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α,β-EPOXYSILANES

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buffer (Na_2CO_3, $NaHCO_3$, Na_2HPO_4, or K_2CO_3) has also been employed. (For typical experimental procedures, see refs. 9, 28, 34, 39–60, 68b.)

Other reagents which have been used for epoxidation of vinylsilanes include dimethyldioxirane[61] and hydrogen peroxide in the presence of As_2O_3 (catalyst).[62] A silyl-substituted quinone was epoxidized with basic *t*-BuOOH.[63] For vinylsilanes which are allylic or homoallylic alcohols, *t*-BuOOH with titanium or vanadium compounds has frequently been used (Section 4).

Vinylsilanes undergo peracid epoxidation at rates comparable to those of simple olefins. However, vinylsilanes are generally somewhat *less* reactive than the corresponding alkyl-substituted olefins, but *more* reactive than the corresponding hydrogen-substituted olefins. (Allylsilanes have been reported to be more reactive than the corresponding vinylsilanes, but the resulting epoxides are rather labile.[3,4,14,36,64]) Some of the results of comparative peracid epoxidations[3,17,65] are summarized in Table 1.

Competitive epoxidations using MCPBA in CH_2Cl_2 indicated the following relative reactivities:[66]

$$\mathrm{Me_2C{=}CH{-}SiMe_3 \gg Me_3Si{-}CH{=}CH{-}SiMe_3}\ \textit{trans},\ \mathrm{CH_2{=}C(SiMe_3)_2 > CH_2{=}CH{-}SiMe_3}$$

Although the large difference between 1-hexene (with MCPBA)[65] and 1-heptene (with PBA)[17] in Table 1 is surprising, all of these studies

Table 1. Relative Epoxidation Rates

Compound	*PPA*[a]	*PBA*[b]	*MCPBA*[c]
$CH_2{=}CH{-}CH_2{-}SiMe_3$	much faster		6.2
$CH_2{=}CH{-}Bu$			13.8
$CH_2{=}CH{-}CH_2{-}Bu$		2.51	
$CH_2{=}CH{-}CH_2{-}CH_2{-}SiMe_3$	slower		
$CH_2{=}CH{-}SiMe_2{-}SiMe_3$			2.7
$CH_2{=}CH{-}SiMe_3$	1.0	1.00	1.0
$CH_2{=}CH{-}SiMe_2Et$		0.82	
$CH_2{=}CH{-}SiMe_2{-}i{-}Pr$		0.86	
$CH_2{=}CH{-}SiMe_2{-}t{-}Bu$		0.80	
$CH_2{=}CH{-}SiMe_2{-}O{-}SiMe_3$			0.5

[a] Using perphthalic acid in ether[3]

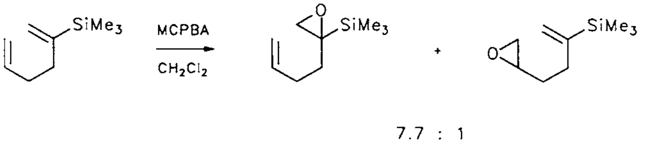
[b] Using perbenzoic acid in benzene[17]

[c] Using MCPBA in CH_2Cl_2[65]

support the generalization that vinylsilanes are *less* reactive toward epoxidation than the corresponding *alkyl*-substituted olefins. Recent studies by Sharpless on the epoxidation of allylic alcohols with MCPBA[67] also support this generalization. The generalization that vinylsilanes are *more* reactive than the corresponding *hydrogen*-substituted olefins is supported by the greater reactivity of bis(trimethylsilyl)ethylene compared with trimethylsilylethylene,[66] and by several examples of peracid epoxidations of the vinylsilane moiety in silicon-substituted dienes (below).

Peracid epoxidations of vinylsilanes are retarded by electron-withdrawing groups on silicon.[7,13,65] Steric effects of the silyl group are usually small. *t*-Butyldimethylsilylethylene was found to be only slightly less reactive than trimethylsilylethylene toward perbenzoic acid (Table 1),[17] and the triisopropylsilyl group was found to retard epoxidation by MCPBA by a factor of three compared to trimethylsilyl.[67]

Many examples of selective epoxidations exist. A number of peracid epoxidations of silicon-substituted dienes have been carried out.[28,53,68–73] In several cases, vinylsilanes have undergone selective epoxidation in the presence of comparable hydrogen-substituted olefins (or olefins of lesser substitution)[28,53,68,70,73] [e.g., eq. (1)[53]].



(1)

Attempted peracid epoxidations of vinylsilanes in the presence of comparable carbon-substituted olefins (or olefins of greater substitution) have produced mixtures of epoxides, or selective epoxidation at the carbon-substituted olefin[69,71] (unless electron-withdrawing groups are on the double bond).[72] In one case, the more reactive double bond was protected by bromination.[68] (In another case the diepoxide was prepared and it was possible to deoxygenate the non-silyl epoxide by treatment with PhSeNa and elimination.[71])

α,β-Epoxysilanes have been prepared by peracid oxidation of vinylsilanes in the presence of a variety of additional functional groups, such as alcohols, ketones, esters, and amides. [In some cases, neighboring group participation occurred, with intramolecular ring-opening of the intermediate epoxysilane (Section 3.4.4).] Of particular note is the epoxidation in the presence of a silylacetylene.[44,74] In vinylsilanes containing a ketone carbonyl group, Baeyer–Villiger rearrangements have occasionally competed with epoxidation, particularly in the case of cyclohexanones[69,75–77] (and occasionally cyclopentanones).[78] In most cases the problem was overcome by converting the ketone to a ketal. In one case (a steroidal enone in which the vinylsilane was also a homoallylic alcohol; see eq. 18 in Section 3.4.4) the vanadium-catalyzed *t*-BuOOH epoxidation worked quite well.[69,77]

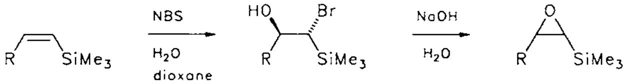
Epoxidation of a vinylsilane in the presence of a Si-Si bond or divalent sulfur is expected to be difficult. $Me_3Si{—}Si(Me)_2CH{=}CH_2$ was reported to undergo peracid oxidation of the Si—Si bond and the vinyl group at comparable rates.[12,65] (The Si—Si bond could be oxidized (to Si-O-Si) *without* epoxidizing the double bond by using trimethylamine-N-oxide.[19]) Dialkyl sulfides are reported to be more reactive than disilanes toward peracids, giving sulfones.[65]

Several 1,1- and 1,2-bis(trialkylsilyl)alkenes[24,59,61,66,79] (and tris(trimethylsilyl)ethylene[80]) have been converted to the epoxides with peracid. The epoxide of 1,3-bis(trimethylsilyl)propene has been prepared (and found to be quite labile),[81,82] and the attempted epoxidation of another 1,3-bis(trimethylsilyl)alkene gave rearranged products.[83]

A number of additional examples have been reported where attempted epoxidations of vinylsilanes failed to give isolable epoxysilanes, and products of rearrangement or hydrolysis were formed.[46,61,84–89] These include attempts to epoxidize vinylsilanes which are also silyl enol ethers,[84] trimethylsilyl allenes[86,87] (in one case using benzonitrile/hydrogen peroxide),[86] a tetrakis(trimethylsilyl)cumulene,[89] and trimethylsilyl cyclopropenes.[61,88]

2.2. Preparation via Halohydrins

An alternative way to convert vinylsilanes to α,β-epoxysilanes is by base-treatment of the corresponding halohydrins (eq. 2).[90] Like peracid epoxidation, the overall process takes place with stereospecific retention of configuration.

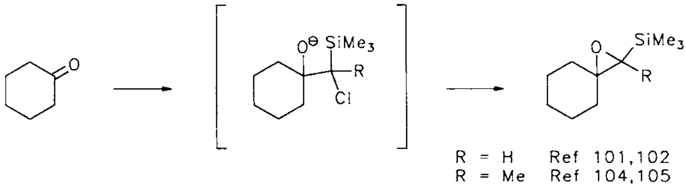


(2)

Vinylsilanes have been converted to halohydrins by treatment with various reagents, including N-bromoacetamide (NBA)[24,91] and N-bromosuccinimide (NBS)[90,92,93] in the presence of water; similar reactions with N-chlorosuccinimide (NCS),[91] *t*-BuOCl,[92] and I_2/HgO[92,95] have been reported. In general the halohydrins are α-halo-β-hydroxysilanes, identical to the isomers obtained by ring opening of the corresponding epoxysilanes with HX[24,91,95] (see Section 3.4.2); however, the reaction of 1-trimethylsilylcyclohexene with NCS in aqueous dioxane was reported to give a 56:44 mixture of regioisomers.[91] (These reactions are of considerable mechanistic interest, as discussed in Section 3.5.3.) The halohydrins have been converted to epoxysilanes by treatment with NaOH,[90] KOH,[91,98] or Pr_3SnOMe.[99] (Halohydrins prepared in other ways have also been converted to epoxysilanes by treatment with KH,[26] *t*-BuOK,[45,100] or NaH.[101,102]

2.3. Preparation from Carbonyl Compounds

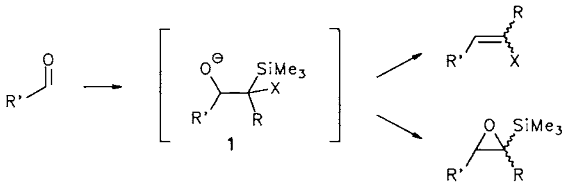
Aldehydes and ketones have been converted to α,β-epoxysilanes by reaction with $R_3SiCR(X)Li$ (X = good leaving group) (eq. 3).[101-109] These reactions were first reported by Magnus, and developed into a useful epoxysilane synthesis by using $Me_3SiCH(Cl)Li$[101,102] and $Me_3SiCMe(Cl)Li$;[104,105] $Me_3SiCH(Br)Li$,[106] $Me_3SiCMe(Br)Li$,[106b] and Ph_3 SiCH(I)Li[107] have also been used. The epoxysilanes have generally been obtained as mixtures of *cis* and *trans* isomers, with the *cis* isomers often predominant. This reaction has been particularly useful for "reductive nucleophilic acylation", in which the epoxysilane is ultimately hydrolyzed to give an aldehyde or ketone (Section 3.4.4).[101-105,109b]



(3)

The presumed intermediates are α-halo-β-oxidosilanes. [These are alkoxides of the same halohydrins obtained in the reactions of vinylsilanes with NBS and related reagents (see above).] In the reaction of benzaldehyde with $Me_3SiCH(Cl)Li$, the reaction mixture was quenched at −55°C and a mixture of stereoisomeric chlorohydrins was isolated and separated; treatment of the major (*threo*) chlorohydrin with NaH in THF gave the pure *cis*-epoxysilane.[101,102]

β-Oxidosilanes normally undergo β-elimination to give olefins (eq. 4) (see also Section 3.1). However, β-oxidosilanes having a good leaving group α to silicon (e.g., **1**, X = halogen or N_2^+ (below)) undergo cyclization to give α,β-epoxysilanes (eq. 5), unless a carbanion-stabilizing group is on the carbon bearing silicon (below). β-Eliminations of α-halo-β-hydroxysilanes do occur under acidic conditions to give vinyl halides (Section 3.4.2).

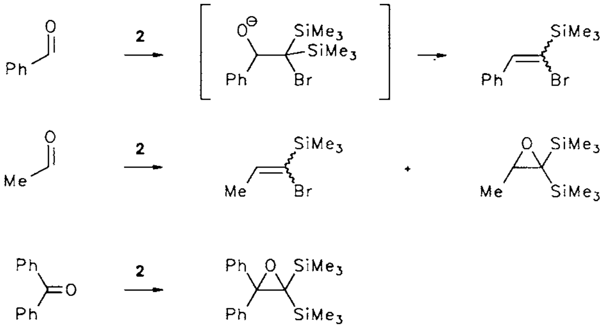


(4)

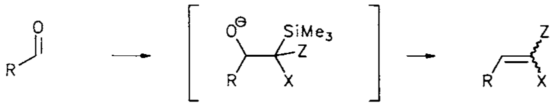
(5)

Reactions of aldehydes and ketones with $Me_3SiCR(X)Li$ (X = poorer leaving group) generally result in olefins (Peterson olefination) in a process which may involve β-elimination of the β-oxidosilane (eq. 4).[37] Consequently, although reactions of aldehydes and ketones with sulfur ylids are useful for the preparation of simple epoxides, the corresponding reactions with silylated sulfur ylids apparently proceed by elimination rather than cyclization and do not give α,β-epoxysilanes.[110,111]

Reactions of carbonyl compounds with bis(trimethylsilyl) bromomethyllithium (**2**) gave products of cyclization and/or elimination, depending on substrate.[112] Aldehydes gave stereoisomeric mixtures of vinyl halides only, except for acetaldehyde, which also gave a small amount of epoxide; in contrast benzophenone gave exclusively the epoxide.



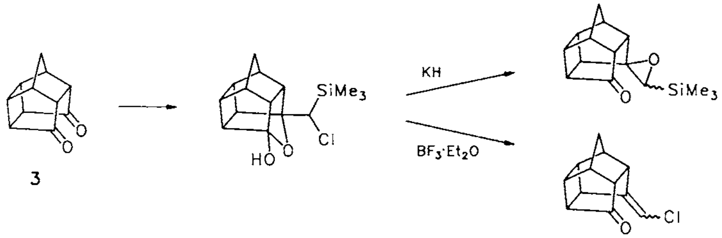
Reactions of aldehydes and ketones with organolithium reagents ($Me_3SiCZXLi$) having more powerful carbanion stabilizing substituents (Z) gave only vinyl halides resulting from β elimination (eq. 6).[113-115]



(6)

X = Cl; Z = CH=CH$_2$ ref 113
X = Cl; Z = CO$_2$*t*-Bu ref 114
X = Br; Z = CO$_2$*t*-Bu ref 115

In an interesting example of neighboring group participation, treatment of the diketone **3** with $Me_3SiCH(Cl)Li$ gave the hemiacetal from cyclization of the presumed lithium alkoxide. Treatment of the hemiacetal with base (KH) gave the epoxide, while treatment with acid ($Bf_3{\cdot}Et_2O$) gave the vinyl chloride.[108]



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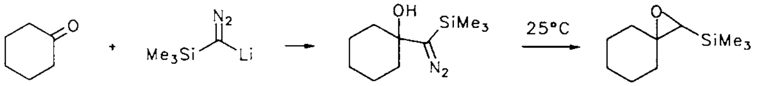
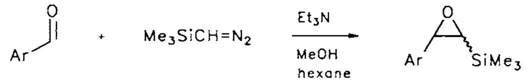
A related method for converting carbonyl compounds to α,β-epoxysilanes involves reaction with lithio trimethylsilyldiazomethane followed by neutralization and warming to room temperature (eq. 7).[116]



(7)

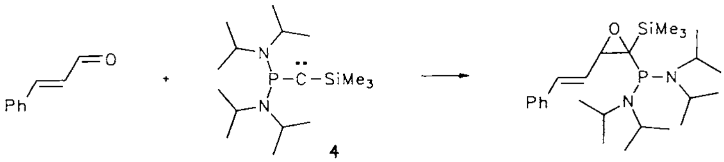
In an analogous process, aromatic aldehydes react with trimethylsilyldiazomethane in the presence of Et_3N to give mixtures of products containing α,β-epoxysilanes.[117]



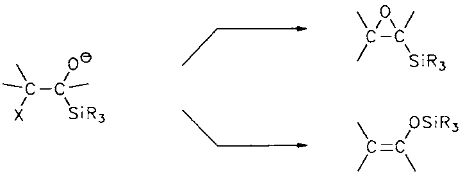
Curiously, when benzophenone is treated with lithio trimethylsilyldiazomethane under similar conditions, the major product is diphenylacetylene.[118]

$$Me_3SiCH{=}N_2 \xrightarrow[\text{(3) warm}]{\text{(1) BuLi} \quad \text{(2) Ph}_2\text{CO}} Ph{-}C{\equiv}C{-}Ph$$

Reactions of the unusual stabilized carbene **4** with benzaldehyde and cinnamaldehyde yield α,β-epoxysilanes.[119]



[It is tempting to consider the possibility of preparing α,β-epoxysilanes from α-oxidosilanes with a leaving group β to silicon (eq. 8). Although a number of systems of this type are known,[120] only one (where X = Cl) has been reported to yield an α,β-epoxysilane;[91] the most common reaction is formation of the silyl enol ether (eq. 9).]



(8)

(9)

2.4. Preparation from Epoxide Anions

In 1976 Eisch and Galle reported that α,β-epoxysilanes could be metallated at the epoxide carbon α to the silicon.[121,122] The reactions are carried out by treating the α,β-epoxysilane with *n*-butyllithium or *t*-butyllithium at low temperatures in ether, THF, TMEDA, or mixtures thereof.[57,102,121-128] [Reactions of α,β-epoxysilanes with organolithium reagents are discussed further in Section 3.3.2.] [Other hetero-substituted epoxides have been similarly metallated (using RLi or *i*-Pr_2NLi (LDA)).[121-123,125,129-133]] These oxiranyllithium reagents react with a variety of electrophilic reagents to give α-substituted α,β-epoxysilanes.

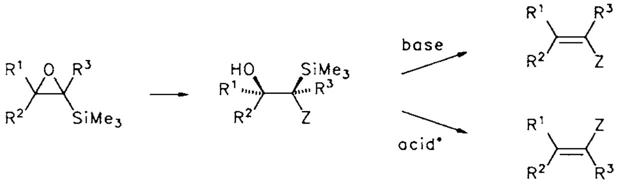
These reactions were first reported with triphenylsilylethylene oxide using *n*-BuLi/THF at −78°C.[121] They have been extended to epoxytrimethylsilanes having a *cis* alkyl substituent on the ring.[122,123] The corresponding reactions of epoxysilanes having a *trans* substituent have been reported to be sluggish[122,123] although in some cases, good yields of trapping products have been obtained[124] (see also ref. 102).

has been widely used, and is now felt to take place via an α opening pathway.[25,27,28] In 1975, Hudrlik and co-workers found that several types of α,β-epoxysilanes underwent regiospecific and stereospecific α ring opening with organocopper reagents to give diastereomerically pure α-substituted β-hydroxysilanes from isomerically pure α,β-epoxysilanes.[23] It had already been shown that olefin-forming β-elimination reactions of β-hydroxysilanes can be stereospecific,[135] and take place by a *syn* pathway under basic conditions and an *anti* pathway under acidic conditions.[23] The ring opening reactions together with the β-elimination reactions were used as the basis of a new stereospecific olefin synthesis (Scheme 1).[23,26]

Ring opening reactions of α,β-epoxysilanes with more electrophilic reagents (first with $MgBr_2$,[24] i-Bu_2AlH,[40] HBr,[25–27] RCO_2H,[26] ROH/acid,[25–27] CH_3CN/acid[26]) were also shown to take place at the α position. The resulting α-substituted-β-hydroxysilanes were also found to undergo stereospecific β-elimination reactions to yield heteroatom-substituted olefins (Scheme 1).[26]

A wide variety of other reagents has since been found to result in regiospecific α opening of α,β-epoxysilanes, including AlH_3, Et_2AlCN, various organometallic reagents, MgI_2, HI, SiF_4, HF-pyridine, amines, azides, silylamides, $KSCN/HClO_4$, organosulfides, n-Bu_3SnLi, and $MeSO_3H$. Most of these reactions have also shown a high degree of stereospecificity, and many have been applied to the olefin synthesis (Scheme 1). These are summarized in Tables 5–13. α,β-Epoxysilanes have been viewed as *stereospecific vinyl cation equivalents.*[26,30]

In addition to the *syn* elimination under basic conditions and the *anti* elimination under acidic conditions, elimination reactions of β-hydroxysilanes have also been achieved by conversion of the hydroxyl to a good leaving group (acetate or sulfonate) and treatment with fluoride;[136] such reactions have been shown to be stereospecific[142] and *anti*.[138,143]



*(or fluoride on hydroxyl derivative)

Scheme 1

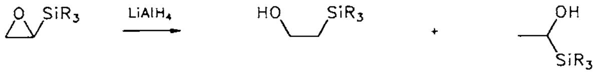
Some limitations to the β-elimination reactions have been observed. The acid-promoted elimination reactions are frequently not useful for the preparation of acid-sensitive compounds; for example, enol ethers and enamines (which can be prepared by base-promoted elimination reactions, Sections 3.4.5 and 3.4.7). The base-promoted elimination reactions are not suitable for β-hydroxysilanes having a good leaving group (e.g., I, Br, OMs) in the α position (epoxide formation results, see Sections 2.2, 2.3, 3.4.2, and 3.4.6), and or for base sensitive compounds. In these cases, the acid-promoted elimination reactions can generally be used. Some β-hydroxysilanes having a β′-OH have undergone elimination reactions involving the β′-OH in competition with those involving the β-OH under acid and basic conditions.[139] β-Hydroxysilanes having a leaving group (OMe) in the β′ position have undergone a base-promoted elimination reaction involving the leaving group[144] similar to that observed in the reactions of β-oxido-β′-sulfonylsilanes (from α,β-epoxysilanes and lithiated sulfones) and related systems (Section 3.3.2). The use of the two-step process of converting the OH to a better leaving group and treatment with fluoride (and the use of protecting groups) have been used to overcome the limitations of the acid- and base-promoted reactions.

The variety of conditions available for the β-elimination reactions give the olefin synthesis flexibility, and a wide variety of olefins can be prepared (see Tables 5–13). Moreover, in many cases a single β-hydroxysilane can be a precursor to either a *cis* or *trans* olefin.

3.2. Hydride Reagents

Reactions of α,β-epoxysilanes with hydride reagents generally give β-hydroxysilanes resulting from regio- and stereospecific α opening. The products have been subjected to β-elimination to give olefins (see Table 5) according to the olefin synthesis of Scheme 1, and have been oxidized to give carbonyl compounds.

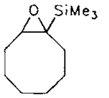
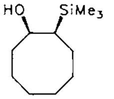
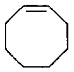
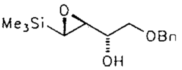
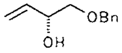
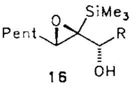
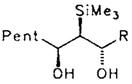
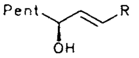
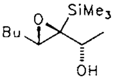
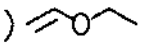
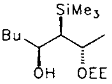
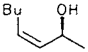
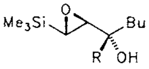
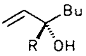
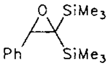
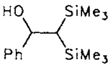
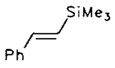
The reactions of silylethylene oxides (**6**) with $LiAlH_4$ to give β-hydroxysilanes (**7**) (eq. 10) were first investigated by Eisch and Trainor.[9a,10] In some cases, a small amount of the α-hydroxysilane (**8**) from β opening was formed (e.g., when a large excess of $LiAlH_4$ was used).



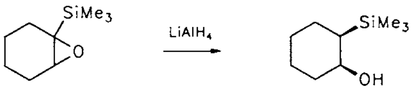
6 7 8 (10)

R = Et, PhCH$_2$, Ar (major) (minor)

Table 5. Olefins From α,β-Epoxysilanes and Hydride Reagents

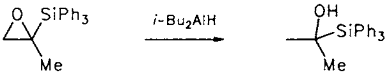
Epoxysilane	Reagent	Product	Conditions	Product	Isomeric Purity	Ref
	$LiAlH_4$	 cis:trans 9:1	NaH DMSO	 cis:trans 9:1		28
 **14**	$LiAlH_4$		KH	 **15**		151
 **16** a: R = Ph; b: R = C≡C-Bu	AlH_3	 **17**	H_2SO_4 MeOH	 **18**		139
 **19**	1)  2) $LiAlH_4$	 **20**	1) Ac_2O Py 2) Bu_4NF 3) HCl			139
 R = Me, Ph	$LiAlH_4$		1) $COCl_2$ 2) Bu_4NF			141
	$LiAlH_4$		KH THF		96%	59

Many other α,β-epoxysilanes have been found to undergo α opening with $LiAlH_4$, including many epoxides of cyclic alkenyltrimethylsilanes[25,28,41,46,56,145–149] (and a $PhMe_2Si$ epoxide[150]), several acyclic β-substituted and α,β-disubstituted α,β-epoxy(trimethyl)silanes,[46,139,145,151] and tripropylsilylethylene oxide.[51] In most cases, the reactions were stereospecific as well as regiospecific; e.g., reaction of trimethylsilylcyclohexene oxide (**9**) with $LiAlH_4$ gave *cis*-2-(trimethylsilyl)cyclohexanol.[25,28] Other hydride reagents have also been used with α,β-epoxysilanes including *i*-Bu_2AlH,[40,123] $LiAlH_4/AlCl_3$,[46,55,56,145] and AlH_3.[60,139,144]



9

The use of *i*-Bu_2AlH resulted in α opening with triphenylsilylethylene oxide (**6b**)[40,123] and with a β-alkyl substituted analog,[123] but the product of β opening was obtained from an α-substituted analog (eq. 11).[123] Apparently the difference in steric hindrance at the two positions is more important in this case than the preference for α opening.



(11)

The magnitude of the preference for α opening of α,β-epoxysilanes with hydride reagents has been tested by using more rigid systems and by using a medium ring epoxide. In reactions of conformationally rigid or biased epoxides with $LiAlH_4$ and with $LiEt_3BH$, the preference for *trans* diaxial opening of an epoxide appears to override the preference for α opening of an α,β-epoxysilane.[28,46,56,145] Epoxidation of 4-*t*-butyl-1-trimethylsilylcyclohexene with MCPBA produced a 40:60 mixture of diastereomeric epoxides. Treatment of the epoxide mixture with $LiAlH_4$ produced mixtures of α- and β-hydroxysilanes from β- and α-opening.[46,145] (The epoxide isomer for which the product of α opening is also the product of *trans* diaxial opening, is the more reactive toward $LiAlH_4$.[28]) However, use of $LiAlH_4/AlCl_3$ mixtures greatly enhanced the percentage of β-hydroxysilanes (from α opening),[46,145] and this reagent has found use in synthesis.[46,55,56,145]

Since medium ring compounds do not undergo facile S_N2-type reactions, the reaction of 1-trimethylsilylcyclooctene oxide with $LiAlH_4$ (in THF) was studied and was found to give a mixture (9:1) of *cis*- and *trans*-2-(trimethylsilyl)cyclooctanol (see Table 5) [in contrast to the clean formation of *cis* silyl alcohol resulting from the corresponding cyclohexene oxide (**9**)].[28] The *trans* isomer may have arisen via prior rearrangement of the epoxide to 2-(trimethylsilyl)cyclooctanone (which was shown to give a 1:1 mixture of the two isomeric β-hydroxysilanes under these conditions).[28] (See also ref. 146.)

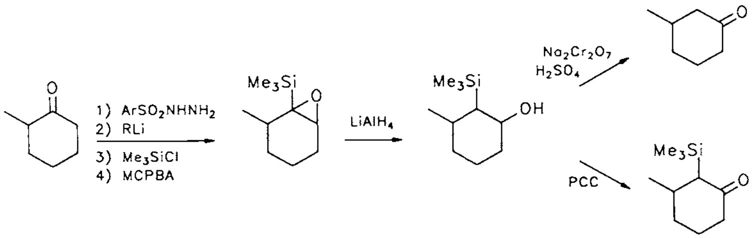
As a test of the limits to the stereospecificity of the β-elimination reactions of β-hydroxysilanes, the above 9:1 mixture of β-hydroxysilanes was treated with NaH/DMSO, giving a mixture of *cis*- and (the highly strained) *trans*-cyclooctene in a 9:1 ratio, consistent with a stereospecific *syn* elimination. However, subjecting the β-hydroxysilanes to $MeSO_2Cl/Et_3N$ gave only the cis isomer (the *trans*-cyclooctene was demonstrated to be stable to these conditions).[28]

The possibility that α,β-epoxysilanes generally react with hydride reagents to give β-hydroxysilanes via prior rearrangement to α-silyl carbonyl compounds rather than by direct α opening was ruled out by the following:

1. Reactions of some α,β-epoxysilanes with $LiAlD_4$,[10] with $LiAlD_4/AlCl_3$,[46] and with $i\text{-}Bu_2AlD$[40,123] resulted in β-hydroxysilanes having deuterium incorporation on the carbon bearing silicon.
2. Reductions of the corresponding α-silyl carbonyl compounds with $LiAlH_4$ have resulted in stereoisomeric mixtures of β-hydroxysilanes[25,41] (in contrast to the single stereoisomer observed in the corresponding reactions of the α,β-epoxysilanes).

Reactions of α,β-epoxysilanes with hydride reagents have been used synthetically to prepare β-hydroxysilanes,[56,60,147,149,152] α-silyl carbonyl compounds (by careful oxidation[135] of the β-hydroxysilanes),[46,51,146,148] silicon-free carbonyl compounds (by oxidation-hydrolysis),[46,145,150] and olefins (by β-elimination reactions of the β-hydroxysilanes—see Table 5).[28,59,139,141,151] The conversion of epoxysilanes to silicon-free carbonyl compounds via hydride reagents was used in a synthesis of d,l-muscone,[150] and in a 1,2-carbonyl transposition[46,145] (Scheme 2).

[Alternative methods for converting α,β-epoxysilanes to carbonyl compounds include Lewis acid-catalyzed rearrangements (Section 3.4.1) and hydrolyses in aqueous acid (Section 3.4.4).]



Scheme 2

Reactions of the epoxides of β- and γ-trimethylsilyl allylic alcohols (which can be obtained in high enantiomeric purity—see Section 4) with hydride reagents followed by β-elimination have given optically active allylic alcohols.[139,141,151] Reaction of epoxide **14** with $LiAlH_4$ followed by elimination with KH led to an olefin (**15**) (see Table 5) which was converted via ozonolysis to a glyceraldehyde derivative.[151] Reactions of epoxides **16a**, **16b**, and **19** with AlH_3 led to β,β′-dihydroxysilanes which could, in principle, undergo β-elimination in two ways to give two regioisomeric allylic alcohols.[139] Under basic conditions, regioselectivity was low. However, under acidic conditions, dihydroxysilanes **17a** and **17b** yielded allylic alcohols **18a** and **18b**, respectively (see Table 5) with high regioselectivity, presumably due to the ability of the developing cation to be stabilized at a benzylic or propargylic position. In contrast, the dihydroxysilane from epoxysilane **19** displayed low regioselectivity under both acidic and basic conditions. A regioselective conversion of **19** to an allylic alcohol was accomplished[139] by protection of the OH as the ethoxyethyl ether, reaction with $LiAlH_4$ to give β-hydroxysilane **20**, and *anti* β-elimination by fluoride treatment of the derived acetate (see Table 5).

3.3. Organometallics

3.3.1. Organocopper Reagents

Reactions of α,β-epoxysilanes with organocopper reagents usually give β-hydroxysilanes from regio- and stereospecific α opening. The products have been transformed into isomerically pure olefins by β-elimination reactions under both basic and acidic conditions (see Table 6) (refs. 23, 58, 81, 82, 153–160). These reactions were the first examples of the olefin synthesis of Scheme 1.[23] (In a few cases, olefins were isolated directly from the reactions with the organocopper reagents, presumably via *in situ* β-elimination of intermediate β-oxidosilanes.) In addition, β-hydroxysilanes having the (i-PrO)Me_2Si group have been transformed into stereoisomerically pure diols by oxidation reactions.[38]

The α opening of simple α,β-epoxysilanes with organocopper reagents was first reported in 1975 by Hudrlik and co-workers using R_2CuLi and RLi/10% CuI (Scheme 3).[23] Grignard reagents in the presence of copper salts have also been used for the ring opening[154] (see also refs. 38, 159, and 161). More recently BF_3 assisted organocopper

Table 6. Olefins From α,β-Epoxysilanes and Organocopper Reagents

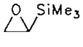
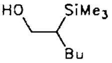
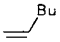
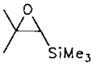
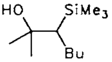
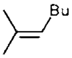
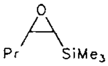
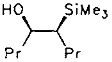
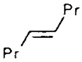
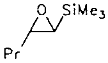
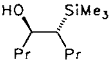
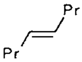
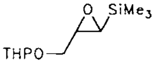
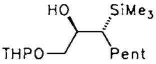
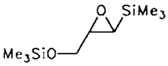
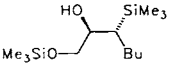
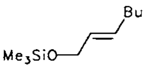
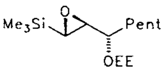
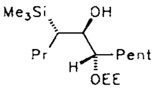
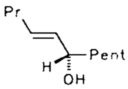
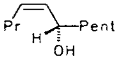
Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
 6a	Bu_2CuLi		KH THF			23
 12a	Bu_2CuLi		NaOAc HOAc			23
 10b	Pr_2CuLi		KH THF		98%	23
			$BF_3 \cdot Et_2O$		98%	23
 11b	Pr_2CuLi		KH THF		100%	23
			$BF_3 \cdot Et_2O$		99.5%	23
	$Pent_2CuLi$		1) KH THF 2) HOAc	 21		153
	Bu_2CuLi		KH THF			82
			$HClO_4$	 R = $SiMe_3$, H		82
	PrMgBr CuI (20%)		KH THF (then HCl)			154
			H_2SO_4 MeOH			154

Table 6. Olefins From α,β-Epoxysilanes and Organocopper Reagents *(Continued)*

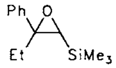
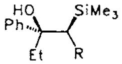
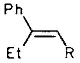
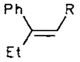
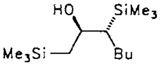
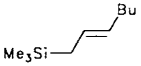
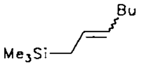
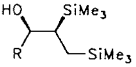
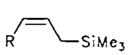
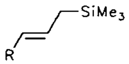
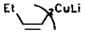
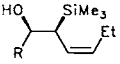
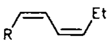
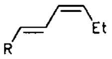
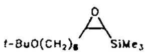
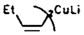
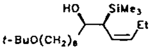
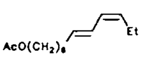
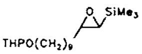
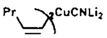
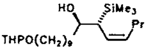
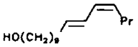
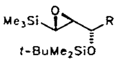
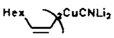
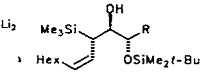
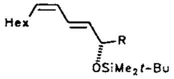
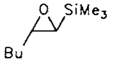
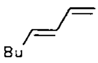
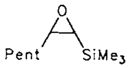
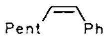
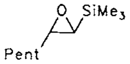
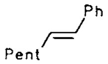
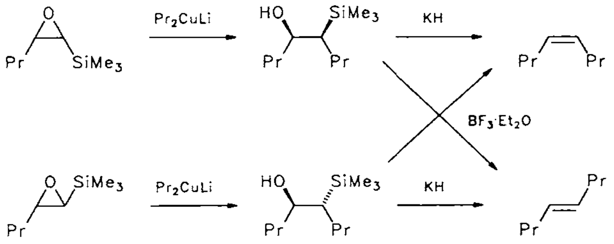
Epoxysilane	Reagent	Product	Conditions	Product	Isomeric Purity	Ref
 **12b**	RLi CuI (2:1) R = Me, Bu		KH THF			158
			$BF_3 \cdot Et_2O$			158
 **22**	Bu_2CuLi	 **23**	NaH DME		98-99%	81, 82
			$BF_3 \cdot Et_2O$		~50%	81, 82
 R = Me, Pr, Bu, *i*-Pr, *t*-Bu R = Ph; use NaH/DME for elimination	$Li_2Cu(CN)(CH_2SiMe_3)_2$		KH THF		>99%	159
R = Me, Pr, Bu, *i*-Pr, *t*-Bu, Ph			$BF_3 \cdot Et_2O$		98%- >99%	159
 R = Hept, Pent	 $BF_3 \cdot Et_2O$		NaH THF		>97%	58
			$BF_3 \cdot Et_2O$		>97%	58
	 $BF_3 \cdot Et_2O$		1) $BF_3 \cdot Et_2O$ 2) $Ac_2O/FeCl_3$	 **24**	96.5%	58, 155-6
	 $BF_3 \cdot Et_2O$		1) NaH 2) H_3O^+	 **25**	97.5%	58, 155-6
	 $BF_3 \cdot Et_2O$		NaH THF			160

Table 6. Olefins From α,β-Epoxysilanes and Organocopper Reagents *(Continued)*

Epoxysilane	Reagent	Product	Conditions	Product	Isomeric Purity	Ref
	Li$_2$Cu(CH=CH$_2$)$_2$CN		in situ		>95%	157
	Li$_2$CuPh$_2$CN		in situ or base		>95%	157
	Li$_2$CuPh$_2$CN		in situ or base		>95%	157

reactions[58,155,156] and higher order organocuprates (2RLi/CuCN),[157,159] have also been found to be effective with epoxysilanes (see Table 6).

Early attempts at opening of epoxysilanes with *alkenyl*copper reagents were unsuccessful,[58,71,155] possibly because of the lesser reactivity of alkenyl (than alkyl) cuprates, steric hindrance in epoxysilanes, thermal lability of cuprates at the higher temperatures necessary for reaction, and/or competing *syn* β-elimination of the intermediate β-oxidosilanes.[58,155] Alexakis and co-workers have found that opening of *cis* and *trans* epoxysilanes with alkenylcuprate reagents (including higher order cuprates) assisted by BF$_3$·OEt$_2$ gives good yields of the corresponding β-hydroxysilanes; stereospecific β-elimination reactions give isomerically pure dienes.[58,155,156] Negishi and co-workers have used higher order organocuprates to open epoxysilanes with vinyl and phenyl groups, giving ultimately dienes and styrenes.[157] In a comparison of Me$_3$SiCH$_2$MgCl/CuI (10%), Me$_3$SiCH$_2$Li/CuI (2:1), and

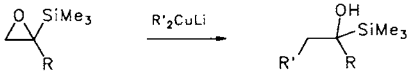


Scheme 3

$Me_3SiCH_2Li/CuCN$ (2:1) for α opening of an epoxysilane, Soderquist and Santiago found the last system to be the most effective, and used these reactions together with the stereospecific β-elimination reactions for a stereospecific synthesis of allylsilanes.[159]

An allylsilane has also been prepared from reaction of epoxysilane **22** (derived from an alkene which is both a vinyl- and allylsilane) with Bu_2CuLi. Although the product β-hydroxysilane (**23**) in principle could undergo β-elimination in two ways, the elimination reactions apparently yielded the allylsilane as only one regioisomer.[81,82]

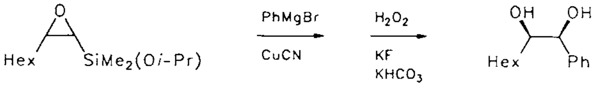
The α opening reactions of α,β-epoxysilanes with organocopper reagents have been demonstrated with unsubstituted, *cis*- and *trans*-β-substituted, and β,β-disubstituted α,β-epoxysilanes. Attempts to extend these reactions to α-substituted α,β-epoxysilanes have led to α-hydroxysilanes from β opening (eq. 12).[153,162] Apparently the additional steric hindrance overrides the preference for α opening in this case. [A diene monoepoxide (having a terminal double bond) which is also an α,β-epoxysilane underwent reaction with an organocopper reagent in the S_N2' manner typical of diene monoepoxides.[163]]



(12)

The α-opening of α,β-epoxysilanes together with the β-elimination reactions have been applied to the synthesis of the natural products *trans*-2-octenyl acetate (**21**), the sex pheromone of the Australian bronze orange bug,[153] and compounds **24** and **25**, pheromones of *Lobesia botrana* and *Bombyx mori*[58,155,156] (see Table 6).

The majority of ring opening reactions of epoxysilanes with organocopper reagents have used the Me_3Si group. Tamao and coworkers found that simple *cis* and *trans* epoxysilanes having the (*i*-PrO)Me_2Si group also undergo stereospecific α ring opening to give β-hydroxysilanes with a variety of organocopper reagents: EtMgBr/CuCN, $(n\text{-}Bu)_2Cu(CN)Li_2/BF_3$, allyl-MgBr/CuCN, PhMgBr/CuCN, 2-thienyl-MgBr/CuCN. Only in one case, the reaction of a *trans* epoxysilane with allyl-MgBr/CuCN, was the competing reaction at silicon a problem. Since C-$SiMe_2OR$ can be converted stereospecifically to C-OH, the intermediate β-hydroxysilanes are precursors to stereochemically defined diols (eq. 13).[38] (In the case of trans epoxysilanes, considerable amounts of the olefin from β-elimination are also formed.[38]) These reactions have been used in a synthesis of the insect pheromone brevicomin.[38]



(13)

In some cases, treatment of epoxysilanes having the $SiMe_2OR$ group with organocopper reagents resulted in deoxygenation reactions to give the corresponding vinylsilanes, in competition with the normal α opening reactions. The deoxygenation reactions could be minimized by the addition of BF_3.[38] These reactions, which did not take place with epoxysilanes having only a $SiMe_3$ group, were found to be favored by the use of a hindered reagent (e.g., *i*-PrMgBr/CuCN (catalytic).[161]

3.3.2. Organolithium Reagents

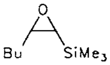
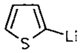
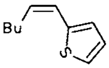
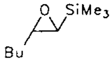
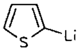
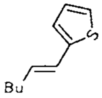
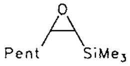
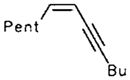
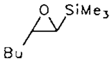
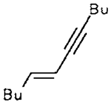
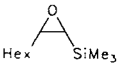
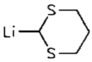
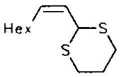
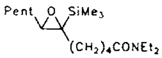
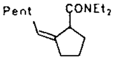
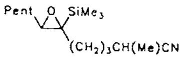
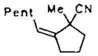
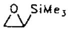
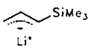
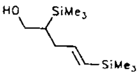
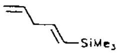
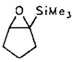
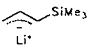
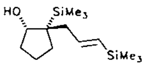
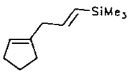
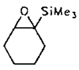
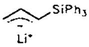
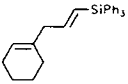
Reactions of epoxysilanes with organolithium reagents such as *n*-BuLi or *t*-BuLi have yielded products which are believed to arise from *proton abstraction* (from the ring carbon α to Si) and in other cases from *attack at silicon*. These reactions have been used to prepare substituted epoxysilanes, vinylsilanes, and silicon-free olefins. In contrast, reactions of epoxysilanes with weaker carbanion bases having lithium as a counterion have yielded products believed to arise from attack at the α carbon (ring opening of the epoxide). These reactions have resulted in β-hydroxysilanes and/or olefins from β-elimination according to the olefin synthesis of Scheme 1 (see Table 7) (or, in reactions with lithium salts Z-CR(Li)-Y (Y = leaving group), α opening with an elimination reaction involving the silicon group and Y).

Treatment of a number of epoxysilanes with alkyllithium reagents (*n*-BuLi, *s*-BuLi, *t*-BuLi) *at low temperatures* followed by a variety of electrophiles has produced substituted epoxysilanes in high yields. This sequence, originally discovered by Eisch and Galle,[121] is becoming a useful method for the preparation of α-substituted α,β-epoxysilanes, as discussed in Section 2.4.

These reactions are believed to proceed via proton abstraction at the epoxide carbon α to the silicon group to generate an oxiranyllithium reagent.[121] A donor solvent was found to be necessary for the reaction to proceed: Treatment of triphenylsilylethylene oxide (**6b**) with *n*-BuLi in hexane at −78°C resulted in no reaction; use of hexane at reflux led to Ph_3SiBu, the product from reaction at silicon.[123]

Reactions of epoxysilanes with an excess of unstabilized organolithium reagents such as *n*-BuLi have been found to give olefins

Table 7. Olefins From α,β-Epoxysilanes and Organolithium Reagents

Epoxysilane	Reagent	Product	Isomeric Purity	Ref
			>95%	157
			>95%	157
	Bu-C≡C-Li		≥98%	157
	Bu-C≡C-Li		>95%	157
			≥98%	157
	LiN(SiMe$_3$)$_2$	KH 	>96%	157
	base	base 	≥96%	157
 6a	 	NaH 15-crown-5 		170
 29	 	NaH 15-crown-5 		170
 9	1)  2) 12-crown-4 3) NH$_4$Cl	 30		170

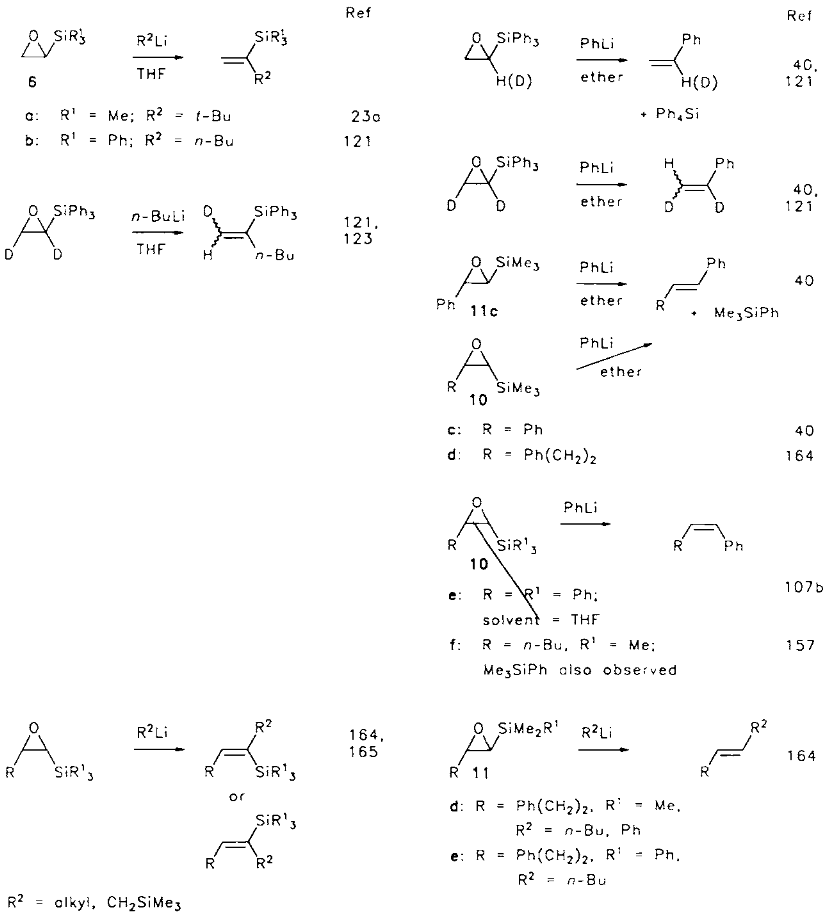
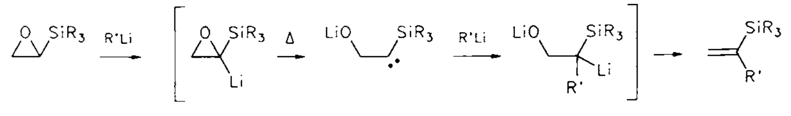


Figure 1

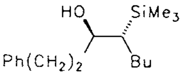
incorporating the organic residue from the organolithium reagent, sometimes as vinylsilanes, sometimes without the silicon (see Figure 1). A reaction pathway involving α proton abstraction by the organolithium to give an oxiranyllithium, α-elimination to give a carbenoid, capture by the organolithium, and loss of lithium oxide, has been considered for the reactions which give vinylsilanes (Scheme 4).[121,166] (Initial coordination of the organolithium with the silicon to form a pentacoordinate silicon anion has also been considered.[167]) An analogous pathway involving initial reaction of the organolithium at silicon (to give the oxiranyllithium without silicon) has been suggested to account for formation of the olefins without silicon.[164] In some cases,



Scheme 4

the product (R′SiR$_3$) from attack of the organolithium (R′Li) at silicon has been observed.[10a,40,121,123,157,164,165,168a]

A reaction pathway (for formation of the olefins without silicon) involving α opening of the epoxysilane by the organolithium (e.g., *n*-BuLi) followed by *in situ* β elimination (i.e., the olefin synthesis of Scheme 1) would not be expected,[169] and was ruled out in the case of epoxysilane **11d** by finding that the corresponding β-hydroxysilane (**26**) was unreactive to *n*-BuLi/ether.[164] However, this reaction pathway does account for products of reactions of α,β-epoxysilanes with stabilized organolithium compounds (i.e., carbanion salts with lithium as the counterion—see below).



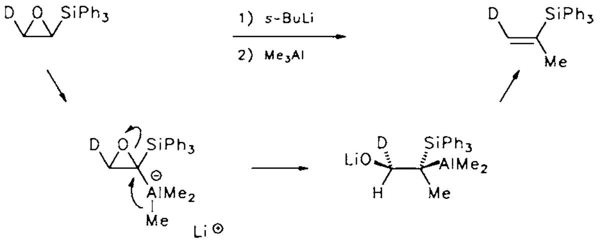
26

The type of olefin formed and the stereochemistry in these reactions depends upon the particular system (and reaction conditions) (see Figure 1). Vinylsilanes have been isolated from reactions of alkyllithium reagents with *cis*[164,165] and unsubstituted [23a,121,123] epoxysilanes (and obtained as minor products from reactions with *trans* epoxysilanes[164]). Olefins without silicon have been isolated from reactions of alkyllithium reagents with *trans* epoxysilanes,[164] and from reactions of phenyllithium with *cis*,[40,107b,157,164] *trans*,[40,164] and unsubstituted[40,121] epoxysilanes. (In some cases, olefins without silicon have been isolated from reactions of alkyllithium reagents with *cis* epoxysilanes as well.[164,165]) The formation of vinylsilanes versus olefins without silicon in these reactions has been suggested to be related to the steric hindrance to attack of the organolithium;[164] additionally PhLi appears to have a preference for attack at silicon.

The process appears to be nonstereospecific for the reaction of an unsubstituted epoxysilane with an alkyllithium reagent: Treatment of *E*-2,3-dideuterio-2-triphenylsilyloxirane with *n*-BuLi gave a 1:1 mixture of *E* and *Z* β-deuteriovinylsilanes[121,123] (see Figure 1). However, reactions of various *cis* epoxysilanes with alkyllithiums frequently have given vinylsilanes as predominantly one stereoisomer.[164,165] The *Z* isomers have been favored in most cases,[164,165] but some epoxysilanes having bulky substituents on the silicon or the ring have given predominantly the *E* isomers.[165] On the other hand, reactions of various *trans* epoxysilanes have given olefins (without silicon) as predominantly *E* isomers.[164] The stereochemistry of the PhLi reactions is variable, and different reaction pathways may be taking place under different conditions. For example, treatment of **10c** (and **11c**) (see Figure 1) with PhLi/ether resulted in *trans*-stilbene,[40] while treatment of the similar epoxide **10e** with PhLi/THF resulted in *cis*-stilbene[107b] (stereochemistry expected from α opening followed by *syn* β-elimination).

When epoxysilanes were treated with unstabilized organolithiums followed by organoaluminum (or zinc) reagents[127] or with dimethylsilacyclobutane,[126] substituted vinylsilanes were isolated. Although in principle the products could be accounted for by a carbenoid pathway analogous to that of Scheme 4, a pathway involving formation of a hypercoordinate Al (Zn) or Si intermediate, 1,2-migration to the epoxide α carbon, and *syn* elimination of R_2Al and OLi was favored. In the case of the aluminum reagent (using Me_3Al), the latter mechanism was supported by the stereochemistry in the reaction using *cis*-2-deuterio-3-triphenylsilyloxirane, which gave only the *Z* vinylsilane (Scheme 5).[127] [It should be noted that conformational inversion was observed when a *cis*-2-alkyl(triphenylsilyl)oxirane was used.[127]] This is in contrast to the above mentioned reaction of *E*-2,3-dideuterio-2-triphenylsilyloxirane with excess BuLi, assumed to take place by the carbenoid pathway of Scheme 4, which gave a 1:1 mixture of *E* and *Z* olefins.[121,123,127]

In the reaction involving the silacyclobutane, the mechanism involving a hypercoordinate intermediate was supported by the fact



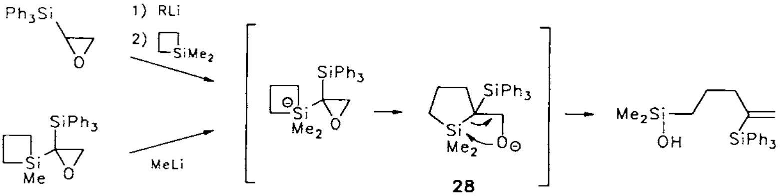
Scheme 5

that the same type of products were obtained by a second route; that is, treatment of the (silacyclobutyl)epoxysilane **27** with MeLi (Scheme 6).[128]

When some simple α,β-epoxysilanes having the silicon incorporated into a 4-membered ring were treated with MeLi or *i*-PrOLi, β-hydroxysilane intermediates corresponding to intermediate **28** (Scheme 6) were isolated (and converted to olefinic alcohols and to triols—see Section 3.4.5).[128]

Negishi and co-workers have found that reactions of α,β-epoxysilanes with organolithium reagents which are relatively weak bases appear to follow the α opening pathway, and therefore can be used in the olefin synthesis of Scheme 1.[157] When *cis* and *trans* disubstituted epoxysilanes were treated with 2-thienyllithium, R—C≡C—Li, or 2-lithio-1,3-dithiane, the products were olefins of high isomeric purity, believed to arise from α opening of the epoxide followed by *syn* β-elimination (see Table 7). (In some cases, initial adducts were treated with KH.) Treatment of a *cis* epoxysilane with $LiCH_2CONEt_2$ led to the β-hydroxysilane expected from α opening. Intramolecular analogs of these reactions show promise for the synthesis of 5-membered carbocyclic rings.[157]

Reactions of several epoxysilanes with lithiated allylsilanes have similarly been used in the olefin synthesis of Scheme 1.[170] Reactions of epoxysilanes **6a** and **29** with lithiated allylsilanes gave the products of α opening together with small amounts of the products of β opening (ratios >9:<1). Treatment of the products with NaH/crown ether resulted in β-elimination giving silyl-substituted 1,4-dienes. Treatment of an α-substituted epoxysilane and of epoxysilane **9** with lithiated allylsilanes gave product mixtures containing higher percentages of the β opening products (together with additional by-products). In some cases, by-products believed to result from 1,3 C → O silicon migration and allyl carbinyl-cyclopropyl carbinyl anion rearrange-

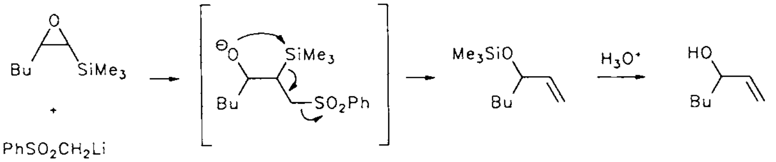


27

Scheme 6

ments were observed. However, a one-pot sequence of ring opening and β-elimination with epoxysilane **9** and lithiated allyltriphenylsilane gave the silyl-substituted diene **30** in 61% (isolated) yield.[170]

In other cases, when additional functionality is present, the initially formed β-oxidosilane can participate in other reaction pathways. In a reaction first demonstrated by Masnyk and Wicha,[171-175] carbanions generated by deprotonation of Z-CRH-Y (in which Z and/or Y is carbanion stabilizing and Z is a leaving group) react with α,β-epoxysilanes to give allylic alcohols (or the silyl ethers) believed to arise via α opening of the epoxide followed by alkoxide-induced elimination of the Si group and Y. Thus, treatment of several epoxysilanes with the lithium salts [$R_2C(Li)SO_2Ph$] of sulfones has produced allylic alcohols (eq. 14) (predominantly *Z* isomers).[171-176] [Under some conditions, the primary products of α opening (β-hydroxy, β′-sulfonylsilanes) were isolated, and these products were converted to the allylic alcohols with fluoride.[171]] When hindered sulfones were used with trimethylsilylethylene oxide in these reactions, the major products were α-hydroxy-γ-sulfonylsilanes, products of β opening.[174,175] However, the expected product of α opening was obtained from a hindered sulfone and a β substituted α,β-epoxysilane.[174] The reaction of an α,β-epoxysilane with the lithium salt of a sulfone was used in a synthesis of disparlure, an attractant of the gypsy moth.[172,173]



(14)

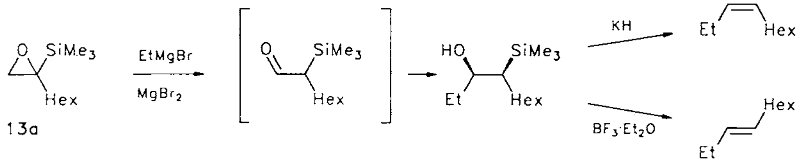
Reaction of the sodium salt of dimethyl sulfoxide with α,β-epoxysilanes has produced allylic alcohols in a manner analogous to that of eq. 14.[176] Similar reactions have been carried out using the lithium salts of Me_3SiCH_2SPh, $MeSCH_2S(O)Me$, and $CH_2(SPh)_2$ (to give vinylsilanes and vinyl sulfides having an allylic OH).[176]

Treatment of trimethylsilylethylene oxide (**6a**) with the lithium salts of the α-trimethylsilyldithianes $Me_3Si(PhS)_2CLi$ and $Me_3Si(MeS)_2CLi$ (**31**) has produced substituted cyclopropanes.[177] The proposed mechanisms involve α opening of the epoxysilane by PhS- in the first case and by **31** (with an elimination involving the Me_3Si group from **31**) in the second.[177]

The reactions of an α,β-epoxysilane with an N-lithioenamine are discussed in Section 3.3.4.

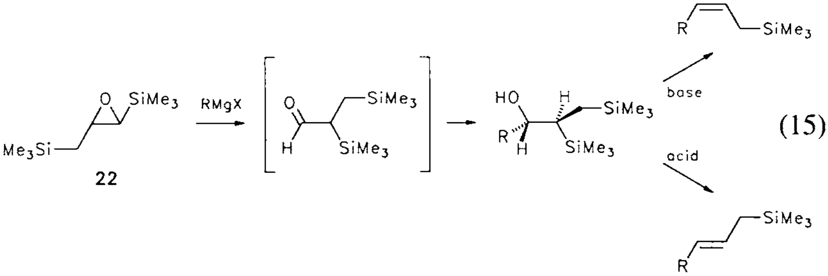
3.3.3. *Organomagnesium Reagents*

In 1961 the reactions of triphenylsilyl- and tribenzylsilylethylene oxide with Grignard reagents were reported to yield α-hydroxysilanes (products of β opening).[7] Subsequently, a number of reactions of α,β-epoxytrimethylsilanes with Grignard reagents have been shown to yield (as major products) β-hydroxysilanes which are isomeric with those expected from direct α opening. The β-hydroxysilanes are believed to arise from magnesium halide-promoted rearrangement of the epoxides to α-silyl carbonyl compounds (see Section 3.4.1), followed by trapping with the Grignard reagents.[23a,59,81,82,168] The β-hydroxysilanes have been used as precursors to *cis* and *trans* olefins via stereospecific β-elimination reactions,[81,82,168] and the stereochemistry of the products suggests the β-hydroxysilanes were produced with a high degree of Cram's rule selectivity (Felkin–Anh model) (as high as 97%).



Addition of $MgBr_2$ to the reaction mixture of a Grignard reagent with an epoxysilane has been used to favor the formation of β-hydroxysilane. For example, reaction of an α-substituted epoxysilane (**13a**) with a Grignard reagent produced the expected β-hydroxysilane along with an α-hydroxysilane, presumably from β opening (6:1 ratio), while a similar reaction with added $MgBr_2$ gave the β-hydroxysilane in good yield.[168] [Treatment of an α,β-epoxysilane with a R_2Mg reagent yielded the simple product of α opening in a very slow reaction.[23b]]

In most cases, the β-hydroxysilane products are consistent with formation of the intermediate α-silyl carbonyl compound by an α opening mechanism. However, reaction of an epoxide (**22**) which is both an α,β- and a β,γ-epoxysilane, with a number of Grignard reagents gave β-hydroxysilanes which may have been derived from β opening of the epoxide (with migration of Me_3Si to give an intermediate α-silyl aldehyde), although an α opening mechanism (with migration of CH_2SiMe_3) was also considered.[81,82] In any event, the products were formed in good diastereomeric purity, and were used for a stereoselective preparation of allylsilanes (eq. 15).[81,82] (See also ref. 159.)



(15)

3.3.4. Miscellaneous Organometallics

The earliest work on reactions of α,β-epoxysilanes with organometallic reagents involved attempted polymerization of the epoxides.[14,18] Reactions with organocopper reagents, organolithium reagents, and Grignard reagents followed as discussed above. Several other types of organometallic reagents have been reacted with epoxysilanes. Reactions of organolanthanoid reagents with epoxysilanes led to the same products as those from the corresponding organolithium reagents.[164,165] Reaction of a titanium acetylide with trimethylsilylethylene oxide (**6a**) gave the simple product of α opening.[178] Attempted reactions of alkynyl- and alkenylorganoaluminum reagents with α,β-epoxysilanes were unsuccessful;[157,179] reaction of $LiAlClEt_2$-($C{\equiv}C$—R) led to the chlorohydrin.[157] [Epoxysilanes have undergone α opening with alkynyllithium[157] and alkenylcopper[58,155–157,160] reagents (discussed above)]. Reaction of Et_3Al with triphenylsilylethylene oxide (**6b**) (in heptane at reflux) led to the reduction product, 2-triphenylsilylethanol.[123] However, reaction of Et_2AlCN with an epoxysilane led to the α,β-unsaturated nitrile, presumably via α opening and *in situ* β-elimination, following the olefin synthesis of Scheme 1 (Table 13).[141]

The reactions of N-metalloenamines (Li and MgBr) (from cyclohexanone) with epoxide **6a** gave mixtures of products derived from both α and β ring openings.[180] The reactions of dimethyl and diethyl sodiomalonate (in methanol and ethanol, respectively) with **6a** gave the products of α ring opening followed by lactonization.[181]

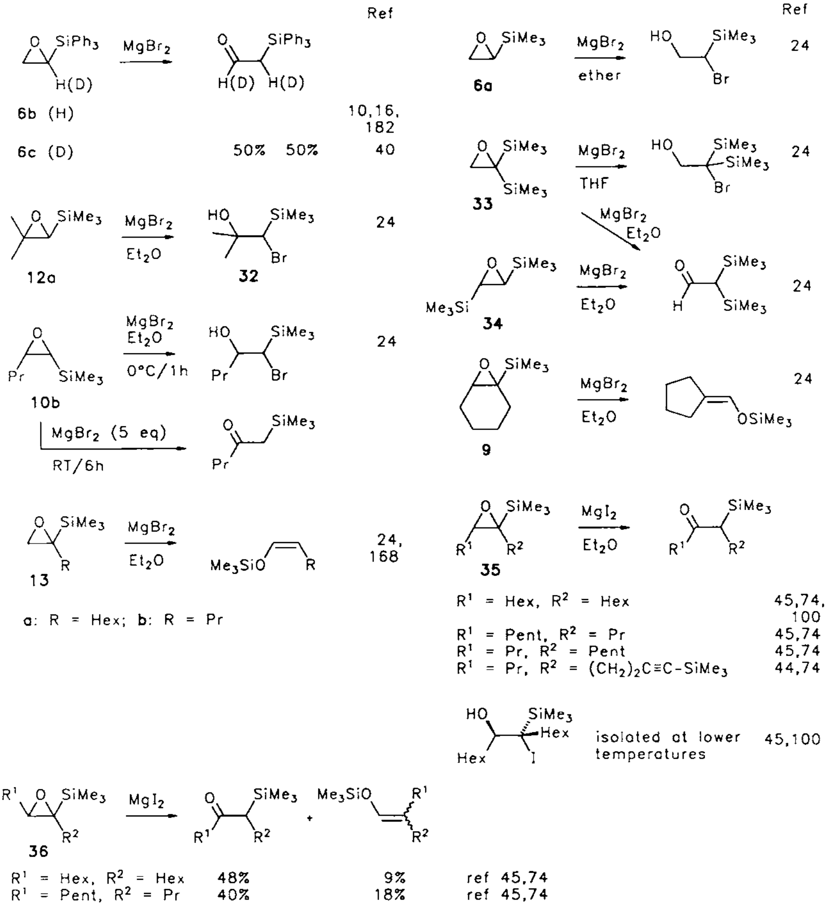


Figure 2

3.4. Heteroatom Reagents

3.4.1. *Magnesium Halides*

Reactions of α,β-epoxysilanes with magnesium halides have been reported to give a variety of products, including halohydrins, carbonyl compounds, and silyl enol ethers, depending on epoxide structure and reaction conditions (see Figure 2). (A similar reaction of trialkylsilylethylene oxides with trialkyltin bromides to give silyl enol ethers via α-silyl aldehydes has also been reported.[99])

Triphenylsilylethylene oxide (**6b**) has been reported to rearrange to triphenylsilylacetaldehyde in the presence of $MgBr_2$ in useful yields.[10,16,182] The use of α-deutero(triphenylsilyl)ethylene oxide (**6c**) led to triphenylsilylacetaldehyde with the deuterium scrambled between the aldehyde and α carbons.[40] An attempt to extend the reaction to the preparation of phenyldimethylsilylacetaldehyde yielded diphenyltetramethyldisiloxane.[16]

A study was carried out on the reactions of trimethylsilyl epoxides with $MgBr_2$, and the reaction products were found to be dependent on the structure of the epoxide.[24] All of the products could be accounted for by initial α opening of the epoxides, and these reactions were the first examples of α opening of α,β-epoxysilanes under acidic conditions. In some cases (with epoxides **6a** and **12a**), only bromohydrins were isolated (after aqueous workup). In other cases (with epoxides **10b** and **33**), bromohydrins were isolated with short reaction times (or use of THF as solvent rather than ether), and α-trimethylsilyl ketones or aldehydes were isolated with longer reaction times. And in some cases (epoxides **9** and **13**), silyl enol ethers were isolated (aldehyde hydrogens were detected by NMR at short reaction times).[24,168] [Attempts to induce rearrangement of the bromohydrin (MgBr salt) from **6a** to trimethylsilylacetaldehyde by extended treatment of **6a** with $MgBr_2$ led to the bromohydrin together with its trimethylsilyl ether. The silyl ether may have arisen by silylation of the bromohydrin salt by trimethylsilylacetaldehyde.[168]] The bromohydrins were shown to be α-bromo-β-hydroxysilanes (from α opening of the epoxides) by the downfield shift in the ^1H NMR of the β protons upon conversion to the acetates, or, for bromohydrin **32**, by β-elimination with $BF_3 \cdot Et_2O$ to give isobutenyl bromide (see also Table 8 below). Although the reactions were not carried out under precisely the same conditions, the difference between the reactions of $MgBr_2$ with *triphenylsilyl*ethylene oxide (**6b**), which gave the aldehyde from rearrangement by apparent pathways of both α and β opening,[40] and *trimethylsilyl*ethylene oxide (**6a**), which gave the bromohydrin by an apparent α opening pathway,[24] is notable.

α-Bromo-β-hydroxysilanes have been found to be useful in the olefin synthesis of Scheme 1, undergoing β-elimination reactions to form vinyl (alkenyl) bromides.[24a,26,27a,140,158] They have most often been prepared by reactions of epoxysilanes with HBr (see below), which generally avoids the rearrangement reactions. However, sometimes $MgBr_2$ has been found to be effective.[24,26,140] Treatment of epoxysilane

37 (see Table 8) (obtained in high enantiomeric purity via kinetic resolution of a γ-trimethylsilyl allylic alcohol (see Section 4)), with $MgBr_2$ led to an α-bromo-β-hydroxysilane, and *anti* elimination (by treatment of the derived mesylate with fluoride) gave the *cis* alkenyl bromide **38** (in high enantiomeric purity), a precursor to a prostaglandin side chain.[140]

Magnesium iodide has been reported[24,44,45,74,100] to effect rearrangements of α,β-epoxytrimethylsilanes similar to those of magnesium

Table 8. Olefins From α,β-Epoxysilanes and Hydrogen Halides (or $MgBr_2$)

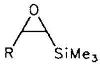
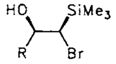
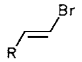
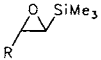
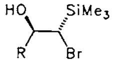
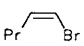
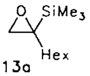
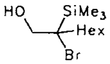
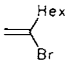
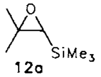
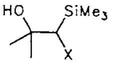
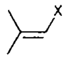
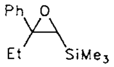
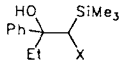
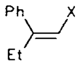
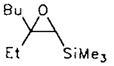
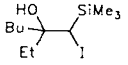
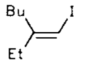
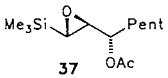
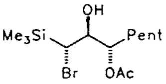
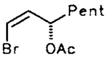
Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
 10 a: R = Hex; b: R = Pr	HBr Et_2O		$BF_3 \cdot Et_2O$		98- >99%	26
 11 a: R = Hex; b: R = Pr	HBr Et_2O		$BF_3 \cdot Et_2O$		>99%	26
 13a	HBr Et_2O		$BF_3 \cdot Et_2O$			26,27a
 12a Reagent = HBr/Et_2O or $MgBr_2/Et_2O$; X = Br Reagent = 57% HI/Et_2O; X = I	Reagent		$BF_3 \cdot Et_2O$			24a,26 45a,100a
 12b Reagent = HCl (conc)/Et_2O; X = Cl Reagent = HBr (conc)/Et_2O; X = Br Reagent = HI (conc)/Et_2O; X = I	Reagent		$BF_3 \cdot Et_2O$			158
	HI (conc) Et_2O		$BF_3 \cdot Et_2O$			158

Table 8. Olefins From α,β-Epoxysilanes and Hydrogen Halides (or $MgBr_2$) *(Continued)*

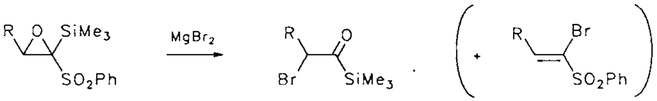
Epoxysilane	Reagent	Product	Conditions	Product	Isomeric Purity	Ref
 **37**	$MgBr_2$		1) MsCl Et_3N 2) Bu_4NF	 **38**		140

bromide (see Figure 2). When α,β-disubstituted α,β-epoxysilanes (**35**) having *cis* alkyl groups were used, α-trimethylsilyl ketones were obtained in good yields.[44,45,74,100] [An iodohydrin was observed at lower temperatures.[45,100]] However, when α,β-disubstituted α,β-epoxysilanes (**36**) having *trans* alkyl groups were used, α-trimethylsilyl ketones were obtained together with silyl enol ethers (apparent products of alkyl migration).[45,74] A modified procedure was developed in which the epoxysilanes were converted to iodohydrins using HI, and then rearranged to the α-silyl ketones using RLi[44,45,100] (see also Section 3.4.2). Using the modified procedure, both epoxysilanes **35** and **36** could be converted in good yields to α-trimethylsilyl ketones.

α-Silyl aldehydes[168,184] and ketones[44,74,135,185] have been found to undergo some nucleophilic addition reactions (hydride, organolithium reagents) with a high degree of stereoselectivity in accord with Cram's rule (Felkin-Anh model) to give β-hydroxysilanes (see also Section 3.3.3). Since β-hydroxysilanes can undergo stereospecific β-elimination reactions (with an *anti* process under acidic conditions and a *syn* process under basic conditions)[23,135] as mentioned above, α-silyl aldehydes and ketones have been used as precursors to stereochemically defined olefins.[135,184,185] The sequence MgI_2-induced rearrangement of an epoxysilane to an α-silyl ketone followed by reaction with an alkyllithium and β-elimination has been used in a synthesis of a tetrahomoterpenoid from the codling moth.[44,74]

α-Silyl aldehydes and ketones undergo facile hydrolysis to silicon-free aldehydes and ketones. Carbonyl compounds obtained from magnesium halide promoted rearrangements of epoxysilanes followed by hydrolysis are generally the opposite regioisomers of those obtained by acid-promoted hydrolysis of epoxysilanes (Section 3.4.4).

Epoxides substituted with an SO_2Ph group generally undergo ring opening with $MgBr_2$ at the β position; in the case of epoxides substituted with SO_2Ph and $SiMe_3$ on the same carbon, the SO_2Ph group is dominant in directing the ring opening.[129,131-133] Thus, α-sulfonyl-α,β-epoxysilanes having minimal steric hindrance at the β position (**39**, R = H or primary alkyl), upon treatment with MgBr$_2$/Et$_2$O, produced α-bromoacylsilanes (**40**) in good yields.[129,131–133] Use of THF at reflux resulted in competing formation of bromoalkenylsulfones (**41**). [The latter compounds were believed to arise via α opening of the epoxides followed by β-elimination.] For such epoxides disubstituted at the β position, reactions with MgBr$_2$/ether were very fast, leading to α-bromoacylsilanes together with other products.[131,133]



39 40 41

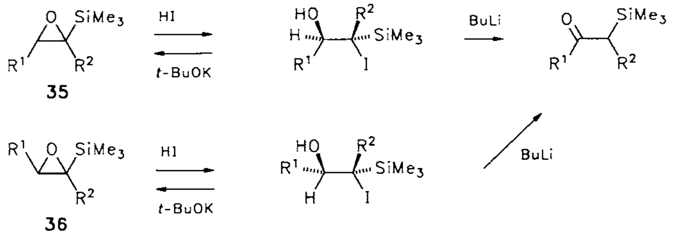
3.4.2. *Hydrogen Halides*

Reactions of a variety of epoxysilanes with HBr[25–28,91,158] and HI[28,44,45,100,158] yield silyl bromo- and iodohydrins (α-halo-β-hydroxysilanes) resulting from stereospecific α opening of the epoxides. These reactions are preferable to the magnesium halide reactions for the preparation of silyl bromo- or iodohydrins, since competing rearrangement reactions do not occur.

These reactions have been used in the olefin synthesis of Scheme 1: Treatment of the bromo- and iodohydrins with BF$_3$·Et$_2$O yields vinyl bromides[26,27a,158] and iodides[45a,100a,158] in high isomeric purity (see Table 8). The base-promoted β-elimination reactions have not been used; treatment of the silyl bromohydrins[26] and iodohydrins[45,100] with base has yielded α,β-epoxysilanes (e.g., see Scheme 7; for similar reactions, see Sections 2.2 and 2.3).

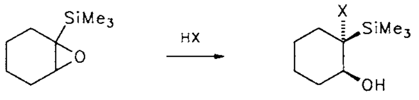
The iodohydrins obtained from reaction of α,β-disubstituted α,β-epoxysilanes (**35** and **36**) with HI, were cleanly rearranged to α-silyl ketones using RLi (see Scheme 7).[44,45,100] When the iodohydrins were treated with MeMgI/MgI$_2$, the results[45,100] were very similar to those from treatment of the starting epoxides with MgI$_2$ (*trans* disubstituted epoxysilanes (**36**) gave α-silyl ketones together with silyl enol ethers derived from alkyl migration—see Figure 2).

Reactions of epoxysilanes with HCl[40,91,158] have given mixed results. The reaction of triphenylsilylethylene oxide (**6b**) with HCl/benzene has been reported to give predominantly the chlorohydrin from β opening together with triphenylsilylacetaldehyde.[40] Reactions of trimethyl-

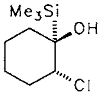


Scheme 7

silylcyclohexene oxide (**9**) with HCl in a number of solvents have been reported to give predominantly the chlorohydrin (**42**, X = Cl) from (stereospecific) α opening together with 2–11% of the chlorohydrin (**43**) from β opening.[91] [For comparison, the reactions of **9** with HBr and HI are reported to give halohydrin **42** (X = Br, I) from a stereospecific α opening.[25,27,28,91]] And reaction of a substituted epoxysilane (**12b**) with HCl (as well as HBr and HI) followed by $BF_3{\cdot}Et_2O$ was reported to give the vinyl halide, suggesting α opening of the epoxysilane had occurred[158] (see Table 8).



9 42



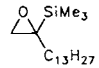
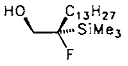
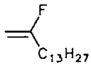
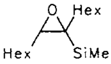
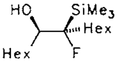
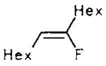
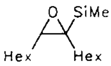
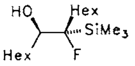
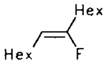
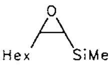
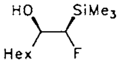
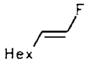
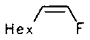
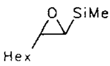
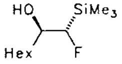
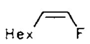
43

3.4.3. *Fluoride Reagents: α Opening*

Reactions of α,β-epoxysilanes with fluoride ion, usually in polar aprotic solvents, generally result in desilylation (Section 3.7.2). However, ring opening to give α-fluoro-β-hydroxysilanes has been accomplished by using SiF_4[186] and HF-pyridine.[187] Using SiF_4, α ring opening was achieved with α-substituted and α,β-disubstituted epoxy(trimethyl)silanes, but the reaction was unsuccessful with an epoxy(tri*ethyl*) silane and with *trans*-β-substituted epoxy(trimethyl)silanes.[186] Using HF-pyridine, α opening was achieved with *cis*- and *trans*-β-substituted epoxy(trimethyl)silanes, although yields of the α-fluoro-β-hydroxysilanes were modest (~30–50%).[187] [Reaction of α,β-difluoro-α,β-epoxysilanes with HF-pyridine gave α-fluoro carbonyl compounds, believed to have been formed via α or β ring opening, depending upon the substituents on the epoxide.[188]]

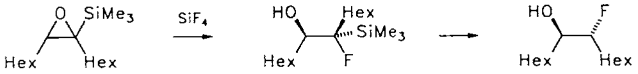
The α-fluoro-β-hydroxysilanes have been used in the olefin synthesis of Scheme 1 (see Table 9). Treatment with basic reagents led to vinyl fluorides[186,187] (in contrast to the analogous reactions of the corresponding bromo compounds which led to epoxides[26]). The stereochemistry was that expected from *syn* β-elimination, but the stereochemical purity was not always as high as that in other systems. Treatment of the α-fluoro-β-hydroxysilane from epoxide **36a** with $KN(SiMe_3)_2$ led to the expected vinyl fluoride in 98% isomeric purity; but treatment of that from the isomeric epoxide **35a** led to a ~50:50 stereoisomeric mixture of vinyl fluorides. Treatment of the α-fluoro-β-hydroxysilanes from epoxides **10a** and **11a** with KH/THF led to vinyl

Table 9. Olefins From α,β-Epoxysilanes and Fluoride Reagents

Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
	SiF_4 $i\text{-}Pr_2NEt$ H_2O	 **44**	$KN(SiMe_3)_2$ THF			186
 36a	SiF_4 $i\text{-}Pr_2NEt$ H_2O		$KN(SiMe_3)_2$ Et_2O		98%	186
 35a	SiF_4 $i\text{-}Pr_2NEt$ H_2O		$KN(SiMe_3)_2$ Et_2O		55%	186
 10a	HF-pyridine		$BF_3 \cdot Et_2O$		>99%	187
			NaH THF		91%	187
 11a	HF-pyridine		$BF_3 \cdot Et_2O$		>99%	187

fluorides in only 81–86% isomeric purity; use of NaH/THF improved the isomeric purity somewhat (91%). *Anti* elimination reactions with $BF_3 \cdot Et_2O$ were highly stereospecific.[187] However, an attempted elimination reaction of the α-fluoro-β-hydroxysilane **44** (in which the hydroxyl is on a primary carbon) with $BF_3 \cdot Et_2O$ or with H_2SO_4 led to rearranged products[186] (in contrast to the successful $BF_3 \cdot Et_2O$ promoted elimination with the related bromo compound[26,27] from epoxysilane **13a**).

The α-fluoro-β-hydroxysilanes were found to undergo a facile stereospecific desilylation with fluoride or with NaH/crown ether leading to stereochemically defined fluorohydrins (eq. 16).[186] Using the latter procedure, the silyl enol ether from a homo-Brook rearrangement could be observed, and the desilylation reaction is most likely related to the base-promoted (KO*t*-Bu) desilylation of simple β-hydroxysilanes and α-methoxy-β-hydroxysilanes.[152,189] As in the case of the methoxy compounds (see Section 3.4.5), α-opening of α,β-epoxysilanes followed by desilylation can be used to prepare products of directed epoxide opening which cannot easily be prepared by opening of the corresponding silicon-free epoxides.[186,189]

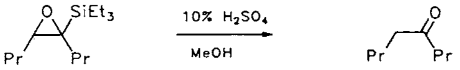


35a

(16)

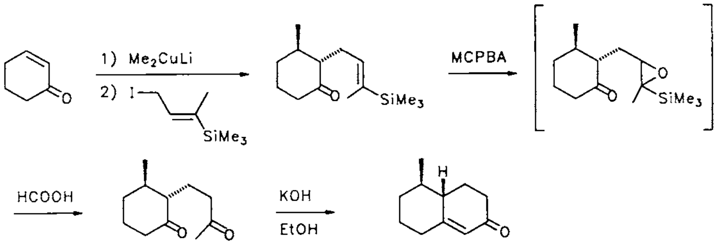
3.4.4. Water (and Acid-Promoted Rearrangements)

The earliest and perhaps most widely used synthetic application of α,β-epoxysilanes is their hydrolysis to carbonyl compounds, first introduced by Stork and Colvin,[20–22,190] in which the carbon bearing silicon becomes the carbonyl carbon.[191] Hydrolyses of α,β-epoxysilanes are typically carried out with aqueous acid (e.g., H_2SO_4 or $BF_3 \cdot Et_2O$) in a water miscible solvent such as methanol or THF. Acetals and ketals have been isolated when alcohols were used as the reaction medium,[20,72,101,102,111b] and internal acetals, ketals, and lactols have been isolated from substrates containing appropriately placed hydroxyls[69,77,103,105,203,205,206] or carbonyls.[21,47,194]



(ref 21)

The hydrolysis of epoxysilanes allows the relatively unreactive vinylsilanes to serve as latent ketones and aldehydes,[21] and has therefore found considerable use in organic synthesis. For example, annulation sequences have been developed[21,22] for the preparation of 5- and 6-membered rings,[21,22,54,191ab,195,198,202] in which a regiospecifically generated enolate can be trapped with a silyl allylic halide, followed by epoxidation[207] and hydrolysis (eq. 17). In this sequence, hydrolysis of the epoxysilane can be considerably more facile than that of simple epoxysilanes, most likely due to participation by the nearby carbonyl group.[21,22,191a] Some trimethylsilylvinyl copper reagents have served as acyl anion and enolate anion equivalents via conjugate addition to enones, epoxidation, and hydrolysis[75,76] (see also refs. 47, 70 and 194). Reactions of silylated allylmetallic reagents (derived from allyl- or vinylsilanes) with a ketone or aldehyde, followed by epoxidation and hydrolysis results in the formation of γ-lactols or O-alkyl lactols; these reactions have been used in the synthesis of various γ lactones including spirolactones[69,77,203,205,206,208] (eq. 18).[69,77] In this sequence, the silyl allyl metallic reagent serves as a β-acyl anion (homoenolate) equivalent.[69,77,205]



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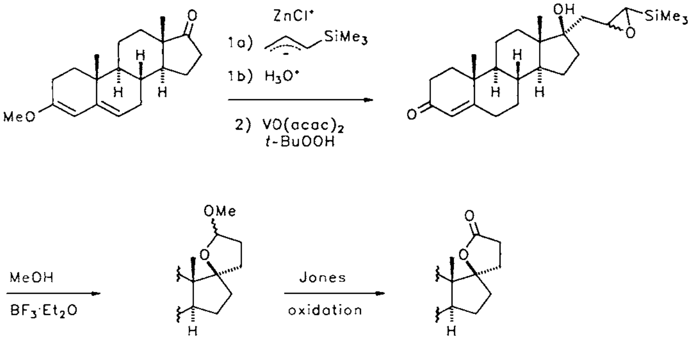
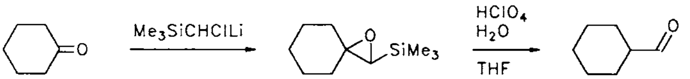


(18)

Procedures for reductive nucleophilic acylation of aldehydes and ketones have been developed, involving treatment with Me$_3$-

SiCHClLi[101,102] or $Me_3SiC(Me)ClLi$[104,105] to form the epoxysilanes (see Section 2.3) followed by hydrolysis to the aldehyde or ketone, respectively (eq. 19).

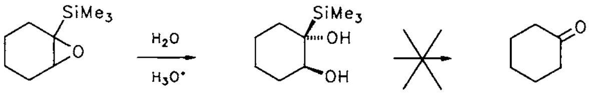


(19)

Hydrolyses of epoxysilanes have been incorporated into a number of total synthesis of compounds of interest to natural products chemistry including frontalin,[103,105] gymnomitrol,[47,194] thromboxane analogs,[195] qinghaosu,[142] *cis*-crobarbatic acid,[206] dihydrojasmone,[196,201,203] and pyrrolizidine alkaloids.[52]

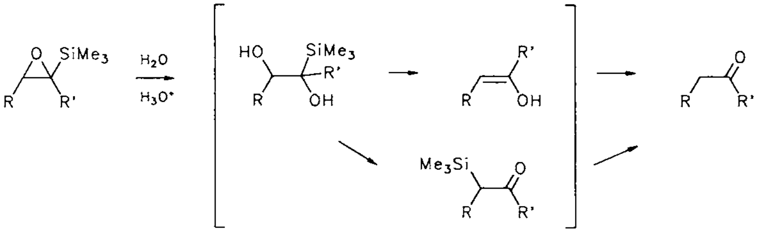
The hydrolysis of epoxysilanes is believed to occur by the general pathway of Scheme 1, i.e., α opening to an α,β-dihydroxysilane followed by acid-promoted β-elimination to an enol (followed by ketonization)[25,27,28] (see Scheme 8). (Another possibility, discussed below, is rearrangement of the dihydroxysilane to an α silyl carbonyl compound, followed by desilylation.[209])

α,β-Dihydroxysilanes have been isolated from hydrolysis reactions of epoxysilanes derived from cyclic (5-membered,[199] 6-membered,[25,27,28,41,91,210,211] and 12-membered[199] ring) vinylsilanes (see also ref. 212). Some of the 5- and 6-membered ring α,β-dihydroxysilanes have been shown to be resistant to further acid treatment;[27,199] the R_3Si and β OH groups in these compounds cannot achieve the *anti* relationship necessary for facile acid-promoted β elimination.[25,27,28]



9

Formation of a complex mixture from hydrolysis of a 7-membered ring epoxysilane,[199] and isolation of products derived from transannular



Scheme 8

reactions from 8-membered ring epoxysilanes[28,48] have been reported. Hydrolysis of an α,β-epoxysilane on the more flexible 12-membered ring gave an α,β-dihydroxysilane which underwent conversion to the ketone with more vigorous conditions.[199] α,β-Dihydroxysilanes have also been isolated from some hydrolysis reactions of epoxysilanes derived from *acyclic* vinylsilanes using mild conditions,[27,28,120a,213] and converted to the expected carbonyl compounds using stronger acid or longer reaction times.[27] [α,β-Dihydroxysilanes have also been prepared from vinylsilanes by hydroxylation with OsO_4. When α,β-dihydroxysilanes are treated with NaH in ether, silyl enol ethers (eq. 9) are formed stereospecifically.[120a]]

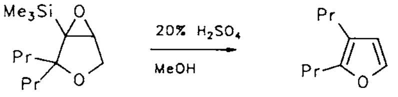
[Gas phase reactions of 1-trimethylsilylcyclohexene oxide with water using Me_2F^+ as the gaseous acid have led to the α-hydroxy-β-methoxysilane expected from α opening as the only product, with stereochemistry as well as regiochemistry analogous to those of the corresponding reactions in solution.[212]]

Using trifluoroacetic acid (0.1 − 2 eq) in $CHCl_3$ (instead of the more commonly employed aqueous acid), Cunico has observed that some α,β-dihydroxysilanes undergo a "silapinacol rearrangement" to give α-silyl aldehydes and ketones.[209] Thus, ring opening to α,β-dihydroxysilanes followed by this rearrangement and desilylation represents an additional mechanistic possibility for the hydrolysis of epoxysilanes[209] (see Scheme 8 above).

Limitations to the use of hydrolysis of epoxysilanes in organic synthesis include the use of some epoxysilanes derived (formally) from cyclic vinylsilanes as discussed above (see also ref. 71), and epoxysilanes in molecules sensitive to the hydrolysis conditions[102,109a] (or with additional functionality to direct the reactions). Most of the hydrolysis reactions have been carried out using Me_3Si (or Et_3Si) epoxides. In one report, a $PhMe_2Si$ epoxide decomposed under hydrolysis conditions;[102] in other systems, a Ph_3Si epoxide underwent normal hydrolysis,[203] and a $PhMe_2Si$ epoxide was converted to an aldehyde 2,4-DNP derivative.[16]

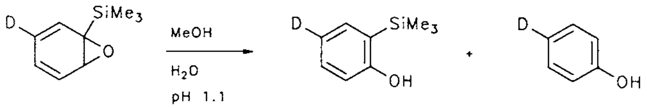
Although hydrolyses of epoxysilanes derived from cyclic vinylsilanes generally yield α,β-dihydroxysilanes, hydrolysis of a few epoxysilanes on four-membered rings has been reported to yield the cyclobutanones (and derived products);[78] in these reactions, the epoxides are β to a carbonyl, and additional pathways for ring opening are possible. Other epoxysilanes on rings having additional functionality (or strain) in the molecule have undergone reactions under hydrolysis conditions which appear to be aided by the additional functionality.

Hydrolysis of epoxysilanes prepared from 3-trimethylsilyl-2,5-dihydrofurans yielded furans which appeared to be derived from α ring opening with rearrangement (eq. 20).[201,214] Hydrolysis of an epoxysilane on a strained 5-membered ring in a bridged system yielded a product of apparent α epoxide opening with rearrangement.[215]



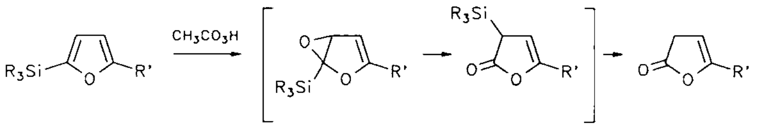
(20)

Some α,β-epoxysilanes (or presumed intermediates) derived from cyclic vinylsilanes in which the β carbon is allylic[68,85,216] have undergone acid-promoted reactions to give products expected from β opening of the epoxide. In some cases, a pathway involving α opening to the α,β-dihydroxysilane followed by loss of the β hydroxyl might also be possible. [α,β-Epoxysilanes derived from *acyclic* vinylsilanes in which the β carbon is allylic, homoallylic, or benzylic have given normal hydrolysis products (or have undergone decomposition).[70,101,102,104,105]] Trimethylsilylbenzene oxides have yielded phenols in an aromatization reaction which appears to exhibit a preference for α opening. With the 5-deuterium-substituted trimethylsilylbenzene oxide, only products expected from α opening were observed at pH 1.1 (eq. 21), while predominantly products expected from α opening together with a product expected from β opening were observed at pH 7.[68b] (Appropriately placed methyl substitution on the aromatic ring was found to lead to products expected from β opening.[68a])



(21)

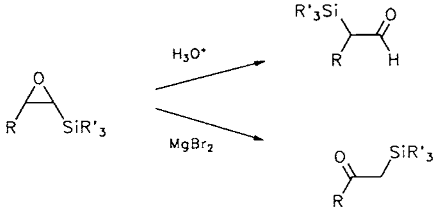
Some α,β-epoxysilanes (or presumed α,β-epoxysilane intermediates) have undergone acid-promoted rearrangements to α-silyl carbonyl compounds in solvents of low nucleophilicity.[83,85,183,209,216] 5-Alkyl-2-trimethylsilylfurans underwent oxidation with peracetic acid in CH_2Cl_2 to yield Δ^3-butenolides in a reaction believed to take place by epoxidation at the silicon site (eq. 22).[216] Intermediate α-silyl lactones were detected spectroscopically in some cases, and isolated in another (R_3Si = t-$BuMe_2Si$).[216]



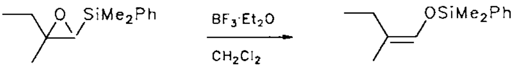
(22)

An olefin which is both a vinyl- and allyl-(trimethyl)silane underwent reaction with MCPBA to give an α,β-bis(trimethylsilyl) aldehyde, suggested to come about via epoxide opening to a carbonium ion (or developing carbonium ion) stabilized by both Me_3Si groups (β opening from the point of view of the α,β-epoxysilane).[83]

Rearrangements of simple α,β-epoxysilanes to α-silyl carbonyl compounds have been reported to take place with magnesium halides (discussed above), with $CF_3CO_2H/CHCl_3$,[209] and with silica gel.[183] Considering the position of the carbonyl, the silyl carbonyl compounds from the CF_3CO_2H and silica gel rearrangements are analogous to those from the hydrolysis reaction of epoxysilanes (and from acid-induced arrangements of α,β-dihydroxysilanes[209] discussed above), but are opposite regioisomers to those from the magnesium halide-induced rearrangements.



Miscellaneous rearrangements involving epoxysilanes have been reported using $BF_3{\cdot}Et_2O$[50,201,217] and R_2AlCl.[50] From an epoxide having two β substituents, the product appeared to be derived from a stereospecific rearrangement involving β opening (eq. 23).[50] The absence of a good nucleophile in the reaction medium may have been an important factor in the regiochemistry of this reaction.



(23)

3.4.5. *Alcohols: α Opening*

As discussed in Section 3.4.4, treatment of α,β-epoxysilanes with alcohols under acidic conditions often yields acetals and ketals. However, under controlled conditions, α-alkoxy-β-hydroxysilanes, products of stereospecific α opening of the epoxides, have been isolated.[26–28,137,152,153,189,218] [Using 1-trimethylsilylcyclohexene epoxides,[25,27,28,41,91,152,210] α-alkoxy-β-hydroxysilanes can be isolated easily (see also ref. 212), since the $SiMe_3$ and OH do not have the proper orientation for facile acid-promoted β-elimination.[25,27,28]]

These reactions have been used in the olefin synthesis of Scheme 1: The α-alkoxy-β-hydroxysilanes have been treated with base (KH/THF, KH/ether, or NaH/DMF), giving alkenyl ethers (enol ethers, vinyl ethers) by *syn* elimination in high isomeric purity[25,26,27a,28,137,152,153,210,219] (see Table 10). The acid promoted (*anti*) elimination reactions

Table 10. Olefins From α,β-Epoxysilanes and Alcohols

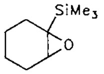
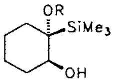
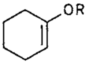
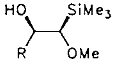
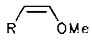
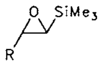
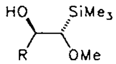
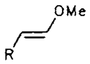
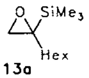
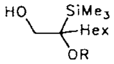
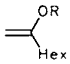
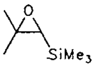
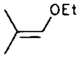
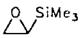
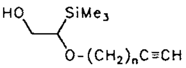
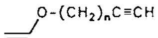
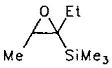
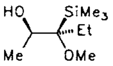
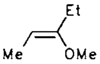
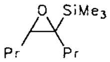
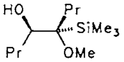
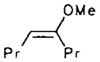
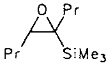
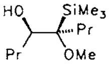
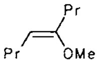
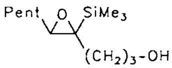
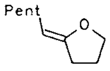
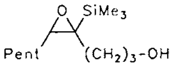
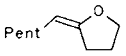
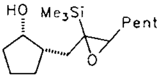
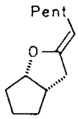
Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
 9	ROH acid R = Me R = CH_2-CH=CH_2		NaH/DMF or KH/THF			25,28,210 28
 10 a: R = Hex f: R = Bu	MeOH CF_3CO_2H		KH THF		98%	26,153 219
 11 R = Hex R = Bu	MeOH CF_3CO_2H		KH THF		98%	26,153 219
 13a	ROH CF_3CO_2H R = Me R = CH_2-CH=CH_2		KH THF			26,27a,153 26,153
 12a	EtOH CF_3CO_2H					153
 6a	HO-$(CH_2)_n$C≡CH BF_3·Et_2O n = 1, 2, 3		KH Et_2O			137

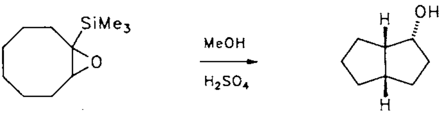
Table 10. Olefins From α,β-Epoxysilanes and Alcohols *(Continued)*

Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
	MeOH H_2SO_4		NaH DMF		95%	28
	MeOH CF_3CO_2H		KH THF		>99%	152
	MeOH CF_3CO_2H		KH THF		98%	152
	KH THF			 **45**	95%- 98%	138
	KH THF			 **46**	≥98%	138
 2 diastereomers	KH			 **47**	97%	138

have not usually been used to convert α-alkoxy-β-hydroxysilanes to alkenyl ethers;[26] an attempt to convert the α-methoxy-β-hydroxysilane from *cis*-1-trimethylsilyl-1-octene oxide (**10a**) to the alkenyl ether using $BF_3{\cdot}Et_2O$ resulted in octanal.[153]

The regiochemistry of epoxysilane opening with MeOH/acid was maintained using α,β-epoxysilanes disubstituted at the β position (**12a**)[153] as well as those having an additional α substituent (and unsubstituted at the β position) (**13a**).[26,27,153,189] Reaction of 1-trimethylsilylcyclohexene oxide (**9**) with MeOH/acid led to the α-methoxy-β-hydroxysilane expected from stereospecific α opening in the gas phase[212] as well as in solution.

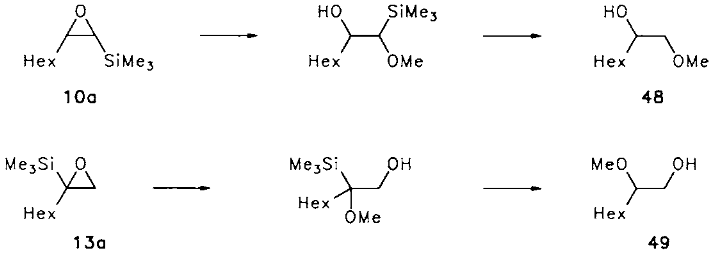
Some limitations to these reactions have been observed. Although treatment of 1-trimethylsilylcyclohexene oxide (**9**) with MeOH/acid results in regiospecific α opening, treatment with MeOH/alumina resulted in a mixture of products from α and β opening in which the α-hydroxysilane resulting from β opening predominated.[210] In the conformationally biased 4-*t*-butylcyclohexyl system, one stereoisomer, for which the product of α opening is also the product of *trans* diaxial opening, cleanly reacted with acidic methanol to give the product of α opening.[28] However, the other stereoisomer gave a mixture of two products, tentatively assigned as products of α and β opening.[28] The medium ring compound, 1-trimethylsilylcyclooctene oxide, reacted with acidic methanol to give a bicyclic alcohol (eq. 24),[28] and other products, depending upon conditions, which suggested that transannular hydride migration (resulting in α opening of the epoxide) is faster than reaction with the external nucleophile.[28,48]



(24)

Intramolecular reactions of α,β-epoxysilanes with alkoxide (generated from treatment of the corresponding alcohols with KH/THF) have been used to prepare cyclic enol ethers (**45–47**, see Table 10) of the type present in some natural products such as prostacyclin. The reactions presumably take place via α opening and *syn* β elimination.[138] An *inter*molecular reaction with alkoxide under more protic conditions resulted in a product of desilylation: Treatment of *cis*-1-trimethylsilyl-1-octene oxide (**10a**) with NaOMe/MeOH resulted in the expected α-methoxy-β-hydroxysilane together with 1-methoxy-2-octanol.[153,210a] [Desilylation has been observed as a side reaction in some β-elimination reactions of α-methoxy-β-hydroxysilanes under some conditions.[210] (See also ref. 152.)]

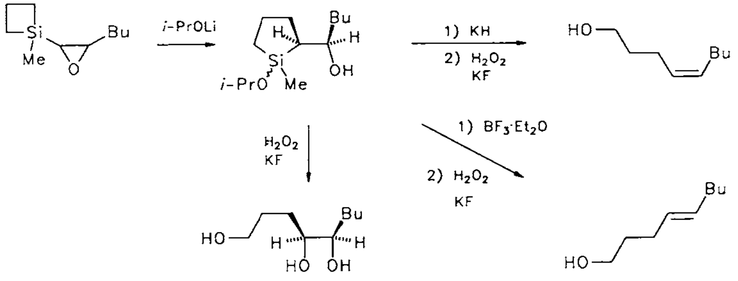
The desilylation reactions have shown some promise for organic synthesis. When some β-hydroxysilanes (including α-methoxy-β-hydroxysilanes) are treated with basic reagents (e.g., *t*-BuOK) in aqueous DMSO (or aqueous HMPA), desilylation (with retention of configuration at carbon) is the major process.[152,189] These desilylation



Scheme 9

reactions allow α,β-epoxysilanes, through their derived β-hydroxysilanes, to serve as precursors to simple (non-silicon) alcohols of defined regio- and stereochemistry. One illustration is shown in Scheme 9. Whereas reaction of 1,2-epoxyoctane with MeOH/CF_3CO_2H gave a mixture ($\sim$1 : 1) of regioisomeric methoxy alcohols (**48** and **49**), similar reactions of epoxysilanes **10a** and **13a** each gave a single α-methoxy-β-hydroxysilane; these were converted by desilylation (*t*-BuOK/DMSO/H_2O) to methoxy alcohols **48** and **49**, respectively.[189]

When α,β-epoxysilanes having the silicon incorporated into a 4-membered ring were treated with *i*-PrOLi (or with MeLi), β-hydroxysilanes were isolated in high diastereomeric purity. They are believed to have arisen from 1,2-rearrangement of a pentacoordinate intermediate (from reaction of the *i*-PrOLi at the silicon). β-Elimination followed by oxidation led to olefinic alcohols; direct oxidation led to triols, all in high isomeric purity (Scheme 10) (see also Section 3.3.2).[128]



Scheme 10

3.4.6. *Carboxylic and Sulfonic Acids*

Carboxylic Acids. Reactions of α,β-epoxysilanes with carboxylic acids have been used for the synthesis of enol esters[26,80,102,103,137,138,187a] according to the olefin synthesis of Scheme 1 (see Table 11). Treatment of the *cis* and *trans* epoxysilanes **10a** and **11a** with acetic acid/

Table 11. Olefins From α,β-Epoxysilanes and Carboxylic or Sulfonic Acids

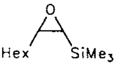
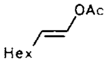
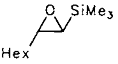
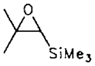
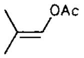
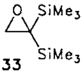
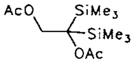
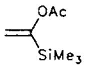
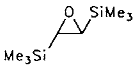
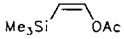
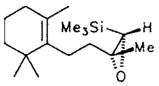
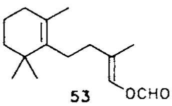
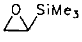
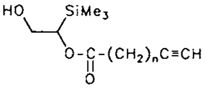
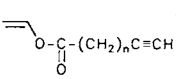
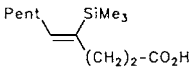
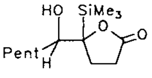
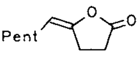
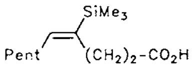
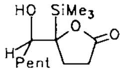
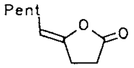
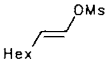
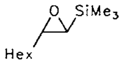
Substrate	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
 10a	HOAc Ac_2O $BF_3 \cdot Et_2O$			 50	97%	26
 11a	HOAc Ac_2O $BF_3 \cdot Et_2O$			 51	97%	26
 12a	HOAc Ac_2O					187a
 33	HOAc Ac_2O $BF_3 \cdot Et_2O$		$BF_3 \cdot Et_2O$			26,80
 34	HOAc Ac_2O $BF_3 \cdot Et_2O$			 (+ $CH_3CH(OAc)_2$)		26,80
 52	HCO_2H			 53	90%	102, 103
 6a	$HOOC-(CH_2)_nC{\equiv}CH$ $BF_3 \cdot Et_2O$ (n=2,8 only) n = 0, 2, 8		1) HOAc DCC 2) Bu_4NF			137

Table 11. Olefins From α,β-Epoxysilanes and Carboxylic or Sulfonic Acids *(Continued)*

Substrate	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
 **54**	MCPBA		1) Ac_2O 2) Bu_4NF		99%	138
 **55**	MCPBA		1) Ac_2O 2) Bu_4NF		99%	138
 **10a**	1) $MeSO_3H$ 2) $BF_3{\cdot}Et_2O$				97%	153
 **11a**	1) $MeSO_3H$ 2) $BF_3{\cdot}Et_2O$				99%	153

acetic anhydride in the presence of $BF_3{\cdot}Et_2O$ gave *trans* and *cis* enol acetates **50** and **51**, respectively in 97% isomeric purity.[26] The reactions were presumed to proceed via α opening of the epoxides followed by *anti* β elimination; when the epoxides were treated with acetic acid without $BF_3{\cdot}Et_2O$, acetoxy β-hydroxysilanes were observed.[26] *Latia* luciferin (**53**), a naturally occurring enol formate, was synthesized by a similar reaction of epoxysilane **52** using anhydrous formic acid.[102,103]

This general reaction has been applied to the synthesis of ω-acetylenic vinyl esters.[137] Trimethylsilylethylene oxide (**6a**) reacted with propynoic acid (without catalyst) to give an α-acetoxy-β-hydroxysilane. This β-hydroxysilane was unreactive to many acidic and basic elimination conditions, and decomposed under others. However, β-elimination was accomplished by conversion to the acetate and treatment with fluoride.[137] 4-Pentynoic acid and 10-undecynoic acid also reacted with **6a** (in the presence of $BF_3{\cdot}Et_2O$) to give α-acetoxy-β-hydroxysilanes, which were converted to the acetylenic vinyl esters by fluoride treatment of the acetates.[137] (This sequence was unsuccessful with 3-butynoic acid.[137])

An intramolecular version of the reaction was used to prepare enol lactones. Treatment of vinylsilanes **54** and **55** with MCPBA gave β-hydroxysilane lactones directly, presumably via intermediate epoxysilanes.[138] As in the case of the acetylenic vinyl esters (above), β-elimination to give the enol lactones was successful using fluoride treatment of the derived acetates (anti elimination), but could not be accomplished using acidic or basic conditions.[138]

Sulfonic Acids. Reactions of α,β-epoxysilanes with methanesulfonic acid have been used for the stereospecific synthesis of alkenyl methanesulfonates according to the olefin synthesis of Scheme 1. Treatment of the *cis* and *trans* epoxysilanes **10a** and **11a** with one equivalent of methanesulfonic acid in dichloromethane followed by addition of $BF_3{\cdot}Et_2O$ (to effect β-elimination) gave the alkenyl methanesulfonates in high isomeric purity (see Table 11).[153] Attempted elimination reactions with KH were not successful, and resulted in epoxide formation.

3.4.7. Nitrogen Nucleophiles

Reactions of α,β-epoxysilanes with amines, nitriles, and azide ion have been used for the synthesis of enamines, enamides, alkenyl azides, and 2-azadienes according to the olefin synthesis of Scheme 1 (see Table 12).

Amines. Initial reports indicated that reactions of α,β-epoxysilanes with amines were sluggish.[40,153] Treatment of triphenylsilylethylene oxide (**6b**) with several amines required relatively high (110–155°C) temperatures, and the only products isolated were triphenylsilanol and hexaphenyldisiloxane.[40] From these products and from NMR monitoring, these reactions were felt to proceed by α opening.[40]

The reactions of *cis* α,β-epoxysilanes with secondary amines in the presence of alumina have been used in the synthesis of enamines according to Scheme 1. Treatment of *cis* epoxysilane **10a** with pyrrolidine or morpholine in the presence of alumina led to the α-amino-β-hydroxysilanes.[220] The *trans* epoxide **11a** was unreactive to these conditions, and therefore, *cis*- *trans* mixtures of epoxide could be used.[220a] When the α-amino-β-hydroxysilanes were treated with KH/

Table 12. Olefins From α,β-Epoxysilanes and Nitrogen Reagents

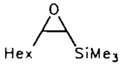
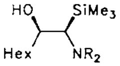
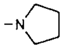
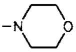
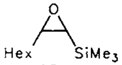
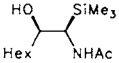
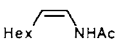
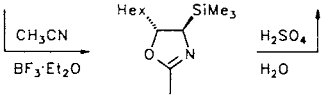
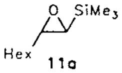
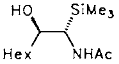
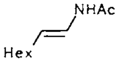
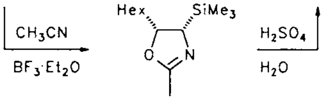
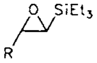
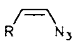
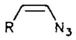
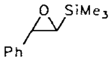
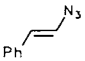
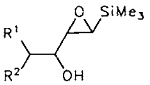
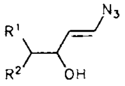
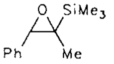
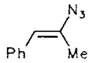
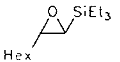
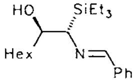
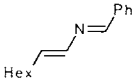
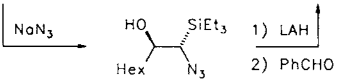
Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
 **10a**	HNR_2 alumina		KH THF			220a
	$-NR_2$ =	 and 				
 **10a**			KH THF		>99%	26
						
 **11a**			KH THF		>99%	26
						
 R = Hex, Oct, $Me_2CH(CH_2)_2$, $Ph(CH_2)_2$	Me_3SiN_3 $BF_3{\cdot}Et_2O$				93- 95%	222a
 R = Ph, CH_2OH	NaN_3 DMF					223a
	NaN_3 DMF					223a
 R^1,R^2 = H; R^1,R^2 = Me; R^1 = Ph, R^2 = H	NaN_3 DMF					223a

Table 12. Olefins From α,β-Epoxysilanes and Nitrogen Reagents *(Continued)*

Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
	NaN$_3$ DMF					223a
 11f			KH THF			222b

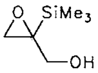


THF, the extremely sensitive *cis* enamines were isolated. (The glassware had to be base washed (aqueous KOH).) Isomerization to the *trans* isomers took place upon standing at room temperature.[220a]

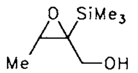
The reactions of α,β-epoxysilanes with primary amines also give α-amino-β-hydroxysilanes, but have not yet been used for the synthesis of enamines. The reaction of a *cis* α,β-epoxysilane with RNHSiMe$_3$ in the presence of AlCl$_3$ followed by hydrolysis (of the intermediate silyl ether) gave the α-amino-β-hydroxysilane.[221] In contrast, the corresponding reaction with lithium cyclohexylamide gave primarily the desilylated epoxide.[221a]

Nitriles. Several epoxysilanes have been reported to undergo an acid-promoted reaction with acetonitrile to form oxazolines, presumably from α opening of the epoxide followed by capture of the resulting intermediate by the hydroxyl.[26,28] The oxazolines from the *cis* and *trans* epoxysilanes **10a** and **11a** were hydrolyzed to α-acylamino-β-hydroxysilanes, and these compounds underwent β-elimination with KH to form isomerically pure enamides.[26] (Elimination reactions using BF$_3$·Et$_2$O were accompanied by some *cis-trans* isomerization.[80])

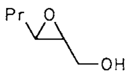
Azides. A number of epoxysilanes have undergone reactions with azide reagents to form α-azido-β-hydroxysilanes or alkenyl azides.[222,223] The use of NaN$_3$/DMF with a variety of epoxysilanes has resulted in alkenyl azides, believed to arise by α opening of the epoxide followed by *in situ syn* β-elimination.[223a] The use of NaN_3/NH_4Cl in $MeOH/H_2O$ has resulted in excellent yields of α-azido-β-hydroxysilanes with a variety of α,β-epoxysilanes.[223] In a study of the regiochemistry of the reaction with epoxides from silyl allylic alcohols, several α-substituted epoxysilanes (e.g., **56**) which were unsubstituted in the β position, gave mixtures of α and β ring opening, while α,β-disubstituted epoxysilanes (e.g., **57**) gave only α ring opening.[223b] (Simple 2,3-epoxyalcohols (without silicon) (e.g., **58**) are known to give predominantly opening at the 3-position under similar conditions.[224])



56



57



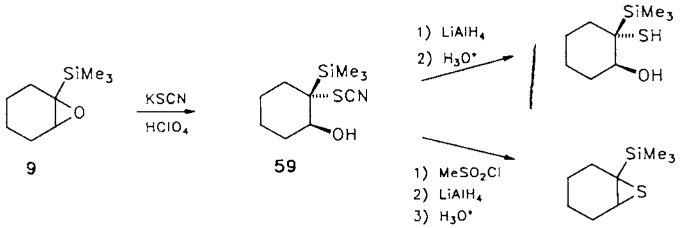
58

α-Azido-β-hydroxysilanes have also been prepared from reaction of epoxysilanes with $NaN_3/ZnCl_2$.[222b] The use of $Me_3SiN_3/BF_3{\cdot}Et_2O$ with some *trans* (and unsubstituted) epoxytrialkylsilanes has been reported to result in α-azido-β-(trialkylsiloxy) silanes[222b] or in *Z*-1-alkenyl azides (presumably via an *anti* β-elimination reaction of the α-azido-β (trialkylsiloxy)silanes).[222a] The α-azido-β-hydroxysilane from *trans* epoxysilane **11f** was converted to a 2-aza-1,3-butadiene by reduction to the amine, conversion to the Schiff base with benzaldehyde, and β-elimination with KH.[222b]

Silylamides. Reactions of some α,β-epoxysilanes (including trimethylsilylethylene oxide) with N-silylated secondary carboxamides in the presence of Me_3SiONa gave products of α opening; α-substituted α,β-epoxysilanes were unreactive to these conditions.[225]

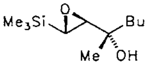
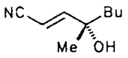
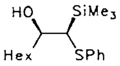
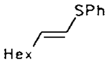
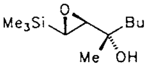
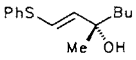
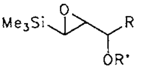
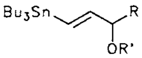
3.4.8. Sulfur and Selenium Reagents

α,β-Epoxysilanes have been converted to the corresponding episulfides using thiourea[98] and 3-methylbenzothiazole-2-thione.[226] Epoxysilane **9** was shown to undergo α opening with $KSCN/HClO_4$, and the major product, hydroxythiocyanate **59**, was converted to the corresponding thiol, and to an episulfide (eq. 25).[28]

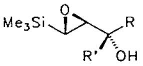
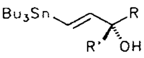


(25)

Table 13. Olefins From α,β-Epoxysilanes and Miscellaneous Reagents

Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
	Et_2AlCN					141
 10a	PhSH alumina		KH THF		98%	187a
			$BF_3 \cdot Et_2O$		97%	187a
	PhSLi					141
	Bu_3SnH LDA					

R = Pent,[140] CH_2OPh,[140,233] CH(OH)-Pent,[229] CH_2CH=CH-Pent,[227,233]
CH_2CH=CH-Et,[231] $CH_2C \equiv C$-Pent,[228,233] CH_2CH=CH-$(CH_2)_5$-$OSiMe_2$t-Bu,[233]
$CH_2C \equiv C$-$(CH_2)_5$-$OSiMe_2$t-Bu,[233] C(Me)(OMe)-Bu[234]

Epoxysilane	Reagent	Product	Elimination Conditions	Product	Isomeric Purity	Ref
	Bu_3SnH LDA					141

R = Pent, R' = Me; R = Bu, R' = Ph

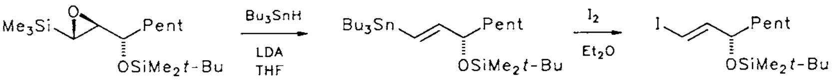
Sulfur nucleophiles have also been used in the olefin synthesis of Scheme 1: Reaction of epoxysilane **10a** with PhSH/alumina led to the product of α opening. Treatment of the product with KH resulted in the *cis* vinyl sulfide; treatment with $BF_3{\cdot}Et_2O$ led to the *trans* vinyl sulfide (see Table 13).[187a] The use of PhSLi converted a *trans* Me_3Si epoxide to a *trans* vinyl sulfide (presumably via α opening with *in situ syn* β elimination).[141] [And the use of PhSNa, followed by $HClO_4$, converted a *cis* Ph_3Ge epoxide to a *trans* vinyl sulfide.[107b]] A reaction of an epoxysilane with PhS- to form a vinyl sulfide was postulated as part of the reaction pathway in the reaction of trimethylsilylethylene oxide (**6a**) with $Me_3Si(PhS)_2CLi$ (see Section 3.3.2).[177]

Acid-promoted reactions of epoxysilanes with $HSCH_2CH_2SH$, $HSCH_2CH_2CH_2SH$, and $HOCH_2CH_2CH_2SH$ have resulted in the corresponding thioacetals,[101,102,104] in an analogous manner to the reactions with diols discussed in Section 3.4.5.

The conversion of α,β-epoxysilanes to vinyl selenides has been mentioned.[104]

3.4.9. Tin Reagents

α,β-Epoxysilanes have been used to prepare alkenyltin compounds (see Table 13) by treatment with *n*-Bu_3SnLi, prepared from *n*-Bu_3SnH and (*i*-$Pr)_2NLi$ (LDA).[140,141,227-234] The reactions presumably take place via α opening of the epoxides with *in situ syn* β elimination according to the olefin synthesis of Scheme 1. The alkenyltin products have been obtained in high enantiomeric purity (the epoxide starting materials have been obtained by Sharpless kinetic resolution of γ-Me_3Si allylic alcohols—see Section 4), and have been used as precursors to alkenylcuprates[141,231] and to alkenyl iodides.[140,227,228,230,232,233] The alkenyl tin compounds have been used in syntheses of optically pure propargylic alcohols[232] and a number of natural products or intermediates of interest to natural products, including prostaglandins and analogs,[140,141,231,234] leukotrienes,[227,230,233] HETE's[228,230] and lipoxin B.[229]

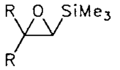


(ref 140)

3.5. Discussion

3.5.1. Summary of α and β Opening

α,β-Epoxysilanes of a number of structural types undergo ring opening α to silicon with a wide variety of reagents. Under acidic conditions, β opening might be expected, especially with epoxysilanes of type **12**, because of the stabilization of a β cation by silicon groups (and evidence that α cations are somewhat destabilized by silicon (relative to carbon)). Under basic or nucleophilic conditions, β opening might be expected, especially with epoxysilanes of type **13**, because of the greater steric hindrance at the α position.



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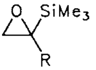

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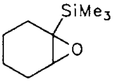

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Epoxysilanes of type **12** have been found to give products of α opening under a wide variety of conditions: organocopper reagents, $MgBr_2$, HBr, HCl, HI, ROH/acid, RCO_2H. An exception is the reaction of **12** with $BF_3{\cdot}Et_2O$ in a non-nucleophilic solvent (CH_2Cl_2), in which case rearrangement took place[50] (Section 3.4.4).

Epoxysilanes of type **13** have been found to give products of α opening from reactions under acidic conditions ($MgBr_2$, HBr, SiF_4, ROH/acid), and products of β opening (or mixtures of products) under more nucleophilic conditions (i-Bu_2AlH (on a Ph_3Si epoxide), organocopper reagents, lithiated allyltrimethylsilane, some Grignard reagents, azide).

With the unsubstituted silylethylene oxides (**6**), the difference in steric hindrance between the α- and β-carbons is not as great as that in epoxide **13**. With *trimethyl*silylethylene oxide (**6a**), only products of (or derived from) α opening have been reported in most cases: using $LiAlH_4$ (on Pr_3Si analog), organocopper reagents, unhindered lithiated sulfones, a titanium acetylide, $MgBr_2$, ROH/acid, RCO_2H, Me_3SiN_3, N-silylated secondary amides, and a presumed PhS- intermediate. Products of β opening were reported from reactions with lithiated allyltrimethylsilane (minor product) and with hindered lithiated sulfones (major product). With *triphenyl*silylethylene oxide (**6b**), products of β opening (or mixtures) have been reported from reactions with $LiAlH_4$ (large excess, minor product), HCl (major product), and $MgBr_2$, while only products of α opening have been reported with $LiAlH_4$ (smaller excess) and with i-Bu_2AlH.

Epoxysilanes having substituents at only the β position, and at both α and β positions, have almost always undergone α opening, with only a few exceptions: In conformationally biased systems, the preference for α opening has not been enough to overcome the preference for *trans* diaxial opening (hydride, ROH/acid). In medium ring compounds, transannular reactions (ROH/acid, H_2O/acid) or loss of stereospecificity (hydride) have sometimes occurred. In the reaction of trimethylsilylcyclohexene oxide (**9**) with MeOH/alumina, the product of β opening was reported as a major product (although reaction of **9** with MeOH/acid gave only α opening); the reaction of **9** with HCl gave the product of β opening as a minor product (although reactions of **9** with HBr and HI are reported to give only α opening). Some reactions of lithiated allyltrimethylsilane was reported to give mixtures of products. As mentioned in Section 3.4.4, some α,β-epoxysilanes (derived from cyclic vinylsilanes) in which the β carbon is substituted with a cation-stabilizing group have undergone acid-promoted rearrangements to give products which might have resulted from initial β opening of the epoxide, although other mechanisms cannot be ruled out in many cases.

Little is known about the effect of the substituents on silicon on the regiochemistry of the ring opening of α,β-epoxysilanes, although it appears that *triphenyl*silylethylene oxide (**6b**) may be more prone to β opening than *trimethyl*silylethylene oxide (**6a**) as discussed above.

3.5.2. Reasons for α Opening

With simple epoxides, the regiochemistry of ring opening under acidic conditions is influenced strongly by the relative stabilities of the two possible carbocations, while the regiochemistry under strongly nucleophilic conditions is influenced largely by steric hindrance. With α,β-epoxysilanes, a high preference for α opening has been observed under both acidic and nucleophilic conditions.

Most of the ring opening reactions of α,β-epoxysilanes are believed to involve little, if any development of cationic character. This is based on the regiochemistry of the reactions (especially in those epoxysilanes substituted in the β position with two alkyl groups or an aryl group), the high stereospecificity of the reactions, and the lack of rearrangements. If cations were involved, one would expect to observe some loss of stereochemistry, as is the case with aryl epoxides.[235] Rearrangements have been observed in few cases, generally when the medium lacks a strongly nucleophilic component and/or substitution on the epoxysilane favors cations (Section 3.4.4). Finally, in ring openings of α,β-epoxysilanes silicon might *not* stabilize a developing positive charge in the β position: As was first pointed out in 1976, "the lack of β opening, although remarkable, is perhaps less surprising in view of the relative orientation of the C-Si bond and the β C-O bond which greatly deviate from the parallel alignment favorable for stabilization of a developing positive charge by the silicon."[24]

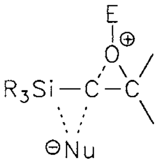
The combined results suggest that most ring opening reactions of α,β-epoxysilanes take place by nucleophilic processes (with electrophilic assistance to ring opening in many cases) in which the presence of the silicon group favors ring opening at the α position. (Another possibility that has not been considered is that silicon in some way retards ring opening β to silicon.)

Results from gas phase reactions are also consistent with the generalizations that a Me_3Si group facilitates nucleophilic displacements at the α carbon (and that silicon destabilizes an α cation relative to carbon). As mentioned in Sections 3.4.4 and 3.4.5, gas phase reactions of 1-trimethylsilylcyclohexene oxide with water/acid and with MeOH/acid have cleanly produced the products of α opening, with stereochemistry as well as regiochemistry analogous to those of the corresponding reactions in solution.[212] Similar gas phase reactions of 1-*t*-butylcyclohexene oxide with methanol and with water produced only products of rearrangement (without participation by the nucleophile), while those of 1-methylcyclohexene oxide produced mixtures of products from rearrangement (major) and substitution (with α opening).[212b]

[Cyclohexene epoxides having *t*-Bu and Me_3Si (and Me_3Ge) groups have also been compared in solution.[41,236] In reactions with acidic methanol and acidic water, the *t*-Bu compounds generally gave mixtures of products derived mostly from rearrangements, depending upon the system (a diol from direct epoxide opening with water has been observed[41]), while the Me_3Si (and Me_3Ge) compounds gave addition products of stereospecific (α) opening. The reactions of the *t*-Bu compounds were suggested to take place via transition states having more cationic character than those of the corresponding Me_3Si compounds.[236] In reactions with $LiAlH_4$, the *t*-Bu compound gave the product of β opening, while the Me_3Si (and Me_3Ge) compounds gave the products of α opening.[41]]

Other evidence indicates that silicon groups facilitate nucleophilic displacements at the α carbon. The reactivity of Me_3SiCH_2X under nucleophilic conditions is considerably greater than that of the analogous neopentyl halides;[237,238] Me_3SiCH_2Cl is more reactive toward nucleophilic substitution than simple *n*-alkyl chlorides under some conditions, and slightly less reactive or of comparable reactivity under others.[237,239] The calculated barrier to hydride exchange in the reaction $H^- + CH_3\text{-}Z \rightarrow H^- + CH_3\text{-}Z$ is considerably lower for $Z = SiH_3$ than for $Z = H$.[238]

In 1954 Eaborn and Jeffrey suggested the enhanced reactivity of Me_3SiCH_2Cl may result from coordination of the incoming nucleophile with both silicon and carbon (or prior coordination with silicon), drawing an analogy to a similar suggestion of Winstein for the high reactivity of α halo ketones toward nucleophilic reagents.[239b] Coordination of the nucleophile to both the silicon and α carbon was proposed by Eisch and Trainor in 1963 for the reaction of silyl ethylene oxides with $LiAlH_4$,[10] and this type of process has been considered for a number of α opening reactions of α,β-epoxysilanes (see **60**).[28,40,41,45,91,100,212a] Initial coordination of the nucleophile with silicon to form a pentacoordinated intermediate, followed by 1,2-rearrangement from Si to the α carbon has also been considered.[28,100,167,212a]



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A precedent for 1,2-rearrangement from Si to the α carbon of an epoxysilane is found in work of Fleming and Newton, in which treatment of epoxy(phenyldimethyl)silanes with Me_2AlCl resulted in modest yields of phenyl-substituted olefins.[50] In addition, some reactions of α,β-epoxysilanes having the silicon incorporated into a 4-membered ring, with alkyllithium or lithium alkoxide reagents,[128] and of α-lithio-α,β-epoxysilanes with a silacyclobutane[126,128] or with R_3Al reagents,[127] have been suggested to proceed via pentacoordinate intermediates with 1,2-rearrangement (see Sections 3.3.2 and 3.4.5).

If 1,2-rearrangement from Si to the α carbon were a general mechanism for the α opening of α,β-epoxysilanes, products from migration of the other groups (e.g., Me) on silicon might be expected in some of the reactions (e.g., with R_2CuLi); this has not been observed.

Some evidence suggests that an "anion" at the carbon α to silicon (carbon-metal bond) is somewhat stabilized by the silicon. Fleming has suggested that the factors which lower the energy of the transition state of an S_N2 reaction at the carbon α to silicon should be at least in part, the same factors as those which stabilize an "anion" at the α carbon.[240] Overlap involving the empty d orbitals on silicon was invoked in early explanations of these phenomena, although now the importance of d orbitals in bonding with second row elements has been questioned. Overlap involving the empty, antibonding orbitals of the Me-Si bond (in the case of a Me_3Si group), for example with the filled orbitals of the carbon-metal bond, has been offered as an alternative explanation.[240]

There is experimental (pyrolysis—Section 3.6) and theoretical[241] evidence to indicate that the C—O bond α to silicon is weaker than the β C—O bond. In this connection, it is interesting to note that the only X-ray structure[242] of an α,β-epoxysilane shows the α C—O bond (1.499 Å) to be considerably longer than the β C—O bond (1.411 Å). This is a rather unusual epoxysilane, with the epoxide ring spirocyclic to a β-lactam ring; it will be interesting to see if this trend is followed for other α,β-epoxysilanes.

3.5.3. Comparison with Other Systems

The acid-promoted ring opening reactions of α,β-epoxysilanes have been compared to reactions of vinylsilanes with reagents expected to result in halonium ion intermediates. Reactions of several vinylsilanes with N-bromoacetamide have led to α-bromo-β-hydroxysilanes[24,91] (the same products that resulted from reactions of the corresponding epoxysilanes with $MgBr_2$ or HBr). Similar reactions have been carried out with N-bromosuccinimide.[90] Reactions of several cyclic vinylsilanes with iodine-based electrophiles have produced α-iodosilanes.[96,97] (See also refs. 69 and 94.) Reactions of other halogen electrophiles[91] (e.g., aqueous NCS) (as well as reactions of several iodine-based electrophiles with an acyclic vinylsilane[97]) have given mixtures of α- and β-halosilanes. These results suggest that the transition states for opening of the halonium ions have more carbonium ion character than that for acid-promoted opening of α,β-epoxysilanes, and can therefore better take advantage of the ability of silicon to stabilize a β carbonium ion.[96,97]

Reactions of vinylsilanes with singlet oxygen have also been compared to ring opening reactions of α,β-epoxysilanes. The products from some substituted vinylsilanes (almost always β-silylated allylic alcohols rather than the α-silylated derivatives after reduction of the initial hydroperoxides) were consistent with the opening of a perepoxide intermediate α to the silicon.[241]

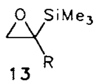
Silylaziridines undergo ring-opening reactions involving cleavage of the α C—N bond, analogous to those of α,β-epoxysilanes. In contrast, some ring-opening reactions of the corresponding aziridinium ions involve cleavage of the β C—N bond.[243]

A comparison of the reactions of α,β-epoxysilanes with the corresponding germanium and tin epoxides is beyond the scope of this review.

3.6. Thermal Reactions

α,β-Epoxysilanes have been found to undergo thermal rearrangements to silyl enol ethers,[40,244-248] and sometimes other products as well. The reactions are more facile than analogous reactions of simple epoxides;[244,245] under conditions (flash vacuum pyrolysis) that resulted in rearrangement of many epoxysilanes, propylene oxide and cyclohexene oxide were unchanged.[245] Many of these reactions appear to involve breaking the α C—O bond.

The majority of the products from thermolysis of epoxysilanes substituted only with deuterium,[40,244] or substituted only in the α position with alkyl or aryl groups,[244,245] are consistent with a mechanism involving cleavage of the α C—O bond of the epoxide. An α-substituted epoxide (**13b**) underwent rearrangement at a lower temperature than analogous β-substituted epoxides (e.g., **11b**), suggesting that silicon facilitates cleavage at the α position.[245] However, the products from epoxysilanes substituted in the β position with phenyl are consistent with a mechanism involving cleavage of the β C—O bond,[244] and for some epoxysilanes, mixtures of reaction pathways may well occur.



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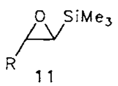

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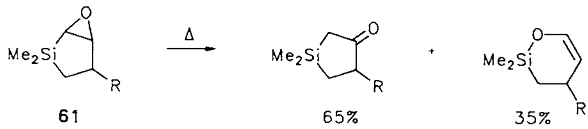
a: R = Hex; b: R = Pr

In some cases, the reactions show considerable stereospecificity, suggesting concerted character. The reactions (α cleavage) have been compared to the thermal rearrangements of α-silyl ketones and aldehydes (to silyl enol ethers),[244] and such compounds have been suggested as possible intermediates.[40,245,246] Thermolysis of the more rigid bicyclic epoxysilane **61** led to a silyl ketone (together with a silyl enol ether believed to arise from β opening).[246,247] Thermolysis of a similar bicyclic α,β-epoxygermane yielded analogous products; but the reaction was less facile than that of the epoxysilane.[247]



In liquid phase thermal reactions of triphenylsilylethylene oxide, traces of acid on the glassware were felt to catalyze the reaction, and the possible role of adventitious catalysts or surface reactions was mentioned.[40] Indeed, the first example of this type of reaction was the rearrangement of phenyldimethylsilylethylene oxide to the corresponding silyl enol ether on gas chromatography at 187°C on an old SE-30 column.[16]

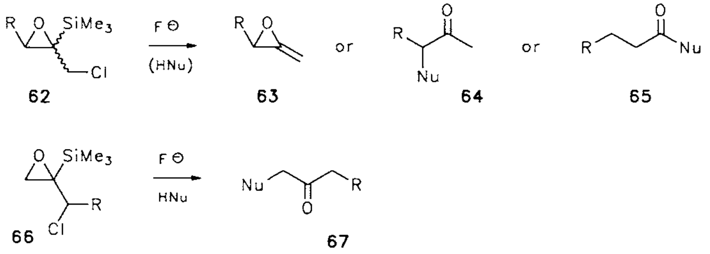
Thermal reactions of α,β-epoxysilanes have not competed with other ways of preparing silyl enol ethers, but they were used to obtain a pure β-substituted (*trans*) epoxysilane (**11a**) from a mixture of β- and α-substituted epoxysilanes (**11a** and **13a**),[248] since, as mentioned above, the α-substituted isomer reacts at a lower temperature than the β-substituted isomer.

3.7. Removal of Silicon

3.7.1. Elimination Reactions to give Allene Oxides

As mentioned in Section 3.1, β-halosilanes and other silanes having a good leaving group in the β position undergo fluoride-induced elimination reactions under very mild conditions. Chan has developed these reactions for the preparation or generation of compounds with strained multiple bonds.[136] Thus allene oxides have been generated from α,β-epoxysilanes with a β′ leaving group.[42,249–254]

Treatment of epoxysilane **62** (R = *t*-Bu) with fluoride resulted in isolation of the allene oxide **63**.[42,250a,252] When epoxysilanes **62** having a sterically less bulky alkyl group (R) were used, allene oxides could not be isolated. α-Chloro ketones **64** (Nu = Cl) were obtained, suggesting the allene oxides had been formed and trapped with chloride.[42,252] When the reactions were carried out in the presence of external nucleophiles (HNu) such as alcohols, thiols, or amines, the analogous trapping products **64** were obtained.[42,250b,252] Similarly, α-substituted ketones **67** were obtained from reaction of epoxysilanes **66** with fluoride in the presence of a nucleophile;[42,250b,252] this type of reaction has been developed into a synthesis of fluoromethyl ketones (and hydroxymethyl ketones[254c]), and has been used to introduce fluorine into steroids.[254a,b]



Reactions of aryl-substituted epoxysilanes **62** (R = Ph, *p*-tolyl) with fluoride in the presence of an external nucleophile led to carbonyl compounds **65**, believed to arise by isomerization of the intermediate allene oxides to cyclopropanones prior to reaction (Favorskii type) with the external nucleophile.[42,249,250b,252] The allene oxide-cyclopropanone rearrangement appears to be especially facile in these cases, suggesting the rate determining step involves breaking the C-1-oxygen bond with development of charge at carbon.[42,250b] Allene oxides and/or cyclopropanones, generated from epoxysilanes, have also been trapped by dienes[249,251,252] and by acrylic esters.[252] In a biomimetic synthesis of a preclavulone A model, a presumed allene oxide having a conjugated double bond (generated from a β′-trifluoroacetoxy-α,β-epoxysilane) underwent cyclization *in situ* giving a cyclopentenone.[253]

[α,β-Epoxysilanes which are allene and butatriene oxides, respectively, were suggested as possible intermediates in the oxidation of a silicon-substituted allenic alcohol (to give a silylated lactone)[86] and in the (peracid) oxidation of a silylated butatriene (to give a silylated acyloxy enone).[89]]

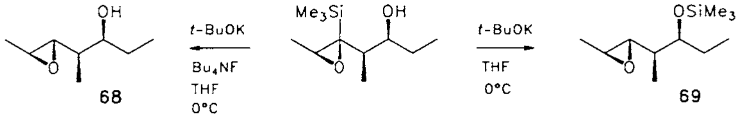
3.7.2. Desilylation Reactions

In 1976[255] (and in 1974[249a]) Chan and co-workers reported that the silicon group (Me_3Si, Ph_3Si) in α,β-epoxysilanes could be replaced by a hydrogen (hydrodesilylation) by using fluoride ion in a polar solvent. This reaction has been widely used (see refs. 68a, 109a, 123, 124a, 151, 229, 234, 255–269) (e.g., see Schemes 11 and 13, and eq. 28 in Section 4), especially for the preparation of (desilylated) epoxides of high diastereomeric and/or enantiomeric purity since, as discussed in Section 4, the selectivity of the epoxidation of allylic alcohols having a β- or γ-silyl group is frequently significantly higher than that of the corresponding desilylated allylic alcohol. This reaction has also been used to introduce deuterium[68a,255] (e.g., by using Et_4NF in CD_3CN for the synthesis of deuterium-labeled arene oxides[68a]). In addition to Me_3Si and Ph_3Si groups, $PhMe_2Si$[264] and R_2SiOH[263,264] groups on epoxides have undergone desilylation with fluoride. These desilylation reactions were first observed with α,β-epoxysilanes having a hydroxyl β to the silicon, but were found to take place with simple α,β-epoxysilanes as well.[255]

An alternate method has been devised for the replacement of a Me_3Si group by hydrogen in α,β-epoxysilanes having a hydroxyl β or γ to the silicon.[270–272,277] This method involves treatment of the hydroxy epoxysilanes with base, and is believed to proceed by migration of Me_3Si from C to O (see eq. 26 below[277]) homologous to the Brook rearrangement. Silyl ethers (e.g., **69**), the initial rearrangement products, have been isolated in some cases (mostly with γ-hydroxysilanes,[271,272,274,277] and a few with β-hydroxysilanes[270a,272]). These reactions have also been widely used (refs. 139, 270–281) especially in the preparation of epoxides of high diastereomeric and/or enantiomeric purity.

In both types of desilylation reactions, retention of configuration at carbon has generally been observed. An exception is the desilylation of an α-acyl-α,β-epoxysilane (using KF/CH_3CN) which was not stereoselective, suggesting the intermediacy of an enolate.[123] And in both types of desilylation reactions, an epoxysilane has been desilylated in the presence of a vinylsilane.[229,270,277] (See also ref. 255.)

The fluoride-induced desilylation reactions of α,β-epoxysilanes have been carried out with KF, n-Bu_4NF, Et_4NF, and CsF. Solvents have included acetonitrile, DMSO, DMF, and THF. In one case, the following order was found for the rate of desilylation in acetonitrile: n-Bu_4NF >> Et_4NF > KF/crown ether.[68a] In the case of α,β-difluoro-α,β-epoxysilanes, the intermediate anions from treatment of the epoxides with fluoride were trapped with various electrophiles (e.g., aldehydes, ketones, and CO_2 to give fluoroepoxy alcohols and fluoroglycidic acids).[188,282]



(26)

The base-induced desilylation reactions of β- or γ-hydroxy-α,β-epoxysilanes have yielded the epoxide products as silyl ethers (**69**) by using t-BuOK/THF,[270a,277] NaH/HMPA,[270a,277] and t-BuOK/t-BuOH/THF,[272] and as alcohols (**68**) by using t-BuOK/n-Bu_4NF/THF.[277] The desilylation reaction with silyl epoxides having a β-OH was much faster than with those having a γ-OH.[272] (See also ref. 189.) [Base-induced reactions of α,β-epoxysilanes having a hydroxyl δ to the silicon have given products of intramolecular α opening by the alkoxide with β elimination,[138] according to the olefin synthesis of Scheme 1 (Section 3.4.5).]

An epoxysilane from epoxidation of a trimethylsilyl quinone was desilylated with Triton B;[63] it should be noted that in this case, the silicon group was α to a carbonyl.

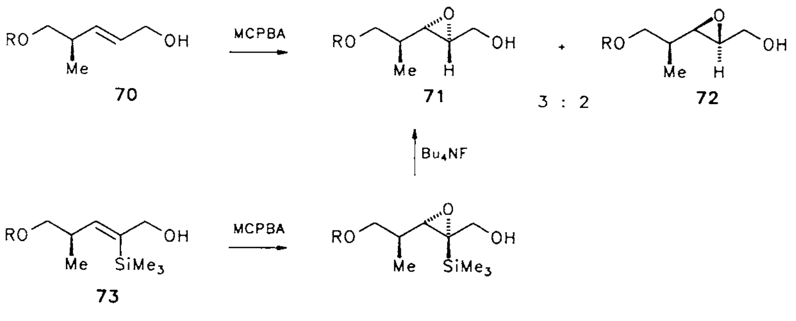
4. STEREOSELECTIVE EPOXIDATION OF ALLYLIC ALCOHOLS

The stereoselectivity of the epoxidation of acyclic allylic alcohols can frequently be enhanced or changed by the replacement of a hydrogen by a silicon group at the β or γ position. As in the case of allylic alcohols without silicon, epoxidation selectivity depends upon the substitution patterns at the double bond and allylic positions (as well as upon the choice of epoxidizing agent), and the stereochemistry of the product epoxides can frequently be predicted by assuming an association between the OH and the epoxidizing agent, and by considering the relative conformational stabilities. Silicon groups have been used as the equivalent of a bulky hydrogen, since they can be stereospecifically replaced by hydrogen in the product epoxides (see Section 3.7.2).

In a 1976 paper introducing the fluoride-induced desilylation of α,β-epoxysilanes, Chan and co-workers observed that epoxidation of a β-triphenylsilyl allylic alcohol with MCPBA yielded the product epoxide as only one diastereomer.[255] Kishi and co-workers were the first to directly compare the epoxidation of silyl allylic alcohols with their non-silylated counterparts, and make use of the selectivity from the silyl compounds in organic synthesis.[256] Allylic alcohol **70** (Scheme 11) upon treatment with MCPBA led to a 3:2 mixture of diastereomeric epoxides (**71** and **72**), while the analogous *silyl* allylic alcohol **73**, upon treatment with MCPBA followed by desilylation with fluoride led exclusively to epoxide **71**. Reactions of this type were used in the total synthesis of rifamycins.[256bc]

Diastereoselectivities of epoxidation of a number of silyl-substituted secondary allylic alcohols, and in some cases, their desilylated counterparts have been determined with peracid (MCPBA), the VO(acac)$_2$/*t*-BuOOH reagent (Hacac = 2,4-pentanedione), and the Sharpless titanium-catalyzed asymmetric epoxidation reagent [Ti(O-*i*-Pr)$_4$/*t*-BuOOH/tartrate ester (such as di-isopropyl tartrate (DIPT))].[283] Results are shown in Table 14. For an additional example using Mo(CO)$_6$/*t*-BuOOH, see ref. 266. In addition, enhanced *enantio*selectivities have been observed with several silyl-substituted allylic alcohols by using the Sharpless asymmetric epoxidation reagent (below).

Diastereoselectivities approaching 100% have frequently been obtained with VO(acac)$_2$/*t*-BuOOH. Thus, silyl allylic alcohols of type **75** (see Table 14) have been used in the synthesis of sugars and sugar building blocks[260,273,275] and of intermediates for the synthesis of arachidonic acid metabolites.[276] And silyl allylic alcohols of type **76** have been used to prepare intermediates for the synthesis of leukotrienes.[278]



Scheme 11

The simple reagent Ti(O-*i*-Pr)$_4$/*t*-BuOOH has been used with a silylated allylic alcohol of type **75** (which had given a low yield with the vanadium reagent), and resulted in a good yield of (*erythro*) epoxide which was used for a synthesis of (+)-blastmycinone.[270]

In 1986, Sato and co-workers reported that γ-trimethylsilyl secondary allylic alcohols (type **74**, Table 14) undergo an efficient kinetic resolution with the Sharpless asymmetric epoxidation reagent.[154,281] In many cases, both the epoxide and remaining allylic alcohol have been isolated with >99% ee each, in almost 90% combined yields. Only in

Table 14. *Threo/Erythro* (T/E) Selectivity in the Epoxidation of Allylic Alcohols

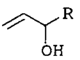
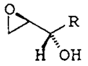
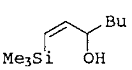
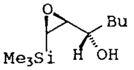
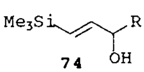
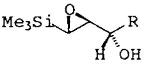
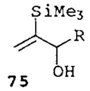
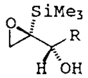
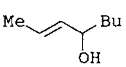
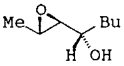
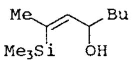
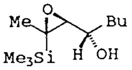
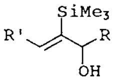
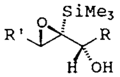
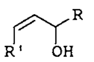
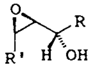
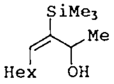
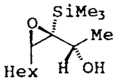
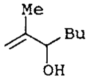
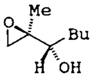
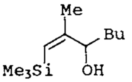
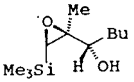
Starting Material	"Erythro" Product	MCPBA T/E[a]	VO(acac)$_2$ t-BuOOH T/E[a]	Tartrate Ti(OiPr)$_4$ t-BuOOH T/E[b]
		58:42[c,d,e]	22:78[c,f,g]	1:99
		87:13[d]	92:8[f]	
 **74**		mixture[h]	1:3[i]	0:1[j,k]
 **75**		39:61[c,d]	1:99[c,l]	0:1[m]
		61:39[d,e]	29:71[e,f]	
		99:1[d]	99:1[f]	
 **76**		15:85[n,o]	1:99[n,p]	0:1[m]

Table 14. *Threo/Erythro* (T/E) Selectivity in the Epoxidation of Allylic Alcohols *(Continued)*

Starting Material	"Erythro" Product	MCPBA T/E[a]	VO(acac)$_2$ t-BuOOH T/E[a]	Tartrate Ti(OiPr)$_4$ t-BuOOH T/E[b]
		95:5[n,q]	80:20[f,g,n]	19:81[r]
		81:19[d,s,t]	7:93[s]	
		41:59[u]	2:98[v]	2:98
		91:9	74:26	

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[a] From ref. 257 unless otherwise indicated. Products were racemic in most cases. [b] Most of these reactions were run as kinetic resolutions of racemic alcohols. Products were non-racemic but not always the same enantiomers as those shown. For the non-silicon compounds, the T/E ratios were determined at an early stage of the reactions (ref. 284c). [c] R = Bu. [d] See also ref. 258b. [e] See also refs. 248ab. [f] See also ref. 258a. [g] See also refs. 284abc. [h] Ref. 229. [i] R = Pent: refs. 140, 154; see also ref. 234. [j] No *threo* isomer detected or only *erythro* isomer isolated; refs. 140, 151, 154, 227–231, 233, 234, 268, 281; see also refs. 141, 232, 289. [k] Only allylic alcohol isolated: refs. 285–287; see also ref. 288. [l] See also refs. 258a, 260, 273, 275, 276, 279. [m] No *threo* isomer detected: refs. 279, 281. [n] R′ = Pent or Hex; R = Me. [o] See also ref. 258b. See also ref. 272 (possibly minor product). [p] See also refs. 139, 144, 258a, 272, 275, 278, 279, 281. [q] See also refs. 258b, 265, 284ab. [r] R = Me, R′ = Me. [s] See also refs. 144, 272. [t] For an exception in a more hindered system, see ref. 265. [u] Ref. 284b; see also refs. 257, 258b, 284a. [v] Ref. 284b; see also refs. 257, 258a, 284ac.

the case of the *t*-Bu substituted compound (type **74**, R = *t*-Bu) were unsatisfactory results obtained.[281] The epoxide products are generally obtained as the *erythro* isomers. (Compare the modest erythro/threo selectivity obtained with the vanadium reagent for allylic alcohols of this type—see Table 14.)

A synthetically useful kinetic resolution of β-trimethylsilyl secondary allylic alcohols of types **75** and **76** has also been accomplished (again with high *erythro* selectivity for the epoxides),[279,281] although not with the extremely high efficiency of the γ-silyl compounds.

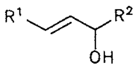
The kinetic resolution of the γ-trimethylsilyl allylic alcohols (type **74**) appears to be considerably more efficient than that of their carbon and hydrogen analogs.[67,229,281] (For non-silicon systems, see ref. 284d.) For example, the phenyl-substituted compound (type **74**, R = Ph) underwent efficient kinetic resolution to give the epoxide with 97.3% ee and allylic alcohol with > 99% ee,[281] while 1-phenyl-2-propen-1-ol has been reported to be a poor substrate for kinetic resolution.[281,284f]

Sharpless and co-workers have found that the ratio of epoxidation rates (k_f/k_s) of the fast and slow reacting enantiomers for γ-trimethylsilyl allylic alcohols of type **74** is significantly higher than for other similar secondary alcohols using conditions for kinetic resolution, $[Ti(DIPT)(O\text{-}i\text{-}Pr)_2]_2/t\text{-}BuOOH$.[67,290] Several examples are shown in Table 15. Increasing steric bulk at the olefin terminus was found to increase the rates of epoxidation of the fast enantiomers, and decrease those of the slow enantiomers, but only within limits. For example, replacing Me_3Si by $(i\text{-}Pr)_3Si$ decreased k_f/k_s. An analogy between the titanium-tartrate process and enzymic catalysis has been drawn.[67]

As in the peracid epoxidations (Section 2.1), silicon-substituted olefins appear to be less reactive to the asymmetric epoxidation conditions than corresponding carbon-substituted olefins,[67,284e] but more reactive than the corresponding hydrogen-substituted olefins.[268] A bis allylic alcohol having one of the double bonds substituted with a Me_3Si group (γ to the hydroxyl) and the other with hydrogen, was epoxidized at the silyl-substituted double bond under these conditions.[268]

Kinetic resolution of silyl allylic alcohols of type **74** with t-BuOOH/$Ti(O\text{-}i\text{-}Pr)_4$/tartrate has been used in the synthesis a number of compounds with high enantiomeric purity, including optically pure propargylic alcohols,[140,232] and intermediates of use for the synthesis of prostaglandins,[140,288] sugars,[151] lipoxin B,[229] and chiral amide allylsilanes (which were converted to parasorbic acid).[285,286] In addition, several

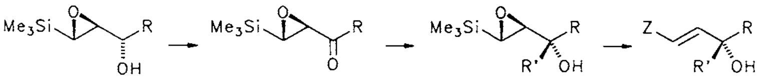
Table 15. Relative Rates of Epoxidation by $[Ti(DIPT)(O\text{-}i\text{-}Pr)_2]_2/t\text{-}BuOOH$

	R¹	*R²*	k_f/k_s
	Me	$c\text{-}C_6H_{11}$	104
	Pent	Me	160
	t-Bu	$c\text{-}C_6H_{11}$	300
	$Si(i\text{-}Pr)_3$	Pent	300
	$SiMe_3$	Pent	700

natural products and analogs have been synthesized including leukotrienes,[227,230,233] prostaglandins, [141,231,234] HETE's,[228,230] and the active component of a family of cyclic tetrapeptides.[268]

A portion of the synthesis[233] of leukotriene B_4 is shown in Scheme 12. Noteworthy is that fact that both the epoxide (**79**) and the recovered allylic alcohol (**78**) from the asymmetric epoxidation of **77** could be used for the synthesis of the same intermediate (iodide **82**) since the Mitsunobu inversion could be used to change the stereochemistry of the hydroxyl of **79**. The conversion of epoxides **80** and **81** to the vinyl tin compound (and then to vinyl iodide **82**) follows along the lines of the olefin synthesis of Scheme 1 (see Section 3.4.9).

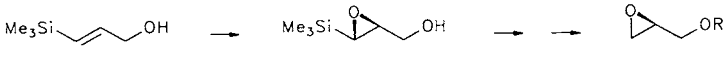
The epoxide products from the kinetic resolution of γ-trimethylsilyl allylic alcohols (type **74**) have been oxidized to the corresponding ketones, and the ketones have been found to undergo highly diastereoselective addition reactions with Grignard reagents (eq. 27, R ≠ Me).[289] The products were used in the olefin synthesis of Scheme 1 (see Sections 3.2, 3.3.4, 3.4.8, and 3.4.9), giving optically active γ-substituted tertiary allylic alcohols.[141]



(27)

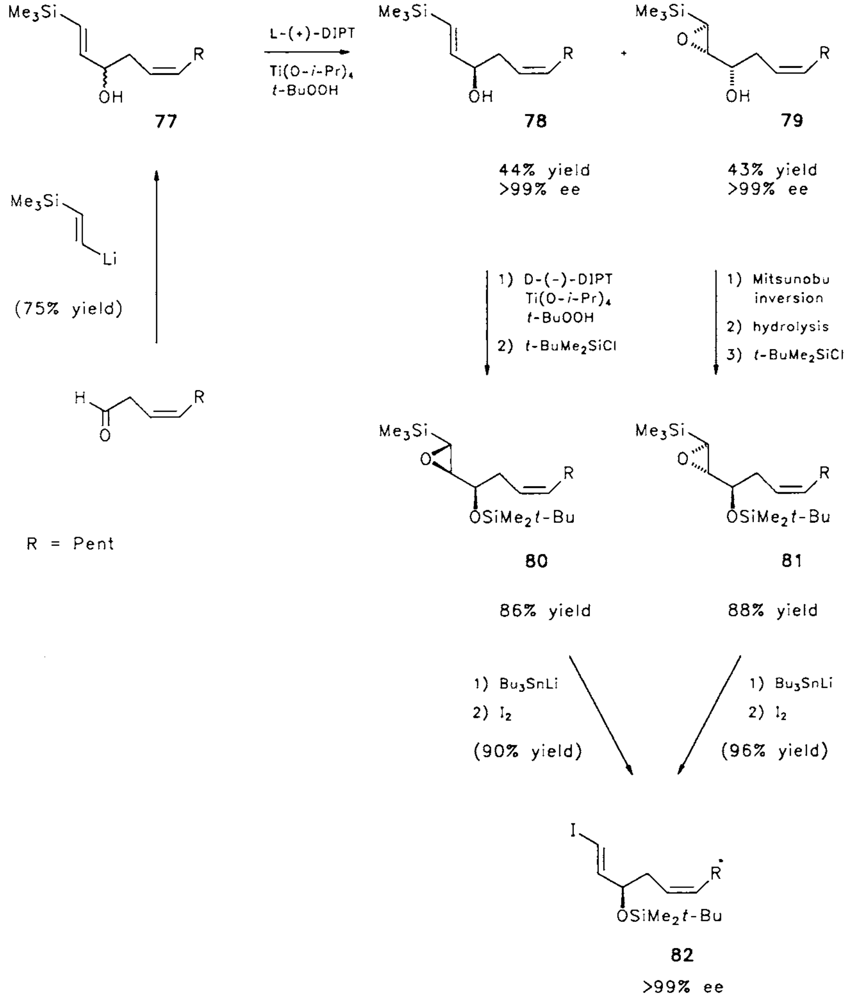
Z = Bu_3Sn, N≡C, PhS, H

The Sharpless asymmetric epoxidation has been used successfully with several primary allylic alcohols having β- or γ-silyl groups, to give α,β-epoxysilanes in high enantiomeric purity,[139,183,259,261,269] Epoxidation of the trimethylsilyl allylic alcohol **83** resulted in the epoxide **84** (silylated glycidol) in up to 99% ee (in contrast to the ca. 90% ee obtained from epoxidation of the simple allyl alcohol).[269] (See also ref. 259.) Glycidol is a versatile synthetic intermediate, but is unstable and difficult to obtain pure.[259,269] Silylated glycidol **84** has been used to prepare several chiral building blocks.[176,269] A similar asymmetric epoxidation of the *i*-Pr_3Si analog of **83** similarly gave the glycidol derivative in ≥98% ee.[183]



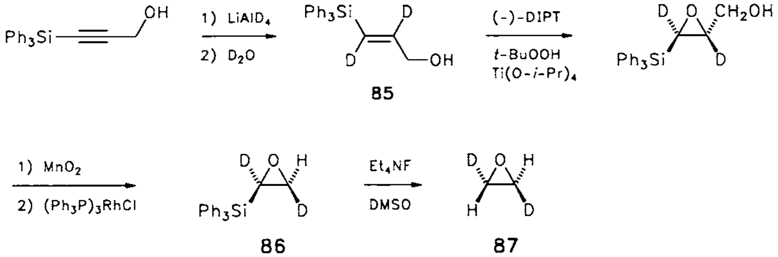
83 84

Another application of asymmetric epoxidation of silylated primary allylic alcohols is in the synthesis of chirally labelled oxirane by



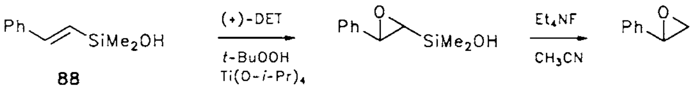
Scheme 12

Schwab and co-workers as shown in Scheme 13.[261] Subjection of allylic alcohol **85** to modified Sharpless conditions using (–)-DIPT followed by oxidation and decarbonylation yielded epoxysilane **86**. The Ph$_3$Si group was stereospecifically replaced by H by using Et$_4$NF (see Section 3.7.2) to give (2S,3S)-[2,3-^{2}H$_2$]oxirane (**87**) in 94% ee. Similarly (2R,3R)-[2,3-^{2}H$_2$]oxirane was prepared from **85** in 92% ee by using (+)-DIPT. The oxiranes were used in a preparation of chirally labeled homoserine lactone.[261c]



Scheme 13

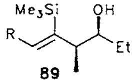
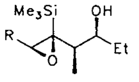
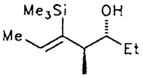
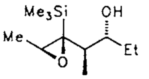
The Sharpless asymmetric epoxidation is normally not useful for simple alkenes without an attached hydroxyalkyl group (for a preparation of a simple epoxide by removal of the CH_2OH group, see Scheme 13). Chan and co-workers have therefore studied the Sharpless asymmetric epoxidation of alkenylsilanols[263] (eq. 28), since silyl epoxides can be desilylated (stereospecifically) by using fluoride ion. Oxidation of silanol **88** under Sharpless conditions with (+)-diethyl tartrate (DET) gave an epoxysilane; treatment with fluoride gave (S)-styrene oxide in 85–95% ee. In a preliminary report, this type of reaction was applied to the synthesis of chirally labelled oxirane by using dimethyl-(E-2-[(dimethyl)phenylsilyl]ethenyl)silanol as the substrate.[264]



(28)

The stereochemistry of epoxidation of some silicon-containing homoallylic alcohols has also been reported.[271,274,291] Some results are shown in Table 16.[271] In some cases, the stereoselectivities were modest, but high stereoselectivity was obtained for compounds of type **89** with the *t*-BuOOH/VO(acac)$_2$ reagent. The $SiMe_3$ group was necessary for the high selectivity; the *t*-BuOOH epoxidation of *syn*-(*E*)-4-methyl-5-hepten-3-ol [prepared by desilylation of **89** (R = Me)] gave a 3:2 mixture of *syn* and *anti* epoxides.[271] Conversion of the homoallylic alcohol **89** (R = Me) to a benzoate ester reversed the selectivity (1:6 ratio) of the MCPBA epoxidation.[271] Epoxidations of homoallylic alcohols analogous to **89** with *t*-BuOOH/VO(acac)$_2$ have been used in syntheses of segments of 6-deoxy-erythronolide B[271] and of tylonolide.[274]

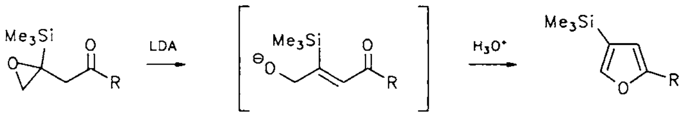
Table 16. Selectivity of Epoxidation of Homoallylic Alcohols

		Reagent	
Substrate	*Major Product*	*MCPBA*	*t-BuOOH/ VO(acac)$_2$*
 89		4:1 (R = Me)	>99:1 (R = Me, H)
		3:1	2:1

5. MISCELLANEOUS REACTIONS

5.1. Elimination Reactions

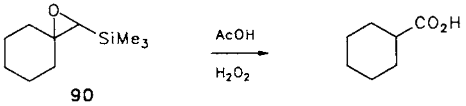
Reactions of lithium dialkylamides with simple epoxides to give allylic alcohols are well known; the analogous reactions with α,β-epoxysilanes have not yet been successful,[49] although the following reaction (eq. 29) can be viewed as a special example.[162] (Vinylsilanes can be directly transformed into allylic alcohols by photooxygenation.[46,241])



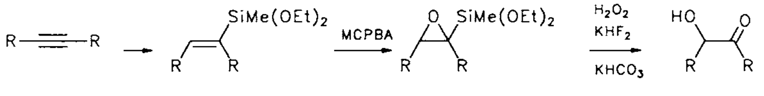
(29)

5.2. Oxidation and Reduction

α,β-Epoxysilanes are stable to a number of reagents used for oxidizing alcohols to carbonyl compounds (e.g., Cr(VI), Swern, etc.). A few examples of ring opening in the presence of an oxidizing agent have been reported.[102,205] For example, treatment of epoxide **90** with hydrogen peroxide in acetic acid gave cyclohexanecarboxylic acid in 60% yield.[102] (For ring-opening reactions of α,β-epoxysilanes with carboxylic acids, see Section 3.4.6.)



α,β-Epoxysilanes having alkoxy groups on the silicon react with $H_2O_2/KHF_2/KHCO_3$ to give α-hydroxy ketones (eq. 30).[292] (Epoxy-*trimethyl*-silanes were stable to these conditions.)

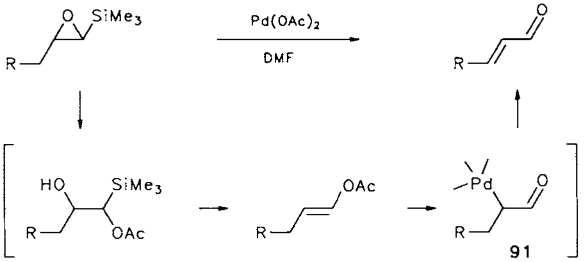


(30)

Although reactions of epoxysilanes with metal hydrides are well known (Section 3.2), few other reducing agents have been investigated. Some deoxygenation reactions of epoxysilanes having $SiMe_2OR$ groups with RMgX/CuCN were discussed in Section 3.3.1. Both *cis* and *trans* β-trimethylsilylstyrene oxide were deoxygenated by Ni(0) complexes to give predominantly *trans* β-trimethylsilylstyrene; *cis*-1-trimethylsilyloctene oxide was inert.[293] A number of α,β-epoxysilanes have been converted to vinylsilanes in good yield by treatment with lithium metal in THF; the reactions were stereoselective (trans products predominated).[294]

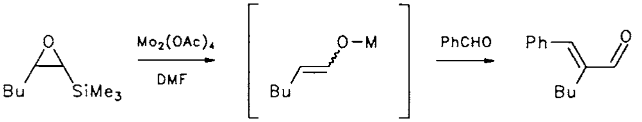
5.3. Reactions with Transition Metal Compounds

Reactions of α,β-epoxysilanes with $Pd(OAc)_2$ in DMF give α,β-unsaturated carbonyl compounds (eq. 31).[295] Several mechanisms have been proposed.[296] Another possible mechanism, analogous to the reactions of α,β-epoxysilanes discussed above, is ring opening α to silicon (by acetate or by solvent), β-elimination, and formation of the palladium complex (**91**)[295,296] as shown below.



(31)

Reactions of α,β-epoxysilanes with $Mo_2(OAc)_4$ or Ti(O-*i*-Pr)$_4$ in DMF generated metal enolates which could be trapped with benzaldehyde to give α,β-unsaturated carbonyl compounds (eq. 32).[297]



(32)

An epoxysilane (derived from a cyclic vinylsilane) has been reacted with CO_2 under Pd(0) catalysis to give a cyclic carbonate.[163] This provides a way to accomplish epoxide ring opening with retention of configuration.

5.4. Spectra

Beyond the routine spectral characterization of α,β-epoxysilanes, there are several reports of additional instrumental studies, including mass spectra,[298] collisional activation mass spectra,[299] photoelectron spectra,[108,300] oxidation potential,[301] vibrational circular dichroism,[261d] and one X-ray crystal structure.[242]

5.5. Miscellaneous[302–306]

In a few cases epoxysilanes were prepared in order to establish the purity[303] or to assign the stereochemistry[305] of the vinylsilanes.

ADDENDA

Eisch and co-workers have recently reported additional studies on the reductions of triphenylsilylethylene oxide with (*i*-Bu)$_3$Al and (*i*-Bu)$_2$-AlH;[307] in contrast to the exclusive α opening by the latter reagent (see also Section 3.2), the reactions with (*i*-Bu)$_3$Al gave mixtures of products from α and β ring opening (by hydride) in which the product of β opening predominated. Yoshida and co-workers have developed an iterative route to optically active polyols, which involves the ring-opening reactions of α,β-epoxysilanes with MeOH/$BF_3 \cdot Et_2O$ (giving α-methoxy-β-hydroxysilanes; see Section 3.4.5) followed by electrochemical oxidation to give α-hydroxy acetals.[308]

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