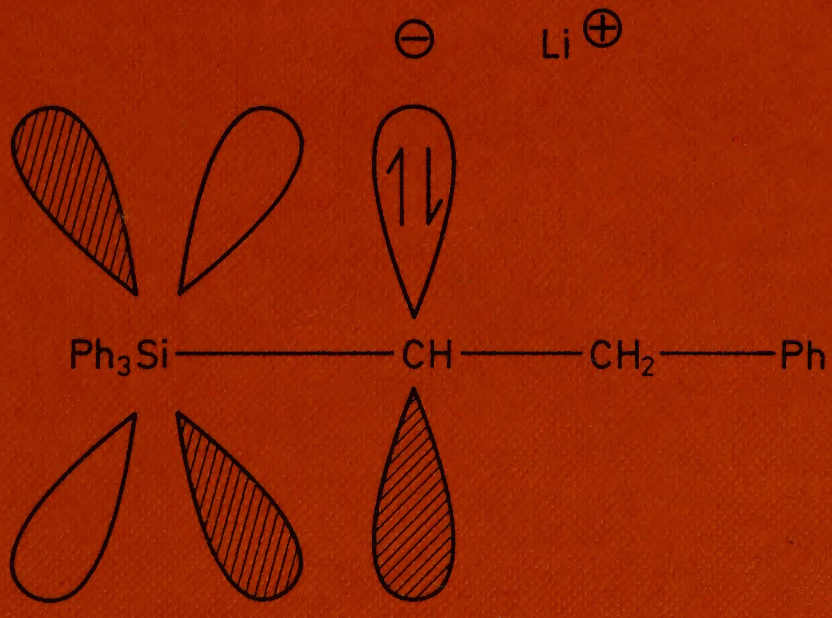
Reactivity and Structure
Concepts in Organic Chemistry 14

W. P. Weber

Silicon Reagents for Organic Synthesis



Springer-Verlag Berlin Heidelberg New York

Reactivity and Structure Concepts in Organic Chemistry

Volume 14

William P. Weber

Silicon Reagents for Organic Synthesis

Springer-Verlag
Berlin Heidelberg New York 1983

William P. Weber

Department of Chemistry, University of Southern California
University Park
Los Angeles, CA 90007/USA

ISBN 3-540-11675-3 Springer-Verlag Berlin Heidelberg New York
ISBN 0-387-11675-3 Springer-Verlag New York Heidelberg Berlin

Library of Congress Cataloging in Publication Data.

Weber, William P., 1940–
Silicon reagents for organic synthesis. (Reactivity and structure; v. 14)
Bibliography: p. Includes index. 1. Chemistry, Organic–Synthesis. 2. Organosilicon compounds. 3. Chemical tests and reagents. 1. Title. II. Series.
QD262.W35 1982 547 .2 82-5890 AACR2

Printing and binding: Konrad Triltsch, Würzburg
2152/3020-543210

To Heather and our sons: Edward, Robert and Justin

Preface

The application of silicon reagents in organic synthesis has grown at an increasingly rapid rate over the last twenty years. This has been the result of truly international interest. Significant contributions have been made by Japanese, Russian, German, French, English, American, Swiss and Canadian as well as by chemists from many other countries. This monograph attempts to comprehensively cover this field. Some seventeen hundred articles reporting contributions by over eighteen hundred scientists are summarized. Nevertheless, I have no doubt that interesting and important work has been left out. I welcome comments about such results which should be included in any future editions of this monograph.

I would like to thank Robert Damrauer who first stimulated my interest in organosilicon chemistry. In addition, I thank a number of chemists who have shared my enthusiasm for silicon chemistry over the years: A Chihi, M.E. Childs, R.A. Felix, H. Firgo, T.Y. Gu, T.I. Ito, I.N. Jung, K.E. Koenig, H. Okinoshima, M.M. Radcliffe, B.I. Rosen, H.S.D. Soysa, K.P. Steele, R.E. Swaim, D. Tzeng, P.B. Valkovich, A.K. Willard, S. Wunderly, and present members of my research group. The opportunity to spend a quiet sabbatical leave at U.C.L.A. greatly assisted in the preparation of this book. Finally, I am indebted to Michelle Dea who typed the entire manuscript, to Jennifer L. Teller who prepared camera ready copies of all equations and figures and to John Carpenter who assisted in collecting literature references.

Los Angeles, California U.S.A.
August 1982

William P. Weber

Table of Contents

Abbreviations

AIBN	azo-isobutyronitrile
$ALCl_3$	aluminium trichloride
aq.	aqueous
$BF_3 \cdot OEt_2$	boron trifluoride etherate
BF_3	boron trifluoride
BF_4^-	tetrafluoroborate
Cl_3SiH	trichlorosilane
CCl_4	carbon tetrachloride
DBU	1,8-diazabicyclo[5,4,0]undec-7-ene
DBN	1,5-diazabicyclo[4,3,0]non-5-ene
DC-18-C-6	dicyclohexyl-18-crown-6
DCC	dicyclohexylcarbodiimide
DDQ	2,3-dichloro-5,6-dicyanoquinone
DIBAL	diisobutyl aluminium hydride
DIOP, (+) or (−)	(+) or (−) 2,3-0-isopropylidene-2,3-dihydroxy-1,4-*bis* (diphenylphosphino)butane
Disiamyl borane	$\left((CH_3)_2CH-\underset{\displaystyle CH_3}{\overset{\displaystyle |}{C}}H\right)_2B-H$
DME	dimethoxyethane
DMF	dimethyl formamide
DMSO	dimethyl sulfoxide
e.e.	enantiomeric excess
eq.	equation
e.u.	entropy unit
HBr	hydrobromic acid
HCl	hydrochloric acid
HI	hydriodic acid
HMPT	hexamethylphosphorous triamide
IR	infrared
KCN	potassium cyanide
$KHSO_4$	potassium hydrogen sulfate
LDA	lithium diisopropyl amide
$LiAlH_4$	lithium aluminium hydride
MCPBA	*meta*-chloroperbenzoic acid
NBS	*N*-bromosuccinimide
NCS	*N*-chlorosuccinimide
$NaBH_4$	sodium borohydride

Pd	palladium
PTC	phase transfer catalysis
$SnCl_4$	stannic chloride
TBAF	tetra-*n*-butylammonium fluoride
TCNE	tetracyanoethylene
Th	thymidine
$TiCl_4$	titanium tetrachloride
THF	tetrahydrofuran
THP	tetrahydropyranyl ether
TMEDA	N,N,N′,N′-tetramethylethylenediamine
TMS-Br	trimethylsilyl bromide
TMS-CN	trimethylsilyl cyanide
TMS-Cl	trimethylsilyl chloride
TMS-F	trimethylsilyl fluoride
TMS-I	trimethylsilyl iodide
$TMS-N_3$	trimethylsilyl azide
TMS-X	trimethylhalosilane
TMU	tetramethylurea
TsOH	*p*-toluene sulfonic acid
UV	ultraviolet
18-C-6	18-crown-6
9-BBN	9-borabicyclo[3,3,1]nonane

1 Fundamental Considerations

The goal of this monograph is to review the use of silicon reagents in organic synthesis. Activity in this area has grown by leaps and bounds in the past decade. The commercial availability of many of these silicon reagents should further encourage development of new chemistry in this area [1–6]. This topic has been the subject of several previous reviews [7–13]. In the present monograph, I have attempted to comprehensively cover this field with the exception of silylation, the protection of O–H, N–H, and S–H bonds as silyl ethers [11, 12]. This choice was dictated by the vast number of examples of the use of silylation whose comprehensive coverage would have easily doubled the length of this already sizeable monograph.

Before beginning, a short summary of some of the physical bases underlying all silicon chemistry is in order. These data will be compared to those for carbon since organic chemists are the intended audience of this book.

The ground electronic configuration of silicon is $1s^2 2s^2 2p^6 3s^2 3p^2$ whereas carbon is $1s^2 2s^2 2p^2$. Both are usually tetracoordinate in their stable compounds and silicon, like carbon, uses four sp^3 hydridized orbitals in its bonding. Suitable organosilicon compounds are capable of optical activity. Chiral compounds such as α-naphthylphenylmethylsilane have proved useful for the study of reaction mechanisms at silyl centers [14].

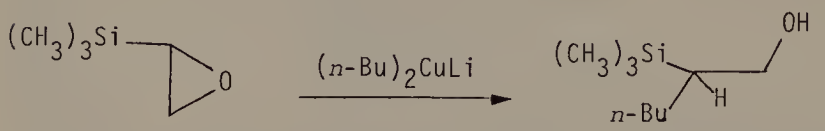
Silylenes are divalent silicon species, and like carbenes, are highly reactive intermediates. While research is active in this area [15], the use of silylenes in organic synthesis has yet to be reported.

Unlike carbon, silicon shows little tendency to form stable compounds possessing multiple bonds. No reagents which possess multiple bonds between silicon and carbon or any other elements have yet been developed. This situation may change, however, since chemists interested in reactive intermediates have intensively studied this area for the past dozen years [16].

Because silicon forms bonds with orbitals of principle quantum number 3 rather than 2, its bonds will be longer than the comparable ones of carbon. The atomic radius of silicon is 1.17 Å while that for carbon is 0.77 Å. In single bonds, carbon and silicon nuclei are 1.87–1.89 Å apart while the carbon-carbon separation in ethane is 1.54 Å [17]. This may reduce the steric bulk of a trimethylsilyl group, making it appear smaller than might be anticipated. For example, chloromethyltrimethylsilane undergoes S_n2 substitution reactions with greater facility than do neopentyl halides [18].

$$(CH_3)_3SiCH_2Cl \xrightarrow[\text{Acetone}]{NaI} (CH_3)_3SiCH_2I \qquad (1.1)$$

Silicon, unlike, carbon, possesses comparatively low lying vacant 3d orbitals. Nucleophiles may associate with these empty orbitals and thus affect the regiochemistry observed in their reactions with organosilicon compounds. For example, α-trimethylsilyl epoxides undergo nucleophilic attack by dialkyl cuprate reagents at the carbon bearing the silyl group. This contrasts with the usual nucleophilic attack on epoxides at the less hindered carbon [19].



(1.2)

3d Orbitals may stabilize transition states as well as pentacoordinate reaction intermediates. These orbitals may provide low energy pathways for nucleophilic displacements in which bond making preceeds bond breaking. Compounds of the type R_3SiX (X = halogen, etc.) undergo facile S_n2 nucleophilic displacement and solvolysis, while similar tertiary alkyl halides generally react by S_n1 pathways.

Several types of compounds in which silicon is penta- and even hexacoordinate are known. These possess electronegative ligands which may cause contraction of the 3d orbitals [20–22]. Recently, dipotassium alkyl or alkenyl pentafluorosilicates have been extensively employed in organic synthesis [23] (See Chapter 10).

Although many electronegativity scales exist and have minor differences in absolute values between them, all agree that silicon is more electropositive than either carbon or hydrogen. In all silicon is relatively close in electronegativity to hydrogen. On Pauling's scale carbon is at 2.5 while silicon is at 1.8. Hydrogen at 2.1 is intermediate [24]. The reactions of methyl lithium with triphenylsilane and triphenylmethane illustrate this difference [25].

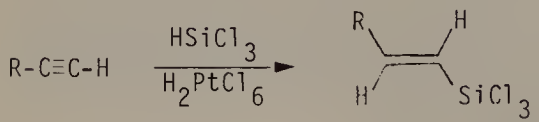
$$Ph_3Si\text{-}H + CH_3Li \longrightarrow Ph_3Si\text{-}CH_3 + Li^+ H^- \quad (1.3)$$

$$Ph_3C\text{-}H + CH_3Li \longrightarrow Ph_3C^- Li^+ + CH_3\text{-}H \quad (1.4)$$

The success of ionic hydrogenation in which silanes serve as hydride donors to carbocations reflects these differences [26].

$$Ph_3C^+ BF_4^- + Et_3Si\text{-}H \longrightarrow Ph_3C\text{-}H + Et_3Si\text{-}F + BF_3 \quad (1.5)$$

On the other hand, silanes, which possess Si−H bonds, may be compared to hydrogen. Hydrosilation and hydrogenation reactions have many common features [27] (see Chapter 10).



(1.6)

Trimethylsilyl groups often react in a manner analogous to a proton. For example, HCN adds to the carbonyl group of aldehydes and ketones to form

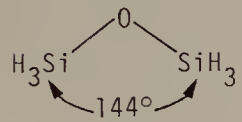
cyanohydrins, while trimethylsilyl cyanide in similar reactions yields trimethylsilyloxynitriles. (See Chapter 2)

(1.7)

(1.8)

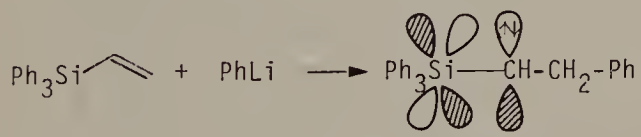
Recent work has determined many silicon bond dissociation energies. Substitution appears to have much less effect on both Si–H and Si–C bond energies than it does on C–H and C–C bond energies. Most Si–H bond dissociation energies (kcal/mole) are about 89.5 whereas C–H bond dissociation energies vary from 104.8 for methane to 87.9 for the alpha C–H bonds of toluene. Silicon-carbon bonds are close to 88.5 kcal/mole in strength, whereas C–C bond energies vary from 88 in ethane to 82 for the C–C bond of neopentane [28]. Silicon forms very strong bonds with electronegative elements such as fluorine and oxygen (see Table for Bond Energies). This has considerable synthetic implications (see Chapter 25).

The strength of Si–O bonds may result from partial double bond character; oxygen 2p lone pairs can overlap with empty 3d orbitals on adjacent silicon. Consistent with this view, the Si–O–Si bond angle of disiloxane is observed to be 144° [29, 30].



(1.9)

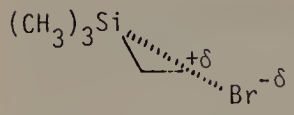
The fact that carbanions alpha to silicon are formed both by metallation of tetraalkylsilanes [31] and by addition of organometallics to vinyl silanes [32, 33] may reflect stabilization of such anions by overlap of the filled 2p orbital on carbon with the adjacent empty 3d orbitals on silicon (see Chapter 6).



(1.10)

However, the importance of 3d orbitals has been questioned [34, 35].

Finally, silicon has a definite stabilizing effect on beta carbocations in cases where the Si–C bond can achieve a *trans*-coplanar arrangement with the vacant 2p orbital of the carbocation center. β-Bromoethyltrimethylsilane undergoes solvolytic elimination to yield ethylene and the elements of TMS-Br. This reaction is as sensitive to solvent polarity as is the ionization of *t*-butyl chloride [36]. This is unusual reactivity results from stabilization of the carbocation by hyperconjugation [37] with the Si–C bond or by bridging of the trimethylsilyl group [38].



$$\xrightarrow{EtOH} (CH_3)_3SiOEt + CH_2{=}CH_2 + HBr \qquad (1.11)$$

Bond Dissociation Energies (kcal/mole) [28]

$H_3Si-SiH_3$	74		
$(CH_3)_3Si-CH_3$	89,4	H_3C-CH_3	88
$(CH_3)_3Si-H$	90.3		
$(CH_3)_3Si-Cl$	113	$(CH_3)_3C-Cl$	80
$(CH_3)_3Si-Br$	96	$(CH_3)_3C-Br$	64
$(CH_3)_3Si-I$	77	$(CH_3)_3C-I$	51
F_3Si-F	160	CF_3-F	130
$(CH_3)_3Si-OH$	128	$(CH_3)_3C-OH$	91
$(CH_3)_3Si-NHCH_3$	100	$(CH_3)_3C-NHCH_3$	80
$(CH_3)_3Si-SC_4H_9$	99	$(CH_3)_3C-S-C_4H_9$	71

These values are in general considerably higher than those for average bond energies given by Ebsworth [39].

Average Bond Energies (kcal/mole) [39]

	C	Si
H	98.7	76.5
C	82.6	73.2
N	72.8	87.3 $(CH_3)_3Si-NEt_2$
O	85.5	106
F	116	142
Cl	81	97.2
Br	68	75.6
I	51	56

In particular chapters where it is pertinent, this minimal information will be supplemented.

References

1. Petrach Systems Inc., Bristol, Pennsylvania, USA.
2. PCR Research Chemicals Inc., Gainesville, Florida, USA.
3. Pierce Chemical Co., Rockford, Illinois, USA.
4. Silar Laboratories, Inc., Scotia, New York, USA.
5. Aldrich Chemical Co., Milwaukee, Wisconsin, USA.
6. Fluka AG CH-9470, Buchs, Switzerland.
7. Hudrilik, P.F. "Organosilicon Compounds in Organic Synthesis", in J. Organometal. Chem. Libr., *1*, 127, Seyferth, D. Ed., Amsterdam, Elsevier, 1976.
8. Colvin, E.W. "Silicon in Organic Synthesis", Chem. Soc. Rev., *7*, 15 (1978)
9. Fleming, I. "Organic Silicon Chemistry" in Comprehensive Organic Chemistry, Barton, D.H.R. and Ollis, W.D. Eds., Vol. 3, 539, Oxford, Pergamon, 1979.

10. Birkofer, L. and Stuhl, O. "Silylated Synthons", Topics Current Chemistry, *88*, 33, Heidelberg, Springer Verlag (1980).
11. Klebe, J. "Silylation in Organic Synthesis", Adv. Org. Chem., *8*, 97 (1972).
12. Pierce, A.F. "Silylation of Organic Compounds", Pierce Chemical Co., Rockford, Ill. 1968.
13. Colvin, E.W. "Silicon in Organic Synthesis", London, Butterworth, 1981.
14. Sommer, L.H.: "Stereochemistry, Mechanism, and Silicon". New York: McGraw Hill 1965
15. For a recent review of silylene chemistry see Gaspar, P.P., in "Reactive Intermediates" (M.Jones, Jr. and R.A.Moss, Eds.). Vol. I, p. 229–277. New York: Wiley-Interscience 1978
16. "Formation and Properties of Unstable Intermediates Containing Multiple P_{π}-P_{π} Bonded Group 4B Metals;" Gusel'nikov, L.E., Nametkin, N.S.: Chem. Rev. *79*, 529–577 (1979)
17. Ebsworth, E.A.V.: "Physical Basis of the Chemistry of the Group IV Elements" in "Organometallic Compounds of the Group IV Elements", MacDiarmid, A.G., Ed. p. 1–104, New York: Marcel Dekker, 1968
18. Bott, R.W., Eaborn, C., Swaddle, T.W.: J. Organometal. Chem. *5*, 233 (1966)
19. Hudrlik, P.F., Peterson, D., Rona, R.J.: J. Org. Chem. *40*, 2263 (1975)
20. Frye, C.L.: J. Am. Chem. Soc. *86*, 3170 (1964)
21. Boer, F.R., Flynn, J., Turley, J.: J. Am. Chem. Soc. *90*, 6973 (1968)
22. Perozzi, E.F., Martin, J.C.: J. Am. Chem. Soc. *101*, 1591 (1979)
23. Müller, R., Organometal: Chem. Rev. *1*, 359 (1966)
24. Pauling, L., "The Nature of the Chemical Bond", 3rd Ed., p. 90. Cornell: 1960
25. Gilman, H., Melvin, Jr., H.W.: J. Am. Chem. Soc. *71*, 4050 (1949)
26. Kursanov, D.N., Parnes, Z.N., Loim, N.M.: Synthesis 633 (1974)
27. Benkeser, R.A.: Pure and Applied Chemistry *13*, 133 (1966)
28. Walsh, R.: Accts. of Chem. Res. *14*, 246 (1981)
29. Mauret, P., Abadie, A., Calas, R., Valade, J.: Bull. Chem. Soc. Fr. 1221 (1967)
30. Almenningen, A., Bastiansen, O., Ewing, V., Hedberg, K., Traetteberg, M.: Acta Chem. Scand. *17*, 2455 (1963)
31. Peterson, D.J.: J. Organometal. Chem. *9*, 373 (1967)
32. Cason, L.F., Brooks, H.G.: J. Am. Chem. Soc. *74*, 4582 (1952)
33. Mulvaney, J.E., Gardlund, Z.G.: J. Org. Chem. *30*, 917 (1965)
34. Baechler, R.D., Andose, J.D., Stackhouse, J., and Mislow, K.: J. Am. Chem. Soc., *94*, 8060 (1972).
35. Baechler, R.D., Casey, J.P., Cook, R.J., Senkler, Jr., G.H., and Mislow, K.: J. Am. Chem. Soc., *94*, 2859 (1972).
36. Sommer, L.H., Braughman, G.A.: J. Am. Chem. Soc. *83*, 3346 (1961)
37. Traylor, T.G., Hanstein, W., Berwin, H.J., Clinton, N.A., Brown, R.S.: J. Am. Chem. Soc. *93*, 5715 (1971)
38. Jarvie, A.W.P., Holt, A., Thompson, J.: J. Chem. Soc. *B*, 852 (1969)
39. Reference 17, p.46.

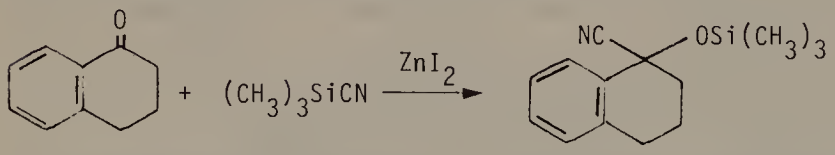
2 Chemistry of Trimethylsilyl Cyanide

2.1 Introduction

Some of the fundamentals of silicon chemistry have been presented in Chapter One. We now consider one of the most versatile of the silicon reagents: trimethylsilyl cyanide (TMS-CN). Its reactivity effectively illustrates one of the fundamentals of silicon chemistry. Specifically, the trimethylsilyl group often reacts as if it were a proton. One might therefore expect TMS-CN to approximate the reactions and toxicity of hydrogen cyanide.

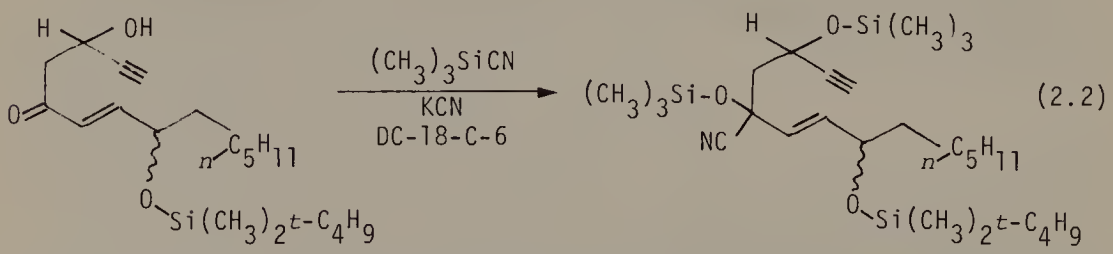
2.2 Addition of Trimethylsilyl Cyanide to Polar Multiple Bonds

TMS-CN reacts with ketones or aldehydes to yield trimethylsilyl ethers of the corresponding cyanohydrins [1–8]. Even sterically congested systems such as camphor and diaryl ketones, which fail to form cyanohydrins under normal conditions, react readily with TMS-CN [4].



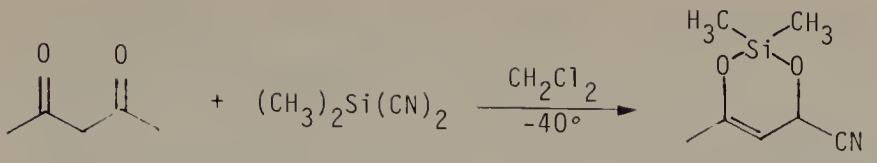
(2.1)

A problem with the reagent is that it will also react with acidic hydrogens such as OH [9], SH, and NH [10] to yield the trimethylsilyl derivative and HCN. This dual reactivity of TMS-CN was used to advantage in a prostaglandin synthesis in which a ketone was converted to a trimethylsilyloxy nitrile group with simultaneous protection of an alcohol as its trimethylsilyl ether [9].



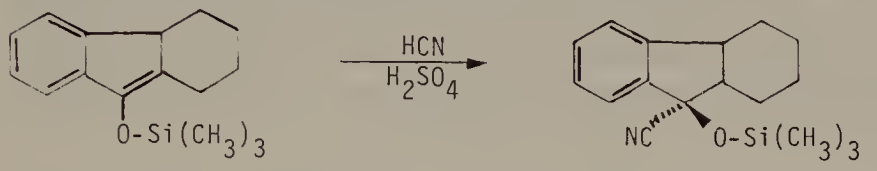
(2.2)

As might be predicted, dimethyldicyanosilane reacts exothermically with enolizable β-diketones to yield six-membered heterocycles [11].



(2.3)

Trimethylsilyloxy nitriles have previously been prepared by the sulfuric acid catalyzed addition of HCN to trimethylsilyl enol ethers [12, 13] or by reaction of TMS-Cl with a cyanohydrin in the presence of tertiary amines [14]. These earlier methods suffered from experimental difficulties and limitations. The two most important advantages of the TMS-CN reaction with ketones or aldehydes are its generality, and high yields [4, 7].

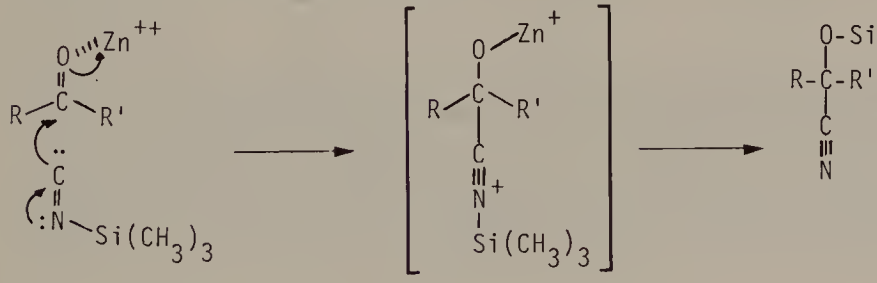


(2.4)

The increased reactivity of TMS-CN toward carbonyl groups compared to HCN has been attributed to the greater heat of reaction [4]. This results primarily from the fact that the Si–C (76 kcal/mole) or Si–N bond (76 kcal/mole) [15] of TMS-CN is weaker than the H–C bond of HCN (111 kcal/mole) [16], rather than from differences in strength of the Si–O (106 kcal/mole) [15], and H–O (110 kcal/mole) [16] bonds. Si–C and Si–N bond strengths must both be considered since TMS-CN is known to exist as an equilibrium mixture of cyanide and isocyanide forms [17–19]. Cyanosilylation may be initiated by alpha [3] addition of the isocyano form to the carbonyl group [4].

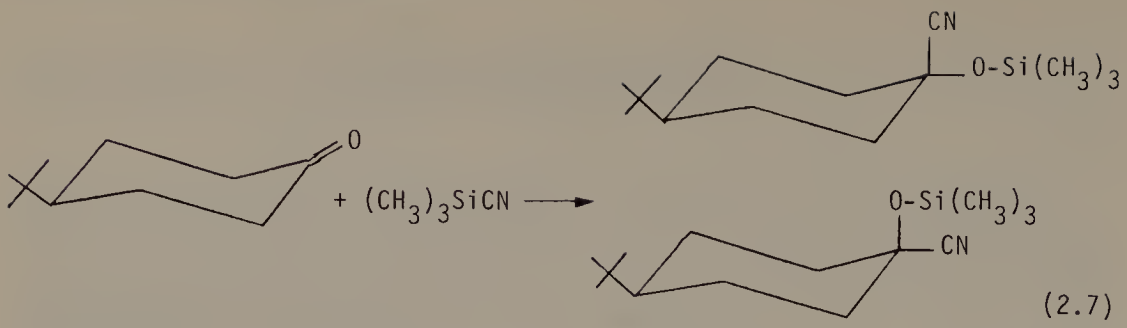
(2.5)

Both electrophilic (zinc iodide) [4, 5, 7] and nucleophilic catalysis by cyanide anion effectively promote the reaction between TMS-CN and ketones or aldehydes [1, 3, 9]. Zinc iodide catalysis presumably involves coordination of the zinc cation with the carbonyl oxygen. The resulting increase in electrophilic character at the carbonyl carbon facilitates nucleophilic attack by the isonitrile form of TMS-CN. This may be followed by transfer of the trimethylsilyl group to oxygen.



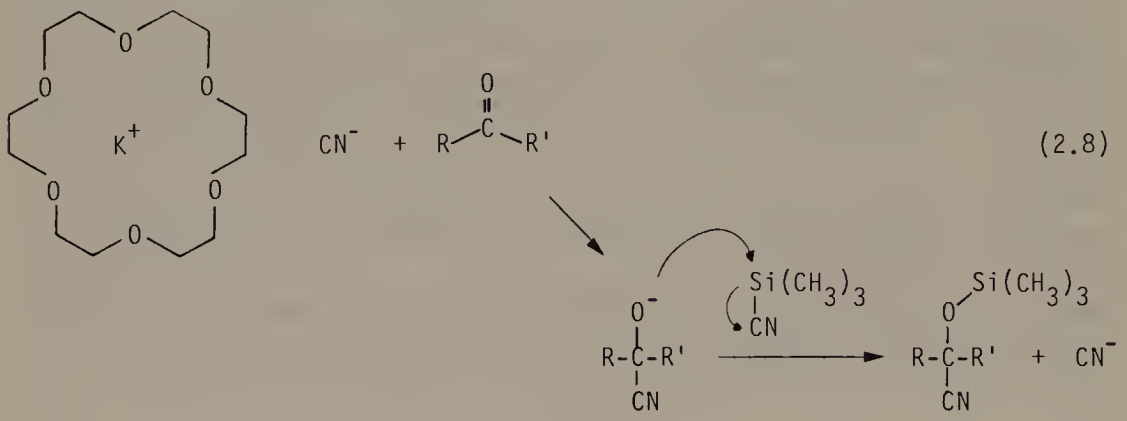
(2.6)

Zinc iodide catalyzed addition of TMS-CN to 4-*t*-butyl cyclohexanone yields a 9:1 ratio of stereoisomers in which the axial cyano group predominates. This results from kinetic rather than thermodynamic control [4].



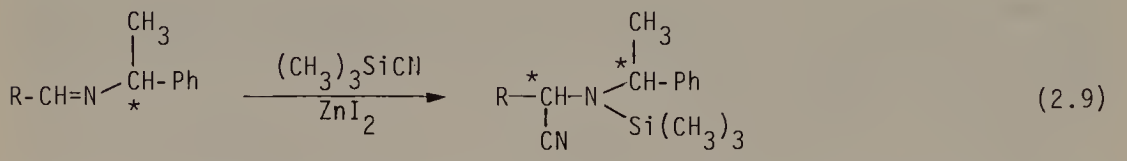
(2.7)

Nucleophilic catalysis requires an organic soluble form of cyanide ion. Both potassium cyanide/18-C-6 complex [1] and tetrabutylammonium cyanide are effective [1]. Cyanide catalysis is thought to occur by addition of cyanide to the carbonyl group. The resulting alkoxide ion reacts at silicon to yield the trimethylsilyloxy nitrile and regenerate cyanide ion. Consistent with this mechanism, azide ion is also an effective catalyst [1].



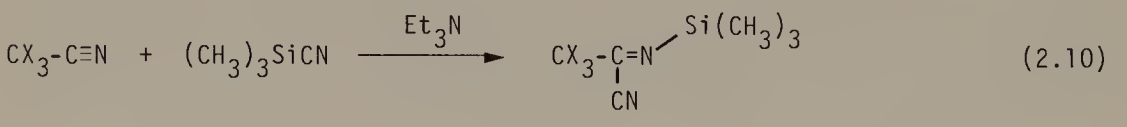
(2.8)

TMS-CN also undergoes Lewis acid catalyzed addition to the C−N double bond of imines. α-Amino nitriles are obtained after hydrolysis. Ojima has shown that if the imine is formed from a chiral amine, such as α-phenethyl amine, asymmetric induction in the addition of TMS-CN occurs 22–58% e.e. [20, 21].



(2.9)

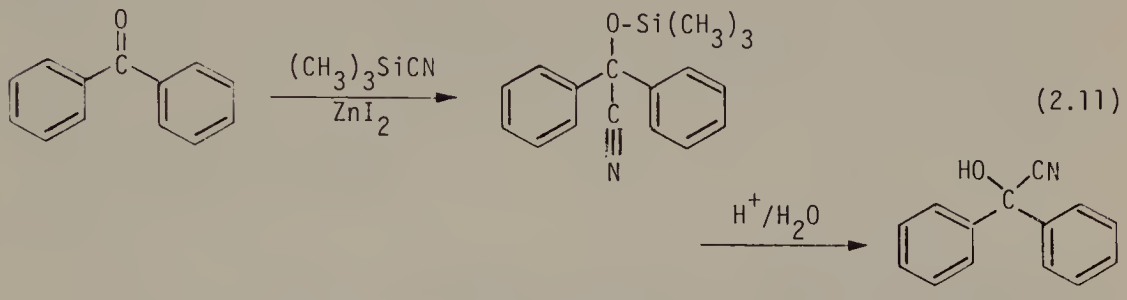
In the presence of triethylamine, TMS-CN will also add to the C−N triple bond of electron deficient nitriles to yield N-trimethylsilyl-α-cyano imines [22].



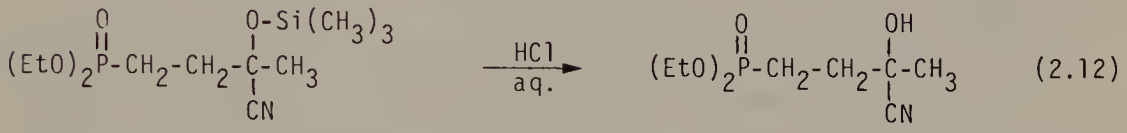
(2.10)

2.3 Utility of Trimethylsilyl Ethers of Cyanohydrins

Cyanohydrin trimethylsilyl ethers are extremely versatile intermediates. Cyanohydrins of ketones which are inaccessible by usual synthetic methods can be formed by use of TMS-CN. Acidic hydrolysis (3 N HCl) of trimethylsilyl ethers of cyanohydrins affords the corresponding cyanohydrin in excellent yields [23–25, 75, 76].

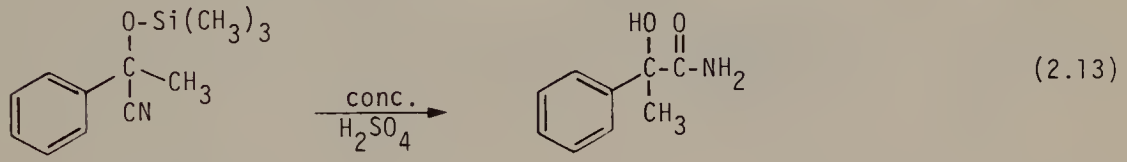


(2.11)



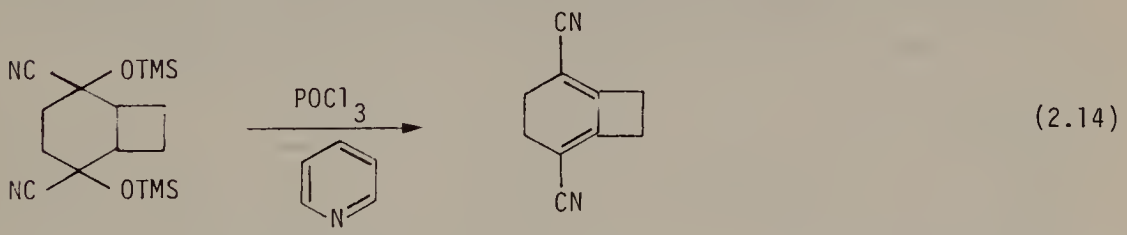
(2.12)

Hydrolysis with conc. sulfuric acid, on the other hand, gives the corresponding α-hydroxy amides [6].



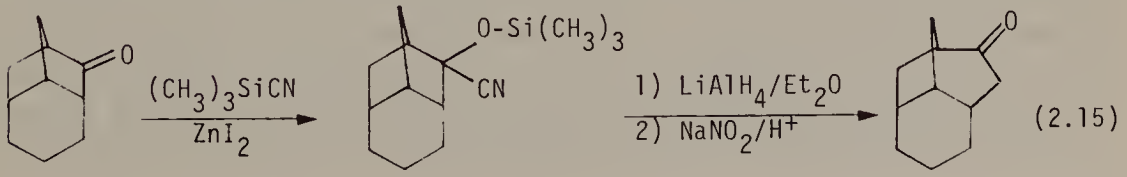
(2.13)

Dehydration of cyanohydrins is a practical way to transform ketones into α,β-unsaturated nitriles. Likewise, the trimethylsilyl ethers of ketone cyanohydrins may be converted into α,β-unsaturated nitriles by treatment with phosphorous oxychloride and pyridine [26].



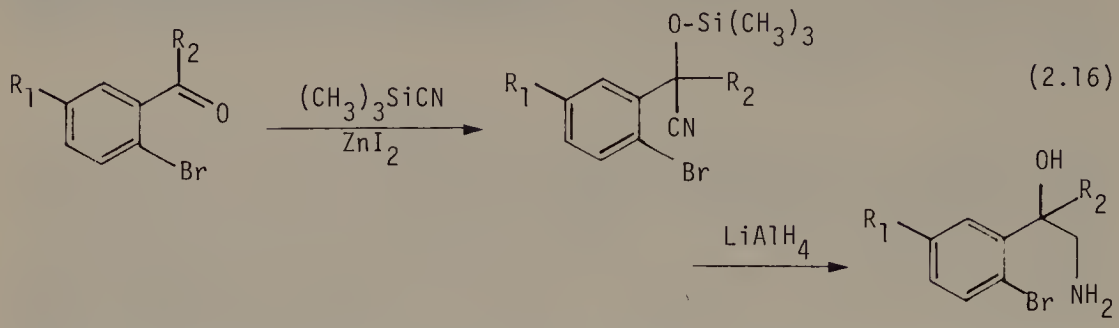
(2.14)

The trimethylsilyl ethers of cyanohydrins can be reduced with $LiAlH_4$ to yield β-aminomethyl alcohols [4, 27, 28]. These can be used in the Tiffeneau-Demjanov reaction [29]. For example, 2,4-*bis*-homobrendan-2-one was prepared from 4-homobrendan-2-one as outlined below (Eq. 2.15) [30].



(2.15)

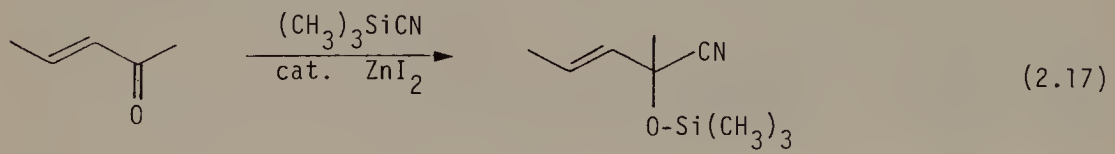
In a similar manner, 7,8,9,10-tetrahydro-6-(5 H)-benzocyclooctenone was prepared from benzosuberone [31]. This methodology was also utilized in the preparation of 8,9:13,14-diseco-18-norestradiol [32]. 2-Amino-1-*o*-bromophenylethanols, which can be converted to indoles, have been prepared from *o*-bromo-acetophenones (Eq. 2.16) [5].



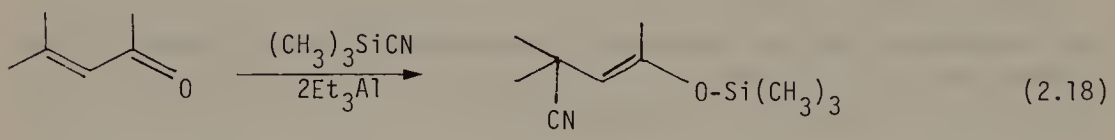
(2.16)

β-Aminomethyl alcohols have been previously prepared by reduction of cyanohydrins or β-hydroxy nitroalkanes [33].

In the presence of a catalytic amount of Lewis acid, TMS-CN adds regiospecifically in a 1,2 sense to α,β-unsaturated ketones or aldehydes (Eq. 2.17) [4, 34, 35]. Hydrogen cyanide, nitromethane anion and TMS-CN with two equivalents of triethylaluminium [Eq. 2.18] give Michael addition products on reaction with α,β-unsaturated ketones or aldehydes [36].

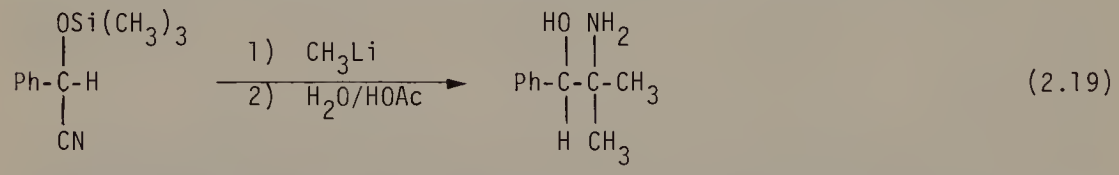


(2.17)



(2.18)

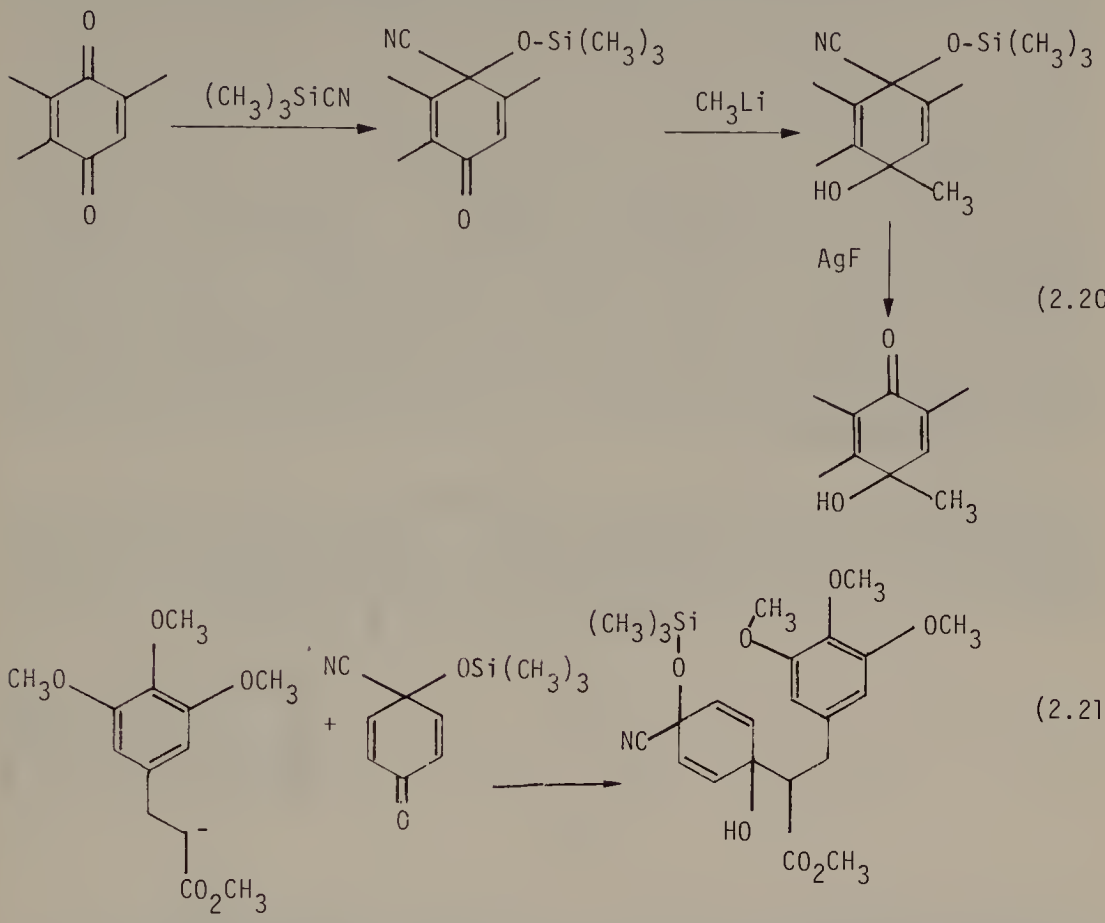
Organolithium reagents add twice to the cyano group of trimethylsilyl ethers of cyanohydrins to yield substituted β-amino alcohols [37].



(2.19)

Trimethylsilyl ethers of cyanohydrins can also be used to protect carbonyl groups. For example, TMS-CN adds in a 1,2-sense to the more electrophilic carbonyl group of both benzo- [3, 39] and naphthoquinones [38]. Selective protection of one of the two quinone carbonyl groups is thus achieved. Organometallic reagents such as Grignards, lithium alkyls [38] (Eq. 2.20) and lithium enolates [39, 40] (Eq. 2.21) add in a regiospecific 1,2-manner to the unprotected carbonyl group of the mono-cyanosilylated benzoquinone. Removal of the trimethylsilyloxy nitrile protecting group by treatment with silver

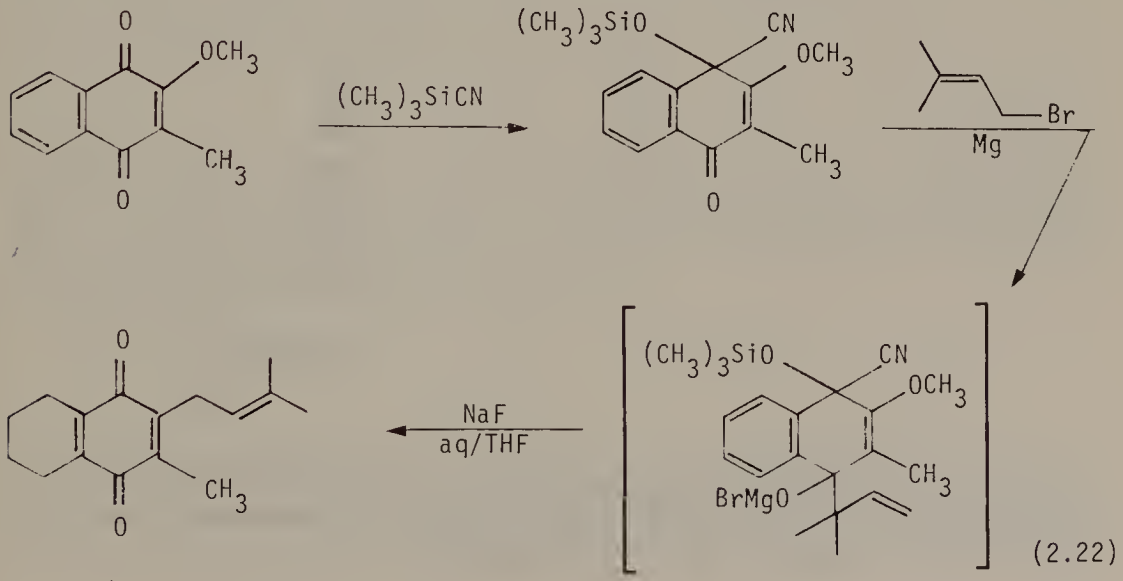
fluoride [38] or aq. sodium fluoride [39] yields *p*-quinols. The driving force for this reaction is the strength of the Si–F bond [15].



(2.20)

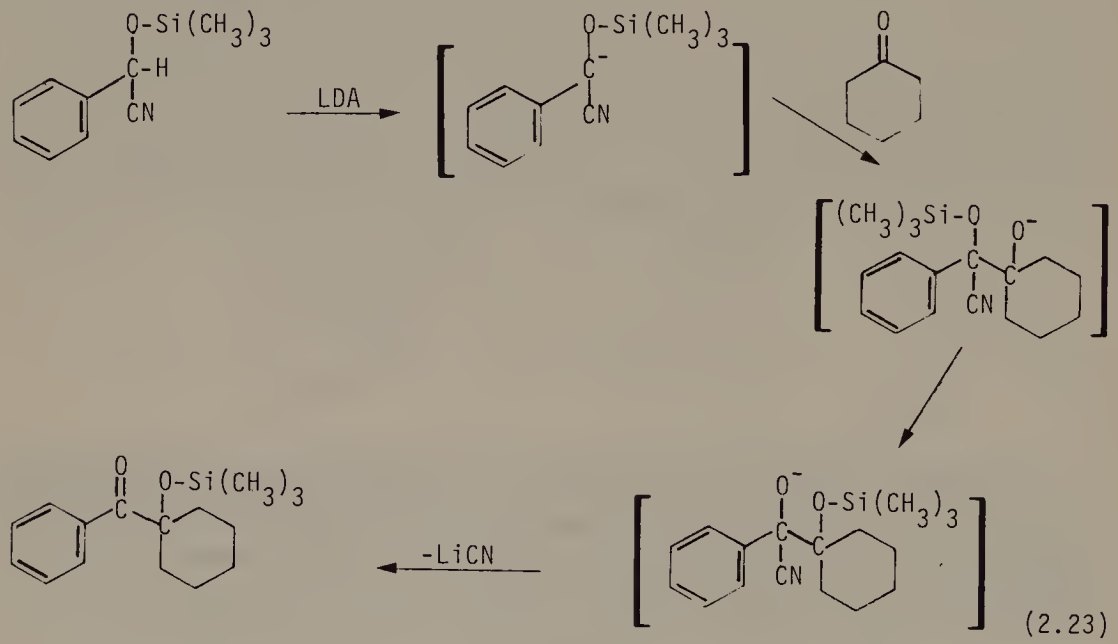
(2.21)

1,2-Addition of allylic Grignard reagents to the unprotected carbonyl group of mono-cyanosilylated benzo- or naphthoquinones yields masked quinols. These then undergo a [3 + 3]-sigmatropic (Cope) rearrangement concurrent with removal of the trimethylsilyloxy protecting group [41, 42].

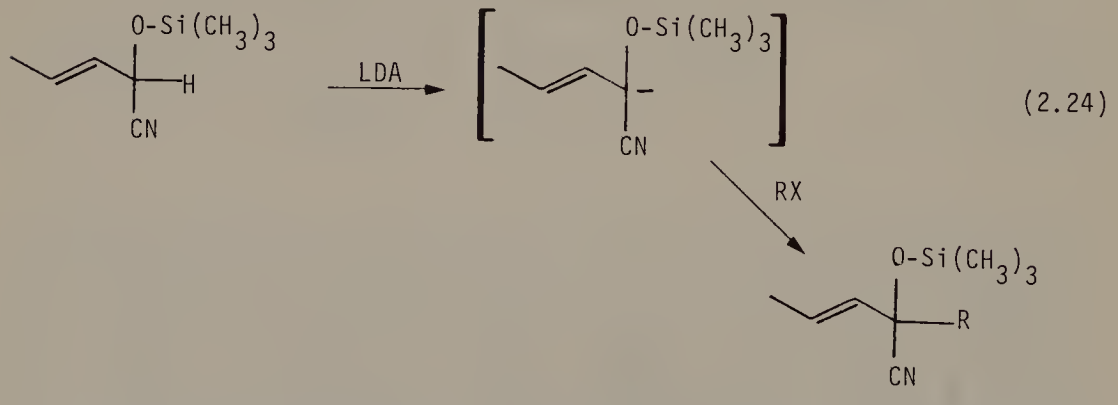


(2.22)

Trimethylsilyl ether derivatives of aldehyde cyanohydrins are particularly useful intermediates due to the acidity of the former aldehydic proton. This proton can be removed by sterically hindered, non-nucleophilic bases such as LDA. The cyano-stabilized carbanion thus formed is an acyl anion equivalent which can be alkylated to yield ketones [34, 35, 43, 44]. It reacts with ketones or aldehydes to afford trimethylsilyl ether derivatives of α-hydroxy ketones via rearrangement of the trimethylsilyl group and loss of lithium cyanide [45, 46] (Eq. 2.23). α-Cyano-α-trimethylsilyloxy allylic anions, formed by deprotonation of the trimethylsilyl ethers of α,β-unsaturated aldehyde cyanohydrins, react with alkyl halides regiospecifically at the α-position to yield trimethylsilyl ethers of α,β-unsaturated ketone cyanohydrins [47] (Eq. 2.24). A particular advantage of these acyl anion equivalents compared to 1,3-dithianes is the ease with which the trimethylsilyloxy nitrile protecting group may be removed.

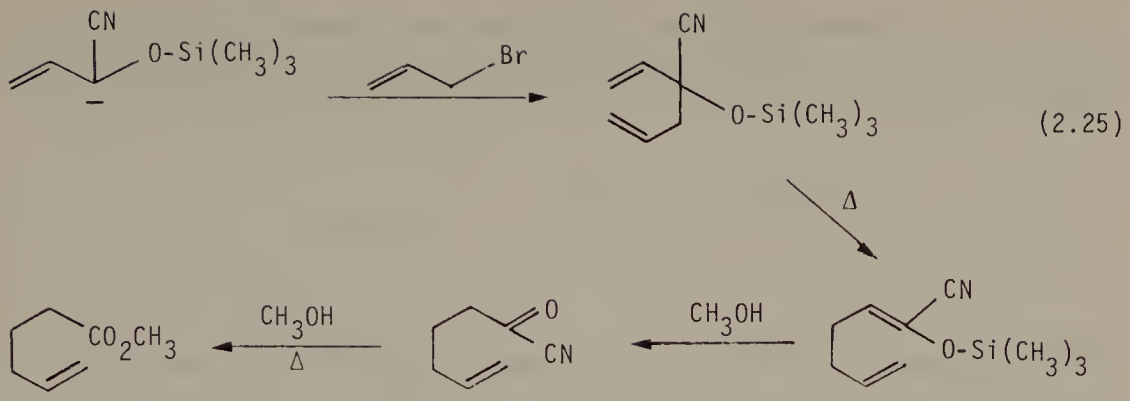


(2.23)



(2.24)

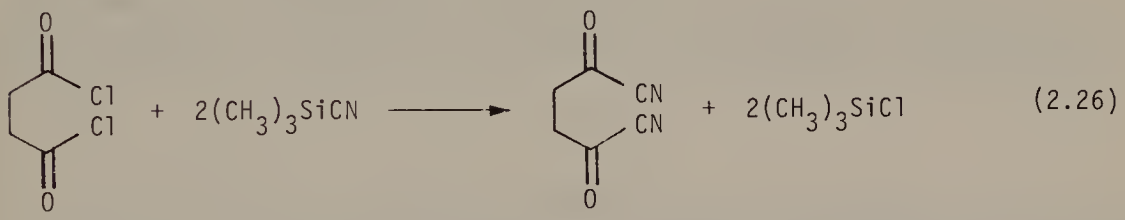
3-Cyano-3-trimethylsilyloxy-1,5-hexadienes undergo Claisen rearrangement on pyrolysis to yield 1-cyano-1-trimethylsilyloxy-1,5-hexadienes. These react with methanol to yield methyl hex-5-enoates [48].



(2.25)

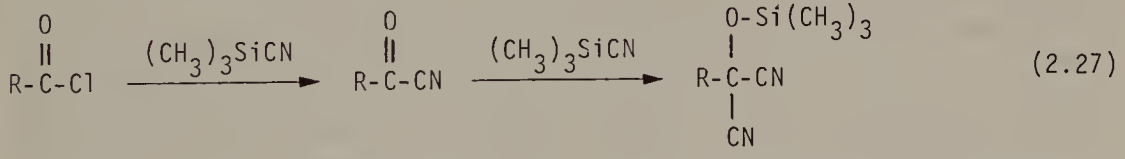
2.4 Acyl Substitution Reactions of Trimethylsilyl Cyanide

Acyl nitriles can be prepared by reaction of TMS-CN with acid chlorides [49, 50]. These reactions may occur by addition of TMS-CN to the carbonyl group of acid chlorides to form unstable adducts which lose TMS-Cl. This results in acyl substitution rather than addition.



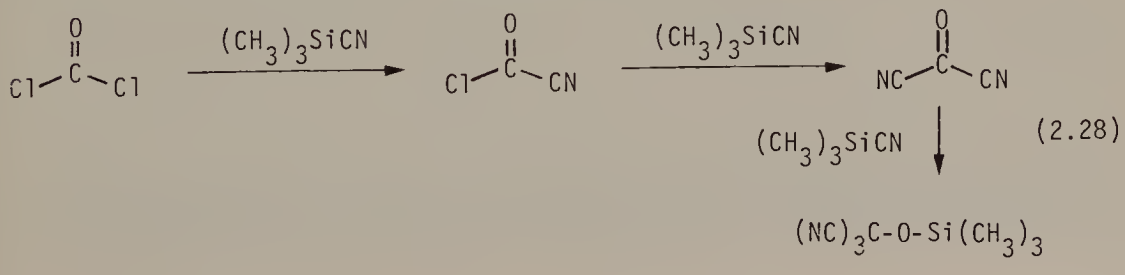
(2.26)

In the presence of pyridine, addition of a second molecule of TMS-CN to the carbonyl group of the acyl nitrile occurs to yield 1,1-dicyano-1-trimethylsilyl-oxyalkanes [50].



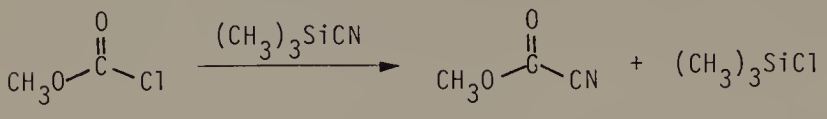
(2.27)

A similar sequence of reactions of TMS-CN with phosgene, oxalyl chloride and trifluoroacetylchloride yields respectively tricyanotrimethylsilyloxy-methane, 1,1,2,2-tetracyano-1,2-*bis*-(trimethylsilyloxy)ethane and 2,2-dicyano-1,1,1-trifluoro-2-trimethylsilyloxyethane [2].



(2.28)

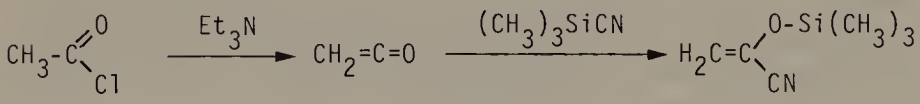
In the case of carbonyl fluoride the initial product is stable [2]. TMS-CN also reacts with methyl and ethyl chloroformate to yield the corresponding alkyl cyanoformates [50, 51].



(2.29)

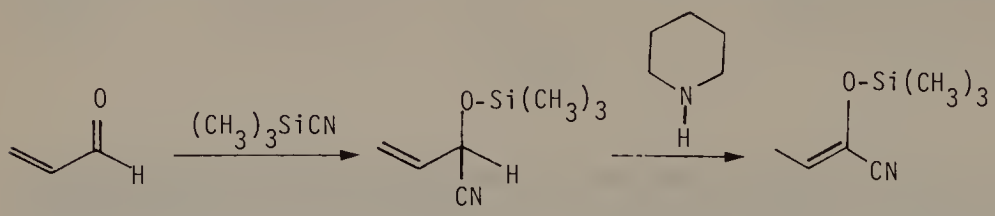
2.5 Reactions of Trimethylsilyl Cyanide with Polar Cumulenes

TMS-CN reacts with the carbonyl group of ketenes to yield 1-cyano-1-trimethylsilyloxy-1-alkenes. Ketenes can be generated *in-situ* in the presence of TMS-CN by dehydrohalogenation of the corresponding acid halides by triethylamine [52].



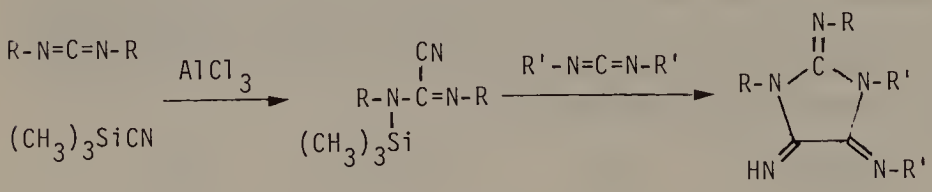
(2.30)

Alternatively, 1-cyano-1-trimethylsilyloxy-1-alkenes can be prepared by base catalyzed isomerization of 1-cyano-1-trimethylsilyloxy-2-alkenes with amines [53].



(2.31)

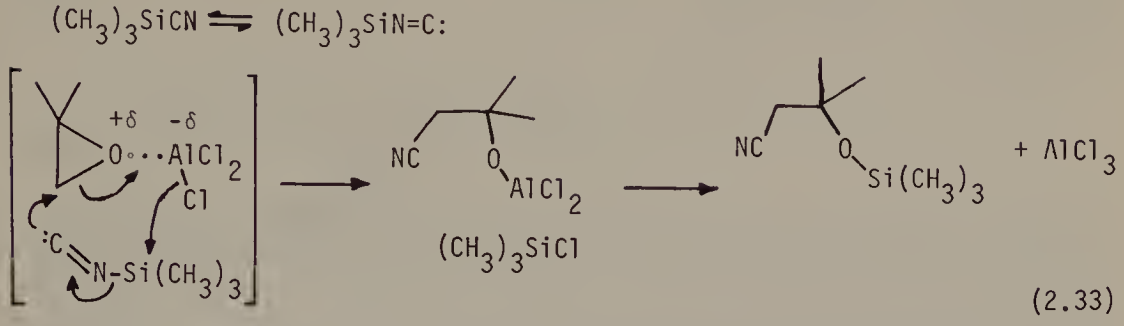
The reaction of TMS-CN with isocyanates [54, 55], isothiocyanates and carbodiimides [56, 57] results in formation of five-membered heterocycles by reaction of one equivalent of TMS-CN with two equivalents of the reactive cumulene. In the case of reactions of TMS-CN with carbodiimides, intermediates formed by addition of TMS-CN across one of the C–N double bonds of the carbodiimides can be isolated. These species will react further with a second equivalent of carbodiimide to yield the five-membered heterocycles.



(2.32)

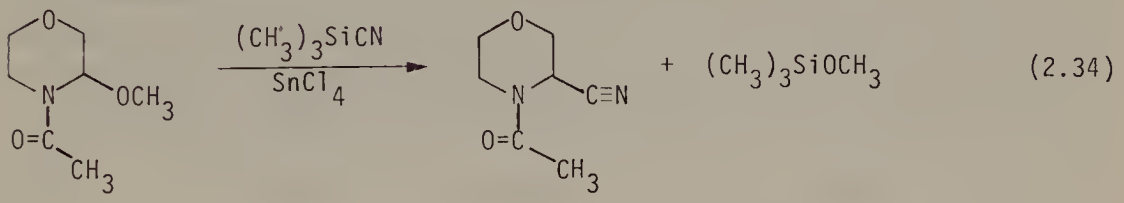
2.6 Substitution Reactions of Trimethylsilyl Cyanide

TMS-CN reacts with epoxides under $AlCl_3$ catalysis to yield 3-trimethylsilyloxy propionitriles [50, 78].



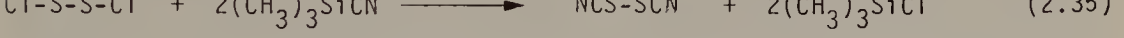
(2.33)

TMS-CN reacts with α-methoxyamides to yield α-cyanoamides and methoxytrimethylsilane. The reaction is catalyzed by Lewis acids, such as $SnCl_4$ or $BF_3 \cdot OEt_2$ [58].



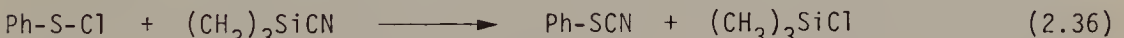
(2.34)

TMS-CN and compounds which possess S–Cl single bonds undergo chloride-cyanide exchange. This leads to TMS-Cl and thiocyanates, which are uncontaminated by isomeric isothiocyanates [2, 50].



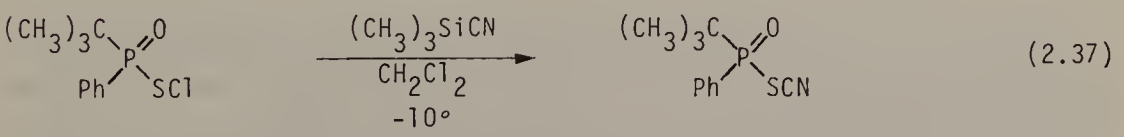
(2.35)

This exchange reaction is useful for the preparation of aryl thiocyanates [61].



(2.36)

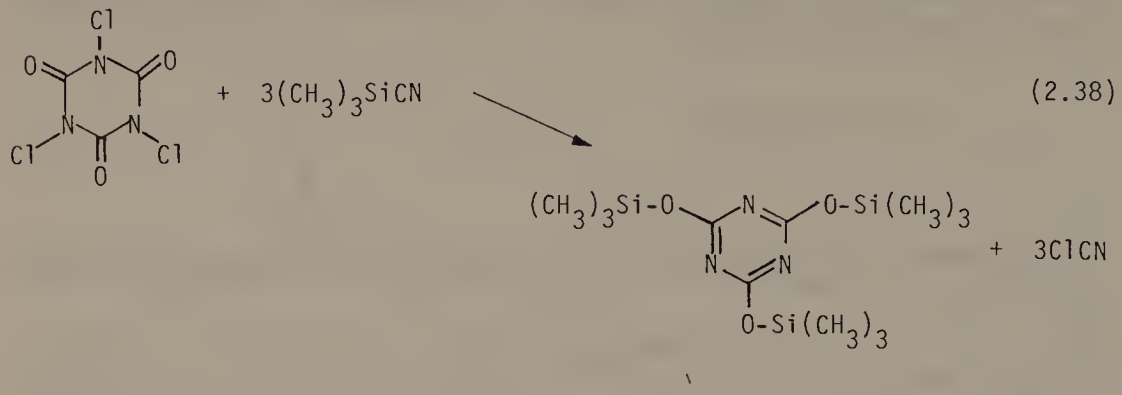
Several phosphorothiocyanatidates and phosphinothiocyanatidates have been prepared in a similar fashion. Such thiocyanatidates rearrange easily to the thermodynamically more stable isothiocyanatidates [59, 60].



(2.37)

TMS-CN also undergoes exchange with the methoxy group of methyl benzene sulfenate to yield phenyl thiocyanate and methoxytrimethylsilane [62].

Chloride cyanide exchange also occurs between N-trichloroisocyanuric acid and TMS-CN to yield *tris*-trimethylsilyl cyanurate and cyanogen chloride [63].



2.7 Synthesis of Trimethylsilyl Cyanide

As the synthetic versatility and potential of TMS-CN has become evident over the last ten years, the methods available for its preparation have dramatically improved. One of the early preparations of TMS-CN involved the reaction of TMS-Cl with silver cyanide [64]. Dimethyldicyanosilane has also been prepared by this procedure [65]. The cost of silver is a problem.

$$(CH_3)_2SiCl_2 + 2AgCN \longrightarrow (CH_3)_2Si(CN)_2 + 2AgCl\downarrow \qquad (2.39)$$

High yields of TMS-CN (88%) result from the reaction of TMS-Cl with thallium (I) cyanide. The toxicity of thallium salts limits the utility of this reaction [66].

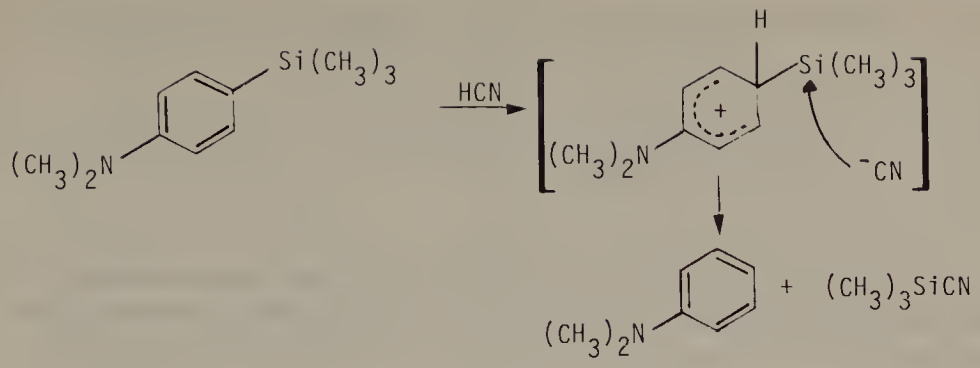
Evans found that lithium cyanide would react with TMS-Cl in ether to yield TMS-CN [4, 77]. However, lithium cyanide is not commercially available and must be prepared by reaction of HCN with lithium hydride or *n*-butyl lithium or by reaction of lithium hydride with acetone cyanohydrin [77].

Durst's report that TMS-CN could be prepared (40–50%) by reaction of TMS-Cl with potassium cyanide in acetonitrile catalyzed by 18-C-6 is an example of solid/liquid PTC and the first really economical synthesis of this reagent [67].

$$(CH_3)_3SiCl \xrightarrow[\substack{18\text{-C-6}\\ CH_3CN}]{KCN} (CH_3)_3SiCN \qquad (2.40)$$

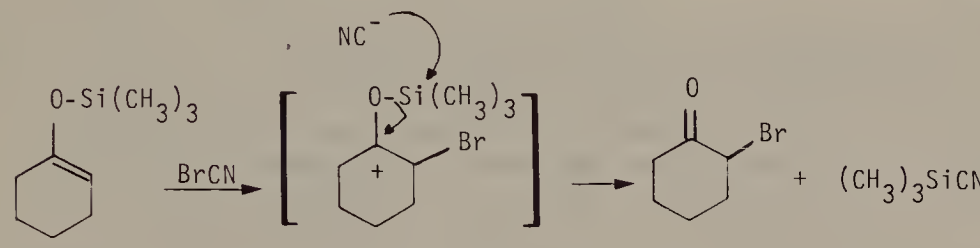
For those who do not mind working with quantities of HCN, the report of Uznanski that TMS-Cl and HCN will react to yield TMS-CN (70%) in the presence of triethylamine and ether may be a useful synthetic method [68].

Anhydrous HCN will also react with *p*-dimethylamino phenyltrimethylsilane via a protodesilylation reaction to yield TMS-CN (89%) and N,N-dimethyl-aniline [69].



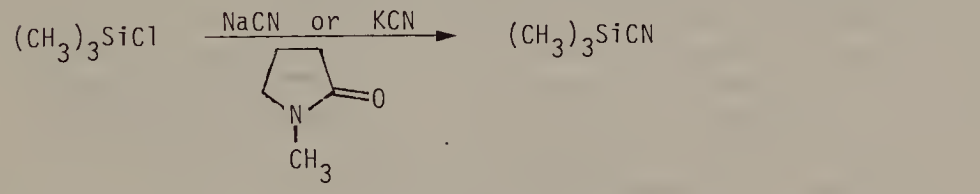
(2.41)

Cyanogen bromide reacts with trimethylsilyl enol ethers to yield the corresponding α-bromo ketone and TMS-CN [70]. The reaction involves addition of a bromonium ion to the C−C double bond of the trimethylsilyl enol ether to yield a carbocation stabilized by both the lone pairs of electrons of the adjacent oxygen and by hyperconjugation of the trimethylsilyl group. Attack by cyanide on the silyl center of this carbocation leads to fragmentation and formation of products.



(2.42)

The simultaneous reports of Hünig [71] and Rasmussen [72] that TMS-Cl will react with sodium or potassium cyanide in dry N-methylpyrrolidone to give a 70% yield of TMS-CN constitutes an excellent procedure. The reaction with sodium cyanide requires catalysis by a small amount of quarternary alkyl ammonium salt (Adogen 1%) while that with potassium cyanide does not.

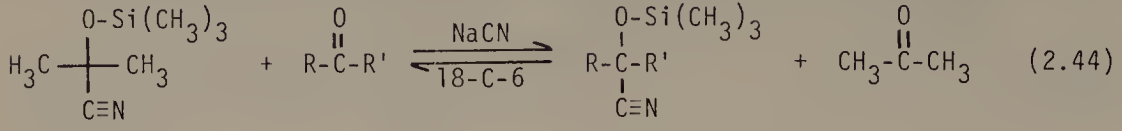


(2.43)

bis-Trimethylsilyl sulfate also reacts with potassium cyanide in dry N-methylpyrrolidone to yield TMS-CN in 96% yield [73].

Finally, both Evans and Rasmussen have developed methods to cyanosilylate ketones and aldehydes which do not involve independent preparation of TMS-CN. *trans*-Cyanosilylation of α-trimethylsilyloxy isobutyronitrile [1] with a less volatile ketone or aldehyde catalyzed by KCN/18-C-6, yields a new trimethylsilyloxy nitrile and acetone. Removal of acetone from the reaction

by distillation shifts the equilibrium to yield the desired trimethylsilyloxy nitrile.



(2.44)

Aromatic aldehydes react directly with TMS-Cl and potassium cyanide in acetonitrile or DMF to yield the corresponding trimethylsilyloxy nitriles. In the case of ketones, the formation of trimethylsilyl enol ethers is a significant side reaction [74].

Less than ten years ago TMS-CN was known only as an inorganic pseudo-halide of unusual structure (cyanide or isocyanide). In the intervening years this compound has rapidly found a valuable place in synthetic organic chemistry. Further utility of this reagent is probably only limited by our imagination and creativity.

References

1. Evans, D.A., Truesdale, L.K.: Tetrahedron Lett. 4929 (1973)
2. Lidy, W., Sundermeyer, W.: Chem. Ber. *106*, 587 (1973)
3. Evans, D.A., Truesdale, L.K., Carroll, G.L.: J. C. S. Chem. Commun. 55 (1973)
4. Evans, D.A., Carroll, G.L., Truesdale, L.K.: J. Org. Chem. *39*, 914 (1974)
5. Fleming, I., Woolias, M.: J. Chem. Soc. Perkin *I*, 829 (1979)
6. Grunewald, G.L., Brouillette, W.J., Finney, J.A.: Tetrahedron Lett. 1219 (1980)
7. Corey, E.J., Tius, M.A., Das, J.: J. Am. Chem. Soc. *102*, 1742 (1980)
8. Demina, M.M., Medvedeva, A.S., Protsuk, N.I., Vyazankin, N.S.: Zhur. Obsh. Khim. *48*, 1563 (1978)
9. Stork, G., Kraus, G.: J. Am. Chem. Soc. *98*, 6747 (1976)
10. Voronkov, M.G., Keiko, N.A., Kuznetsova, T.A., Tsetlina, E.O.: Zhur. Obsh. Khim. *48*, 2138 (1978)
11. Ryu, I., Murai, S., Shinonaga, A., Horiike, T., Sonoda, N.: J. Org. Chem., *43*, 780 (1978)
12. Parham, W.E., Roosevelt, C.S.: Tetrahedron Lett. 923 (1971)
13. Parham, W.E., Roosevelt, C.S.: J. Org. Chem. *37*, 1975 (1972)
14. Frisch, K.C., Wolf, M.: J. Org. Chem. *18*, 657 (1953)
15. Ebsworth, E.A.V., in "Organometallic Chemistry of the Group IV Elements" Vol. I, part I, (MacDiarmid, A.G., Ed.) p. 46. New York: Marcel Dekker, 1968
16. Cottrell, T.L., "The Strength of Chemical Bonds", London: Butterworths 1958
17. Booth, M.R., Frankiss, S.G.: Spectrochim. Acta. Part A, *26*, 859 (1970)
18. Seckar, J.A., Thayer, J.S.: Inorganic Chem. *15*, 501 (1976)
19. Seyferth, D., Kahlen, N.: J. Am. Chem. Soc. *82*, 1080 (1960)
20. Ojima, I., Inaba, S.I., Nagai, Y.: Chem. Lett 737 (1975)
21. Ojima, I., Inaba, S.I., Nakatsugawa, K., Nagai, Y.: Chem. Lett. 331 (1975)
22. Lazukina, L.A., Kukhar, V.P.: Synthesis, 747 (1979)
23. Gassman, P.G., Talley, J.J.: Tetrahedron Lett., 3773 (1978)
24. Boutte, D., Auronx, A., Demande, Fr.: 2, 321, 484 Chem. Abst. *88*, P37454i
25. Gassman, P.G., Talley, J.J.: J. Am. Chem. Soc. *102*, 4138 (1980)
26. Oda, M., Yamamuro, A., Watabe, T.: Chem. Lett. 1427 (1979)
27. Takadate, A., Fishman, J.: J. Org. Chem. *44*, 67 (1979)

28. Bartholow, R.M., Walaszek, E.J.: J. Med. Chem. *19*, 189 (1976)
29. Smith, P.A.S., Baer, D.R.: Org. React. *11*, 157 (1960)
30. Takaishi, N., Fujikura, Y., Inamoto, Y., Aigami, K.: J. Org. Chem. *42*, 1737 (1977)
31. Thies, R.W., Seitz, E.P.: J. Org. Chem. *43*, 1050 (1978)
32. Thies, R.W., Yue, S.: J.C.S. Chem. Commun. 950 (1980)
33. Dauben, Jr., H.J., Ringold, H.J., Wade, R.H., Anderson, A.G. Jr.: J. Am. Chem. Soc. *73*, 2359 (1951)
34. Deuchert, K., Hertenstein, U., Hünig, S.: Synthesis, 777 (1973)
35. Hertenstein, U., Hünig, S., Öller, M.: Synthesis, 416 (1976)
36. Utimoto, K., Obayashi, N., Shishiyama, Y., Inoue, M., Nozaki, H.: Tetrahedron Lett. 3389 (1980)
37. Amouroux, R., Axiotis, G.P.: Synthesis, 270 (1981)
38. Evans, D.A., Hoffman, J.M., Truesdale, L.K.: J. Am. Chem. Soc. *95*, 5822 (1973)
39. Evans, D.A., Wong, R.Y.: J. Org. Chem. *42*, 350 (1977)
40. Evans, D.A., Cain, P.A., Wong, R.Y.: J. Am. Chem. Soc. *99*, 7083 (1977)
41. Evans, D.A., Hoffman, J.M.: J. Am. Chem. Soc. *98*, 1983 (1976)
42. Hegedus, L.S., Evans, B.R.: J. Am. Chem. Soc. *100*, 3461 (1978)
43. Hünig, S., Wehner, G.: Synthesis, 180 (1975)
44. Deuchert, K., Hertenstein, U., Hünig, S., Wehner, G.: Chem. Ber. *112*, 2045 (1979)
45. Hünig, S., Wehner, G.: Synthesis, 391 (1975)
46. Hünig, S., Öller, M.: Chem. Ber. *114*, 959 (1981)
47. Hertenstein, U., Hünig, S., Öller, M.: Chem. Ber. *113*, 3783 (1980)
48. Ziegler, F.E., Nelson, R.V., Wong, T.F.: Tetrahedron Lett. 2125 (1980)
49. Heermann, K., Simchen, G.: Synthesis, 204 (1979)
50. Lidy, W., Sundermeyer, W.: Tetrahedron Lett. 1449 (1973)
51. Childs, M.E., Weber, W.P.: J. Org. Chem. *41*, 3486 (1970)
52. Hertenstein, U., Hünig, S.: Angew. Chem. Int. Ed. *14*, 179 (1975)
53. Voronkov, M.G., Keiko, N.A., Kuznetsova, T.A., Keiko, V.V., Tsetlina, E.O., Pestunovich, V.A.: Izv. Akad. Nauk. SSSR Ser. Khim. 906 (1978)
54. Ojima, I., Inaba, S.T., Nagai, Y.: J.C.S. Chem. Commun. 826 (1974)
55. Lutz, W., Sundermeyer, W.: Chem. Ber. *112*, 2158 (1979)
56. Ojima, I., Inaba, S.I.: Tetrahedron Lett. 817 (1979)
57. Ojima, I., Inaba, S.I., Nagai, Y.: J. Organometallic Chem. *99*, C5 (1975)
58. Asher, V., Becu, C., Anteunis, M.J.O., Callens, R.: Tetrahedron Lett. 141 (1981)
59. Łopusiński, A., Michalski, J., Stec, W.J.: Angew. Chem. Int. *14*, 108 (1975)
60. Łopusiński, A., Michalski, J., Stec, W.J.: Liebigs Ann. Chem. 924 (1977)
61. Harpp, D.N., Friedlander, B.T., Smith, R.A.: Synthesis, 181 (1979)
62. Harpp, D.N., Friedlander, B.T., Larsen, C., Steliou, K., Stockton, A.: J. Org. Chem. *43*, 3481 (1978)
63. Nachbaur, E., Kosmus, W, Krannich, H.J., Sundermeyer, W.: Monat. für Chem. *109*, 1211 (1978)
64. Evers, K.C., Freitag, W.O., Keith, J.N., Kriner, W.A., MacDiarmid, A.G., Sujishi, S.: J. Am. Chem. Soc. *81*, 4493 (1959)
65. Ryu, I., Murai, S., Horiike, T., Shinonaga, A., Sonoda, N.: Synthesis, 154 (1978)
66. Taylor, E.C., Andrade, J.G., John, K.C., McKillop, A.: J. Org. Chem. *43*, 2280 (1978)
67. Zubrick, J.W., Dunbar, B.I., Durst, H.D.: Tetrahedron Lett., 71 (1975)
68. Uznanski, B., Stec, W.J.: Synthesis, 154 (1978)
69. Häbich, D., Effenberger, F.: Synthesis, 755 (1978)
70. Lazukina, L.A., Kukhar, V.P., Pesotskaya, G.V.: Zhur. Obsh. Khim. *45*, 2100 (1975)

71. Hünig, S., Wehner, G.: Synthesis, 522 (1979)
72. Rasmussen, J.K., Heilmann, S.M.: Synthesis, 523 (1979)
73. Kantehner, W., Haug, E., Mergen, W.W.: Synthesis, 460 (1980)
74. Rasmussen J.K., Heilmann, S.M.: Synthesis, 219 (1978)
75. Gassman, P.G., Saito, K., Talley, J.J.: J. Am. Chem. Soc. *102*, 7613 (1980)
76. Gassman, P.G., Talley, J.J.: Org. Syn. *60*, 14 (1981)
77. Livinghouse, T.: Org. Syn. *60*, 126 (1981)
78. Mullis, J.C., Weber, W.P.: J. Org. Chem. *47*, 2873 (1982).

3 Trimethylsilyl Iodide and Bromide

3.1 Introduction

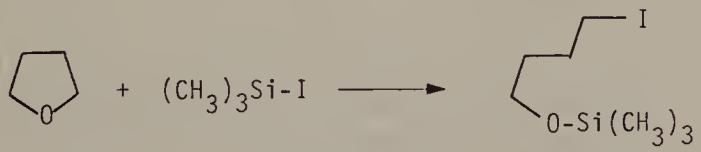
Both trimethylsilyl bromide [1] and iodide [2, 3] have been known since the late 1940's.

$$Ph\text{-}Si(CH_3)_3 \xrightarrow{I_2} Ph\text{-}I + (CH_3)_3Si\text{-}I \qquad (3.1)$$

Nevertheless, it has only been in the last six years that their use as reagents in organic synthesis has been actively explored.

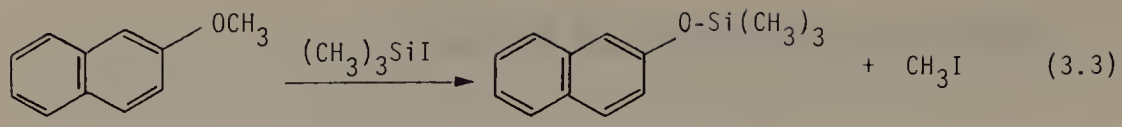
3.2 Cleavage of Ethers

TMS-I's greatest utility is in the removal of ether, ester, and carbamate protecting groups. Key requirements for a protecting group are ease of reaction with the functional group to be protected and mild reaction conditions for removal after its protective function has been fulfilled [4]. The difficulty of cleaving methyl and ethyl ethers has limited their use as protecting groups. The chemistry developed with TMS-I during the last five years has changed this situation. Between 1948 when Whitmore prepared TMS-I and 1976 when Jung and Olah simultaneously began work on its use in organic synthesis, there were at least three reports that TMS-I, would easily cleave ethers [5–7].



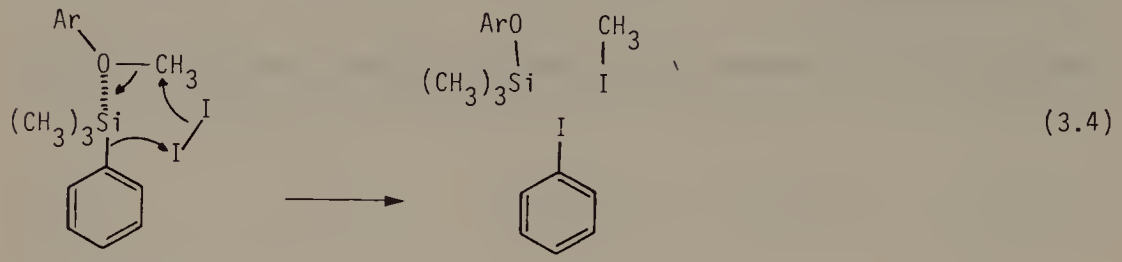
(3.2)

In 1976 this situation changed. Voronkov found that tetrahydropyran reacts with TMS-I to yield 1-iodo-5-trimethylsilyloxypentane [9]. Both Olah and Voronkov reported that TMS-I would cleave aryl methyl ethers under neutral conditions to yield methyl iodide and aryloxytrimethylsilanes [8]. The latter could be easily hydrolyzed to phenols [10, 11].



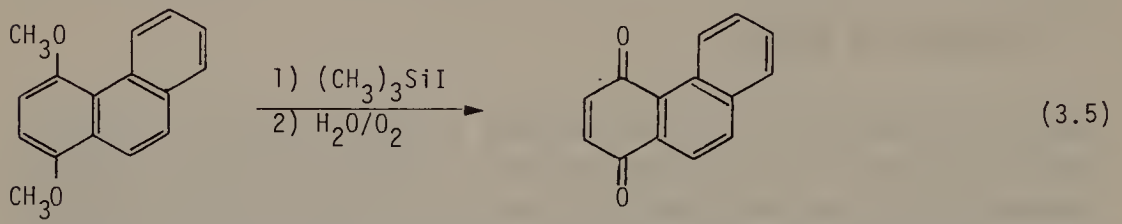
(3.3)

TMS-I, generated *in-situ* by reaction of trimethylphenylsilane with a 10% molar excess of iodine at 110°C, reacts with aryl methyl ethers to give high yields (90%) of cleavage products. In the proposed cyclic six-membered ring transition state the hard acid silicon interacts with the hard oxygen of the ether, while simultaneously, the soft iodine interacts with carbon. Free TMS-I may not be involved [12, 13].



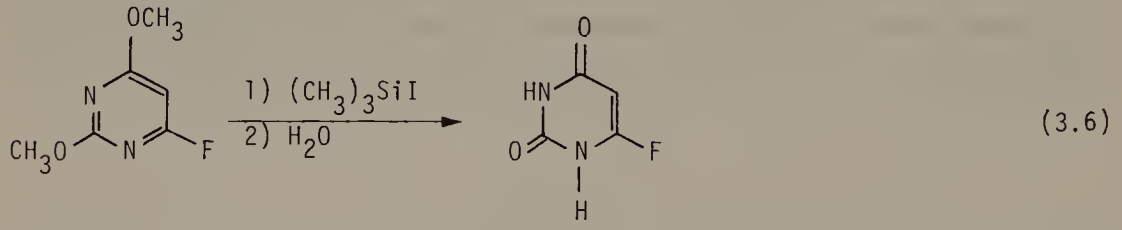
(3.4)

This reactions is general. For example, TMS-I cleaves sterically congested aryl methyl ethers, such as 1,4-dimethoxyphenanthrene, to yield 1,4-dihydroxyphenanthrene which is oxidized during work-up to 1,4-phenanthraquinone [14].



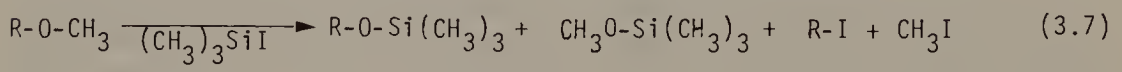
(3.5)

Likewise, treatment of 2,4-dimethoxy-6-substituted pyrimidines with TMS-I followed by work-up yields 6-substituted uracils. Other methods of hydrolysis often result in loss of the 6-substituent in this system [15].



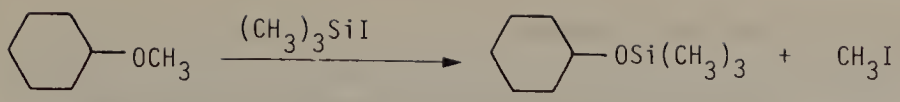
(3.6)

Jung found that TMS-I would cleave trityl, benzyl, and *t*-butyl ethers much faster than methyl, ethyl, isopropyl or cyclohexyl ethers. The cleavage of unsymmetrical dialkyl ethers is often not regioselective.



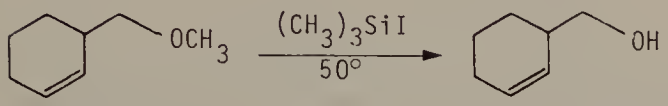
(3.7)

However, methyl cyclohexyl ether reacts with TMS-I to yield predominantly methyl iodide and cyclohexanoxytrimethylsilane.



(3.8)

An alternative mechanism has been proposed to account for this specificity. Transfer of a trimethylsilyl group to the ether oxygen may form a dialkyltrimethylsilyloxonium/iodide ion pair. S_n2 nucleophilic attack by iodide on a methyl carbon would be favored over attack on a cyclohexyl carbon [16]. C–C double and triple bonds, ketone carbonyls, and aryl halides are stable to the reaction conditions [17].

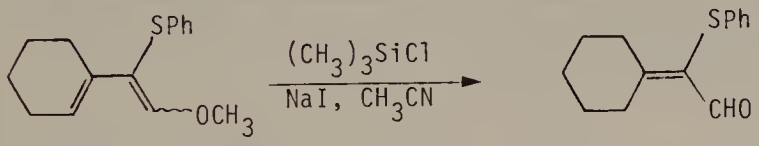


(3.9)

Among the problems associated with TMS-I are its extreme hydrolytic instability and sensitivity to light. Freshly distilled, TMS-I (bp 106°C) is almost water white. It rapidly develops a pink color and further darkens on exposure to light. Its ease of hydrolysis suggests that HI may often be involved in reactions of TMS-I.

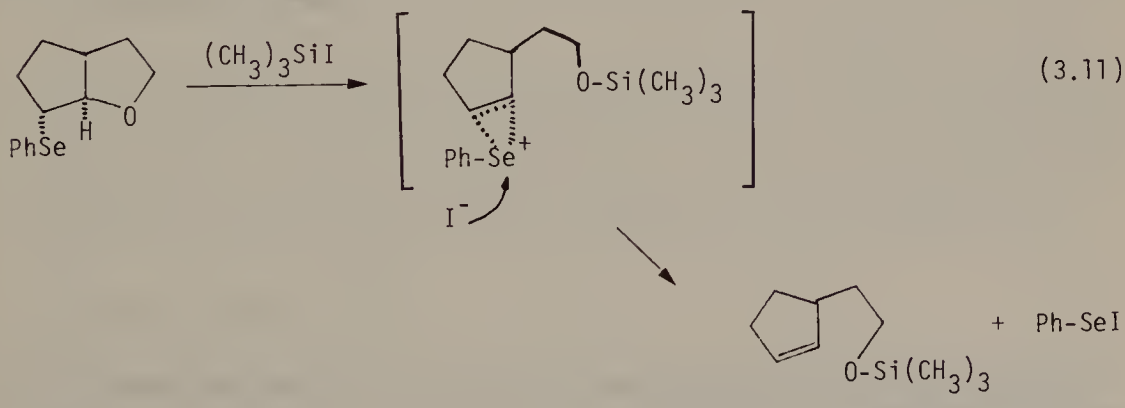
Olah has found that TMS-Cl reacts with sodium iodide in acetonitrile to yield TMS-I. This reagent cleaves ethers at room temperature even more rapidly than TMS-I itself. Apparently, excess iodide acts as a catalyst [18].

TMS-I generated *in-situ* by reaction of TMS-Cl and sodium iodide in acetonitrile [18] cleaves enol and dienol methyl ethers [19]. Aq. work-up provides aldehydes or ketones in quantitative yield. This is noteworthy since such dienol methyl ethers are susceptible to acid catalyzed polymerization.



(3.10)

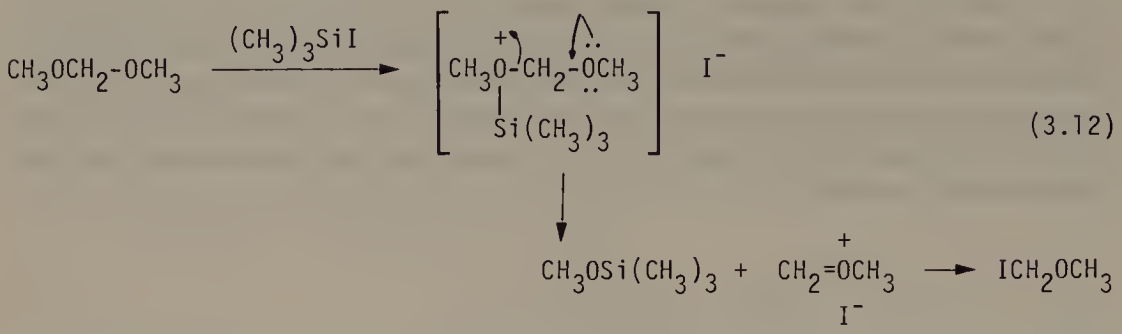
β-Phenylseleno cyclic ethers react with TMS-I, generated as above, to yield ω-hydroxy alkenes [20] as outlined in Eq. 3.11.



(3.11)

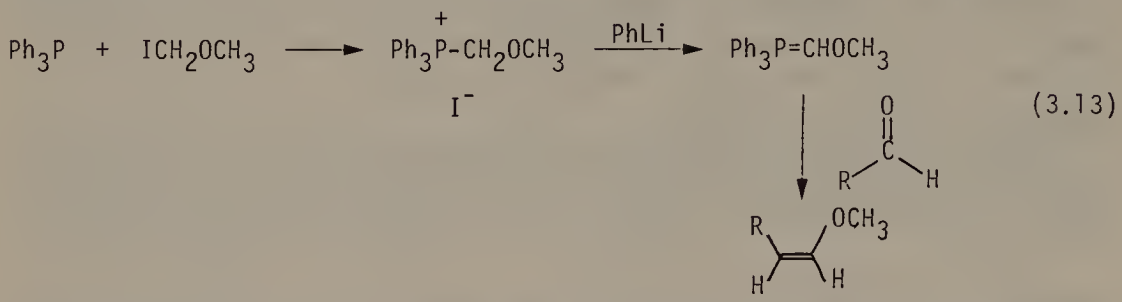
3.3 Cleavage of Acetals and Ketals

TMS-I reacts with dimethoxymethane to yield iodomethyl methyl ether [21].



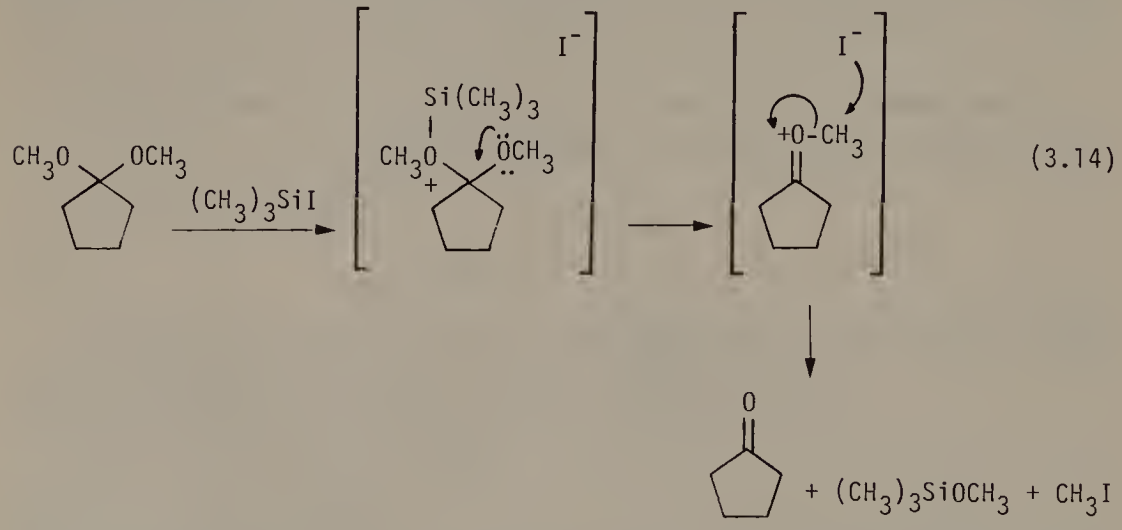
(3.12)

Iodomethyl methyl ether is not only a viable substitute for chloromethyl methyl ether, a restricted carcinogen, but also a valuable synthetic intermediate [22].



(3.13)

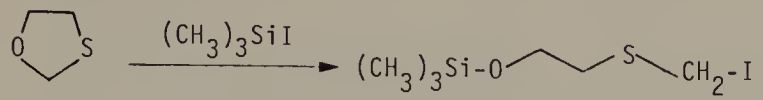
Ketones and aldehydes are frequently protected by conversion to dimethyl or diethyl acetals and ketals. Deprotection and regeneration of the ketone or aldehyde functionality is normally carried out by treatment with aq. acid. Jung has found that both dimethyl and diethyl acetals and ketals can be converted back to aldehydes and ketones under neutral conditions by treatment with TMS-I in chloroform or CCl_4 [23].



(3.14)

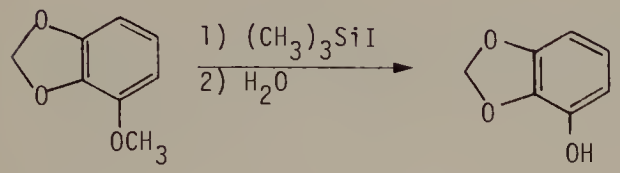
Unfortunately, TMS-I does not react cleanly with the ethylene ketal or the ethylene thioketal of cyclohexanone [23]. On the other hand, TMS-I reacts

with 1,3-dioxolanes and 1,3-oxathiolanes to yield iodomethyl-2-trimethylsilyloxyethyl ether and iodomethyl-2-trimethylsilyloxyethyl sulfide respectively. Both of these are valuable alkylating agents [24, 25].



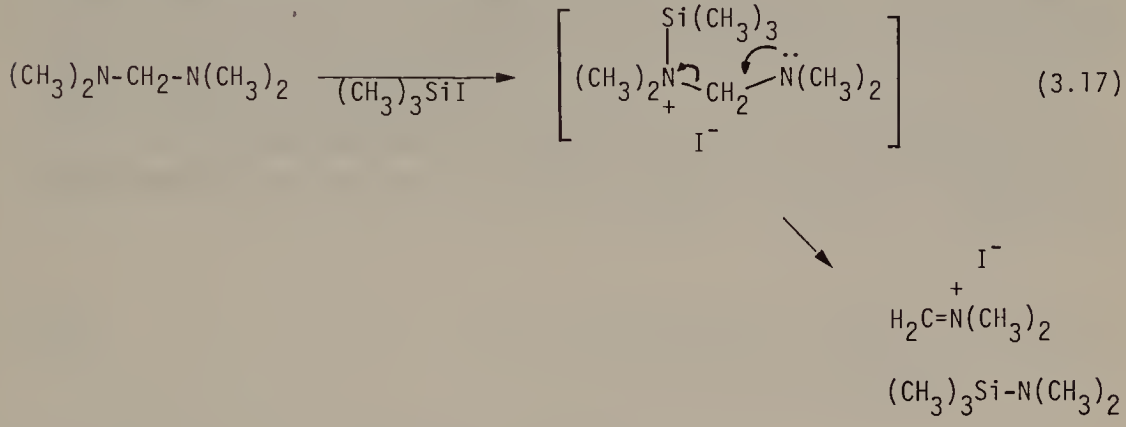
(3.15)

The methyl ether of sesamol methyl ether is selectively cleaved by reaction with TMS-I in quinoline [26].



(3.16)

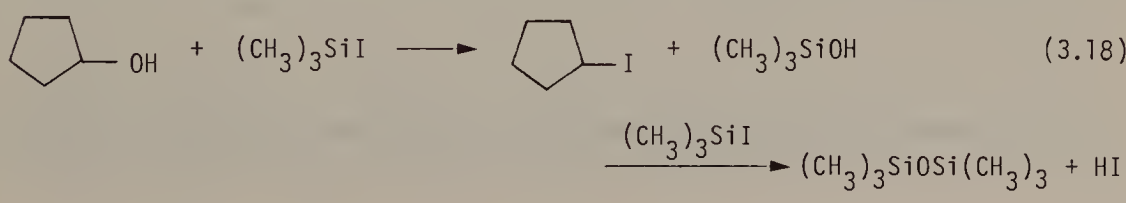
TMS-I reacts with *bis*(dimethylamino)methane to yield dimethyl(methylene)-ammonium iodide, a valuable synthetic intermediate [27, 28]. Other *bis*(dialkylamino)methanes react in a similar manner [27].



(3.17)

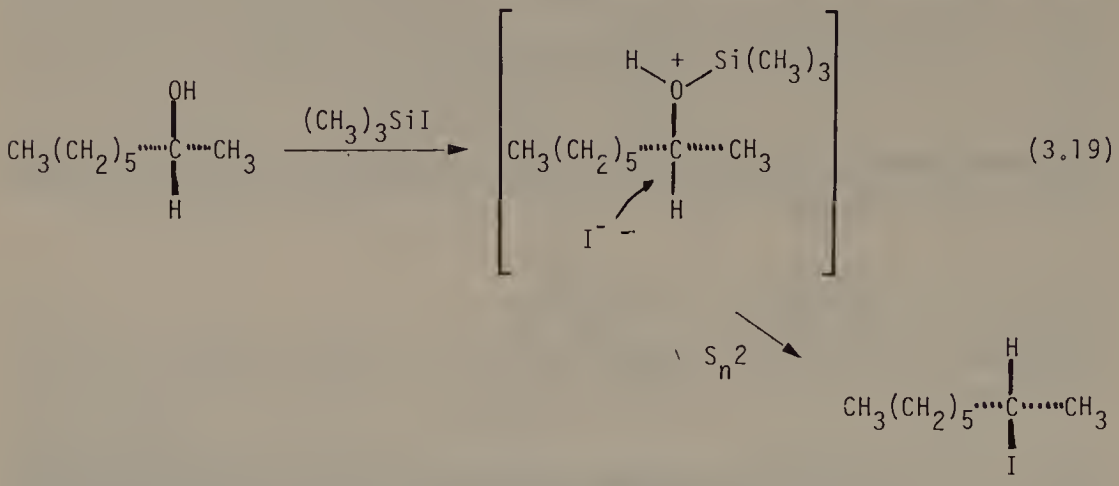
3.4 Conversion of Alcohols and Alkoxytrimethylsilanes to Alkyl Iodides

Red phosphorous and iodine or HI convert alcohols to alkyl iodides. TMS-I is also an excellent reagent for this purpose. TMS-I (2 equivalents) react with alcohols at 25 °C in methylene chloride, chloroform, or CCl_4 to yield alkyl iodides, HI, and hexamethyldisiloxane. The presence of HI makes this reaction unsuitable for alcohols which possess acid-sensitive functional groups [29].



(3.18)

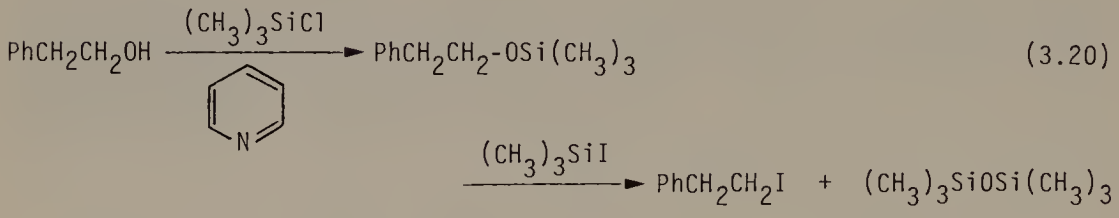
The reaction apparently proceeds largely by an S_n2 type process since treatment of optically active 2-octanol with TMS-I yields 2-octyl iodide whose configuration is 94% inverted.



(3.19)

Similar results have been obtained by treatment of primary, secondary, and tertiary, allylic and benzylic alcohols with TMS-Cl and sodium iodide in acetonitrile [18]. In fact, this *in-situ* method results in more rapid reaction. This acceleration may result from the difference in solvent. However, the reaction of TMS-I itself can be accelerated by the addition of sodium iodide.

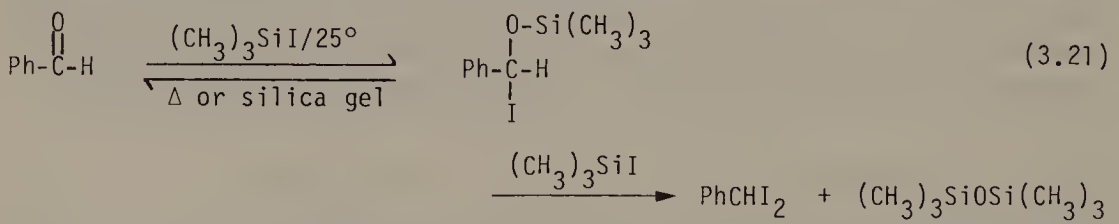
Alkoxytrimethylsilanes are cleaved regiospecifically by TMS-I under neutral conditions to yield alkyl iodides and hexamethyldisiloxane [30, 31]. This reaction is general for primary, secondary, and tertiary alkoxytrimethylsilanes [29].



(3.20)

Similar results were obtained with TMS-I generated *in-situ* by reaction of TMS-Cl and sodium iodide in acetonitrile [32].

TMS-I and aldehydes react in a 1 : 1 ratio to yield iodohydrin trimethylsilyl ethers. Attempts to purify these compounds by distillation or chromatography led to regeneration of the starting aldehyde.

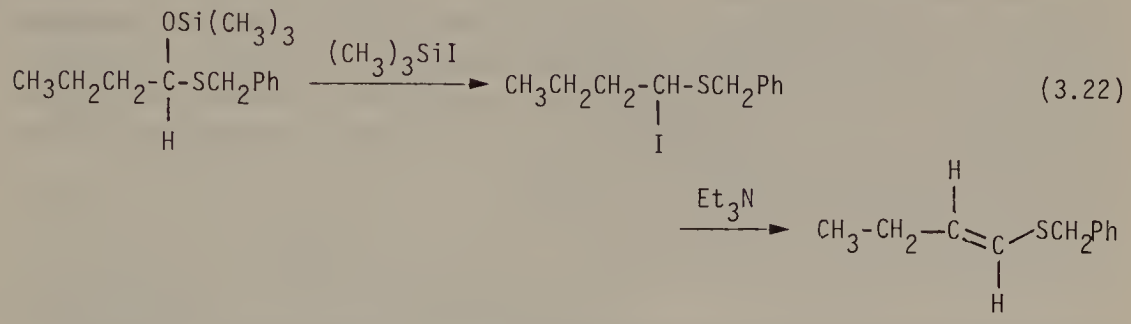


(3.21)

If a 2:1 ratio is used, the initial aldehyde iodohydrin trimethylsilyl ether is converted to a 1,1-diiodide and hexamethyldisiloxane [33]. This reaction is

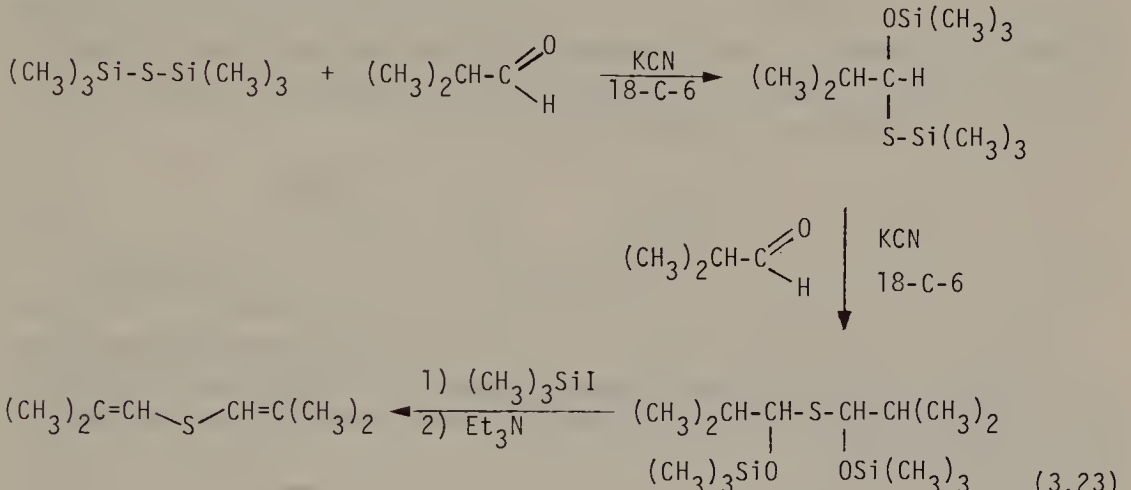
related to the cleavage of alkoxytrimethylsilanes by TMS-I to yield alkyl iodides. Phenylacetaldehyde is an exception. It undergoes slow reaction with excess TMS-I at 0°C to give 2,3,6,7-dibenzo-9-oxabicyclo[3,3,1]nona-2,6-diene [33].

O-Trimethylsilyl hemithioacetals and ketals react with TMS-I to form α-iodosulfides and hexamethyldisiloxane. α-Iodosulfides were previously virtually unknown. They undergo facile dehydrohalogenation on treatment with triethylamine or with sodium hydroxide under PTC conditions to yield vinyl sulfides [34].



(3.22)

α,α'-*bis*(Trimethylsilyloxy) sulfides react with TMS-I to give α,α'-diiodo sulfides as intermediates which undergo dehydrohalogenation with triethylamine to yuield divinylsulfides [35].

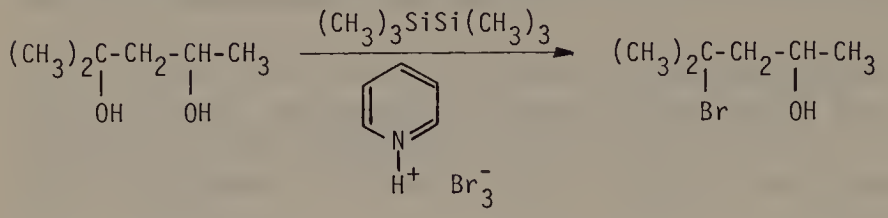


(3.23)

3.5 Reaction of TMS-Br with Alcohols

Unlike TMS-I, TMS-Br does not rapidly cleave esters of carboxylic acids carbonates, ethers, or alkoxytrimethylsilanes under mild conditions. This difference has been attributed to the lower electrophilicity of TMS-Br. Alcohols are converted to bromides by reaction with two equivalents of TMS-Br. HBr is generated in the reaction. The reaction is rapid at 25°C for tertiary, allylic, and benzylic alcohols but slower for primary and secondary alcohols which require heating at 50°C for several hours to effect reaction. This

difference permits the conversion of these more reactive alcohols to bromides in the presence of primary and secondary alcohols [36].

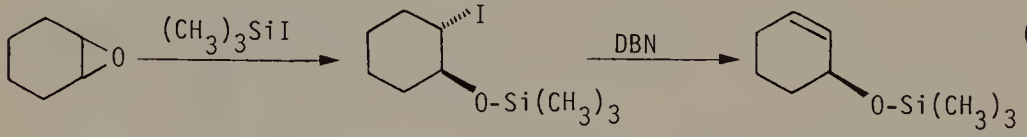


(3.24)

The reaction of TMS-Br with optically active 2-octanol proceeds with 94% inversion of configuration via an S_n2 type process [37]. TMS-Br, generated *in-situ* by reaction of TMS-Cl and lithium bromide in acetonitrile, reacts faster with alcohols. This acceleration has been attributed to catalysis by bromide ion. TMS-Br may also be generated *in-situ* by reaction of hexamethyldisilane with pyridinium perbromide at 25 °C [36].

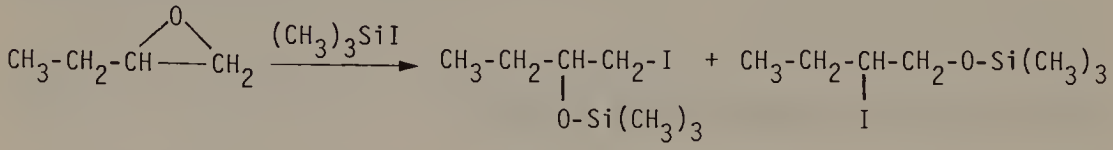
3.6 Reaction of Oxiranes with TMS-I – Conversion to Allylic Alcohols

Epoxides react with TMS-I, which was generated by reaction of hexamethyldisilane with iodine, to give 2-iodoalkoxytrimethylsilanes. These can be converted to allylic alcohols by treatment with tertiary amine bases, such as DBU or DBN, followed by hydrolysis [38].



(3.25)

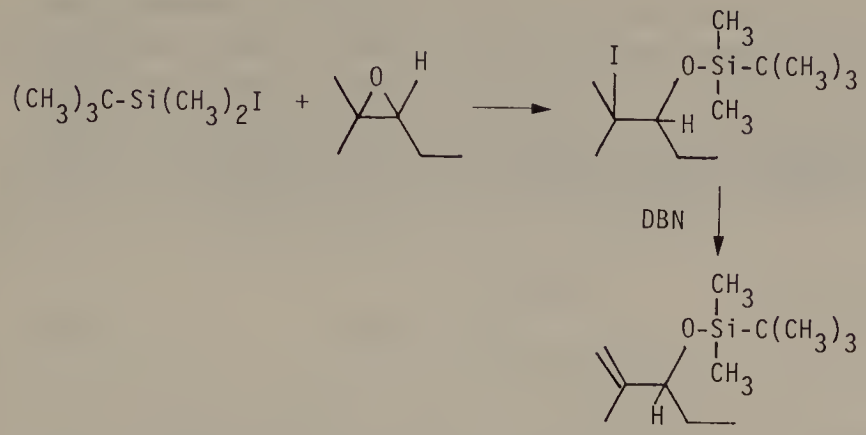
Epoxides of terminal alkenes react with TMS-I to yield approximately a 4:1 ratio of 1-iodo-2-trimethylsilyloxyalkanes [39] and 2-iodo-1-trimethylsilyloxyalkanes [38]. 1-Iodo-2-trimethylsilyloxyalkanes can be oxidized to yield α-iodo ketones.



84 : 16 (3.26)

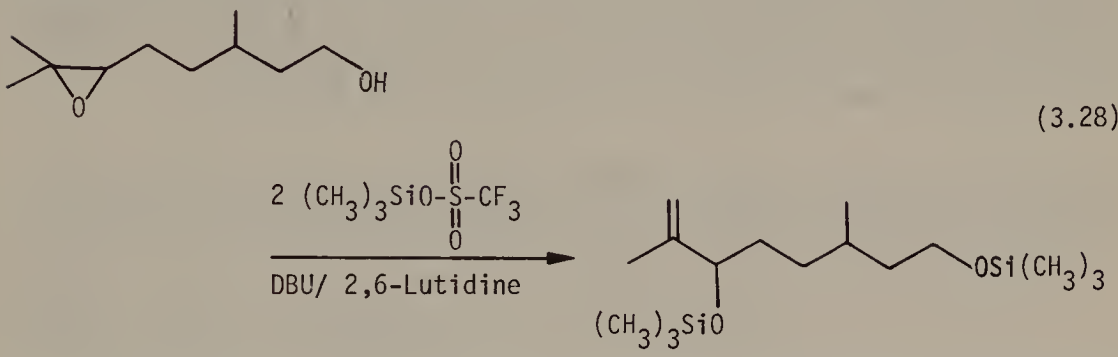
TMS-I reacts with an oxirane in preference to a methyl ester or ethylene ketal functional groups [40]. Similar results have been obtained with *t*-butyldimethylsilyl iodide. The *t*-butyldimethylsilyl ethers of allylic alcohols are more stable to hydrolysis than the corresponding trimethylsilyl ethers. They can be hydrolyzed by treatment with tetraalkylammonium fluoride in moist

DMSO or THF or with potassium fluoride in the presence of a catalytic amount of 18-C-6 [41, 42].



(3.27)

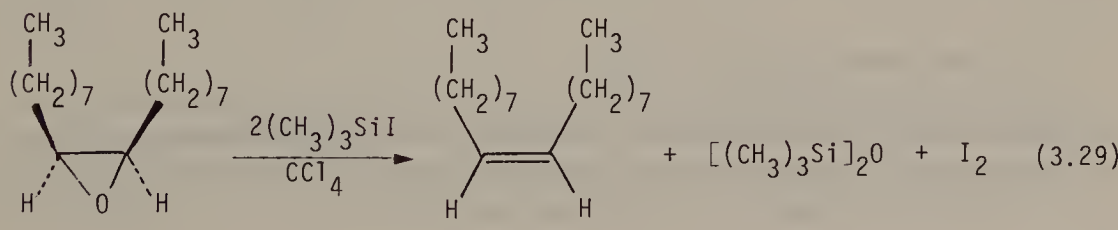
The conversion of oxiranes to allylic alcohols has previously been accomplished by a variety of methods [43]. This transformation can be accomplished by treatment of the oxirane with equimolar amounts of trimethylsilyl trifluoromethanesulfonate, DBU and 2,6-lutidine [44].



(3.28)

The regiospecificity of this transformation with electrophilic TMS-I or trimethylsilyl trifluoromethanesulfonate is different than that with nucleophilic sodium phenylselenide [43].

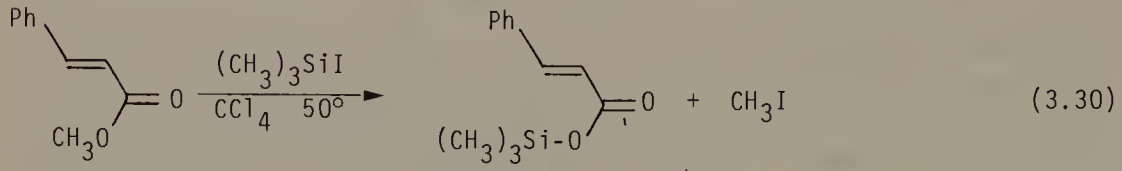
Reaction of epoxides with two equivalents of TMS-I in CCl_4 results in deoxygenation of the epoxide to yield an alkene with retention of stereochemistry. Thus *cis*-9,10-octadecene oxide reacts with TMS-I to yield *cis*-9,10-octadecene. Similar results have been obtained with *trans*-9,10-octadecene oxide [45]. This reaction probably proceeds by initial formation of 9-iodo-10-trimethylsilyloxyoctadecane. Cleavage of the C–O single bond of this alkoxytrimethylsilane with a second equivalent of TMS-I yields 9,10-diiodooctadecane which is unstable relative to octadecene and iodine.



(3.29)

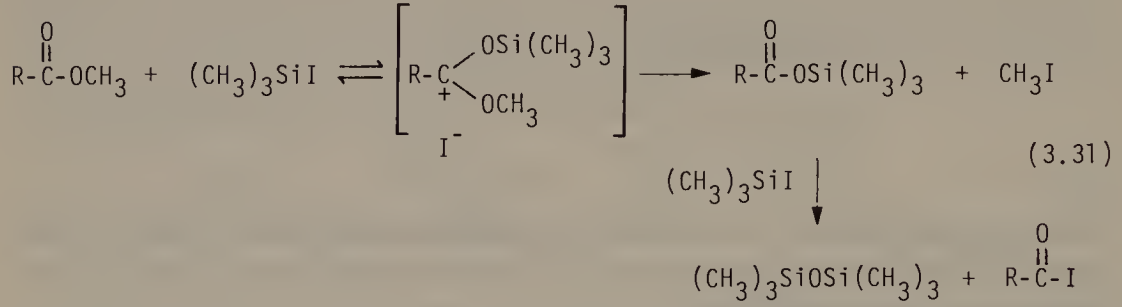
3.7 Hydrolysis of Esters

The hydrolysis of alkyl esters has been accomplished in a number of ways [46–49]. TMS-I rapidly cleaves methyl, ethyl, *i*-propyl, *t*-butyl, and benzyl esters in CCl_4 at 50°C to yield the corresponding trimethylsilyl esters and alkyl iodides. The wide generality of ester hydrolysis by TMS-I makes this method a major synthetic advance. Phenyl esters do not react. The reaction tolerates a large number of functional groups such as C–C double bonds.



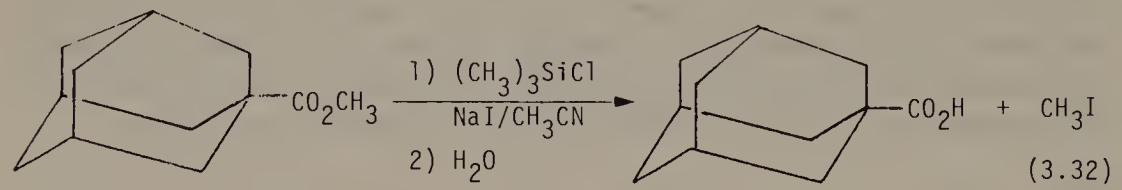
(3.30)

The following reaction mechanism has been proposed. TMS-I reacts in a rapid reversible reaction with the carbonyl oxygen of the ester to yield trimethylsilyloxy alkoxy-stabilized carbocation/iodide ion pair. Rate limiting nucleophilic attack by iodide on the α-carbon of the alkoxy group yields alkyl iodide and the trimethylsilyl ester. In the presence of excess TMS-I the trimethylsilyl ester is converted to an acyl iodide (IR C=O 1,830–1,800 cm^{-1}) and hexamethyldisiloxane [50]. The fact that TMS-I is usually contaminated by traces of HI acid may account for the hydrolysis of *t*-butyl esters, since nucleophilic attack on a *t*-butyl group is improbable.



(3.31)

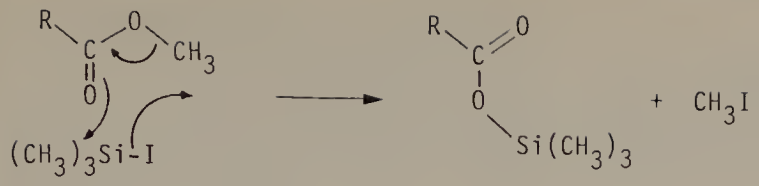
Similar results were obtained for ester hydrolysis with TMS-I generated *in-situ* by the reaction of trimethylphenylsilane [10, 12] or hexamethyldisilane [51, 52], with iodine or by reaction of TMS-Cl and sodium iodide in acetonitrile [18].



(3.32)

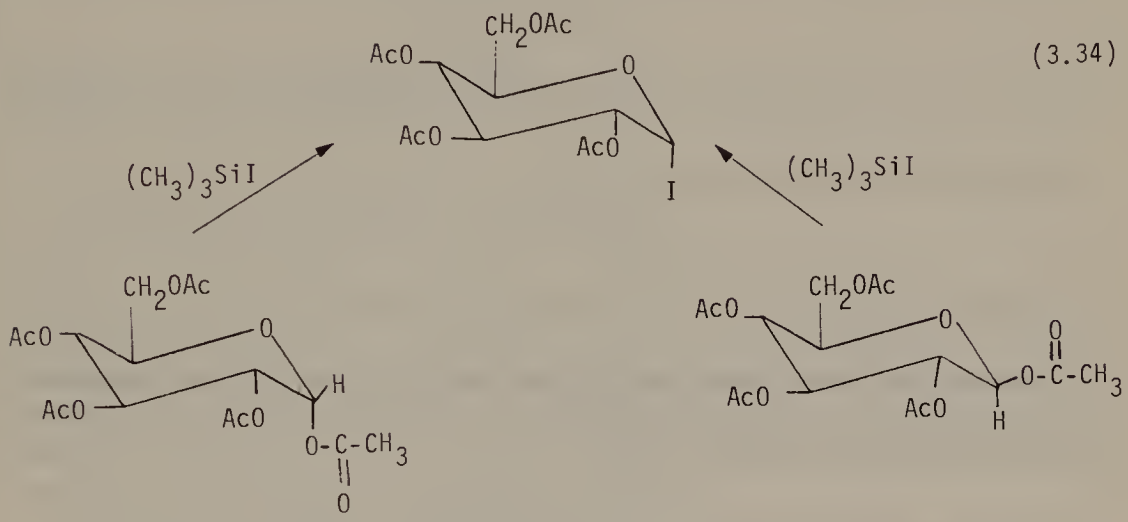
TMS-Br is ineffective in this reaction.

An alternative molecular mechanism which involves a six-membered cyclic transition state has been proposed. The silyl center of TMS-I serves as a hard acid which may coordinate to the carbonyl oxygen of the ester while the soft iodide attacks the α-carbon of the alkoxy group [13].



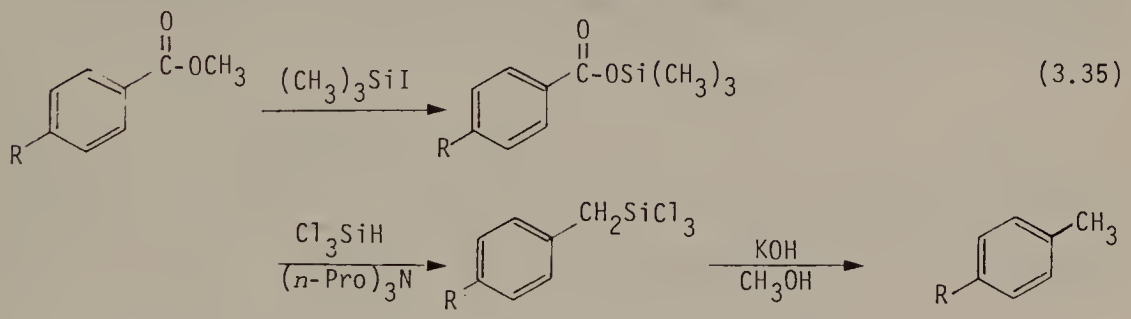
(3.33)

TMS-I and TMS-Br permit stereoselective iodination or bromination of anomeric glycosyl acetates. Under these conditions TMS-Br does not affect ether, ester, or acetal protecting groups [53, 54].



(3.34)

Trimethylsilyl esters of aromatic carboxylic acids can be reduced by trichlorosilane and tertiary aliphatic amines to benzyltrichlorosilanes which then can be cleaved by potassium hydroxide in methanol to yield the corresponding methyl aromatics. Alkyl esters of aromatic carboxylic acids, are not reduced under these conditions [55] (see Chapter 20).

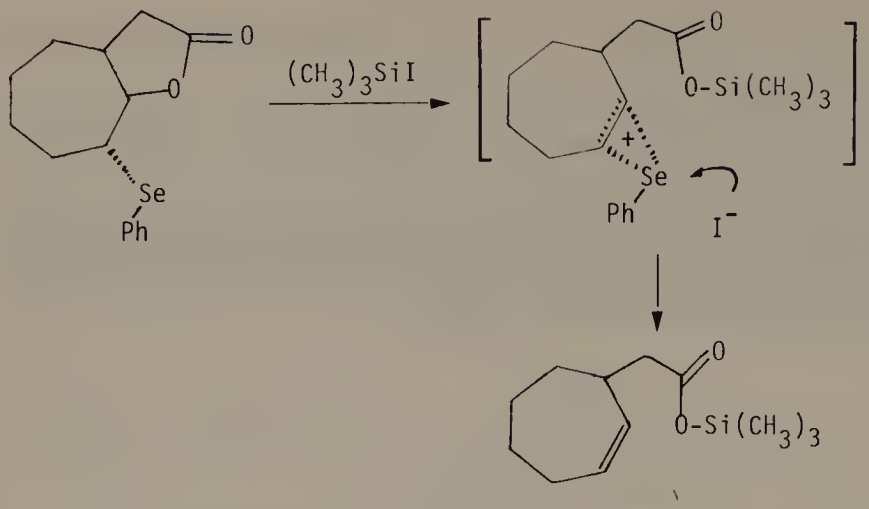


(3.35)

γ-Lactones are cleaved by both TMS-I and TMS-Br [18, 56, 57].

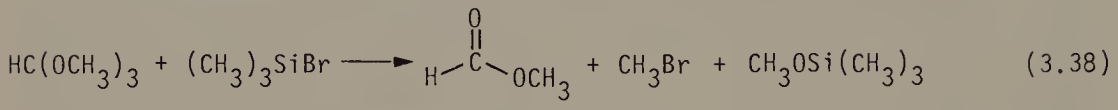
(3.36)

TMS-I generated *in-situ* by reaction of TMS-Cl and sodium iodide in acetonitrile reacts with β-phenylselenolactones to yield olefinic carboxylic acids [20].



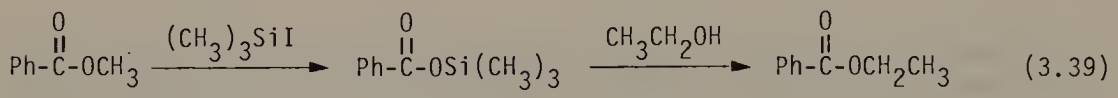
(3.37)

TMS-Br reacts with ortho esters [37].



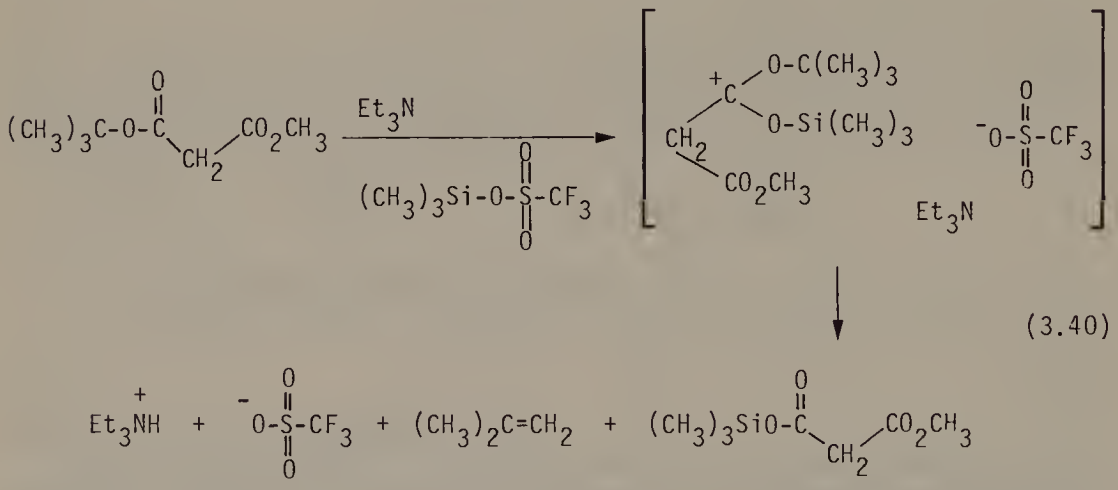
(3.38)

Trimethylsilyl esters react with two equivalents of primary or secondary alcohols to yield the corresponding alkyl esters. This permits transesterification under neutral conditions [58].



(3.39)

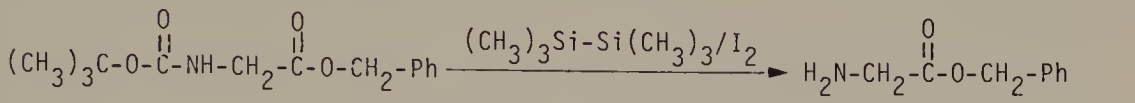
Trimethylsilyl trifluoromethanesulfonate/triethylamine does not react with methyl or benzyl esters but selectively converts *t*-butyl esters into trimethylsilyl esters [59]. This reaction may occur as outlined (Eq. 3.40).



(3.40)

3.8 Hydrolysis of Carbamates

Alkyl carbamates have been utilized to protect primary and secondary amine groups. TMS-I preferentially cleaves carbamates under conditions which do not affect peptide amide bonds, alkyl esters, or benzyl ether protecting groups [18, 52, 60].



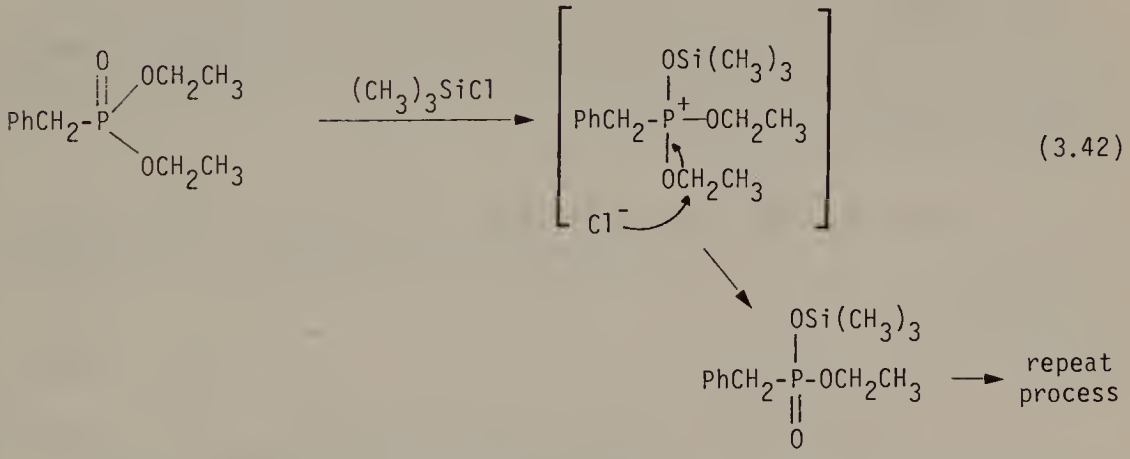
(3.41)

Extensive work on the removal of carbamate protecting groups from dipeptides by TMS-I has been reported [61].

3.9 Hydrolysis of Dialkyl Phosphonates

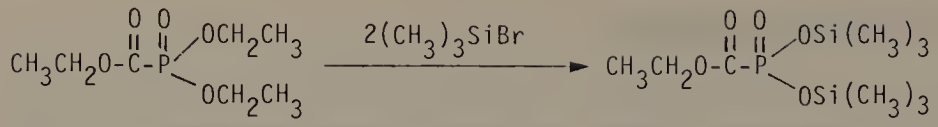
Alkaline hydrolysis of dialkyl phosphonates to the corresponding phosphonic acids requires vigorous conditions which are not compatible with many functional groups. On the other hand, *bis*(trimethylsilyl) phosphonates are readily hydrolyzed by treatment with water. The problem of hydrolysis of dialkyl phosphonates hence becomes one of transesterification, converting a methyl or ethyl ester to a trimethylsilyl ester.

Rabinowitz found that dialkyl phosphonates react slowly (one week) with TMS-Cl at 120° to yield *bis*(trimethylsilyl) phosphonates. The reaction may proceed in a manner similar to the Arbuzov reaction as outlined [62].



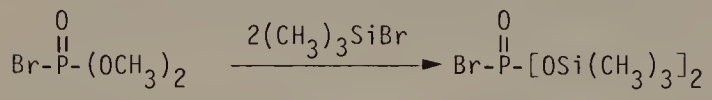
(3.42)

Analysis by McKenna led to the suggestion that the rate limiting step might be reaction of the phosphonium cation/chloride ion pair. On this basis, TMS-Br might be a more reactive reagent due to the increased nucleophilicity of bromide compared to chloride [63]. In fact, TMS-Br rapidly converts dialkyl phosphonates into *bis*(trimethylsilyl) phosphonates at 25°C [63, 64]. C–C double and triple bonds, esters, ethers, benzoyl, and diazo functionalities are compatible with the reaction conditions. No halogen exchange is observed when diethyl iodomethyl phosphonate is treated with TMS-Br.



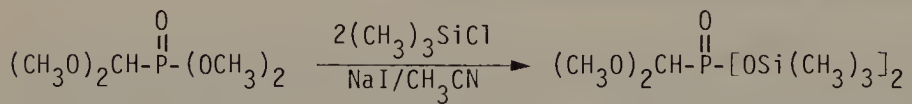
(3.43)

TMS-Br converts dialkyl phosphorochloridates, dialkyl phosphorobromidates, and dialkyl phosphoramidates to the corresponding *bis*(trimethylsilyl) esters [65].



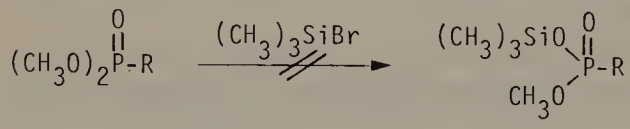
(3.44)

Transesterifications can also be achieved with TMS-I [66–69]. TMS-I reacts with dialkyl phosphonates in preference to dimethyl acetals, or methyl esters.



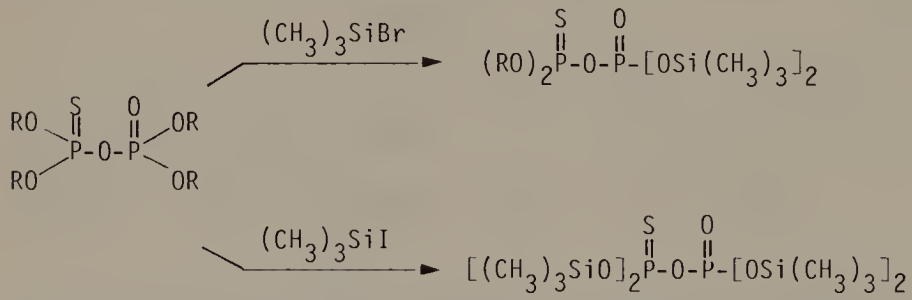
(3.45)

Neither TMS-Br nor TMS-I reacts with dialkyl phosphonates to yield alkyl trimethylsilyl phosphonate intermediates.



(3.46)

While TMS-I reacts more rapidly than TMS-Br with dialkyl phosphonates, both yield *bis*(trimethylsilyl)phosphonates. However, only TMS-I permits transesterification of dialkyl thiophosphonates (P=S) to yield *bis*(trimethylsilyl)thiophosphonates (P=S) [65].



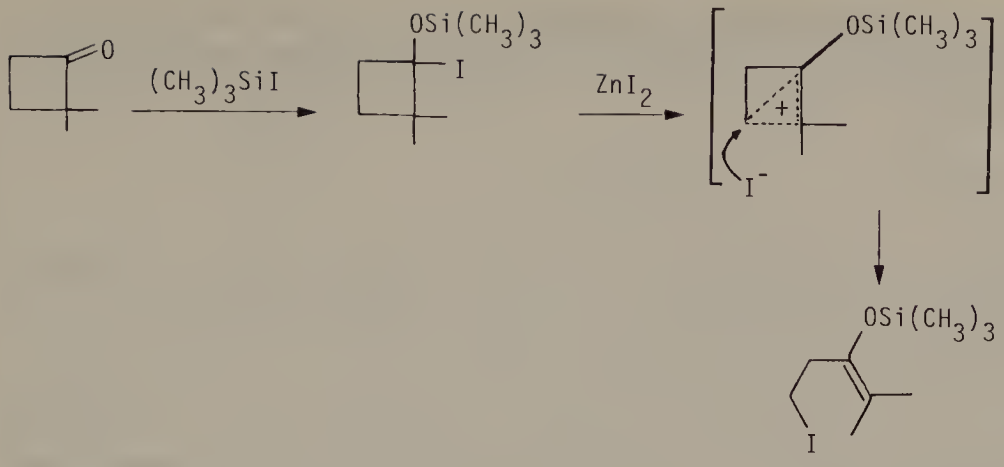
(3.47)

(3.48)

Reductions with TMS-I are considered in Chapter 20.

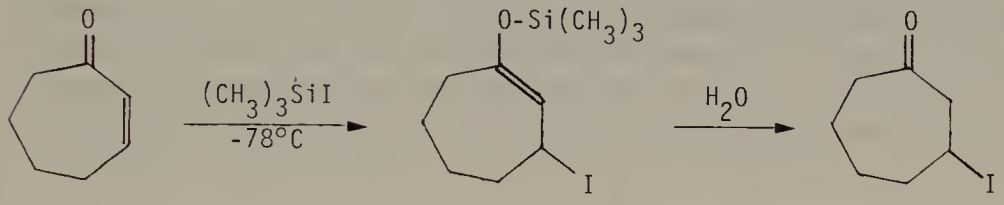
3.10 Preparation of β- and γ-Iodo Ketones

Zine iodide catalyzed reaction of TMS-I with cyclobutanones yields after hydrolysis ring opened β-iodoketones [70]. This may occur as outlined below.



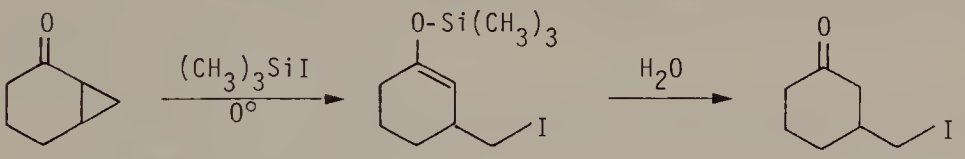
(3.49)

β-Iodoketones undergo facile reaction with various nucleophiles, such as cyanide and phenylthiolate ions. β-Iodoketones can also be prepared by Michael addition of TMS-I to α,β-unsaturated ketones [71].



(3.50)

TMS-I reacts with α,β-cyclopropylketones to yield γ-iodoketones [71, 72].



(3.51)

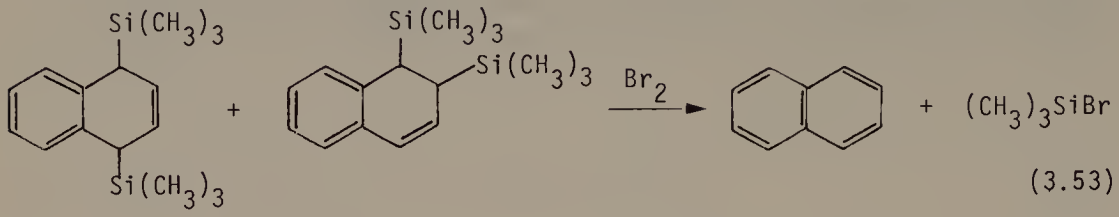
TMS-I and TMS-Br undergo halogen exchange with acyl chlorides to yield respectively, acyl iodides and acyl bromides [73].

(3.52)

3.11 Preparation of TMS-Br and TMS-I

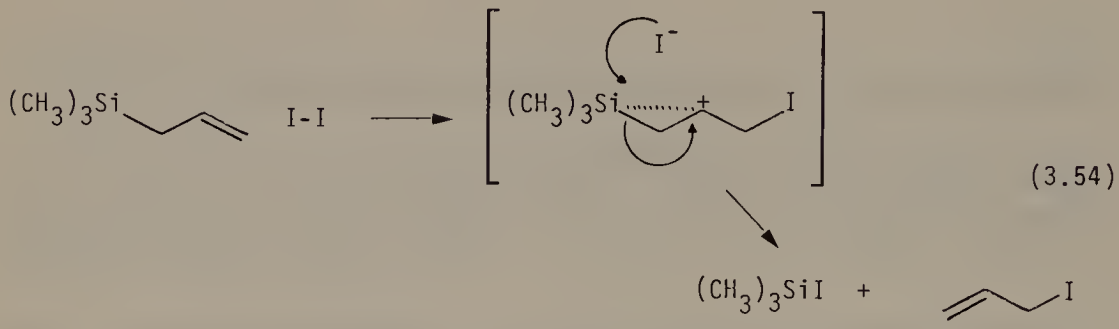
TMS-Br, a water white liquid (bp 80°C) has been prepared by the reaction of hexamethyldisiloxane with phosphorous tribromide catalyzed by ferric chloride [1]. It reacts immediately with moisture but is otherwise reasonably stable. Reaction of phenyltrimethylsilane with bromine at steam bath temperature for one hour, results in an 85% yield of TMS-Br. Reaction of bromine with a mixture of 1,2-*bis*(trimethylsilyl)-1,2-dihydronaphthalene and 1,4-*bis*-(trimethylsilyl)-1,4-dihydronaphthalene also yields TMS-Br [74]. TMS-Br has

also been generated *in-situ* by reaction of TMS-Cl with lithium bromide in acetonitrile solvent or by reaction of hexamethyldisilane with pyridinium perbromide [36].



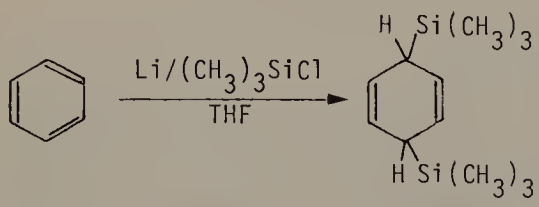
(3.53)

TMS-I has been prepared by reaction of hexamethyldisiloxane with iodine and aluminum powder [5, 75]. Freshly distilled TMS-I is a colorless liquid (bp 107 °C) which reacts rapidly with water. It is therefore usually contaminated with small amounts of HI. It rapidly darkens on standing in the light. TMS-I has been prepared by several *in-situ* reactions. Among these are the reaction of trimethylphenylsilane with iodine at 120 °C [2, 12]. This reaction may be catalyzed by aluminium iodide [3, 76]. TMS-I results from *in-situ* reaction of allyltrimethylsilane with iodine. A problem is that allyl iodide is itself a reactive electrophile which may alkylate nucleophilic centers in the substrate or product. Further, only half the iodine atoms are productively utilized [77].



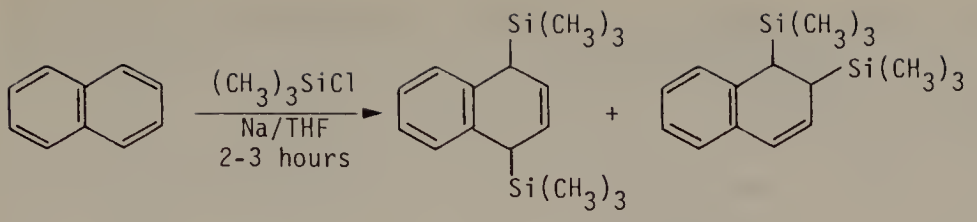
(3.54)

The reaction of iodine with 3,6-*bis*(trimethylsilyl)-1,4-cyclohexadiene yields two molecules of TMS-I and benzene which can easily be removed from the reaction mixture [77]. However, the preparation of 3,6-*bis*(trimethylsilyl)-1,4-cyclohexadiene is time consuming [78].



(3.55)

Reaction of a mixture of 1,2-*bis*(trimethylsilyl)-1,2-dihydronaphthalene and 1,4-*bis*(trimethylsilyl)-1,4-dihydronaphthalene with iodine also yields TMS-I. The precursor mixture is easily prepared [79].



(3.56)

TMS-I has also been generated *in-situ* by the reaction of iodine with phenylseleno-trimethylsilane [80]. Phenylseleno-trimethylsilane (bp 110–115°C/18 mm) has been prepared by reaction of phenylselenol, TMS-Cl and triethylamine [81] or by the reaction of sodium phenylselenide and TMS-Cl in THF [82].

$$2\ PhSe\text{-}Si(CH_3)_3 \xrightarrow{I_2} PhSe\text{-}SePh + 2(CH_3)_3SiI \qquad (3.57)$$

The reaction of iodine with hexamethyldisilane to yield TMS-I is most direct [38, 51, 52, 83, 84]. However, hexamethyldisilane is not easily prepared except by reaction of TMS-Cl with sodium-potassium alloy.

$$(CH_3)_3SiCl \xrightarrow{Na/K} (CH_3)_3SiSi(CH_3)_3 \xrightarrow{I_2} 2(CH_3)_3SiI \qquad (3.58)$$

t-Butyldimethylsilyl iodide may be prepared by reaction of iodine with phenylseleno-*t*-butyldimethylsilane [41, 42]. Phenylseleno-*t*-butyldimethylsilane may be prepared by reaction of sodium or lithium phenylselenide with *t*-butyldimethylchlorosilane [41, 42]. *t*-Butyldiphenylsilyl iodide can be prepared in a similar manner.

In conclusion, it appears to us that for most reactions Olah's procedure which involves reaction of TMS-Cl with sodium iodide in acetonitrile is the most economical and facile [18]. For TMS-I it appears that the simplest method really is best.

$$(CH_3)_3SiCl \xrightarrow[CH_3CN]{NaI} (CH_3)_3SiI \qquad (3.59)$$

References

1. Gilliam, W.G., Meals, R.N., Sauer, R.D.: J. Am. Chem. Soc. *68*, 1161 (1946)
2. Pray, B.O., Sommer, L.H., Goldberg, G.M., Kerr, G.T., DiGiorgio, P.A., Whitmore, F.C.: J. Am. Chem. Soc. *70*, 433 (1948)
3. Eaborn, C.: J. Chem. Soc. 2755 (1949)
4. Reese, C.B., "Protection of Alcoholic Hydroxyl Groups and Glycol Systems", in Protecting Groups in Organic Chemistry, (McOmie, J.F.W., Ed.) p. 95–143. New York: Plenum Press, 1973
5. Voronkov, M.G., Khudobin, Y.I.: Izv. Akad. Nauk. SSSR Otd. Khim. Nauk, 713 (1956)
6. Voronkov, M.G., Khudobin, Y.I.: Zh. Obsh. Khim. *26*, 584 (1956)
7. Krürke, U.: Chem. Ber. 174 (1962)

8. Voronkov, M.G., Puzanova, V.E., Pavlov, S.F., Dubinskaya, E.I.: Izv. Akad. Nauk. SSSR Ser. Khim. 448 (1975)
9. Voronkov, M.G., Dubinskaya, E.I., Komarov, V.G., Pavlov, S.F.: Zh. Obsh. Khim. *46*, 1908 (1976)
10. Ho, T.L., Olah, G.A.: Angew. Chem. Int. Ed. *15*, 774 (1976)
11. Voronkov, M.G., Dubinskaya, E.I., Pavlov, S.F., Gorokhova, V.G.: Izv. Akad. Nauk SSSR Ser. Khim. 2355 (1976)
12. Ho, T.L., Olah, G.A.: Synthesis, 417 (1977)
13. Ho, T.L., Olah, G.A.: Proc. Natl. Acad. Sci. USA, *75*, 4 (1978)
14. Rosen, B.I., Weber, W.P.: J. Org. Chem. *42*, 3463 (1977)
15. Silverman, R.B., Radak, R.E., Hacker, N.P.: J. Org. Chem. *44*, 4970 (1979)
16. Jung, M.E., Lyster, M.A.: J. Org. Chem. *42*, 3761 (1977)
17. Seitz, D.E., Ferreira, L.: Syn. Commun. *9*, 931 (1979)
18. Olah, G.A., Narang, S.C., Gupta, B.G.B., Malhotra, R.: J. Org. Chem. *44*, 1247 (1979)
19. Kosarych, Z., Cohen, T.: Tetrahedron Lett., 3959 (1980)
20. Clive, D.L.J., Kalé, V.N.: J. Org. Chem. *46*, 231 (1981)
21. Jung, M.E., Mazurek, M.A., Lim, R.M.: Synthesis, 588 (1978)
22. Wittig, G., Schlosser, W.: Chem. Ber. *94*, 1373 (1961)
23. Jung, M.E., Andrus, W.A., Ornstein, P.L.: Tetrahedron Lett. 4175 (1977)
24. Keyser, G.E., Bryant, J.D., Barrio, J.R.: Tetrahedron Lett. 3263 (1979)
25. Bryant, J.D., Keyser, G.E., Barrio, J.R.: J. Org. Chem. *44*, 3733 (1979)
26. Minamikawa, J., Brossi, A.: Tetrahedron Lett. 3085 (1978)
27. Bryson, T.A., Bonitz, G.H., Reichel, C.J., Dardis, R.E.: J. Org. Chem. *45*, 524 (1980)
28. Schreiber, J., Maag, H., Hashimoto, N., Eschenmoser, A.: Angew. Chem. Int. Ed. *10*, 330 (1971)
29. Jung, M.E., Ornstein, P.L.: Tetrahedron Lett. 2659 (1977)
30. Voronkov, M.G., Pavlov, S.F., Dubinskaya, E.I.: Izv. Akad. Nauk. SSSR Ser. Khim. 657 (1975)
31. Voronkov, M.G., Pavlov, S.F., Dubinskaya, E.I.: Akad. Nauk. SSSR, *227*, 607 (1976)
32. Morita, T., Yoshida, S., Okamoto, Y., Sakurai, H.: Synthesis, 379 (1979)
33. Jung, M.E., Mossman, A.B., Lyster, M.A.: J. Org. Chem. *43*, 3698 (1978)
34. Aida, T., Harpp, D.N., Chan, T.H.: Tetrahedron Lett. 3247 (1980)
35. Aida, T., Chan, T.H., Harpp, D.N.: Tetrahedron Lett. 1089 (1981)
36. Olah, G.A., Gupta, B.G.B., Malhotra, R., Narang, S.C.: J. Org. Chem. *45*, 1638 (1980)
37. Jung, M.E., Hatfield, G.L.: Tetrahedron Lett. 4483 (1978)
38. Sakurai, H., Sasaki, K., Hosomi, A.: Tetrahedron Lett. 2329 (1980)
39. Denis, J.N., Krief, A.: Tetrahedron Lett. 1429 (1981)
40. Kraus, G.A., Fraiser, K.: J. Org. Chem. *45*, 2579 (1980)
41. Detty, M.R.: J. Org. Chem. *45*, 924 (1980)
42. Detty, M.R., Seidler, J.D.: J. Org. Chem. *46*, 1283 (1981)
43. Sharpless, K.B., Lauer, R.F.: J. Am. Chem. Soc. *95*, 2697 (1973)
44. Murata, S., Suzuki, M., Noyori, R.: J. Am. Chem. Soc. *101*, 2738 (1979)
45. Denis, J.N., Magnane, R., Eenoo, M.V., Krief, A.: Nouv. J. Chim. *3*, 705 (1979)
46. Haslam, E., "Protection of Carboxyl Groups" in Protecting Groups in Organic Chemistry, edited by (McOmie, J.F.W., Ed.) pp. 183–215. New York 1973, Plenum Press.
47. Woodward, R.B., Heusler, K., Gosteli, J., Naegeli, P., Oppolzer, W., Ramage, R., Ranganathan, S., Vorbruggen, H.: J. Am. Chem. Soc. *88*, 852 (1966)

48. Elsing, E., Schreiberg, J., Eschenmoser, A.: Helv. Chim. Acta. *43*, 113 (1960)
49. Bartlett, P.A., Johnson, W.S.: Tetrahedron Lett. 4459 (1970)
50. Jung, M.E., Lyster, M.A.: J. Am. Chem. Soc. *99*, 969 (1977)
51. Sakurai, H., Shirahata, A., Sasaki, K., Hosomi, A.: Synthesis, 740 (1979)
52. Olah, G.A., Narang, S.C., Gupta, B.G.B., Malhotra, R.: Angew. Chem. Int. Ed. *18*, 612 (1979)
53. Thiem, J., Meyer, B.: Chem. Ber. *113*, 3075 (1980)
54. Gillard, J.W., Israel, M.: Tetrahedron Lett. 513 (1981)
55. Benkeser, R.A., Mozdzen, E.C., Muth, C.L.: J. Org. Chem. *44*, 2185 (1979)
56. Voronkov, M.G., Komarov, V.G., Albanov, A.I., Kositsina, E.I., Dubinskaya, E.I.: Izv. Akad. Nauk. SSSR Ser. Khim. 1692 (1978)
57. Kricheldorf, H.R.: Angew. Chem. Int. Ed. *18*, 689 (1979)
58. Olah, G.A., Narang, S.C., Salem, G.F., Gupta, B.G.B.: Synthesis, 142 (1981)
59. Borgulya, J., Bernauer, K.: Synthesis, 545 (1980)
60. Jung, M.E., Lyster, M.A.: J. Chem. Soc. Chem. Commun. 315 (1978)
61. Lott, R.S., Chauhan, V.S., Stammer, C.H.: J. Chem. Soc. Chem. Commun. 495 (1979)
62. Rabinowitz, R.: J. Org. Chem. *28*, 2975 (1963)
63. McKenna, C.E., Higa, M.T., Cheung, N.H., McKenna, M.C.: Tetrahedron Lett. 155 (1977)
64. McKenna, C.E., Schmidhauser, J.: J. Chem. Soc. Chem. Commun. 739 (1979)
65. Chojnowski, J., Cypryk, M., Michalski, J.: Synthesis, 777 (1978)
66. Blackburn, G.M., Ingleson, D.: J. Chem. Soc. Chem. Commun. 870 (1978)
67. Blackburn, G.M., Ingleson, D.: J. Chem. Soc. Perkin, *I*, 1150 (1980)
68. Zygmunt, J., Kafarski, P., Mastalerz, P.: Synthesis, 609 (1978)
69. Morita, T., Okamoto, Y., Sakurai, H.: Tetrahedron Lett. 2523 (1978)
70. Miller, R.D., McKean, D.R.: Tetrahedron Lett. 2639 (1980)
71. Miller, R.D., McKean, D.R.: Tetrahedron Lett. 2305 (1979)
72. Miller, R.D., McKean, D.R.: J. Org. Chem. *46*, 2412 (1981)
73. Schmidt, A.H., Russ, M., Grosse, D.: Synthesis, 216 (1981)
74. Birkofer, L., Krämer, E.: Chem. Ber. *100*, 2776 (1967)
75. Jung, M.E.: Org. Synthesis, in press
76. Eaborn, C., Walton, D.R.M., Young, D.J.: J. Chem. Soc. *B*, 15 (1969)
77. Jung, M.E., Blumenkopf, T.A.: Tetrahedron Lett. 3657 (1978)
78. Weyenberg, D.R., Toporcer, L.H.: J. Am. Chem. Soc. *84*, 2843 (1960)
79. Weyenberg, D.R., Toporcer, L.H.: J. Org. Chem. *30*, 943 (1965)
80. Detty, M.R.: Tetrahedron Lett. 4189 (1979)
81. Derkach, N.Y., Pasmurtseva, N.A., Levchenko, E.S.: Zhur. Org. Khim. *7*, 1543 (1971)
82. Detty, M.R.: Tetrahedron Lett. 5087 (1978)
83. Kumada, M., Shiina, K., Yamaguchi, M.: Kogyo, Hagakn Zasshi, *57*, 230 (1954)
84. Bundel, Y.G., Bobrovskii, S.I., Smirnov, V.V., Novikova, I.A., Sergeev, G.B., Reutov, O.A.: Izv. Akad. Nauk. SSSR Ser. Khim. 2129 (1979)

4 Silyl Azides

4.1 Introduction

Organosilyl azides have proved themselves useful as reagents in organic synthesis. On the basis of the analogy between a trimethylsilyl group and a proton, trimethylsilyl azide (TMS-N_3) might be expected to demonstrate reactivity and toxicity similar to that of hydrazoic acid.

4.2 Preparation and Properties of Organosilyl Azides

TMS-N_3, a colorless liquid boiling at 95–96°C/760 mm, is more convenient to handle than hydrazoic acid. Organosilyl azides are considerably more thermally stable than organic azides [1–4]. For example, triphenylsilyl azide does not decompose in the vapor phase at 590°C [5]. The thermal stability has been attributed to dative $d_\pi - p_\pi$ bonding between silicon and nitrogen which increases the bond order for the Si–N bond [2, 3]. Nevertheless, these compounds should be handled with care, since diazidodimethylsilane is reported to explode unpredictably [6]. Organosilyl azides also react rapidly with water to release toxic hydrazoic acid [2].

TMS-N_3 has been prepared by reaction of TMS-Cl with lithium azide in 2,4-lutidine [5] or THF [4].

$$(CH_3)_3SiCl + LiN_3 \xrightarrow[\text{or 2,4-Lutidine}]{\text{THF}} (CH_3)_3SiN_3 \qquad (4.1)$$

TMS-N_3 can also be prepared by reaction of TMS-Cl with the more commonly available sodium azide in THF in the presence of $AlCl_3$ [7]. DMF [8], HMPT [8] or diethylene glycol dimethyl ether [1] can also be used as solvents for this reaction.

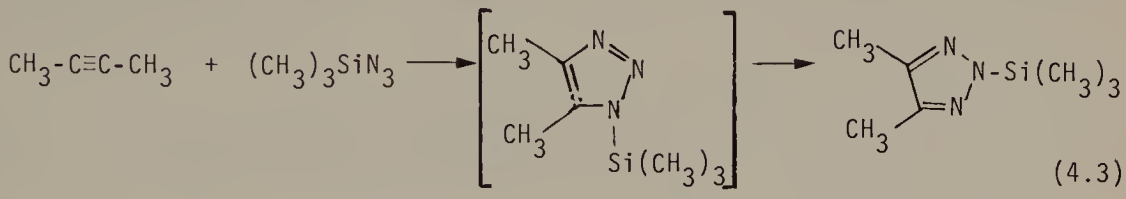
These procedures are quite general and permit the preparation of a variety of organosilyl azides [9, 10]. However, they do not permit preparation of organosilyl azides possessing Si–H, Si–NH_2 or C–C double bonds. Methylphenylsilyl azide has been prepared by an exchange reaction between TMS-N_3 and methylphenylchlorosilane [11, 12].

$$(CH_3)_3SiN_3 + \begin{matrix} & CH_3 & \\ & | & \\ Ph- & Si- & Cl \\ & | & \\ & H & \end{matrix} \longrightarrow (CH_3)_3SiCl + \begin{matrix} & CH_3 & \\ & | & \\ Ph- & Si- & N_3 \\ & | & \\ & H & \end{matrix} \qquad (4.2)$$

A rather detailed comparison of synthetic methods for the preparation of organosilyl azides has been published [13]. A number of them are commercially available from Petrach [14].

4.3 Cycloaddition Reactions

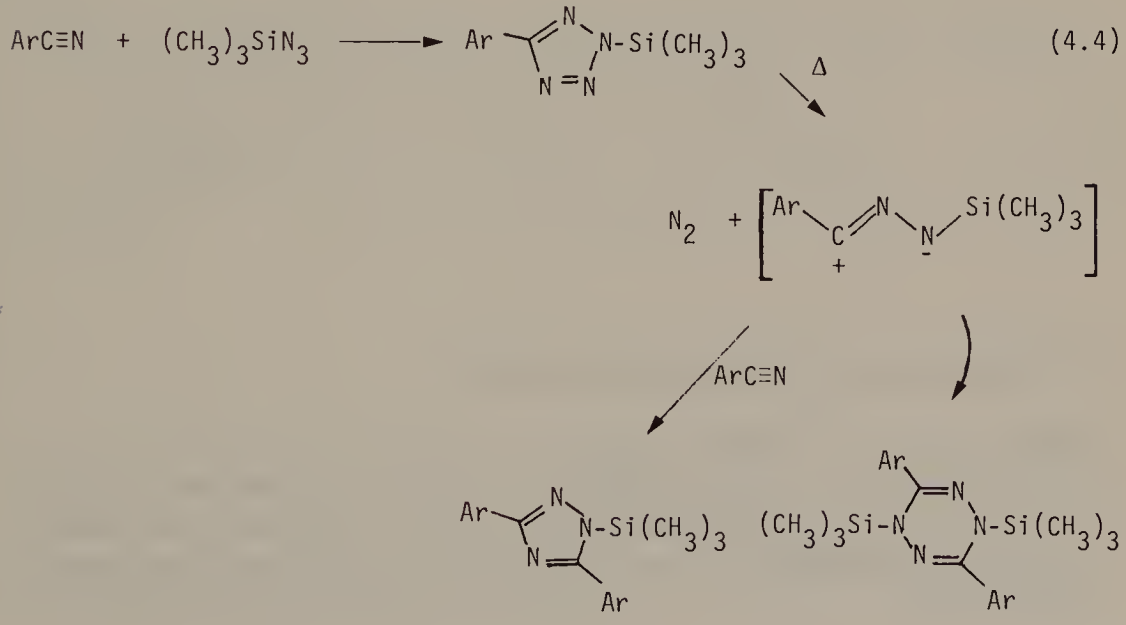
TMS-N_3 undergoes [2 + 3] cycloaddition reactions with acetylenes to yield 2-trimethylsilyl-1,2,3-triazoles. These result from isomerization, via a 1,5-sigmatropic shift of the trimethylsilyl group, of the initially formed 1-trimethylsilyl 1,2,3-triazoles [15–18].



(4.3)

The trimethylsilyl group of such 2-trimethylsilyl-1,2,3-triazoles can easily be removed by hydrolysis to yield 1,2,3-triazoles.

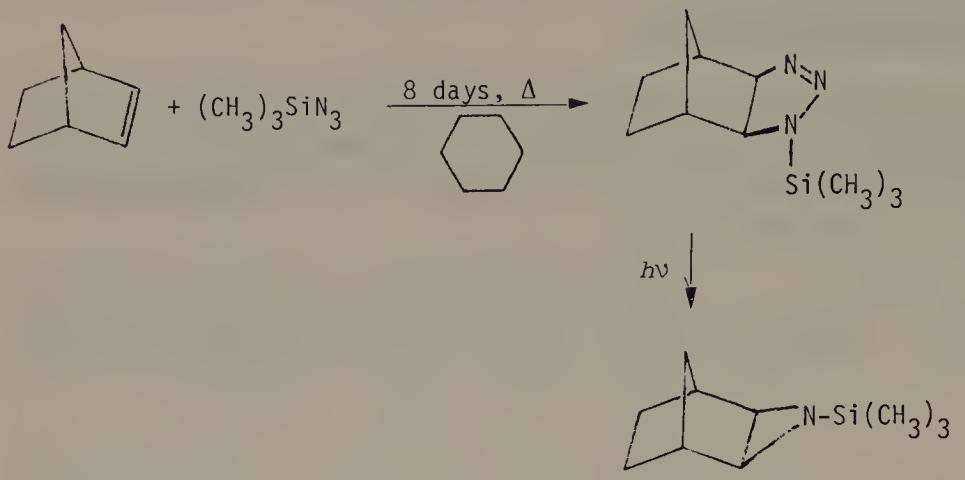
TMS-N_3 undergoes thermal [2 + 3] cycloaddition reaction with aryl nitriles to give mixtures of 5-aryl-2-trimethylsilyl tetrazoles [11], 3,5-diaryl-2-trimethylsilyl-1,2,4-triazoles and 3,6-diaryl-1,4-*bis*(trimethylsilyl)-1,2,4,5-tetrazines [19]. The latter two products result from thermal decomposition of the initial 5-aryl-2-trimethylsilyl tetrazole to give nitrogen and a N-trimethylsilyl substituted nitrile imine [20]. Such reactive 1,3-dipolar species react with an additional molecule of aryl nitrile to yield 3,5-diaryl-2-trimethylsilyl-1,2,4-triazoles or dimerize to yield 3,6-diaryl-1,4-*bis*(trimethylsilyl)-1,2,4,5-tetrazines.



(4.4)

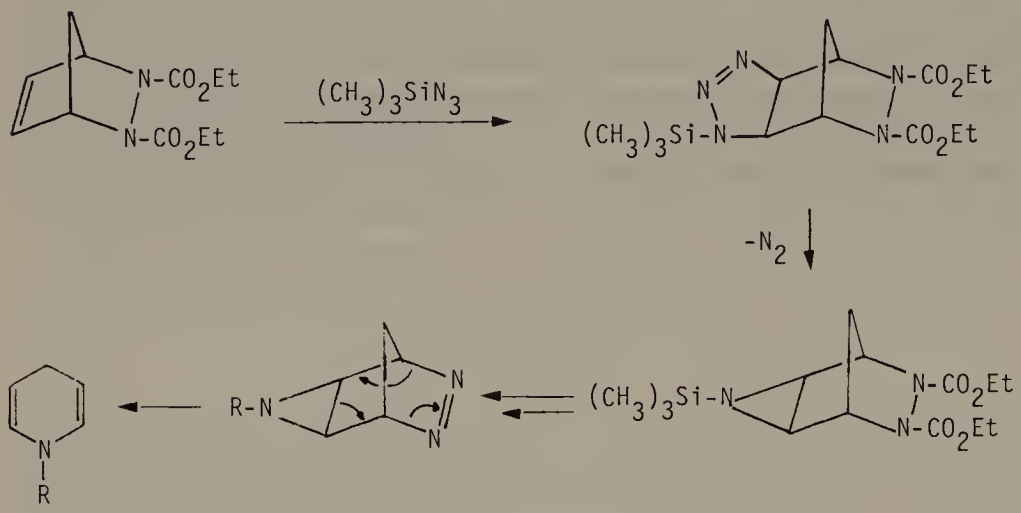
However, ferrocenyl nitrile reacts with TMS-N_3 under $AlCl_3$ catalysis to yield exclusively 2-trimethylsilyl-5-ferrocenyl tetrazole (75%) [19].

TMS-N_3 undergoes slow thermal [2 + 3] cycloaddition reactions with alkenes to yield 1-trimethylsilyl-Δ^2-1,2,3-triazoles. These lose nitrogen on heating at higher temperature or on photolysis to give N-trimethylsilyl aziridines [11, 21].



(4.5)

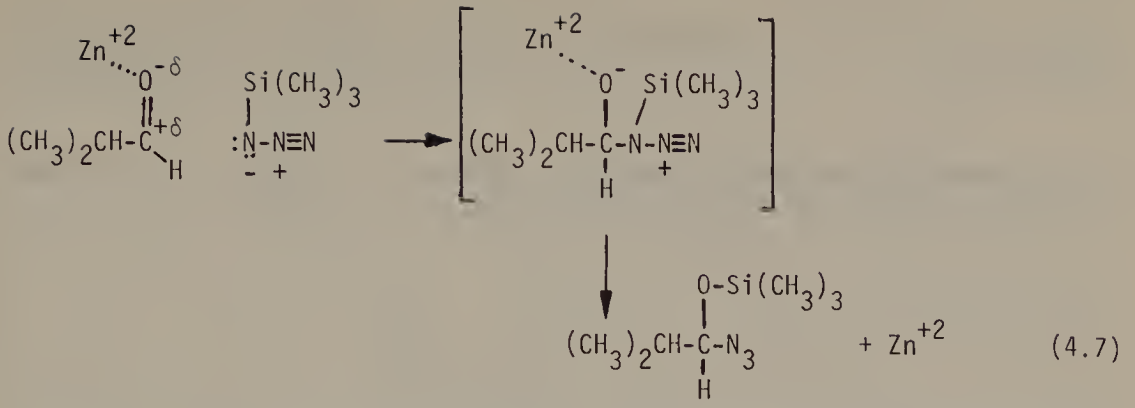
This reaction has been utilized in an unequivocal synthesis of N-substituted-1,4-dihydropyridines [22].



(4.6)

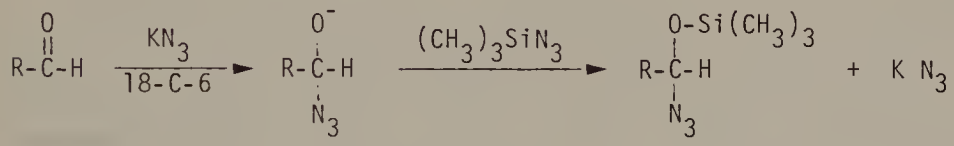
4.4 Reactions with Aldehydes or Ketones

TMS-N_3 reacts with aliphatic aldehydes under both electrophilic catalysis by zinc chloride [23, 24] or anionic activation by potassium azide and 18-C-6 [25] to yield α-trimethylsilyloxyalkyl azides. Catalysis by zinc chloride may involve coordination of zinc cation to the carbonyl oxygen increasing its electrophilicity.



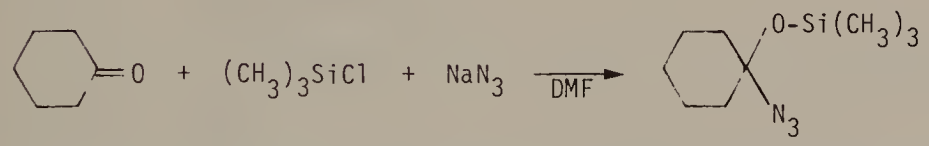
(4.7)

Anionic catalysis occurs by addition of azide ion to the carbonyl group to yield an alkoxide anion. This then reacts with TMS-N_3 to give the product and regenerate azide ion.



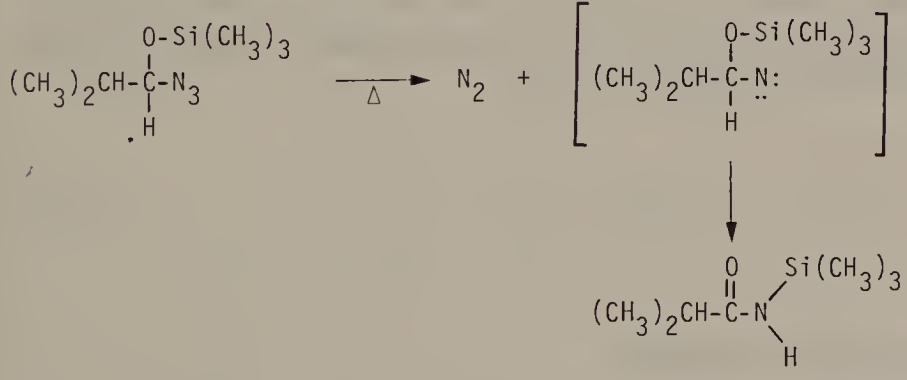
(4.8)

Higher yields are obtained with anionic activation. Recently it has been shown that aliphatic aldehydes or ketones react with TMS-Cl and sodium azide in DMF to yield α-trimethylsilyloxyalkyl azides directly [26]. Although TMS-N_3 can be prepared under similar reaction conditions [8], it is not clear whether this reaction involves prior *in-situ* formation of TMS-N_3 or not.



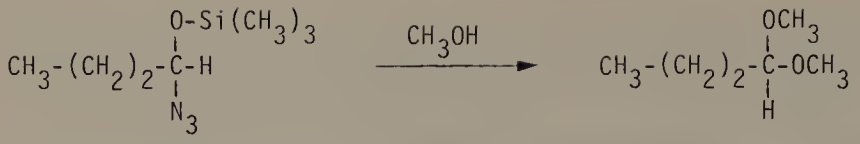
(4.9)

α-Trimethylsilyloxyalkyl azides undergo pyrolysis at 280° to yield N-trimethylsilyl amides and nitrogen [11, 24].



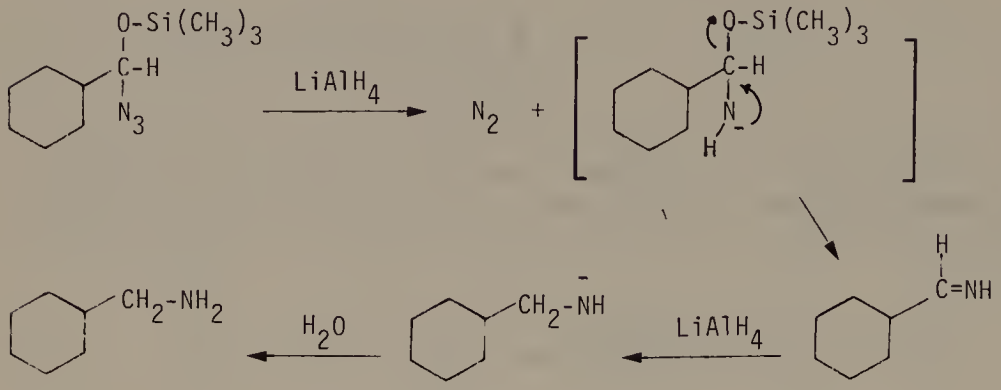
(4.10)

α-Trimethylsilyloxyalkyl azides react with methanol to give the corresponding dimethyl acetal and hydrazoic acid [24].



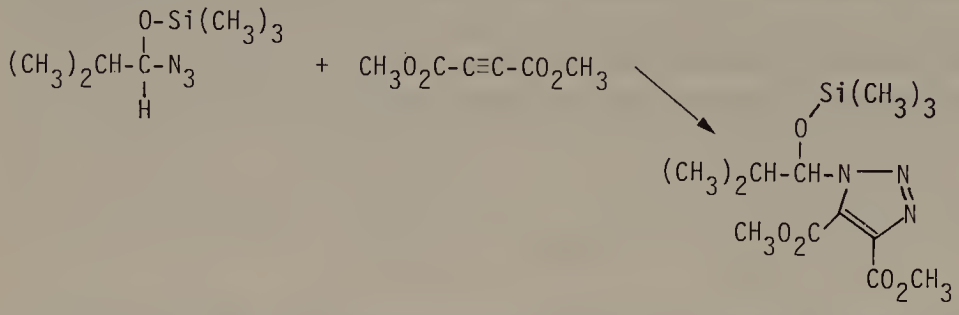
(4.11)

α-Trimethylsilyloxyalkyl azides are reduced by $LiAlH_4$ to yield after hydrolysis, primary alkyl amines (Eq. 4.12)[27].



(4.12)

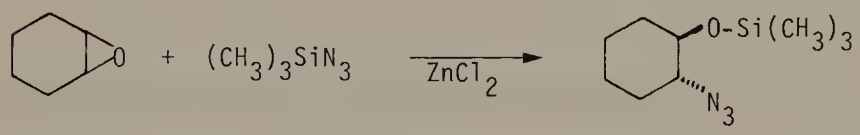
Finally, α-trimethylsilyloxyalkyl azides react as organic azides in thermal [2 + 3] cycloaddition reactions with polar acetylenes to yield substituted triazoles [24].



(4.13)

4.5 Reactions with Epoxides

Cyclohexene oxide reacts with TMS-N_3 in the presence of zinc chloride to yield *trans*-1-azido-2-trimethylsilyloxycyclohexane while styrene oxide yields 2-azido-1-trimethylsilyloxyphenylethane [24].

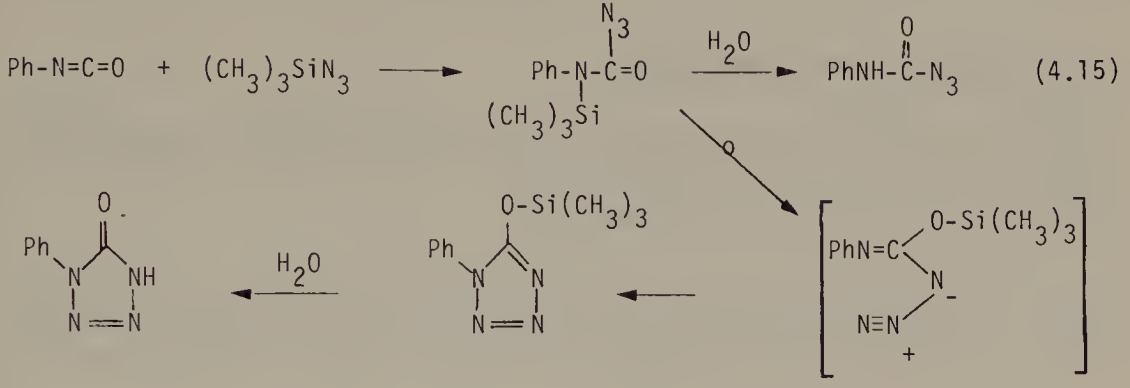


(4.14)

4.6 Reactions with Cumulenes

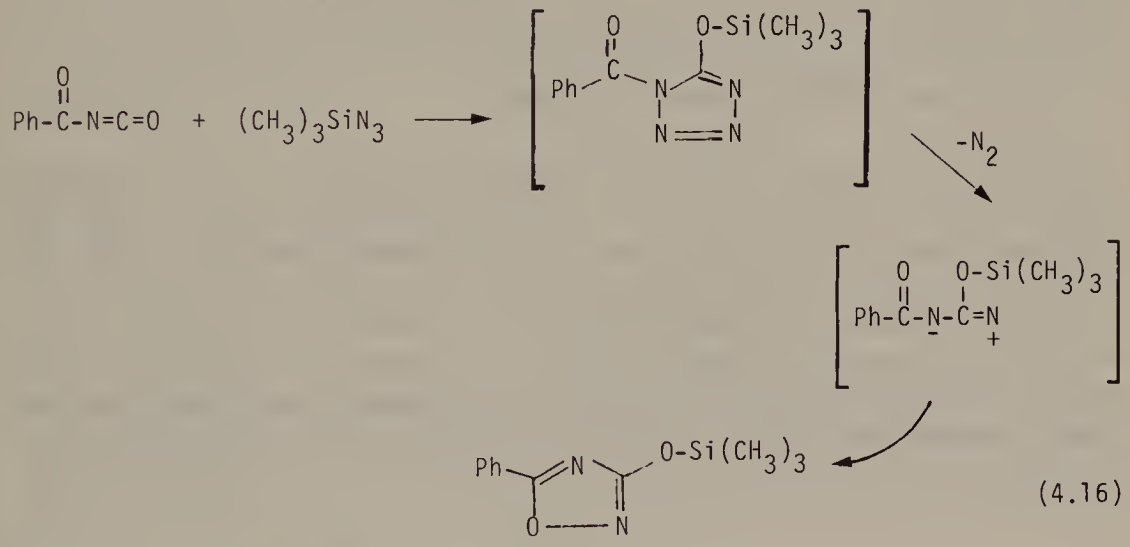
Phenyl isocyanate reacts with TMS-N_3 in a 1 : 1 ratio to give phenyl carbamoyl azide (32%) and 1-phenyl-5-(4 H)-tetrazolinones (62%) after hydrolysis as

outlined in Eq. 4.15. If a 1:2 ratio is used, only 1-phenyl-5-(4 H)-tetrazolinone is obtained [55].



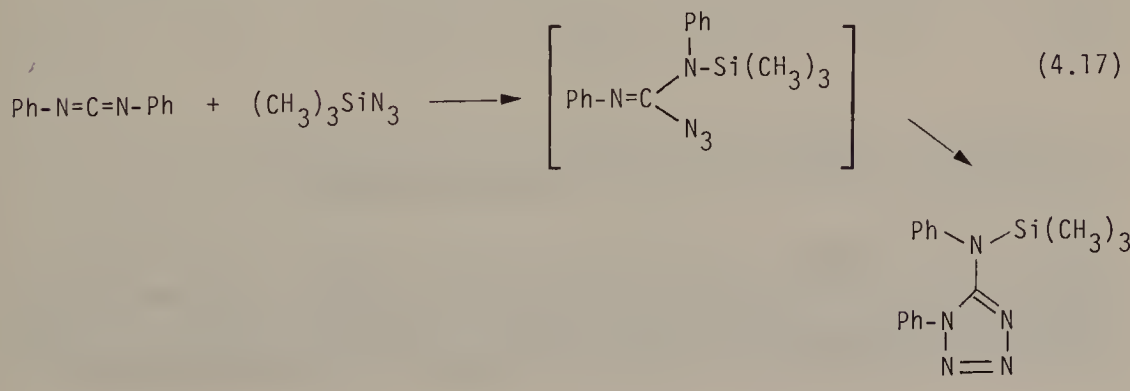
(4.15)

Benzoyl isocyanate reacts with TMS-N_3 in a similar manner to yield initially 1-benzoyl-5-trimethylsilyloxy-tetrazole. Loss of nitrogen yields a reactive 1,3-dipolar species which undergoes an intramolecular electrocyclic reaction with the carbonyl group to give 5-phenyl-3-trimethylsilyloxy-1,2,4-oxadiazole [55].



(4.16)

Carbodiimides react with TMS-N_3 in an analogous manner [55].



(4.17)

Phenyl isothiocyanate, on the other hand gives 5-anilino-1,2,3,4-thiotriazole [26].

4.7 Reactions with Phosphines

Organosilyl azides react with tertiary aliphatic and aromatic phosphines to yield N-organosilyl tertiary phosphineimines and nitrogen [9, 28]. These can be hydrolyzed to tertiary phosphineimines.

$$Et_3P + (CH_3)_3SiN_3 \longrightarrow Et_3P{=}N\text{-}Si(CH_3)_3 \xrightarrow{CH_3OH/H^+} Et_3P{=}N\text{-}H \qquad (4.18)$$

$$+ N_2$$

N-Trimethylsilyltriphenylphosphineimines react with acid chlorides or anhydrides to yield N-acyl triphenylphosphineimines [29].

$$Ph_3P{=}N\text{-}Si(CH_3)_3 + Ph\text{-}\overset{\overset{O}{\|}}{C}\text{-}Cl \longrightarrow Ph_3P{=}N\text{-}\overset{\overset{O}{\|}}{C}\text{-}Ph \qquad (4.19)$$

4.8 Reactions with Grignard Reagents

Aryl Grignard reagents react with triorganosilyl azides via two competing pathways. This first results in magnesium bromide N-silyl amides and nitrogen. These can be hydrolyzed to give primary amines (Eq. 4.20). The second gives magnesium azide bromide and a tetraorganosilane (Eq. 4.21) [30]. The ratio of these two processes depends on solvent, triorganosilyl azide, and the organometallic reagent. Addition is favored by less polar solvents, triphenylsilyl azide compared to TMS-N_3, and diphenyl magnesium rather than phenyl magnesium bromide. With phenyl lithium only substitution occurs [31, 32].

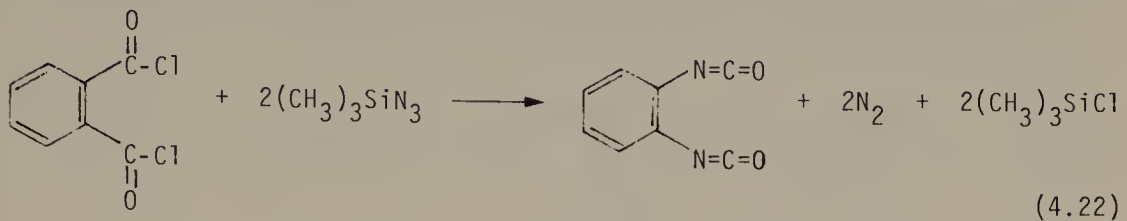
$$Ph_3SiN_3 + PhMgBr \longrightarrow Ph_3SiN(Ph)(MgBr) + N_2 \xrightarrow{H_2O} PhNH_2 \qquad (4.20)$$

$$Ph_3SiN_3 + PhMgBr \longrightarrow Ph_4Si + BrMgN_3 \qquad (4.21)$$

4.9 Reactions with Acid Chlorides or Anhydrides

TMS-N_3 reacts rapidly with both aliphatic and aromatic acid chlorides to yield TMS-Cl and the corresponding acyl azide which undergoes loss of nitrogen. Rearrangement of the acyl nitrene intermediate thus formed gives high yields of isocyanate. TMS-N_3 thus permits the Curtis degradation to

be carried out under mild neutral conditions (Eq. 4.22) [33, 34]. ω-Bromo aliphatic acid chlorides are readily converted to ω-bromo alkyl isocyanates [33, 35].

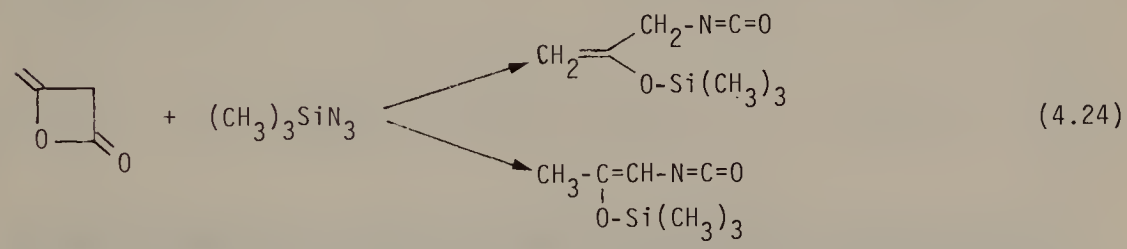


(4.22)

While alkenes undergo [2 + 3] cycloaddition reactions with TMS-N_3 [21, 22], TMS-N_3 reacts with acid chlorides more rapidly. This permits the conversion of unsaturated carboxylic chlorides to the corresponding isocyanates [33, 34].

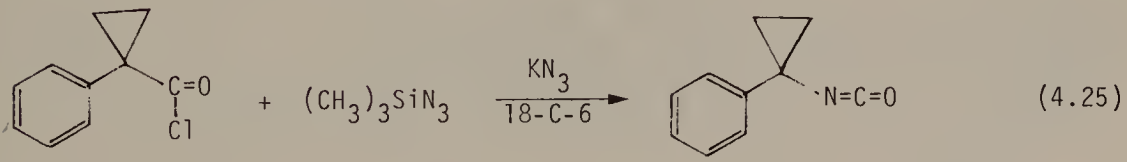
(4.23)

ω-Methoxycarbonyl alkanoyl chlorides can be converted to ω-methoxycarbonyl alkyl isocyanates in high yields [34]. On the other hand, reactive esters such as diketene and β-propiolactone react with TMS-N_3. Diketene yields a 1:1 mixture of 2-trimethylsilyloxy-2-propenyl isocyanate and 2-trimethylsilyloxy-1-propenyl isocyanate while β-propiolactone gives trimethylsilyl-3-azido propionate [36].



(4.24)

Cyclopropanoyl chloride reacts with diphenyldiazosilane to yield cyclopropyl isocyanate [37]. However, catalysis by potassium azide and 18-C-6 proved necessary in the reaction of 1-phenylcyclopropanoyl chloride with TMS-N_3 [38].



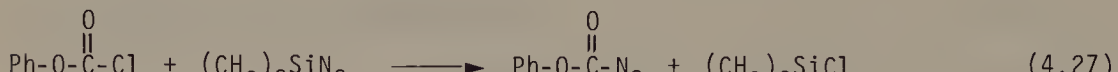
(4.25)

Even perfluoroalkyl acid chlorides have been smoothly converted to the perfluoroalkyl isocyanates [39, 40]

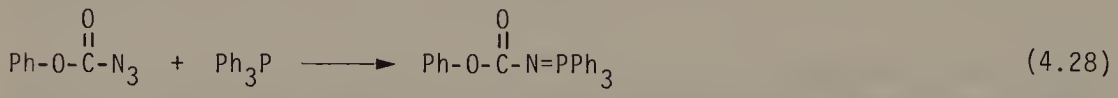
(4.26)

Aryl chloroformates react with TMS-N_3 in chloroform to yield aryl azido

formates. Pyridine catalyzes the reaction at room temperature (Eq. 4.27). At higher temperatures (90°) aryl azido formates decompose to yield the corresponding nitrenes which react with solvent. Aryl azido formates react with triphenylphosphine as outlined below (Eq. 4.28) [29].

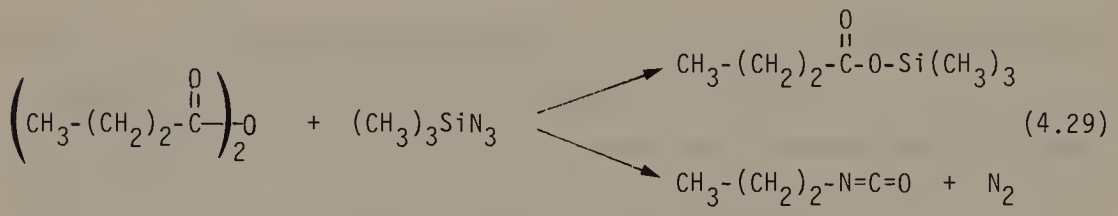


(4.27)



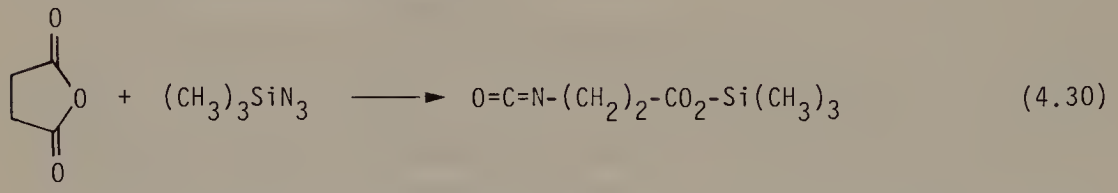
(4.28)

Anhydrides react with TMS-N_3 in a similar manner to acid chloride to give equal amounts of trimethylsilyl esters and isocyanates [34, 41, 42].



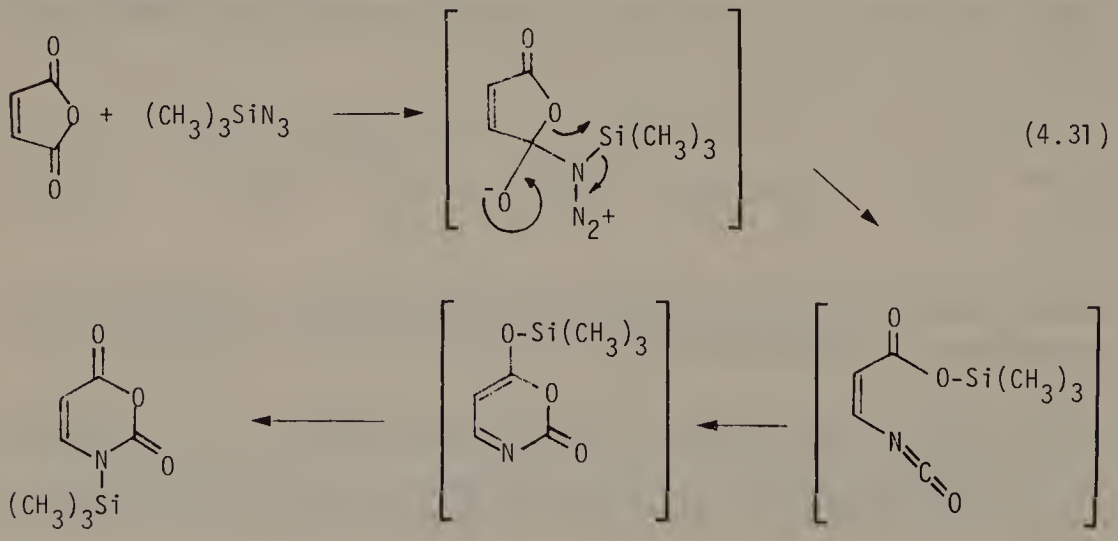
(4.29)

Cyclic saturated anhydrides react with TMS-N_3 to give ω-trimethylsilyloxycarbonyl alkyl isocyanates [42, 43].



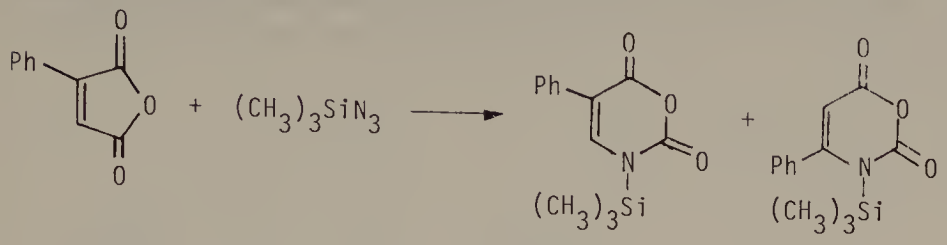
(4.30)

α,β-Unsaturated cyclic anhydrides such as maleic and phthalic anhydride react with TMS-N_3 to yield N-trimethylsilyl-1,3-oxazine-2,6-diones [41] as outlined below (Eq. 4.31).



(4.31)

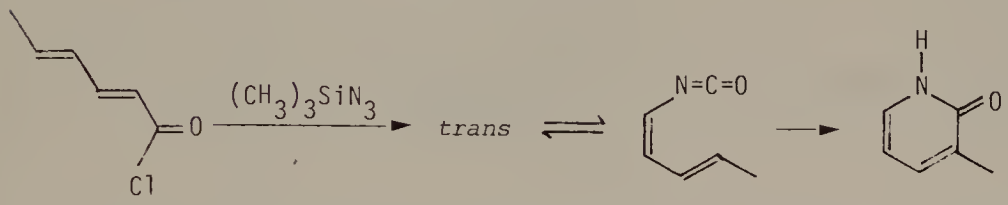
Halogen, alkyl and aryl substituted maleic anhydrides react with TMS-N_3 to yield mixtures of 4 and 5 substituted N-trimethylsilyl-1,3-oxazine-2,6-diones. Surprisingly, the 4-substituted isomers are always predominant [45-48].



(4.32)

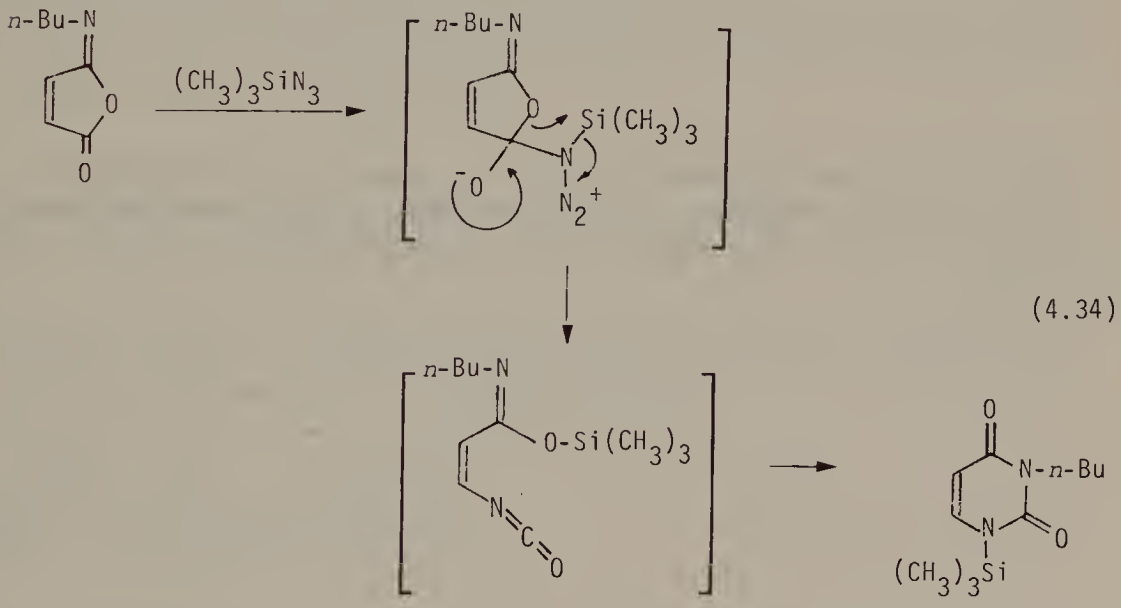
1:9

In a similar manner, *cis*-1,3-pentadienyl isocyanate, prepared by reaction of sorboyl chloride with TMS-N_3, undergoes intramolecular electrocyclic reaction to yield 3-methyl-2-pyridone [44].



(4.33)

N-Butyl isomaleimide reacts with TMS-N_3 to yield 3-butyl uracil after hydrolysis [41].



(4.34)

4.10 Reactions with Lead Tetraacetate or Phenyliodosodiacetate

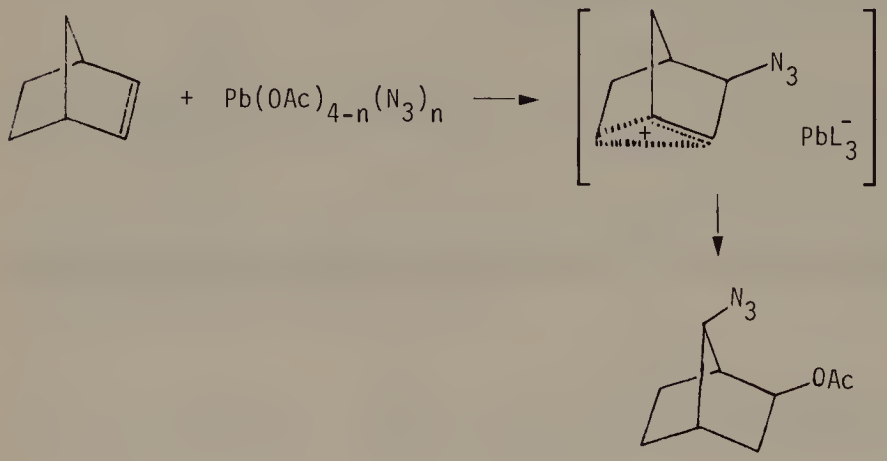
The reactivity of lead tetraacetate has been modified by reaction with TMS-N_3 [56]. An exchange reaction results in formation of species, such as lead diacetate diazide and acetoxytrimethylsilane.

$$Pb(OAc)_4 + 2(CH_3)_3SiN_3 \longrightarrow Pb(OAc)_2(N_3)_2 + 2(CH_3)_3SiOAc \qquad (4.35)$$

This system reacts with activated alkenes, such as styrene, to yield mixtures of 1,2-diazido phenylethane, 1-acetoxy-2-azido phenylethane and α-azidomethyl phenyl ketone. This regiospecificity suggests an intermediate benzylic carbocation [49].

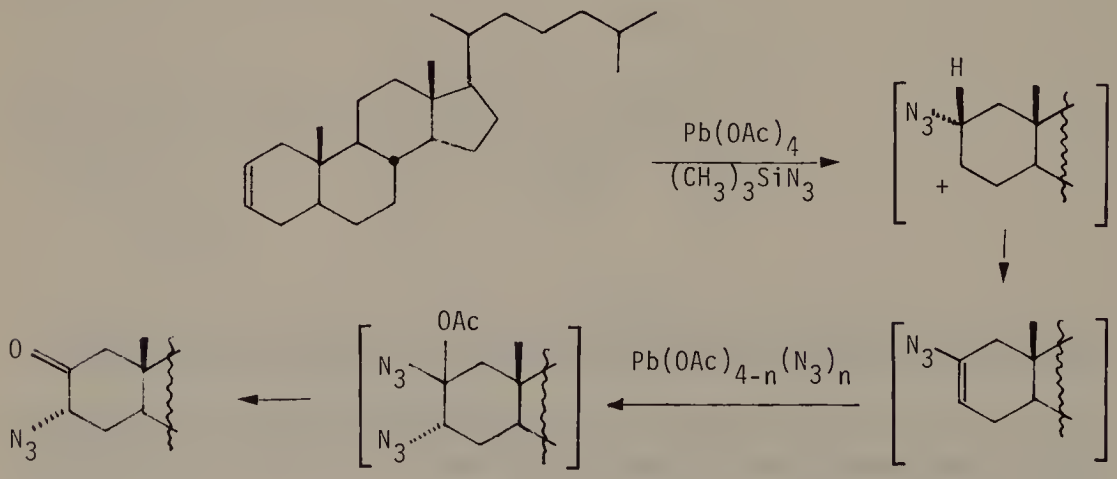
$$Ph\text{-}CH{=}CH_2 + Pb(OAc)_{4-n}(N_3)_n \longrightarrow Ph\text{-}\underset{N_3}{\overset{N_3}{CH}}\text{-}CH_2 + Ph\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_2N_3 + Ph\text{-}\underset{OAc}{CH}\text{-}CH_2\text{-}N_3 \qquad (4.36)$$

Oxidation of norbornene with this system yields 5-*exo*-acetoxy-7-*syn* azidonorbornane. This result is consistent with a carbocation intermediate [50].



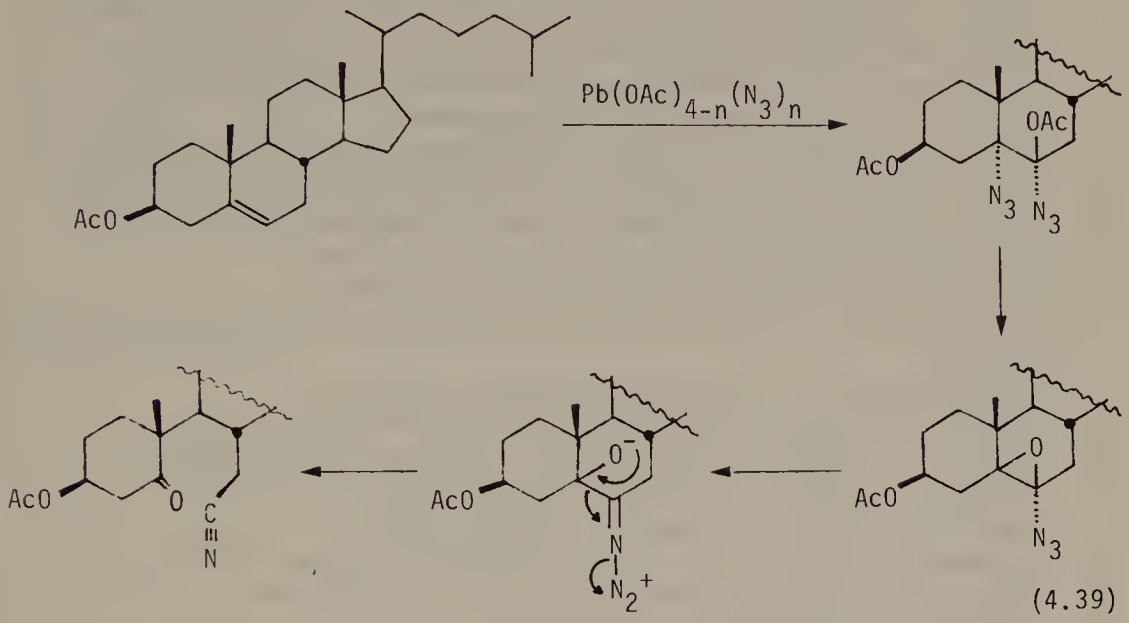
(4.37)

With disubstituted steroidal alkenes this system regiospecifically yields α-azido ketones. A mechanism, in which the initial α-azido carbocation loses a proton to form a vinyl azide which is further oxidized, has been suggested [51].



(4.38)

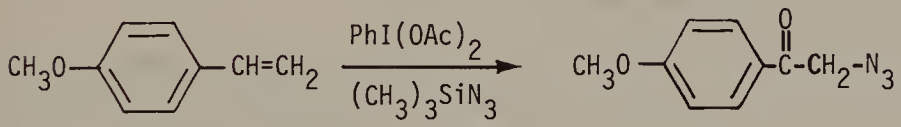
Trisubstituted steroidal alkenes undergo oxidative cleavage of the C–C double bond to yield ε-keto nitriles. A mechanism involving ionic intermediates has been proposed. An azido epoxide intermediate may be involved in framentation of the C–C double bond [52].



(4.39)

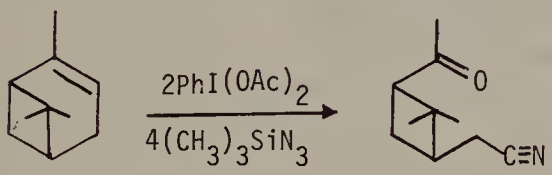
It should be noted that lead azides are explosive. This system has the obvious advantage of generating these species *in-situ.*

The reactivity of phenyliodosodiacetate has also been modified by equilibration with TMS-N_3. Phenyliodosodiacetate/TMS-N_3 reacts with disubstituted alkenes to give α-azido ketones [53].



(4.40)

With phenyliodosodiacetate/TMS-N_3, trisubstituted alkenes undergo oxidative cleavage of the C–C double bond to give ε-keto nitriles in slightly lower yields than with lead tetraacetate/TMS-N_3 [54].



(4.41)

An advantage of phenyliodosodiacetate/TMS-N_3 is that it is potentially less hazardous since no explosive lead azides can be formed.

References

1. Birkofer, L., Wegner, P.: Org. Syn. *50*, 107 (1970)
2. West, R., Thayer, J.S.: J. Am. Chem. Soc. *87*, 1763 (1962)
3. Thayer, J.S., West, R.: Inorg. Chem. *3*, 889 (1964)
4. Wiberg, N., Raschig, F., Sustmann, R.: Angew. Chem. Int. Ed. *1*, 335 (1962)
5. Reichle, W.T.: Inorg. Chem. *3*, 402 (1964)
6. Wolfsberger, W., Schmidbauer, H.: J. Organometal. Chem. *28*, 301 (1971)
7. Thayer, J.S., West, R.: Inorg. Chem. *3*, 406 (1964)
8. Washburne, S.S., Peterson, Jr., W.R.: J. Organometal. Chem. *33*, 153 (1971)
9. Wiberg, N., Raschig, F., Sustmann, R.: Angew. Chem. Int. Ed. *1*, 335 (1962)
10. Wiberg, N., Raschig, F., Sustmann, R.: Angew. Chem. Int. Ed. *1*, 551 (1962)
11. Ettenhuber, E., Rühlmann, K.: Chem. Ber. *101*, 743 (1968)
12. Sundermeyer, W.: Angew. Chem. Int. Ed. *1*, 595 (1962)
13. Peterson, Jr., W.R.: Reviews on Silicon, Germanium, Tin and Lead Compounds *I*, 193 (1974)
14. Petrach Systems, Inc., Bristol Pennsylvania, 19007, USA.
15. Birkhofer, L., Wegner, P.: Chem. Ber. *99*, 2512 (1966)
16. Birkofer, L., Ritter, A., Uhlenbrauck, H.: Chem. Ber. *96*, 3280 (1963)
17. Tanaka, Y., Velen, S.R., Miller, S.I.: Tetrahedron, *29*, 3271 (1973)
18. Birkofer, L., Wegner, P.: Chem. Ber. *100*, 3485 (1967)
19. Washburne, S.S., Peterson, Jr. W.R.: J. Organometal. Chem. *21*, 427 (1970)
20. Birkofer, L., Ritter, A., Richter, P.: Chem. Ber. *96*, 2750 (1963)
21. Scheiner, P.: Tetrahedron, *24*, 2757 (1968)
22. Stout, D.M., Takaya, T., Meyers, A.I.: J. Org. Chem. *40*, 563 (1975)
23. Birkofer, L., Müller, F., Kaiser, W.: Tetrahedron Lett. 2781 (1967)
24. Birkofer, L., Kaiser, W.: J. Lieligs. Ann. *1975*, 266
25. Evans, D.A., Truesdale, L.K.: Tetrahedron Lett. 4929 (1973)
26. Vorbrüggen, H., Krolikiewicz, K.: Synthesis 35 (1979)
27. Kyba, E.P., John, A.M.: Tetrahedron Lett. 2737 (1977)
28. Birkofer, L., Kim, S.M.: Chem. Ber. *97*, 2100 (1969)
29. Kricheldorf, H.R.: Synthesis 695 (1972)
30. Wiberg, N., Schmid, K.H., Joo, W.C.: Angew. Chem. Int. Ed. *4*, 90 (1965)
31. Wiberg, N., Joo, W.C.: J. Organometal. Chem. *22*, 333 (1970)
32. Wiberg, N., Joo, W.C., Olbert, P.: J. Organometal. Chem. *22*, 341 (1970)
33. Kricheldorf, H.R.: Synthesis 551 (1972)
34. Washburne, S.S., Peterson, Jr., W.R.: Syn. Commun. *2*, 227 (1972)
35. Kricheldorf, H.R.: Angew. Chem. Int. Ed. *18*, 689 (1979)
36. Kricheldorf, H.R.: Chem. Ber. *106*, 3765 (1973)
37. Kricheldorf, H.R., Regel, W.: Chem. Ber. *106*, 3757 (1973)
38. Warren, J.D., Press, J.B.: Syn. Commun. *10*, 107 (1980)
39. Peterson, Jr., W.R., Radell, J., Washburne, S.S.: J. Flourine Chem. *2*, 437 (1972/1973)
40. Lutz, W., Sundermeyer, W.: Chem. Ber. *112*, 2158 (1979)
41. Washburne, S.S., Peterson, Jr., W.R., Berman, D.A.: J. Org. Chem. *37*, 1738 (1972)
42. Kricheldorf, H.R.: Chem. Ber. *105*, 3958 (1972)
43. Kricheldorf, H.R., Regel, W.: Chem. Ber. *106*, 3753 (1973)
44. MacMillan, J.H., Washburne, S.S.: J. Org. Chem. *38*, 2982 (1973)
45. Warren, J.D., MacMillan, J.H., Washburne, S.S.: J. Org. Chem. *40*, 743 (1975)
46. Washburne, S.S., Lee, H.: J. Org. Chem. *43*, 2719 (1978)

47. Farkas, J., Fliegerova, O., Skoda, J.: Collect. Czech. Chem. Commun. *41*, 2059 (1976)
48. MacMillan, J.H., Washburne, S.S.: J. Heterocyclic Chem. *12*, 1215 (1975)
49. Zbiral, E., Kischa, K.: Tetrahedron Lett. 1167 (1969)
50. Zbiral, E., Stütz, A.: Tetrahedron, *27*, 4953 (1971)
51. Zbiral, E., Nestler, G.: Tetrahedron, *27*, 2293 (1971)
52. Zbiral, E., Nestler, G., Kischa, K.: Tetrahedron, *26*, 1427 (1970)
53. Ehrenfreund, E., Zbiral, E.: Tetrahedron, *28*, 1697 (1972)
54. Zbiral, E., Nestler, G.: Tetrahedron, *26*, 2945 (1970)
55. Tsuge, O., Urano, S., Oe, K.: J. Org. Chem. *45*, 5130 (1980)
56. Zbiral, E.: Synthesis, 285 (1972)

5 Silyl Nitronates

5.1 Introduction – Physical and Spectroscopic Properties

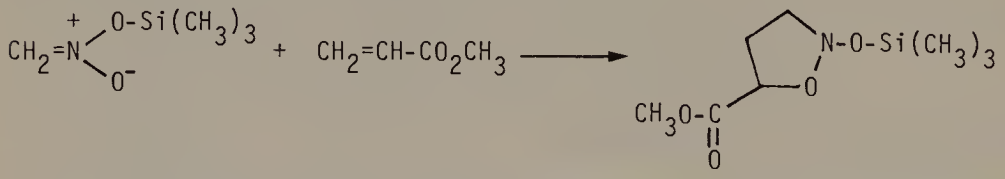
A limited amount of synthetic work has been carried out with silyl nitronates (silyl esters of nitronic acids). IR, UV, and variable temperature NMR spectra, as well as, a low temperature X-ray structure of a silyl nitronate have been reported [2]. The concentration independent variable temperature NMR behavior of these species is consistent with fast intramolecular migration of the silyl group between the two oxygens of the nitronate [2]. Although

(5.1)

silyl nitronates are more thermally stable than the corresponding alkyl nitronates [1, 2], they readily undergo hydrolysis to regenerate the nitroalkanes. *t*-Butyldimethylsilyl nitronates are less susceptible to hydrolysis than trimethylsilyl nitronates [2].

5.2 Cycloaddition Reactions

Silyl nitronates undergo thermal [2 + 3] cycloaddition reactions with alkenes substituted by electron withdrawing groups to yield regiospecifically 5-substituted-2-N-silyloxyisoxazolidines [1, 3, 4].



(5.2)

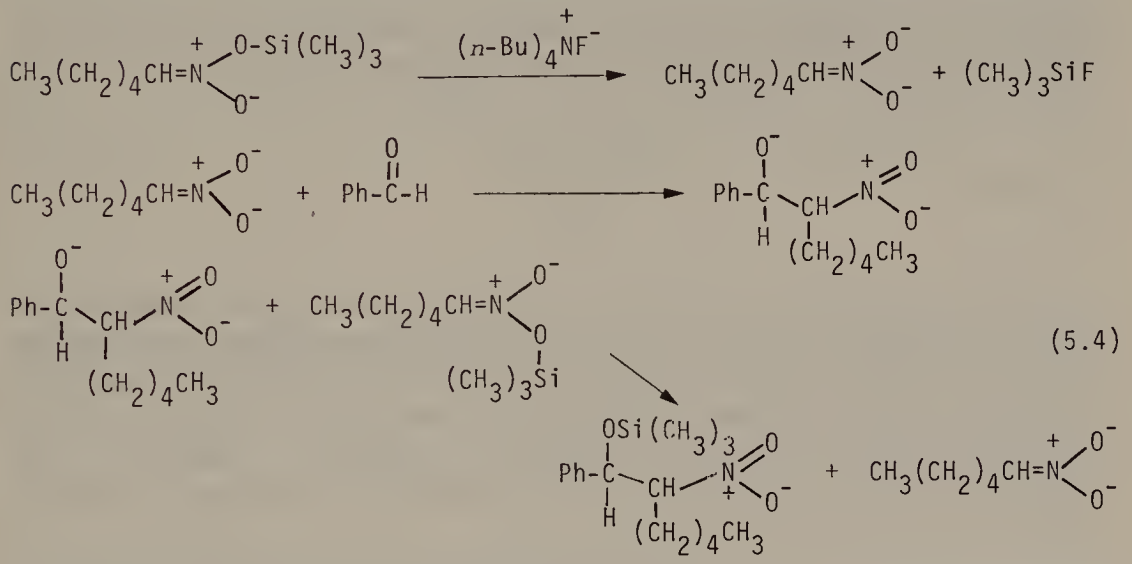
Such 2-N-silyloxyisoxazolidines undergo loss of trimethylsilanol on treatment with acid (HCl or TsOH [3]) or heat [4] to yield 2-isoxazolines [1, 3].

(5.3)

Treatment of 2-N-trimethylsilyloxyisoxazolidines with potassium methoxide in benzene, followed by acidic work-up, gives γ-hydroxy oximes [1, 4]. 2-N-Trimethylsilyloxyisoxazolidines have been converted to 3-substituted isoxazoles and 1,3-substituted pyrazoles [3].

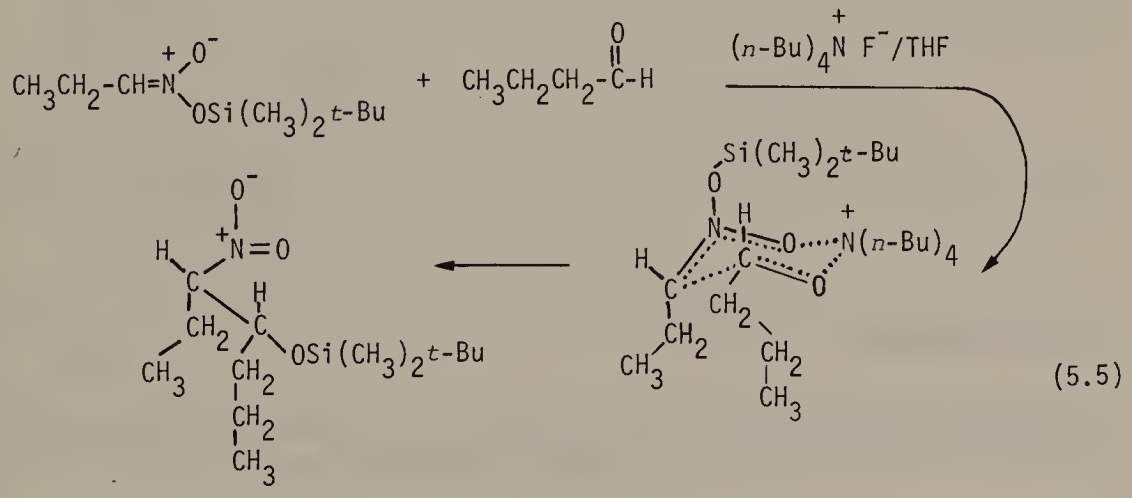
5.3 Nitro-Aldol Reactions

Silyl nitronates react with aliphatic and aromatic aldehydes under nucleophilic catalysis by TBAF to yield 2-silyloxy nitroalkanes [5]. The reaction may proceed by fluoride ion attack on the silyl group to yield the nitro stabilized carbanion. This adds to the aldehyde carbonyl group to give an alkoxide anion which attacks the silyl center of another silyl nitronate molecule. Transfer of the silyl group yields the product and regenerates the nitro stabilized carbanion.



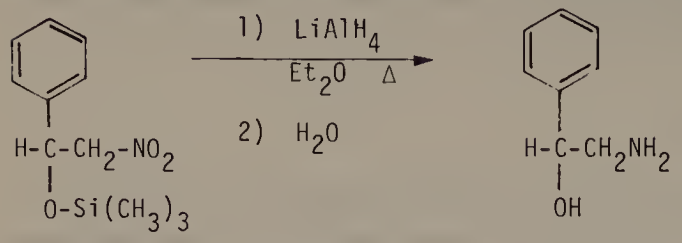
(5.4)

Fluoride ion catalyzed nitro-Aldol reactions of *t*-butyldimethylsilyl nitronates with aliphatic aldehydes proceed diastereoselectively to yield practically pure *erythro* isomers. Lower diastereoselectivity is observed with benzaldehyde. The preferential formation of one diastereomer is consistent with a chair transition state which minimizes steric interactions [6].



(5.5)

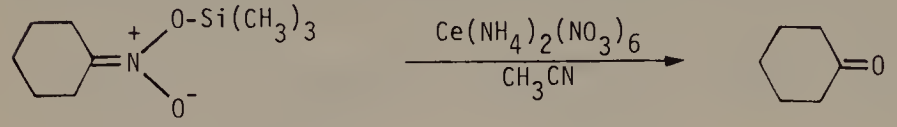
Unfortunately the reaction fails with ketones. 2-Silyloxy nitroalkanes are successfully reduced with $LiAlH_4$ to 2-amino alcohols [5].



(5.6)

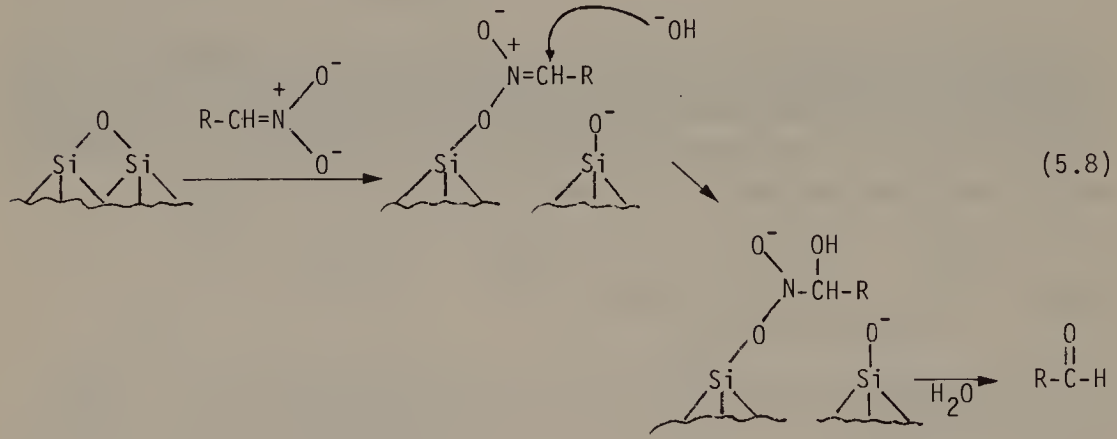
5.4 Oxidation

Secondary silyl nitronates undergo oxidative cleavage by ceric ammonium nitrate in acetonitrile to yield the corresponding ketones [7].



(5.7)

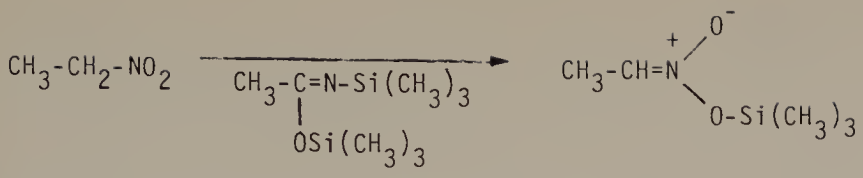
Nitroalkanes have been converted into the corresponding aldehydes or ketones by treatment with basic silica gel, followed by elution of the carbonyl compound with ether. The reaction may occur by interaction of the nitronate ion with the surface siloxane functionality of the silica gel to yield a surface bound silyl nitronate. Attack by absorbed hydroxide or silanoate on the silyl nitronate, converts it to the carbonyl compound and nitrogen oxides [8].



(5.8)

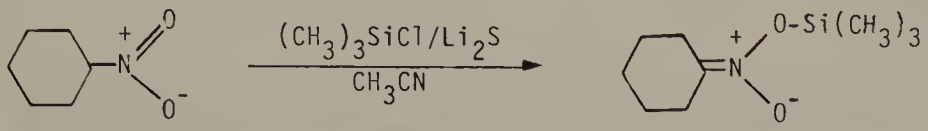
5.5 Preparation

Trimethylsilyl nitronates have been prepared by reaction of primary and secondary nitroalkanes with N,O-*bis*(trimethylsilyl)acetamide [1,3].



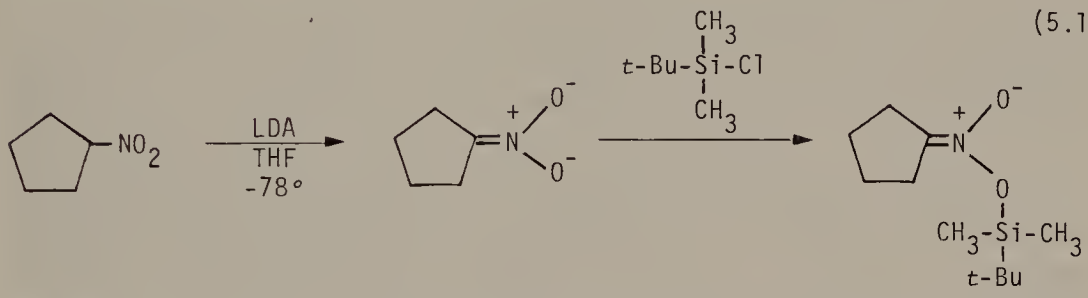
(5.9)

Nitromethane, -ethane and -propane can be converted to the corresponding trimethylsilyl nitronates by treatment with TMS-Cl and triethylamine [3]. Reaction of TMS-Cl with nitrocyclohexanes and lithium sulfide in acetonitrile provides an efficient route to the corresponding trimethylsilyl nitronates [9].



(5.10)

Perhaps the most general method involves reaction of the lithium nitronates, generated by treatment of primary and secondary nitroalkanes with LDA in THF at −78°, with the desired trialkylchlorosilane. *t*-Butyldimethylsilyl nitronates, as well as trimethylsilyl nitronates, have been prepared by this method [2].



(5.11)

Since silyl nitronates are now readily available, new chemistry with these interesting compounds may be forthcoming.

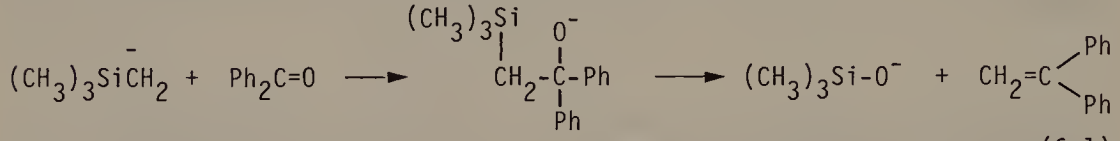
References

1. Kashutina, M.V., Ioffe, S.L., Tartakovskii, V.A.: Dokl. Akad. Nauk. SSSR, *218*, 109 (1974)
2. Colvin, E.W., Beck, A.K., Bastani, B., Seebach, D., Kai, Y., Dunitz, J.D.: Helv. Chim. Acta. *63*, 697 (1980)
3. Sharma, S.C., Torssell, K.: Acta, Chem. Scand. *B33*, 379 (1979)
4. Torssell, K., Zeuthen, O.: Acta. Chem. Scand. *B32*, 118 (1978)
5. Colvin, E.W., Seebach, D.: J. Chem. Soc. Chem. Commun. 689 (1978)
6. Seebach, D., Beck, A.K., Lehr, F., Weller, T., Colvin, E.: Angew. Chem. Int. Ed. *20*, 397 (1981)
7. Olah, G.A., Gupta, B.G.B.: Synthesis, 44 (1980)
8. Keinan, E., Mazur, Y.: J. Am. Chem. Soc. *99*, 3861 (1977)
9. Olah, G.A., Gupta, G.B.G., Narang, S.C., Malhotra, R.: J. Org. Chem. *44*, 4272 (1979)

6 Peterson Reaction

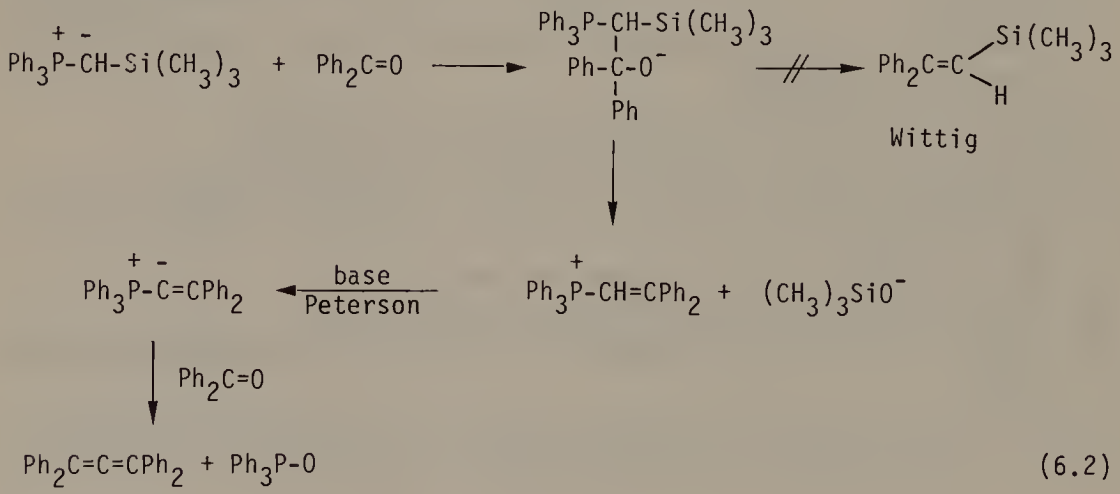
6.1 Introduction

The Silyl-Wittig or Peterson reaction involves addition of a stoichiometric quantity of an α-silyl carbanion to the carbonyl group of a ketone or aldehyde. This yields a β-silyl alkoxide which decomposes by alkoxide attack on silicon to yield an alkene and a silanoate. The ease of this decomposition is dependent on the cation. Potassium and sodium alkoxides decompose far more readily than the more covalent magnesium alkoxides [1].

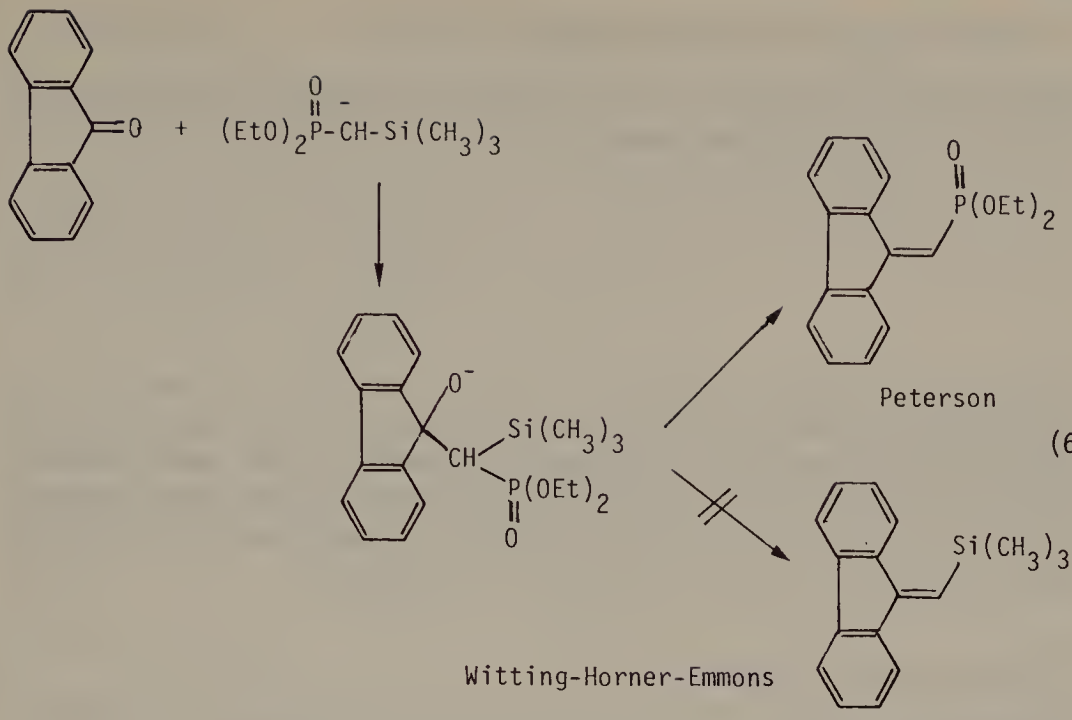


(6.1)

The similarity of this reaction sequence to the Wittig reaction is apparent: α-trimethylsilyl carbanions are analogous to ylids, while β-trimethylsilyl alkoxides are similar to betaines. Finally the trimethylsilanoate may be compared to triphenylphosphine oxide. The driving force for this reaction results from the formation of a strong Si–O single bond. In fact, given a choice the alkoxide oxygen prefers to attack silicon rather than phosphorous. The Peterson reaction occurs in preference to both the Wittig [2] (Eq. 6.2) and the Wittig-Horner-Emmons reactions (Eq. 6.3) [3]. This permits synthesis of vinyl phosphonates.

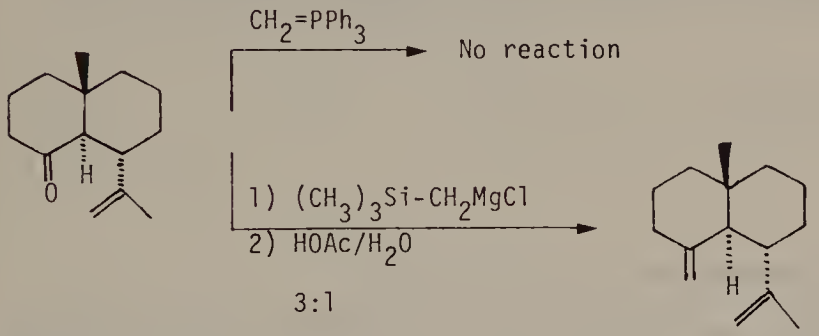


(6.2)



(6.3)

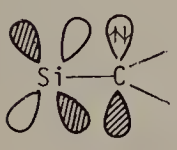
The Peterson reaction is successful with enolizable ketones while the Wittig reaction often fails. This is because alkylidenetriphenylphosphoranes may react as strong bases with enolizable ketones rather than undergoing nucleophilic addition to form betaines. α-Trimethylsilyl carbanions, on the other hand, add to such ketones as nucleophiles [4].



(6.4)

6.2 α-Silyl Organometallics

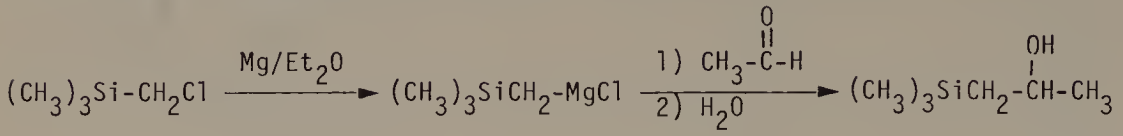
The synthetic utility of the Peterson reaction has generated interest in α-silyl organometallics [5]. These have been generated in a number of ways. The ease of formation and the stability of carbanions alpha to silicon have been attributed to delocalization of the extra electron density centered in a 2p orbital on carbon into an empty 3d orbital on silicon.



(6.5)

A. α-Silyl Grignard and Organolithium Reagents

α-Haloalkyltrimethylsilanes or α-haloalkyltriphenylsilanes can be converted to Grignard or organolithium reagents [9, 10].

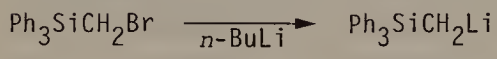


(6.6)

α-Trimethylsilyl Grignard reagents will add to ketones or aldehydes to yield after hydrolysis β-hydroxyalkyltrimethylsilanes. This occurs because the intermediate magnesium β-trimethylsilyl alkoxides do not easily undergo elimination [1]. Treatment of β-hydroxyalkyltrimethylsilanes with sodium or potassium hydride converts them to sodium or potassium β-trimethylsilyl alkoxides which lose trimethylsilanoate and form alkenes.

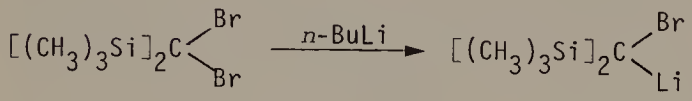
B. Halogen-Metal Exchange

Halogen-metal exchange between bromomethyltriphenylsilane and *n*-butyl lithium yields triphenylsilylmethyl lithium [11].



(6.7)

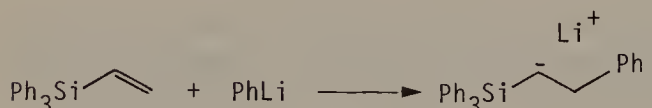
Halogen-metal exchange has also been used to generate bromo-*bis*(trimethylsilyl)methyl lithium [12] and *tris*(trimethylsilyl)methyl lithium [13].



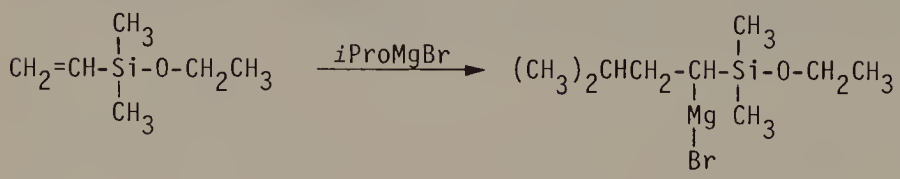
(6.8)

C. Addition of Organometallics to Vinyl Silanes

While Grignard reagents and organolithium compounds will not, in general, add to isolated C–C double bonds, they will add to the C–C double bond of vinyl silanes to form a carbanion adjacent to silicon [14–18].



(6.9)



(6.10)

D. Metallation

While tetramethylsilane can be metallated by *n*-butyl lithium/TMEDA [6–8], the reaction is more facile when a second carbanion stabilizing group is present. *bis*(Trimethylsilyl)methane [19] and *tris*(trimethylsilyl)methane [13, 19] are easily metallated to yield carbanions stabilized by two and three adjacent trimethylsilyl groups respectively.

$$[(CH_3)_3Si]_2CH_2 \xrightarrow[\substack{t\text{-BuLi}\\ -78°C}]{\text{THF/HMPT}} [(CH_3)_3Si]_2\bar{C}HLi^+ \qquad (6.11)$$

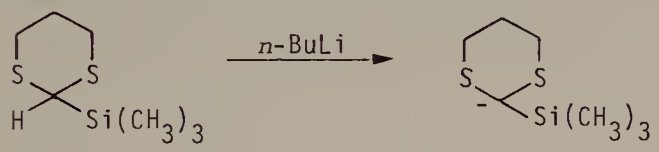
Adjacent aryl, ester and nitrile groups stabilize carbanions. Both benzyltriphenylsilane [20] and benzyltrimethylsilane [21] are readily metallated by reaction with *n*-butyl lithium. 2-(Trimethylsilylmethyl)pyridine is easily deprotonated by LDA in THF at −78 °C [22, 23].

(6.12)

t-Butyl and ethyl esters of trimethylsilylacetic acid [24–27] and trimethylsilylacetonitrile [28, 29] can be converted to α-silyl carbanions by treatment with LDA.

$$(CH_3)_3SiCH_2CO_2\text{-}t\text{-}Bu \xrightarrow[-78°]{\text{LDA}} (CH_3)_3Si\underset{\substack{|\\ Li^+}}{\bar{C}}H\text{-}CO_2\text{-}t\text{-}Bu \qquad (6.13)$$

2-Trimethylsilyl-1,3-dithiane and other such trimethylsilyl-substituted thioacetals are easily metallated [30].



(6.14)

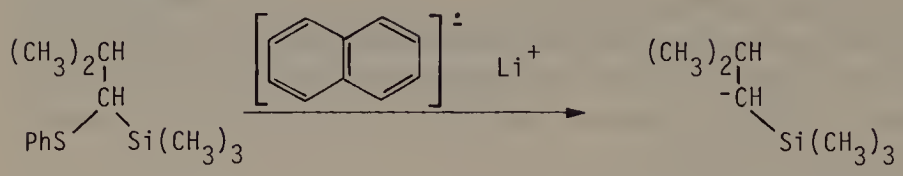
E. Displacement Reactions

α-Trimethylsilyl carbanions have been formed by displacement reactions. *tetrakis*(Trimethylsilyl)methane reacts with sodium methoxide in HMPT to form *tris*(trimethylsilyl)methyl sodium and methoxytrimethylsilane [31]. The driving force for this reaction may be the formation of the strong Si−O single bond of methoxytrimethylsilane. Similar reactions occur with *tris*(trimethylsilyl)methane and *bis*(trimethylsilyl)methane, to yield the corresponding α-silyl carbanions via loss of one trimethylsilyl group as methoxytrimethylsilane [31].

$$[(CH_3)_3Si]_2CH_2 \xrightarrow[\text{HMPT}]{CH_3O^-Na^+} (CH_3)_3SiCH_2^-Na^+ + (CH_3)_3SiOCH_3 \qquad (6.15)$$

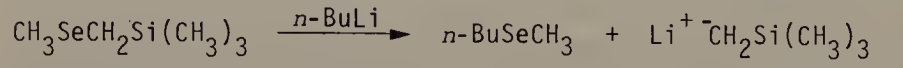
Displacement of phenylthiolate from 1-phenylthio-1-trimethylsilylalkanes

by reaction with lithium naphthalide yields α-trimethylsilyl alkyl lithium reagents [32].



(6.16)

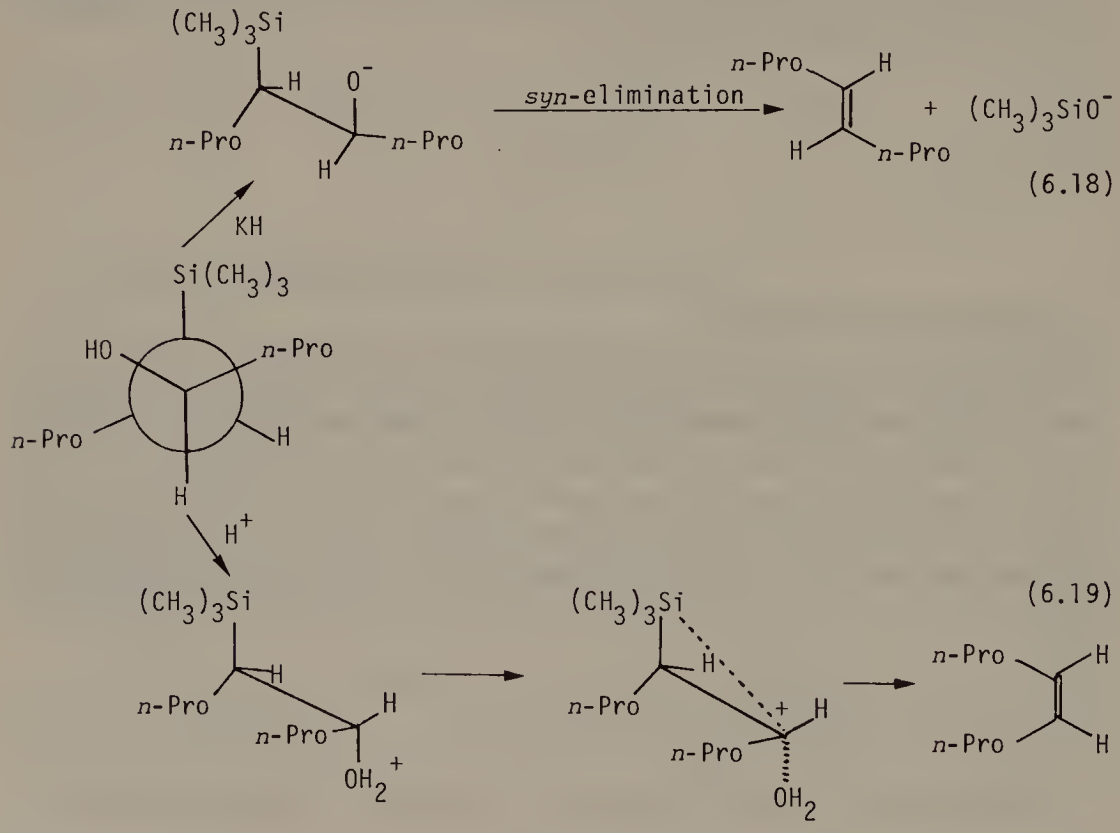
Similarly, displacement of methyl selenide from methyl trimethylsilylmethyl selenide by *n*-butyl lithium yields trimethylsilylmethyl lithium [33].



(6.17)

6.3 Stereochemical Control of Elimination

The Peterson reaction is of synthetic interest, not only due to the wide variety of alkenes which can be prepared, but also because the reaction can be controlled to yield either *cis* or *trans* alkenes. Treatment of *threo* 5-trimethylsilyloctan-4-ol with potassium hydride in THF yields exclusively *trans*-4-octene via a *syn*-elimination (Eq. 6.18). On the other hand, β-hydroxyalkylsilanes also undergo elimination under acidic conditions [9]. Treatment of this diastereomer with a catalytic amount of sulfuric acid in THF or $BF_3 \cdot OEt_2$ in methylene chloride, yields *cis*-4-octene via an *anti*-elimination (Eq. 6.19) [34, 35]. Trimethylsilyl groups stabilize developing beta carbocation centers when they can assume a *trans*-diaxial relationship to the leaving group (see Chapter 7).



(6.18)

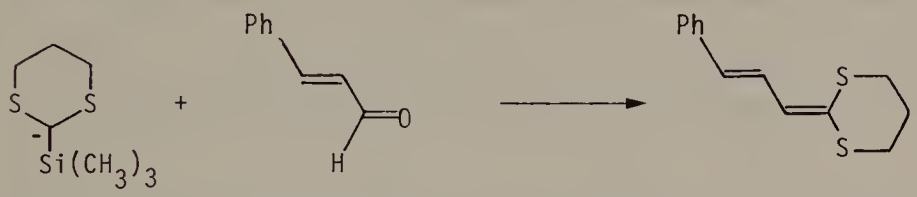
(6.19)

The necessary *threo*-5-trimethylsilyloctan-4-ol is prepared by reduction of 5-trimethylsilyloctan-4-one with DIBAL in pentane at −120°C. This stereoselectivity is predicted by Cram's rule [36] and the assumption that the trimethylsilyl group is larger than the *n*-propyl group.

6.4 Preparation of Substituted Alkenes

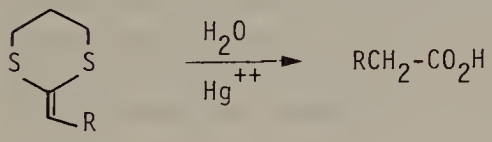
A. Ketene Thioacetals

The Peterson reaction has been used to prepare ketene thioacetals [37–39]. α-Trimethylsilyl carbanions stabilized by two adjacent sulfur atoms are easily formed by metallation reactions. For example, 2-trimethylsilyl-1,3-dithiane reacts with *n*-butyl lithium to yield 2-lithio-2-trimethylsilyl-1,3-dithiane [42, 43]. Reaction of this α-silyl carbanion with ketones or aldehydes yields ketene thioacetals. With α,β-unsaturated ketones and aldehydes, only 1,2-addition is observed (Eq. 6.20) [30, 40, 44, 45]. *bis*-(Methylmercapto)methane. *bis*-(phenylmercapto)methane, and *bis*(phenylseleno)methane react similarly [19, 40, 41].



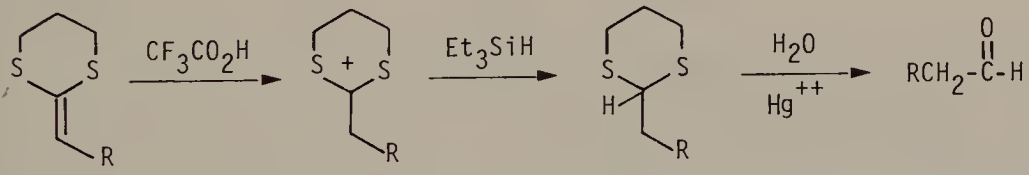
(6.20)

Ketene thioacetals are valuable synthetic intermediates. They can be hydrolyzed to yield carboxylic acids [39].



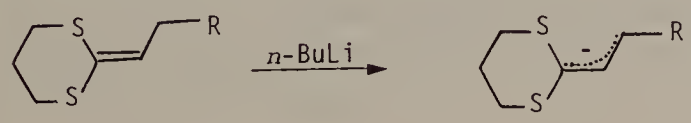
(6.21)

The C–C double bond of ketene thioacetals can be reduced by treatment with triethylsilane and trifluoracetic acid to yield thioacetals [46] (see Chapter 17).



(6.22)

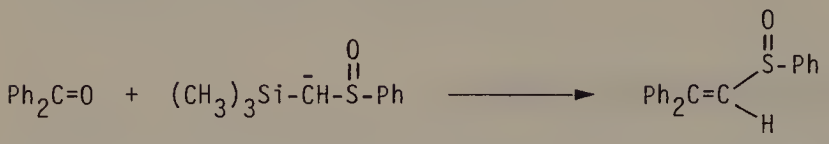
Ketene thioacetals can be metallated with *n*-butyl lithium to yield allylic carbanions [47, 48].



(6.23)

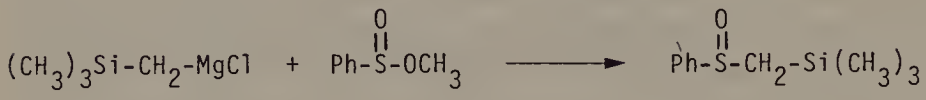
B. Vinyl Sulfoxides

Trimethylsilylmethyl phenyl sulfoxide can be metallated to yield 1-trimethylsilyl-1-phenylsulfinylmethyl lithium which reacts with ketones or aldehydes to yield 1-phenylsulfinyl alkenes [49].



(6.24)

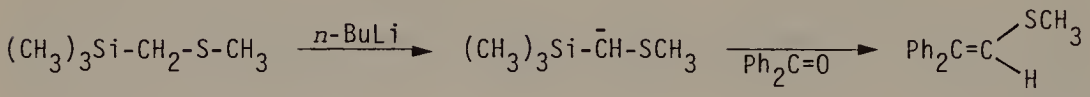
The necessary sulfoxide was prepared by reaction of trimethylsilylmethyl magnesium chloride with methyl benzene sulfinate [50].



(6.25)

C. Thio Enol Ethers

Metallation of trimethylsilylmethyl methyl sulfide yields a carbanion which reacts with ketones or aldehydes to yield methyl vinyl sulfides [1, 3].

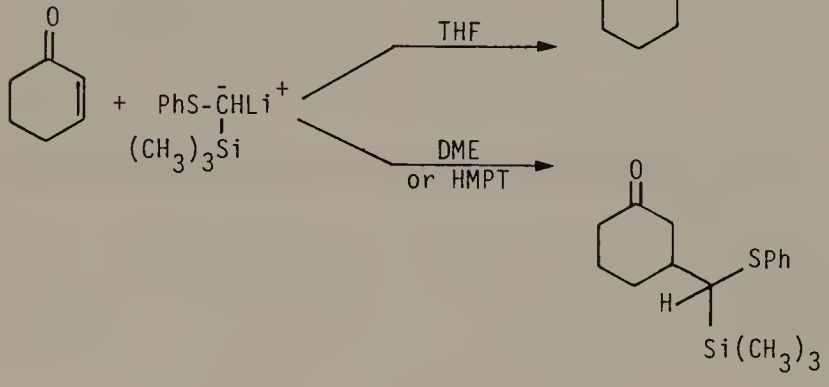


(6.26)

Thio enol ethers can be hydrolyzed to ketones, albeit under vigorous conditions [51].

Phenylthio trimethylsilylmethyl lithium reacts with N,N-dialkyl benzamides to yield 2-phenylthio-1-dialkylamino alkenes [52]. This lithium reagent reacts with 2-cyclohexenone in THF to give the expected vinyl sulfide (Eq. 6.27). On the other hand, in HMPT or DME, 1,4-conjugate addition occurs (Eq. 6.28) [53].

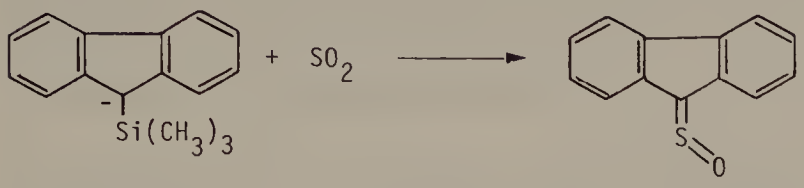
(6.27)



(6.28)

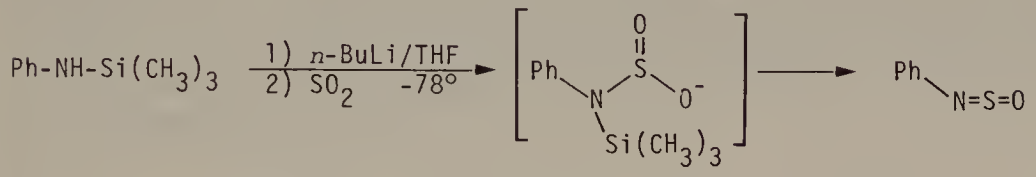
D. Sulfines

The Peterson reaction has been used to prepare sulfines. α-Trimethylsilyl carbanions add to a S–O double bond of SO_2. Loss of trimethylsilanoate results in formation of a S–C double bond [54, 55].



(6.29)

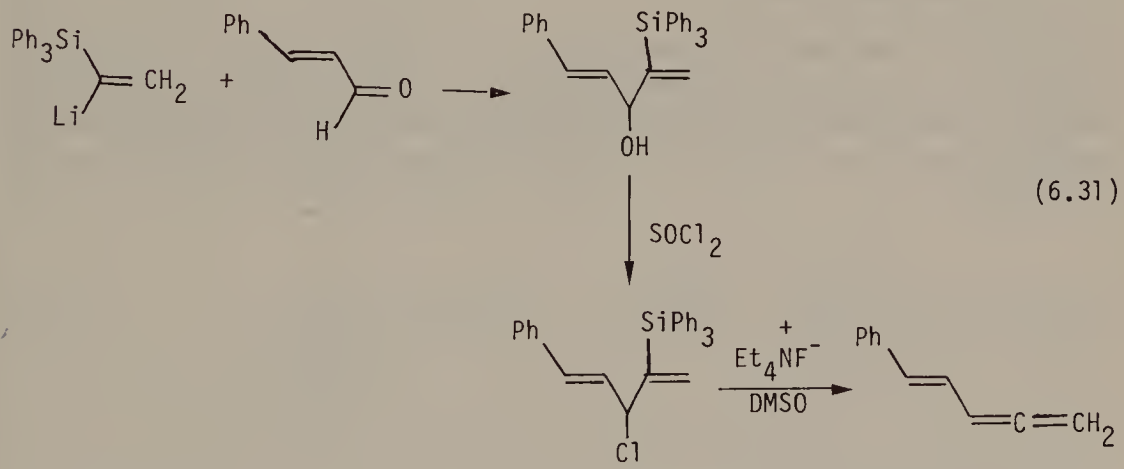
N-Sulfinylamines have also been prepared by reaction of lithium N-aryl-N-trimethylsilylamides with SO_2 in THF [56].



(6.30)

E. Allenes

Allenes have also been prepared by the Peterson reaction. α-Bromotriphenylsilylethylene undergoes halogen-metal exchange with *n*-butyl lithium to yield α-lithio-triphenylsilylethylene. This reacts with ketones and aldehydes to yield 2-triphenylsilyl substituted allylic alcohols. Unlike other β-hydroxyalkylsilanes, these do not undergo facile elimination on treatment with either acid or base [57]. However, reaction of the alcohol with thionyl chloride gives an allylic chloride which loses the elements of triphenylchlorosilane when treated with tetraethylammonium fluoride in DMSO [58].



(6.31)

The driving force for this elimination is the formation of a strong Si–F bond. Similar results are obtained with α-lithio trimethylsilylethylene generated by halogen-metal exchange of α-bromo trimethylsilylethylene with *t*-butyl lithium at −78° [59].

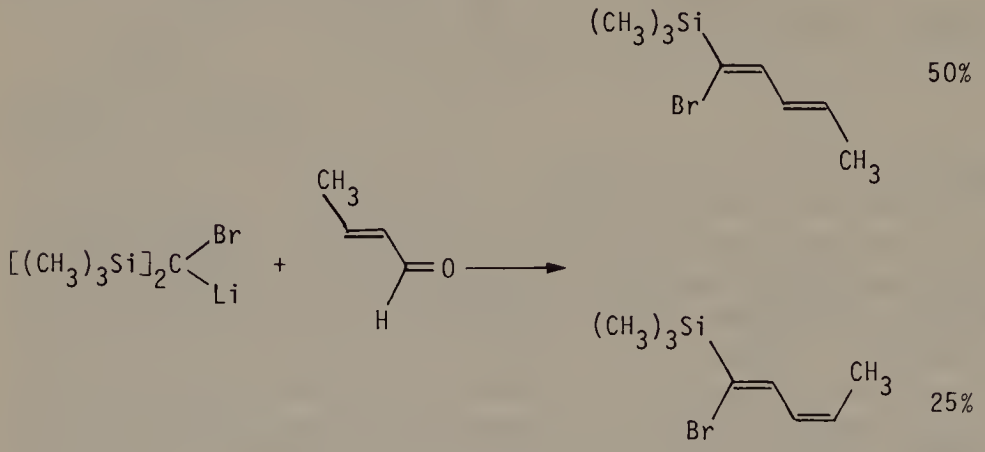
F. Vinyl Silanes (see Chapter 7)

Metallation of *tris*(trimethylsilyl)methane with methyl lithium yields a carbanion which reacts with formaldehyde to give 1,1-*bis*(trimethylsilyl)ethylene [19, 60].

$$[(CH_3)_3Si]_3C^-Li^+ + CH_2{=}O \longrightarrow [(CH_3)_3Si]_2C{=}CH_2 \qquad (6.32)$$

bis-(Trimethylsilyl)methyl sodium reacts with benzophenone to yield 1,1-diphenyl-2-trimethylsilyl ethylene [31].

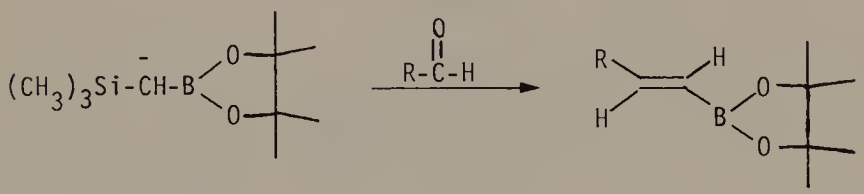
One of the few cases where the Peterson reaction fails involves bromo-*bis*-(trimethylsilyl)methyl lithium. This reagent reacts normally with aldehydes to yield the expected α-bromo-trimethylsilylalkenes. However, it fails to add to enolizable ketones and reacts with benzophenone to give 1,1-*bis*-(trimethylsilyl)-2,2-diphenylethylene oxide [12].



(6.33)

G. Vinyl Boronic Esters

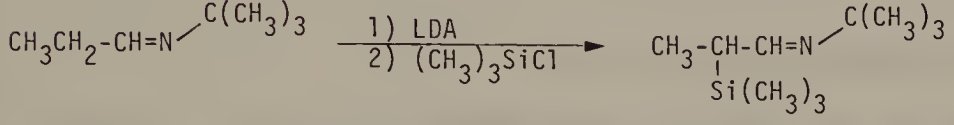
The Peterson reaction has been utilized to prepare vinyl boronic esters. Metallation of pinacol trimethylsilylmethane boronate with the sterically hindered base, lithium 2,2,6,6-tetramethylpiperidide, gives a carbanion which reacts with ketones or aldehydes to yield the desired pinacol alkenyl boronic esters [61].



(6.34)

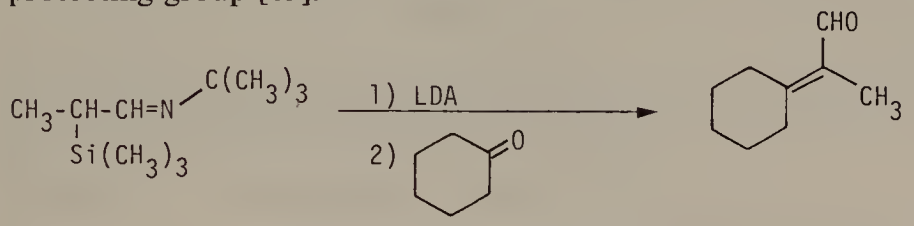
H. Cross Aldol Reaction—α,β-Unsaturated Aldehydes

The formal "cross-aldol" coupling of two aldehydes, RCHO and $R'CH_2CHO$, to yield an α,β-unsaturated aldehyde $RCH{=}CR'{-}CHO$ has been achieved in several ways [62–64]. The Peterson reaction provides a general method to accomplish this transformation. The necessary precursors, α-trimethylsilyl aldimines have been prepared by metallation of aldehyde-*t*-butylimines with LDA followed by addition of TMS-Cl.



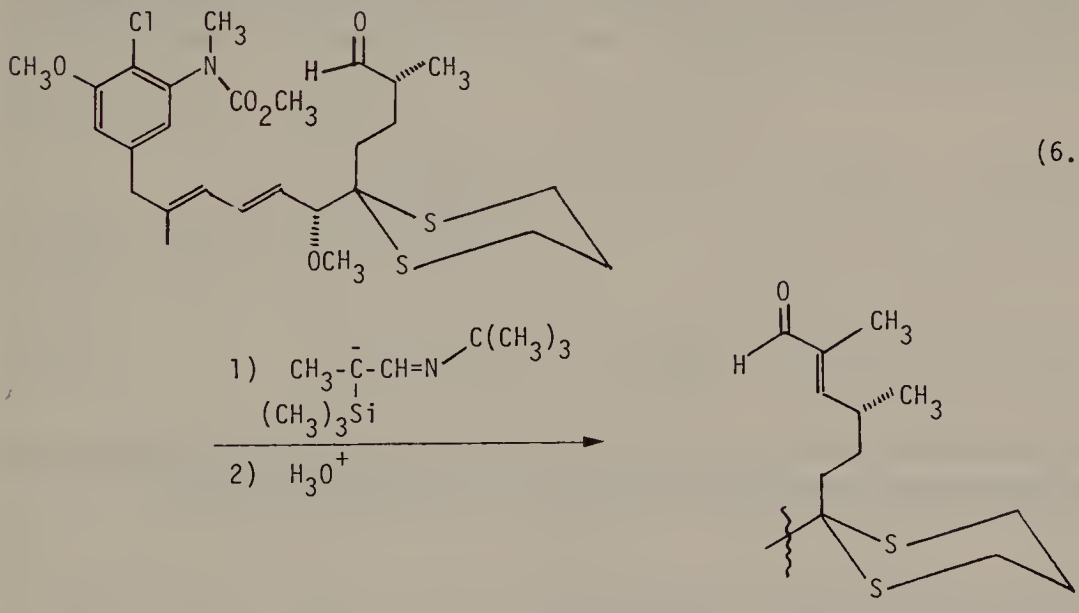
(6.35)

Metallation of α-trimethylsilylaldehyde-*t*-butylimines with LDA occurs readily. This carbanion reacts with ketones or aldehydes to yield the desired α,β-unsaturated aldehydes after mild acidic hydrolysis of the *t*-butyl imine protecting group [65].



(6.36)

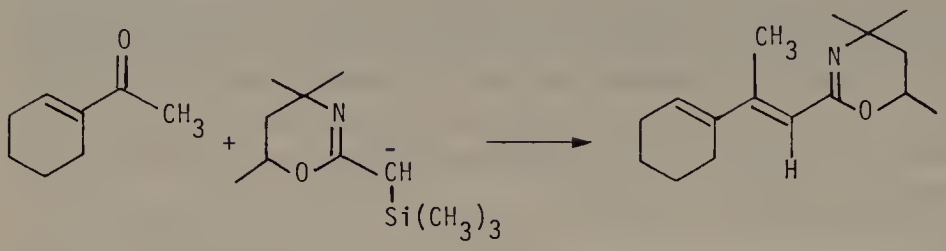
This methodology was recently utilized in Corey's synthesis of (±) N-methyl-maysenine [66, 67].



(6.37)

Metallation of 2-trimethylsilylmethyl-4,4,6-trimethyl-5,6-dihydro-1,3-oxazine with *t*-butyl lithium followed by reaction with ketones or aldehydes

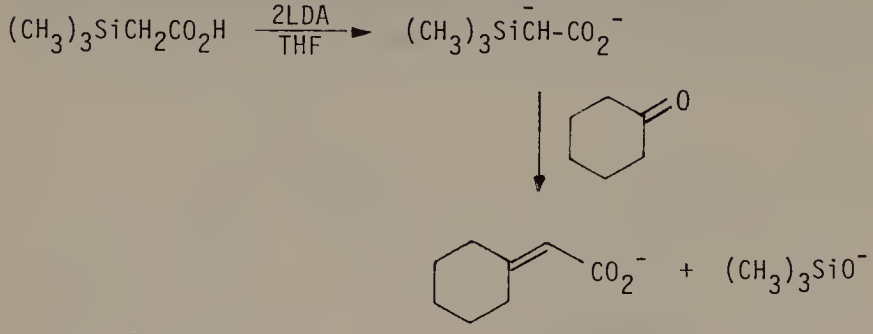
yields α,β-unsaturated oxazines [68]. These can be hydrolyzed to α,β-unsaturated aldehydes.



(6.38)

I. α,β-Unsaturated Carboxylic Acids

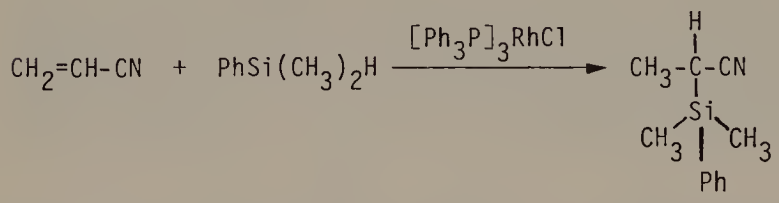
α,β-Unsaturated carboxylic acids can be prepared by reaction of the dianion of trimethylsilyl acetic acid with ketones or aldehydes [69].



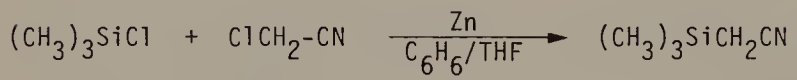
(6.39)

J. α,β-Unsaturated Nitriles

α-Trimethylsilylnitriles have been prepared by $[Ph_3P]_3RhCl$ catalyzed hydrosilation of α,β-unsaturated nitriles (Eq. 6.40) [28]. On the other hand, reaction of TMS-Cl with chloroacetonitrile and zinc in benzene/THF yields trimethylsilylacetonitrile (Eq. 6.41) [29].

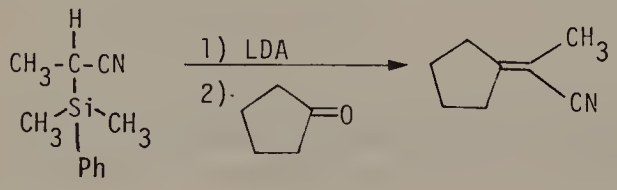


(6.40)



(6.41)

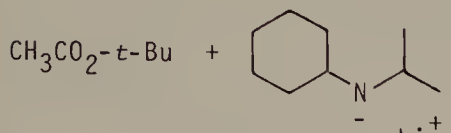
Deprotonation of these α-silylnitriles with LDA gives carbanions which react with both ketones and aldehydes to yield α,β-unsaturated nitriles.



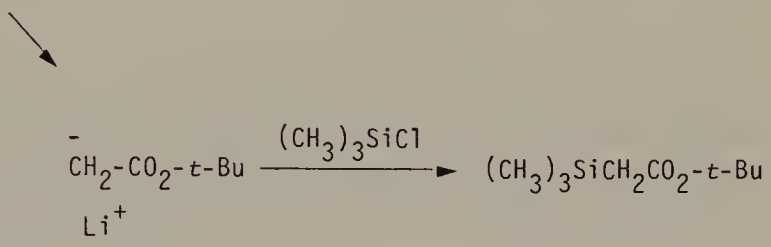
(6.42)

K. α,β-Unsaturated Esters

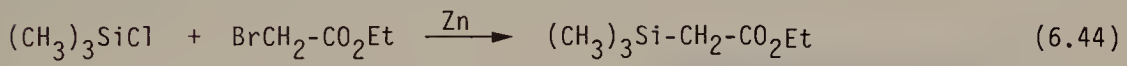
The synthesis of α,β-unsaturated esters by the Peterson reaction requires α-trimethylsilyl esters as precursors. *t*-Butyl trimethylsilylacetate can be prepared by reaction of TMS-Cl with the lithium enolate of *t*-butyl acetate in THF at −78°C [70].



(6.43)

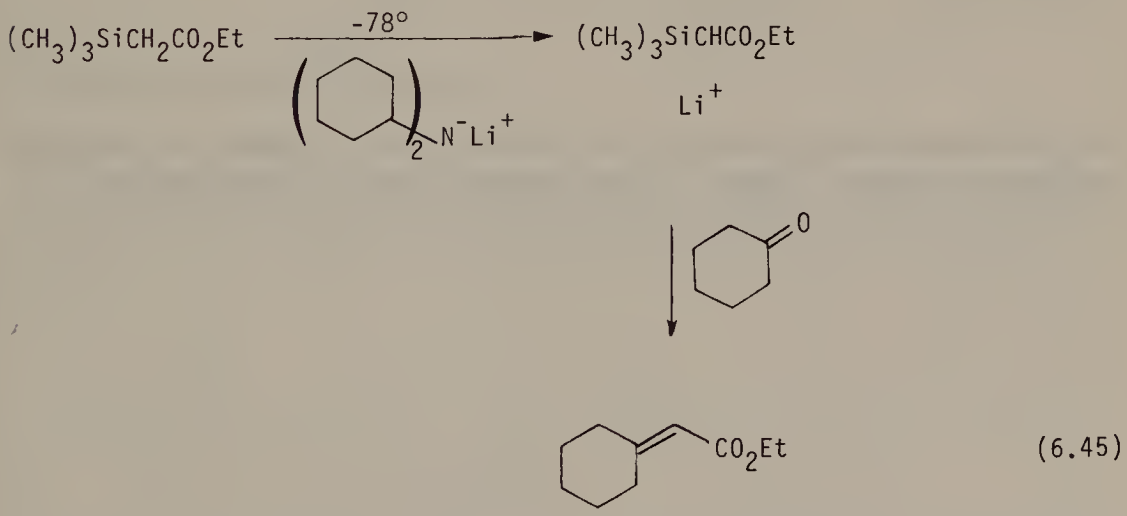


Ethyl trimethylsilylacetate has been prepared by a modified Reformatsky reaction of ethyl bromoacetate and TMS-Cl with zinc [71].



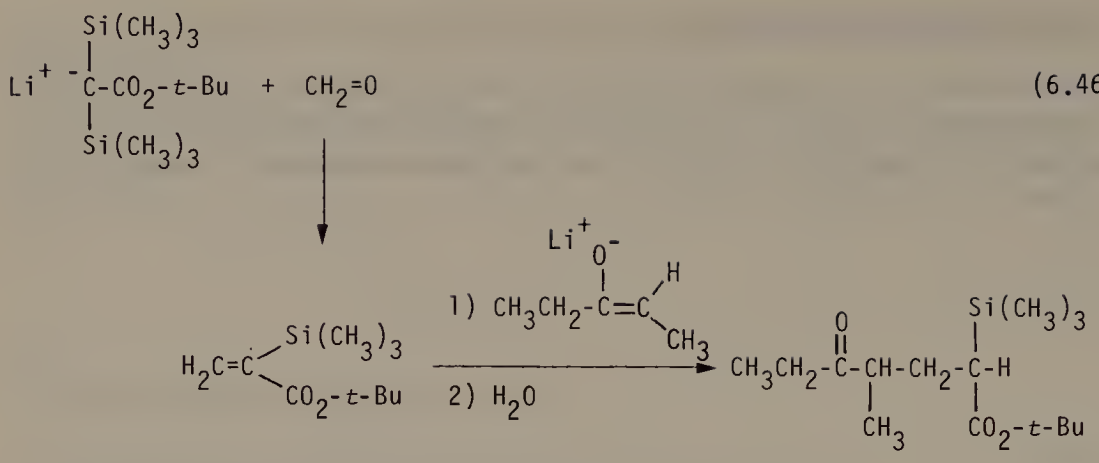
(6.44)

Both *t*-butyl trimethylsilylacetate and ethyl trimethylsilylacetate are converted to α-trimethylsilyl lithium enolates by treatment at low temperature with LDA or lithium dicyclohexylamide. They react ketones or aldehydes to yield α,β-unsaturated esters [25–27, 72]. Lithio-*t*-butyl trimethylsilylacetate is quite stable.



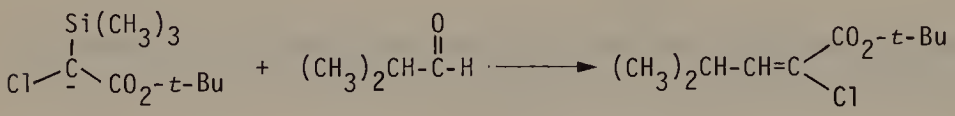
(6.45)

LDA readily converts *t*-butyl *bis*(trimethylsilyl)acetate to an enolate which reacts with aldehydes but not ketones to yield α-trimethylsilyl-α,β-unsaturated esters. These are useful Michael acceptors [25].



(6.46)

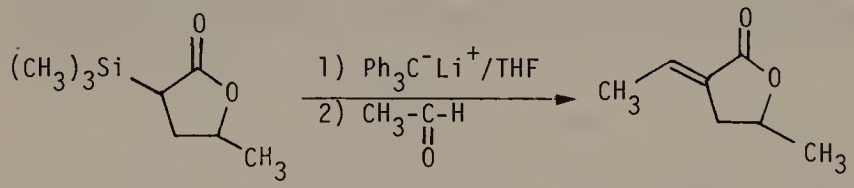
t-Butyl trimethylsilylchloroacetate has been prepared by reaction of the lithium enolate of *t*-butyl chloroacetate with TMS-Cl. Deprotonation of this silyl reagent with LDA forms an ester enolate which reacts with ketones or aldehydes to yield α-chloro-α,β-unsaturated esters [24].



(6.47)

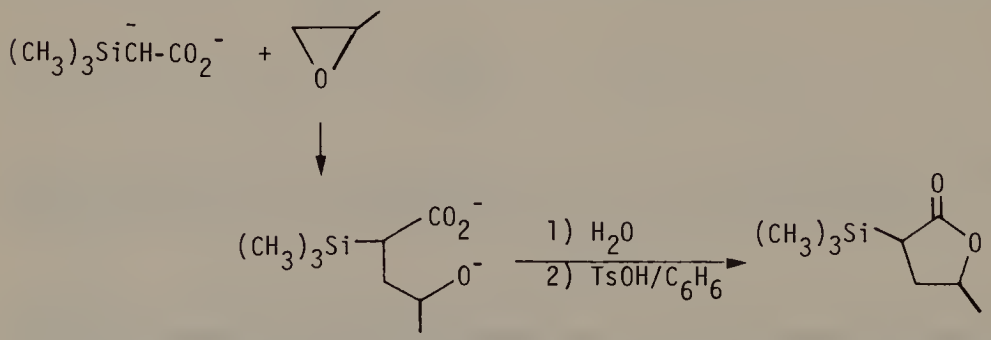
L. α-Ylidene-γ-butyrolactones

α-Ylidene-γ-butyrolactones have been prepared by Peterson reaction of aldehydes with the enolate anion generated from α-trimethylsilyl γ-butyrolactones.



(6.48)

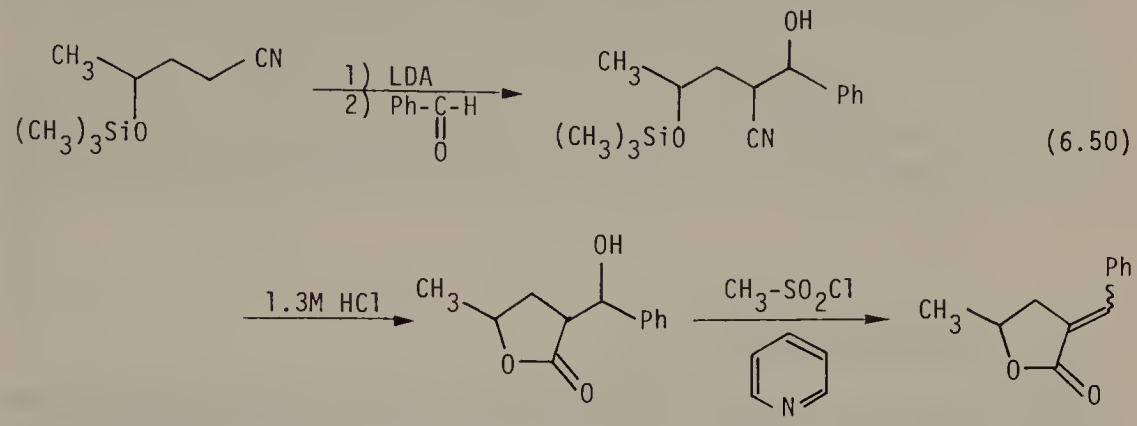
The necessary α-trimethylsilyl-γ-butyrolactones were prepared by reaction of epoxides with the dianion of trimethylsilyl acetic acid (Eq. 6.49) [69].



(6.49)

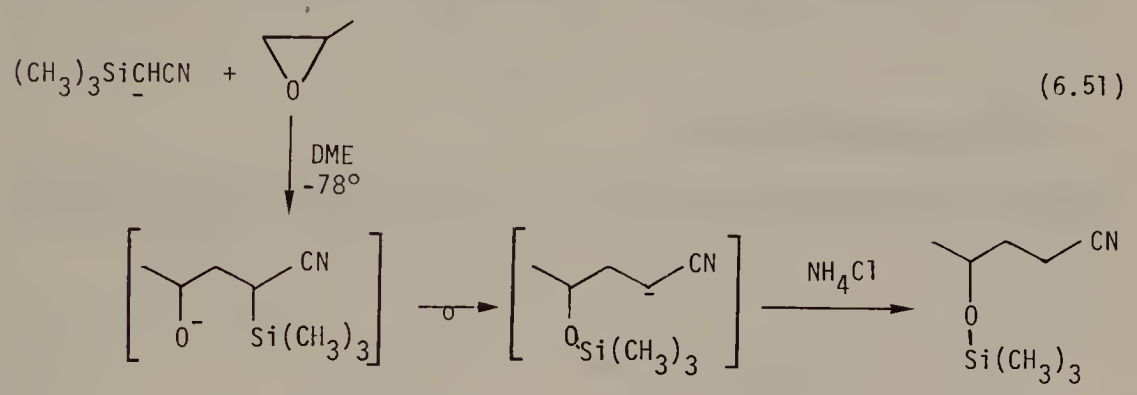
α-Ylidene-γ-lactones have also been prepared from γ-trimethylsilyloxypropionitriles. These can be deprotonated with LDA to yield cyano-stabilized

anions which react with aldehydes to give α-(1-hydroxyalkyl)-γ-trimethylsilyloxy nitriles. These undergo acidic hydrolysis to α-(1-hydroxyalkyl)-γ-lactones which can be dehydrated to α-ylidene γ-lactones [92].



(6.50)

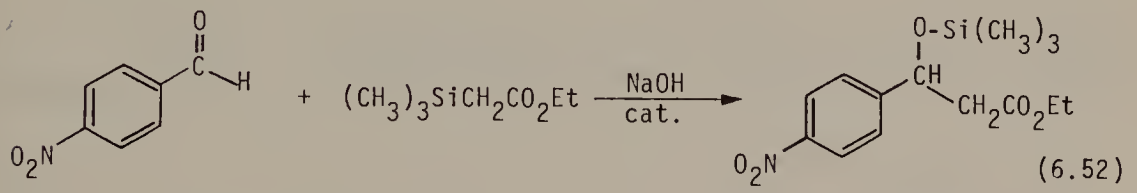
α-Lithio trimethylsilylacetonitrile reacts with epoxides to produce γ-trimethylsilyloxy propionitriles via a 1,4-shift of the trimethylsilyl group from carbon to the alkoxide oxygen [91].



(6.51)

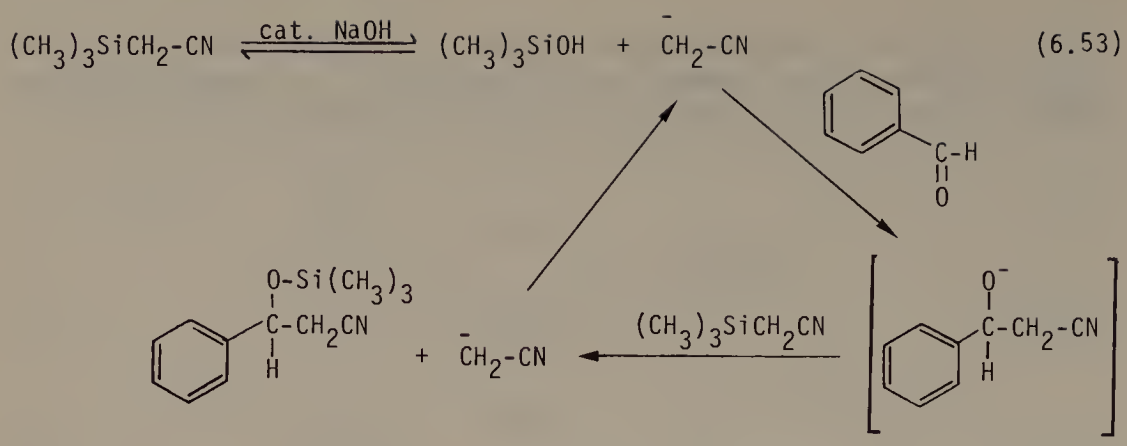
M. Silyl Reformatsky Reaction

The Peterson reaction is not catalytic in base but rather requires one equivalent of α-silyl carbanion. In the presence of a catalytic amount of sodium hydroxide at 160–180°, ethyl trimethylsilylacetate reacts with aromatic aldehydes to yield ethyl β-aryl β-trimethylsilyloxy propionates (Eq. 6.52) [90].



(6.52)

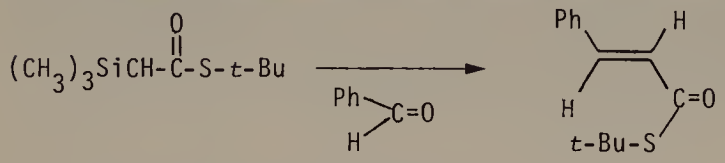
Likewise, trimethylsilylacetonitrile reacts with aromatic aldehydes in the presence of a catalytic amount of sodium hydroxide at 160–180° to give β-aryl-β-trimethylsilyloxy-propionitrile [90].



(6.53)

N. α,β-Unsaturated Thiol Esters

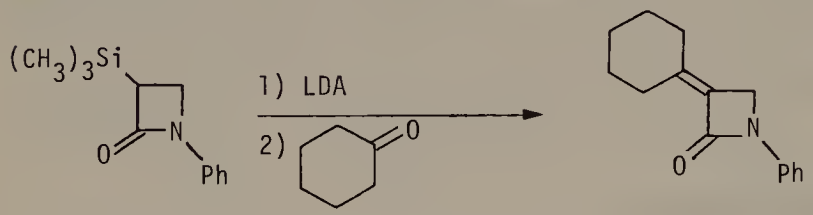
Deprotonation of *t*-butyl α-trimethylsilythioacetate with LDA yields an ester enolate which reacts with both ketones and aldehydes to give α,β-unsaturated thio esters [73].



(6.54)

O. α,β-Unsaturated Amides

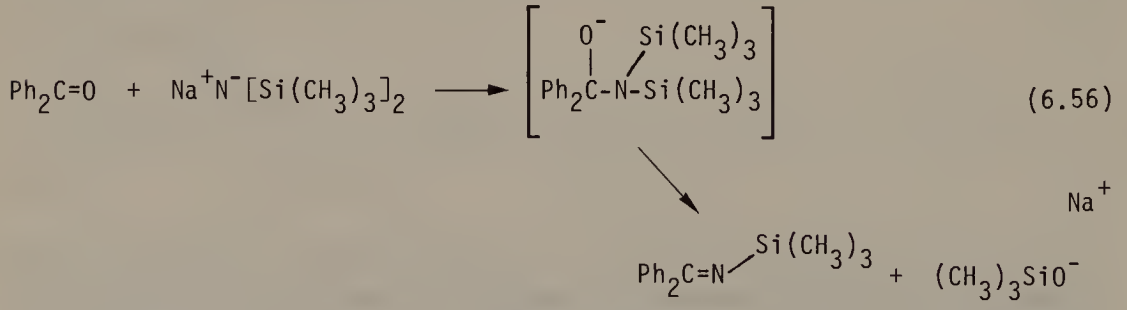
N-Phenyl-3-alkylidene azetidin-2-ones have been prepared by the Peterson reaction [74].



(6.55)

P. Imines

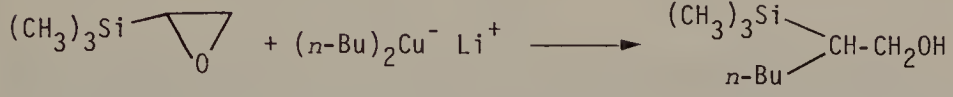
The reaction of the sodium salt of hexamethyldisilazane with non-enolizable ketones yields N-trimethylsilyl imines [75].



(6.56)

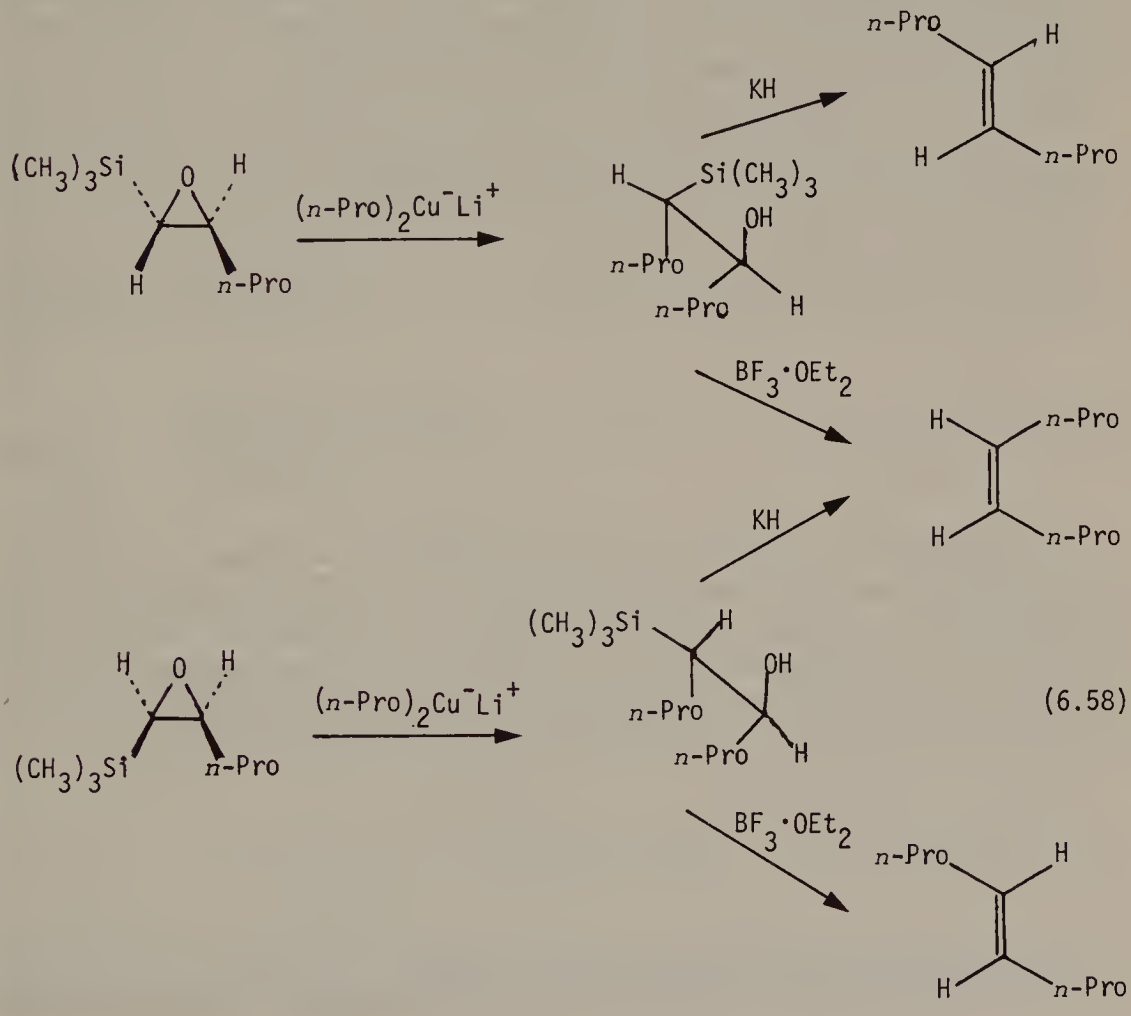
6.5 Related Reactions

There are several related reactions which involve formation of either β-hydroxyalkyltrimethylsilanes or β-trimethylsilyl alkoxide intermediates by alternative routes. For example, Hudrlik found that β-hydroxyalkyltrimethylsilanes can be prepared regio- and stereospecifically by the reaction of dialkyl cuprates with α-trimethylsilyl epoxides (see Chapter 7). Nucleophilic attack by dialkyl cuprates occurs on the backside of the carbon atom of the epoxide which bears the trimethylsilyl group and results in opening the epoxide ring.



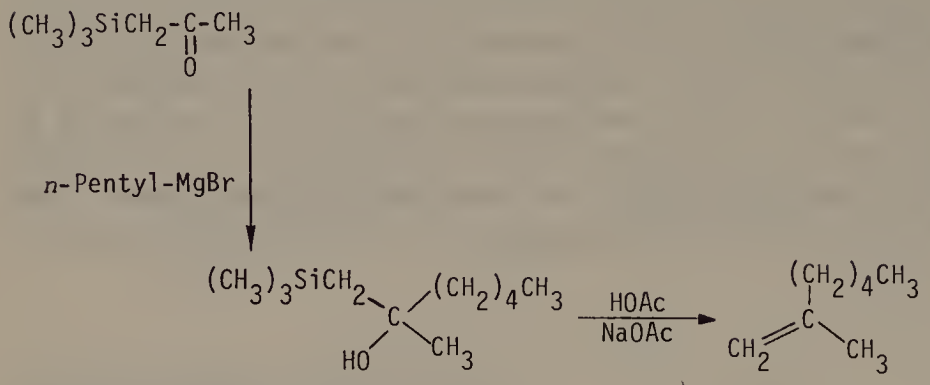
(6.57)

Di-*n*-propyl copper lithium reacts with *cis*-1-trimethylsilylpentene oxide to yield *erythro*-5-trimethylsilyloctan-4-ol and with *trans*-1-trimethylsilylpentene oxide to yield *threo*-5-trimethylsilyloctan-4-ol. Both of these diastereomeric β-hydroxyalkyltrimethylsilanes can be converted to either *cis* or *trans*-4-octene by the appropriate choice of conditions for the elimination step [76].



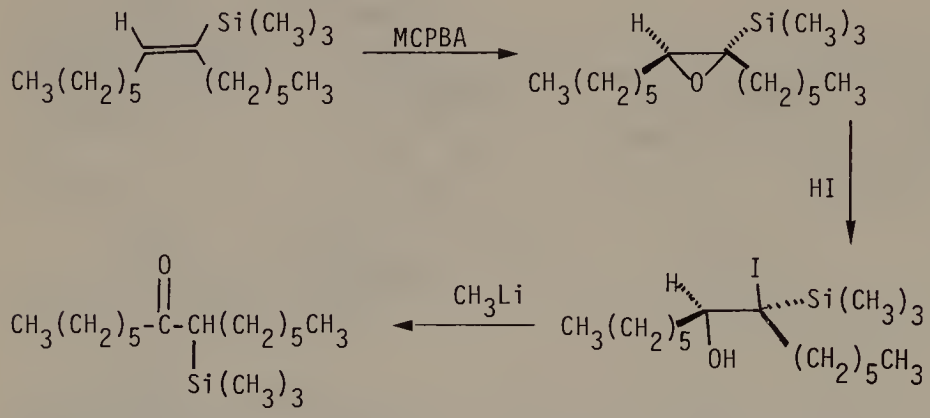
(6.58)

The addition of Grignard or organolithium reagents to β-ketosilanes, also yields β-hydroxyalkyltrimethylsilanes [77].



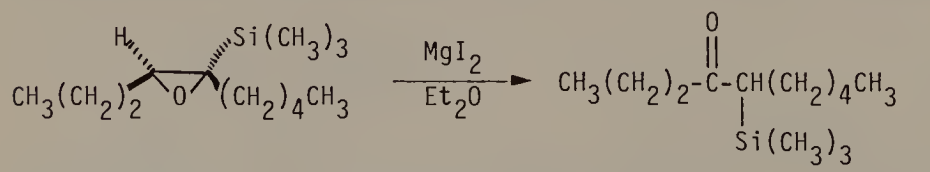
(6.59)

Organolithium reagents add to β-keto silanes, such as 5-trimethylsilyldecan-4-one, to yield β-hydroxysilanes with high stereoselectivity as predicted by Cram's rule. These undergo *syn* elimination on treatment with potassium *t*-butoxide to yield tri-substituted alkenes of predominantly *E*-configuration whereas treatment with glacial acetic acid leads to alkenes of predominantly *Z* configuration via *trans* elimination [78, 79]. The necessary β-keto silanes are easily prepared by treatment of 2-trimethylsilyl-2,3-dialkyl oxiranes with HI followed by reaction of the iodohydrins with one equivalent of methyl lithium in ether [79] or *n*-butyllithium in hexane/ether [80].



(6.60)

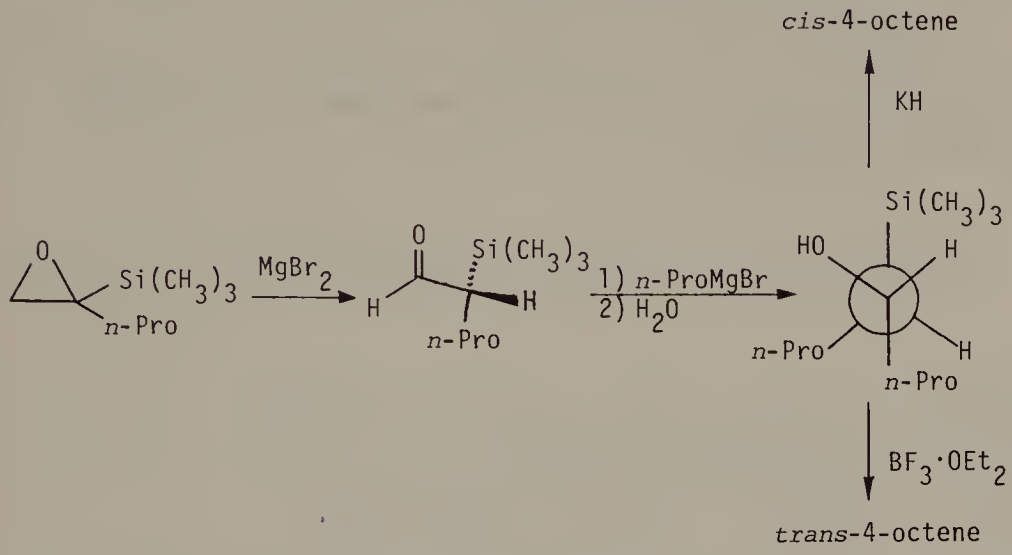
α-Trimethylsilyl epoxides react with Grignard reagents to yield β-hydroxyalkylsilanes. This reaction proceeds by initial rearrangement of the α-trimethylsilyl epoxides under the influence of magnesium bromide to α-bromo-β-hydroxysilanes which react with additional magnesium bromide to give β-silyl aldehydes or ketones [81]. α-Trimethylsilyl epoxides also rearrange to β-keto silanes on treatment with magnesium iodide [82, 93].



(6.61)

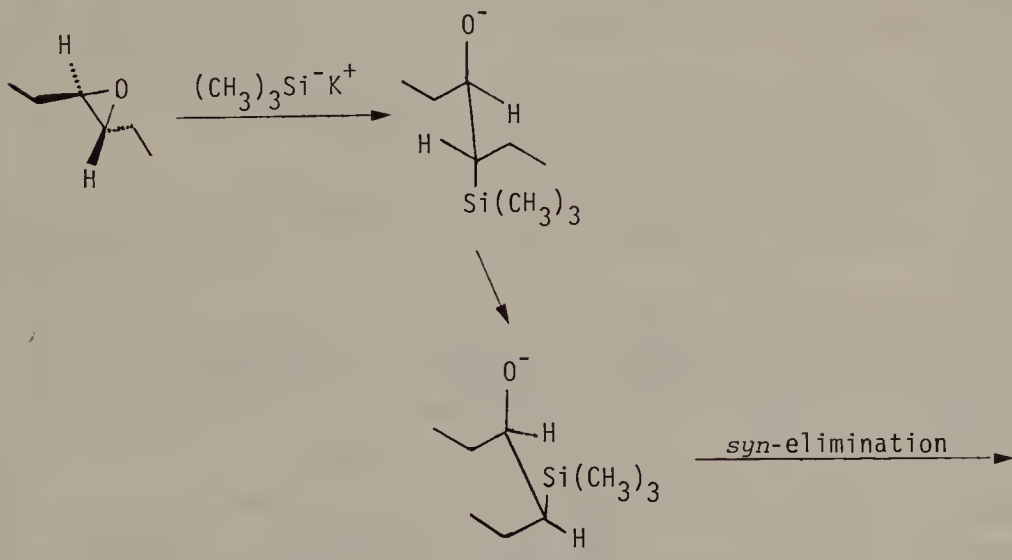
β-Silyl aldehydes react stereoselectively with Grignard reagents to yield

β-hydroxyalkyl silanes [83]. The stereoselectivity of this addition is predicted by Cram's Rule. 2-Trimethylsilyl-1-pentene oxide reacts with *n*-propyl magnesium bromide to yield a β-hydroxyalkylsilane which undergoes a *syn* elimination on treatment with potassium hydride to yield *cis*-4-octene or *trans* elimination on treatment with $BF_3 \cdot Et_2O$ to yield *trans*-4-octene [83].



(6.62)

Dervan found that trimethylsilyl potassium would react with epoxides in a stereospecific manner to yield olefins of inverted geometry. For example, *trans*-3-hexene oxide reacts with trimethylsilyl potassium to yield *cis*-3-hexene. This result was explained as follows. Backside nucleophilic attack by trimethylsilyl potassium on the epoxide yields a *β*-trimethylsilyl alkoxide. This must rotate about the 3,4 C–C single bond by 180° in order to achieve the necessary geometry for *syn* elimination of potassium trimethylsilanoate [84].



(6.63)

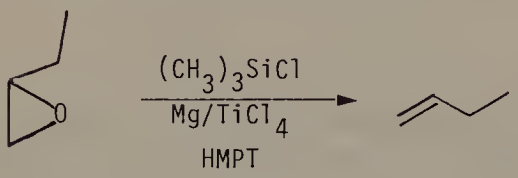
The required trimethylsilyl potassium can be prepared by reaction of hexamethyldisilane with potassium methoxide in HMPT or THF/18-C-6 [85–87].

$$(CH_3)_3SiSi(CH_3)_3 \xrightarrow[THF/18\text{-}C\text{-}6]{K^+\ ^-OCH_3} (CH_3)_3Si^-K^+ + (CH_3)_3SiOCH_3 \qquad (6.64)$$

Likewise, triethylsilyl potassium results from reaction of triethylsilane with potassium hydride in DME or HMPT [88].

$$Et_3SiH \xrightarrow[DME\ or\ HMPT]{KH} Et_3Si^-\ K^+ + H_2 \qquad (6.65)$$

The deoxygenation of epoxides on treatment with TMS-Cl and magnesium in HMPT may be related [89].



(6.66)

References

1. Peterson, D.J.: J. Org. Chem. *33*, 780 (1968)
2. Gilman, H., Tomasi, R.A.: J. Org. Chem. *27*, 3647 (1962)
3. Carey, F.A., Court, A.S.: J. Org. Chem. *37*, 939 (1972)
4. Boeckman, Jr., R.K., Silver, S.M.: Tetrahedron Lett. 3497 (1973)
5. For a review see Peterson, D.J.: Organometal. Chem. Rev. *A*, *7*, 295 (1972)
6. Peterson, D.J.: J. Organometal. Chem. *9*, 373 (1967)
7. Langer, Jr., A.W.: Trans. N.Y. Acad. Sci. *27*, 741 (1965)
8. Eberhardt, G.G., Butte, W.A.: J. Org. Chem. *29*, 2928 (1964)
9. Whitmore, F.C., Sommer, L.H., Gold, J., van Strien, R.E.: J. Am. Chem. Soc. *69*, 1551 (1947)
10. Hauser, C.R., Hance, C.R.: J. Am. Chem. Soc. *74*, 5091 (1952)
11. Brook, A.G., Duff, J.M., Anderson, D.G.: Can. J. Chem. *48*, 651 (1970)
12. Seyferth, D., Lefferts, J.L., Lambert, Jr., R.L.: J. Organometal. Chem. *142*, 39 (1977)
13. Cook, M.A., Eaborn, C., Jukes, A.E., Walton, D.R.M.: J. Organometal. Chem. *24*, 529 (1970)
14. Cason, L.F., Brooks, H.G.: J. Am. Chem. Soc. *74*, 4582 (1952)
15. Cason, L.F., Brooks, H.G.: J. Org. Chem. *19*, 1278 (1954)
16. Mulvaney, J.E., Gardlund, Z.G.: J. Org. Chem. *30*, 917 (1965)
17. Hudrlik, P.F., Peterson, D.: Tetrahedron Lett. 1133 (1974)
18. Buell, G.R., Corriu, R., Guerin, C., Spialter, L.: J. Am. Chem. Soc. *92*, 7424 (1970)
19. Gröbel, B.T., Seebach, D.: Chem. Ber. *110*, 852 (1977)
20. Brooks, A.G., Duff, J.M., Anderson, D.G.: Can. J. Chem. *48*, 561 (1970)
21. Chan, T.H., Chang, E., Vinokur, E.: Tetrahedron Lett. 1137 (1970)
22. Konakahara, T., Takagi, Y.: Synthesis, 192 (1979)
23. Konakahara, T., Takagi, Y.: Tetrahedron Lett. 2073 (1980)
24. Chan, T.H., Moreland, M.: Tetrahedron Lett. 515 (1978)
25. Hartzell, S.L., Rathke, M.W.: Tetrahedron Lett. 2757 (1976)
26. Hartzell, S.L., Sullivan, D.F., Rathke, M.W.: Tetrahedron Lett. 1403 (1974)
27. Shimoji, E., Taguchi, H., Oshima, K., Yamamoto, H., Nozaki, H.: J. Am. Chem. Soc. *96*, 1620 (1974)
28. Ojima, I., Kumagai, M., Nagai, Y.: Tetrahedron Lett. 4005 (1974)

29. Matsuda, I., Murata, S., Ishii, Y.: J. Chem. Soc. Perkin I, 26 (1979)
30. Carey, F.A., Court, A.S.: J. Org. Chem. *37*, 1926 (1972)
31. Sakurai, H., Nishiwaki, K., Kira, M.: Tetrahedron Lett. 4193 (1973)
32. Ager, D.J.: Tetrahedron Lett. 2923 (1981)
33. Dumont, W., Krief, A.: Angew. Chem. Int. Ed. *15*, 161 (1976)
34. Hudrlik, P.F., Peterson, D.: Tetrahedron Lett. 1133 (1974)
35. Hudrlik, P.F., Peterson, D.: J. Am. Chem. Soc. *97*, 1464 (1975)
36. Cram, D.J., Abd. Elhafez, F.A.: J. Am. Chem. Soc. *74*, 5828 (1952)
37. Larsson, F.C.V., Lawesson, S.O.: Tetrahedron, *28*, 5341 (1972)
38. Dalgaard, L., Kolind-Andersen, H., Lawesson, S.O.: Tetrahedron, *29*, 2077 (1973)
39. Corey, E.J., Markl, G.: Tetrahedron Lett. 3201 (1967)
40. Seebach, D., Gröbel, B.T., Beck, A.K., Braum, M., Geiss, K.H.: Angew. Chem. Int. Ed. *11*, 433 (1972)
41. Seebach, D., Kolb, M., Gröbel, B.T.: Chem. Ber. *106*, 2277 (1973)
42. Brook, A.G., Duff, J.M., James, P.F., Davis, N.R.: J. Am. Chem. Soc. *89*, 431 (1967)
43. Corey, E.J., Seebach, D., Freedman, R.: J. Am. Chem. Soc. *89*, 434 (1967)
44. Jones, P.F., Lappert, M.F.: J. Chem. Soc. Chem. Commun. 526 (1972)
45. Jones, P.F., Lappert, M.F., Szary, A.C.: J. Chem. Soc. Perkin I, 2272 (1973)
46. Carey, F.A., Neergaard, J.R.: J. Org. Chem. *36*, 2731 (1971)
47. Seebach, D.: Synthesis, 17 (1969)
48. Coffen, D.L., McEntee, Jr., T.E. Williams, D.R.: J. Chem. Soc. Chem. Commun. 913 (1970)
49. Carey, F.A., Hernandez, O.: J. Org. Chem. *38*, 2670 (1973)
50. Brook, A.G., Anderson, D.G.: Can. J. Chem. *46*, 2115 (1968)
51. Seebach, D., Bürstinghaus, R., Gröbel, B.T., Kolb, M.: Liebigs Ann., 830 (1977)
52. Agawa, T., Ishikawa, M., Komatsu, M., Ohshiro, Y.: Chem. Lett. 335 (1980)
53. Ager, D.J.: Tetrahedron Lett. 2803 (1981)
54. van der Leij, M., Porskamp, P.A.T., Lammerink, B.G.M., Zwanenburg, B.: Tetrahedron Lett. 811 (1978)
55. van der Leij, M., Zwanenburg, B.: Tetrahedron Lett. 3383 (1978)
56. Porskamp, P.A.T.W., Zwanenburg, B.: Synthesis, 368 (1981)
57. For a review of such elimination reactions see: Jarvie, A.W.P.: Organometal. Chem. Rev. *A*, *6*, 153 (1970)
58. Chan, T.H., Mychajlowskij, W.: Tetrahedron Lett. 171 (1974)
59. Chan, T.H., Mychajlowskij, W., Ong, B.S., Harpp, D.N.: J. Org. Chem. *43*, 1526 (1978)
60. Gröbel, B.T., Seebach, D.: Angew. Chem. Int. Ed. *13*, 83 (1974)
61. Matteson, D.S., Majumdar, D.: J. Chem. Soc. Chem. Commun. 39 (1980)
62. Wittig, G., Reiff, H.: Angew. Chem. Int. Ed. *7*, 7 (1968)
63. Trippett, S., Walker, D.M.: J. Chem. Soc. 2130 (1961)
64. Cresp, T.M., Sargent, M.J., Vogel, P.: J. Chem. Soc. Perkin *I*, 37 (1974)
65. Corey, E.J., Enders, D., Bock, M.G.: Tetrahedron Lett. 7 (1976)
66. Corey, E.J., Weigel, L.O., Floyd, D., Bock, M.G.: J. Am. Chem. Soc. *100*, 2916 (1978)
67. Corey, E.J., Weigel, L.O., Chamberlain, R.A., Lipshutz, B.: J. Am. Chem. Soc. *102*, 1439 (1980)
68. Sachdev, K.: Tetrahedron Lett. 4041 (1976)
69. Grieco, P.A., Wang, C.L.J., Burke, S.D.: J. Chem. Soc. Chem. Commun. 537 (1975)
70. Rathke, M.W., Sullivan, D.F.: Syn. Commun. *3*, 67 (1973)

71. Fessenden, R.J., Fessenden, J.S.: J. Org. Chem. *32*, 3535 (1967)
72. Taguchi, T., Shimoji, K., Yamamoto, Y.Y., Nozaki, H.: Bull. Soc. Chem. Japan, *47*, 2529 (1974)
73. Lucast, D.H., Wemple, J.: Tetrahedron Lett. 1103 (1977)
74. Kano, S., Ebata, T., Funaki, K., Shibuya, S.: Synthesis, 746 (1978)
75. Krüger, C., Rochow, E.G., Wannagat, U.: Chem. Ber. *96*, 2132 (1963)
76. Hudrlik, P.F., Peterson, D., Rona, R.J.: J. Org. Chem. *40*, 2263 (1975)
77. Hudrlik, P.F., Peterson, D.: Tetrahedron Lett. 1785 (1972)
78. Utimoto, K., Obayashi, M., Nozaki, H.: J. Org. Chem. *41*, 2940 (1976)
79. Obayashi, M., Utimoto, K., Nozaki, H.: Bull. Chem. Soc. Japan, *52*, 1760 (1979)
80. Obayashi, M., Utimoto, K., Nozaki, H.: Tetrahedron Lett. 1383 (1978)
81. Hudrlik, P.F., Misra, R.N., Withers, G.P., Hudrlik, A.M., Rona, R.J., Arcoleo, J.P.: Tetrahedron Lett. 1453 (1976)
82. Obayashi, M., Utimoto, K., Nozaki, H.: Tetrahedron Lett. 1807 (1977)
83. Hudrlik, P.F., Hudrlik, A.M., Misra, R.N., Peterson, D., Withers, G.P., Kulkarni, A.K.: J. Org. Chem. *45*, 4444 (1980)
84. Dervan, P.B., Shippey, M.A.: J. Am. Chem. Soc. *98*, 1265 (1976)
85. Sakurai, H., Okada, A., Kira, M., Yonezawa, K.: Tetrahedron Lett. 1511 (1971)
86. Sakurai, H., Okada, A.: J. Organometal. Chem. *35*, C13 (1972)
87. Sakurai, H., Kondo, F.: J. Organometal. Chem. *92*, C46 (1975)
88. Corriu, J.R.P., Guerin, C.: J. Chem. Soc. Chem. Commun. 168 (1980)
89. Dunoguès, J., Calas, R., Duffant, N., Picard, J.P.: J. Organometal. Chem. *26*, C13 (1971)
90. Birkofer, L., Ritter, A., Wieden, H.: Chem. Ber. *95*, 971 (1962)
91. Matsuda, I., Murata, S., Ishii, Y.: J. Chem. Soc. Perkin *I*, 26 (1979)
92. Matsuda, I., Murata, S., Izumi, Y.: Bull. Chem. Soc. Japan, *52*, 2389 (1979)
93. Obayashi, M., Utimoto, K., Nozaki, H.: Bull. Chem. Soc. Japan, *52*, 2646 (1979)

7 Vinyl Silanes

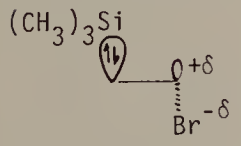
7.1 Introduction

The material of this chapter has been divided into seven parts. The first six are concerned with synthetically useful reactions of β-halosilanes, vinyl silanes, and α-silyl epoxides. The seventh deals with the preparation of vinyl silanes.

First will be elimination reactions of β-halosilanes. Second will be electrophilic substitution reactions of vinyl silanes and α-silyl epoxides. This often results in regio- and stereospecific formation of substituted alkenes. These reactions frequently proceed by electrophilic addition to the vinylsilane to yield a β-halosilane followed by loss of the elements of trimethylhalosilane (TMS-X) from the intermediate β-halosilane. Third will be regiospecific addition of carbanions to the C–C double bond of vinyl silanes to yield α-silyl carbanions. Touched on fourth will be vinyl silanes as masked carbonyl compounds. Fifth will be the 1,2-transposition of carbonyl groups and six cycloaddition reactions of vinyl silanes.

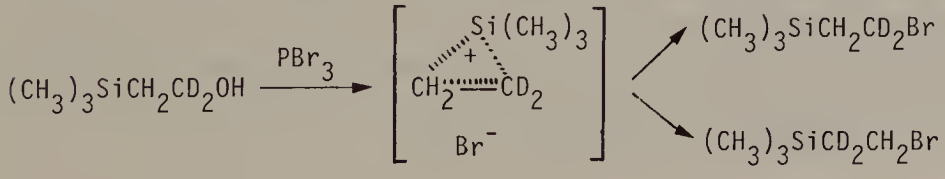
7.2 Elimination of Trimethylhalosilanes from β-Halosilanes

β-Halosilanes, such as β-bromoethyltrimethylsilane, undergo facile Sn1 solvolysis to yield alkenes with loss of the elements of TMS-X [1]. This may result from the stabilization of the developing primary carbocation by hyperconjugation with the C–Si sigma bond [2] or by bridging of the trimethylsilyl group.



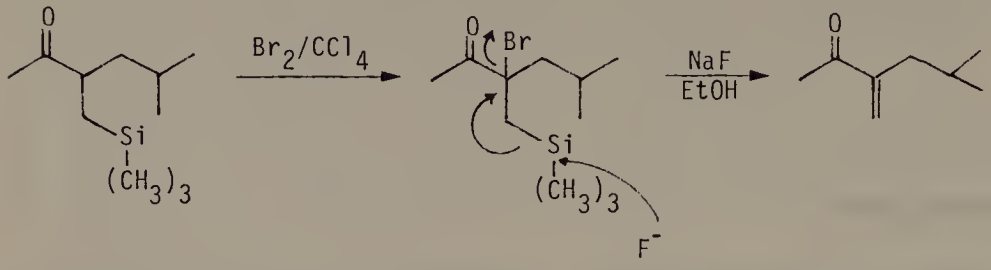
(7.0)

This latter hypothesis [3] is supported by the fact that 2-trimethylsilylethanol 1,1-d_2 reacts with phosphorous tribromide to yield 2-bromoethyltrimethylsilane in which the deuterium is scrambled.



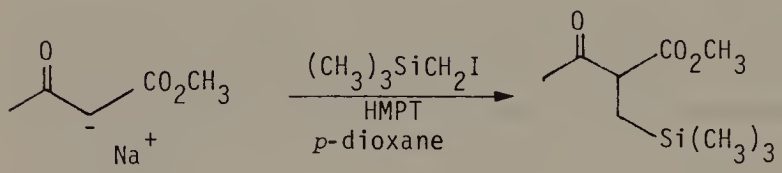
(7.1)

This elimination reaction of β-halosilanes has been exploited synthetically. Thus β-trimethylsilyl ketones can be converted to α,β-unsaturated ketones by α-bromination followed by loss of TMS-Br [4–6]. The loss of TMS-Br may be accelerated by fluoride ion attack on the silyl center.

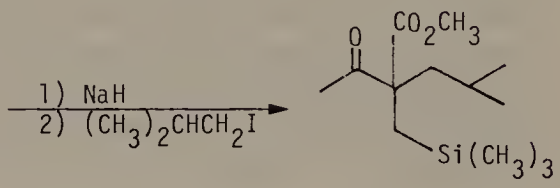


(7.2)

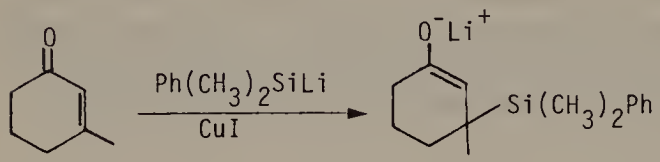
β-Trimethylsilyl ketones can be prepared by C-alkylation of the enolate anions of β-keto-esters with iodomethyltrimethylsilane in HMPT.



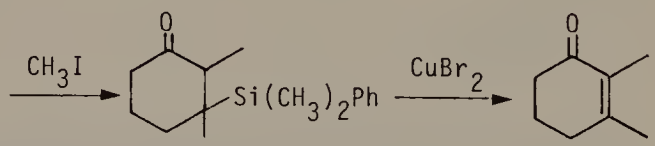
(7.3)



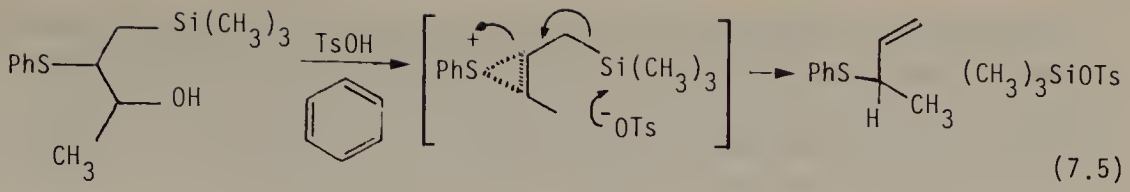
Alternatively, β-phenyldimethylsilyl ketones can be prepared by the conjugate addition of phenyldimethylsilyl lithium [7] to α,β-unsaturated ketones under the influence of cuprous iodide [8].



(7.4)

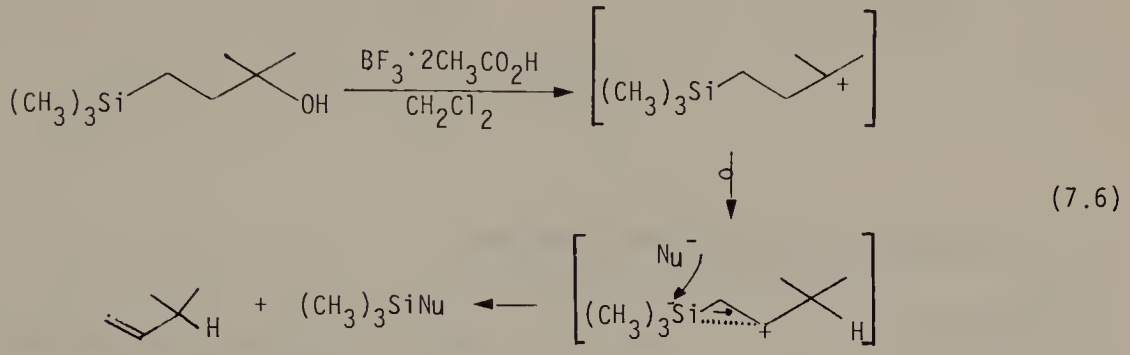


This stabilizing effect of trimethylsilyl groups on a β-carbocation has been utilized to direct carbocation rearrangements. Treatment of 3-trimethylsilyl-2-phenylthio substituted alcohols with acid leads to specific allylic phenyl sulfides. The trimethylsilyl group encourages the migration of the phenylthio group to the initial carbocation center to form a new carbocation located *beta* to the trimethylsilyl group. Nucleophilic attack on the silyl center leads to regiospecific C–C double bond formation [9, 10].



(7.5)

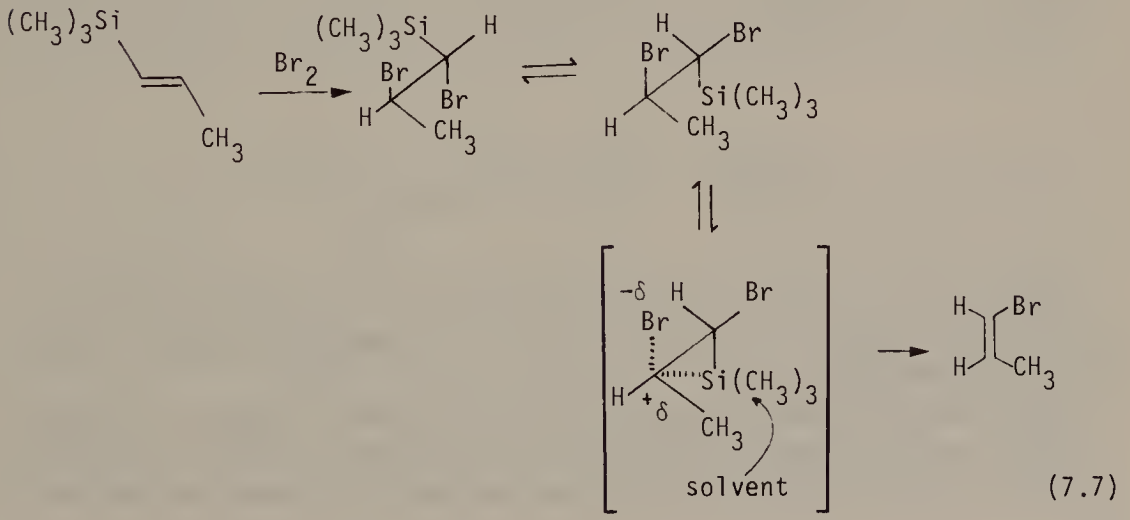
Likewise, 3-trimethylsilyl substituted undergo tertiary alcohols acid catalyzed rearrangement and loss of trimethylsilanol to yield particular alkenes [11].



(7.6)

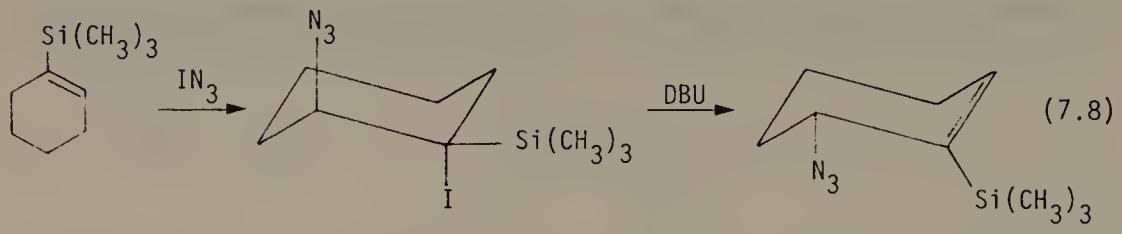
7.3 Stereospecificity of Elimination

Synthetic chemists were intrigued by the report that *E*-propenyltrimethylsilane reacts with bromine to yield a single diastereomeric dibromide which then undergoes solvolysis with loss of TMS-Br to yield predominantly *Z*-bromopropene. These results could be accounted for by a *trans*-addition of bromine to *E*-propenyltrimethylsilane to yield *erythro*-1,2-dibromopropyltrimethylsilane followed by *trans*-elimination of TMS-Br. The trimethylsilyl group must be *trans* coplanar to the bromide which is lost in order to stabilize the incipient primary carbocation. This causes stereospecific *trans*-elimination. Nucleophilic attack by solvent on the bridging trimethylsilyl group leads to products [3].



(7.7)

6-Substituted-1-trimethylsilyl cyclohexenes have been prepared by addition of iodine electrophiles (IN_3) to 1-trimethylsilylcyclohexene followed by dehydrohalogenation of the initial adducts with DBU in benzene. The success of the reaction is dependent on the inability of the trimethylsilyl to achieve a *trans* coplanar orientation with the adjacent azide group [12].

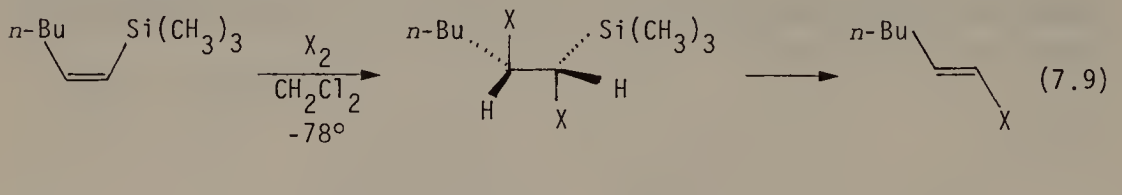


(7.8)

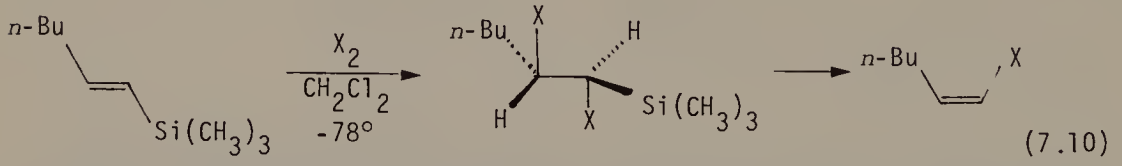
7.4 Electrophilic Substitution Reactions

A. Halogens

Stereospecific *trans* addition of electrophiles to vinyl silanes followed by *trans* elimination of the elements of TMS-X permits the stereospecific preparation of a variety of substituted alkenes. *Z*-1-trimethylsilyl hexene reacts with either chlorine or bromine at −78°C to yield the respective *threo*-1-trimethylsilyl-1,2-dihalohexanes. These undergo *trans* elimination of the elements of TMS-X on treatment with sodium methoxide in methanol, potassium fluoride dihydrate in DMSO or alumina in pentane to yield *E*-1-bromohexene or *E*-1-chlorohexene. Lower stereoselectivity is observed with alumina. Likewise, *E*-1-trimethylsilyl hexene reacts with chlorine or bromine to yield the respective *erythro*-1-trimethylsilyl-1,2-dihalohexanes which undergo elimination under comparable conditions to yield *Z*-1-bromohexene or *Z*-1-chlorohexene [13, 15].



(7.9)

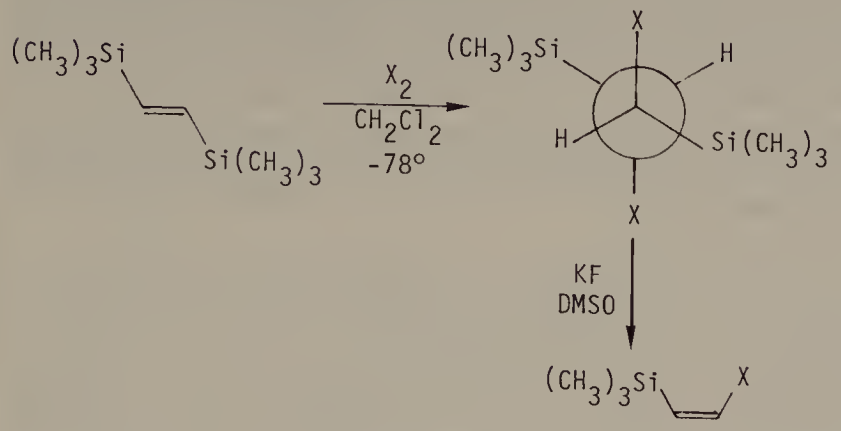


(7.10)

Similar stereospecificity has been observed with *Z*- and *E*-2-cyclohexyl-1-trimethylsilylethylene. Lower stereospecificity is observed with *Z*-2-*t*-butyl-1-trimethylsilylethylene.

E-1,2-*bis*(trimethylsilyl)ethylene also reacts with chlorine or bromine to yield *meso*-1,2-dihalo-1,2-*bis*(trimethylsilyl)ethanes. These undergo elimination of the elements of TMS-X on treatment with potassium fluoride in

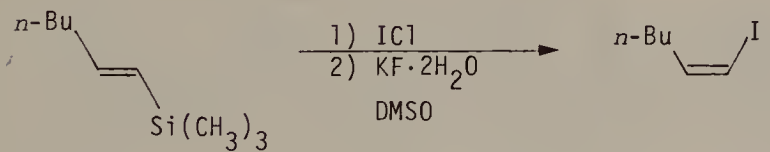
DMSO to yield *Z*-1-chloro-2-trimethylsilylethylene or *Z*-1-bromo-2-trimethylsilylethylene, respectively [16].



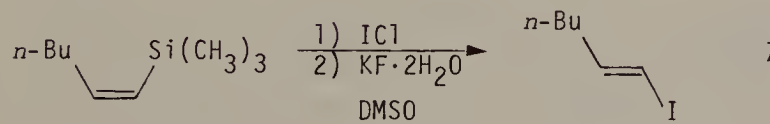
(7.11)

Trisubstituted alkenes have also been prepared in this manner. For example, *Z*-2-cyclohexyl-1-ethyl-1-trimethylsilylethylene reacts with bromine to yield a dibromide which loses TMS-Br in acetonitrile to give *E*-1-bromo-2-cyclohexyl-1-ethyl ethylene. Likewise, *E*-2-cyclohexyl-1-ethyl-1-trimethylsilyl ethylene reacts with bromine to yield *Z*-1-bromo-2-cyclohexyl-1-ethyl ethylene [17]. Similar results have been obtained with *E*- and *Z*-2-*n*-butyl-1-methyl-1-trimethylsilylethylene [18].

The reaction of iodine with vinyl trimethylsilanes followed by elimination of TMS-I to yield vinyl iodides is more complex. For example, *E*-1,2-*bis*(trimethylsilyl)ethylene reacts with iodine in CCl_4 to give equal amounts of *Z*- and *E*-1-iodo-2-trimethylsilylethylene [16]. On the other hand, *Z*-1-trimethylsilylhexene reacts with iodine in methylene chloride to yield *Z*-1-iodohexene [14]. The stereoselectivity of this reaction can be controlled by the use of silver trifluoroacetate and iodine followed by elimination with potassium fluoride in DMSO. Under these conditions *Z*-1-trimethylsilylhexene yields *E*-1-iodohexene. However, iodine monochloride has proved more effective. *E*-1-Trimethylsilylhexene reacts with iodine monochloride in CCl_4 at 0° to give an adduct which loses the elements of TMS-Cl on treatment with potassium fluoride in DMSO to yield almost pure *Z*-1-iodohexene. While *Z*-1-trimethylsilylhexene reacts with iodine monochloride to give predominantly *E*-1-iodohexene [19, 20].



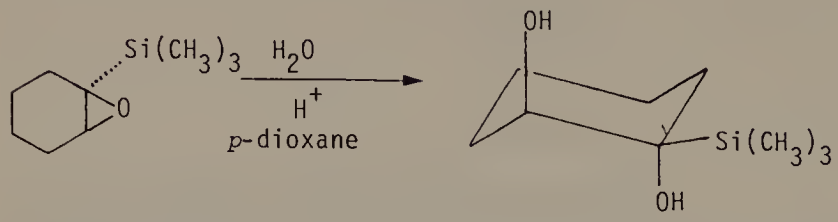
(7.12)



(7.13)

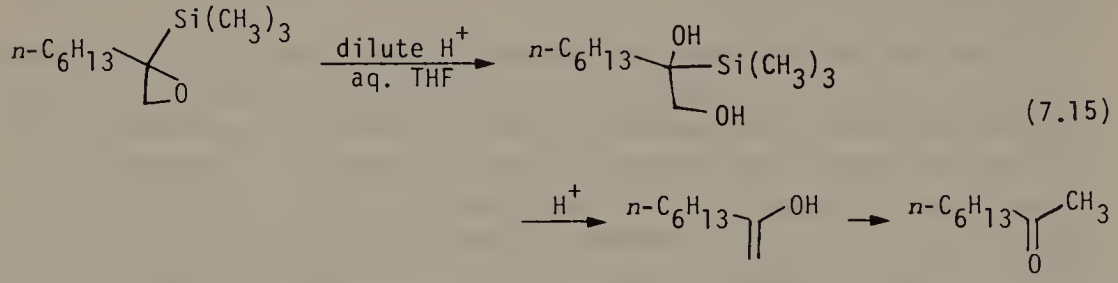
B. Reactions of α-Trimethylsilyl Epoxides with Electrophiles

α-Trimethylsilyl epoxides undergo acid catalyzed opening of the epoxide with simultaneous nucleophilic attack on the carbon bearing the trimethylsilyl group. For example, treatment of 1-trimethylsilylcyclohexene oxide with aq. acid leads to 1-trimethylsilyl-*trans*-1,2-cyclohexanediol. This α,β-dihydroxyalkyl trimethylsilane does not undergo acid catalyzed loss of trimethylsilanol since the trimethylsilyl group and the adjacent β-hydroxyl group cannot achieve a *trans*-coplanar arrangement [21].



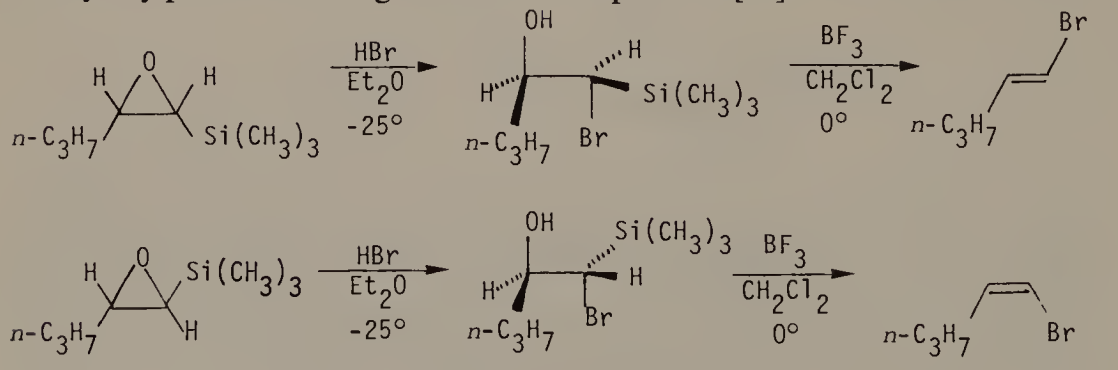
(7.14)

On the other hand, mild acid catalyzed hydrolysis of 2-trimethylsilyl-1,2-octene oxide yields 2-trimethylsilyl-1,2-octanediol. Treatment with stronger mineral acids results in elimination of trimethylsilanol and formation of 2-octanone [22].



(7.15)

α-Trimethylsilyl epoxides also undergo acid catalyzed ring opening on treatment with HBr in ethyl ether to yield α-bromo-β-hydroxyalkyl trimethylsilanes. These *trans*-bromohydrins undergo loss of trimethylsilanol on treatment with $BF_3 \cdot OEt_2$ in methylene chloride. Thus *Z*-1-trimethylsilylpentene oxide reacts with HBr to give a bromohydrin which reacts with $BF_3 \cdot OEt_2$ to yield *E*-1-bromopentene. A similar reaction sequence starting with *E*-1-trimethylsilylpentene oxide gives *Z*-1-bromopentene [23].

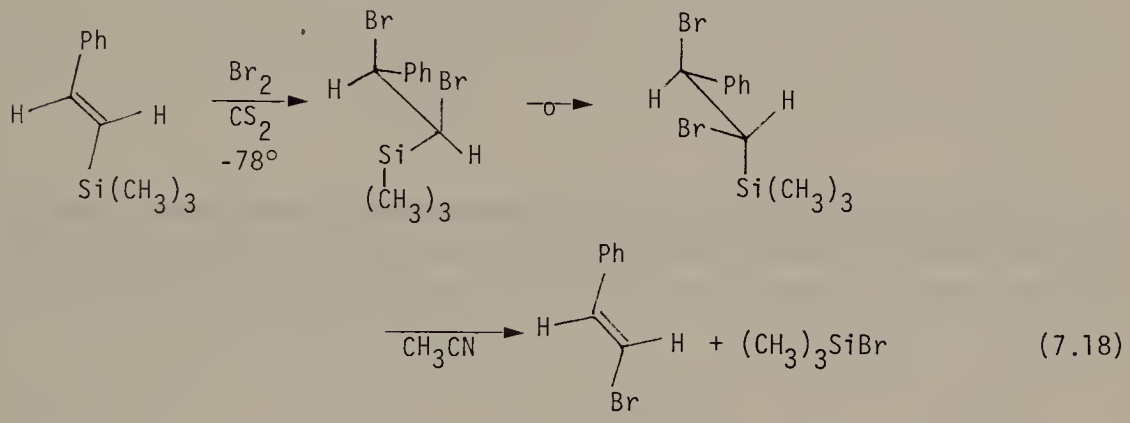


(7.17)

The stereospecific formation of enol acetates occurs when α-trimethylsilyl epoxides are treated sequentially with acetic acid and then a catalytic amount of $BF_3 \cdot OEt_2$. Reaction of α-trimethylsilyl epoxides with methanol under acidic conditions permits the stereospecific preparation of methyl enol ethers [23].

C. β-Silyl Styrenes

trans-Addition of electrophiles to vinyl trimethylsilanes followed by *trans* elimination of TMS-X fails to account for the stereochemistry observed on reaction of *Z* and *E*-β-trimethylsilylstyrene with bromine. *E* and *Z*-β-trimethylsilylstyrene react with bromine to yield dibromo adducts. Subsequent addition of acetonitrile leads to stereospecific elimination of TMS-Br. *Z*-β-Bromostyrene from the dibromo adduct of results *Z*-β-trimethylsilylstyrene.. Similarly the dibromo adduct of *E*-β-trimethylsilylstyrene gives *E*-β-bromostyrene [24]. This retention of stereochemistry may result from *cis* addition of bromine followed by a *trans* elimination of the elements of TMS-Br.

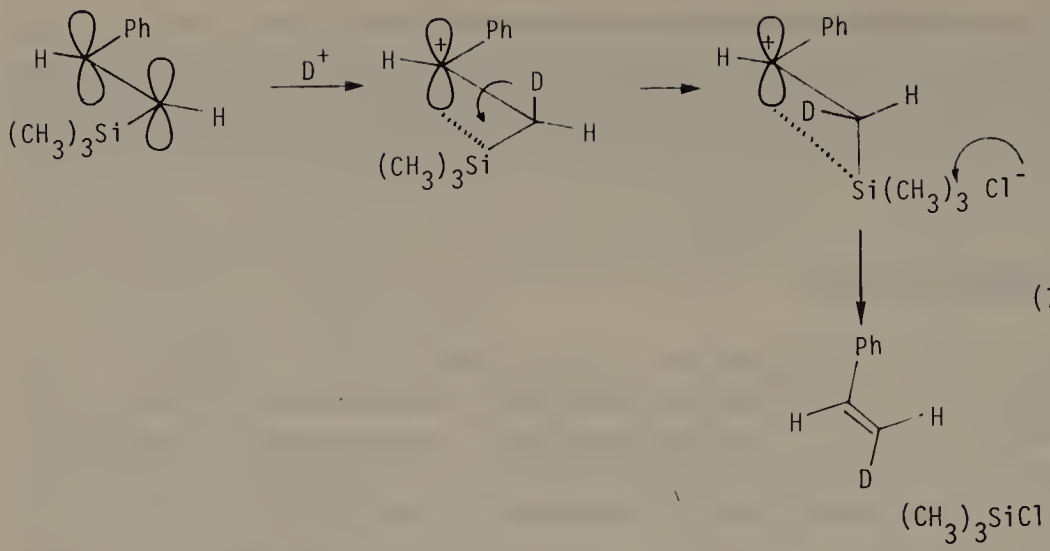


(7.18)

Similar results were obtained with *Z* and *E*-β-triphenylsilylstyrene. Evidence for *cis* addition of bromine to *E*-β-triphenylsilylstyrene was obtained by X-ray crystallography [25].

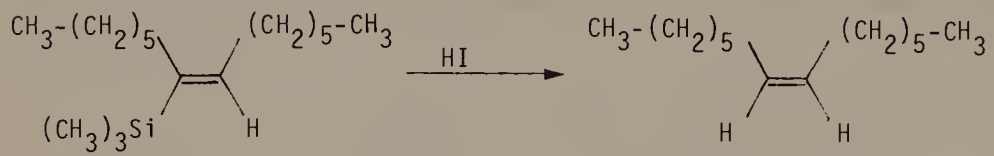
D. Protodesilylation of Vinyl Silanes

Vinyl silanes undergo protodesilylation on treatment with acids. In those cases where stereochemistry can be determined, substitution of the trimethylsilyl group by a proton occurs with retention. For example, *Z* and *E*-β-trimethylsilylstyrene react with DCl or DBr in dry acetonitrile to yield *Z*-β-deuteriostyrene and *E*-β-deuteriostyrene, [26] respectively. This may result from protonation of the double bond and simultaneous rotation about the developing C–C single bond in a direction which permits the trimethylsilyl group to continuously stabilize the incipient benzylic carbocation center [2, 27, 28]. Attack by the nucleophilic anion then occurs on silicon to yield products.



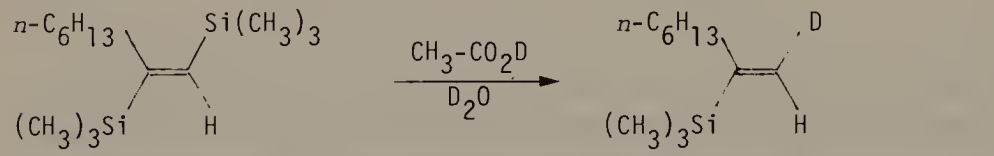
(7.19)

Similar results have been observed in the protodesilylation of *E*-7-trimethylsilyl-7-tetradecene with HI [29].



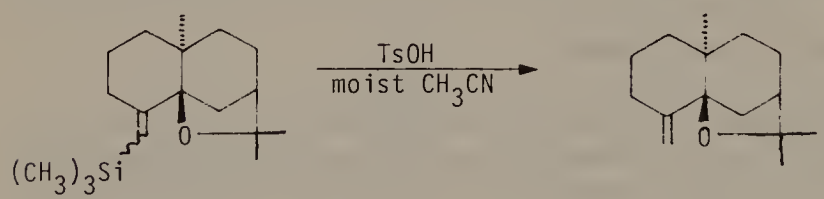
(7.20)

The selective protodesilylation of the terminal trimethylsilyl group of *E*-1,2-*bis*(trimethylsilyl)-1-octene with acetic acid-O-d_1 also proceeds with retention [30].



(7.21)

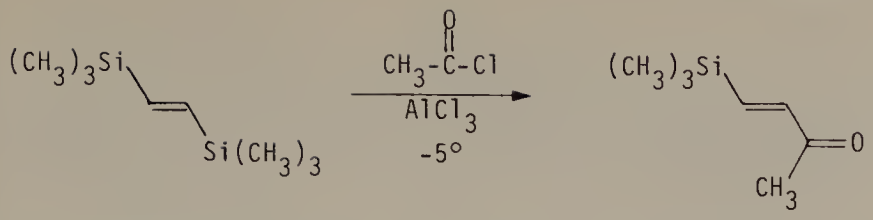
p-Toluenesulfonic acid is also effective for protodesilylation of vinyl silanes [31].



(7.22)

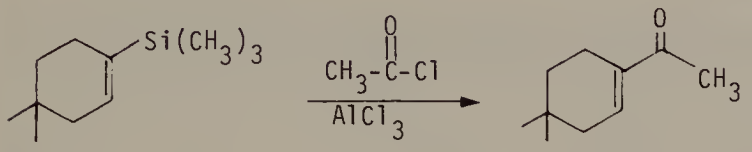
E. Friedel-Crafts Acylation Reactions

Vinyltrimethylsilanes also undergo Friedel-Crafts acylation reactions in which an acyl group replaces the trimethylsilyl group [32].



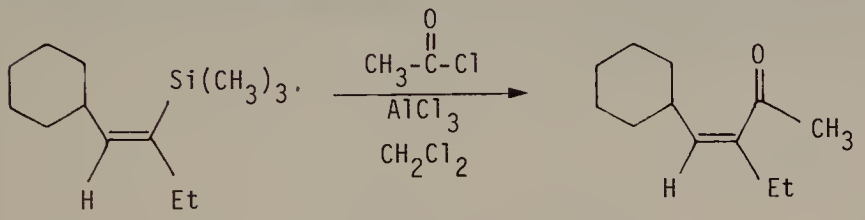
(7.23)

Friedel-Crafts acylation of cyclohexenyl-1-trimethylsilanes provides an efficient synthesis of 1-acetyl cyclohexenes [33–34].



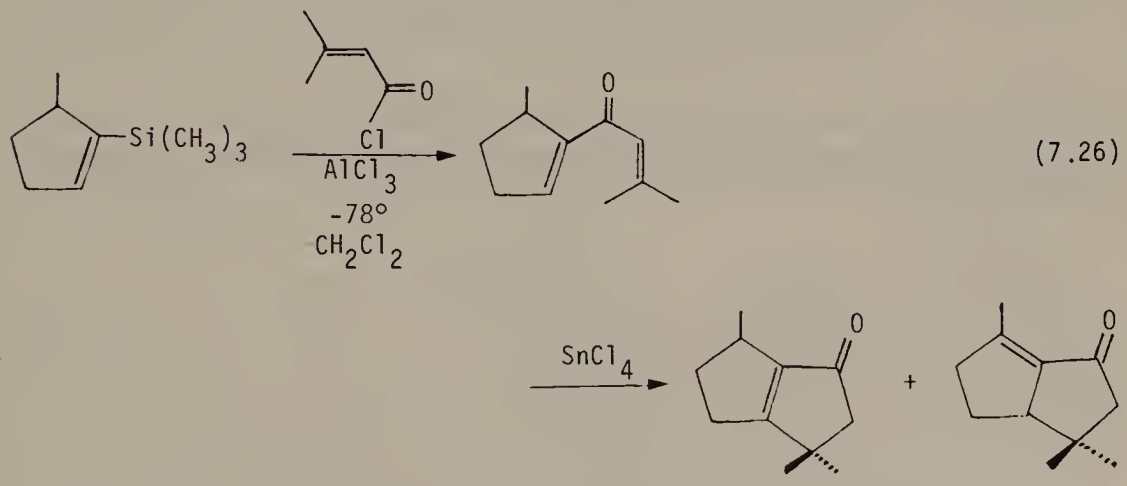
(7.24)

Similar reactions of β-trimethylsilylstyrene with either benzoyl chloride or phenylacetyl chloride have been carried out. These electrophilic substitutions proceed with retention [17].



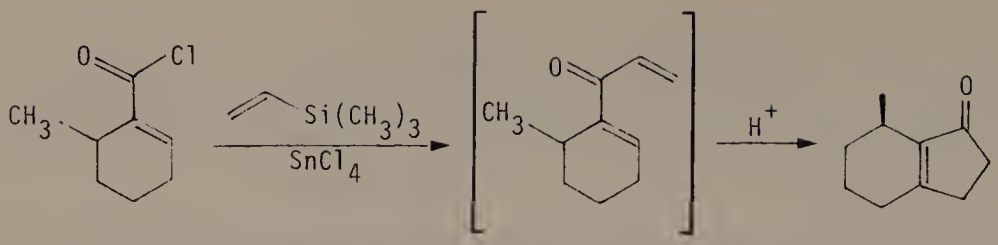
(7.25)

Friedel-Crafts acylation/desilylation of vinyl silanes is also successful with α,β-unsaturated acid chlorides [35]. This procedure has been combined with the termally allowed acid catalyzed cyclization of penta-1,4-dien-3-ones to yield cyclopentenones [36–38].



(7.26)

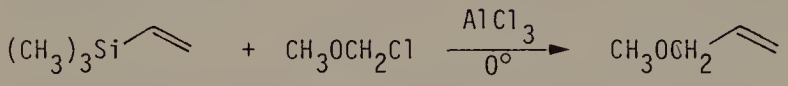
Vinyltrimethylsilane has been used as an ethylene equivalent in Nazarov-type reactions [39]. Thus, α,β-unsaturated carboxylic acid chlorides undergo Friedel-Crafts acylation/desilylation with vinyltrimethylsilane in the presence of $SnCl_4$ to yield cyclopentenones directly [40, 41].



(7.27)

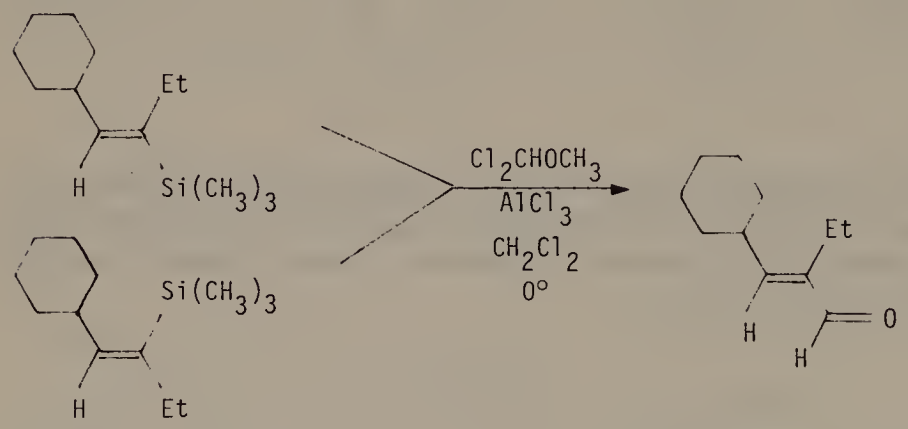
F. Friedel-Crafts Alkylation

Chloromethyl methyl ether reacts with vinyltrimethylsilane and $AlCl_3$ to give allyl methyl ether.



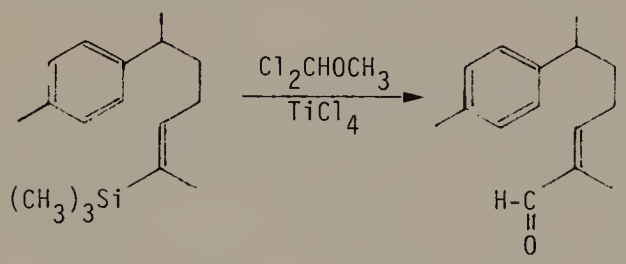
(7.28)

α,α-Dichloromethyl methyl ether reacts with *E*-1,2-*bis*(trimethylsilyl)-ethylene to yield β-trimethylsilylacrolein [35]. This reaction permits the synthesis of α,β-unsaturated aldehydes from vinyl silanes. Unfortunately, this electrophilic substitution is *not* stereospecific [17].



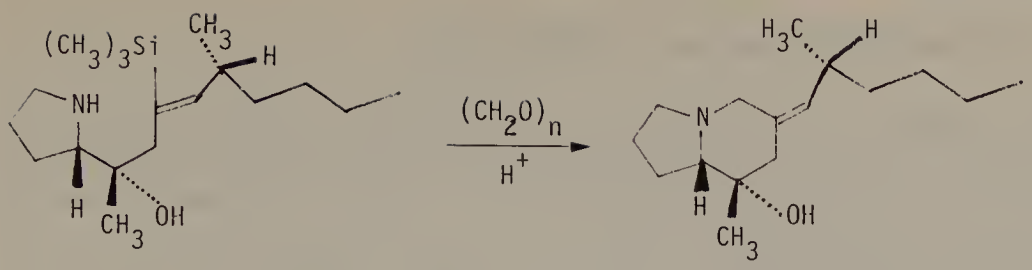
(7.29)

Yields in this reaction are greatly improved if $TiCl_4$ is utilized in place of $AlCl_3$ [42]. This methodology has been used in an efficient synthesis of Nuciferal [43].



(7.30)

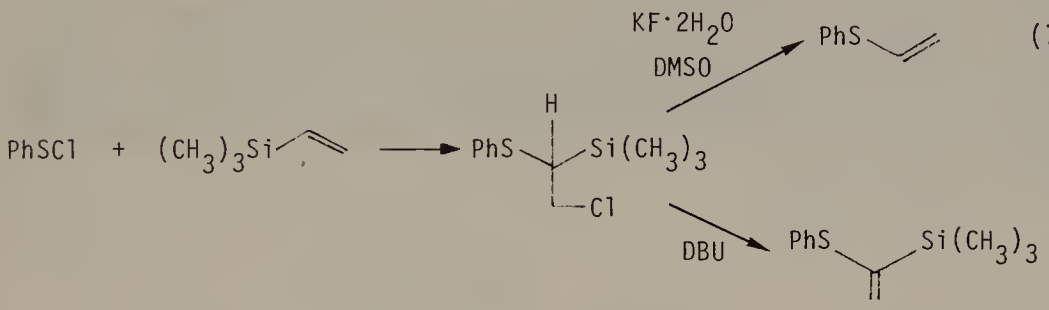
Intramolecular reaction of iminium ions with vinylsilanes provides a new method for forming unsaturated nitrogen heterocycles [143]. This electrophilic substitution proceeds with retention of the stereochemistry of the vinylsilane.



(7.31)

G. Sulfenyl Halides

Aryl sulfenyl halides add to vinyltrimethylsilane to give adducts. These undergo elimination of the elements of TMS-X on treatment with potassium fluoride dihydrate in DMSO to yield aryl vinyl sulfides [41]. On the other hand, treatment of these adducts with the tertiary amine bases such as DBU or DBN leads to 1-arylthio-1-trimethylsilylethylenes [41].

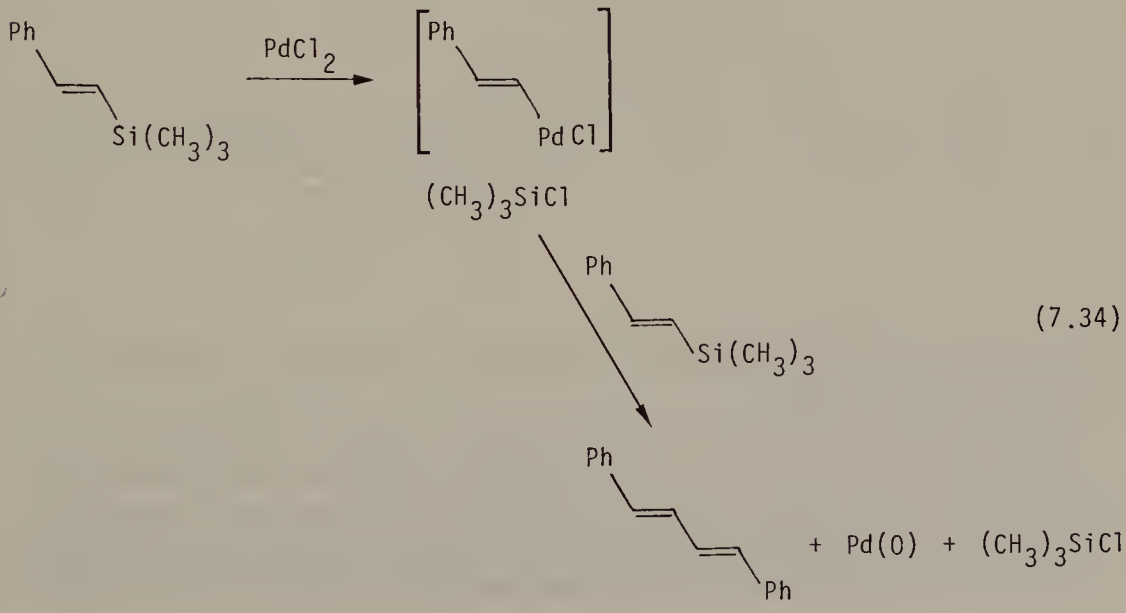


(7.32)

(7.33)

H. Palladium Chloride

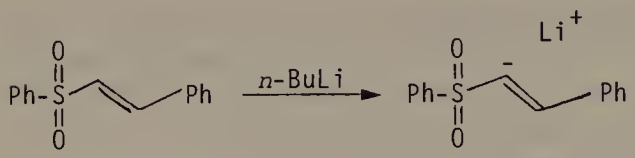
E-β-Trimethylsilylstyrene undergoes reaction with palladium chloride in methanol to yield *E,E*-1,4-diphenylbutadiene. This reaction may involve *E*-β-palladiostyrene as a reactive intermediate (Eq. 7.34) [44].



(7.34)

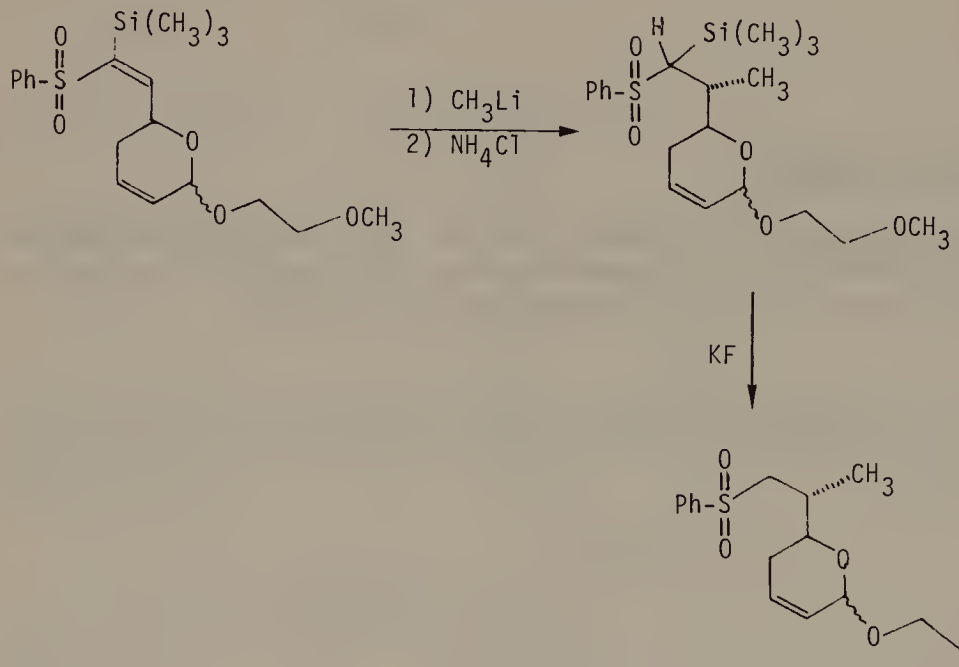
7.5 Addition of Carbanions to Vinyl Silanes

Many examples of the addition of organometallics to vinyl silanes were considered in Chapter Six. Silyl groups not only stabilize adjacent carbanions but may prevent undesired reactions. For example, treatment of phenyl β-styrenyl sulphone with *n*-butyl lithium does not result in addition to the C–C double bond to yield a sulphone stabilized carbanion, but rather in abstraction of the vinyl hydrogen adjacent to the sulphone group [45].



(7.35)

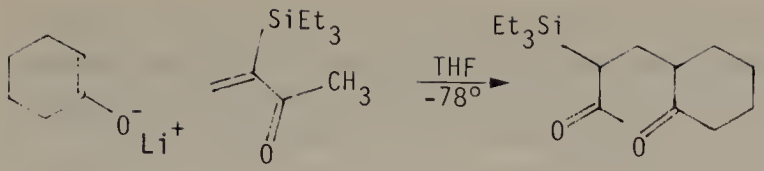
This problem can be solved by use of a trimethylsilyl protecting group. Reaction of phenyl α-trimethylsilylvinyl sulphones with methyl or *n*-butyl lithium results in addition of the alkyl lithium and formation of a carbanion stabilized by both the adjacent phenyl sulphone and trimethylsilyl groups. After protonation, the trimethylsilyl group can be removed by treatment with potassium fluoride [46].



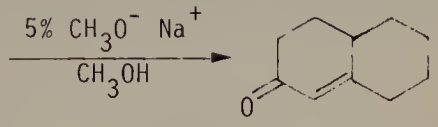
(7.36)

Such phenyl α-trimethylsilylvinyl sulphones have been prepared by the Peterson reaction [46, 47].

Regiospecific addition of enolate anions to methyl vinyl ketone fails in aprotic solvents. This problem has been overcome by the use of methyl α-trimethylsilylvinyl ketone in place of methyl vinyl ketone. The enolate anion formed by the initial Michael addition is stabilized by the silyl group. With this reagent aprotic conditions can be applied successfully [48].

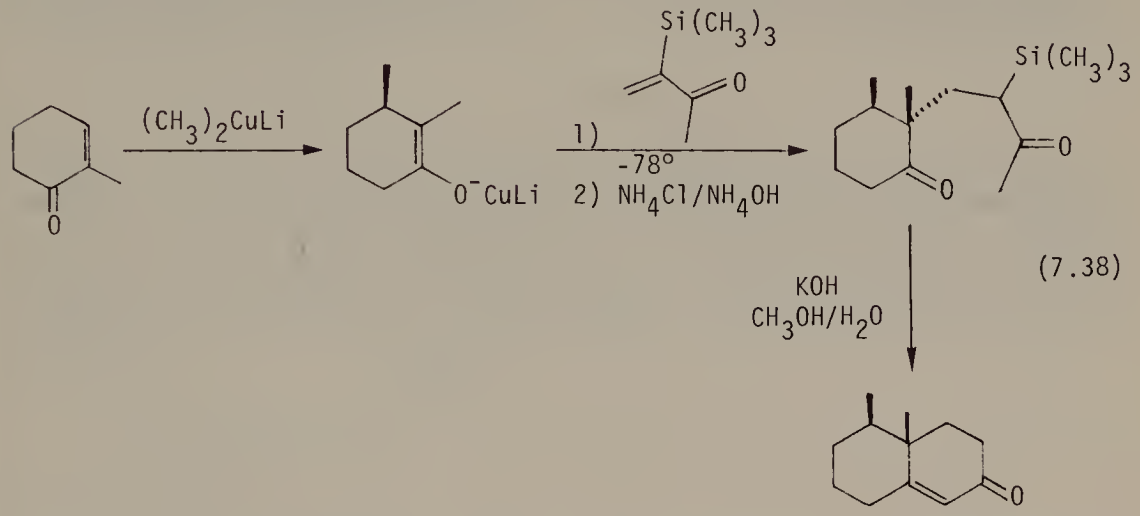


(7.37)



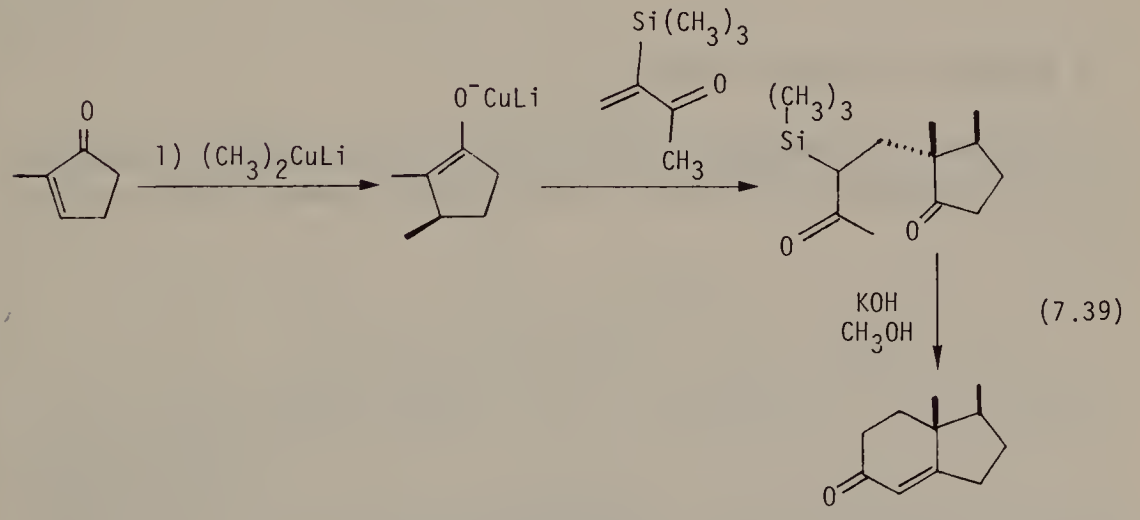
The silyl group is easily removed under the conditions of the subsequent cross-Aldol cyclization process.

Organo-copper enolates also undergo Michael addition with methyl α-trimethylsilyl vinyl ketone [49, 50].



(7.38)

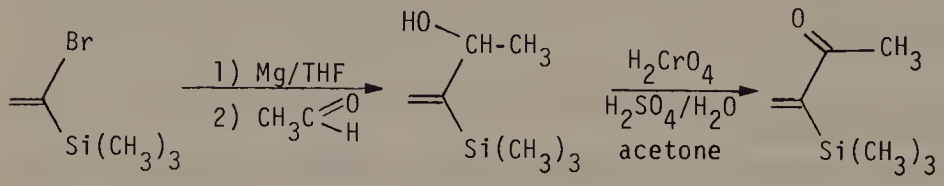
This reaction sequence is also effective with α,β-unsaturated cyclopentenones [51].



(7.39)

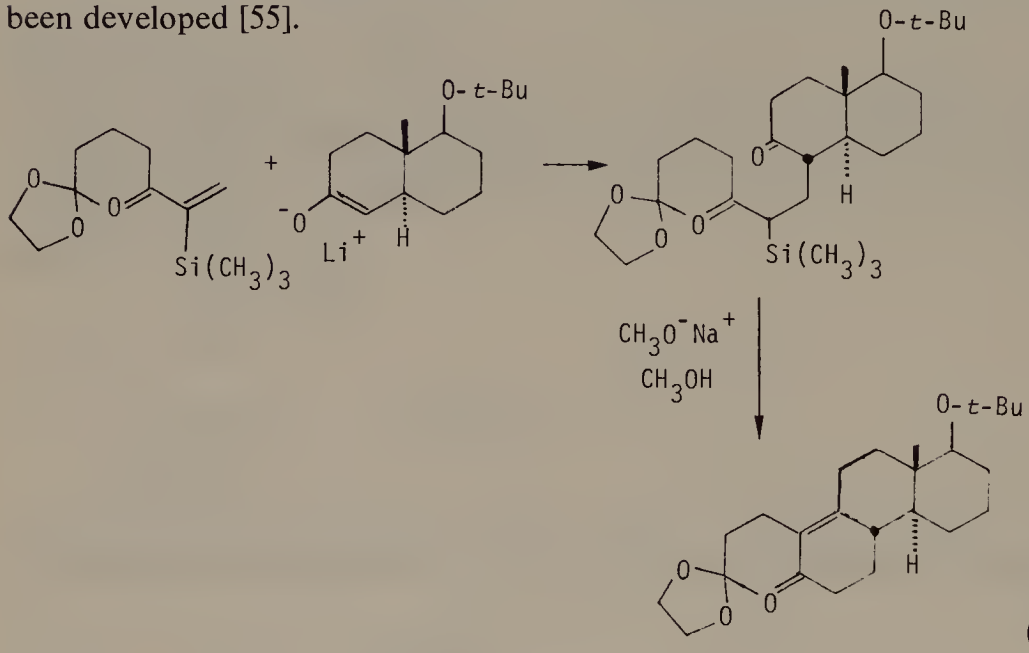
Methyl α-trimethylsilylvinyl ketone has been prepared as outlined below. Addition of bromine at −78 °C to vinyltrimethylsilane yields the expected

dibromide which undergoes dehydrohalogenation on treatment with diethylamine to yield α-bromovinyltrimethylsilane [52]. α-Bromovinyltriphenylsilane has been prepared in a similar manner [53]. Reaction of the Grignard reagent prepared from α-bromovinyltrimethylsilane with acetaldehyde yields 3-trimethylsilyl-but-3-en-2-ol. Jones oxidation of this alcohol yields the desired methyl α-trimethylsilylvinyl ketone [54].



(7.40)

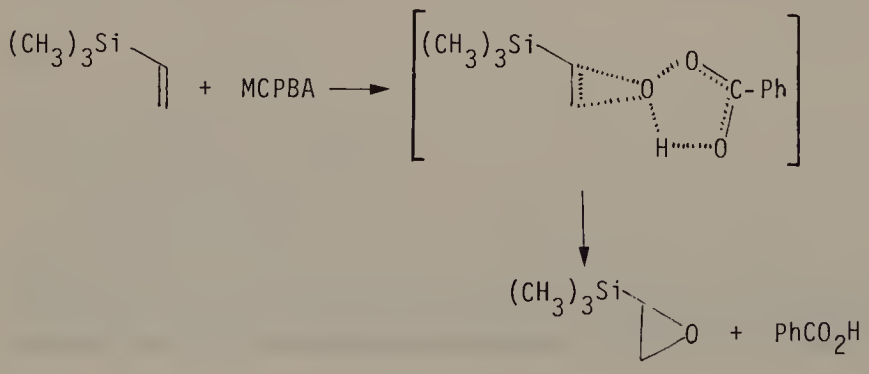
Bis-annelation reagents based on α-trimethylsilylvinyl ketones have been developed [55].



(7.41)

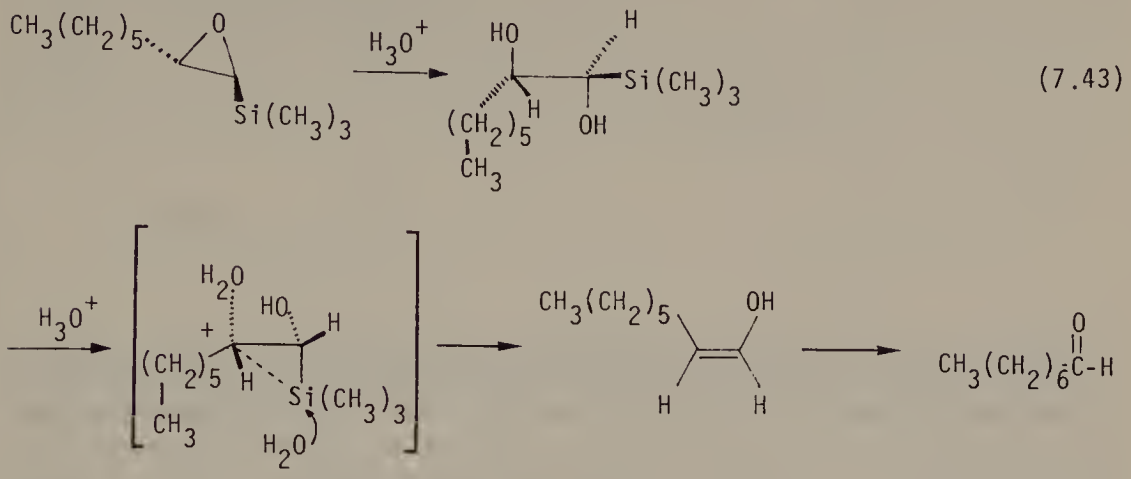
7.6 Masked Carbonyl Groups

Vinyl silanes are equivalent to masked carbonyl functionalities. Epoxidation of vinyl silanes with peracids, such as MCPBA, yields α-trimethylsilyl epoxides [56, 57].



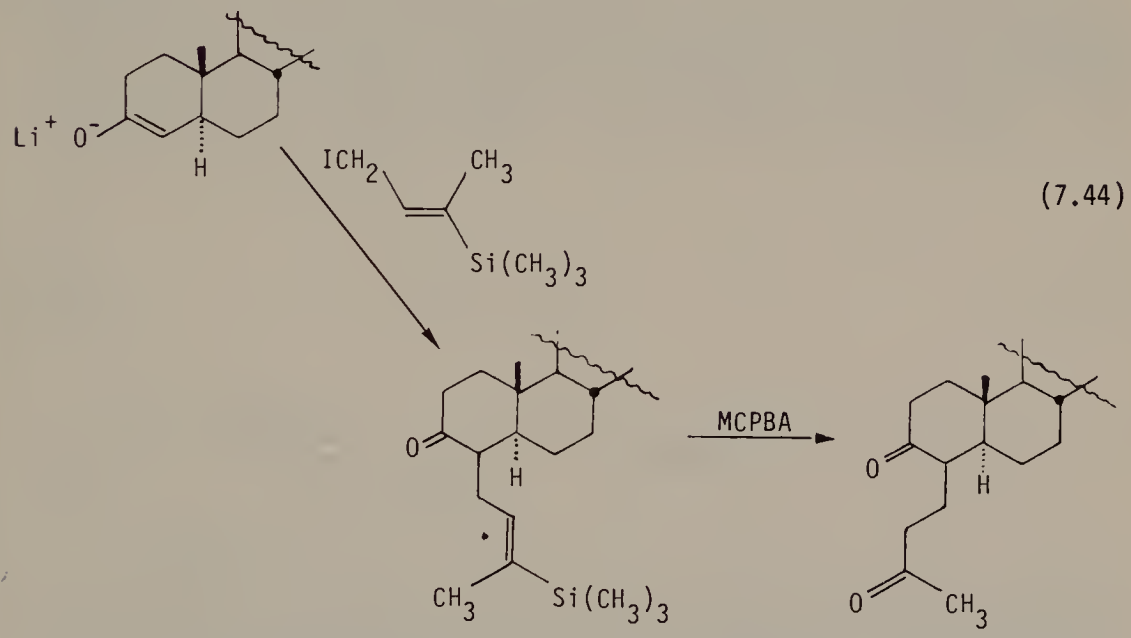
(7.42)

These undergo acid catalyzed ring opening to generate a carbonyl functional group at the carbon which formerly bore the trialkylsilyl group [58]. This may occur as outlined.



(7.43)

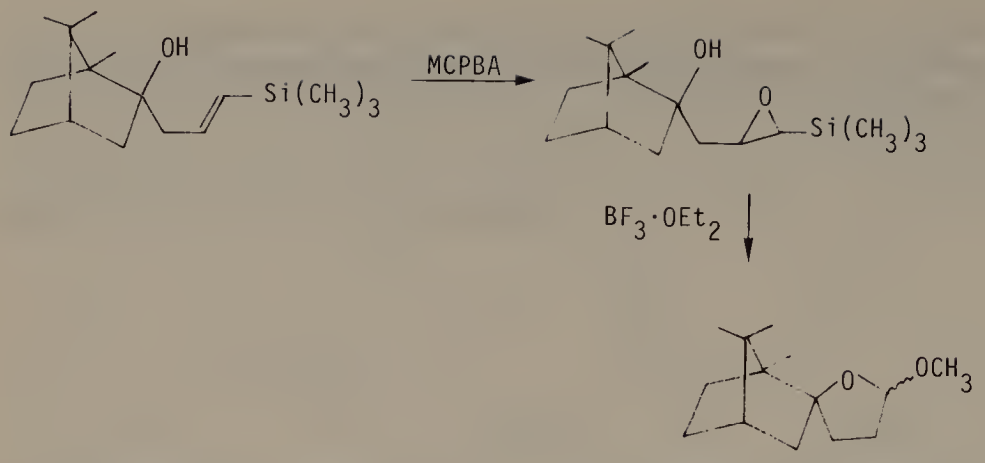
This information may have led to the design of 1-iodo-3-trimethylsilyl-2-butene as an ketone annulation reagent. C-Alkylation of lithium enolates by this allylic iodide yields δ-trimethylsilyl-γ,δ-unsaturated ketones. Subsequent treatment with MCPBA yields δ-trimethylsilyl γ,δ-epoxy ketones which are converted to 1,5-diketones by *m*-chlorobenzoic acid with loss of the trimethylsilyl group [59].



(7.44)

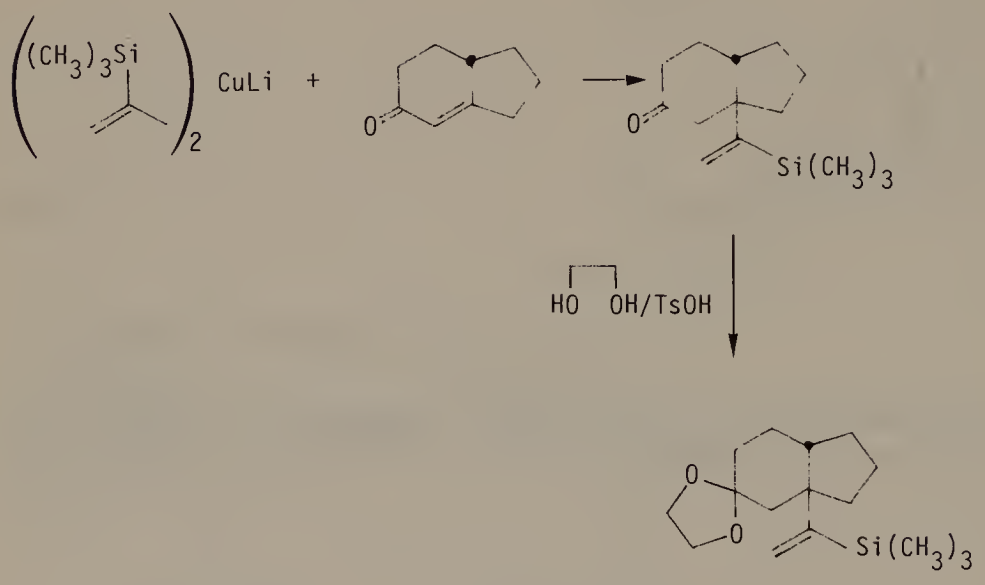
1-Iodo-3-trimethylsilyl-2-butene has been prepared from 3-trimethylsilylpropyn-1-ol [60, 61].

Treatment of *E*-1-(2′-hydroxyalkyl)-2-trimethylsilylethylenes with MCPBA leads to α-trimethylsilyl epoxides. These react with $BF_3 \cdot OEt_2$ in methanol to yield lactol methyl ethers which can be oxidized with Jones reagents to the corresponding γ lactones [62].

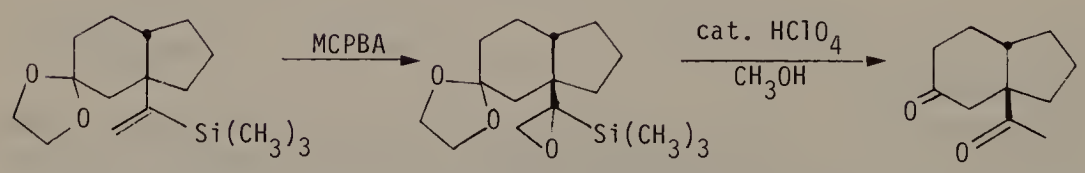


(7.45)

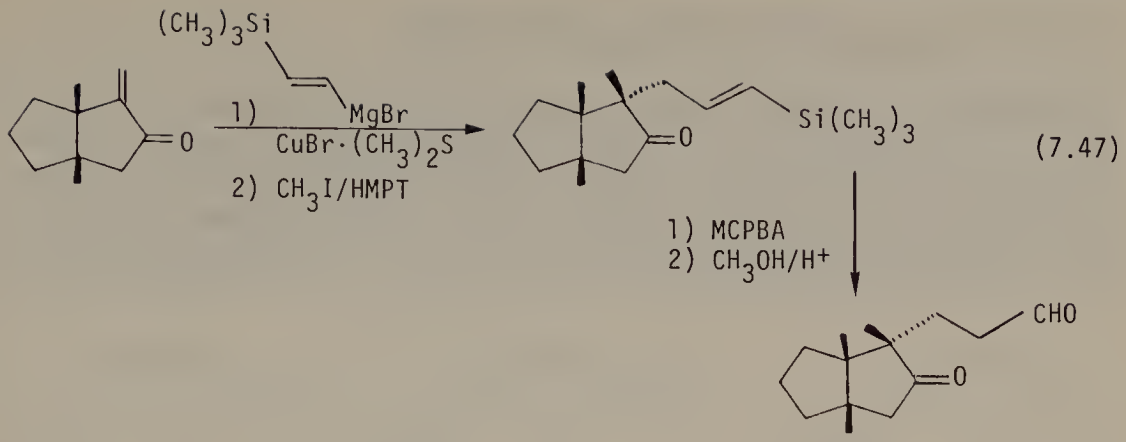
The conjugate addition of *bis*(α-trimethylsilylvinyl)copper lithium to α,β-unsaturated ketones is synthetically equivalent to a Michael addition of an acyl anion. This results from the fact that vinyl trimethylsilanes can be readily oxidized by MCPBA to α-trimethylsilyl epoxides which undergo acid catalyzed hydrolysis to yield ketones or aldehydes. This synthetic sequence permits the generation of 1,4-dicarbonyl compounds. Due to the low reactivity of vinyl silanes toward MCPBA, it may be necessary to protect the ketone prior to epoxidation to prevent competitive Baeyer-Villiger oxidation [63, 64].



(7.46)

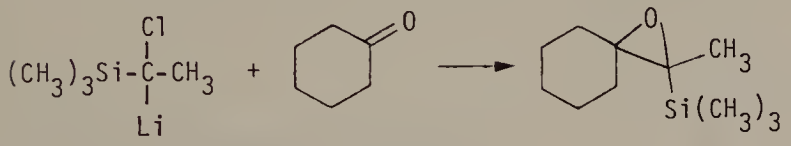


1,5-Keto aldehydes have been prepared as outlined below (Eq. 7.47) [65].



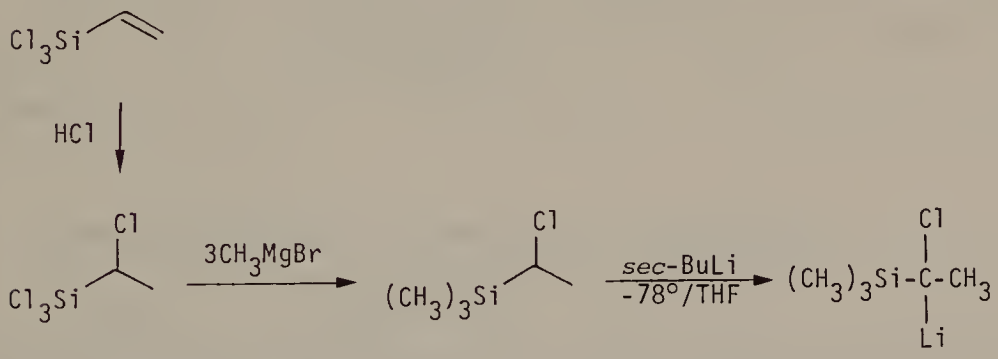
(7.47)

An alternative approach to the synthesis of α-trimethylsilyl epoxides involves the reaction of ketones or aldehydes with α-chloro-α-trimethylsilylethyl lithium [66, 67].



(7.48)

This methodology has been exploited in an efficient synthesis of R(+)-Frontalin [69]. α-Chloro-α-trimethylsilylethyl lithium has been prepared by metallation of α-chloroethyltrimethylsilane by *sec*-butyl lithium in THF at $-78°$. α-Chloro-α-trimethylsilylethane has been prepared as outlined (Eq. 7.49). This provides an example of a limitation in the ability of silicon to stabilize a β-carbocation [68]. Thus HCl adds in an anti-Markovnikoff sense to vinyltrimethylsilane but in a Markovnikoff sense to the vinyltrichlorosilane.

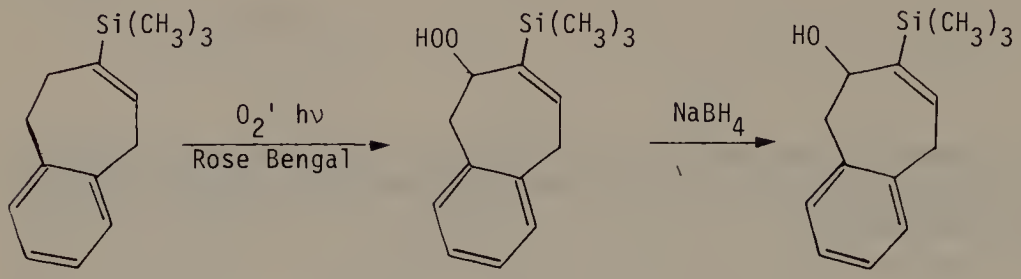


(7.49)

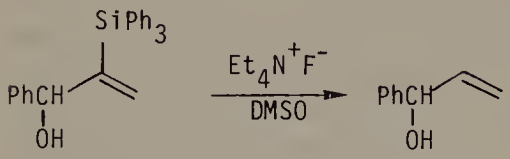
α-Trimethylsilyl epoxides have also been prepared by reaction of α-lithiotrimethylsilyldiazomethane with ketones. This reagent is formed by metallation of α-trimethylsilyldiazomethane with *n*-butyl lithium in THF/*n*-pentane at $-100°$ [70]. However, the preparation of α-trimethylsilyldiazomethane is rather difficult [71].

7.7 1,2-Transposition of Carbonyl Groups

Photochemically generated singlet oxygen undergoes regiospecific reaction with vinyl trimethylsilanes to yield 2-trimethylsilylallylic hydroperoxides. These can be reduced with $NaBH_4$ to yield 2-trimethylsilylallylic alcohols (Eq. 7.50) [72]. The adjacent hydroxyl functionality facilitates removal of the trimethylsilyl group by fluoride ion in DMSO or acetonitrile (Eq. 7.51) [73].

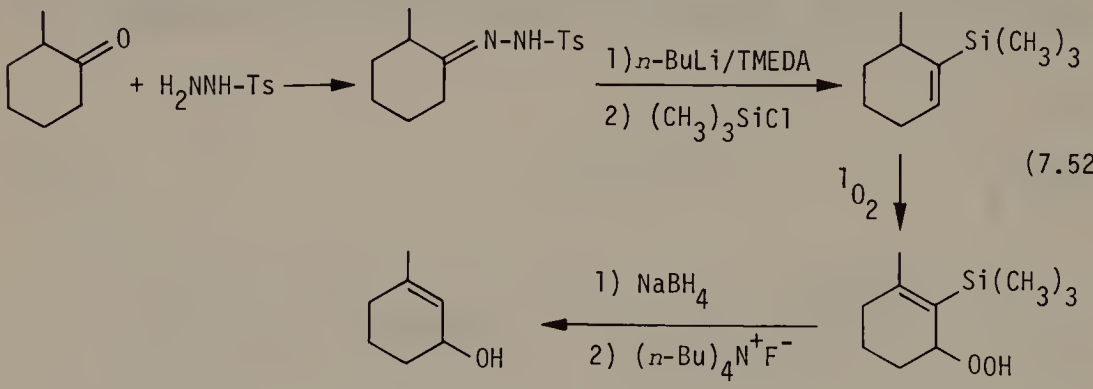


(7.50)



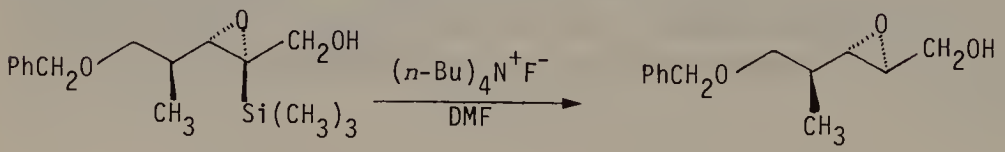
(7.51)

Combining these reactions with the efficient synthesis of vinyltrimethylsilanes from ketones (outlined below Eq. 7.52) permits the regiospecific conversion of ketones to allylic alcohols [72, 76]. The 1,2-transposition of the oxygen functionality in this process should be noted.



(7.52)

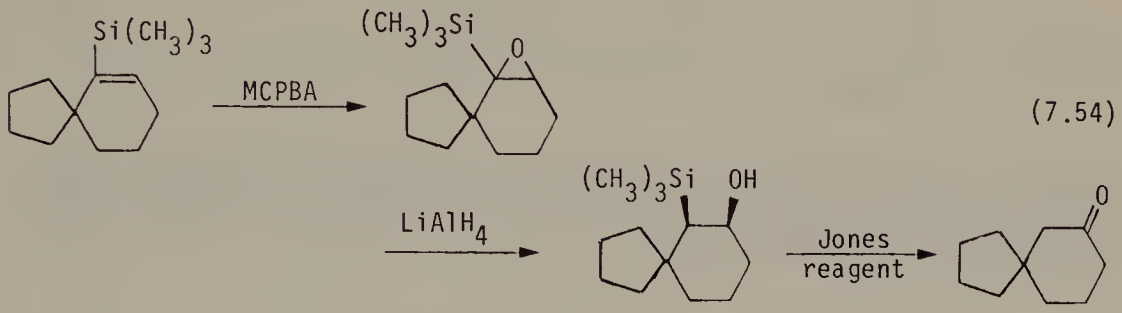
An adjacent hydroxyl functionality also facilitates removal of trimethylsilyl groups from α-trimethylsilyl epoxides by fluoride [74, 75].



(7.53)

By comparison neither vinyltriphenylsilane nor vinyltrimethylsilane are desilylated under these conditions [73].

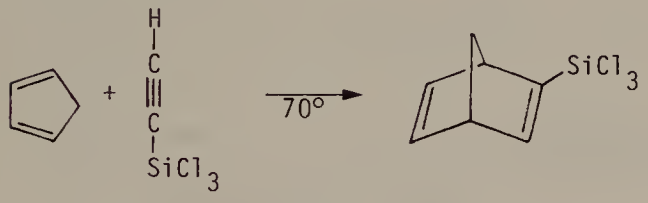
1,2-Transposition of a ketone carbonyl functionality can be efficiently achieved by the use of vinyl silanes. Epoxidation of vinyl trimethyl silanes with MCPBA followed by treatment of the α-trimethylsilyl epoxides with $LiAlH_4$ yields β-hydroxyalkyltrimethylsilanes [21, 77]. This results from nucleophilic attack by the hydride at the silyl substituted carbon of the epoxide ring [77]. Oxidation of the β-hydroxyalkyltrimethylsilane with Jones reagent yields the desired ketone [76, 78]. Such 2-trimethylsilyl ketones easily suffer cleavage of the C–Si bond under acidic conditions [79, 80].



(7.54)

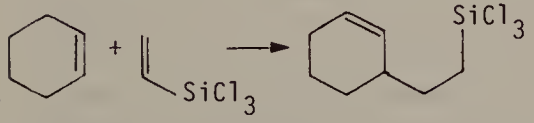
7.8 Cycloaddition Reactions

Limited work has been done on cycloaddition reactions of vinyl silanes. Diels-Alder reaction of trichlorosilylacetylene with cyclopentadiene provides an efficient route to 2-trichlorosilylnorbornadiene. Similar reaction of trimethylsilylacetylene with cyclopentadiene requires higher temperatures (270°) [81].



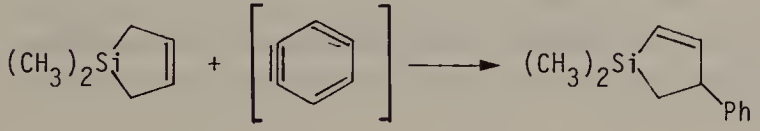
(7.55)

Vinyltrichlorosilane also undergoes ene reactions [82].

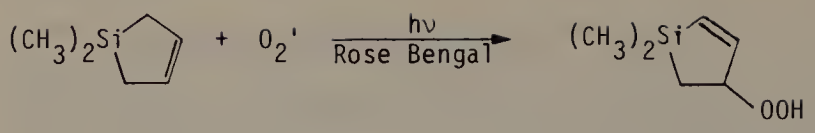


(7.56)

Ene reactions of allylic silanes with maleic anhydride, diethylazodicarboxylate, benzyne, formaldehyde, 4-phenyl-1,2,4-triazoline-3,5-dione and singlet oxygen provide efficient routes to functionally-substituted vinyl silanes [82–87].

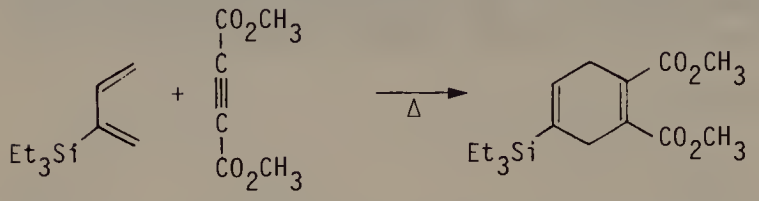


(7.57)



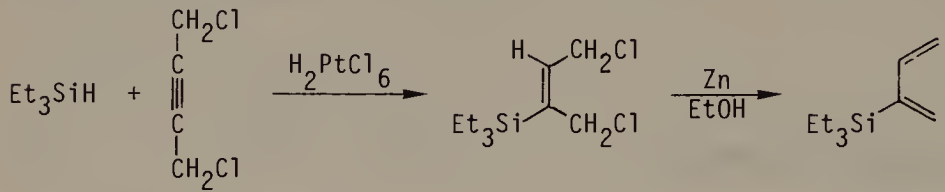
(7.58)

2-Triethylsilyl-1,3-butadiene undergoes Diels-Alder reactions with a variety of dienophiles.



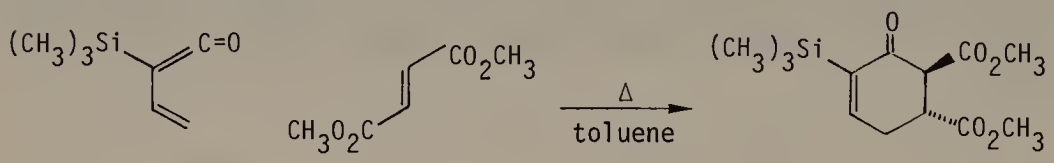
(7.59)

Hydrosilation of 1,4-dichloro-2-butyne with triethylsilane catalyzed by chloroplatinic acid followed by dechlorination with zinc dust in ethanol yields 2-triethylsilyl-1,3-butadiene [88].



(7.60)

Trimethylsilyl vinyl ketene also undergoes Diels Alder reactions with a variety of dienophiles [89].



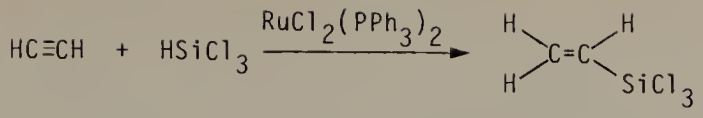
(7.61)

This ketene was prepared by dehydrohalogenation of *Z*-2-trimethylsilyl-3-butenoyl chloride with triethylamine [89].

7.9 Preparation of Vinyl Silanes

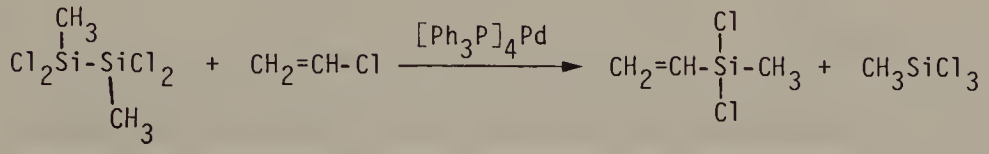
The variety of stereo- and regiospecific transformations which can be accomplished by use of vinyl silanes has led to considerable interest in methods to prepare these compounds with specific substitution patterns and defined stereochemistry.

Industrially, vinyltrichlorosilane and vinylmethyldichlorosilane may be produced by heating either trichlorosilane, or methyldichlorosilane and vinyl chloride at 600° [90, 91]. A more convenient laboratory method is the atmospheric pressure hydrosilation of acetylene by trichlorosilane, triethoxysilane, methyldichlorosilane, or methyldiethoxysilane catalyzed by ruthenium, rhodium, or platinum complexes [92].



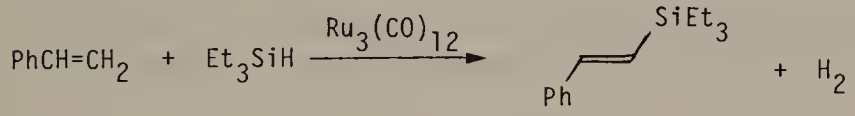
(7.62)

tetrakis(Triphenylphosphine) palladium (O) catalyzes the reaction of vinyl chloride with either *sym*-dichlorotetramethyldisilane or *sym*-tetrachlorodimethyldisilane to yield vinyldimethylchlorosilane or vinylmethyldichlorosilane respectively [93].



(7.63)

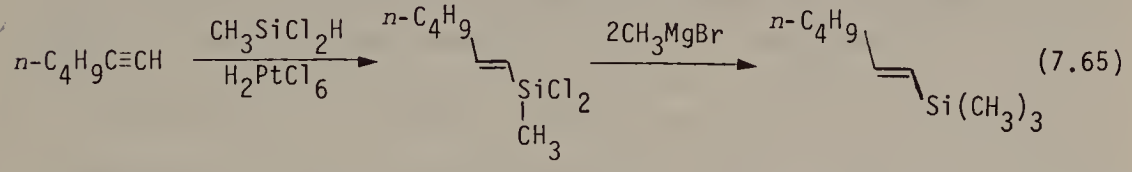
Based on the similarities between catalytic hydrogenation and hydrosilation, a direct synthesis of vinyl silanes would involve a catalytic reaction of a silane with an alkene to yield an alkylsilane as an intermediate which would lose hydrogen and give a vinyl silane as a final product. This concept has been demonstrated in practice for a few cases. Trialkylsilanes react both thermally [94] and photochemically [95] with alkenes to give a mixture of vinyltrialkylsilanes and tetraalkylsilanes under catalysis by iron pentacarbonyl. Similar results have been obtained with a rhodium catalyst [96]. Triethylsilane reacts with α-olefins under catalysis by a dimeric rhodium complex to give mixtures of alkyltriethylsilanes, alkenyltriethylsilanes, and allylic triethylsilanes. The desired alkenyltrimethylsilane is the predominant product at high ratios of olefin to triethylsilane [97]. Most recently, encouraging results have been reported when a ruthenium carbonyl cluster is used as catalyst [98].



(7.64)

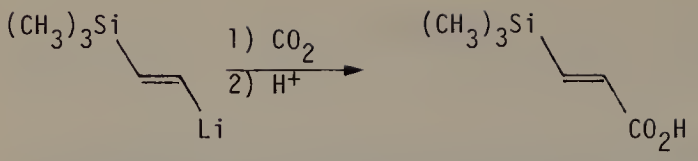
A. E-1-Trimethylsilyl-1-alkenes

E-1-trimethylsilyl-1-alkenes are readily prepared by the chloroplatinic acid catalyzed hydrosilation of terminal alkynes with either trichlorosilane or methyldichlorosilane followed by addition of methylmagnesium bromide [99].



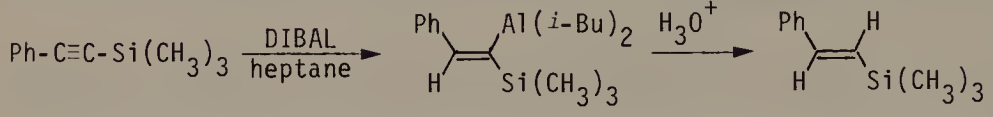
(7.65)

E-1-Lithio-2-trimethylsilylethylene, prepared form *E*-1-bromo-2-trimethylsilylethylene by halogen-metal exchange with *t*-butyl lithium [63] or by direct reaction with lithium [100, 101] permits the preparation of a variety of *E*-1-trimethylsilylethylene derivatives.



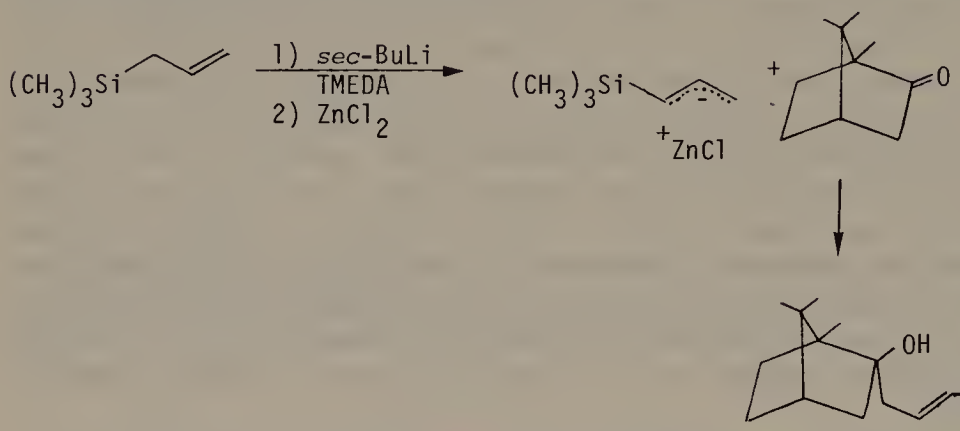
(7.66)

Treatment of 1-trimethylsilylalkynes with DIBAL in hydrocarbon solvents followed by protonolysis leads to *E*-1-trimethylsilyl alkenes [102].



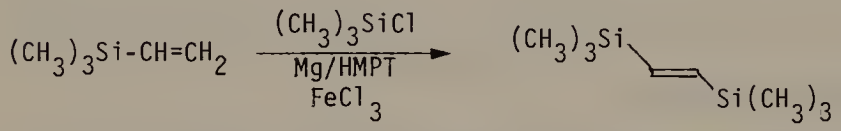
(7.67)

Metallation of allyltrimethylsilane with *sec*-butyl lithium in THF/TMEDA yields 1-trimethylsilylallyl lithium. This reagent reacts regiospecifically at its 3-position with ketones or aldehydes to yield *E*-1-(2′-hydroxyalkyl)-2-trimethylsilylethylenes [62, 103, 104].



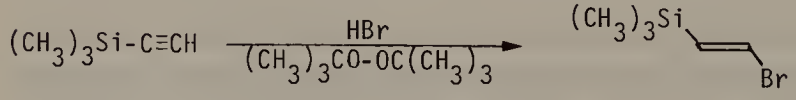
(7.68)

E-1,2-*bis*(Trimethylsilyl)ethylene has been prepared by treatment of vinyltrimethylsilane with TMS-Cl and magnesium powder in HMPT [105].



(7.69)

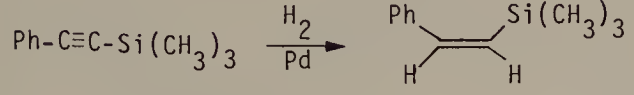
E-1,2-*bis*(Trimethylsilyl)ethylene has also been prepared by hydrosilation of trimethylsilylacetylene with dimethylchlorosilane catalyzed by chloroplatinic acid followed by addition of methylmagnesium iodide [106]. Reaction of *E*-2-trimethylsilyl vinyl magnesium bromide with TMS-Cl also gives *E*-1,2-*bis*(trimethylsilyl)ethylene. *E*-1-Bromo-2-trimethylsilylethylene is readily available by the addition of dry HBr to trimethylsilylacetylene under free radical catalysis by di-*t*-butyl peroxide [107, 108].



(7.70)

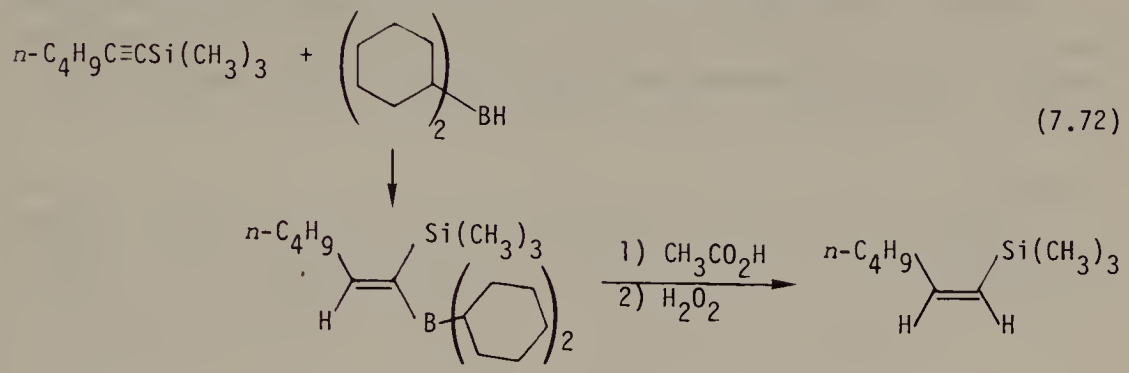
B. *Z*-1-Trimethylsilyl-1-alkenes

A variety of methods permit preparation of *Z*-1-trimethylsilyl-1-alkenes. Among these is the low pressure catalytic hydrogenation of 1-trimethylsilyl alkynes over either Raney nickel [109] or a nickel boride catalyst (P-2-Ni) [15].



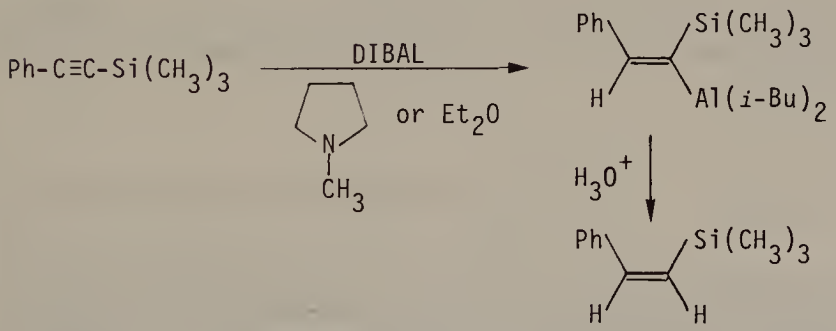
(7.71)

Hydroboration of 1-trimethylsilyl alkynes with dicyclohexyl borohydride [14] or disiamyl borohydride, followed by protonolysis of the sp^2 hybridized C–B bond by acetic acid also yields *Z*-1-trimethylsilyl-1-alkenes.



(7.72)

Treatment of 1-trimethylsilyl alkynes with DIBAL in ether [15, 110] or in heptane in the presence of one equivalent of tertiary amines [102] leads to *Z*-1-trimethylsilyl alkenes after protonolysis of the sp^2 hybridized C–Al bond.



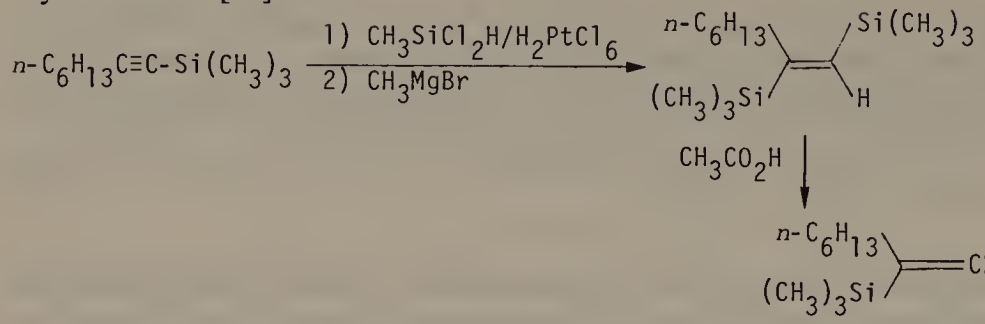
(7.73)

Such *Z*-1-trimethylsilyl alkenes undergo facile isomerization on irradiation with a sunlamp in pyridine with a catalytic amount of NBS (5 mole %) to yield *E*-1-trimethylsilyl alkenes [110].

C. 2-Trimethylsilyl-1-alkenes

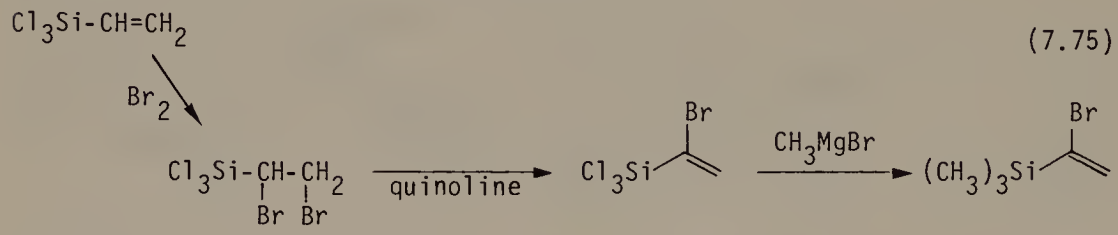
2-Trimethylsilyl-1-alkenes have been prepared by a variety of methods. Chloroplatinic acid catalyzed hydrosilation of 1-trimethylsilyl alkynes with methyldichlorosilane, followed by addition of methylmagnesium bromide generally yields *E*-1,2-*bis*(trimethylsilyl)alkenes [30]. 1-*t*-Butyl-2-trimethylsilyl acetylene is an exception [111]. Protodesilylation with acetic acid/water

selectively removes the terminal trimethylsilyl group to yield 2-trimethylsilyl-1-alkenes [30].



(7.74)

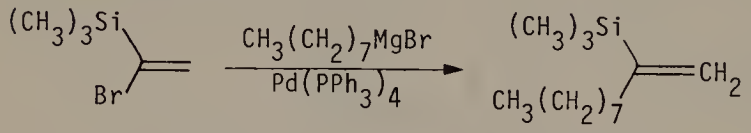
α-Bromovinyltrimethylsilane is an extremely versatile precursor for the preparation of 2-trimethylsilyl-1-alkenes. Addition of bromine to vinyltrichlorosilane, followed by dehydrohalogenation with quinoline or N,N-diethylaniline yields α-bromovinyltrichlorosilane. This reacts with excess methyl Grignard reagent to yield α-bromovinyltrimethylsilane [112].



(7.75)

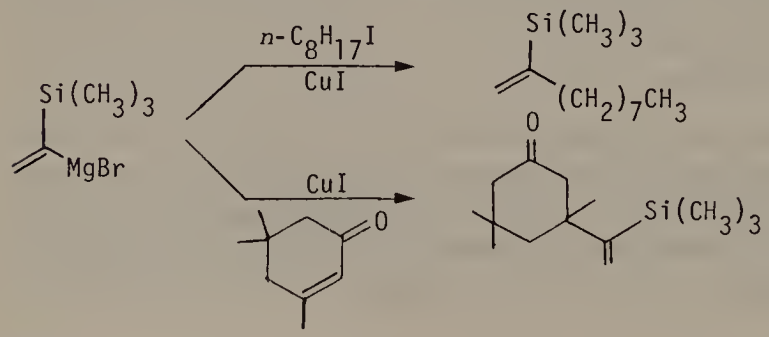
Alternatively, α-bromovinyltrimethylsilane can be prepared from vinyltrimethylsilane by addition of bromine, followed by dehydrohalogenation with diethylamine [52, 54]. The reaction of 1,1-*bis*-(trimethylsilyl)ethylene with bromine [113] also yields α-bromovinyltrimethylsilane.

α-Bromovinyltrimethylsilane undergoes coupling reactions with Grignard reagents catalyzed by *tetrakis*(triphenylphosphine) palladium (O) to yield 2-trimethylsilyl-1-alkenes [20].



(7.76)

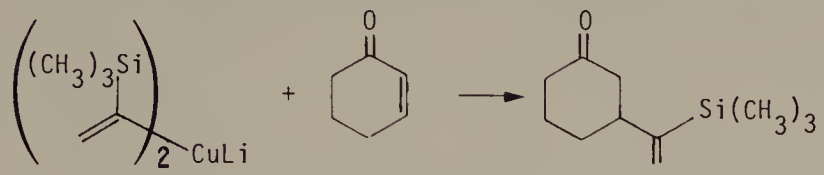
α-Bromovinyltrimethylsilane can be converted to a Grignard reagent which will couple with primary alkyl iodides or tosylates (Eq. 7.77), or undergo conjugate addition to α,β-unsaturated ketones in the presence of copper (I) salts (Eq. 7.78) [20].



(7.77)

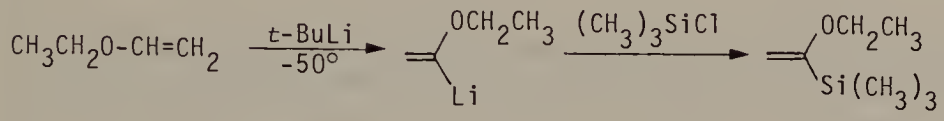
(7.78)

Halogen-metal exchange between α-bromovinyltrimethylsilane and *t*-butyl lithium at −78 °C gives the expected vinyl lithium reagent. Reaction of this with cuprous iodide yields *bis*(α-trimethylsilylvinyl)copper lithium which undergoes conjugate addition to α,β-unsaturated ketones [63, 64].



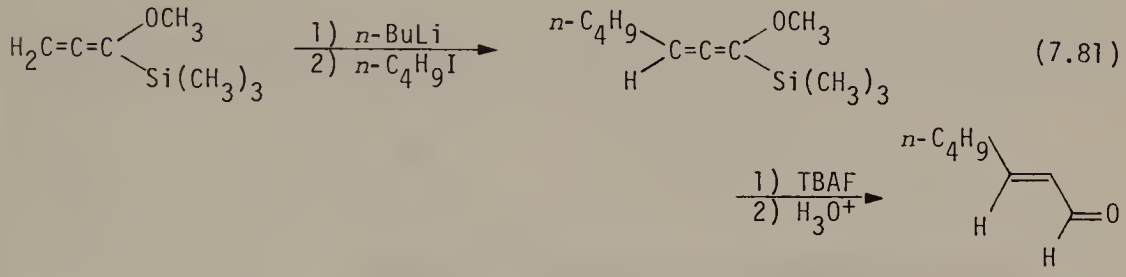
(7.79)

α-Ethoxy-α-trimethylsilyl ethylene has been prepared by reaction of α-ethoxy vinyl lithium with TMS-Cl [114].



(7.80)

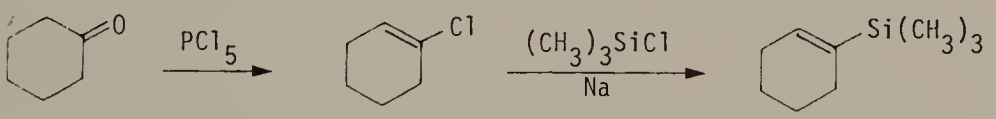
In a similar manner, reaction of 1-lithio-1-methoxy-1,3-butadiene with TMS-Cl yields 1-methoxy-1-trimethylsilyl-1,3-butadiene [115, 116]. 1-Methoxy-1-trimethylsilylallene, prepared from 1-methoxyallene, can be converted to 1-methoxy-1-trimethylsilyl-1,2-heptadiene (Eq. 7.81). This reacts with fluoride ion to yield *E*-2-heptenal [117].



(7.81)

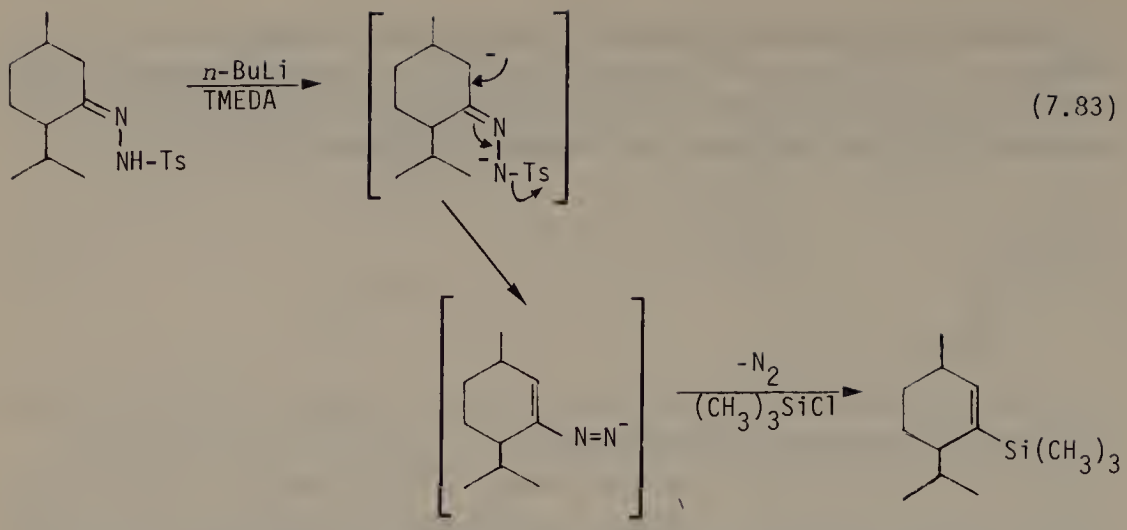
D. 1-Cycloalkenyltrimethylsilanes

Cyclic ketones can easily be converted to 1-cycloalkenyltrimethylsilanes. The ketone is reacted with PCl_5 to give a 1-chlorocycloalkene, which undergoes a Wurtz type coupling with TMS-Cl in the presence of sodium [33, 118, 119].



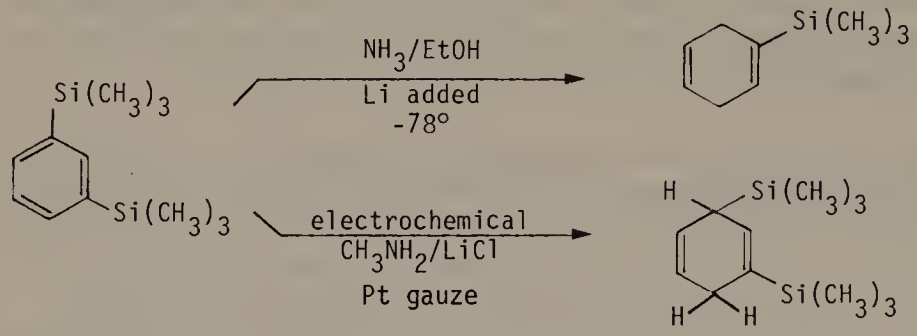
(7.82)

An alternative method involves conversion of the ketone to a benzene or *p*-toluene sulfonyl hydrazone. Such hydrazones react with excess *n*-butyl lithium/TMEDA to yield the least substituted vinyl lithium reagent. This can be quenched with TMS-Cl to yield the corresponding vinyl trimethylsilane [38, 78, 118, 120, 121].



(7.83)

Birch reduction (Eq. 7.84) or the related electrochemical reduction (Eq. 7.85) of aryltrimethylsilanes is not generally useful for the preparation of 1-trimethylsilylcyclohexene derivatives because trimethylsilyl groups are often lost under the reaction conditions. Nevertheless, in specific cases good to excellent yields are achieved [122, 123].

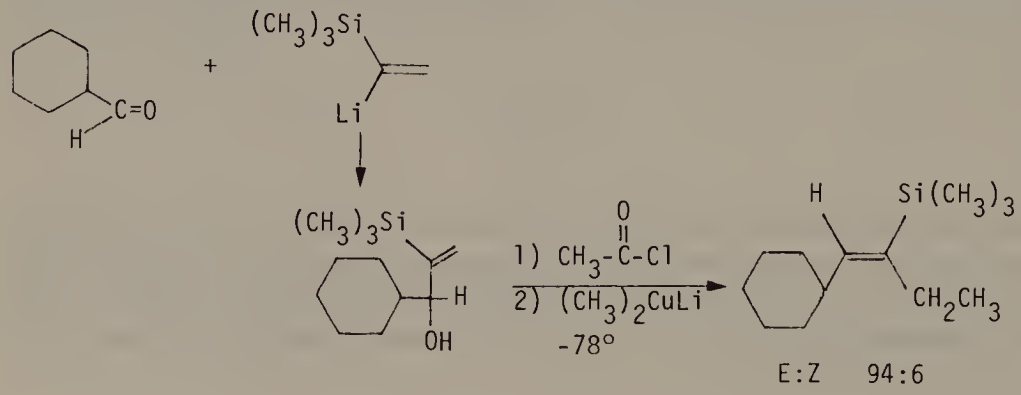


(7.84)

(7.85)

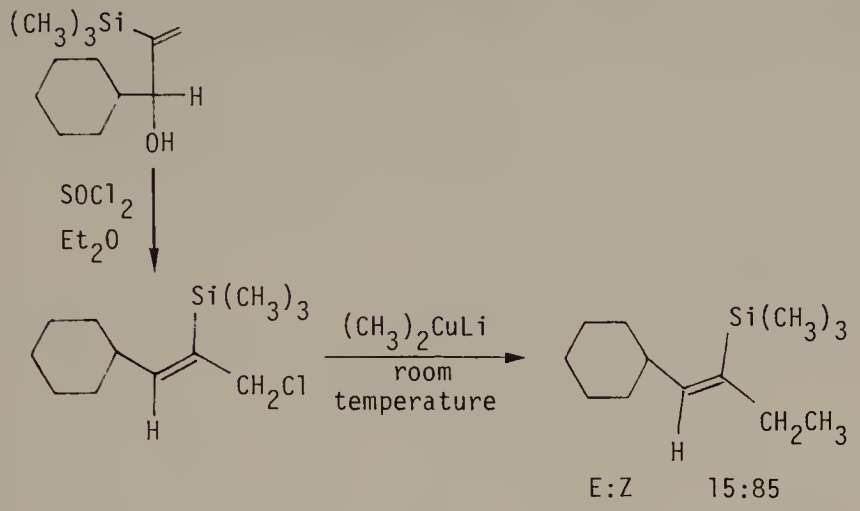
E. *E* and *Z*-1,2-Dialkyl-1-trimethylsilyl ethylenes

α-Lithiovinyl trimethylsilane reacts with aldehydes or ketones to yield 2-trimethylsilyl allylic alcohols. These can be converted to 2-trimethylsilyl allylic acetates which undergo S_N2' coupling with dialkyl copper lithium reagents to yield predominantly *E*-1,2-dialkyl-1-trimethylsilylethylenes [124].



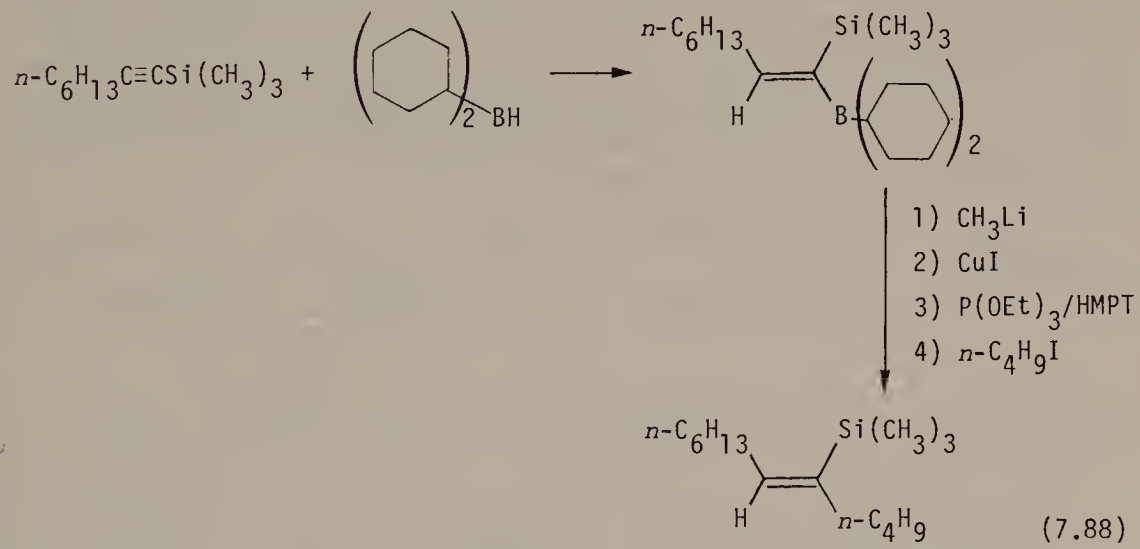
(7.86)

On the other hand, treatment of 2-trimethylsilyl allylic alcohols with thionyl-chloride yields rearranged 2-trimethylsilyl allylic chlorides [124, 125]. These undergo coupling with dialkyl copper lithium reagents to yield predominantly *Z*-1,2-dialkyl-1-trimethylsilylethylenes [124].



(7.87)

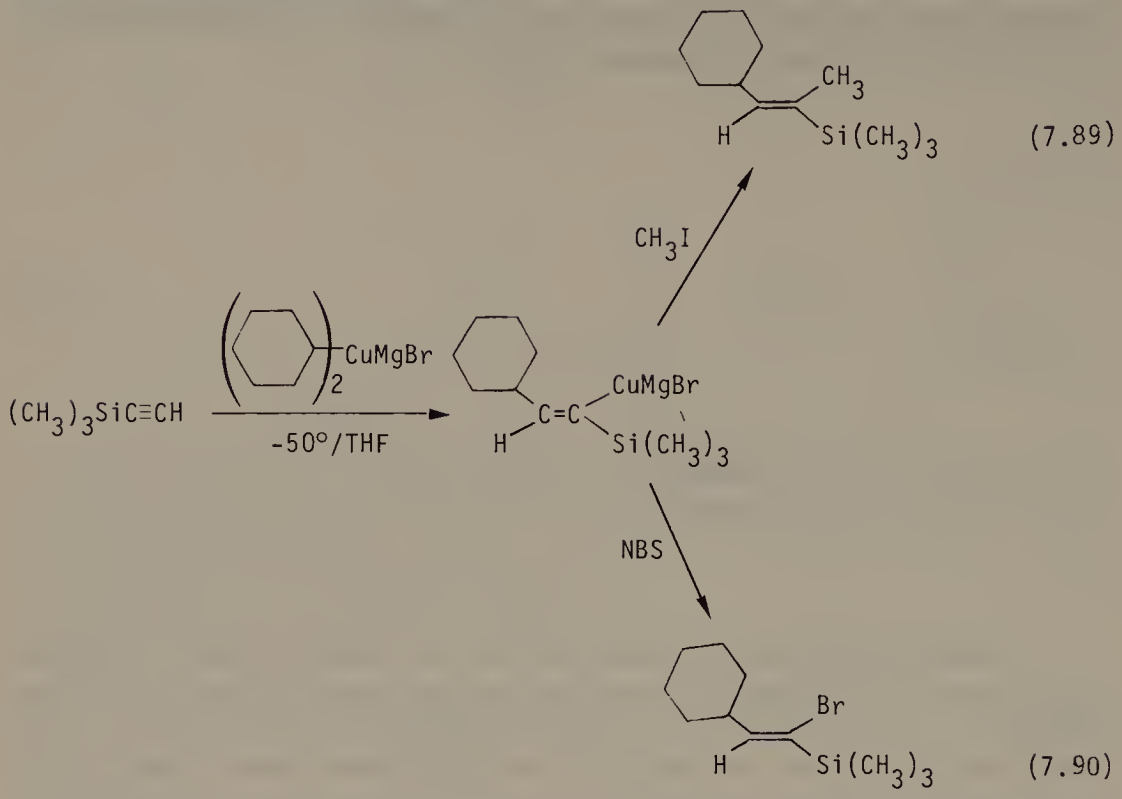
Z-1,2-dialkyl-1-trimethylsilylethylene can be prepared from 1-trimethyl-silylalkynes. Hydroboration of 1-trimethylsilyl alkynes with dicyclohexylborane proceeds in a *cis* manner regiospecifically to yield vinyl boranes in which both boron and silicon are bonded to the same carbon atom. Treatment of this intermediate sequentially with methyl lithium, cuprous iodide, triethyl phosphite in HMPT and finally a primary alkyl iodide yields the desired *Z*-1,2-dialkyl-1-trimethylsilylethylene [126].



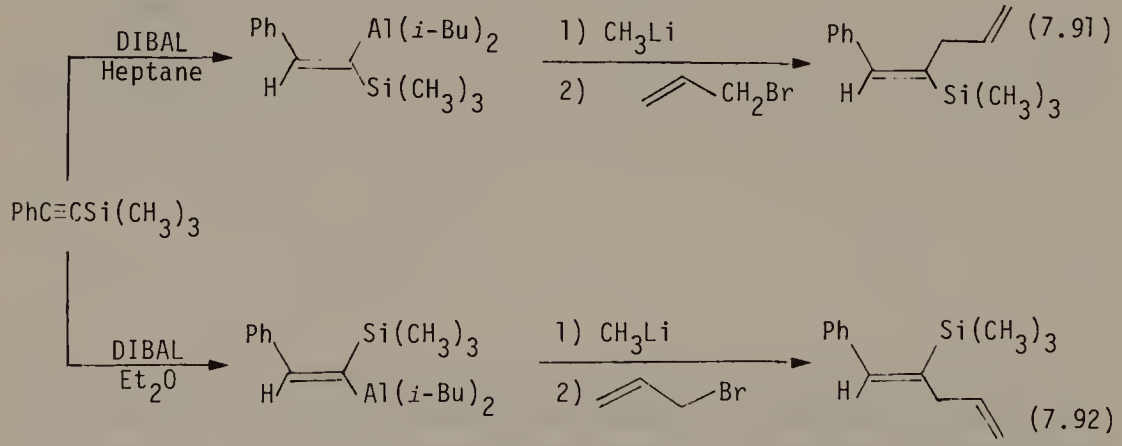
(7.88)

Dialkylcopper magnesium halides add in a stereospecific *cis* manner to both trimethylsilylacetylene [127] and triphenylsilylacetylene [128] to yield regio-specifically intermediates in which both copper and silicon are bonded to the same carbon atom. These α-silyl vinyl cuprate reagents can be alkylated with primary alkyl iodides in HMPT (Eq. 7.89) [127, 128]. The vinyl-copper

bond is cleaved stereospecifically with retention by cyanogen, bromine, iodine and *NBS* (Eq. 7.90) [128].

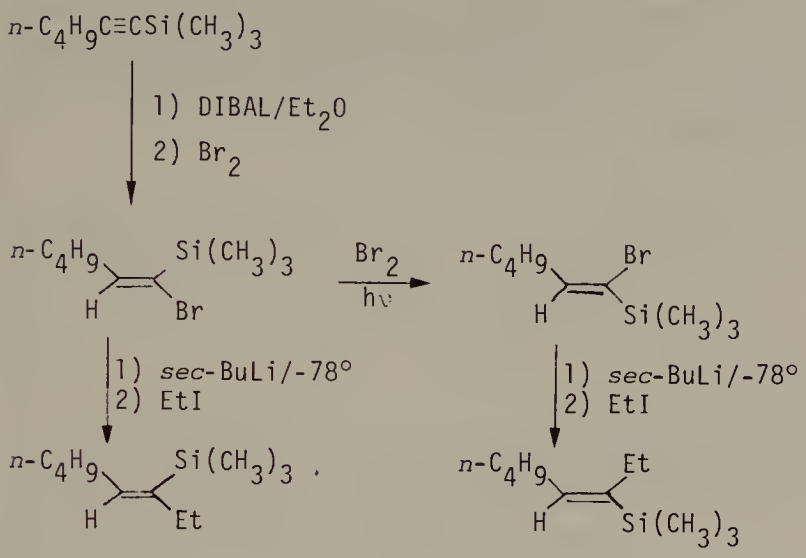


Both *Z*- and *E*-1,2-dialkyl-1-trimethylsilyl ethylenes can be prepared from 1-trimethylsilyl alkynes. Reaction of 1-trimethylsilyl alkynes with DIBAL in hydrocarbon solvent proceeds regiospecifically [102] in a *trans* manner (Eq. 7.91). On the other hand, in the presence of a donor solvent such as ether or one equivalent of tertiary amine, the addition proceeds in a *cis* manner (Eq. 7.92) [15, 102, 110]. These vinyl aluminum reagents can be converted to ate complexes by reaction with methyl lithium. Reaction with alkyl halides occurs with retention of stereochemistry [129, 130].



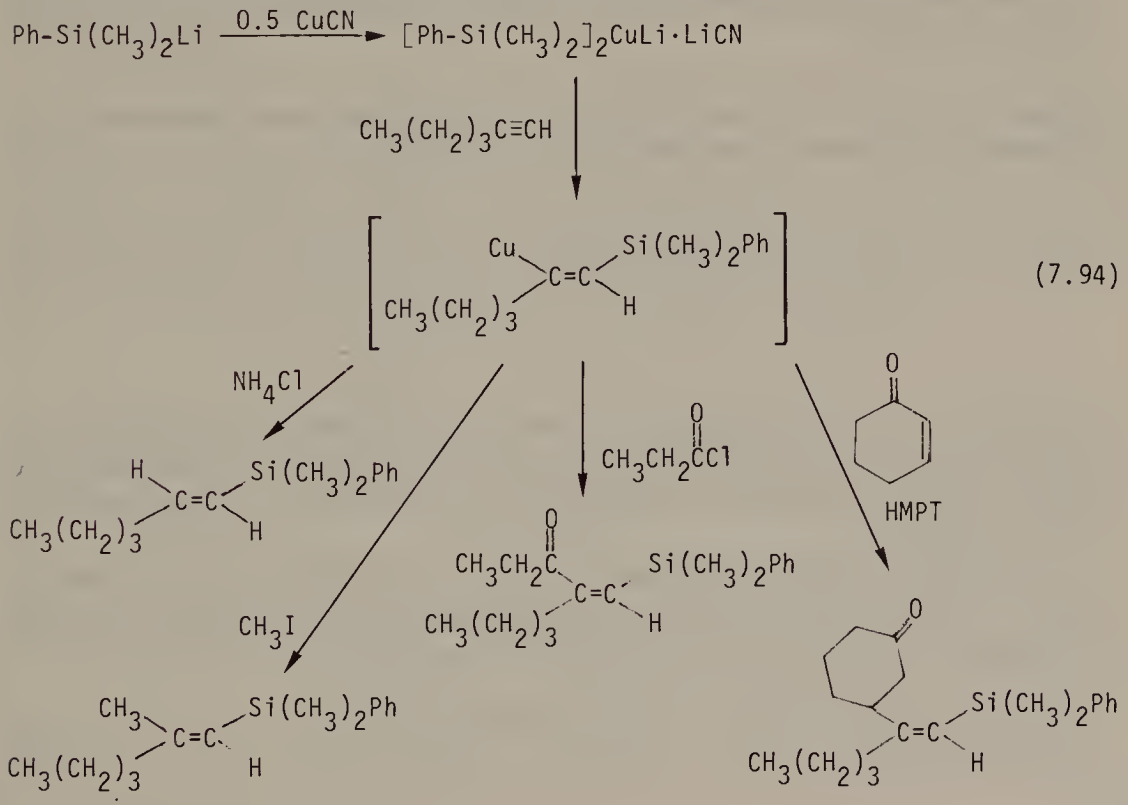
These *E*-vinyl aluminum species react with bromine to give *E*-1-bromo-1-trimethylsilyl-2-alkyl ethylenes. These will undergo photoisomerization

in the presence of bromine to the corresponding *Z*-1-bromo-1-trimethylsilyl-2-alkyl-ethylenes. Both of these vinyl bromides undergo halogenmetal exchange with retention of stereochemistry on treatment with *sec*-butyl lithium. Such *E*- or *Z*-1-lithio-1-trimethylsilyl-2-alkyl ethylenes couple efficiently with primary alkyl iodides to yield stereospecifically *E*- or *Z*-1,2-dialkyl-1-trimethylsilyl ethylenes [18] or Reaction with iodine yields similar results [75].



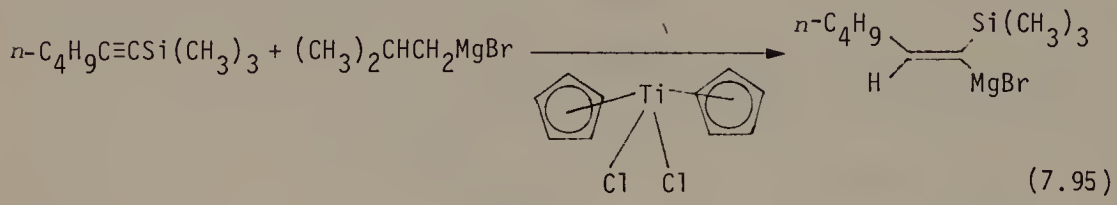
(7.93)

bis-Silyl lithium cuprate reagents add in a *cis* manner to terminal alkynes. The silyl substituted vinyl copper reagents thus formed are most versatile [131]. Some of their chemistry is summarized below [Eq. 7.94].

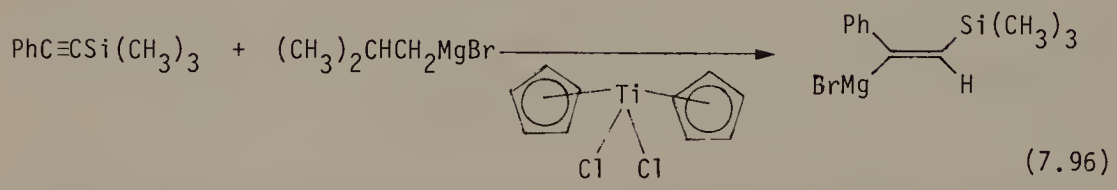


(7.94)

bis-Cyclopentadienyl titanium dichloride catalyzes the *cis*-addition of magnesium hydride across the C–C triple bond of 1-trimethylsilyl alkynes. Opposite regiospecificity is observed with aliphatic and aromatic 1-trimethylsilyl substituted acetylenes (Eq. 7.95 and 7.96). It seems probable that the reaction proceeds by initial reaction of *iso*-butylmagnesium bromide with the *bis*-cyclopentadienyl titanium dichloride to yield an *iso*-butyl titanium species which undergoes β-hydride elimination. The titanium hydride species thus formed adds in a stereospecific *cis*-manner to the 1-trimethylsilyl alkyne to yield a vinyl titanium species which untergoes a metal-exchange with more *iso*-butylmagnesium bromide to yield the vinyl magnesium product and regenerate the *iso*-butyl titanium species [132].



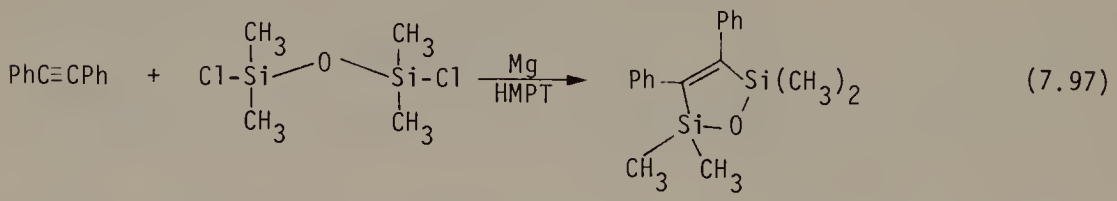
(7.95)



(7.96)

F. 1,2-Disubstituted-1,2-*bis*(trimethylsilyl)ethylenes, 1,1-Disubstituted-2,2-*bis*(trimethylsilyl)ethylenes and 1,1,2-Trisubstituted-2-trimethylsilyl ethylenes

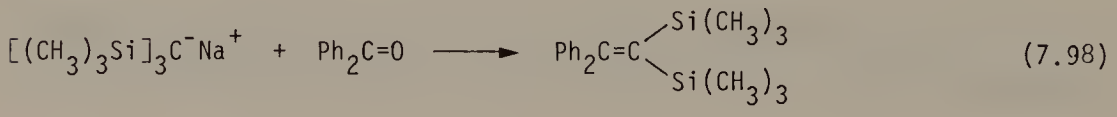
Reductive silylation with magnesium in HMPT of diphenyl acetylene [133] or trimethylsilyl phenyl acetylene [134] is successful.



(7.97)

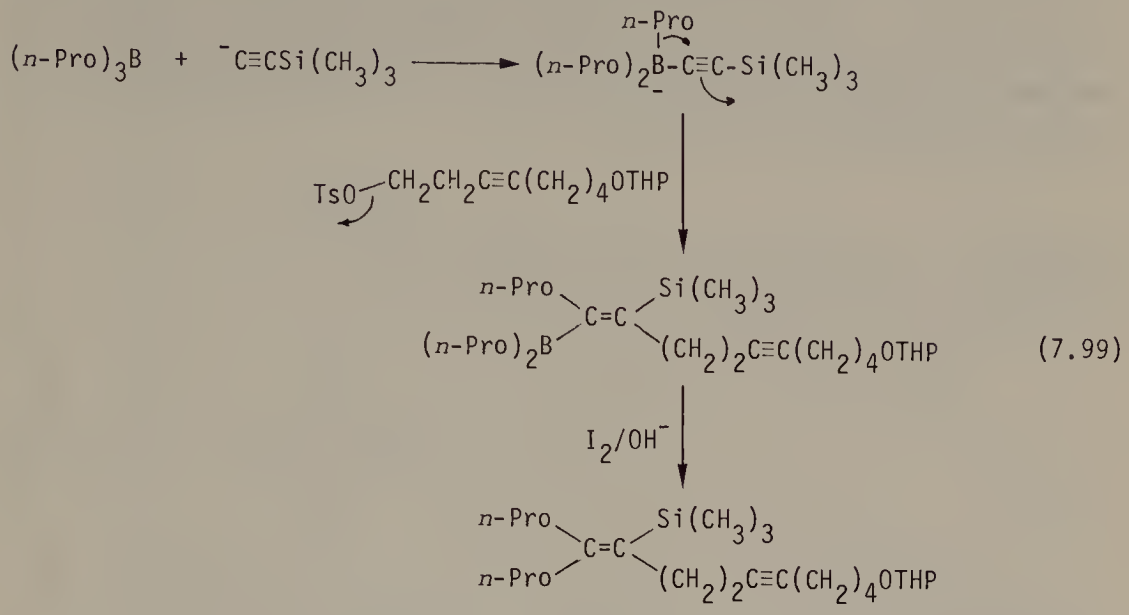
Bromine has been reported to add to *bis*(trimethylsilyl)acetylene to yield *E*-1,2-dibromo-1,2-*bis*(trimethylsilyl)ethylene [135]. Zinc chloride also catalyzes the *trans* addition of both chlorine and bromine to *bis*(trimethylsilyl)-acetylene [106].

1,1-*bis*(Trimethylsilyl) alkenes have been prepared by the Peterson reaction. Thus, reaction of *tris*(trimethylsilyl)methyl sodium with non-enolizable ketones yields 1,1-*bis*(trimethylsilyl)alkenes [136].



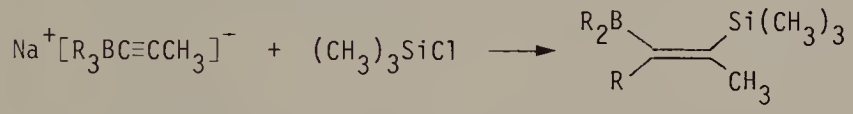
(7.98)

The following reaction sequence based on the reaction of trialkyl(trimethylsilylethynyl)borates with electrophiles has been used to prepare 1,1,2-trialkyl-2-trimethylsilyl ethylenes [137, 139].



(7.99)

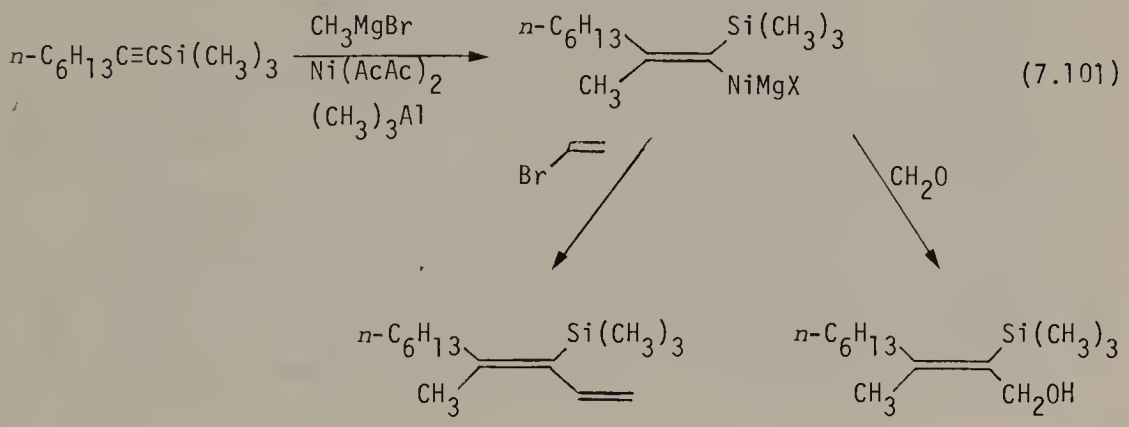
Addition of TMS-Cl to sodium trialkylpropynylborates gives *E*-2-trimethylsilyl vinyl boranes [138].



(7.100)

Such vinyl boranes can be converted to *E*-1,2-dialkyl-2-trimethylsilylethylene by protonolysis.

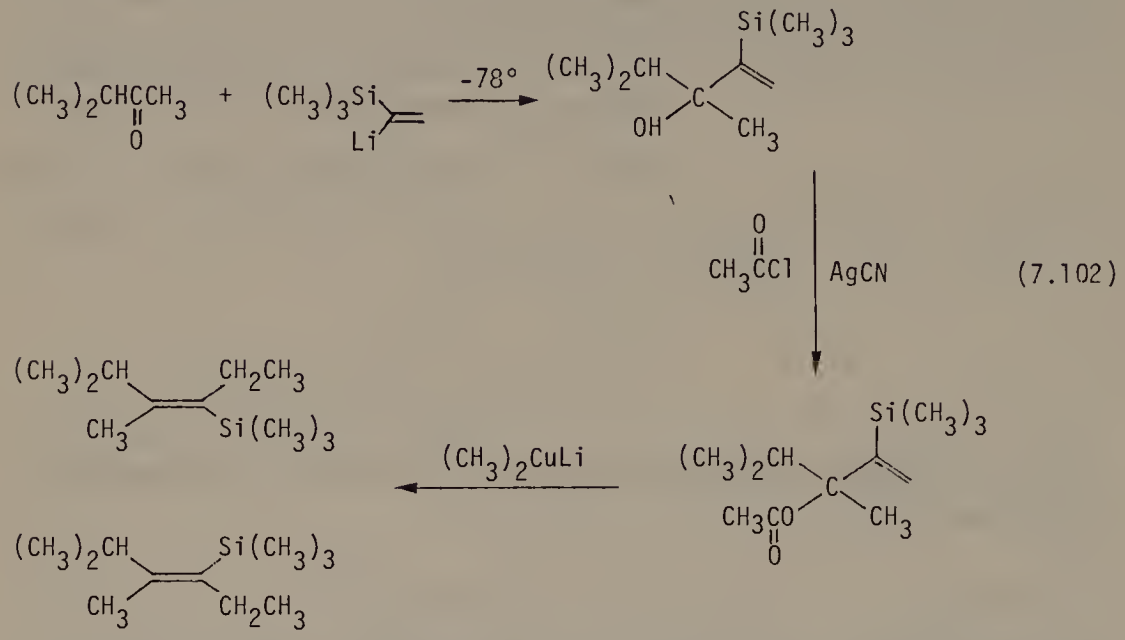
A reactive methyl nickel species, generated by reaction of methylmagnesium bromide in the presence of a catalytic amount of nickel (II) acetylacetonate and trimethylaluminium, adds in a *cis* manner to 1-trimethylsilyl alkynes. The addition is both stereo and regiospecific such that nickel and silicon are bonded to the same carbon. This intermediate reacts with water (D_2O), aldehydes, carbon dioxide, iodine, vinyl bromide, and alkyl bromide to yield a variety of specific trimethylsilyl substituted alkenes [140].



(7.101)

The reaction is limited to methylmagnesium bromide since with larger alkyl groups β-hydride elimination occurs [141].

Finally, α-lithiovinyltrimethylsilane reacts with ketones to yield 2-trimethylsilylallylic alcohols which can be converted to allylic acetates by treatment with acetyl chloride and silver cyanide. These will undergo S_N2' coupling with dialkylcopper lithium reagents to yield predominantly *E*-1,1,2-trialkyl-2-trimethylsilyl ethylenes [142].



References

1. Sommer, L.H., Braughman, G.A.: J. Am. Chem. Soc. *83*, 3346 (1961)
2. Traylor, T.G., Hanstein, W., Berwin, H.J., Clinton, N.A., Brown, R.S.: J. Am. Chem. Soc. *93*, 5715 (1971)
3. Jarvie, A.W.P., Holt, A., Thompson, J.: J. Chem. Soc. B, 852 (1969)
4. Fleming, I., Goldhill, J.: J. Chem. Soc. Chem. Comm. 176 (1978)
5. Fleming, I., Goldhill, J.: J. Chem. Soc. Perkin I, 1493 (1980)
6. Eberson, L.: Acta Chem. Scand. *10*, 633 (1956)
7. Gilman, H., Lichtenwalter, G.D.: J. Am. Chem. Soc. *80*, 608 (1958)
8. Ager, D.J. Fleming, I.: J. Chem. Soc. Chem. Comm. 177 (1978)
9. Brownbridge, P., Fleming, I., Pearce, A., Warren, S.: J. Chem. Soc. Chem. Comm. 751 (1976)
10. Fleming, I., Paterson, I., Pearce, A.: J. Chem. Soc. Perkin I, 256 (1981)
11. Fleming, I., Patel, S.K.: Tetrahedron Lett. 2321 (1981)
12. Thomas, E.J., Whitman, G.H.: J. Chem. Soc. Chem. Comm. 212 (1979)
13. Miller, R.B., McGarvey, G.: Syn. Comm. *7*, 475 (1977)
14. Miller, R.B., Reichenbach, T.: Tetrahedron Lett. 543 (1974)
15. Miller, R.B., McGarvey, G.: J. Org. Chem. *43*, 4424 (1978)

16. Pillot, J.P., Dunoguès, J., Calas, R.: Syn. Comm. *9*, 395 (1979)
17. Chan, T.H., Lau, P.W.K., Mychajlowskij, W.: Tetrahedron Lett. 3317 (1977)
18. Miller, R.B., McGarvey, G.: J. Org. Chem. *44*, 4623 (1979)
19. Miller, R.B., McGarvey, G.: Syn. Comm. *8*, 291 (1978)
20. Huynh, C., Linstrumelle, G.: Tetrahedron Lett. 1073 (1979)
21. Robbins, C.M., Whitman, G.H.: J. Chem. Soc. Chem. Comm. 697 (1976)
22. Hudrilik, P.F., Arcoleo, J.P., Schwartz, R.H., Misra, R.N., Rona, R.J.: Tetrahedron Lett. 591 (1977)
23. Hudrilik, P.F., Hudrilik, A.M., Rona, R.J., Misra, R.N., Withers, G.P.: J. Am. Chem. Soc. *99*, 1993 (1977)
24. Koenig, K.E., Weber, W.P.: Tetrahedron Lett. 2533 (1973)
25. Brook, A.G., Duff, J.M., Reynolds, W.F.: J. Organometal. Chem. *121*, 293 (1976)
26. Koenig, K.E., Weber, W.P.: J. Am. Chem. Soc. *95*, 3416 (1973)
27. Cook, M.A., Eaborn, C., Walton, D.R.M.: J. Organometal. Chem. *24*, 301 (1970)
28. Bourne, A.J., Jarvie, A.W.P.: J. Organometal. Chem. *24*, 335 (1970)
29. Utimoto, K., Kitai, M., Nozaki, H.: Tetrahedron Lett. 2825 (1975)
30. Hudrilik, P.F., Schwartz, R.H., Hogan, J.C.: J. Org. Chem. *44*, 155 (1979)
31. Büchi, G., Wüest, H.: Tetrahedron Lett. 4305 (1977)
32. Pillot, J.P., Dunoguès, J., Calas, R.: C.R. Acad. Sci, Paris, Ser. C, 789 (1974)
33. Fleming, I., Pearce, A.: J. Chem. Soc. Perkin I, 2485 (1980)
34. Fleming, I., Pearce, A.: J. Chem. Soc. Chem. Comm. 633 (1975)
35. Pillot, J.P., Dunoguès, J., Calas, R.: Bull. Soc. Chim. Fr. 2143 (1975)
36. Woodward, R.B., Hoffman, R., "The Conservation of Orbital Symmetry": Verlag. Chem. 58 (1971)
37. Fristad, W.E., Dime, D.S., Bailey, T.R., Paquette, L.A.: Tetrahedron Lett. 1999 (1979)
38. Paquette, L.A., Fristad, W.E., Dime, D.S., Bailey, T.R.: J. Org. Chem. *45*, 3017 (1980)
39. Nazarov, I.N., Zaretskaya, I.I.: Zh. Obsh. Khim. *27*, 693 (1957)
40. Cooke, F., Schwindeman, J., Magnus, P.: Tetrahedron Lett. 1995 (1979)
41. Cooke, F., Moerck, R., Schwindeman, J., Magnus, P.: J. Org. Chem. *45*, 1046 (1980)
42. Yamamoto, K., Nunokawa, O., Tsuji, J.: Synthesis, 721 (1977)
43. Yamamoto, K., Yoshitake, J., Qui, N.T., Tsuji, J.: Chem. Lett., 859 (1978)
44. Weber, W.P., Felix, R.A., Willard, A.K., Koenig, K.E.: Tetrahedron Lett. 4701 (1971)
45. Isobe, M., Kitamura, M., Goto, T.: Chem. Lett. 331 (1980)
46. Isobe, M., Kitamura, M., Goto, T.: Tetrahedron Lett. 239 (1981)
47. Grobel, B.T., Seebach, D.: Chem. Ber. *110*, 852 (1977)
48. Stork, G., Ganem, B.: J. Am. Chem. Soc. *95*, 6152 (1973)
49. Boeckman, Jr., R.K.: J. Am. Chem. Soc. *95*, 6867 (1973)
50. Boeckman, Jr., R.K., Blum, D.M., Ganem, B.: Org. Syn. *58*, 158 (1978)
51. Boeckman, Jr., R.K.: J. Am. Chem. Soc. *96*, 6179 (1974)
52. Ottolenghi, A., Fridkin, M., Zilkha, A.: Can. J. Chem. *41*, 2977 (1963)
53. Brook, A.G., Duff, J.M., Legrow, G.E.: J. Organometal. Chem. *122*, 31 (1976)
54. Boeckman, Jr., R.K., Blum, D.M., Ganem, B., Halvey, N.: Org. Syn. *58*, 152 (1978)
55. Stork, G., Singh, J.: J. Am. Chem. Soc. *96*, 6181 (1974)
56. Eisch, J.J., Trainor, J.T.: J. Org. Chem. *28*, 487 (1963)
57. Sakurai, H., Hayashi, N., Kumada, M.: J. Organometal. Chem. *18*, 351 (1969)
58. Stork, G., Colvin, E.: J. Am. Chem. Soc. *93*, 2080 (1971)
59. Stork, G., Jung, M.E.: J. Am. Chem. Soc. *96*, 3682 (1974)

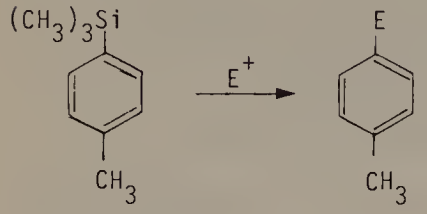
60. Stork, G., Jung, M.E., Colvin, E., Noei, Y.: J. Am. Chem. Soc. *96*, 3684 (1974)
61. Altnau, G., Rösch, L., Bohlmann, F., Lonitz, M.: Tetrahedron Lett. 4069 (1980)
62. Ehlinger, E., Magnus, P.: J. Am. Chem. Soc. *102*, 5004 (1980)
63. Boeckman, Jr., R.K., Bruza, K.J.: Tetrahedron Lett. 3365 (1974)
64. Boeckman, Jr., R.K., Bruza, K.J.: J. Org. Chem. *44*, 4781 (1979)
65. Han, Y.K., Paquette, L.A.: J. Org. Chem. *44*, 3731 (1979)
66. Cooke, F., Magnus, P.: J. Chem. Soc. Chem. Comm. 513 (1977)
67. Burford, C., Cooke, F., Ehlinger, E., Magnus, P.: J. Am. Chem. Soc. *99*, 4536 (1977)
68. Cook, M.A., Eaborn, C., Walton, D.R.M.: J. Organometal. Chem. *29*, 389 (1971)
69. Magnus, P., Roy, G.: J. Chem. Soc. Chem. Commun. 297 (1978)
70. Schollkopf, U., Scholz, H.U.: Synthesis, 271 (1976)
71. Seyferth, D., Dow, A.W., Menzel, H., Flood, T.C.: J. Am. Chem. Soc. *90*, 1080 (1968)
72. Fristad, W.E., Bailey, T.R., Paquette, L.A., Gleiter, R., Böhm, M.C.: J. Am. J. Am. Chem. Soc. *101*, 4420 (1979)
73. Chan, T.H., Mychajlowskij, W.: Tetrahedron Lett. 3479 (1974)
74. Chan, T.H., Lau, P.W.K., Li, M.P.: Tetrahedron Lett. 2667 (1976)
75. Hasan, I., Kishi, Y.: Tetrahedron Lett. 4229 (1980)
76. Fristad, W.E., Bailey, T.R., Paquette, L.A.: J. Org. Chem. *45*, 3038 (1980)
77. Eisch, J.J., Trainor, J.T.: J. Org. Chem. *28*, 2870 (1963)
78. Fristad, W.E., Bailey, T.R., Paquette, L.A.: J. Org. Chem. *43*, 1620 (1978)
79. Whitmore, F.C., Sommer, L.H., Gold, J., Van Strien, R.E.: J. Am. Chem. Soc. *69*, 1551 (1947)
80. Hauser, C.R., Hance, C.R.: J. Am. Chem. Soc. *74*, 5091 (1952)
81. Cunico, R.F.: J. Org. Chem. *36*, 929 (1971)
82. Laporterie, A., Dubac, J., Lesbre, M.: C. R. Acad. Sci. Paris, Ser. C, *278*, 375 (1974)
83. Laporterie, A., Dubac, J., Lesbre, M.: J. Organometal. Chem. *101*, 187 (1975)
84. Lesbre, M., Laporterie, A., Dubac, J., Manuel, G.: C. R. Acad. Sci. Paris, Ser. C, *280*, 787 (1975)
85. Laporterie, A., Dubac, J., Mazerolles, P.: J. Organometal. Chem. *202*, C89 (1980)
86. Laporterie, A., Dubac, J., Manuel, G., Déléris, G., Kowalski, J., Dunoguès, J., Calas, R.: Tetrahedron *34*, 2669 (1978)
87. Ohashi, S., Ruch, W.E., Butler, G.B.: J. Org. Chem. *46*, 614 (1981)
88. Batt, D.G., Ganem, B.: Tetrahedron Lett. 3323 (1978)
89. Danheiser, R.L., Sand, H.: J. Org. Chem. *45*, 4810 (1980)
90. Mironov, V.F., Petrov, A.D., Pisarenko, V.V.: Dokl. Akad. Nauk. SSSR, *124*, 102 (1959)
91. Weyenberg, D.R., German Federal Republic Patent 936, 445, December 15, 1955
92. Watanabe, H., Asami, M., Nagai, Y.: J. Organometal. Chem. *195*, 363 (1980)
93. Matsumoto, H., Nagashima, S., Kato, T., Nagai, Y.: Angew. Chem. Int. *17*, 279 (1978)
94. Nesmeyanov, A.N., Freidlina, R.K., Chukovskaya, E.C., Petrova, R.G., Belyavsky, A.B.: Tetrahedron, *17*, 61 (1962)
95. Schroeder, M.A., Wrighton, M.S.: J. Organometal. Chem. *128*, 345 (1977)
96. Schepinov, S.A., Khidekef, M.L., Lagodzinskaya, G.V.: Izv. Akad. Nauk. SSSR, Ser. Khim. 2165 (1968)
97. Millan, A., Towns, E., Maitlis, P.M.: J. Chem. Soc. Chem. Comm. 673 (1981)
98. Seki, Y., Takeshita, K., Kawamoto, K., Murai, S., Sonoda, N.: Angew. Chem. Int. *19*, 928 (1980)

99. Benkeser, R.A., Burraus, M.L., Nolse, L.E., Schisler, J.V.: J. Am. Chem. Soc. *83*, 4385 (1961)
100. Husk, G.R., Vilitchko, A.M.: J. Organometal. Chem. *49*, 85 (1973)
101. Cunico, R.F., Clayton, F.J.: J. Org. Chem. *41*, 1480 (1976)
102. Eisch, J.J., Foxton, M.W.: J. Org. Chem. *36*, 3520 (1971)
103. Ayalon-Chass, D., Ehlinger, E., Magnus, P.: J. Chem. Soc. Chem. Comm. 772 (1977)
104. Ehlinger, E., Magnus, P.: J. Chem. Soc. Chem. Comm. 421 (1979)
105. Dunoguès, J., Pillot, J.P., Duffaut, N., Calas, R.: C. R. Acad. Sci. Paris, Ser. C. 467 (1974)
106. Birkofer, L., Kühn, T.: Chem. Ber. *111*, 3119 (1978)
107. Yarosh, O.G., Voronkov, V.K., Komarov, N.V.: Izv. Akad. Nauk SSSR Ser. Khim. 875 (1971)
108. Komarov, N.V., Yarosh, O.G.: Izv. Akad. Nauk. SSSR Ser. Khim. 1573 (1971)
109. Weber, W.P., Willard, A.K., Boettger, H.G.: J. Org. Chem. *36*, 1620 (1971)
110. Zwiefel, G., On, H.P.: Synthesis, 803 (1980)
111. Bock, M., Seidel, H.: J. Organometal. Chem. *13*, 87 (1968)
112. Mironov, V.F., Petrov, A.D., Maksimova, N.G.: Izv. Akad. Nauk. SSSR, Otd. Khim. Nauk. 954 (1958)
113. Fritz, G., Grobe, J.: Z. Anorg. Allg. Chem. *309*, 77 (1961)
114. Dexheimer, E.M., Spialter, L.: J. Organometal. Chem. *107*, 229 (1976)
115. Soderquist, J.A., Hassner, A.: J. Am. Chem. Soc. *102*, 1577 (1980)
116. Soderquist, J.A., Hassner, A.: J. Org. Chem. *45*, 541 (1980)
117. Clinet, J.C., Linstrumelle, G.: Tetrahedron Lett. 3987 (1980)
118. Chan, T.H., Baldassarre, A., Massuda, D.: Synthesis, 801 (1976)
119. Nagendrappa, G.: Synthesis, 704 (1980)
120. Taylor, R.T., Degenhardt, C.R., Melega, W.P., Paquette, L.A.: Tetrahedron Lett. 159 (1977)
121. Chamberlin, A.R., Stemke, J.E., Bond, F.T.: J. Org. Chem. *43*, 147 (1978)
122. Eaborn, C., Jackson, R.A., Pearce, R.: J. Chem. Soc. Perkin I, 2055 (1974)
123. Eaborn, C., Jackson, R.A., Pearce, R.: J. Chem. Soc. Perkin I, 470 (1975)
124. Mychajlowskij, W., Chan, T.H.: Tetrahedron Lett. 4439 (1976)
125. Chan, T.H., Mychajlowskij, W., Ong, B.S., Harpp, D.N.: J. Organometal. Chem. *107*, C1 (1976)
126. Uchida, K., Utimoto, K., Nozaki, H.: J. Org. Chem. *41*, 2941 (1976)
127. Obayashi, M., Utimoto, K., Nozaki, H.: Tetrahedron Lett. 1807 (1977)
128. Westmijze, H., Meijer, J., Vermeer, P.: Tetrahedron Lett. 1823 (1977)
129. Eisch, J.J., Damasevitz, G.A.: J. Org. Chem. *41*, 2214 (1976)
130. Uchida, K., Utimoto, K., Nozaki, H.: J. Org. Chem. *41*, 2215 (1976)
131. Fleming, I., Roessler, F.: J. Chem. Soc. Chem. Comm. 276 (1980)
132. Sato, F., Ishikawa, H., Sato, M.: Tetrahedron Lett. 85 (1981)
133. Calas, R., Dunoguès, J.: C.R. Acad. Sci. Paris, Ser. C, 554 (1971)
134. Dunoguès, J., Bourgeois, P., Pillot, J.P., Merault, G., Calas, R., Lapouyade, P.: J. Organometal. Chem. *87*, 169 (1975)
135. Frisch, K.C., Young, R.B.: J. Am. Chem. Soc. *74*, 4853 (1952)
136. Sakurai, H., Nishiwaki, K.I., Kira, M.: Tetrahedron Lett. 4193 (1973)
137. Utimoto, K., Kitai, M., Naruse, M., Nozaki, H.: Tetrahedron Lett. 4233 (1975)
138. Binger, P., Köster, R.: Synthesis, 309 (1973)
139. Köster, R., Hagelee, L.A.: Synthesis, 118 (1976)
140. Snider, B.B., Karras, M., Conn, R.S.E.: J. Am. Chem. Soc. *100*, 4624 (1978)
141. Snider, B.B., Conn, R.S.E., Karras, M.: Tetrahedron Lett. 1679 (1979)
142. Amouroux, R., Chan, T.H.: Tetrahedron Lett. 4453 (1978)
143. Overman, L.E., Bell, K.L.: J. Am. Chem. Soc. 103, 1851 (1981)

8 Aryl Silanes

8.1 Introduction

Electrophilic cleavage of aryl silanes result, in general, in specific substituted aromatic compounds in which the electrophile occupies the position to which the silyl group was previously bonded. Unlike normal electrophilic substitution reactions which involve loss of a proton, mixtures of isomers are *not* obtained.



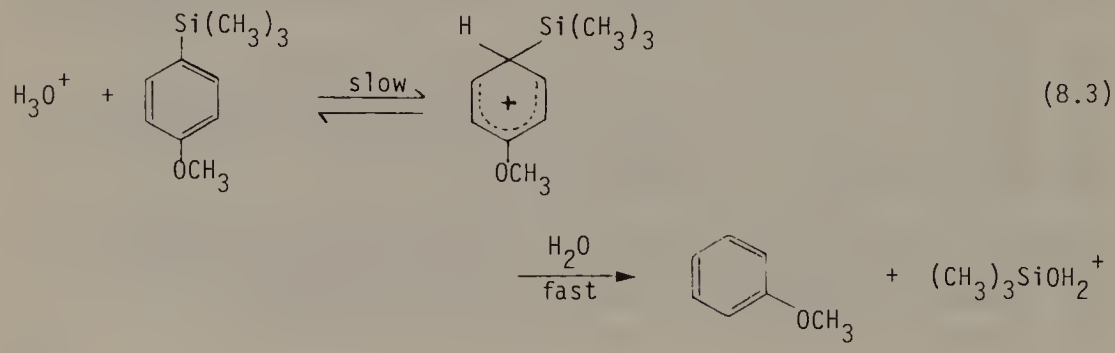
(8.1)

8.2 Protodesilylation

The first example of protodesilylation was reported by Kipping [1].

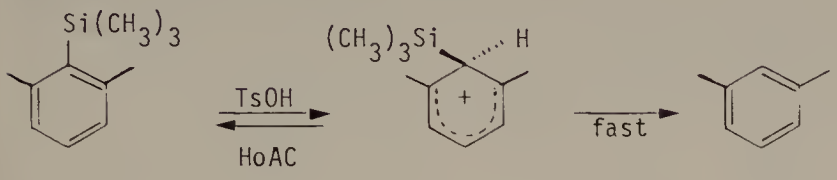
(8.2)

The mechanism of this reaction has been extensively studied by Eaborn [2, 3]. The observations that protodesilylation of *p*-methoxyphenyltrimethylsilane occurs 1.55 times faster with HCl in H_2O/*p*-dioxane than with DCl in D_2O/*p*-dioxane [4] and 7.3 times [5] as fast in CF_3CO_2H/H_2O as in CF_3CO_2D/D_2O are consistent with a mechanism in which proton transfer to form the sigma complex is rate limiting.



(8.3)

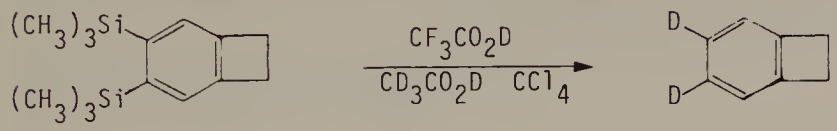
Substituent effects on the rate of protodesilylation of aryltrimethylsilanes have been determined [6]. The effect of two methyl groups in 2,4-dimethylphenyltrimethylsilane and 2,5-dimethylphenyltrimethylsilane is additive. However, 2,6-dimethylphenyltrimethylsilane undergoes protodesilylation significantly faster (~ 10 times). This acceleration is consistent with a decrease of steric strain in the sigma complex [7, 8].



(8.4)

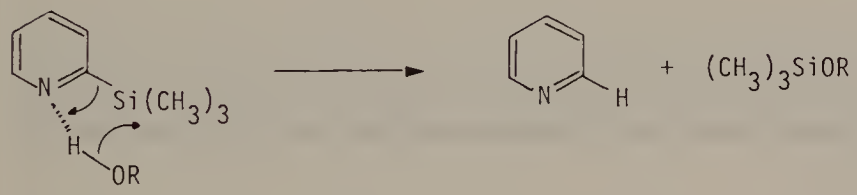
Although the C–Si bond is not broken in the rate determining step, phenyltrimethylsilane undergoes protodesilylation ten thousand times faster than benzene-d_1 undergoes dedeuteration in aq. sulfuric acid. This acceleration has been attributed to inductive electron release by the trimethylsilyl group [9].

From a synthetic viewpoint the reaction has been utilized to introduce deuterium into specific positions of aromatic nuclei [10, 11].



(8.5)

2-Trimethylsilylpyridine undergoes protodesilylation by water, methanol, or ethanol. The reaction has been proposed to occur by a four-center transition state which is stabilized by hydrogen bonding [12].



(8.6)

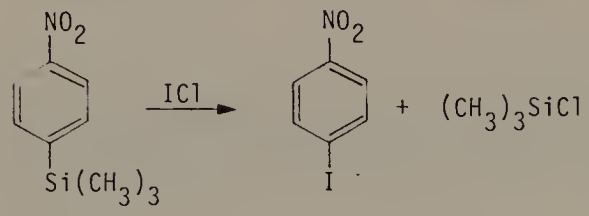
The large negative entropy of activation for the reaction ($\Delta H^{\neq} = 16$, $\Delta S^{\neq} = -29$ e.u.) is consistent with this proposal. This type of protodesilylation does not occur with 3 or 4-trimethylsilylpyridines.

8.3 Halodesilylation

Although benzene can not be directly iodinated to yield iodobenzene, phenyltrimethylsilane reacts with iodine to yield TMS-I and iodobenzene [13].

(8.7)

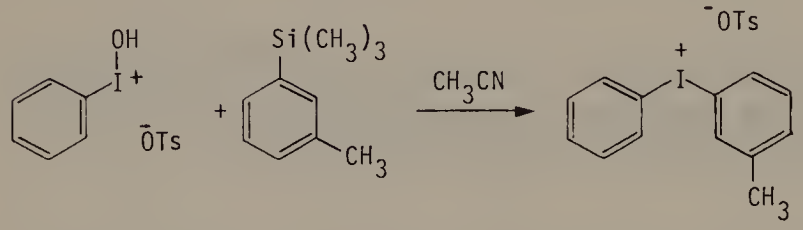
Iodine and aluminium powder [14, 15] have also been utilized. Iodine monochloride has proved particularly effective. Aryl iodides and TMS-Cl are obtained. The reaction is successful even when the aromatic ring is substituted by strongly electron withdrawing groups. *o*-, *m*-, and *p*-Iodo nitrobenzenes, have been prepared [16].



(8.8)

o-, *m*-, and *p*-*bis*(Trimethylsilyl) benzenes have been converted to *o*-, *m*-, and *p*-diiodobenzenes, respectively, by reaction with iodine monochloride [17, 18].

[Hydroxy(tosyloxy)iodo]arenes react with aryltrimethylsilanes in acetonitrile to yield diaryl iodonium tosylates [19, 20].

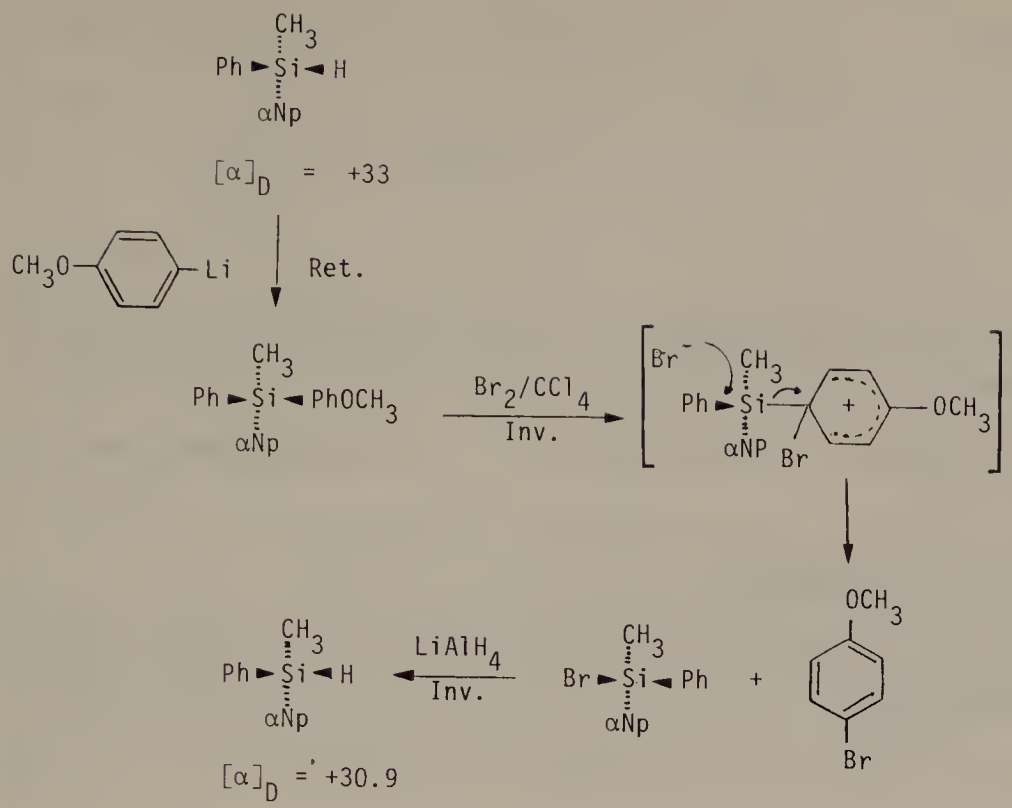


(8.9)

The reaction of bromine with tetraphenylsilane [21] or phenyltrimethylsilane [13, 22] yields bromobenzene and triphenylbromosilane [21] or TMS-Br, respectively, [13, 22].

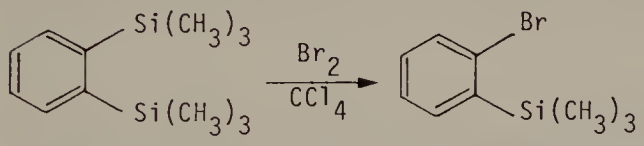
(8.10)

Reaction of bromine with optically active α-naphthyl *p*-methoxyphenylphenylmethylsilane leads predominantly to α-naphthylphenylmethylbromosilane and *p*-bromo anisole. Inversion of stereochemistry at the silyl center is observed. This is consistent with electrophilic attack by a bromonium ion on the carbon bearing the silyl group to form a sigma complex. Backside attack of bromide ion on the silyl center yields the products [23, 25]. A four-center mechanism, on the other hand, would be expected to result in retention of stereochemistry at the silyl center.



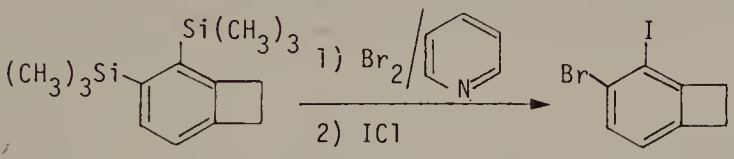
(8.11)

o-bis(Trimethylsilyl)benzene undergoes monobromo-desilylation to yield *o*-bromophenyltrimethylsilane [15].



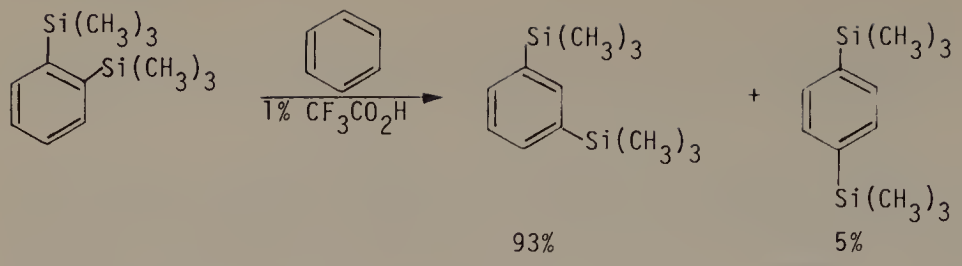
(8.12)

Sequential electrophilic desilylations of 4,5- [10] and 3,4- [11] *bis*(trimethylsilyl)benzocyclobutenes, as well as 5,6-*bis*(trimethylsilyl)benzocyclopentene, and 6,7-*bis*(trimethylsilyl)benzocyclohexene [10] by bromine, followed by iodine monochloride, yield the corresponding *ortho* bromo iodo aromatics.



(8.13)

With 3,4-*bis*(trimethylsilyl)benzocyclobutene, 4-bromo-3-iodo-benzocyclobutene is obtained. This regiospecificity results from the fact that desilylation occurs at the 4-position 500 times faster than at the 3-position [11]. *ortho-bis*(Trimethylsilyl)benzenes have a tendency to rearrange under acid catalysis to the corresponding *meta* isomers [26]. This results in relief of steric strain. Pyridine prevents this acid catalyzed rearrangement from competing with the bromodesilylation above.



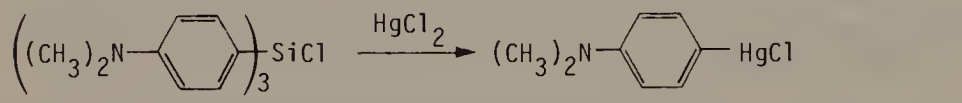
(8.14)

Unexpectedly, bromination of 2-*n*-octyl-4-trimethylsilyl furan with pyridinium bromide perbromide in THF gives 2-bromo-3-trimethylsilyl-5-*n*-octyl furan. Electrophilic substition apparently occurs in preference to bromodesilylation [27].

The mechanism of chlorodesilylation of aryltrimethylsilanes has been studied [18, 22].

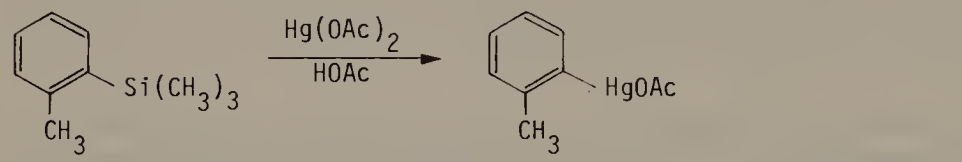
8.4 Metallo-desilylation

Electrophilic desilylation of aryl silanes by mercuric was reported eighty-five years ago [28].



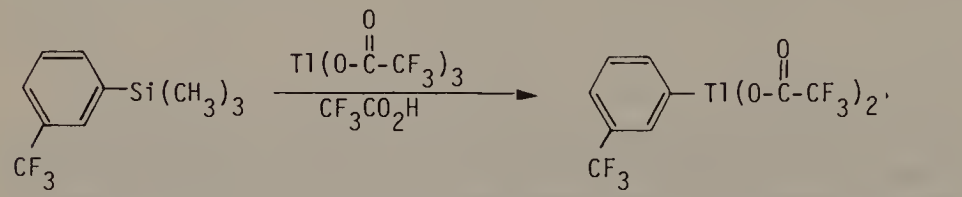
(8.15)

The reaction of mercuric acetate with aryltrimethylsilanes in glacial acetic acid has been thoroughly studied. The mercuric acetate group in the product unequivocally assumes the position occupied by the trimethylsilyl group in the starting material [29].



(8.16)

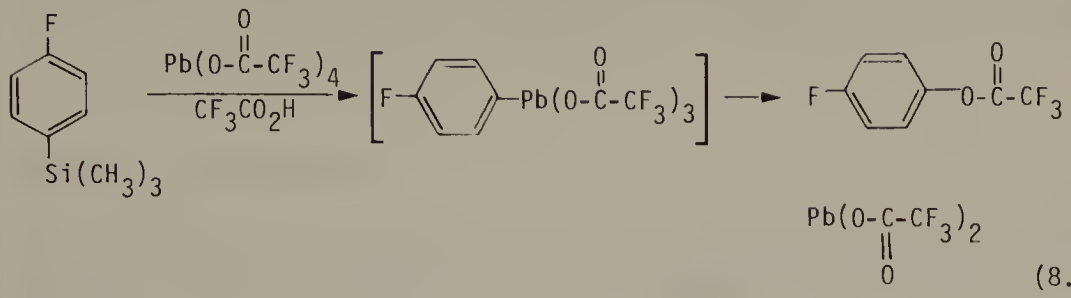
Aryltrimethylsilanes undergo regiospecific electrophilic desilylation on treatement with thallium (III) *tris*-trifluoroacetate in trifluoracetic acid to yield aryl thallium *bis*-trifluoroacetate derivatives. The reaction proceeds readily even with moderately electron withdrawing substituents on the aromatic ring [30–32].



(8.17)

Lead *tetrakis* trifluoroacetate affects electrophilic desilylation of aryltrimethylsilanes in trifluoracetic acid to yield regiospecifically aryl trifluoroacetates. The reaction may involve an aryl lead *tris*-trifluoracetate as an intermediate [33].

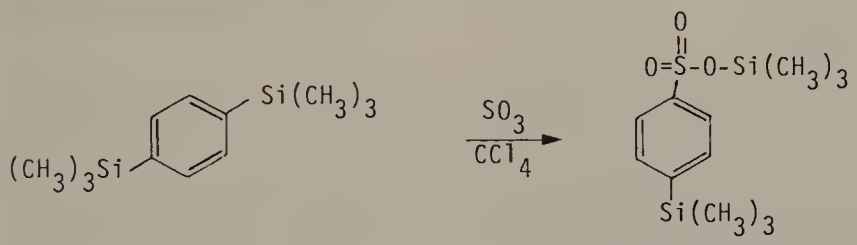
Lead tetraacetate in acetic acid is not effective.



(8.18)

8.5 Sulfo-desilylation

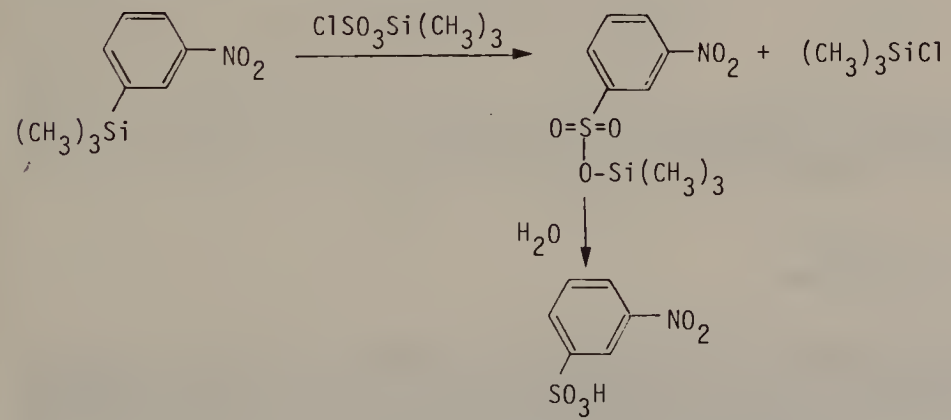
The reaction of tetraphenylsilane with sulfuric acid to yield benzene sulfonic acid and silica was reported by Kipping [1]. Similarly the reaction of sulfur trioxide with aryltrimethylsilanes regiospecifically yields trimethylsilyl benzenesulfonates. This reaction permits introduction of a sulfonic acid group at a specific position of the aromatic ring [34, 35]. *o*- [15], *m*- [35], and *p*- [34] *bis*(Trimethylsilyl)benzenes react with sulfur trioxide to yield *o*-, *m*-, and *p*-trimethylsilyl trimethylsilylbenzenesulfonates, respectively.



(8.19)

Trimethylsilyl chlorosulfonate reacts with aryltrialkylsilanes to yield trialkylsilyl arylsulfonates and TMS-Cl [36].

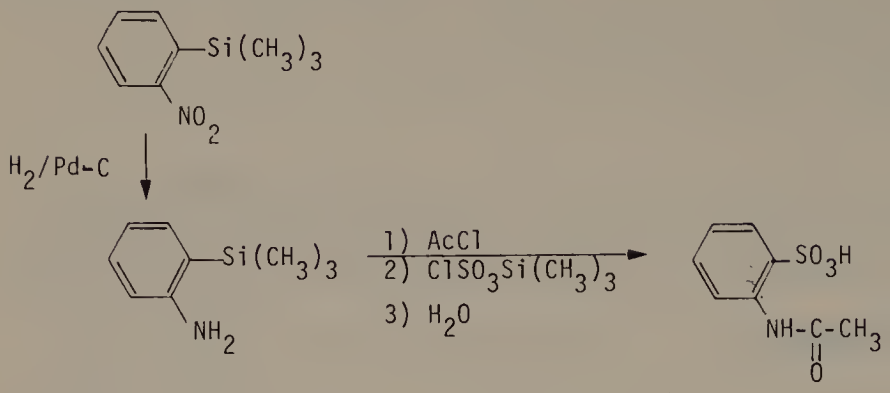
o-, *m*-, and *p*-Nitrophenyltrimethylsilanes undergo electrophilic desilylation with trimethylsilyl chlorosulfonate to yield the corresponding *o*-, *m*-, and *p*-nitrobenzene sulfonic acids after aq. work-up [16].



(8.20)

Treatment of *o*-, *m*-, or *p*-trimethylsilyl acetanilide with trimethylsilyl chloro-

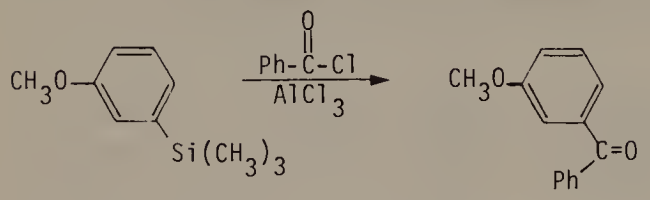
sulfonate followed by aq. work-up gives the corresponding N-acetyl aminobenzene sulfonic acids [16].



(8.21)

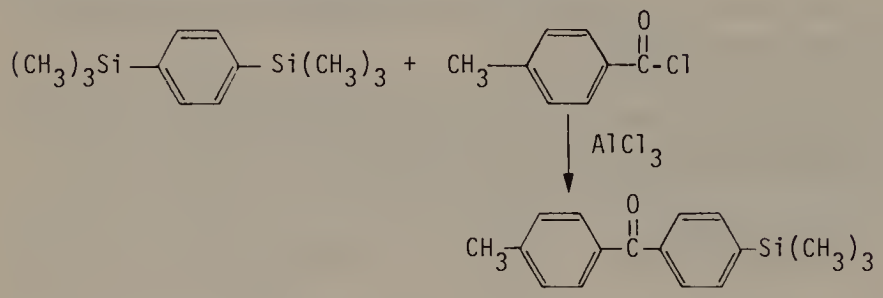
8.6 Acyl-desilylation

Aryltrimethylsilanes undergo acyl-desilylation on treatment with acid chlorides in the presence of $AlCl_3$ [10, 37].



(8.22)

Only one of the two trimethylsilyl groups of 1,2- [15] or 1,4-*bis*(trimethylsilyl)benzene undergoes acyl-desilylation.

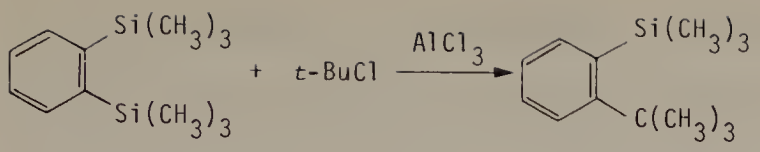


(8.23)

Phenyltrichlorosilane undergoes acyl-desilylation with acetyl chloride and $AlCl_3$ to yield acetophenone and tetrachlorosilane [38].

8.7 Alkyl-desilylation

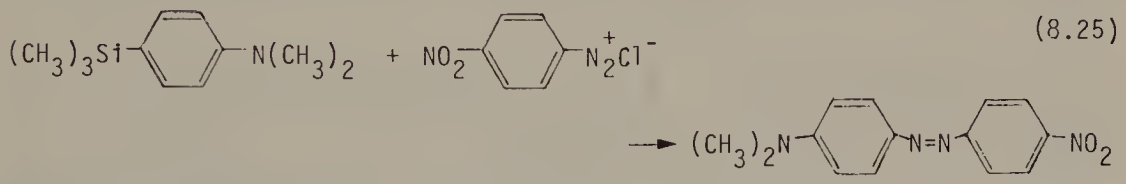
A very limited number of alkyl-desilylation reactions have been reported. Phenyltrimethylsilane reacts with benzyl bromide and $AlCl_3$ to give diphenylmethane [37]. While 1,2-*bis*(trimethylsilyl)benzene reacts with *t*-butyl chloride and $AlCl_3$ to give *o*-*t*-butylphenyltrimethylsilane [15].



(8.24)

8.8 Diazo-desilylation

Aryltrimethylsilane substituted by electron donating groups *ortho* or *para* to the trimethylsilyl group react regiospecifically with aryl diazonium salts via diazo-desilylation [39–41].

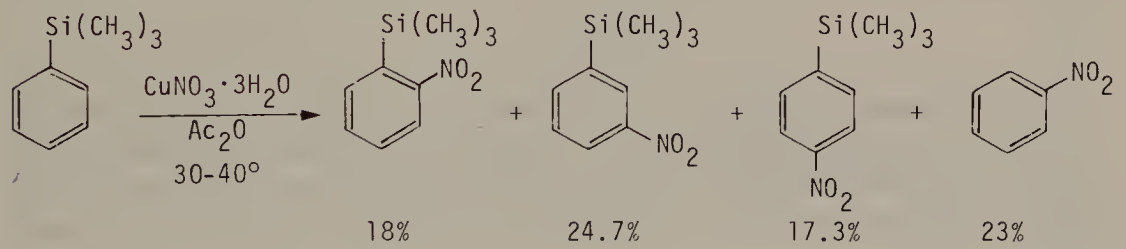


(8.25)

meta-Dimethylaminophenyltrimethylsilane, however, undergoes normal diazo coupling [42].

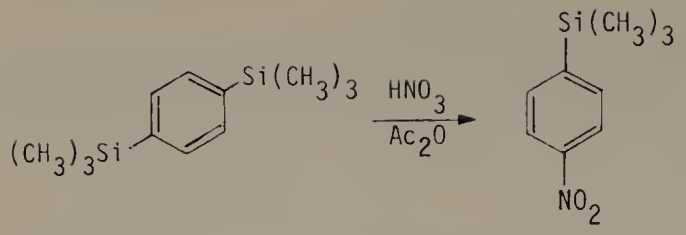
8.9 Nitrodesilylation

Nitration of aryltrimethylsilanes is rather complicated. The usual conditions (H_2SO_2/HNO_3) can not be used due to competition from protodesilylation. Nitric acid in acetic anhydride or cupric nitrate trihydrate in acetic acid are successful [43–45]. The course of the reaction is highly dependent on temperature and the conditions used to prepare the nitric acid/acetic anhydride mixture. For example, if nitric acid and acetic anhydride are mixed at low temperature and reacted with phenyltrimethylsilane between large 0°–10°, nitration principally occurs. Nitrodesilylation is the minor process. Similar results are obtained with cupric nitrate. From the distribution of *o-*, *m-*, and *p*-nitro-phenyltrimethylsilane products it appears that a trimethylsilyl group is a weak *ortho/para* director.



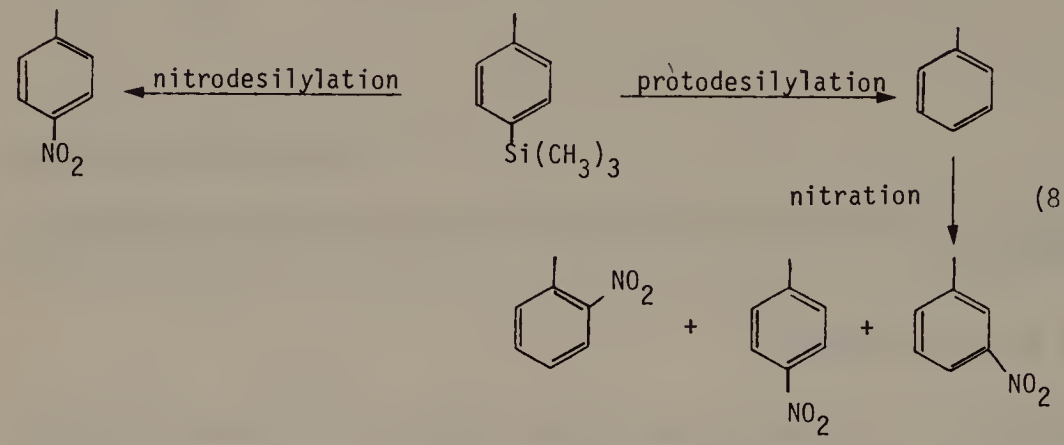
(8.26)

On the other hand, aryltrimethylsilanes have been reported to undergo nitrodesilylation on treatment with nitric acid (71%) and acetic anhydride at reflux [46]. Likewise, 1,4-*bis*(trimethylsilyl)benzene undergoes nitrodesilylation on treatment with nitric acid in acetic anhydride [47].



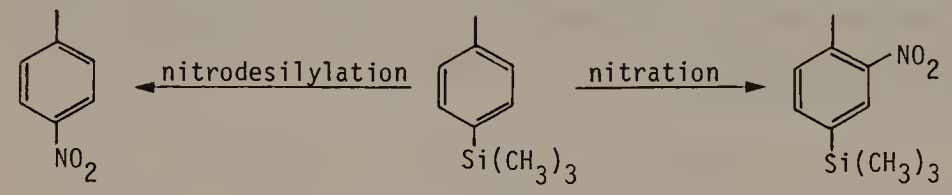
(8.27)

Formation of *p*-nitrophenyltrimethylsilane does not result from protodesilylation of 1,4-*bis*(trimethylsilyl)benzene, followed by nitration of phenyltrimethylsilane, because this would lead to a mixture of isomers. In a similar manner, *p*-tolytrimethylsilane permits a clear distinction to be drawn between nitrodesilylation and protodesilylation followed by nitration.



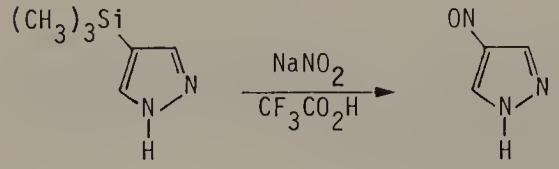
(8.28)

When nitric acid/acetic anhydride are heated briefly to 100° and then reacted with *p*-tolyltrimethylsilane at 15°, nitrodesilylation is the predominant process. Nitrodesilylation results from initial nitrosodesilylation, followed by oxidation. On the other hand, when nitric acid and acetic anhydride are prepared at 15° and reacted with *p*-tolyltrimethylsilane at this temperature, nitration and nitrodesilylation occur with almost equal facility [48].



(8.29)

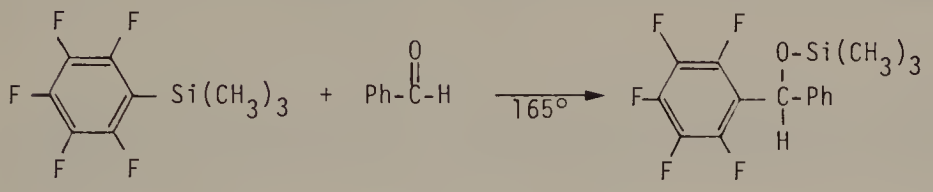
The electrophile involved in nitrosodesilylation is highly selective for the C–Si bond. Nitrosodesilylation can be achieved by treatment of aryltrimethylsilanes with isoamyl nitrite or sodium nitrite and trifluoroacetic acid. These nitroso aromatics can easily be oxidized to nitro aromatics with hydrogen peroxide [49, 74].



(8.30)

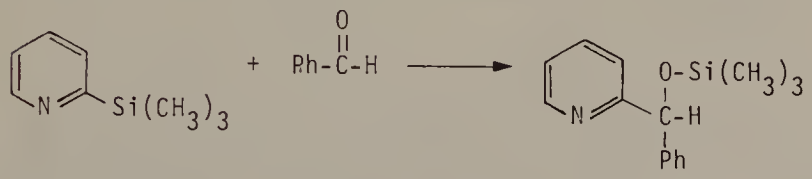
8.10 Aryl Silanes as Organometallic Reagents

On the basis of differences in electronegativity, the C–Si bond possesses 12% ionic character. Silicon is the positive end and carbon is the negative end of the dipole. In a limited number of cases, aryl silanes react with aldehydes as if they were aryl Grignard or aryl lithium reagents. Both pentafluoro and pentachlorophenyltrimethylsilane react with benzaldehyde to give the corresponding α-pentahalophenyl benzyl trimethylsilyl ethers [50].



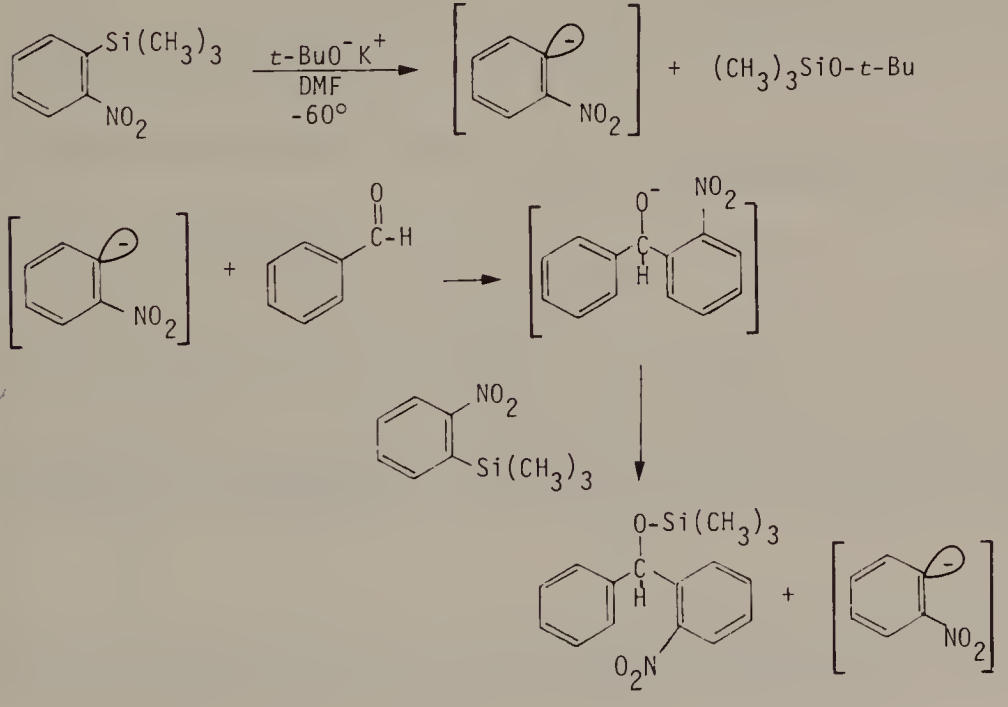
(8.31)

In a similar manner, 2-trimethylsilyl pyridine [51, 52], 1-methyl-2-trimethylsilyl imidazole [53], and 2-trimethylsilyl benzthiazoles [54], react with benzaldehydes to give α-(2-pyridinyl), α-[2-(1-methylimidazolyl)] or α-(2-benzthiazolyl)benzyl trimethylsilyl ethers, respectively.



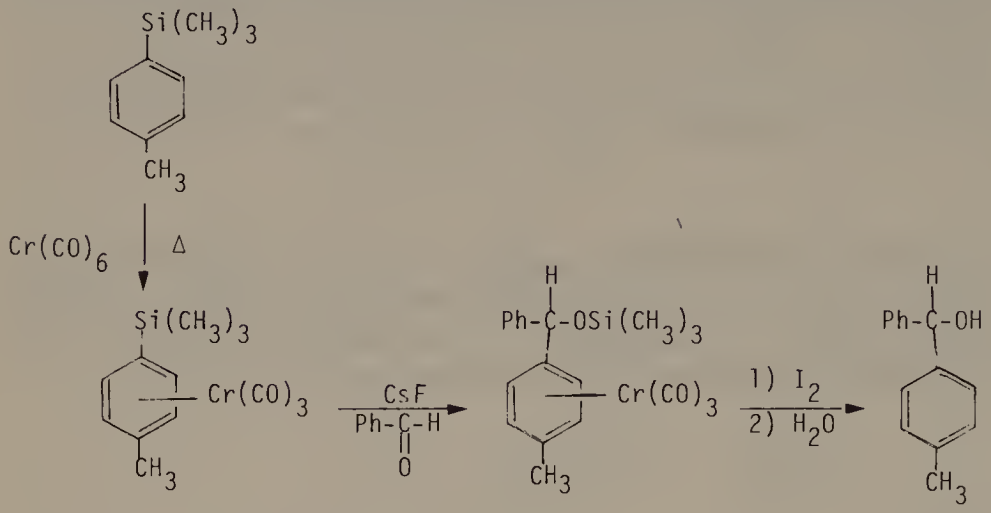
(8.32)

While phenyltrimethylsilane does not react thermally with benzaldehyde, aryltrimethylsilanes substituted with electron withdrawing groups in the *ortho* position react with benzaldehyde, under nucleophilic catalysis by potassium *t*-butoxide, potassium or cesium fluoride as outlined below [55].



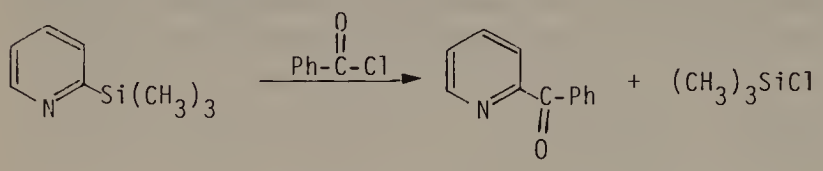
(8.33)

Similar reactions occur with alkyl aryl ketones, acyl fluorides, anhydrides and CO_2. On the other hand, the reaction fails when the aryl nucleus is substituted by electron donating groups. This difficulty can be overcome by use of trimethylsilyl arene chromium tricarbonyl complexes. These undergo reaction with aldehydes or ketones under nucleophilic catalysis by cesium fluoride. Oxidative removal of the chromium tricarbonyl group by treatment with iodine followed by hydrolysis yields benzylic alcohols [75].



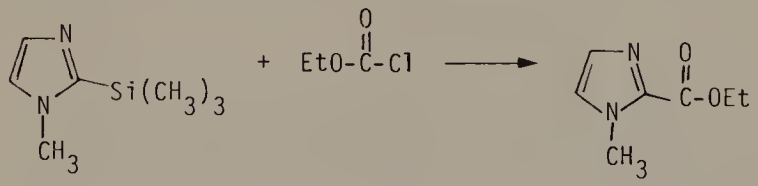
(8.34)

2-Trimethylsilyl pyridine undergoes acyl-desilylation on reaction with acid chlorides, anhydrides and ethyl chloroformate. These reactions do not require Lewis acids and presumably depend on the unusual polarity of the C–Si bond which is cleaved [52].



(8.35)

Similar results have been obtained with 1-methyl-2-trimethylsilyl imidazole and 2-trimethylsilyl benzthiazole [54, 56].

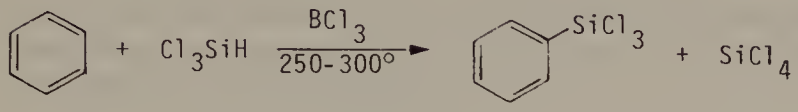


(8.36)

While 1-methyl-2-trimethylsilyl pyrrole fails to react with benzaldehyde, it undergoes acyl-desilylation with acid chlorides, and anhydrides in the absence of Lewis acids [53].

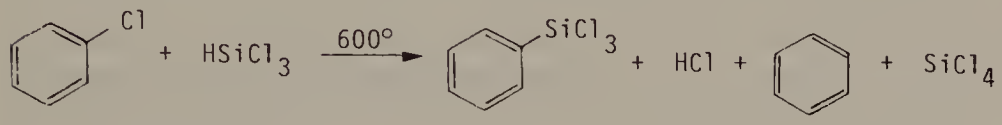
8.11 Preparation

The preparation of aryl silanes has been recently reviewed [57]. Benzene reacts with trichlorosilane under the influence of Lewis acid catalysts to yield phenyltrichlorosilane [58].



(8.37)

Aryl chlorides undergo thermal reaction with trichlorosilane to yield aryltrichlorosilanes and HCl. In a side reaction, the aryl chloride is reduced by trichlorosilane to the corresponding aromatic hydrocarbon and tetrachlorosilane [59, 60].



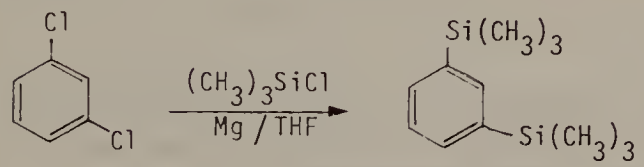
(8.38)

Free radical chain processes have been proposed to account for these results.

Many aryltrimethylsilanes have been prepared by *in-situ* Grignard reactions. These are carried out by addition of the aryl halide to a mixture of TMS-Cl, ether and magnesium turnings [61].

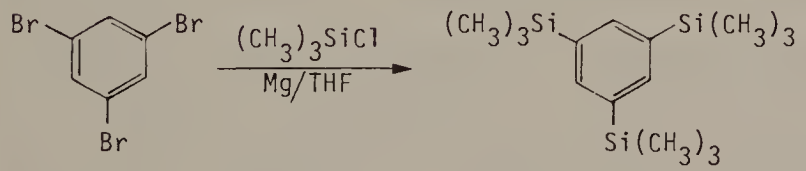
(8.39)

o-, *m-*, and *p-bis*(Trimethylsilyl)benzene have been prepared by addition of the corresponding *o-*, *m-*, or *p*-dichlorobenzene to a mixture of TMS-Cl in HMPT and magnesium [62].



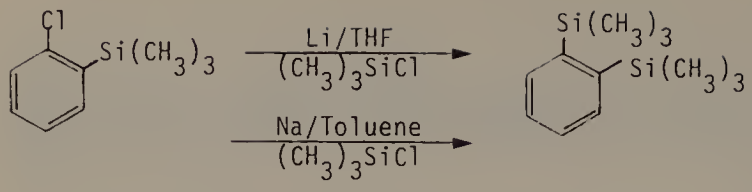
(8.40)

1,3,5-*tris*(Trimethylsilyl)benzene and 2,4,6-*tris*(trimethylsilyl) anisole have been prepared by *in-situ* Grignard reactions [63, 64].



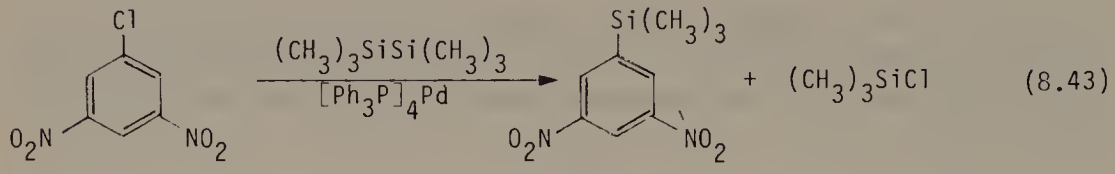
(8.41)

Aryl trimethylsilanes have also been prepared by *in-situ* formation of aryl lithium or sodium derivatives in the presence of TMS-Cl [65].



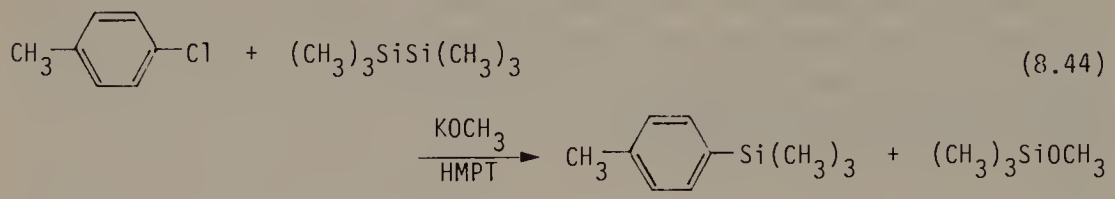
(8.42)

tetrakis(Triphenylphosphine) palladium (O) catalyzes the reaction of aryl chlorides and bromides with hexamethyldisilane to yield aryltrimethylsilanes. Of particular note, this reaction is successful with nitrohalobenzenes [66–69].



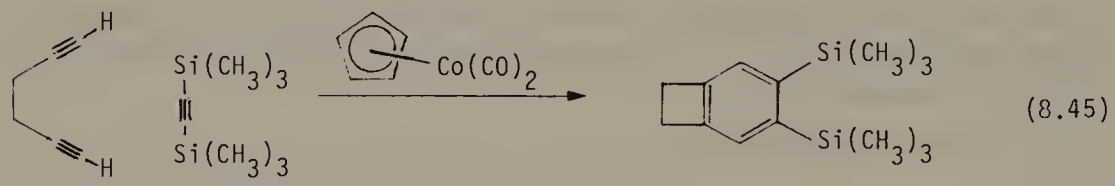
(8.43)

Trimethylsilyl lithium, sodium or potassium react with aryl halides to yield aryltrimethylsilanes. The necessary reagents may be prepared *in-situ* by reaction of hexamethyldisilane with methyl lithium, sodium methoxide or potassium methoxide in HMPT [70].



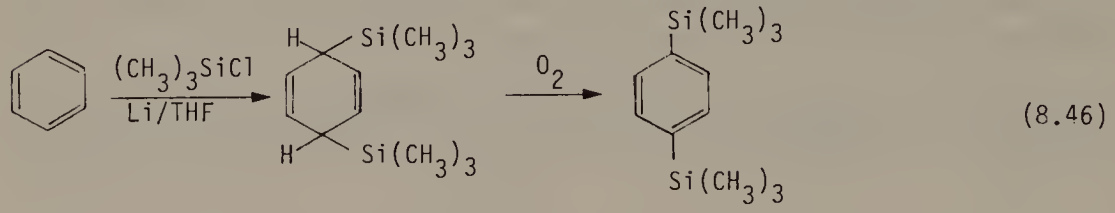
(8.44)

Aryltrimethylsilanes have also been prepared by transition metal catalyzed cycloaddition reactions of 1-trimethylsilyl alkynes (see Chapter 9).



(8.45)

Dissolving metal reduction of aromatic hydrocarbons in the presence of TMS-Cl yields 1,4-*bis*(trimethylsilyl)-1,4-dihydroaromatics. These can be oxidized by air to yield 1,4-*bis*(trimethylsilyl) aromatics [71–73].



(8.46)

References

1. Kipping, F.S., Lloyd, L.L.: J. Chem. Soc. 449 (1901)
2. Eaborn, C.: Pure and Applied Chemistry, *19*, 375 (1969)
3. Eaborn, C., Bott, R.W., "Synthesis and Reaction of the Silicon Carbon Bond" in Organometallic Compounds of the Group IV Element, Vol I, (MacDiarmid, A.G., Ed.), p. 407–435, New York: Marcel Dekker, 1968
4. Bott, R.W., Eaborn, C., Greasley, P.M.: J. Chem. Soc. 4804 (1964)
5. Eaborn, C., Jackson, P.M., Taylor, R.: J. Chem. Soc. *B*, 613 (1966)
6. See Ref. 3, p. 410–411 and 414.
7. Benkeser, R.A., Krysiak, H.R.: J. Am. Chem. Soc. *76*, 6353 (1954)
8. Eaborn, C., Moore, R.C.: J. Chem. Soc. 3640 (1959)
9. Eaborn, C., Pande, K.C.: J. Chem. Soc. 1566 (1960)
10. Hillard, III, R.L., Vollhardt, K.P.C.: J. Am. Chem. Soc. *99*, 4058 (1977)
11. Hillard, III, R.L., Vollhardt, K.P.C.: Angew. Chem. Int. *16*, 399 (1977)
12. Anderson, D.G., Bradney, M.A.M., Webster, D.E.: J. Chem. Soc. *B*, 450 (1968)
13. Pray, B.O., Sommer, L.H., Goldberg, G.M., Kerr, G.T., DiGiorgio, P.A., Whitmore, F.C.: J. Am. Chem. Soc. *70*, 433 (1948)
14. Eaborn, C.: J. Chem. Soc. 2755 (1949)
15. Eaborn, C., Walton, D.R.M., Young, D.J.: J. Chem. Soc. *B*, 15 (1969)
16. Félix, G., Dunoguès, J., Calas, R.: Angew. Chem. Int. Ed. *18*, 402 (1979)
17. Félix, G., Dunoguès, J., Pisciotti, F., Calas, R.: Angew. Chem. Int. Ed. *16*, 488 (1977)
18. Stock, L.M., Spector, A.R.: J. Org. Chem. *28*, 3272 (1963)
19. Koser, G.F., Wettach, R.H., Smith, C.S.: J. Org. Chem. *45*, 1543 (1980)
20. Beringer, F.M., Dehn, Jr., J.W., Winicov, M.: J. Am. Chem. Soc. *82*, 2948 (1960)
21. Ladenburg, A.: Chem. Ber. *40*, 2274 (1907)
22. Eaborn, G., Webster, D.E.: J. Chem. Soc. 179 (1960)
23. Eaborn, C., Steward, O.W.: Proc. Chem. Soc. 59 (1963)
24. Eaborn, C., Steward, O.W.: J. Chem. Soc. 521 (1965)
25. Sommer, L.H., Michael, K.W., Korte, W.D.: J. Am. Chem. Soc. *89*, 868 (1967)
26. Seyferth, D., White, D.L.: J. Am. Chem. Soc. *94*, 3132 (1972)
27. Nolan, S.M., Cohen, T.: J. Org. Chem. *46*, 2473 (1981)
28. Combes, C.: Compt. Rend. Acad. Sci. Paris, *122*, 622 (1896)
29. Benkeser, R.A., Hoke, D.I., Hickner, R.A.: J. Am. Chem. Soc. *80*, 5294 (1958)
30. Bell, H.C., Kalman, J.R., Pinhey, J.T., Sternhall, S.: Tetrahedron Lett. 3391 (1974)
31. Taylor, E.C., Kienzle, F., Robey, R.L., McKillop, A., Hunt, J.D.: J. Am. Chem. Soc. *93*, 4845 (1971)
32. McKillop, A., Fowler, J.S., Zeleska, M.J., Hunt, J.D., Taylor, E.C., McGillivray, G.: Tetrahedron Lett. 2423 (1969)
33. Kalman, J.R., Pinhey, J.T., Sternhall, S.: Tetrahedron Lett. 5369 (1972)
34. Eaborn, C., Hashimoto, T.: Chem. and Ind. 1081 (1961)
35. Bott, R.W., Eaborn, C., Hashimoto, T.: J. Organometal. Chem. *3*, 442 (1965)
36. Calas, R., Bourgeois, P., Duffaut, N.: Compt. Rend, Acad. Sci. Paris, *263*, C243 (1966)
37. Dey, K., Eaborn, C., Walton, D.R.M.: Organometal. Chem. Syn. *1*, 151 (1970/71)
38. Austin, J.D., Eaborn, C., Smith, J.D.: J. Chem. Soc. 4744 (1963)
39. Sunthankar, S.V., Gilman, H.: J. Org. Chem. *15*, 1200 (1950)
40. Sakata, Y., Hashimoto, T.: Yakugaku Zasshi, *80*, 728 (1960), CA *54*, 24480 (1960)
41. Sakata, Y., Hashimoto, T.: Yakugaku Zasshi, *79*, 878 (1959), CA *54*, 358a (1960)
42. Hashimoto, T., Seki, M.: Yakugaku Zasshi, *81*, 204 (1961), CA *55*, 14340 (1961)
43. Speier, J.L.: J. Am. Chem. Soc. *75*, 2930 (1953)

44. Benkeser, R.A., Brumfield, P.E.: J. Am. Chem. Soc. *73*, 4770 (1951)
45. Benkeser, R.A., Landesman, H.: J. Am. Chem. Soc. *76*, 904 (1954)
46. Chvalovsky, V., Bazant, V.: Collect. Czech. Chem. Commun. *16*, 580 (1951)
47. Deans, F.B., Eaborn, C.: J. Chem. Soc. 498 (1957)
48. Eaborn, C., Salih, Z.S., Walton, D.R.M.: J. Chem. Soc. Perkin II, 172 (1972)
49. Birkofer, L., Franz, M.: Chem. Ber. *104*, 3062 (1971)
50. Webb, A.F., Sethi, D.S., Gilman, H.: J. Organometal. Chem. *21*, P61 (1970)
51. Pinkerton, F.H., Thames, S.F.: J. Heterocyclic Chem. *6*, 433 (1969)
52. Pinkerton, F.H., Thames, S.F.: J. Organometal. Chem. *24*, 623 (1970)
53. Pratt, J.R., Pinkerton, F.H., Thames, S.F.: J. Organometal. Chem. *38*, 29 (1972)
54. Pinkerton, F.H., Thames, S.F.: J. Heterocyclic Chem. *8*, 257 (1971)
55. Effenberger, F., Spiegler, W.: Angew. Chem. Int. Ed. *20*, 265 (1981)
56. Pinkerton, R.H., Thames, S.F.: J. Heterocyclic Chem. *9*, 67 (1972)
57. Häbich, D., Effenberger, F.: Synthesis, 84 (1979)
58. Barry, A.J., Gilkey, J.W., Hook, D.E.: Ind. Eng. Chem. *51*, 131 (1959)
59. Chernyshev, E.A., Li, G.L., Petrov, A.D.: Dokl. Akad. Nauk. SSSR, *127*, 808 (1959)
60. Petrov, A.D., Mironov, V.F., Ponomarenko, V.A., Chernyshev, E.A., Synthesis of Organosilicon Monomers, p. 288, New York: Consultants Bureau, 1964
61. Anderson, D.G., Bradney, M.A.M., Webster, D.E.: J. Chem. Soc. *B*, 450 (1968)
62. Félix, G., Dunoguès, J., Pisciotti, F., Calas, R.: Angew. Chem. Int. Ed. *16*, 488 (1977)
63. Chaffee, R.G., Beck, H.N.: J. Chem. and Eng. Data, *8*, 453 (1963)
64. Beck, H.N., Chaffee, R.G.: J. Chem. and Eng. Data, *8*, 602 (1963)
65. Eaborn, C., Walton, D.R.M., Young, D.J.: J. Chem. Soc. *B*, 15 (1969)
66. Matsumoto, H., Shono, K., Nagai, Y.: J. Organometal. Chem. *208*, 145 (1981)
67. Matsumoto, H., Nagashima, S., Yoshihiro, K., Nagai, Y.: J. Organometal. Chem. *85*, C1 (1975)
68. Azarian, A., Dua, S.S., Eaborn, C., Walton, D.R.M.: J. Organometal. Chem. *117*, C55 (1976)
69. Matsumoto, H., Yoshihiro, K., Nagashima, S., Watanabe, H., Nagai, Y.: J. Organometal. Chem. *128*, 409 (1977)
70. Shippey, M.A., Dervan, P.B.: J. Org. Chem. *42*, 2654 (1977)
71. Laguerre, M., Dunoguès, J., Calas, R., Duffaut, N.: J. Organometal. Chem. *112*, 49 (1976)
72. Dunoguès, J., Calas, R., Ardoin, N.: J. Organometal. Chem. *43*, 127 (1972)
73. Laguerre, M., Dunoguès, J., Calas, R.: J. Chem. Res. *8*, 295 (1978)
74. Sakata, Y., Hashimoto, T.: Yakugaku Zasshi, *80*, 728 (1960), CA *54*, 24480 (1960)
75. Effenberger, F., Schöllkopf, K.: Angew. Chem. Int. Ed. *20*, 266 (1981)

9 Silyl Acetylenes

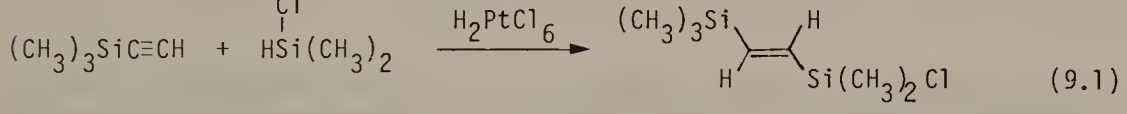
9.1 Introduction

Silyl acetylenes have proved to be versatile reagents in a number of reactions. This chapter will be organized into five major sections: first, addition reactions to 1-silyl alkynes; second, electrophilic substitution reactions; third, the use of 1-silyl alkynes as protecting groups for terminal alkynes; fourth, cycloaddition reactions; and fifth, the preparation of these compounds.

9.2 Addition Reactions

1-Trimethylsilylalkynes undergo a variety of addition reactions to yield vinyl silanes. These have been discussed in chapter 7. Nevertheless we will summarize them here since they were previously organized from a different viewpoint.

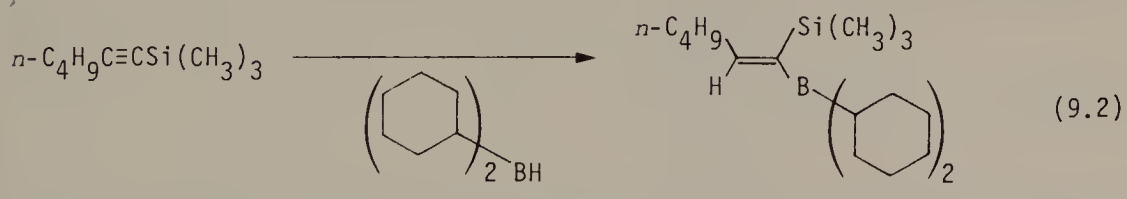
1-Trimethylsilylalkynes undergo both catalytic hydrogenation [1] and hydrosilation [2] reactions to yield vinyl silanes. HBr adds to trimethylsilyl



(9.1)

acetylene under the influence of peroxides to yield *E*-1-bromo-2-trimethylsilyl ethylene [3, 4]. Both chlorine and bromine add to *bis*(trimethylsilyl)-acetylene to yield *E*-1,2-dihalo-1,2-*bis*(trimethylsilyl)ethylene [2].

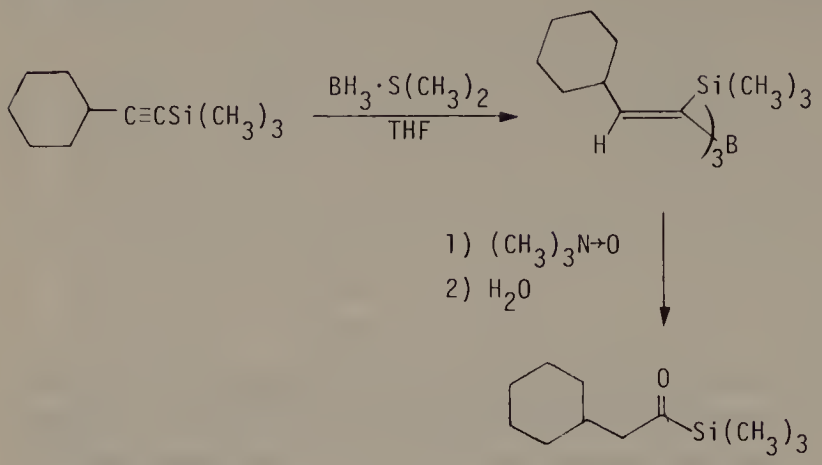
Dialkyl boranes undergo *cis* addition to 1-trimethylsilylalkynes to yield vinyl organometallic species in which the silicon and boron are bonded to the same carbon atom [5].



(9.2)

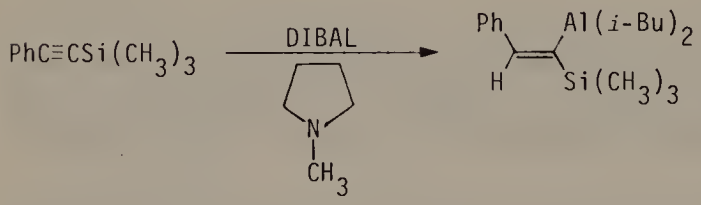
Such vinyl organometallics are useful intermediates for the preparation of acyl silanes. Oxidation of *tris*-vinyl borane intermediates with anhydrous

trimethylamine oxide followed by hydrolysis affords acyl silanes in high yield [10].

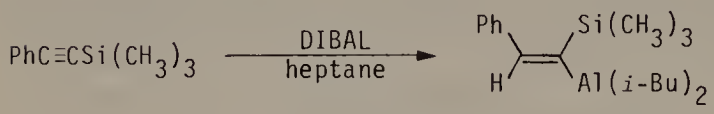


(9.3)

Cis-addition of DIBAL to 1-trimethylsilylalkynes occurs in ether solvents [1, 6, 8, 9] or in the presence of one equivalent of a tertiary amine [7]. *Trans*-addition is observed in hydrocarbon solvent [7, 8]. These vinyl alumium-silanes have proved to be synthetically useful (see Chapter 7.9).

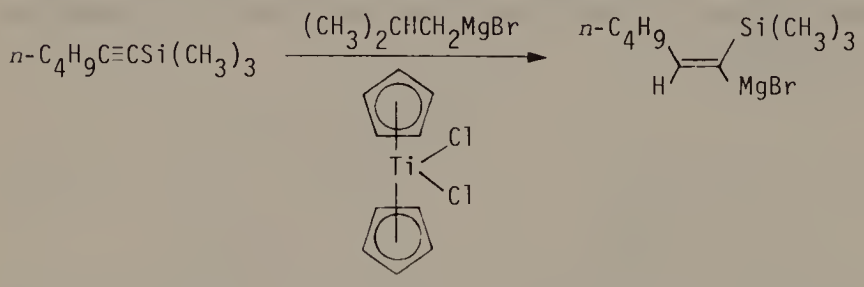


(9.4)



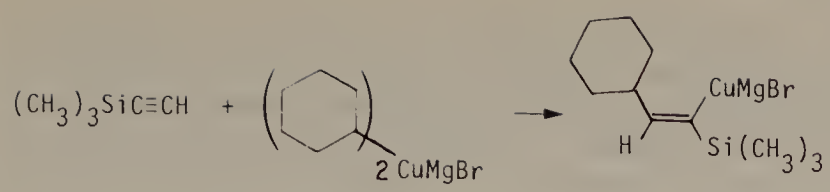
(9.5)

The reaction of 1-trialkylsilylalkynes with isobutylmagnesium bromide catalyzed by *bis*(cyclopentadienyl)titanium dichloride results in *cis* addition of magnesium hydride. This reaction regiospecifically yields a vinyl magnesium species with both the magnesium and silicon bonded to the same carbon (see Vinyl Silanes 7.9) [11].



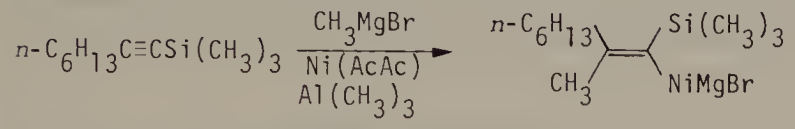
(9.6)

Magnesium dialkyl cuprate reagents also add in a *cis* manner to 1-trimethylsilylalkynes to yield vinyl cuprates [12, 13].



(9.7)

The same regiospecificity is observed in the nickel catalyzed addition of methyl Grignard reagent to 1-trimethylsilyl alkynes [14].



(9.8)

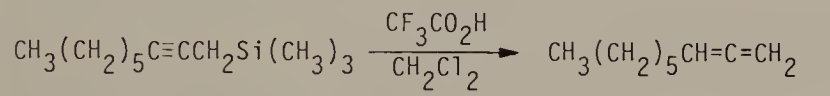
9.3 Electrophilic Substitution

The chemistry of 1-trimethylsilyl-1-alkynes, 2-alkynes, 1,2-dienes, and 2,3-dienes with electrophiles is similar in many respects and will therefore be considered together. All four types of compounds react with a variety of electrophiles. These reactions usually involve substitution of the trimethylsilyl group by an electrophile. The reactions are often accompanied by rearrangement.

(9.9)

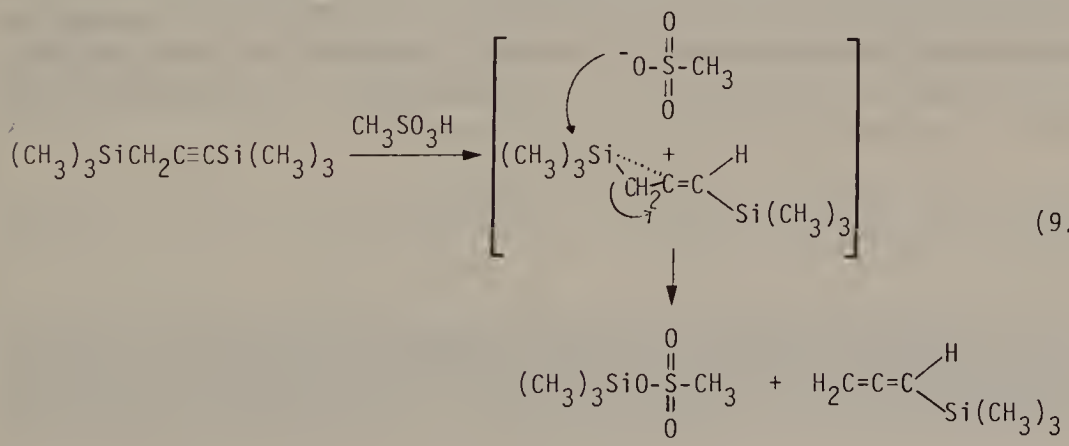
A. Protic Acids

1-Trimethylsilyl-2-nonyne reacts with trifluoroacetic acid in methylene chloride to give 1,2-nonadiene [15].



(9.10)

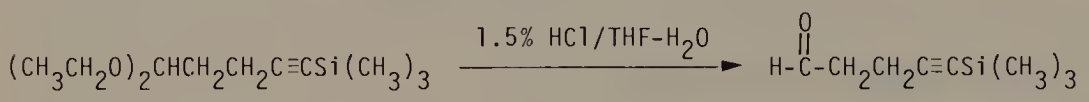
1,3-*bis*(Trimethylsilyl)propyne reacts with methanesulfonic acid to yield trimethylsilyl methanesulfonate and the rearranged product, trimethylsilylallene [16]. This reaction may proceed by protonation of the C–C triple bond to yield a vinyl carbocation stabilized by a β-trimethylsilyl group. Attack by methanesulfonate ion on the stabilizing silyl center leads to products.



(9.11)

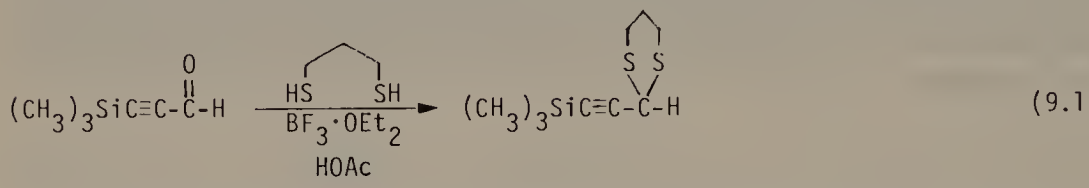
On the other hand, 1-trimethylsilyl-2-alkynes are stable to a variety of reagents and reaction conditions: mild acid hydrolysis (10% HCl/THF), propionic acid, basic hydrolysis (10% NaOH), alkylidenetriphenylphosphoranes, $LiAlH_4$, and methyl lithium. This stability permits incorporation of the propargyltrimethylsilane functionality into a variety of complex molecules [17].

1-Trimethylsilylalkynes are also stable to mild protic and Lewis acid conditions. For example, the diethyl acetal group of 5,5-diethoxy-1-trimethylsilyl-1-pentyne can be removed by hydrolysis with 1,5% HCl in THF without rearrangement to yield 5-trimethylsilylpent-4-yn-1-al [18].



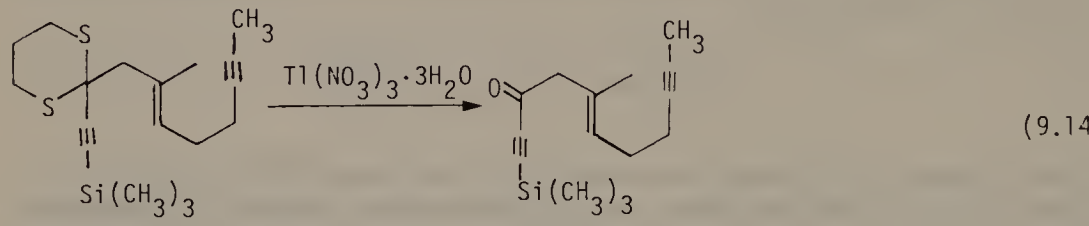
(9.12)

Likewise, the aldehyde functional group of 3-trimethylsilylprop-2-yn-1-al can be converted to a 1,3-dithiane by use of the Lewis acid $BF_3 \cdot OEt_2$ [19].



(9.13)

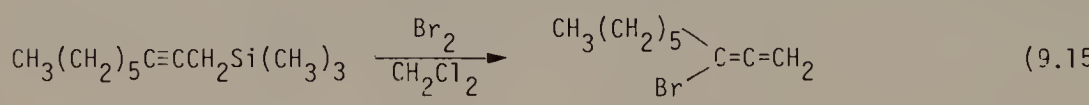
1-Trimethylsilylalkynes are stable to thallium (III) nitrate in methanol, the conditions required to hydrolyze a 1,3-dithiane to the corresponding ketone [19].



(9.14)

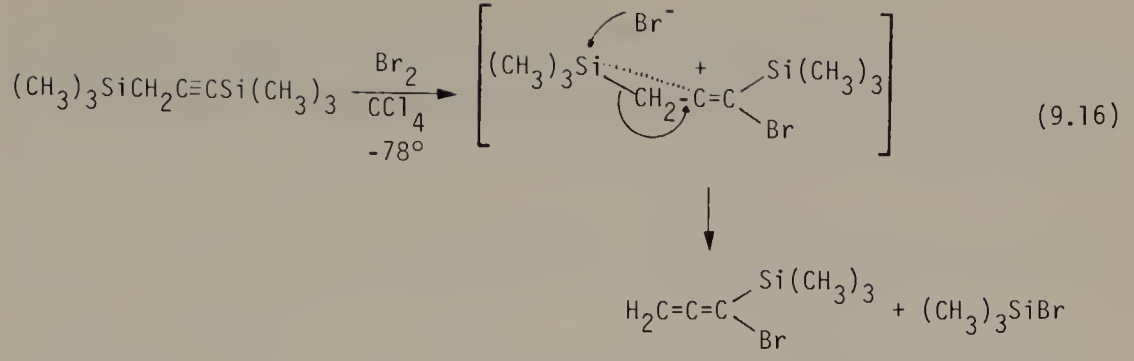
B. Halogens

1-Iodo-2-trimethylsilylacetylene, formed by reaction of iodine monochloride with *bis*(trimethylsilyl)acetylene, is a valuable precursor for Castro coupling with aryl cuprate reagents [20, 21]. 1-Trimethylsilyl-2-nonyne reacts with bromine or iodine to yield 3-halo-1,2-nonadienes [15].



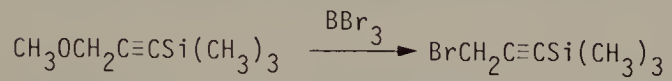
(9.15)

1,3-*bis*(Trimethylsilyl)propyne reacts with bromine in CCl_4 to yield 1-bromo-1-trimethylsilylallene as the major product [16]. This reaction may occur as outlined below.



(9.16)

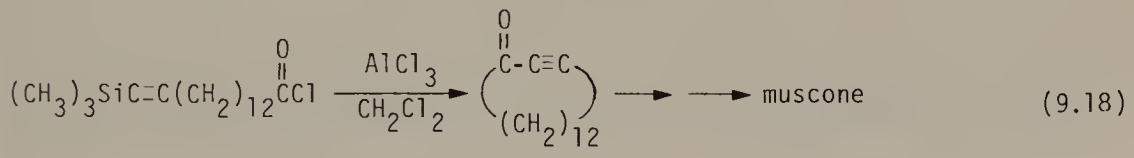
3-Bromo-1-trimethylsilylpropyne has been prepared by reaction of 3-methoxy-1-trimethylsilylpropyne with boron tribromide [22].



(9.17)

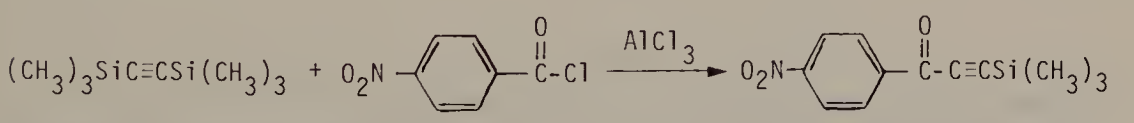
C. Acyl Chlorides

1-Trimethylsilylalkynes react with acid chlorides and $AlCl_3$ to yield conjugated alkynones [23]. This reaction probably proceeds by addition of the acylium ion to the C−C triple bond to yield a β-trimethylsilyl stabilized vinyl carbocation. Attack by chloride on the silyl center causes loss of TMS-Cl and formation of product. The $AlCl_3$ catalyzed intramolecular electrophilic cyclization of 15-trimethylsilylpentadec-14-ynoyl chloride yields 2-cyclopentadecynone [24].



(9.18)

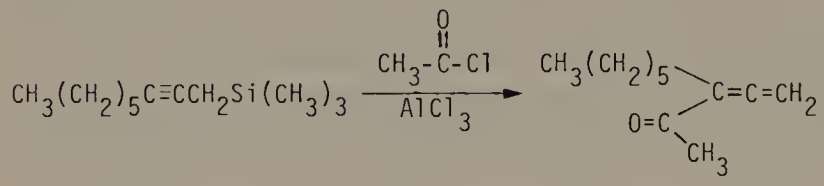
When *bis*(trimethylsilyl)acetylene is subjected to similar conditions, only one of the two trimethylsilyl groups is replaced even in the presence of excess acid chloride [23, 25]. Apparently the electron withdrawing carbonyl group deactivates the triple bond toward further electrophilic attack by acylium ions. This difference provides a useful route to 1-trimethylsilyl alkyn-3-ones [23].



(9.19)

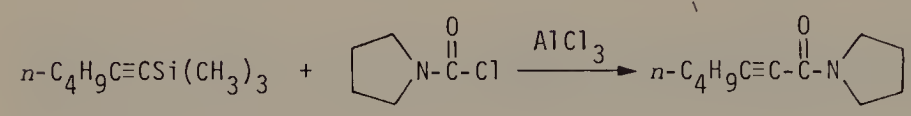
Similar electrophilic substitutions have been carried out with *bis*-1,4-(trimethylsilyl)-1,3-butadiyne and aromatic acid chlorides to give 1-aroyl-4-trimethylsilyl-1,3-butadiynes in moderate yield [26]. Isobutyryl chloride, 1,4-

bis(trimethylsilyl)-1,3-butadiyne, and $AlCl_3$ react to give 6-methyl-1-trimethylsilyl-1,3-heptadiyn-5-one [27].
1-Trimethylsilyl-2-nonyne reacts with acetyl chloride and $AlCl_3$ to give 3-acetyl-1,2-nonadiene [15].



(9.20)

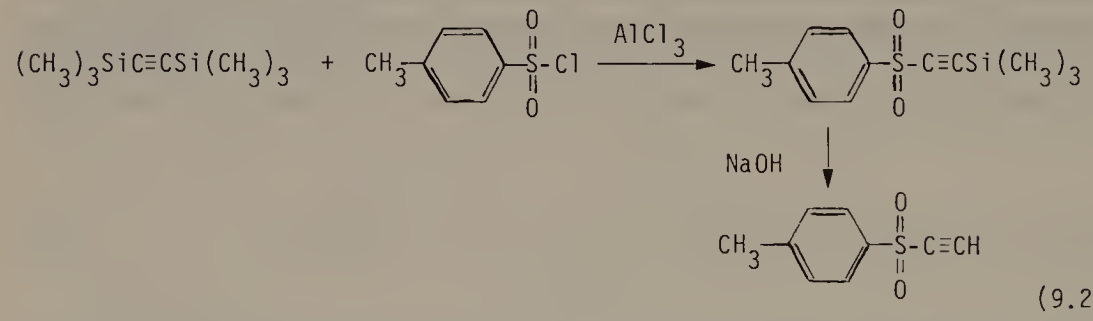
Carbamyl chlorides react with 1-trimethylsilylalkynes in essentially the same way as acid chlorides [28].



(9.21)

D. Sulfonyl Chlorides – Sulfur Trioxide

Arylsulfonyl halides react with *bis*(trimethylsilyl)acetylene under Friedel-Crafts conditions to yield 1-arylsulfonyl-2-trimethylsilylacetylenes [29].



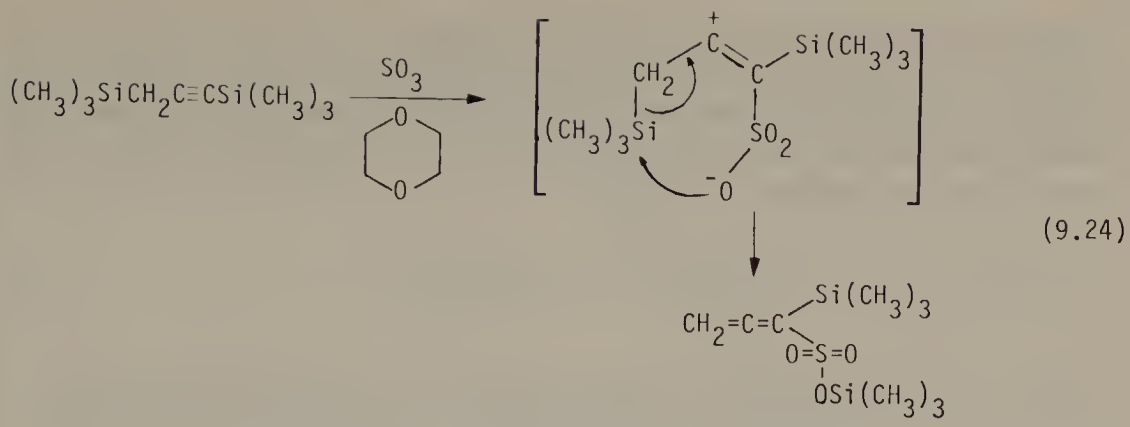
(9.22)

Trimethylsilyl chlorosulfonate also reacts with 1-trimethylsilylalkynes to yield, in general, trimethylsilyl esters of ethynylsulfonic acids [30].

(9.23)

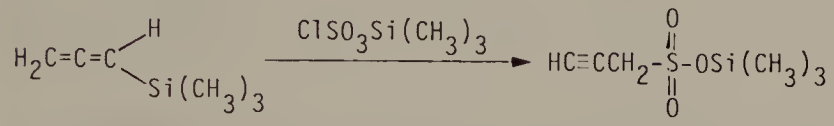
Similar results are obtained from the reaction of trimethylsilylacetylenes with the sulfur trioxide complex of *p*-dioxane [31].

Propargyltrimethylsilanes react with either trimethylsilyl chlorosulfonate or the sulfur trioxide complex of *p*-dioxane to yield rearranged trimethylsilylallene sulfonates [32]. 1,3-*bis*(Trimethylsilyl)propyne reacts under these conditions as a propargylsilane rather than an alkynylsilane to yield the rearrangement product: trimethylsilyl 1-trimethylsilylallene-1-sulfonate [32].



(9.24)

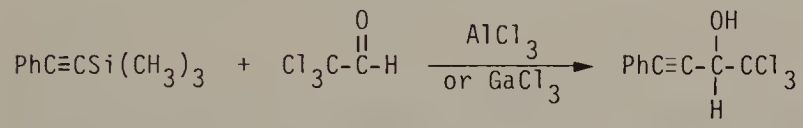
The reaction of trimethylsilylallene with trimethylsilyl chlorosulfonate to yield trimethylsilyl propargylsulfonate may occur by a similar process [33].



(9.25)

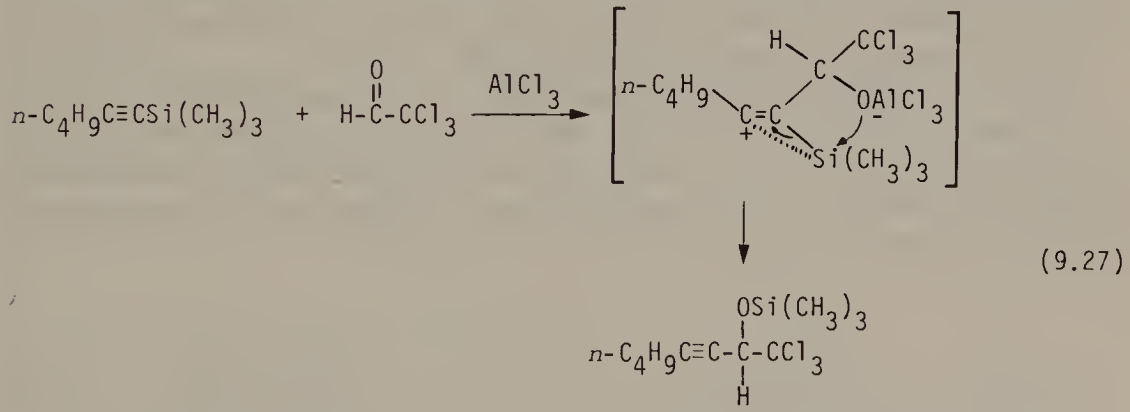
E. Aldehydes and Ketones

Trimethylsilylacetylenes undergo Lewis acid catalyzed electrophilic substitution reactions with ketones and aldehydes to yield propargyl alcohols [34, 35].



(9.26)

The reaction may occur by Lewis acid coordination to the carbonyl group rending it sufficiently electrophilic to attack the silyl substituted acetylene.

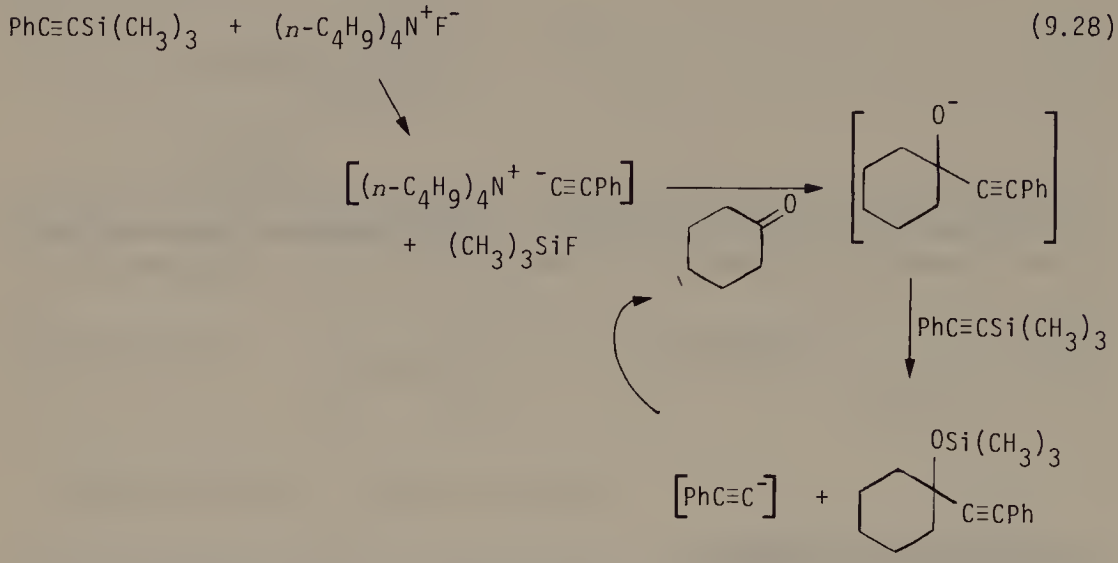


(9.27)

When a similar reaction is attempted on *bis*(trimethylsilyl)acetylene only one of the trimethylsilyl groups undergoes reaction [36].

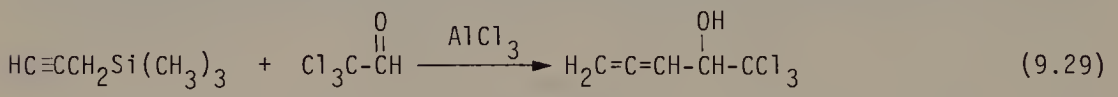
1-Trimethylsilylalkynes also react with aldehydes and ketones under nucleophilic catalysis by TBAF [37] or potassium fluoride/18-C-6 [38] to yield

propargyl trimethylsilyl ethers. Presumably, these reactions are initiated by fluoride anion attack on the 1-trimethylsilylalkyne to form TMS-F. The resulting acetylide anion then reacts with the ketone. The alkoxide anion thus formed then attacks the 1-trimethylsilylalkyne affording the product and regenerating the acetylide anion [37].



(9.28)

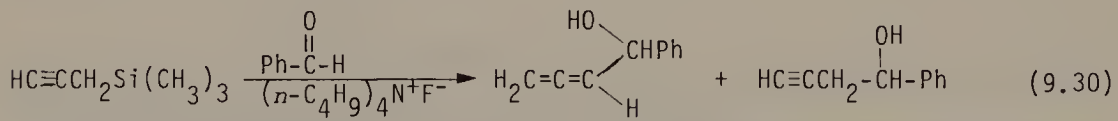
Propargylsilanes, on the other hand, undergo $AlCl_3$ catalyzed reactions with ketones and aldehydes to yield rearranged allenic alcohols [35].



(9.29)

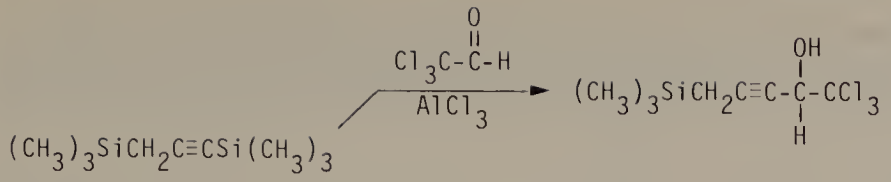
Propargyltrimethylsilanes react with aldehydes, ketones [39, 40] and acetals [41] in the presence of $TiCl_4$ at low temperature to yield respectively rearranged allenic carbinols or ethers. If the allenic carbinol is desired, these reactions must be hydrolyzed at low temperature (−60°). Warming prior to hydrolysis yields 2-chloro-1,3-butadiene derivatives by reaction of the initial allenic trimethylsilyl ethers with $TiCl_4$ [39, 40].

Reaction between propargyltrimethylsilanes and aldehydes may also be catalyzed by TBAF in THF. In the case of aliphatic aldehydes, the products are isomerically pure rearranged allenic carbinols. With benzaldehyde, however, a mixture of the expected allenic carbinol and the unrearranged propargyl alcohol are obtained in a 70 : 30 ratio [42].

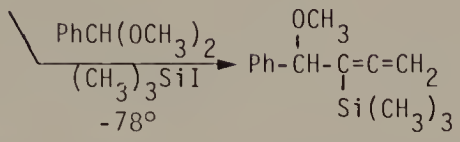


(9.30)

Although *bis*-1,3-(trimethylsilyl)propyne undergoes electrophilic reaction with chloral as a silylacetylene (Eq. 9.30) [35], it reacts as a propargylsilane with acetals under catalysis by TMS-I to yield 1-alkoxy-2-trimethylsilyl-2,3-butadienes (Eq. 9.31) [43]. The reason for this difference is not clear at present.

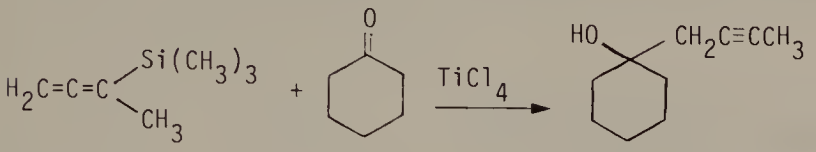


(9.31)



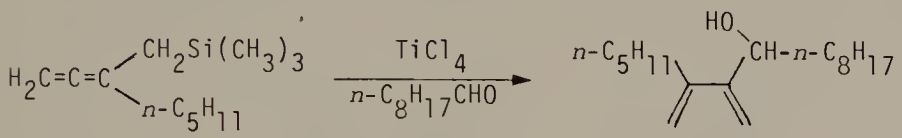
(9.32)

1-Trimethylsilylallenes react with ketones or aldehydes in the presence of $TiCl_4$ to yield rearranged homopropargyl alcohols [44].



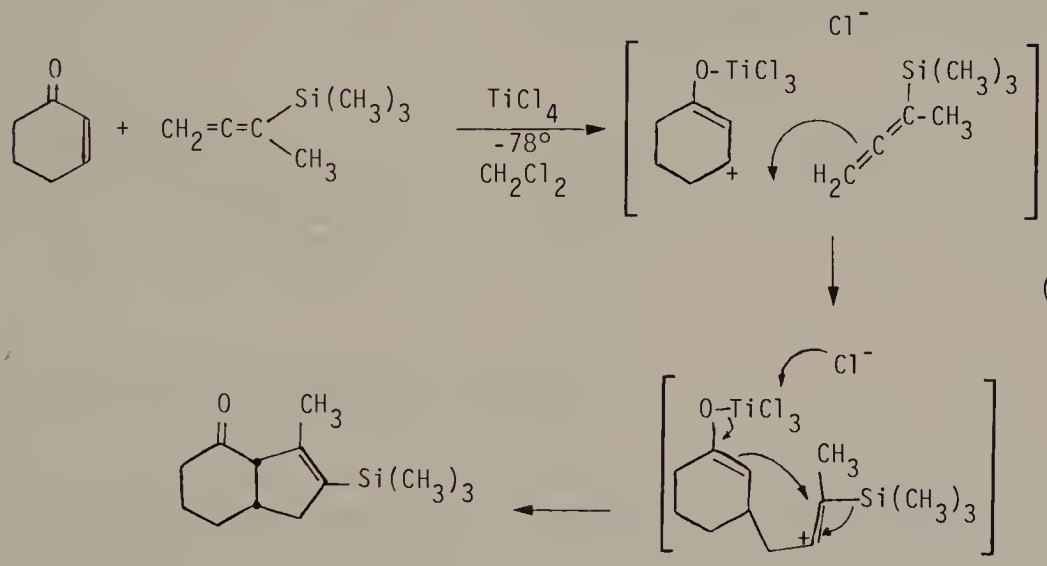
(9.33)

The $TiCl_4$ catalyzed reaction of 1-trimethylsilyl-2,3-dienes with aldehydes affords rearranged 2-(1′-hydroxyalkyl)-1,3-butadienes [45].



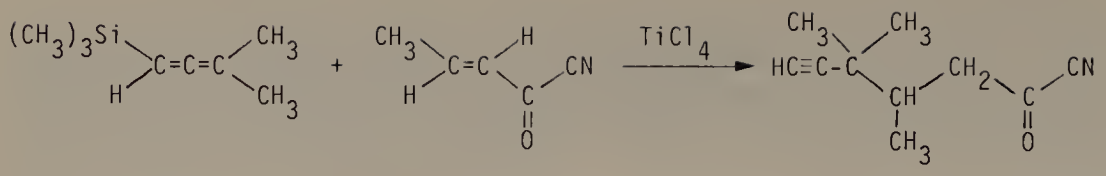
(9.34)

1-Trimethylsilylallenes react with α,β-unsaturated ketones to yield trimethylsilylcyclopentene products. This approach to cyclopentenes by [2 + 3]cycloannulation provides a unique regiospecific synthesis of such compounds. The sequence of events outlined in Eq. 9.35 has been proposed to account for these results [46].



(9.35)

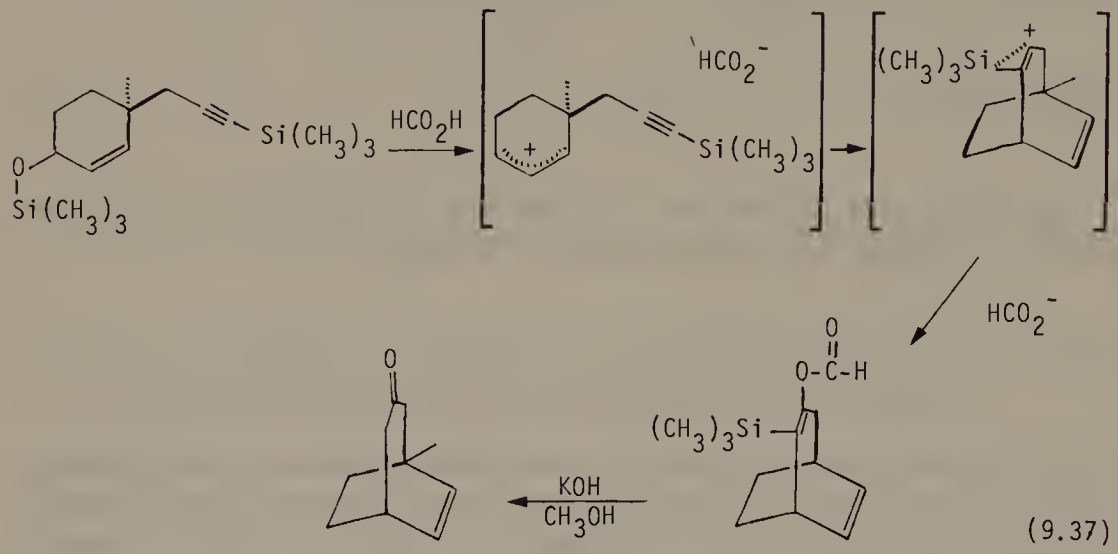
1-Trimethylsilylallenes react with α,β-unsaturated acyl nitriles and $TiCl_4$ in a conjugate 1,4-Michael-type reaction to yield rearranged products [47].



(9.36)

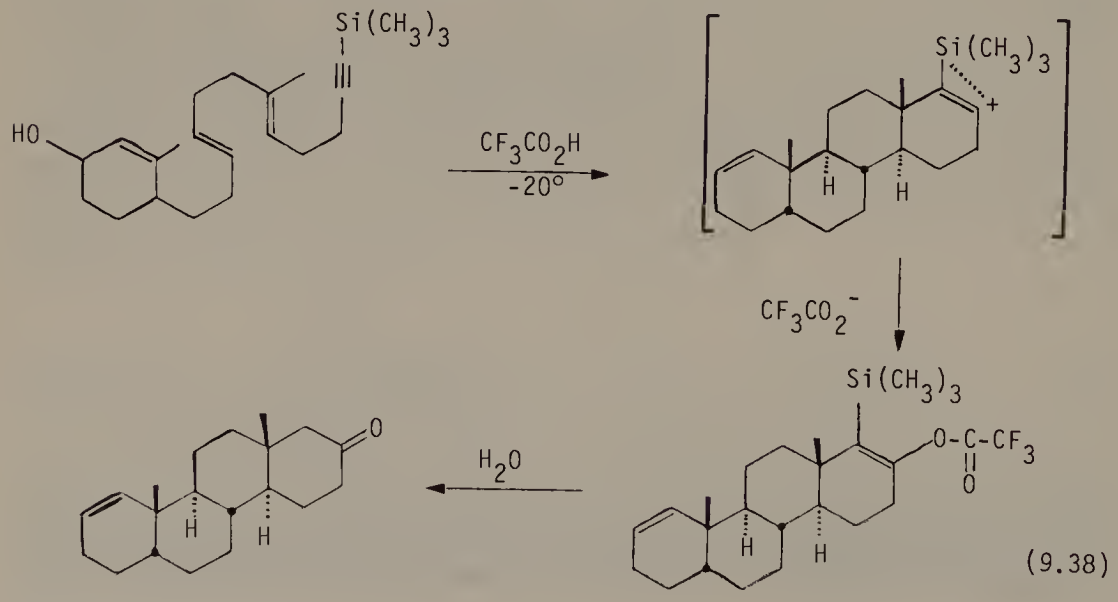
F. Carbocations

1-Trimethylsilylalkynes undergo intramolecular ring-closure with carbocations to yield cyclic ketones as outlined below [48].



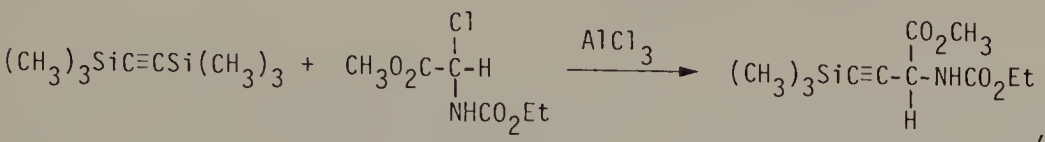
(9.37)

A 1-trimethylsilylalkyne has been used as a terminator in a biomimetic type cyclization to form D-homosteroids [18].



(9.38)

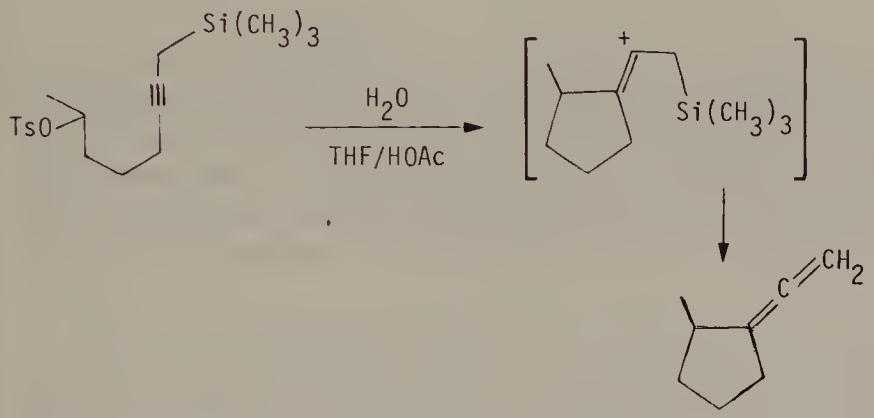
Methyl trimethylsilylacetylene N-carboethoxyglycinate has been prepared by reaction of *bis*(trimethylsilyl)acetylene with methyl-2-chloro-N-carboethoxy glycinate and $AlCl_3$ in methylene chloride [49].



(9.39)

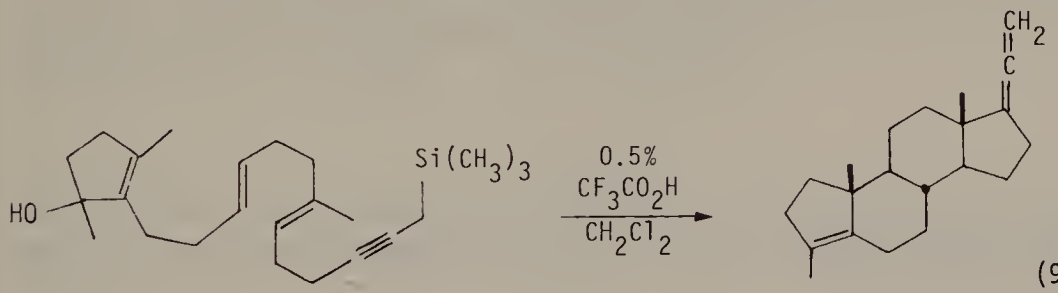
Both trimethylsilyl groups of *bis*(trimethylsilyl)acetylene may be substituted by carbocations under electrophilic conditions [23].

Propargyltrimethylsilanes undergo intramolecular reaction with carbocations to yield vinylene cycloalkanes [50].



(9.40)

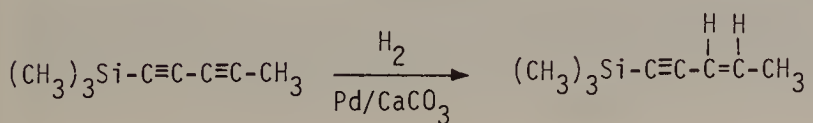
Propargyltrimethylsilanes have also proved effective as terminators in biomimetic carbocation cyclization reactions as outlined below [17].



(9.41)

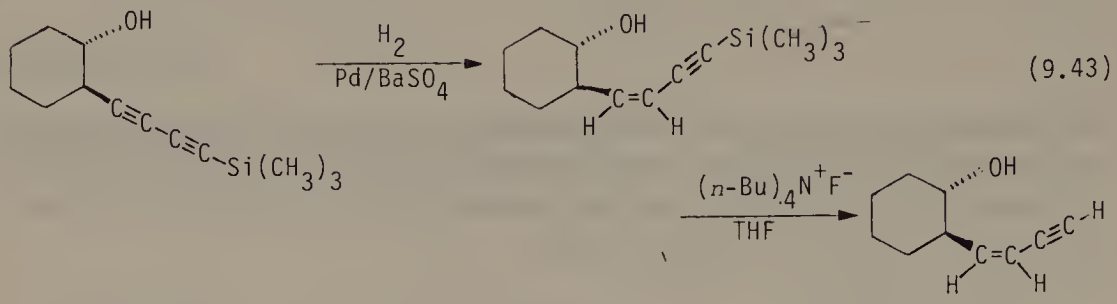
9.4 Protection of Terminal Alkynes

Trimethylsilyl groups have been used to protect terminal alkynes from reduction during the hydrogenation of internal acetylenes to *cis*-alkenes [51].



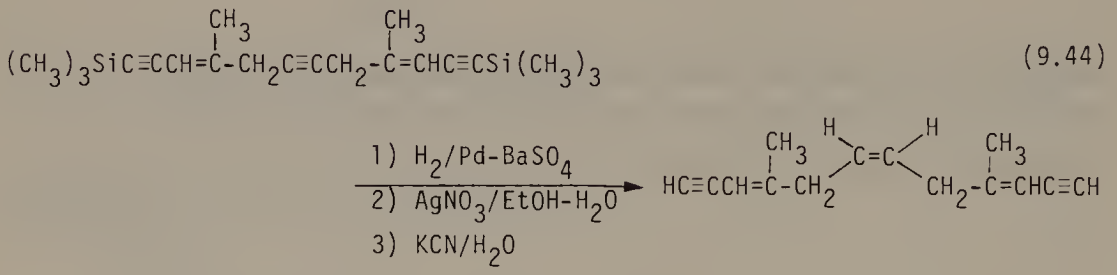
(9.42)

This approach has been utilized in a highly stereoselective synthesis of a terminal *cis*-enyne. After partial reduction of the internal acetylene by catalytic hydrogenation, the trimethylsilyl protecting group was removed by treatment with TBAF in THF [52].



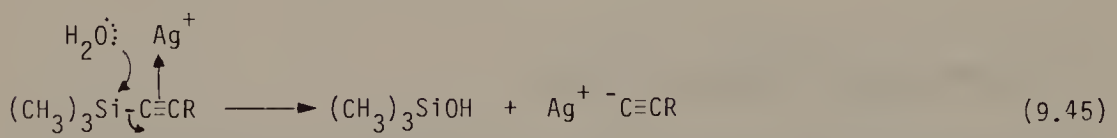
(9.43)

The conversion of 4,9-dimethyl-3,9-dodecadien-1,6,11-triyne into 4,9-dimethyl-3,6,9-dodecatrien-1,11-diyne was achieved in a similar manner. The terminal acetylenic groups were protected by deprotonation with ethyl Grignard reagent followed by addition of TMS-Cl. The internal triple bond was then catalytically hydrogenated. Finally, the terminal trimethylsilyl groups were removed by treatment with silver nitrate in aq. ethanol followed by potassium cyanide in water [53].



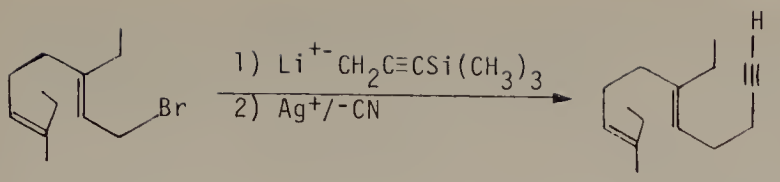
(9.44)

It has been proposed that coordination of the silver cation with the triple bond facilitates attack by water on the silyl center which results in cleavage of the Si–C bond [53].



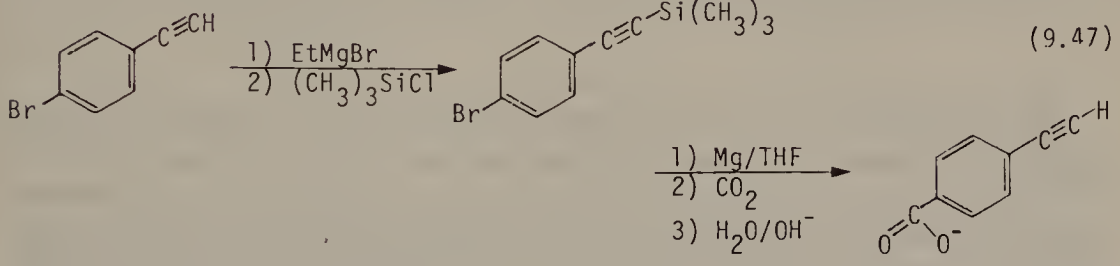
(9.45)

This deprotection technique may be the mildest method yet developed for the cleavage of Si–C sp hybridized bonds. This procedure has been utilized by Corey [54] in a stereospecific synthesis of *d,l*-C_{18}-Cecropia juvenile hormone, Eq. 9.46 [55], as well as in the preparation of α-Santalol [56].



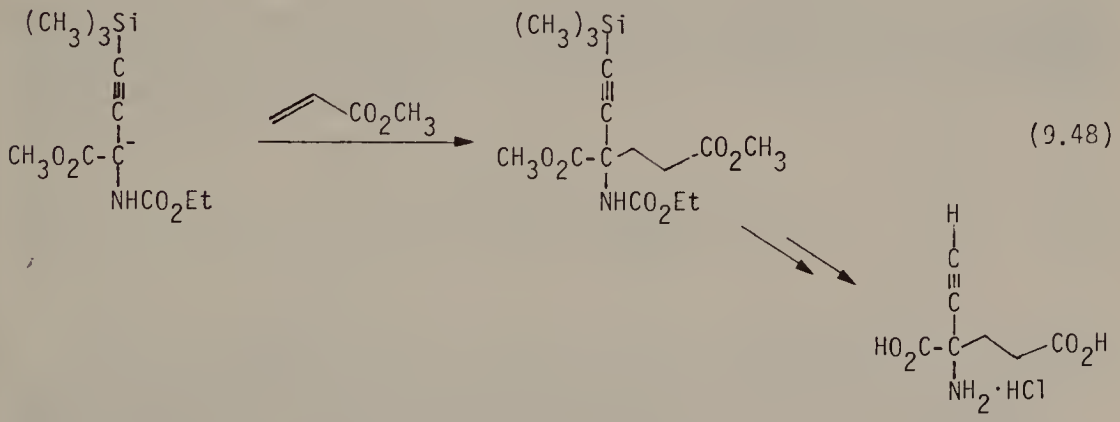
(9.46)

Trimethylsilyl groups have been utilized to protect terminal acetylene not only from reduction but in a number of other reactions. For example, it is not possible to prepare a Grignard reagent from *p*-bromophenylacetylene due to the acidity of the sp hybridized C–H bond. This difficulty has been overcome by trimethylsilyl protection. Carbonation of the protected Grignard, followed by aq. alkaline cleavage of the Si–C bond yields 4-ethynylbenzoic acid [57].



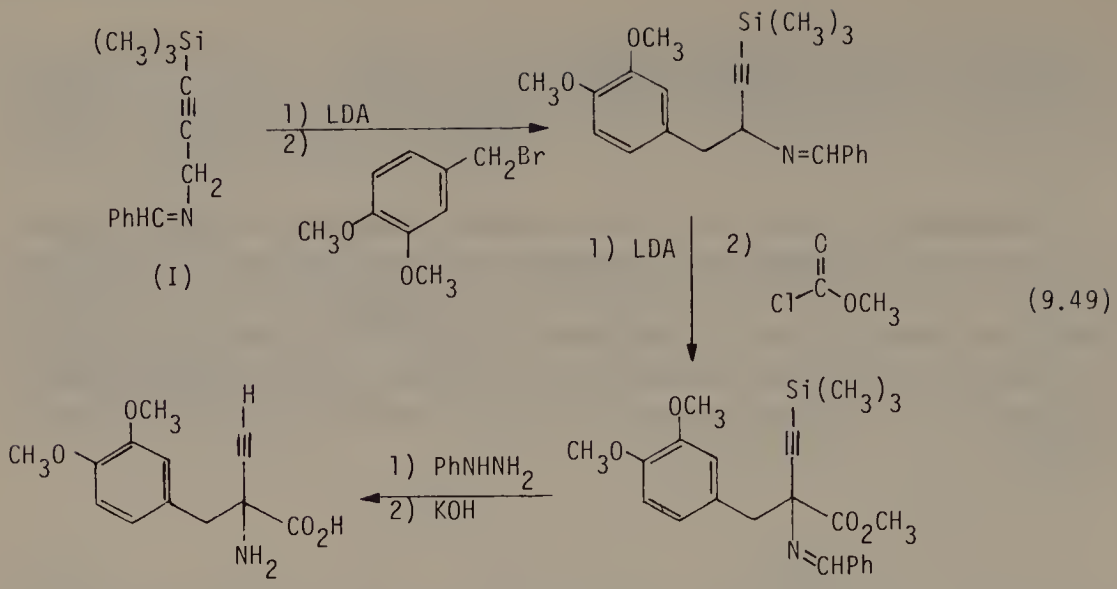
(9.47)

The trimethylsilyl group has been used to protect terminal alkynes in the synthesis of α-acetylenic amines and α-acetylenic α-amino acids. Methyl trimethylsilylacetylene-N-carboethoxyglycinate can be deprotonated with LDA in HMPT to yield a reactive anion which can be alkylated with allylic and benzylic bromides or primary alkyl iodides. This anion can also undergo Michael addition with methyl acrylate α-Acetylene glutamic acid has been prepared as outlined. The trimethylsilyl protecting group is removed by treatment with aq. KOH [58].



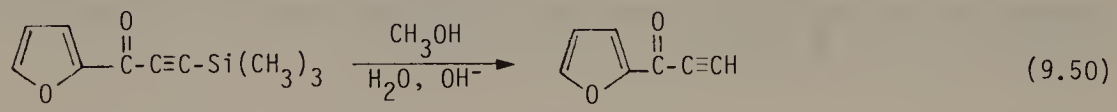
(9.48)

The alidimine (I) has been used to prepare α-acetylenic α-amino acids and α-acetylenic amines. For example, an α-acetylenic DOPA derivative was prepared as outlined below [59].

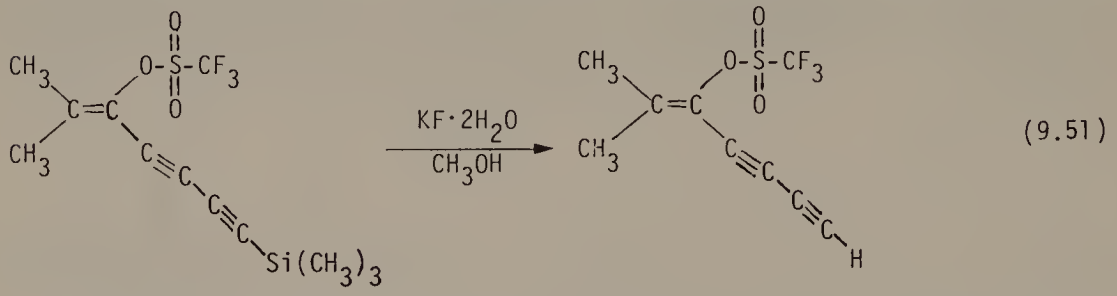


The first example of basic cleavage of a Si–C sp hybridized bond was reported by Gilman. He observed that the base-catalyzed cleavage of the Si–C bond of phenyl triphenylsilyl acetylene was qualitatively fast compared to the cleavage of benzyltriphenylsilane [60]. Quantitative data shows that methanolic sodium hydroxide cleaves the Si–C bond of phenyl trimethylsilyl acetylene 2×10^7 times faster than the Si–C bond of benzyltrimethylsilane. This may reflect the greater stability of an acetylide anion compared to a benzylic anion [61, 62].

The Si–C bond of both 1-aroyl-2-trimethylsilylacetylenes and 1-aroyl-4-trimethylsilyl-1,3-butadiynes are cleaved on treatment with aq. borax and methanol to yield the corresponding aroyl acetylenes or 1-aroyl-1,3-butadiynes [26].



Potassium fluoride dihydrate in methanol will also cleave Si–C sp hybridized bonds [27].



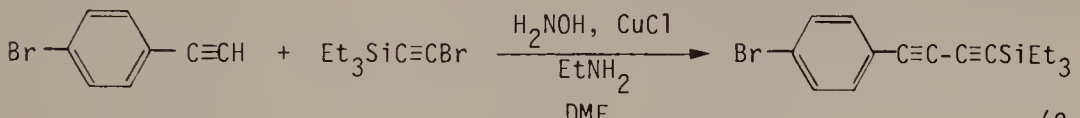
Trimethylsilyl protecting groups permit the oxidative coupling of trimethylsilyl acetylenes to yield *α,ω-bis*(trimethylsilyl)polyacetylenes. The Hay modification [64] of the Glaser reaction has proved effective in this respect. For example, treatment of trimethylsilylacetylene with cuprous chloride,

TMEDA and oxygen yields 1,4-*bis*(trimethylsilyl)-1,3-butadiyne. Similar treatment of 1-trimethylsilyl-1,3-butadiyne yields, 1,8-*bis*(trimethylsilyl)-1,3,5,7-octatetrayne.

$$(CH_3)_3SiC{\equiv}C\text{-}C{\equiv}CH \xrightarrow[O_2]{CuCl/TMEDA} (CH_3)_3SiC{\equiv}C\text{-}C{\equiv}C\text{-}C{\equiv}C\text{-}C{\equiv}CSi(CH_3)_3 \qquad (9.52)$$

Reaction of these products with aq. methanolic alkali yields 1,3-butadiyne and 1,3,5,7-octatetrayne respectively [65]. Triethylsilyl protecting groups have been used in the preparation of 1,3,7,9,13,15,19,21-octadehydro-24-annulene [67]. The rates of base catalyzed cleavage of Si–C bonds in trimethylsilyl-substituted polyacetylenes have been determined [66].

Likewise Cadiot-Chodkiewicz coupling [68] of 1-bromo-2-trialkylsilyl-acetylenes with terminal acetylenes yields 1-trialkylsilyl polyacetylenes [65, 69].

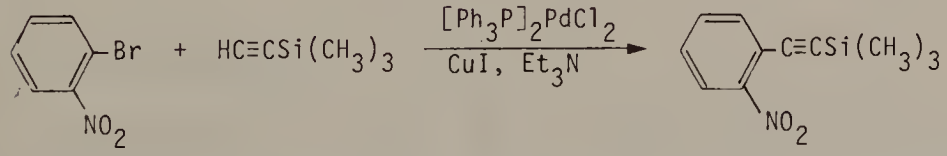


(9.53)

The reaction of phenylacetylene with 1-bromo-4-triethylsilyl-1,3-butadiyne yields 1-phenyl-6-triethylsilylhexatriyne. The necessary 1-bromo or 1-iodo-4-triethylsilyl-1,3-butadiyne was prepared from 1-triethylsilylbutadiyne. Reaction of 1-triethylsilylbutadiyne with N,N-dimethylamino-tri-*n*-butyltin gave 1-tri-*n*-butylstannyl-4-triethylsilyl-1,3-butadiyne which undergoes selective destannylation on treatment with bromine or iodine monochloride [70].

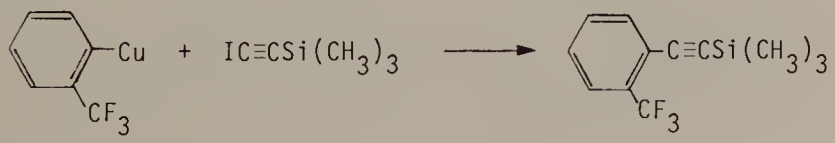
$$Et_3SiC{\equiv}C\text{-}C{\equiv}CH \xrightarrow{(n\text{-}Bu)_3SnN(CH_3)_2} Et_3SiC{\equiv}C\text{-}C{\equiv}CSn(n\text{-}Bu)_3 \xrightarrow{ICl} Et_3SiC{\equiv}C\text{-}C{\equiv}CI \qquad (9.54)$$

The inverse reaction of an α-bromoacetylene with a trimethylsilyl acetylene fails under Cadiot-Chodkiewicz conditions. However, aryl trimethylsilyl acetylenes can be efficiently prepared by *bis*(triphenylphosphine) palladium dichloride catalyzed coupling of aryl bromides or iodides with trimethylsilyl acetylene [71].



(9.55)

The Castro coupling of aryl copper reagents with 1-iodo-2-trimethylsilyl-acetylene to yield 1-aryl-2-trimethylsilylacetylenes is closely related [20].



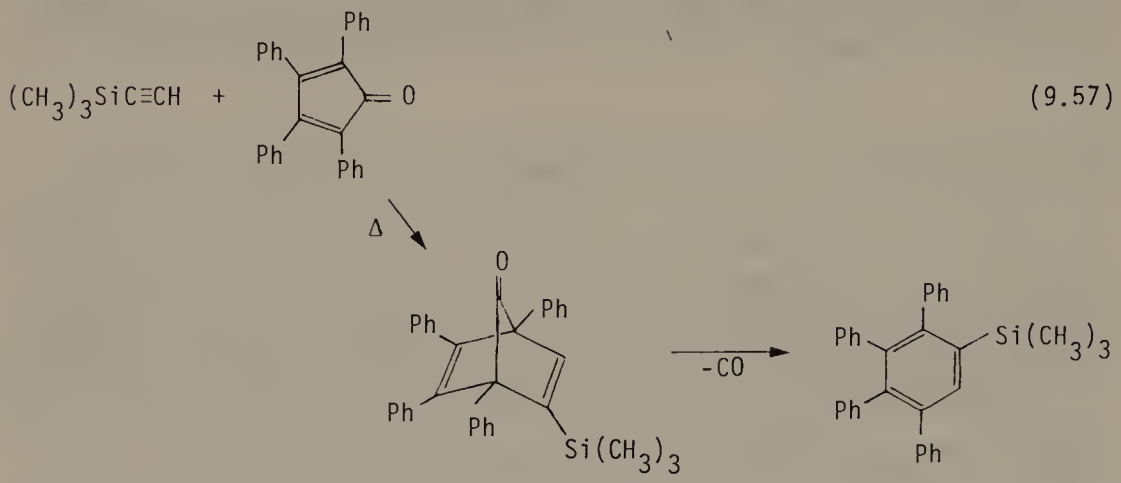
(9.56)

Trimethylsilyl groups have been used to protect terminal acetylenes while Castro coupling was carried out between an aryl iodide and a terminal acetylenic copper reagent [72].

9.5 Cycloaddition Reactions

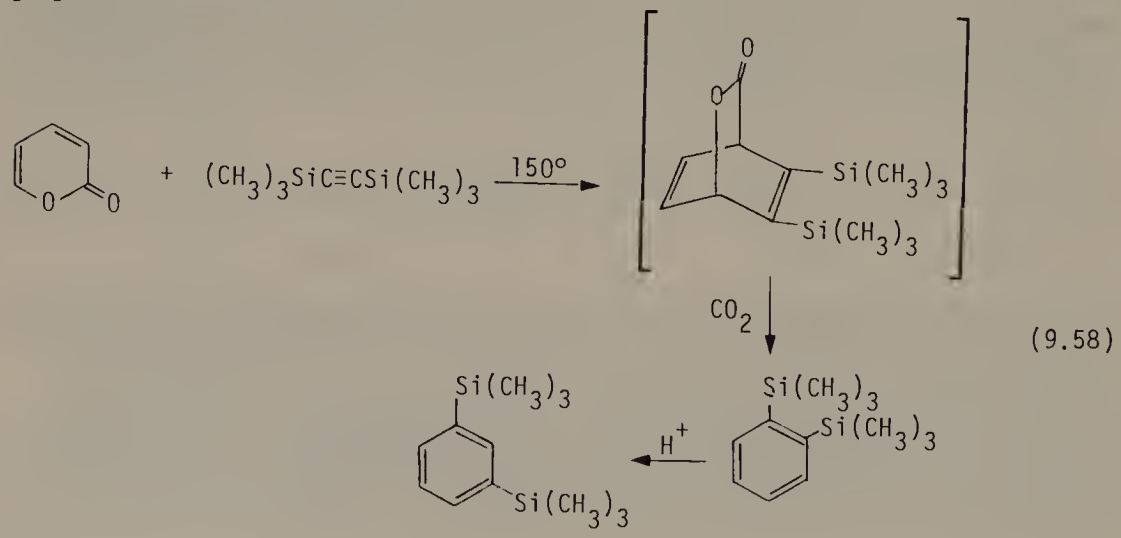
A. Diels-Alder Reactions

Silylacetylenes undergo a variety of cycloaddition reactions. Diels-Alder reactions of silylacetylenes are valuable for the preparation of certain silyl-substituted aromatic compounds [73].



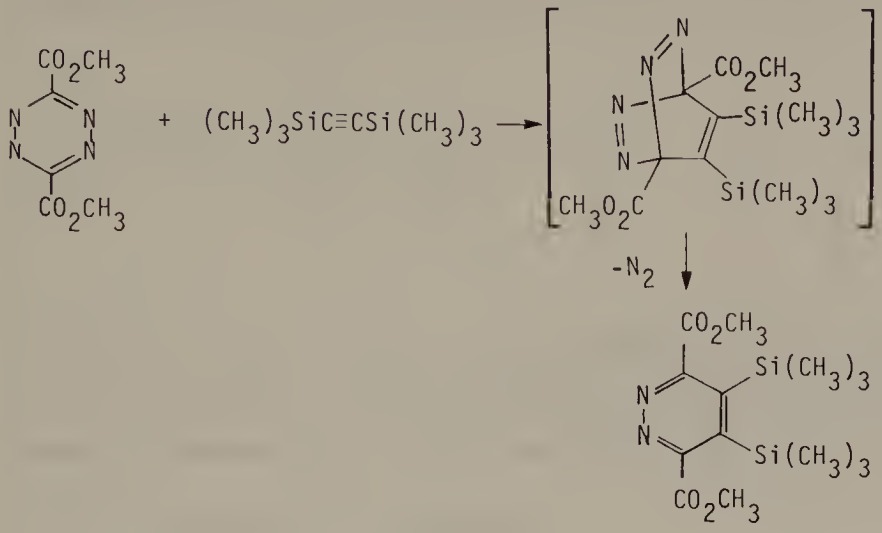
(9.57)

In a similar manner, *bis*(trimethylsilyl)acetylene undergoes a Diels-Alder reaction with α-pyrone in refluxing bromobenzene. The initial adduct decarboxylates to yield 1,2-*bis*(trimethylsilyl)benzene which readily undergoes acid catalyzed rearrangement to 1,3-*bis*(trimethylsilyl)benzene. The driving force for this rearrangement probably is relief of steric strain. Addition of 10 mole percent of triethylamine to the solvent prevents this rearrangement [74].



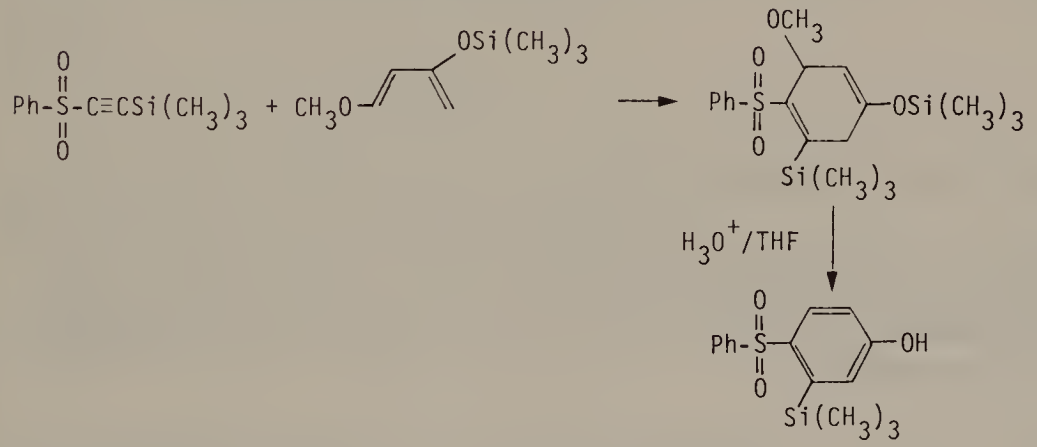
(9.58)

Both *mono*- and *bis*-(trimethylsilyl)acetylene undergo Diels-Alder reactions with 3,6-*bis*(carbomethoxy)-1,2,4,5-tetrazine to yield substituted pyridazines [75].



(9.59)

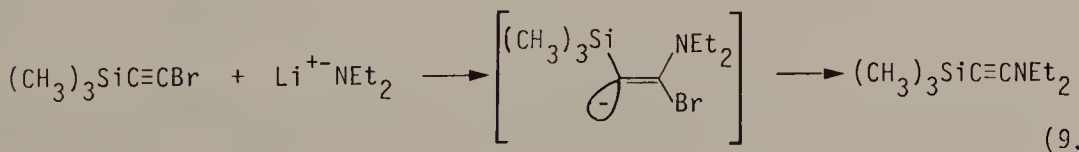
1-Arylsulfonyl-2-trimethylsilylacetylenes undergo Diels-Alder reactions with 1-methoxy-3-trimethylsilyloxy-1,3-butadiene to yield 2-arylsulfonyl-3-methoxy-1-trimethylsilyl-5-trimethylsilyloxy-1,4-cyclohexadienes. On treatment with acid in aq. THF, these lose methanol and hydrolyze to yield 4-arylsulfonyl-3-trimethylsilyl substituted phenols [76].



(9.60)

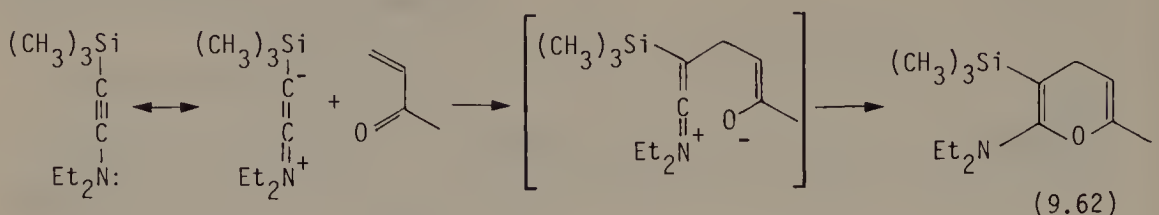
B. Silyl-ynamines

Silyl-ynamines are prepared by the reaction of 1-bromo-2-trimethylsilylacetylene with lithium amides. This reaction probably occurs by an additions–elimination sequence.



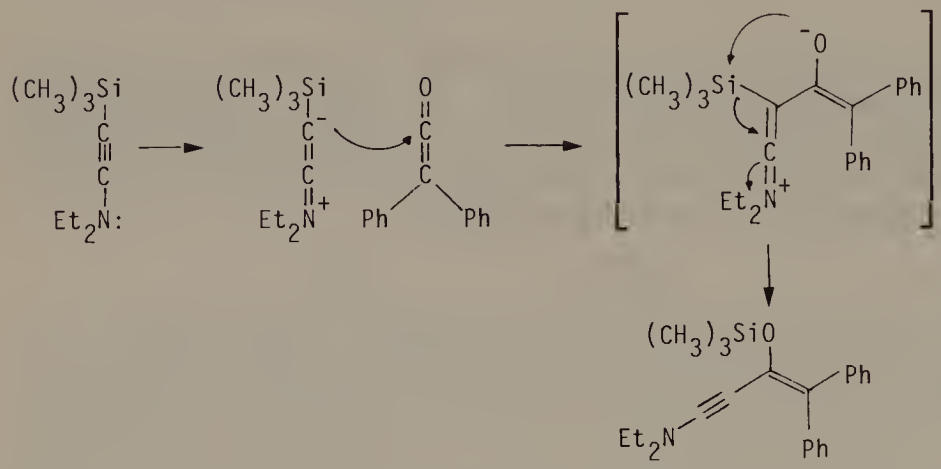
(9.61)

Silyl-ynamines undergo Diels-Alder reactions with α,β-usaturated ketones, to yield 2-dialkylamino-3-trimethylsilyl pyran derivatives. The regiospecificity observed may result from the zwitterionic intermediates formed by Michael addition of the nucleophilic carbon of the silyl-ynamine to the α,β-unsaturated ketone [77].



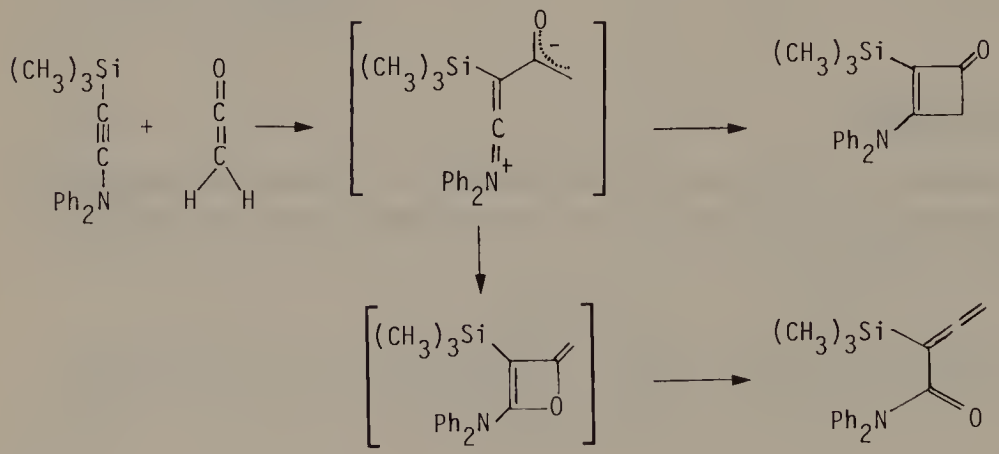
(9.62)

Silyl-ynamines react with diphenylketene to yield 3-silyloxy-3-buten-1-ynyl amines. Initial nucleophilic attack by the C-2 carbon of the silyl-ynamine on the carbonyl carbon of the ketene leads to a zwitterionic intermediate. Migration of the silyl group from carbon to the negatively charged oxygen yields the product [78].



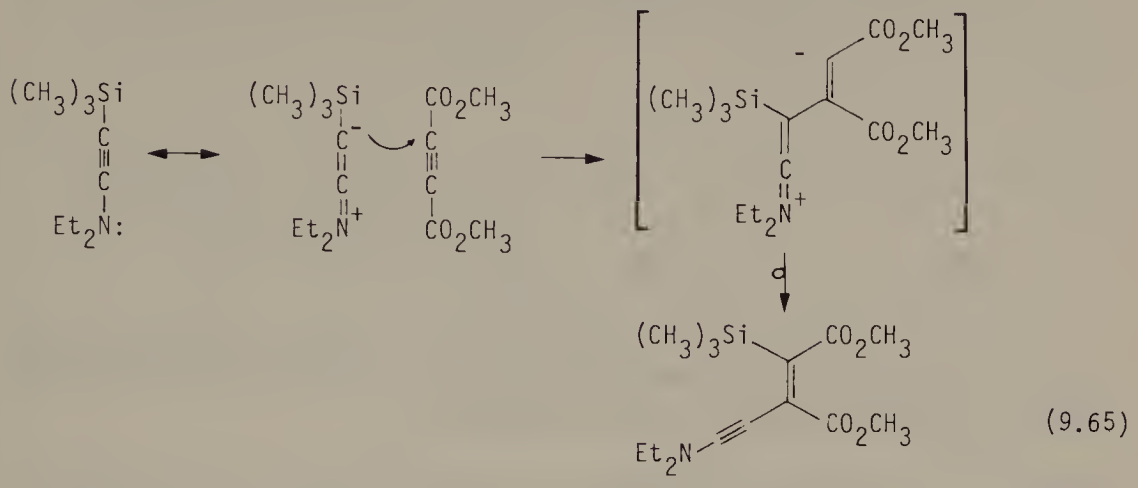
(9.63)

On the other hand, silyl-ynamines react with ketene to yield 3-amino-2-silyl-2-cyclobuten-1-ones and 2-silyl-2,3-butadieneamides [79]. The reaction may proceed as indicated. The reason for the different behavior of the two ketenes is at present unknown.



(9.64)

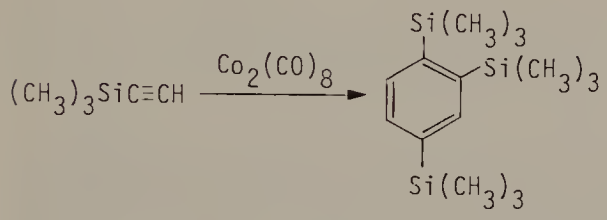
The reaction of silyl-ynamines with dimethyl acetylenedicarboxylate probably involves a similar zwitterionic intermediate [80].



(9.65)

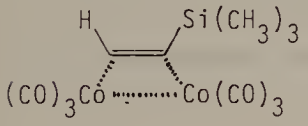
C. Cobalt-Catalyzed Cycloadditions

Dicobalt octacarbonyl catalyzed trimerization of trimethylsilylacetylene provides an efficient route to 1,2,4-*tris*-(trimethylsilyl)benzene [81].



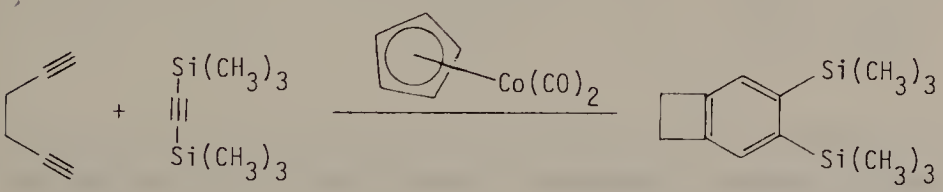
(9.66)

A dicobalt hexacarbonyl complex of trimethylsilylacetylene, which is formed in the reaction, is also an effective catalyst [82].



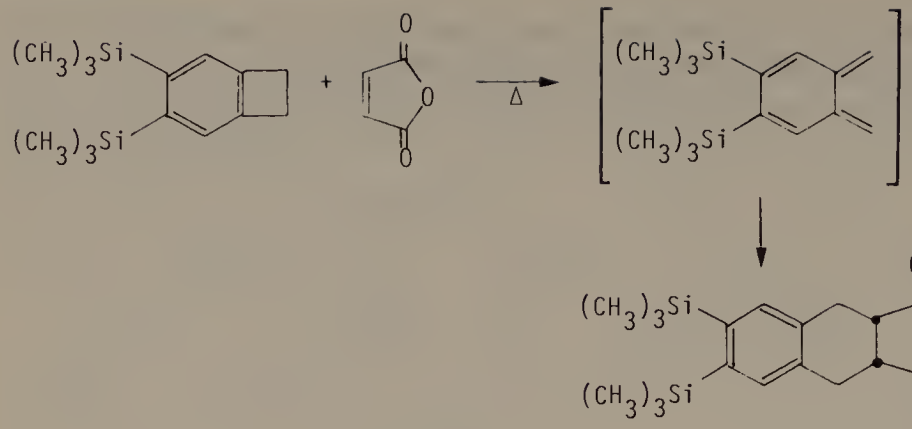
(9.67)

η^5-Cyclopentadienyl cobalt dicarbonyl catalyzes cross-trimerization reactions between silylacetylenes and α,ω-diynes [83–85].



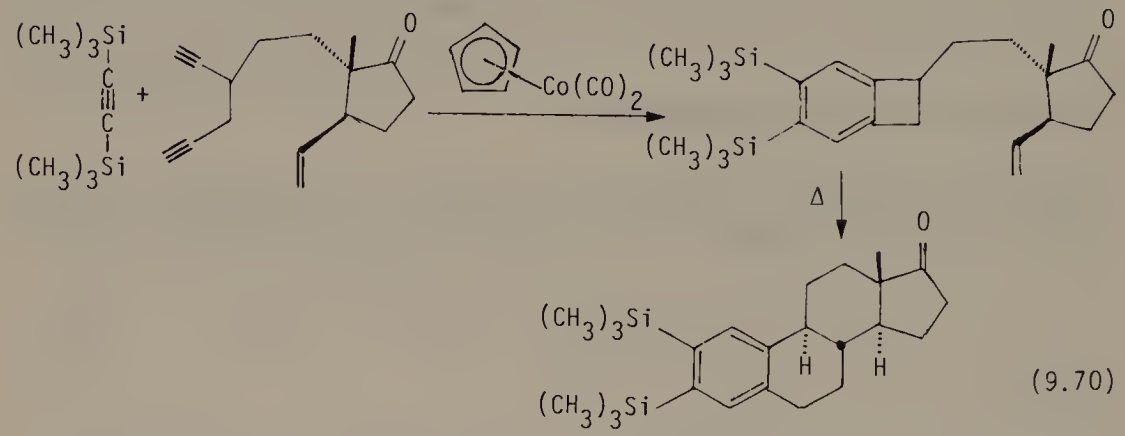
(9.68)

Benzocyclobutenes undergo thermal electrocyclic ring opening to reactive *ortho*-quinone methides which can participate in Diels-Alder reactions [84].



(9.69)

This approach has been utilized in the synthesis of 2,3-*bis*(trimethylsilyl)-estra-1,3,5-(10) trien-17-one as outlined below [86].

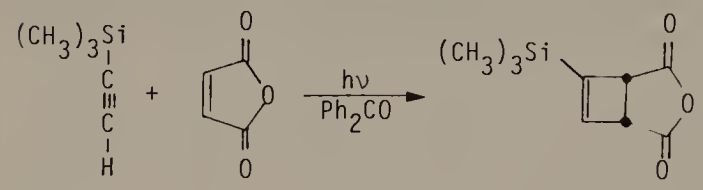


(9.70)

η^5-Cyclopentadienyl cobalt dicarbonyl catalyzes the reaction of 3-trimethylsilyloxy-1,5-hexadiyne and an excess of *bis*(trimethylsilyl)acetylene to yield 2,3,6,7-*tetrakis*(trimethylsilyl)naphthalene [87].

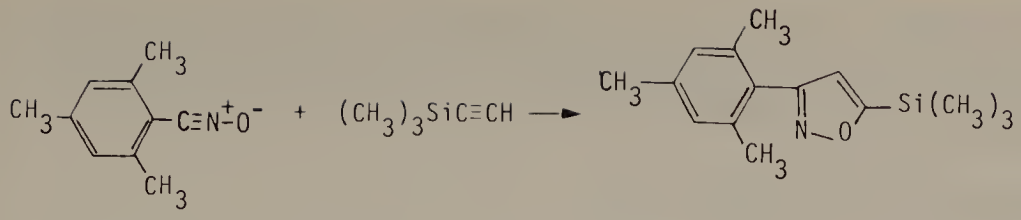
D. [2 + 2] and [2 + 3] Cycloadditions

Trimethylsilylacetylene undergoes benzophenone triplet sensitized [2 + 2] photocycloaddition reaction with maleic anhydride to yield 1-trimethylsilylcyclobutene-3,4-dicarboxylic acid anhydride [88].



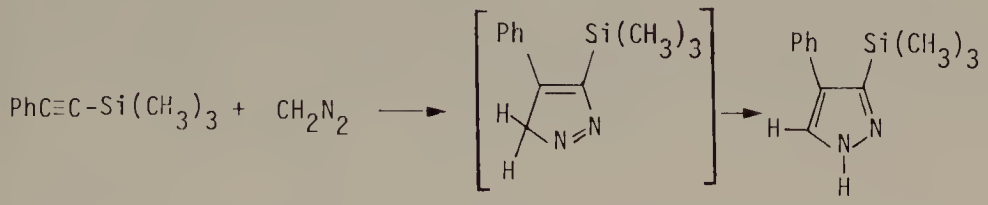
(9.71)

[2 + 3] Cycloaddition reactions between silylacetylenes and a variety of 1,3-dipolar species provide a reasonable synthetic route to silyl-substituted five-membered aromatic heterocycles.
For example, nitrile oxides react regiospecifically with silyl substituted acetylenes to yield 5-silyl isoxazoles [89].



(9.72)

Likewise, diazomethane slowly reacts with silylacetylenes to yield 3-silylpyrazoles.

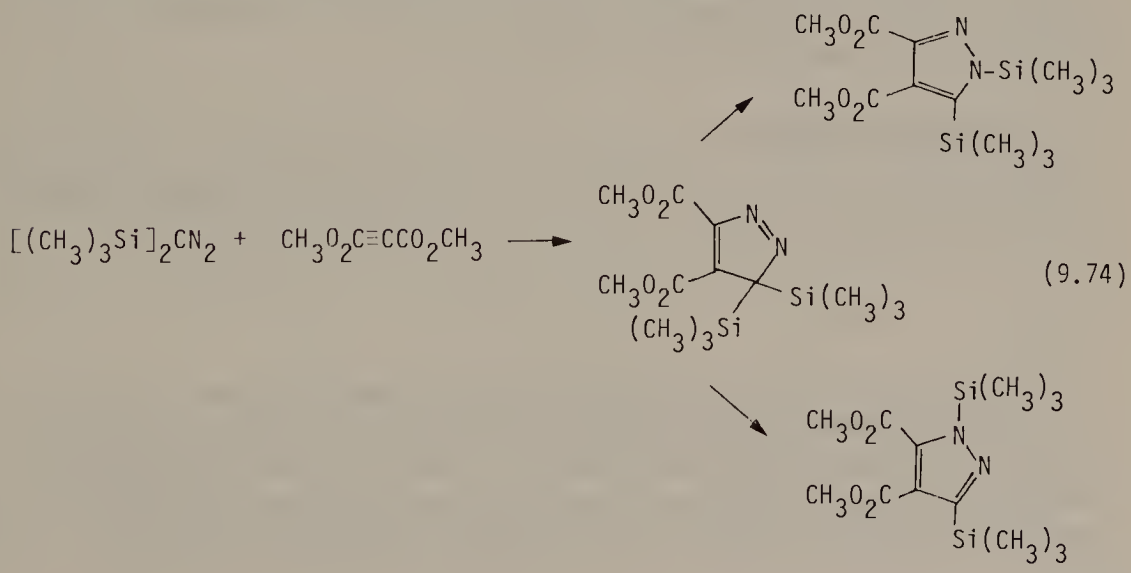


(9.73)

Ethyl diazoacetate reacts with *bis*(trimethylsilyl)acetylene to yield 3,4-*bis*-(trimethylsilyl)-5-carboethoxypyrazole [90, 91]. Although French workers have obtained similar results [92], they assign the N−H hydrogen to nitrogen-2. Which assignment is correct is not certain at this time.

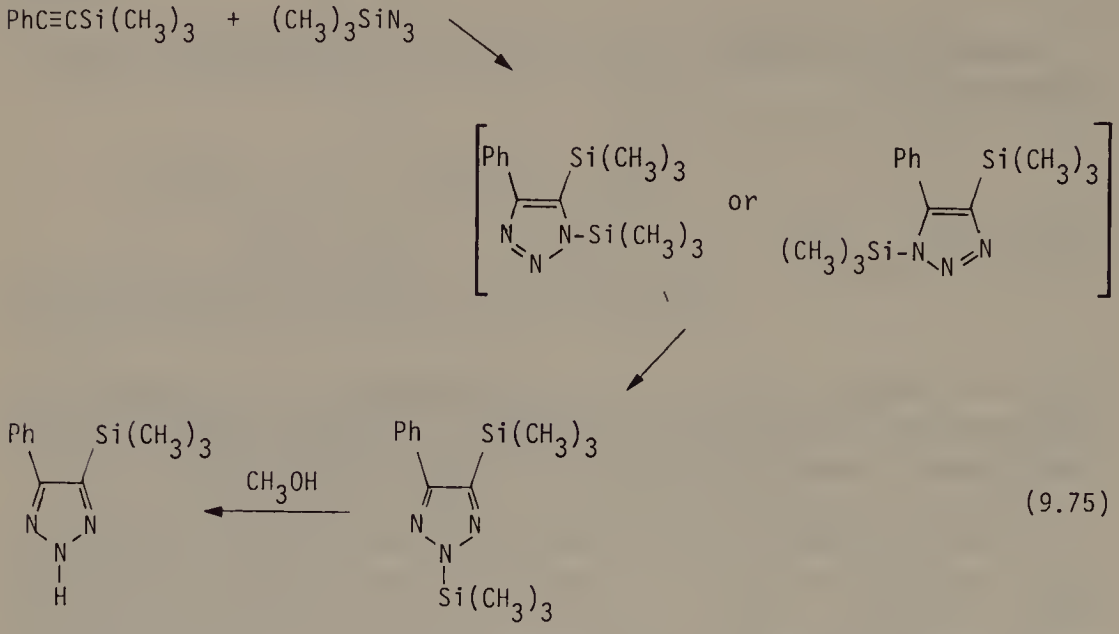
On the other hand, reaction of diazomethane with methyl 2-trimethylsilylacetylenecarboxylate yields a mixture of 3- and 4-trimethylsilylpyrazole isomers. Similarly, a mixture of 3- and 4-trimethylsilylpyrazoles was obtained with 3-trimethylsilylpropynal [92]. Reaction of methyl 2-trimethylsilylacetylenecarboxylate with dimethyldiazomethane yields 5,5-dimethyl-3-trimethylsilyl-4-carbomethoxypyrazole, which loses nitrogen on photolysis to give 3,3-dimethyl-1-trimethylsilyl-2-carbomethoxycyclopropene [92].

The inverse reaction of *bis*(trimethylsilyl)diazomethane with dimethyl acetylenedicarboxylate initially yields dimethyl 5,5-*bis*(trimethylsilyl)-3,4-pyrazoledicarboxylate. Migration of a trimethylsilyl group from carbon to nitrogen results in the formation of either dimethyl 1,3-*bis*(trimethylsilyl)-4,5-pyrazoledicarboxylate or dimethyl 1,5-*bis*(trimethylsilyl)-3,4-pyrazoledicarboxylate [93, 94]. N-Trimethylsilyl groups are easily removed by hydrolysis.



(9.74)

Silylacetylenes undergo [2 + 3] cycloaddition reactions with TMS-N_3 to yield initially 1,5 or 1,4-*bis*(trimethylsilyl)-1,2,3-triazoles which rearrange by a 1,2-shift of the trimethylsilyl group to yield 2,4-*bis*(trimethylsilyl)-1,2,3-triazoles [23, 95] (see 4.3).



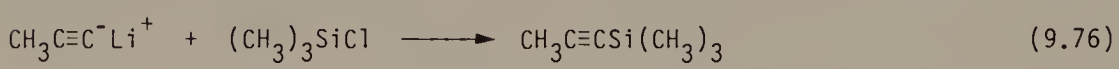
Phenyl-2-trimethylsilylacetylene reacts with phenylazide to yield 1,5-diphenyl-4-trimethylsilyl-1,2,3-triazole. This regiospecificity is opposite that observed in the reaction of phenyl azide with phenylacetylene [23].

9.6 Preparation of Silylacetylenes

Since 1-trialkylsilyl-1,2-dienes, 2,3-dienes, 1-alkynes, and 2-alkynes are versatile synthetic intermediates, a variety of methods to prepare these compounds have been developed. Certain experimental conditions, such as high temperature lead to mixtures [96, 97].

A. 1-Trialkylsilylalkynes

1-Trimethylsilylalkynes may be prepared by reaction of alkali metal acetylides with TMS-Cl [54, 98].

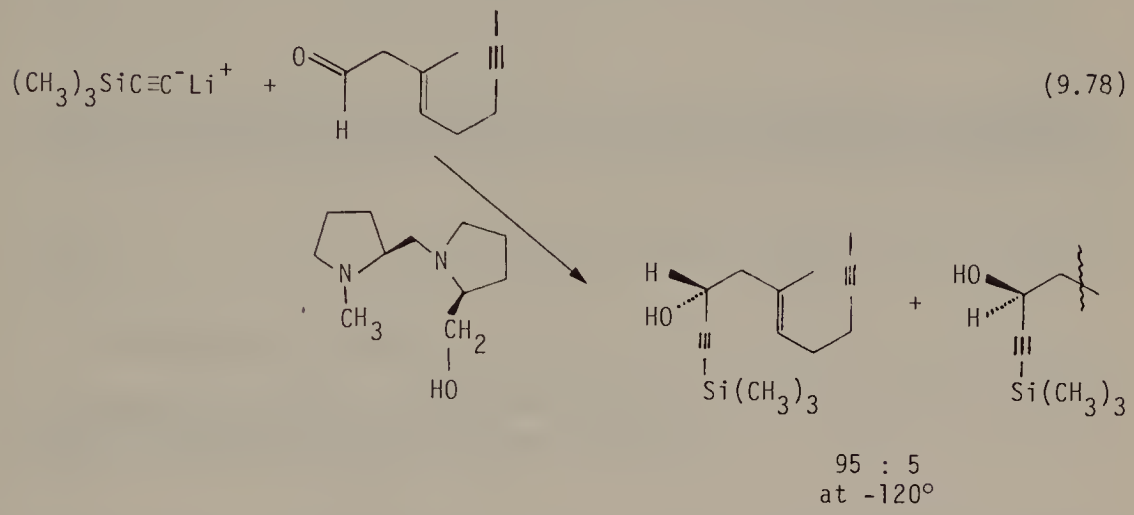


The inverse reaction of trimethylsilyl-substituted acetylide anions with primary alkyl halides, is also effective. For example, 1,4-*bis*-(trimethylsilyl)-1,3-butadiyne reacts with methyl lithium to yield 1-lithio-4-trimethylsilyl-1,3-butadiyne and tetramethylsilane. This lithium reagent reacts efficiently with primary alkyl iodides to yield 1-trimethylsilyl-1,3-alkadiynes [38, 99].

$$(CH_3)_3SiC{\equiv}C\text{-}C{\equiv}CSi(CH_3)_3 \xrightarrow{CH_3Li} (CH_3)_3SiC{\equiv}C\text{-}C{\equiv}C^-Li^+$$

$$\xrightarrow[(CH_3)_4Si]{EtI/THF\text{-}HMPT} (CH_3)_3SiC{\equiv}C\text{-}C{\equiv}C\text{-}Et \qquad (9.77)$$

1-Lithio-2-trimethylsilylacetylene reacts with ketones and aldehydes to yield 3-trimethylsilylprop-2-yn-1-ols. In the presence of the chiral chelating ligand (2S,2'S)-2-hydroxymethyl-1-[(1-methylpyrrolidin-2-yl)-methyl]pyrrolidine [100], this reaction gives propargyl alcohols of high e.e. [19, 101].



(9.78)

95 : 5
at -120°

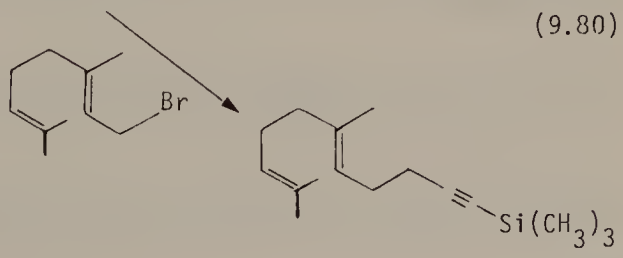
1-Alkyn-3-ols can be used to prepare 1-trimethylsilylalkynes. Deprotonation of 1-alkyn-3-ols with *n*-butyl lithium followed by addition of TMS-Cl yields after aq. work-up 1-trimethylsilylalkyn-3-ols. Treatment of these alkynols with acetic anhydride affords the corresponding propargyl acetates. These undergo S_n2 displacement with dialkyl copper lithium reagents [102, 103].

$$(CH_3)_3SiC{\equiv}C\underset{OH}{CH}\text{-}n\text{-}C_5H_{11} \xrightarrow[2)\ (CH_3)_2CuLi]{1)\ Ac_2O} (CH_3)_3SiC{\equiv}C\underset{CH_3}{CH}\text{-}n\text{-}C_5H_{11} \qquad (9.79)$$

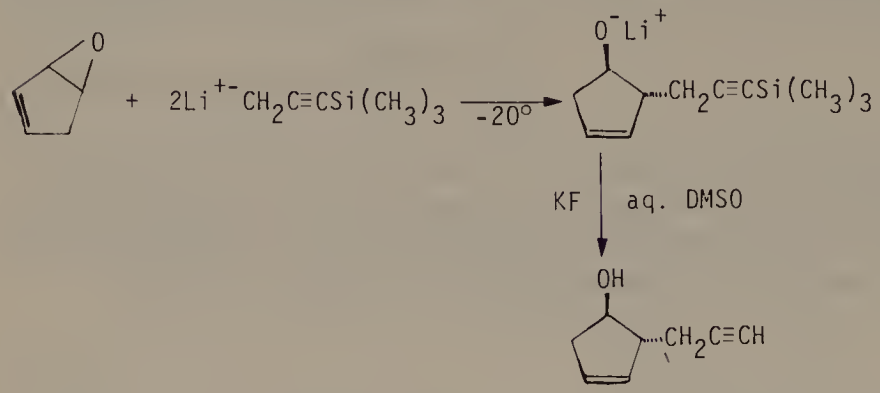
Metallation of 1-trimethylsilylpropyne with *n*-butyl lithium/TMEDA followed by addition of primary alkyl iodides or allylic bromide gives 1-trimethylsilylalkynes [54–56, 104].

$$CH_3C{\equiv}CSi(CH_3)_3 \xrightarrow[TMEDA]{n\text{-}BuLi} Li^{+-}CH_2C{\equiv}CSi(CH_3)_3$$

(9.80)

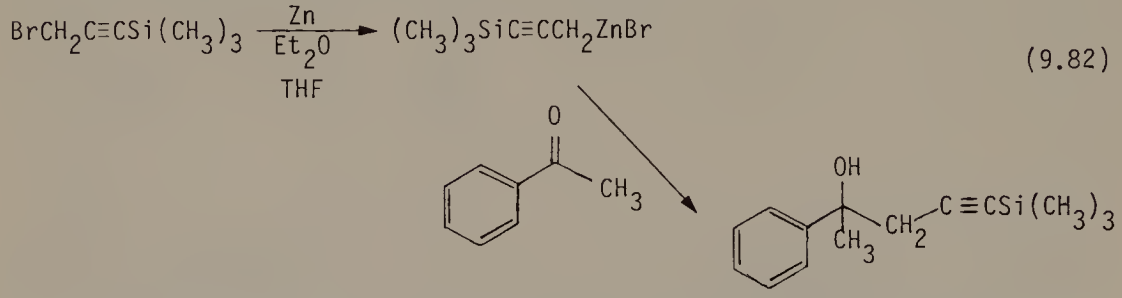


3-Lithio-1-trimethylsilylpropyne reacts with epoxides to yield 5-trimethylsilyl pent-4-yn-1-ols. The reaction of this reagent with the mono-epoxide of cyclopentadiene was utilized in a general synthesis of prostaglandins [105].



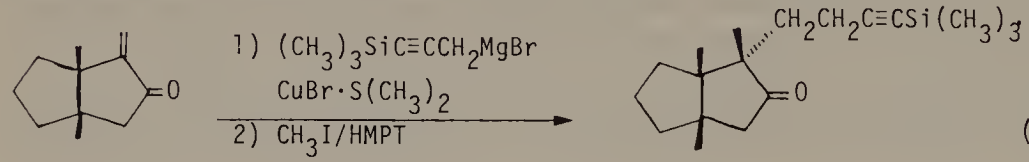
(9.81)

Ketones and aldehydes react with 1-trimethylsilylpropargylzinc bromide [22] to yield 4-trimethylsilylbut-3-yn-1-ols [106].



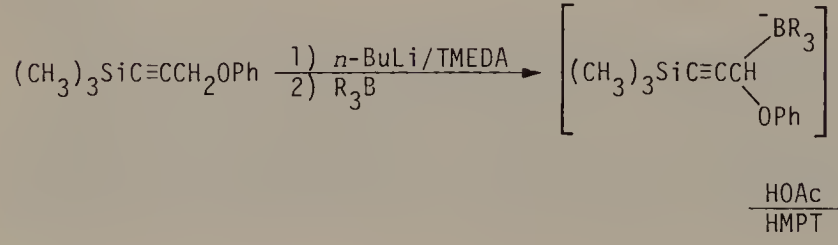
(9.82)

Cuprous bromide dimethyl sulfide complex facilitates the conjugate addition of 1-trimethylsilylpropargylmagnesium bromide to α,β-unsaturated ketones [107].



(9.83)

1-Trimethylsilylalkynes can be prepared from 3-phenoxy-1-trimethylsilylpropyne. Metallation with *n*-butyl lithium/TMEDA yields a propargyl lithium species which reacts with trialkylboranes to give propargyltrialkylborates. Treatment of these with acetic acid in HMPT yields 1-trimethylsilylalkynes. In this process, one of the alkyl groups migrates from boron to carbon [108].

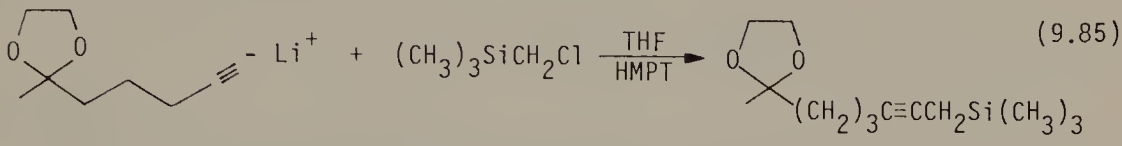


(9.84)

B. 1-Trialkylsilyl-2-alkynes

1-Trimethylsilyl-2-alkynes can be prepared by reaction of 1-bromo-2-alkynes with magnesium in ether in the presence of TMS-Cl. Isomeric allenes are found in small yield in these reactions [109].

Reaction of lithium acetylides with either trimethylsilylmethyl trifluoromethane sulfonate or chloromethyltrimethylsilane in HMPT [116] yields 1-trimethylsilyl-2-alkynes [110]. The reaction of sodium acetylides with iodomethyltrimethylsilane [17] is also effective.



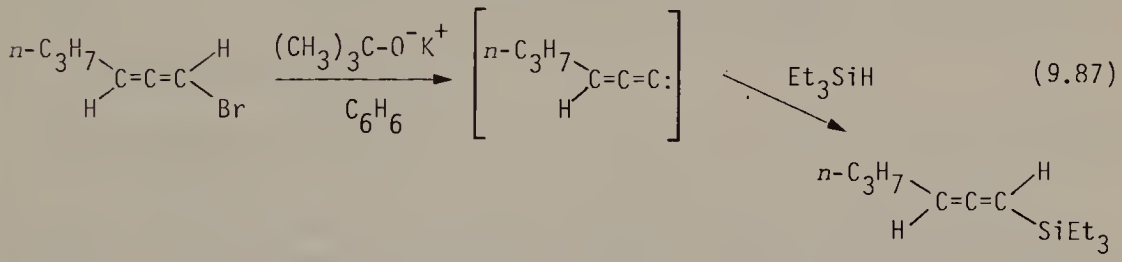
(9.85)

1,3 *bis*(Trimethylsilyl)propyne can be easily prepared by a dissolving metal reaction of ether methyl or trimethylsilyl propargyl ethers with TMS-Cl and lithium in THF [111].

(9.86)

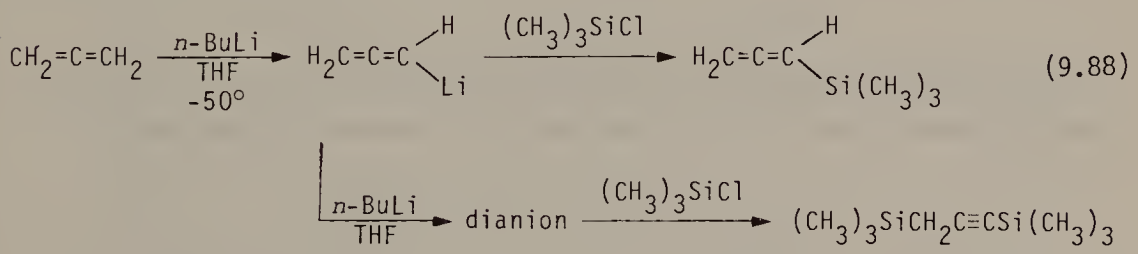
C. 1-Trialkylsilyl-1,2-dienes

1-Trialkylsilyl-1,2-dienes have been prepared by insertion of vinylidene carbenes into the Si–H bond of trialkylsilanes [96, 112].



(9.87)

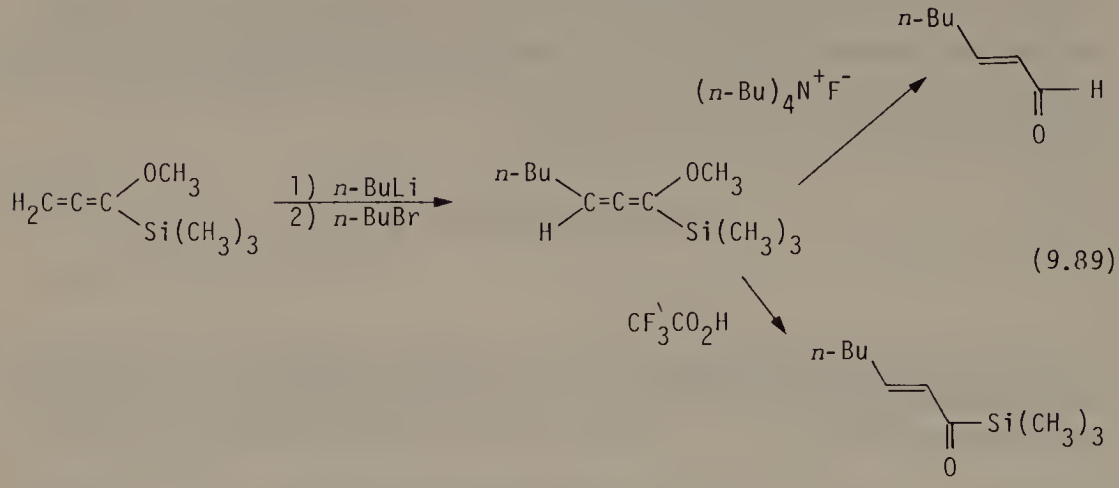
Metallation of allene with one equivalent of *n*-butyl lithium in THF at −50° yields allenyl lithium which reacts with TMS-Cl to yield trimethylsilylallene On the other hand, treatment of allene with two equivalents of *n*-butyl lithium yields a dianion which reacts with TMS-Cl to yield 1,3-*bis*-(trimethylsilyl)-propyne [113].



(9.88)

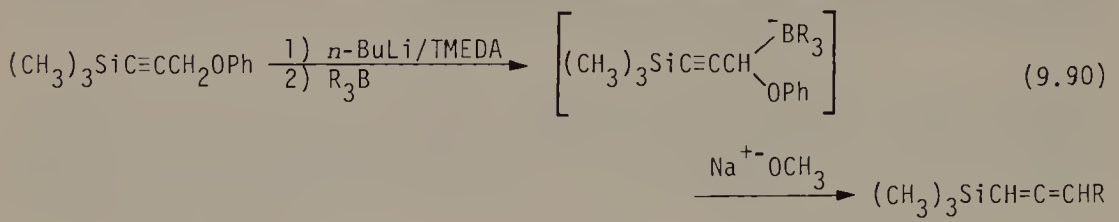
1-Methoxy-1-trimethylsilylallene can be prepared by metallation of methoxyallene with *n*-butyl lithium followed by addition of TMS-Cl. Further

metallation of 1-methoxy-1-trimethylsilylallene with *n*-butyl lithium followed by reaction with primary alkyl halides yields 1-methoxy-1-trimethylsilyl-1,2-dienes. These react with trifluroacetic acid to yield α,β-unsaturated acyltrimethylsilanes or with TBAF to give α,β-unsaturated aldehydes [114].



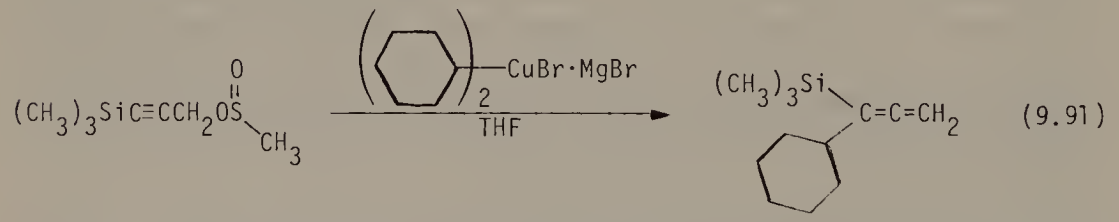
(9.89)

Metallation of 3-phenoxy-1-trimethylsilylpropyne yields a propargyl anion which reacts with trialkylboranes to yield propargyltrialkylborates. Treatment of these with sodium methoxide gives 1-trimethylsilyl-1,2-dienes in which an alkyl group has migrated from boron to carbon [115].



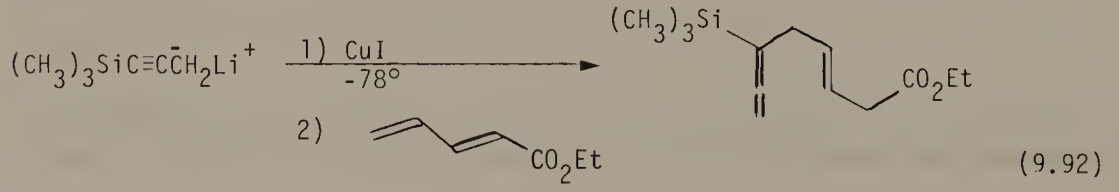
(9.90)

Treatment of the methanesulfinate esters of 1-trimethylsilylalkyn-3-ols with magnesium dialkyl cuprates in THF [46, 116] yields 1-trimethylsilyl-1,2-dienes.



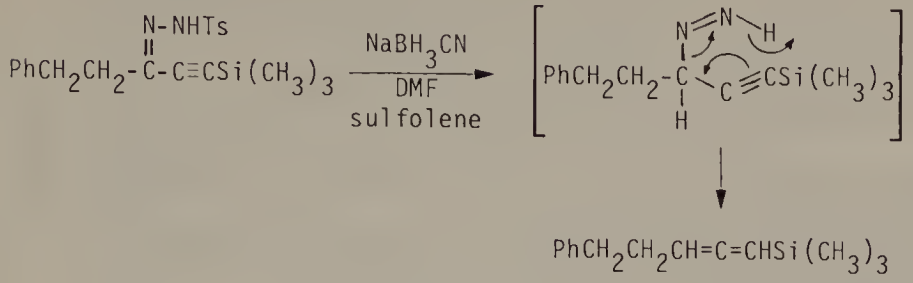
(9.91)

Conjugate 1,6-addition of 1-trimethylsilylpropargyl cuprates to alkyl 2,4-pentadienoates yields alkyl 6-trimethylsilyl-3,6,7-octatrienoates [117].



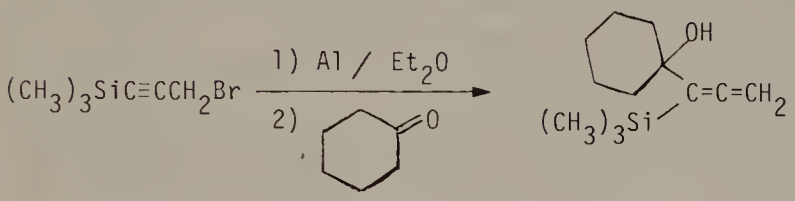
(9.92)

1-Trimethylsilyl-1,2-dienes result from treatment of the tosyl hydrazones of 3-trimethylsilyl alkynones with an excess of sodium cyanoborohydride in DMF/sulfolene [44].



(9.93)

Reaction of 3-bromo-1-trimethylsilylpropyne with aluminum yields an organometallic reagent which reacts with ketones and aldehydes to yield rearranged products: 1-(1′-hydroxyalkyl)-1-trimethylsilylallenes [106].

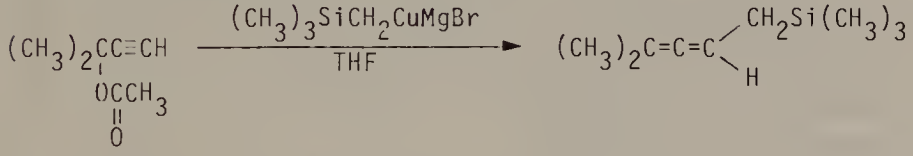


(9.94)

As previously mentioned, the corresponding zinc reagent reacts with ketones and aldehydes with no rearrangement (Eq 9.82). The reason for this difference in regiospecificity between the zinc and aluminum reagents is not clear.

D. 1-Trimethylsilyl-2,3-dienes

1-Trimethylsilyl-2,3-dienes can be prepared by reaction of trimethylsilylmethylmagnesium cuprates with propargyl acetates or tosylates [45].



(9.95)

References

1. Miller, J.B., McGarvey, G.: J. Org. Chem. *43*, 4424 (1978)
2. Birkofer, L., Kühn, T.: Chem. Ber. *111*, 3119 (1978)
3. Komarov, V.M., Yarosh, O.G.: Isv. Akad. Nauk. SSSR. Ser. Khim. 1573 (1971)
4. Yarosh, O.G., Vovenkov, V.K., Kamarov, N.V.: Izv. Akad. Nauk. SSSR Ser. Khim. 875 (1971)
5. Miller, R.B., Reichenbach, T.: Tetrahedron Lett. 543 (1974)
6. Zweifel, G., On, H.P.: Synthesis, 803 (1980)
7. Eisch, J.J., Foxton, M.W.: J. Org. Chem. *36*, 3520 (1971)
8. Uchida, K., Utimoto, K., Nozaki, H.: J. Org. Chem. *41*, 2941 (1976)
9. Hasan, I., Kishi, Y.: Tetrahedron Lett. 4229 (1980)

10. Miller, J.A., Zweifel, G.: Synthesis, 288 (1981)
11. Soto, F., Ishikawa, H., Soto, M.: Tetrahedron Lett. 85 (1981)
12. Obayashi, M., Utimoto, K., Nozaki, H.: Tetrahedron Lett. 1805 (1979)
13. Westmijze, H., Meijer, J., Vermeer, P.: Tetrahedron Lett. 1823 (1977)
14. Snider, B.B., Karras, M., Conn, R.S.E.: J. Am. Chem. Soc. *100*, 4624 (1978)
15. Flood, T., Peterson, P.E.: J. Org. Chem. *45*, 5006 (1980)
16. Bourgeois, P., Mérault, G.: J. Organometal. Chem. *39*, C44 (1972)
17. Schmid, R., Huesmann, P.L., Johnson, W.S.: J. Am. Chem. Soc. *102*, 5122 (1980)
18. Johnson, W.S., Yarnell, T.M., Myers, R.F., Morton, D.R.: Tetrahedron Lett. 2549 (1978)
19. Johnson, W.S., Frei, B., Gopalan, A.S.: J. Org. Chem. *46*, 1512 (1981)
20. Walton, D.R.M., Webb, M.J.: J. Organometal. Chem. *37*, 41 (1972)
21. Oliver, R., Walton, D.R.M.: Tetrahedron Lett. 5209 (1972)
22. Eiter, K., Lieb, F., Disselnkötter, H., Oediger, H.: Liebigs. Ann. Chem. *658*, (1978)
23. Birkofer, L., Ritter, A., Uhlenbrauck, H.: Chem. Ber. *96*, 3280 (1963)
24. Utimoto, K., Tanaka, M., Kitai, M., Nozaki, H.: Tetrahedron Lett. 2301 (1978)
25. Ladika, M., Stang, P.J.: J.C.S. Chem. Commun. 459 (1981)
26. Walton, D.R.M., Waugh, F.: J. Organometal. Chem. *37*, 45 (1972)
27. Stang, P.J., Ladika, M.: Synthesis, 29 (1981)
28. Bourgeois, P., Merault, G., Calas, R.: J. Organometal. Chem. *59*, C-4 (1973)
29. Bhattacharya, S.N., Josiah, B.M., Walton, D.R.M.: Organometal. Chem. Synthesis, *1*, 145 (1970/1971)
30. Bourgeois, P., Calas, R.: J. Organometal. Chem. *22*, 89 (1970)
31. Bourgeois, P., Mérault, G., Duffaut, N., Calas, R.: J. Organometal. Chem. *59*, 145 (1973)
32. Bourgeois, P., Mérault, G.: C.R. Acad. Sci. Paris Ser. C, *273*, 714 (1971)
33. Bourgeois, P., Calas, R., Mérault, G.: J. Organometal. Chem. *141*, 23 (1977)
34. Calas, R., Dunoguès, J., Deleris, G., Pisciotti, F.: J. Organometal. Chem. *69*, C15 (1974)
35. Deleris, G., Dunoguès, J., Calas, R.: J. Organometal. Chem. *93*, 43 (1975)
36. Deleris, G., Dunoguès, J., Calas, R.: Tetrahedron Lett. 2449 (1976)
37. Nakamura, E., Kuwajima, I.: Angew. Chem. Int. Ed. *15*, 498 (1976)
38. Holmes, A.B., Jennings-White, C.L.D., Schulthess, A.H., Akinde, B., Walton, D.R.M.: J. Chem. Soc. Chem. Commun. 840 (1979)
39. Pornet, J., Randrianoelina, B.: Tetrahedron Lett. 1327 (1981)
40. Pornet, J.: Tetrahedron Lett. 453 (1981)
41. Pornet, J.: Tetrahedron Lett. 2049 (1980)
42. Pornet, J.: Tetrahedron Lett. 455 (1981)
43. Sakurai, H., Sasaki, K., Hosomi, A.: Tetrahedron Lett. 745 (1981)
44. Danheiser, R.L., Carini, D.J.: J. Org. Chem. *45*, 3925 (1980)
45. Montury, M., Psaume, B., Gore, J.: Tetrahedron Lett. 163 (1980)
46. Danheiser, R.L., Carini, D.J., Basak, A.: J. Am. Chem. Soc. *103*, 1604 (1981)
47. Jellal, A., Santelli, M.: Tetrahedron Lett. 4487 (1980)
48. Kozar, L.G., Clark, R.D., Heathcock, C.H.: J. Org. Chem. *42*, 1386 (1977)
49. Casara, P., Metcalf, B.W.: Tetrahedron Lett. 1581 (1978)
50. Despo, A.D., Chiu, S.K., Flood, T., Peterson, P.E.: J. Am. Chem. Soc. *102*, 5120 (1980)
51. Shakhovskoi, B.G., Stadnichuk, M.D., Petrov, A.A.: J. Gen. Chem. USSR, *34*, 2646 (1964)
52. Holmes, A.B. Raphel, R.A., Welland, N.K.: Tetrahedron Lett. 1539 (1976)

53. Schmidt, H.M., Arens, J.F.: Rec. Trav. Chim de bas Pays, *86*, 1138 (1967)
54. Corey, E.J., Kirst, H.A.: Tetrahedron Lett. 5041 (1968)
55. Corey, E.J., Katzenellenbogen, J.A., Gilman, N.W., Roman, S.A., Erickson, B.W.: J. Am. Chem. Soc. *90*, 5618 (1968)
56. Corey, E.J., Kirst, H.A., Katzenellenbogen, J.A.: J. Am. Chem. Soc. *92*, 6314 (1970)
57. Eaborn, C., Thompson, A.R., Walton, D.R.M.: J. Chem. Soc. *C*, 1364 (1967)
58. Metcalf, B.W., Jund, K.: Tetrahedron Lett. 3689 (1977)
59. Metcalf, B.W., Casara, P.: Tetrahedron Lett. 3337 (1975)
60. Gilman, H., Brook, A.G., Miller, L.S.: J. Am. Chem. Soc. *75*, 4531 (1953)
61. Eaborn, C., Walton, D.R.M.: J. Organometal. Chem. *4*, 217 (1965)
62. Eaborn, C., Thompson, A.R., Walton, D.R.M.: J. Organometal. Chem. *17*, 149 (1969)
63. Newman, H.: J. Org. Chem. *38*, 2254 (1973)
64. Hay, A.S.: J. Org. Chem. *27*, 3320 (1962)
65. Eastmond, R., Walton, D.R.M.: J. Chem. Soc., Chem. Commun. 204 (1968)
66. Eastmond, R., Johnson, T.R., Walton, D.R.M.: J. Organometal. Chem. *50*, 87 (1973)
67. McQuilkin, R.M., Garrett, P.J., Sondheimer, F.: J. Am. Chem. Soc. *92*, 6682 (1970)
68. Eglinton, G., McCrae, W.: Adv. Org. Chem. *4*, 225 (1963)
69. Eaborn, C., Thompson, A.R., Walton, D.R.M.: J. Chem. Soc. *B*, 357 (1970)
70. Ghose, B.N., Walton, D.R.M.: Synthesis, 890 (1974)
71. Takahashi, S., Kuroyama, Y., Sonogashira, K., Hagihara, N.: Synthesis, 627 (1980)
72. Mitchell, R.H., Sondheimer, F.: Tetrahedron, *26*, 2141 (1970)
73. Seyferth, D., Sarafidis, C., Evnin, A.B.: J. Organometal. Chem. *2*, 417 (1964)
74. Seyferth, D., White, D.L.: J. Organometal. Chem. *34*, 119 (1972)
75. Birkofer, L., Stilke, R.: J. Organometal. Chem. *74*, C-1 (1974)
76. Kloek, J.A.: J. Org. Chem. *46*, 1951 (1981)
77. Shchukovskaya, L.L., Budakova, L.D., Pal'chik, R.I.: Zhur. Obsh. Khim. *43*, 1989 (1973)
78. Himbert, G.: Angew. Chem. *88*, 59 (1976)
79. Henn, L., Himbert, G.: Chem. Ber. *114*, 1015 (1981)
80. Sato, Y., Kobayashi, Y., Sugiura, M., Shirai, H.: J. Org. Chem. *43*, 199 (1978)
81. Hübel, W., Hoogzand, C.: Chem. Ber. *93*, 103 (1960)
82. Greenfield, H., Sternberg, H.W., Friedel, R.A., Wotiz, J.H., Markby, R., Wender, I.: J. Am. Chem. Soc. *78*, 120 (1965)
83. Hillard, III, R.L., Vollhardt, K.P.C.: Angew. Chem. Int. Ed. *14*, 712 (1975)
84. Aalbersberg, W.G.L., Barkovich, A.J., Funk, R.L., Hillard, III, R.L., Vollhardt, K.P.C.: J. Am. Chem. Soc. *97*, 5600 (1975)
85. Hillard, III, R.L., Vollhardt, K.P.C.: Angew. Chem. Int. Ed. *16*, 399 (1977)
86. Funk, R.L., Vollhardt, K.P.C.: J. Am. Chem. Soc. *99*, 5483 (1977)
87. Funk, R.L., Vollhardt, K.P.C.: J. Chem. Soc. Chem. Commun. 833 (1976)
88. Birkofer, L., Eichstädt, D.: J. Organometal. Chem. *145*, C29 (1978)
89. Birkofer, L., Stilke, R.: Chem. Ber. *107*, 3717 (1974)
90. Birkofer, L., Franz, M.: Chem. Ber. *100*, 2681 (1967)
91. Birkofer, L., Franz, M.: Chem. Ber. *105*, 17 (1972)
92. Guillerm, G., Honoré, A.L., Veniard, L., Pourcelot, G., Benaim, J.: Bull. Soc. Chem. Fr. 2739 (1973)
93. Seyferth, D., Dows, A.W., Menzel, H., Flood, T.C.: J. Am. Chem. Soc. *90*, 1080 (1968)

94. Seyferth, D., Flood, T.C.: J. Organometal. Chem. *29*, C25 (1971)
95. Birkofer, L., Wegner, P.: Chem. Ber. *99*, 2512 (1966)
96. Patrick, T.B., Haynie, E.C., Probst, W.J.: J. Org. Chem. *37*, 1553 (1972)
97. Slutsky, J., Kwart, H.: J. Am. Chem. Soc. *95*, 8678 (1973)
98. Eaborn, C., Walton, D.R.M.: J. Organometal. Chem. *4*, 217 (1965)
99. Holmes, A.B., Jones, G.E.: Tetrahedron Lett. 3111 (1980)
100. Mukaiyama, T., Soai, K., Sato, T., Shimizu, H., Suzuki, K.: J. Am. Chem. Soc. *101*, 1455 (1979)
101. Mukaiyama, T., Suzuki, K., Soai, K., Sato, T.: Chem. Lett. 447 (1979)
102. Brinkmeyer, R.S., MacDonald, T.L.: J. Chem. Soc. Chem. Commun. 876 (1978)
103. MacDonald, T.L., Reagan, D.R., Brinkmeyer, R.S.: J. Org. Chem. *45*, 4740 (1980)
104. Ireland, R.E., Dawson, M.I., Lipinski, C.A.: Tetrahedron Lett. 2247 (1970)
105. Stork, G., Kowalski, C., Garcia, G.: J. Am. Chem. Soc. *97*, 3258 (1975)
106. Daniels, R.G., Paquette, L.A.: Tetrahedron Lett. 1579 (1981)
107. Han, Y.K., Paquette, L.A.: J. Org. Chem. *44*, 3731 (1979)
108. Yogo, T., Koshino, J., Suzuki, A.: Syn. Commun. *9*, 809 (1979)
109. Masson, J.C., Quan, M.L., Cadiot, P.: Bull. Soc. Chim. Fr. 777 (1967)
110. Chiu, S.K., Peterson, P.E.: Tetrahedron Lett. 4047 (1980)
111. Laguerre, M., Dunoguès, J., Calas, R.: J. Organometal. Chem. *145*, C34 (1978)
112. Beard, C.D., Craig, J.C.: J. Am. Chem. Soc. *96*, 7950 (1974)
113. Jaffe, F.: J. Organometal. Chem. *23*, 53 (1970)
114. Clinet, J.C., Linstrumelle, G.: Tetrahedron Lett. 3987 (1980)
115. Yogo, T., Koshino, J., Suzuki, A.: Tetrahedron Lett. 1781 (1979)
116. Westmijze, H., Vermeer, P.: Synthesis, 390 (1979)
117. Ganem, B.: Tetrahedron Lett. 4467 (1974)

10 Tetraalkylsilanes, Alkylpentafluorosilicates and Alkenylpentafluorosilicates

10.1 Introduction

This chapter is concerned with the synthetically useful chemistry of tetraalkylsilanes and dipotassium alkyl-and alkenylpentafluorosilicates.

10.2 Electrophilic Cleavage of Tetraalkylsilanes

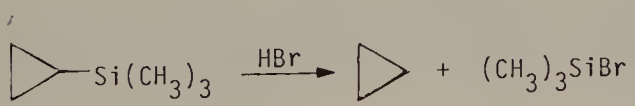
Like vinyl silanes many reactions of tetraalkylsilanes involve electrophilic cleavage of C–Si bonds.

A. Protic Acids

Reaction of chloromethyltrimethylsilane with sulfuric acid yields methane and chloromethyldimethylsilyl sulfate [1]. Similar reactions with 4-trimethylsilyl-2-butanone and 3-trimethylsilylpropionic acid yield methane and the corresponding silyl sulfate [2, 3].

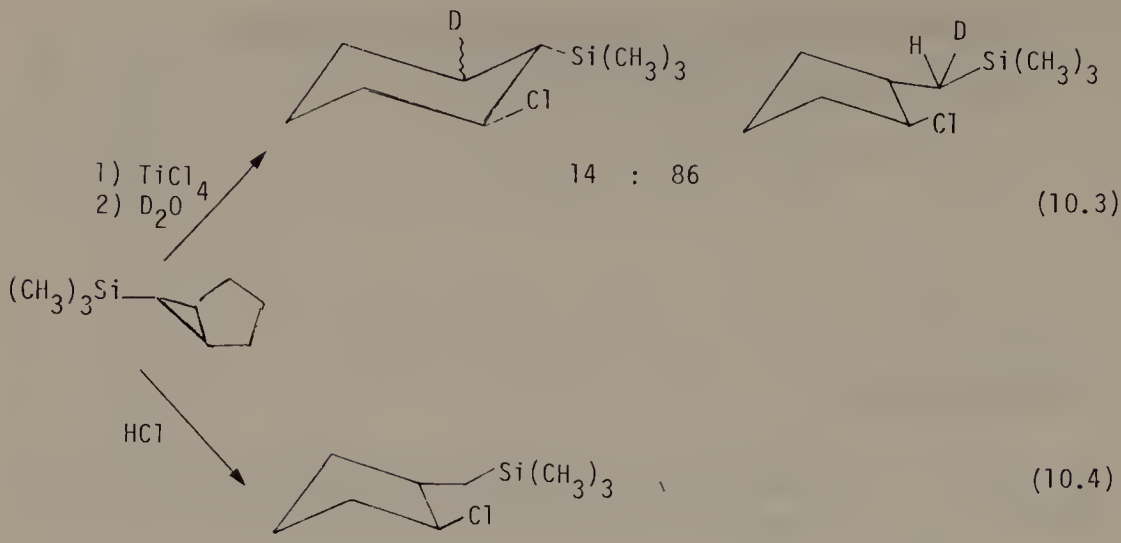
$$(CH_3)_3SiCH_2CH_2CO_2H \xrightarrow{H_2SO_4} CH_4 + HO\text{-}\overset{\overset{O}{\|}}{\underset{\underset{O}{\|}}{S}}\text{-}O\text{-}\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{Si}}\text{-}CH_2CH_2CO_2H \qquad (10.1)$$

Cyclopropyltrimethylsilane reacts with HBr or sulfuric acid to yield cyclopropane [4].



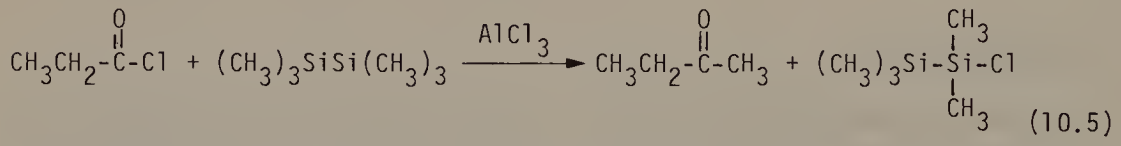
$$+ (CH_3)_3SiBr \qquad (10.2)$$

However, reaction of substituted cyclopropyltrimethylsilanes with HCl or $TiCl_4$ results in cleavage of a C–C bond of the cyclopropane rather a C–Si bond. The ratio of electrophilic cleavage of C–C bonds adjacent to the trimethylsilyl group compared to scission of the remote C–C bond of the cyclopropane varies with structure of the substrate and the electrophile [5].

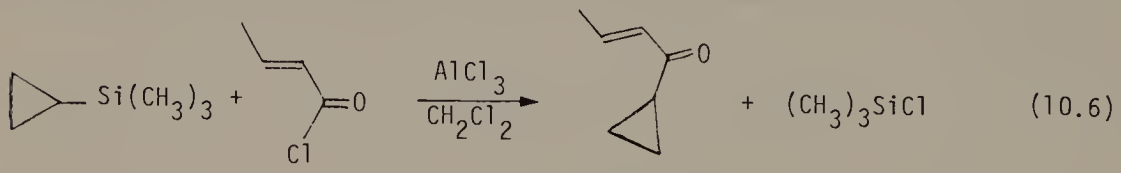


B. Acylium Ions

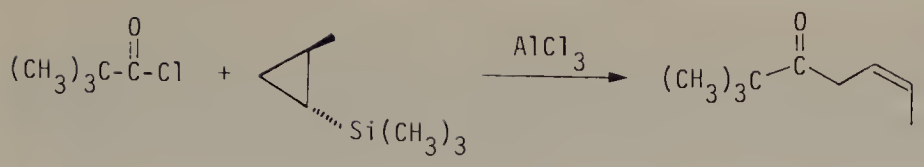
Acylium ions formed by reaction of acid chlorides and $AlCl_3$ cleave terminal C–Si bonds of octamethyltrisilane and hexamethyldisilane to yield methyl ketones and 1,3-dichlorohexamethyltrisilane [6] and pentamethylchlorodisilane [7] respectively.



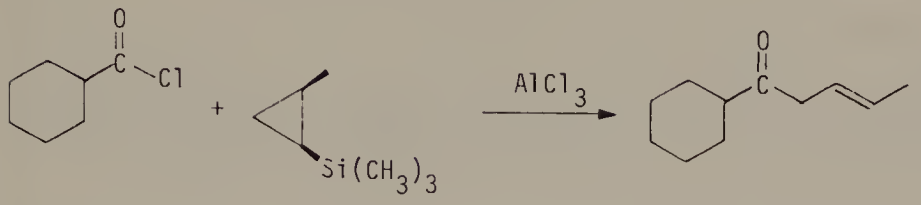
This reaction was probably not widely appreciated due to the necessity to prepare either octamethyltrisilane or hexamethyldisilane. Recently, electrophilic cleavage of tetraalkylsilanes by acylium ions has been utilized in two related ketone syntheses [8, 9]. Unfortunately, only one of the four C–Si bonds of tetraalkylsilanes undergoes electrophilic cleavage by acylium ions [9]. Cyclopropyl alkyl ketones are efficiently prepared since the cyclopropyl group is selectively cleaved from cyclopropyltrimethylsilane [8]. The π-character of the cyclopropyl group may increase its susceptibility to electrophilic attack.



On the other hand, 2-methylcyclopropyltrimethylsilane reacts with acid chlorides and $AlCl_3$ via opening of the cyclopropyl ring and loss of the trimethylsilyl group to yield 2-butenyl ketones [10]. The reaction is stereospecific: *cis*-2-methylcyclopropyltrimethylsilane yields *E*-2-butenyl ketones while the *trans* isomer gives *Z*-2-butenyl ketones.

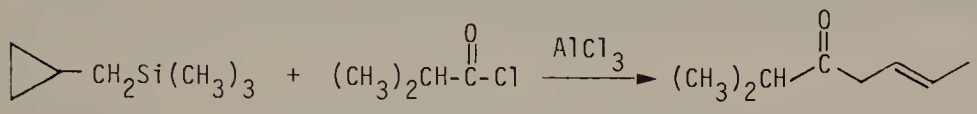


(10.7)



(10.8)

Likewise, cyclopropylmethyltrimethylsilane reacts with aliphatic acid chlorides and $AlCl_3$ with cleavage of the cyclopropyl ring and loss of the trimethylsilyl group to yield β,γ-unsaturated ketones [11].



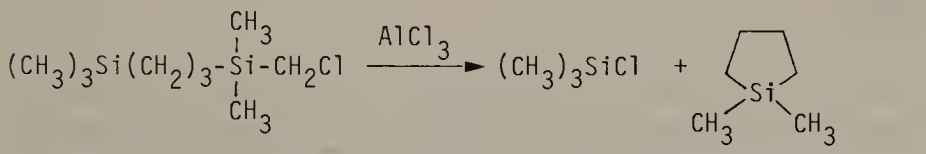
(10.9)

C. Carbocations

Carbocations also cleave C–Si bonds. Thus 3-bromopropyltrimethylsilane and a catalytic amount of $AlCl_3$ undergoes an intramolecular reaction to yield TMS-Br and cyclopropane [12].

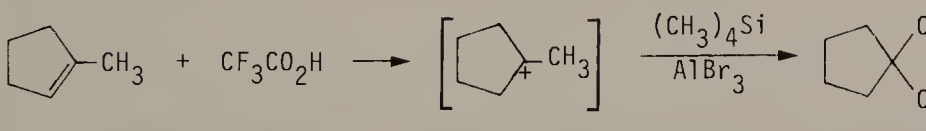
(10.10)

A related intramolecular electrophilic cleavage reaction provides a reasonable synthesis of 1,1-dimethylsilacyclopentane [13].



(10.11)

Recently, intermolecular examples of carbocation cleavage of sp^3 hybridized C–Si bonds have been observed. Protonation of tri- and tetra-substituted alkenes by trifluoroacetic acid yields tertiary carbocations. Tetramethylsilane reacts with these to transfer a methyl group from silicon to the tertiary carbocation centers [14].



(10.12)

D. Halogens

Tetraalkylsilanes undergo reaction with iodine catalyzed by aluminium iodide to yield trialkyliodosilanes and alkyl iodides [15]. Cyclopropyltrimethylsilane reacts with iodine monochloride to give cyclopropyl iodide and TMS-Cl [16].

(10.13)

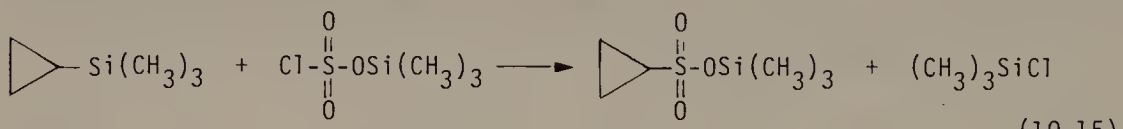
On the other hand, cyclopropyltrimethylsilane reacts with bromine with or without assistance from aluminium bromide to yield a mixture of products resulting from scission of C−C bonds of the cyclopropane ring [16].

E. Trimethylsilyl Chlorosulfonate

Tetraalkylsilanes react with trimethylsilyl chlorosulfonate to yield trimethylsilyl alkylsulfonates and trialkylchlorosilanes [17].

(10.14)

Cyclopropyltrimethylsilane is cleaved by trimethylsilyl chlorosulfonate to yield trimethylsilyl cyclopropylsulfonate and TMS-Cl [18].



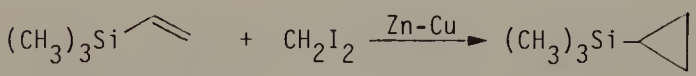
(10.15)

By contrast, 2-methylcyclopropyltrimethylsilane reacts with trimethylsilyl chlorosulfonate to yield trimethylsilyl 2-butenylsulfonate [10].

10.3 Preparation

Excellent methods exist to prepare alkyl silanes. Hydrosilation of alkenes can be carried out by a free radical chain process or by catalysis with chloroplatinic acid [19]. This latter method is generally regiospecific. For example, reaction of trichlorosilane with either 1- or 2-pentene catalyzed by chloroplatinic acid yields essentially pure 1-pentyltrichlorosilane [20]. This reacts with excess methyl Grignard reagent to yield *n*-pentyltrimethylsilane.

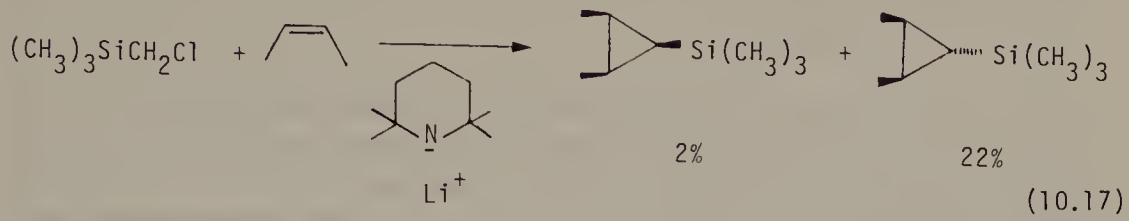
Cyclopropyltrimethylsilane is readily prepared by treatment of trimethylvinylsilane with Simmons-Smith reagent [21].



(10.16)

Alternatively, cyclopropyltrimethylsilanes may be prepared by addition of trimethylsilyl carbene to appropriate olefins.

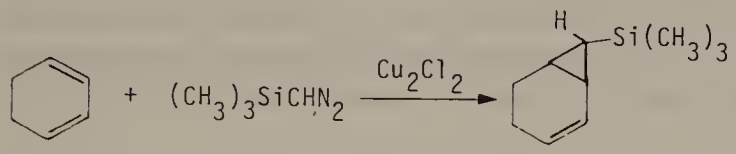
α-Elimination of lithium chloride from α-chloro-α-lithiomethyltrimethylsilane yields trimethylsilyl carbene, which reacts stereospecifically with alkenes, to give cyclopropyltrimethylsilanes [22]. Chloromethyltrimethylsilane can be deprotonated by lithium 2,2,6,6-tetramethylpiperidide to yield α-chloro-α-lithiomethyltrimethylsilane.



(10.17)

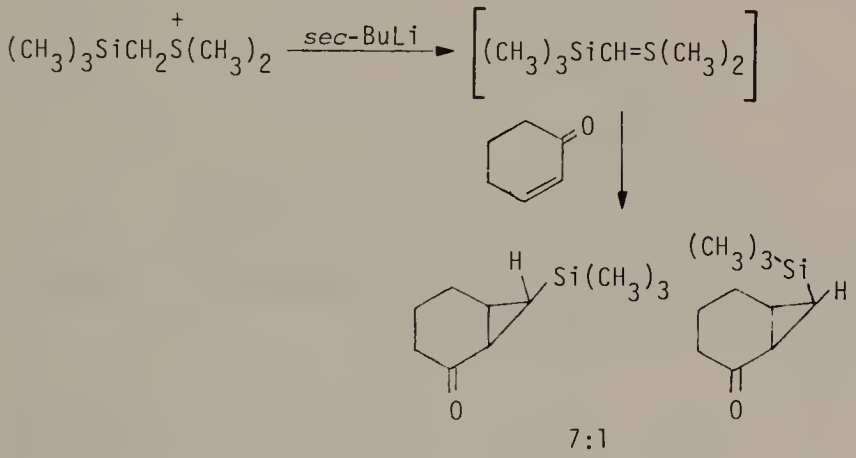
Metallation of chloromethyltrimethylsilane with *sec*-butyl lithium in TMEDA/THF does not yield trimethylsilyl carbene [23, 24].

Copper (I) catalyzed addition of trimethylsilyldiazomethane [25, 26] to olefins also yields trimethylsilylcyclopropanes [25, 27, 28].



(10.18)

The ylid, dimethyltrimethylsilylmethylene sulphurane, reacts with α,β-unsaturated ketones to give trimethylsilylcyclopropyl ketones [29].



(10.19)

10.4 Alkylpentafluorosilicates

While the C–Si bond of alkyltrichlorosilanes is not easily cleaved by electrophiles, Kumada has found that the C–Si bond of the corresponding dipotassium alkylpentafluorosilicates is [30]. These are easily prepared by reaction of alkyltrichlorosilanes with potassium fluoride. Silicon can expand its coordination number beyond four by utilization of empty 3d orbitals to coordinate ligands such as fluoride. It is reasonable that alkylpentafluoro-

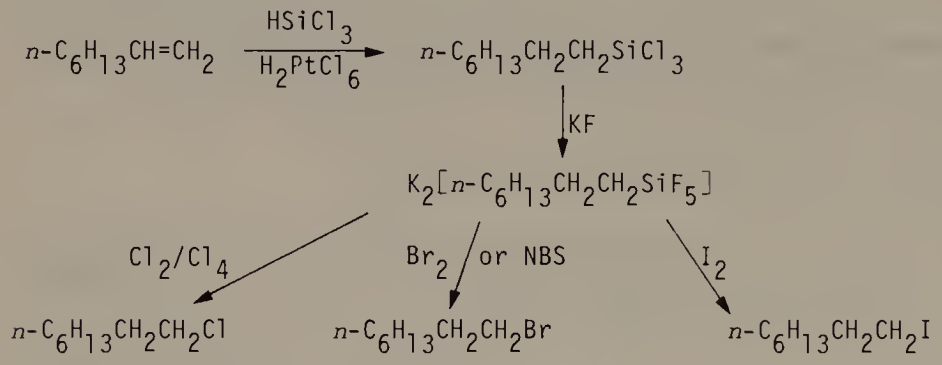
silicates which have a double negative charge should be readily attacked by electrophiles. One might, in fact, imagine that they would possess carbanionic character. However, unlike organolithium reagents or Grignard reagents, dipotassium alkylpentafluorosilicates are air stable, crystalline solids which can be isolated by filtration.

$$R\text{-}SiCl_3 \xrightarrow{\text{aq. KF}} K_2[R\text{-}SiF_5] \qquad (10.20)$$

While the water solubility of dipotassium alkylpentafluorosilicates is very limited, the solubility of ammonium alkylpentafluorosilicates is considerably greater [31, 32]. PTC by quaternary alkyl ammonium salts or crown ethers capable of chelation to potassium tions might overcome this solubility problem.

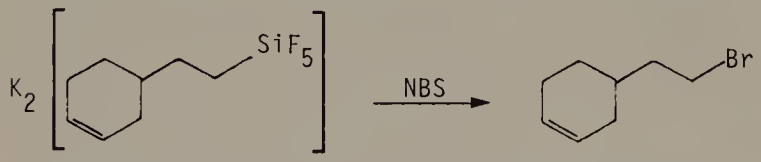
10.5 Reaction of Alkylpentafluorosilicates with Halogens

1-Alkenes have been converted to 1-haloalkanes as outlined below. This constitutes a method to add the elements of HX to an alkene in a regiospecific anti-Markovnikoff manner. Such reactions are much less efficient with secondary alkylpentafluorosilicates.



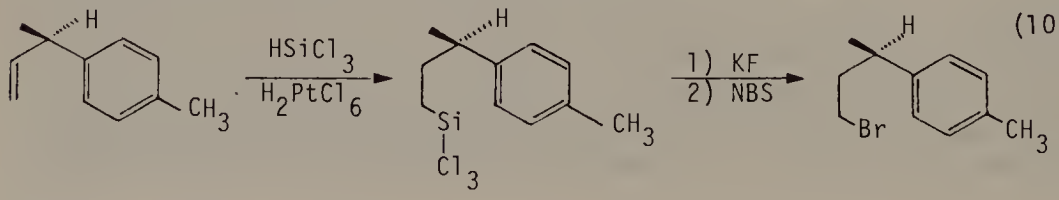
(10.21)

The reaction of alkylpentafluorosilicates with NBS to yield 1-bromo alkanes tolerates esters, as well as C–C double bonds [33].



(10.22)

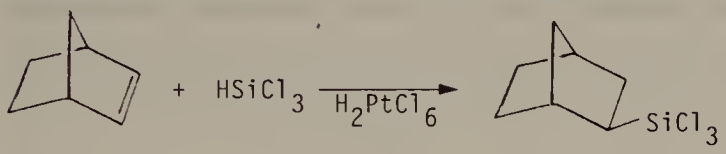
This procedure permits efficient synthesis of R-(−)-α-curcumene (Eq. 10.23) It should be noted that NBS preferentially cleaves the primary sp^3 C–Si bond rather than brominates the benzylic C–H bonds [34].



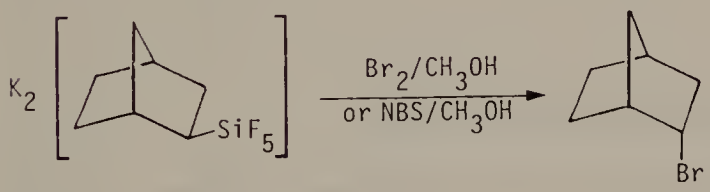
(10.23)

Alkyl pentafluorosilicates also undergo electrophilic cleavage by anhydrous cupric chloride or bromide to yield respectively alkyl chlorides or bromides. The reaction is synthetically useful with primary alkyl and arylpentafluorosilicates; but not with secondary alkylpentafluorosilicates [35]..

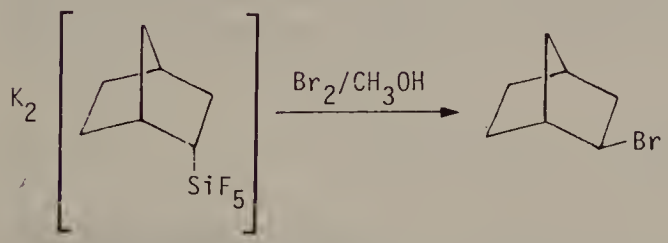
Stereochemistry has been used to probe the mechanism of these reactions. Hydrosilation of 2-norbornene with trichlorosilane catalyzed by chloroplatinic acid yields exclusively *exo*-2-trichlorosilyl norbornane (Eq. 10.24). Preparation of *endo*-2-trichlorosilyl norbornane is more complicated. A Diels-Alder reaction of vinyltrichlorosilane and cyclopentadiene yields a mixture of *exo*- and *endo*-2-trichlorosilyl-5-norbornene, which can be separated by fractional distillation. Catalytic hydrogenation of *endo*-2-trichlorosilyl-5-norbornene over Pd/C yields *endo*-2-trichlorosilylnorbornane. Both *exo* and *endo*-2-trichlorosilylnorbornane react with potassium fluoride to yield the corresponding norbornylpentafluorosilicates with retention of configuration. These react with bromine or NBS in polar solvents such as methanol or THF to yield 2-norbornyl bromides of inverted (at least 95%) stereochemistry (Eq. 10.25 and 10.26). Reaction of *exo*-2-norbornylpentafluorosilicate with cupric bromide in methanol, on the other hand, yields 2-norbornyl bromide with predominant retention of configuration [36].



(10.24)

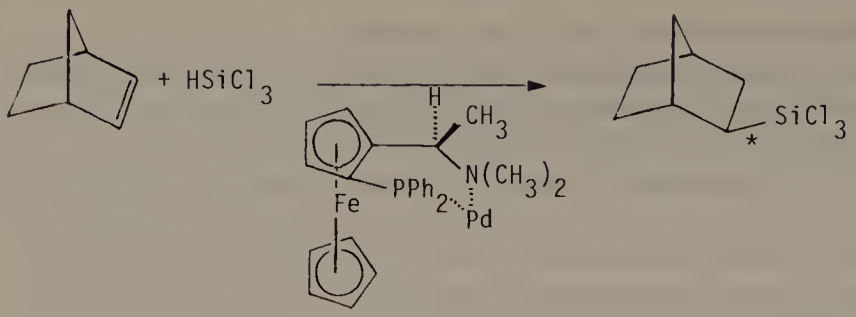


(10.25)



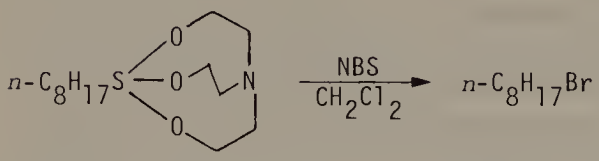
(10.26)

Asymmetric hydrosilation of prochiral olefins with trichlorosilane can be achieved by use of chiral catalysts such as menthyldiphenylphosphine, neomenthyldiphenylphosphine [37], or dichloro [(R)-N,N-dimethyl-1-(S)-2-(diphenylphosphine)ferrocenyl] ethyl amino Pd(II) [38]. Reaction of optically active *exo*-trichlorosilyl norbornane with potassium fluoride followed by NBS in methanol yields *endo*-norbornyl bromide $[\alpha]_D^{20} = -9.1{,}53\%$ e.e. [39].



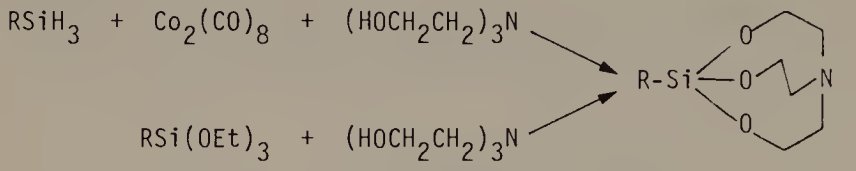
(10.27)

^{1}H and ^{29}Si NMR chemical shifts indicate that organosilatranes and alkylpentafluorosilicates both have high charge density at the silyl center. Both primary alkyl and aryl organosilatranes react with NBS to yield the corresponding bromides [40].



(10.28)

While organosilatranes are readily prepared [41, 42] (see Eq. 10.29), they should be handled with care since certain of them have high mammalian toxicity [43].



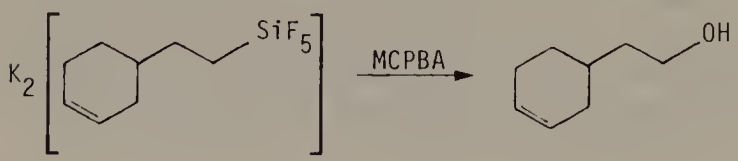
(10.29)

10.6 Reaction with *m*-Chloroperbenzoic Acid

The following sequence permits the anti-Markovnikoff addition of water to 1-alkenes. Hydrosilation of 1-alkenes with trichlorosilane regiospecifically yields 1-alkyltrichlorosilanes which react with potassium fluoride to yield 1-alkylpentafluorosilicates. These undergo oxidative cleavage by MCPBA to yield alcohols.

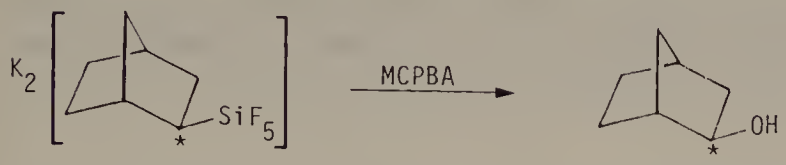
(10.30)

MCPBA reacts faster with the sp^3 hybridized C–Si bond of alkylpentafluorosilicates than with disubstituted C–C double bonds to yield epoxides [44].



(10.31)

Oxidation of optically active *exo*-2-norbornylpentafluorosilicate, gives optically *exo*-2-norboranol in 50% e.e. with retention of configuration.

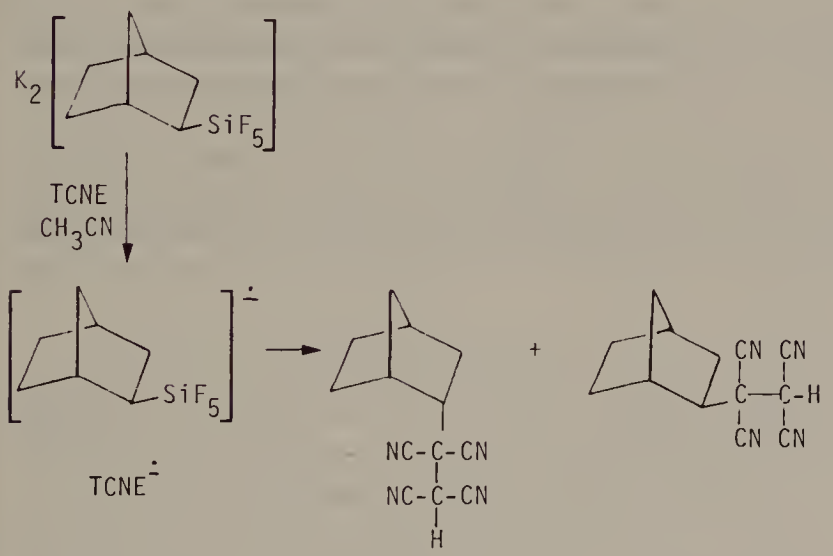


(10.32)

Primary alkyl and aryl organotriethoxysilanes and organosilatranes also undergo oxidation by MCPBA to yield primary alcohols or phenols [40].

10.7 Reaction with TCNE

Unlike the previous reactions, the reaction of alkylpentafluorosilicates with TCNE is not stereospecific. *exo*-2-Norbornylpentafluorosilicate reacts with TCNE to give a 1 : 1 ratio of *exo* and *endo* products [45]. This result has been accounted for in terms of an initial one electron transfer from the alkylpentafluorosilicate to TCNE to give an alkylpentafluorosilicate monoanion radical and the TCNE anion radical. Loss of configuration of the alkyl group in such a radical anion species is expected. In fact, on mixing *exo*-2-norbornylpentafluorosilicate and TCNE in acetonitrile at −40 °C, the ESR spectra of the TCNE anion radical can be observed.



(10.33)

10.8 Reduction

Alkylpentafluorosilicates react with protic acids to yield alkyl trifluorosilanes. On the other hand, they react with cupric fluoride dihydrate in the solid state to yield the corresponding alkanes [46].

$$K_2[n\text{-}C_{12}H_{25}SiF_5] \xrightarrow[\Delta]{CuF_2 \cdot 2H_2O} n\text{-}C_{12}H_{26} \qquad (10.34)$$

10.9 Exchange

Ammonium methylpentafluorosilicate reacts with mercuric chloride to yield methyl mercuric chloride or at higher temperatures dimethyl mercury [47, 48]. This reaction may occur by electrophilic attack of $^{+}HgCl$ on the C–Si bond of methylpentafluorosilicate.

$$HgCl_2 + (NH_4)_2[CH_3SiF_5] \xrightarrow[25°C]{H_2O} CH_3HgCl \qquad (10.35)$$

$$CH_3HgCl + (NH_4)_2[CH_3SiF_5] \xrightarrow[100°C]{H_2O} CH_3HgCH_3 \qquad (10.36)$$

Alkylpentafluorosilicates react with cuprous chloride at 250 °C to yield virtually equal amounts of the corresponding alkene and alkane. These may result from disproportionation of an alkyl copper (I) species [46].

$$K_2[CH_3O_2C(CH_2)_{10}SiF_5] \xrightarrow[250°C]{CuCl} \underset{56\%}{CH_3O_2C(CH_2)_{10}H} + \underset{44\%}{CH_3O_2C(CH_2)_8CH{=}CH_2} \qquad (10.37)$$

10.10 Alkenylpentafluorosilicates

Z or *E* alkenyltrichlorosilanes react with potassium fluoride to yield *Z* or *E* alkenylpentafluorosilicates. Hydrosilation of alkynes by trichlorosilane can be controlled to yield either *Z*-or *E*-alkenyltrichlorosilanes. Hydrosilation of terminal alkynes with trichlorosilane catalyzed by chloroplatinic acid yields *E*-1-alkenyltrichlorosilanes (Eq. 10.38). On the other hand, hydrosilation of terminal alkynes catalyzed by peroxides yields predominantly *Z*-1-alkenyltrichlorosilanes (Eq. 10.39). Finally, hydrosilation of internal alkynes with trichlorosilane catalyzed by chloroplantinic acid yields *E*-alkenyltrichlorosilanes (Eq. 10.40) [49–51].

$$CH_3CH_2CH_2C{\equiv}CH \xrightarrow[H_2PtCl_6]{HSiCl_3} \underset{100\%}{CH_3(CH_2)_2CH{=}CHSiCl_3} \qquad (10.38)$$

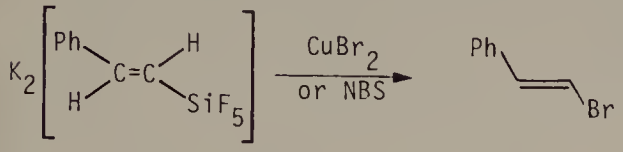
$$CH_3(CH_2)_2C{\equiv}CH \xrightarrow[\text{peroxides}]{HSiCl_3} \underset{79:21}{CH_3(CH_2)_2CH{=}CHSiCl_3 + CH_3(CH_2)_2CH{=}CHSiCl_3} \qquad (10.39)$$

$$CH_3C{\equiv}CCH_3 \xrightarrow[H_2PtCl_6]{HSiCl_3} CH_3CH{=}C(CH_3)SiCl_3 \qquad (10.40)$$

Most of the work so far has been done with *E*-1-alkenylpentafluorosilicates.

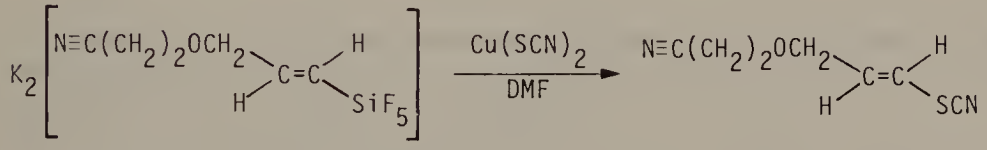
10.11 Electrophilic Cleavage of Alkenylpentafluorosilicates

E-1-alkenylpentafluorosilicates undergo electrophilic cleavage by NBS, cupric chloride or cupric bromide to yield the corresponding vinyl bromides or chlorides with retention of stereochemistry [52].



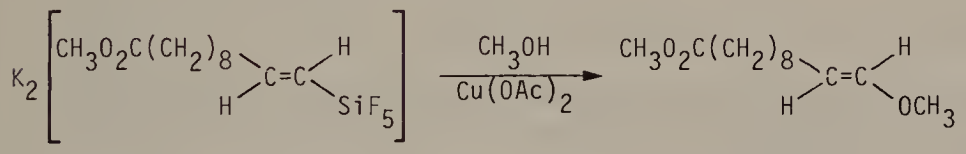
(10.41)

Alkenylpentafluorosilicates react with cupric thiocyanate to yield alkenyl thiocyanates, with retention of stereochemistry [53–56]. The reaction tolerates ether, cyano, and ester functional groups.



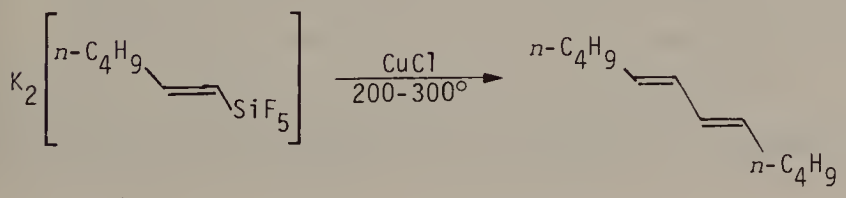
(10.42)

E-1-alkenylpentafluorosilicates are converted regio- and stereospecifically to the corresponding *E*-alkenyl ethers by treatment with a catalytic amount of cupric acetate in a primary alcohol solvent under an oxygen atmosphere. Cyano and ester functional groups are tolerated. Similarly, *E*-1-alkenyl pentafluorosilicates react with water in acetonitrile in the presence of a catalytic amount of cupric acetate to yield aldehydes [57].



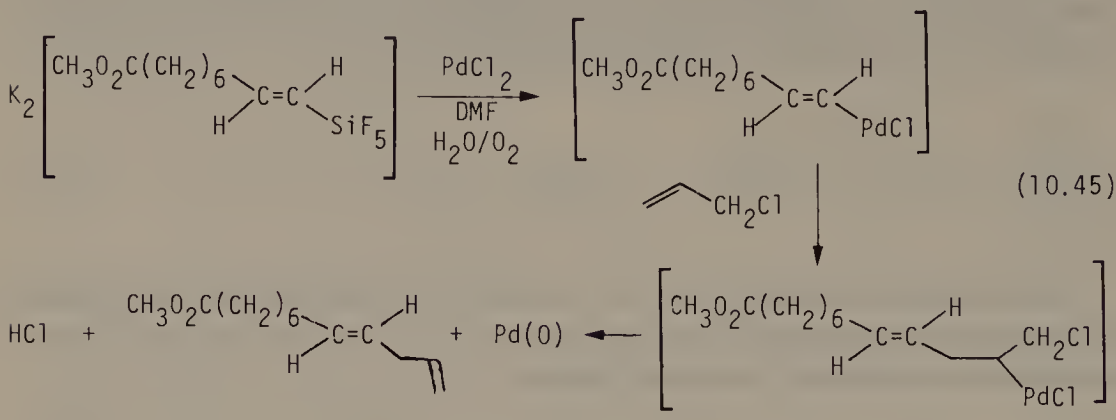
(10.43)

E-1-Alkenylpentafluorosilicates react with silver salts in homogeneous solution [31] or with cuprous chloride in the solid state [58] to yield symmetrical *E,E*-1,3-dienes. Thus, vinyl pentafluorosilicate yields 1,3-butadiene on treatment with silver fluoride. The highest yields are obtained with silver fluoride in acetonitrile or silver nitrate in water [59]. The heterogeneous reaction of *E*-1-alkenylpentafluorosilicate with cuprous chloride is carried out between 200° and 300°C under vacuum. The product, *E,E*-1,3-diene, distills out as it is formed [58]. Ether and ester functional groups are unaffected by this reaction.



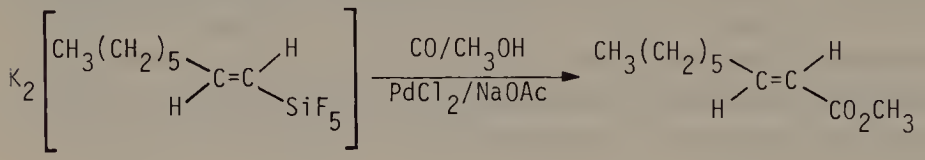
(10.44)

E-1-Alkenylpentafluorosilicates react with palladium chloride and allyl chloride to yield 1,4-dienes [60–63]. The reaction probably occurs by transfer of the *E*-1-alkenyl group from silicon to Pd(II) as outlined.



(10.45)

Likewise, *E*-1-alkenylpentafluorosilicates react with CO (1 atm) in methanol under catalysis by palladium chloride to yield methyl-*E*-α,β-unsaturated esters [64]. The reaction may be analogous to that of vinyl mercurials with CO and methanol catalyzed by Pd(II) to yield acrylate esters [65]. While the chemistry may be similar, alkenylpentafluorosilicates are less toxic than organo-mercurial compounds.



(10.46)

References

1. Sommer, L.H., Baire, W.B., Gould, J.R.: J. Am. Chem. Soc. *75*, 3765 (1953)
2. Sommer, L.H., Marans, N.S., Goldberg, G.M., Rockett, J., Pioch, R.P.: J. Am. Chem. Soc. *73*, 882 (1951)
3. Sommer, L.H., Pioch, R.P., Marans, N.S., Goldberg, G.M., Rockett, J., Kerlin, J.: J. Am. Chem. Soc. *75*, 2932 (1953)
4. Mironov, V.F., Sheladyakov, V.D., Schcherbinin, V.V., Viktorov, E.A.: Zh. Obsh. Khim. *45*, 1796 (1975)
5. Daniels, R.G., Paquette, L.A.: J. Org. Chem. *46*, 2901 (1981)
6. Sakurai, H., Tominaga, K., Watanabe, T., Kumada, M.: Tetrahedron Lett. 5493 (1966)
7. Frainnet, E., Calas, R., Gerval, P., Dentone, Y., Bonastre, J.: Bull. Soc. Chim. Fr. 1259 (1965)
8. Grignon-Dubois, M., Dunoguès, J., Calas, R.: Synthesis, 737 (1976)
9. Olah, G.A., Ho, T.L., Prakash, G.K.S., Gupta, B.G.B.: Synthesis, 677 (1977)
10. Grignon-Dubois, M., Dunoguès, J., Calas, R.: Tetrahedron Lett. 2883 (1981)
11. Grignon-Dubois, M., Dunoguès, J., Calas, R.: Can. J. Chem. *59*, 802 (1981)
12. Sommer, L.H., Van Strien, R.E., Whitmore, F.C.: J. Am. Chem. Soc. *71*, 3056 (1949)
13. Nametkin, N.S., Vdovin, V.M., Pushchevaya, K.S.: Dokl. Akad. Nauk. SSSR, *150*, 562 (1963)

14. Parnes, Z.N., Bolestova, G.I., Akhrem, I.S., Vol'pin, M.E., Kursanov, D.N.: J. Chem. Soc. Chem. Commun. 748 (1980)
15. Eaborn, C.: J. Chem. Soc. 2755 (1949)
16. Grignon-Dubois, M., Dunoguès, J., Calas, R.: J. Chem. Res. Miniprint, 379 (1979)
17. Calas, R., Bourgeois, P., Duffant, N.: C.R. Acad. Sci. Ser. C., *263*, 243 (1966)
18. Grignon-Dubois, M., Dunoguès, J., Calas, R.: Tetrahedron Lett. 1197 (1976)
19. Eaborn, C., Bott, R.W.: Synthesis and Reactions of the Silicon-Carbon Bond in "Organometallic Compounds of the Group IV Elements", Vol. 1, (MacDiarmid, A.G., Ed.), p. 213–278. New York: Marcel Dekker, 1968
20. Speier, J.L., Webster, J.A., Barnes, G.H.: J. Am. Chem. Soc. *79*, 974 (1957)
21. Seyferth, D., Cohen, H.M.: Inorg. Chem. *1*, 913 (1962)
22. Olofson, R.A., Hoskin, D.H., Lotts, K.D.: Tetrahedron Lett. 1677 (1978)
23. Burford, C., Cooke, F., Ehlinger, E., Magnus, P.: J. Am. Chem. Soc. *99*, 4536 (1977)
24. Cooke, F., Magnus, P.: J. Chem. Soc. Chem. Commun. 513 (1977)
25. Seyferth, D., Dow, A.W., Menzel, H., Flood, T.C.: J. Am. Chem. Soc. *90*, 1080 (1969)
26. Seyferth, D., Menzel, H., Dow, A.W., Flood, T.C.: J. Organometal. Chem. *44*, 279 (1972)
27. Ashe, A.J.: J. Am. Chem. Soc. *95*, 818 (1973)
28. Taylor, R.T., Paquette, L.A.: J. Org. Chem. *43*, 242 (1978)
29. Cooke, F., Magnus, P., Bundy, G.L.: J. Chem. Soc. Chem. Commun. 714 (1978)
30. Tamao, K., Yoshida, J.I., Kumada, M.: J. Syn. Org. Chem. Japan, *38*, 769 (1980)
31. Müller, R.: Organometal. Chem. Rev. *1*, 359 (1966)
32. Müller, R., Dathe, Chr.: Z. Anorg. Allg. Chem. *341*, 49 (1965)
33. Tamao, K., Yoshida, J.I., Takahashi, M., Yamamoto, H., Kakui, T., Matsumoto, H., Kurita, A., Kumada, M.: J. Am. Chem. Soc. *100*, 290 (1978)
34. Tamao, K., Hayashi, T., Matsumoto, H., Yamamoto, H., Kumada, M.: Tetrahedron Lett. 2155 (1979)
35. Yoshida, J.I., Tamao, K., Kurita, A., Kumada, M.: Tetrahedron Lett. 1809 (1978)
36. Yoshida, J.I., Tamao, K., Kumada, M., Kawamura, T.: J. Am. Chem. Soc. *102*, 3267 (1980)
37. Yamamoto, K., Kiso, Y., Ito, R., Tamao, K., Kumada, M.: J. Organometal. Chem. *210*, 9 (1981)
38. Hayashi, T., Mise, T., Fukushima, M., Kagotani, M., Nagashima, N., Hamada, Y., Matsumoto, A., Kawakami, S., Konishi, M., Yamamoto, K., Kumada, M.: Bull. Chem. Soc. Japan, *53*, 1138 (1980)
39. Hayashi, T., Tamao, K., Katsuro, Y., Nakae, I., Kumada, M.: Tetrahedron Lett. 1871 (1980)
40. Hosomi, A., Iijima, S., Sakurai, H.: Chem. Lett. 243 (1981)
41. Frye, C.L., Vogel, G.E., Hall, J.A.: J. Am. Chem. Soc. *83*, 996 (1961)
42. Voronkov, M.G.: Pure and Applied Chem. *13*, 35 (1966)
43. Voronkov, M.G., Biological Activity of Silatranes in Topics in Current Chem. Vol. 84, p. 78–88, Berlin: Springer, 1979
44. Tamao, K., Kakui, T., Kumada, M.: J. Am. Chem. Soc. *100*, 2268 (1978)
45. Yoshida, J.I., Tamao, K., Kumada, M., Kawamura, T.: J. Am. Chem. Soc. *102*, 3269 (1980)
46. Yoshida, J.I., Tamao, K., Kakui, T., Kumada, M.: Tetrahedron Lett. 1141 (1979)
47. Müller, R., Dathe, Chr.: J. Prakt. Chem. *22*, 232 (1963)
48. Müller, R., Dathe, Chr.: Chem. Ber. *98*, 235 (1965)
49. Benkeser, R.A.: Pure and Applied Chemistry, *13*, 133 (1966)
50. Benkeser, R., Cunico, R.F.: J. Organometal. Chem. *4*, 284 (1965)

51. Benkeser, R.A., Burrous, M.L., Nelson, L.E., Swisher, J.V.: J. Am. Chem. Soc. *83*, 4385 (1961)
52. Yoshida, J.I., Tamao, K., Kurita, A., Kumada, M.: Tetrahedron Lett. 1809 (1978)
53. Tamao, K., Kakui, T., Kumada, M.: Tetrahedron Lett. 111 (1980)
54. Reeves, W.P., White, M.R., Hilbrich, R.G., Biegert, L.L.: Syn. Commun. *6*, 509 (1976)
55. Liotta, C.L., Grisdale, E.E., Hopkins, H.P.: Tetrahedron Lett. 4205 (1975)
56. Guy, R.G., "The Chemistry of Cyanates and Their Thio Derivatives", (S. Patai, Ed.), Part 2, p. 819–886, New York: J. Wiley, 1977
57. Tamao, K., Kakui, T., Kumada, M.: Tetrahedron Lett. 4105 (1980)
58. Yoshida, J.I., Tamao, K., Kakui, T., Kumada, M.: Tetrahedron Lett. 1141 (1979)
59. Tamao, K., Matsumoto, M., Kakui, T., Kumada, M.: Tetrahedron Lett. 1137 (1979)
60. Yoshida, J.I., Tamao, K., Takahashi, M., Kumada, M.: Tetrahedron Lett. 2161 (1978)
61. Heck, R.F.: J. Am. Chem. Soc. *90*, 5518 (1968)
62. Heck, R.F.: J. Am. Chem. Soc. *90*, 5526 (1968)
63. Heck, R.F.: J. Am. Chem. Soc. *90*, 4431 (1968)
64. Tamao, K., Kakui, T., Kumada, M.: Tetrahedron, 619 (1979)
65. Larock, R.C.: J. Org. Chem. *40*, 3237 (1975)

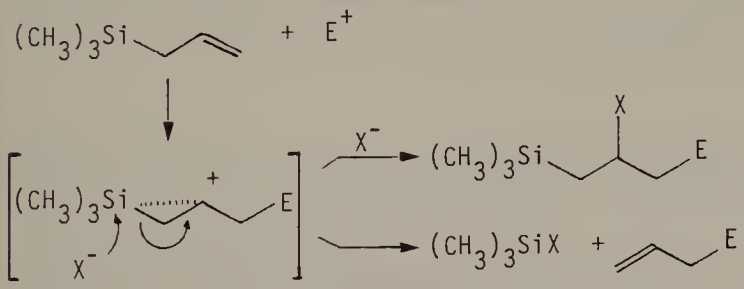
11 Allylic Silanes

11.1 Introduction

Allylic trimethylsilanes are highly versatile synthetic intermediates. We will consider five aspects of their chemistry in this chapter. First will be electrophilic substitution reactions; second, cycloaddition reactions; third, synthesis of allylic silanes; fourth, reactions of silyl substituted allylic anions, and fifth, the chemistry of boron substituted allylic silanes.

11.2 Electrophilic Substitution

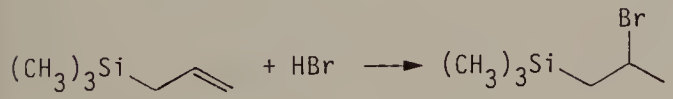
Many reactions of allylic trimethylsilanes involve electrophilic substitution with allylic rearrangement and loss of the trimethylsilyl group. These reactions often occur by addition of the electrophile to the C−C double bond to yield a carbocation which is stabilized by a β-trimethylsilyl group. Nucleophilic attack on silicon by the associated anion or solvent results in loss of the silyl group and formation of products. On the other hand, addition of the anion to the carbocation center results in electrophilic addition.



(11.1)

A. Protic Acids

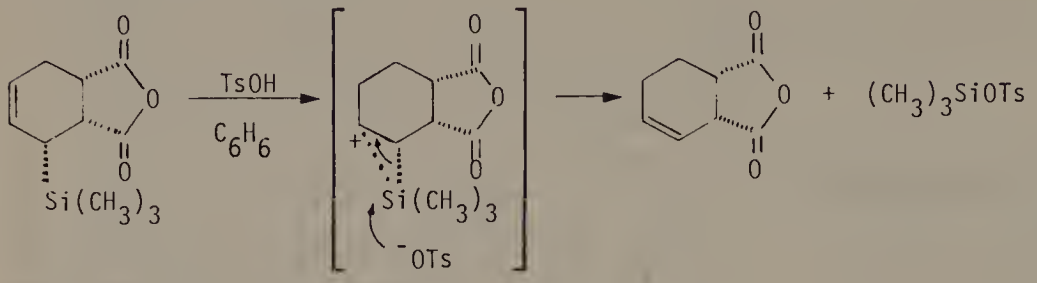
Both HBr and HI add to allyltrimethylsilane in an anti-Markovnikoff sense. On the other hand, HCl reacts with allyltrimethylsilane to yield TMS-Cl



(11.2)

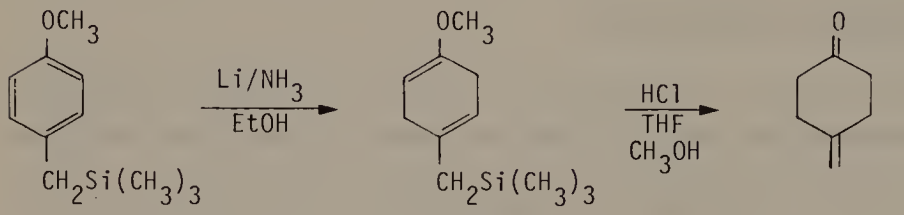
and propene. Electrophilic substitution results from attack by chloride ion at the silyl center rather than at the carbocation center [1].

In such electrophilic-substitution reactions of allylic trimethylsilanes, the position of the C–C double bond shifts. For example, treatment of the Diels-Alder adduct of 1-trimethylsilyl-1,3-butadiene and maleic anhydride with TsOH results in loss of the trimethylsilyl group and a specific 1,2-shift of the C–C double bond [2].



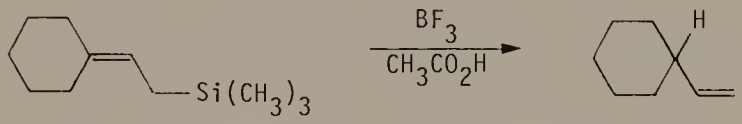
(11.3)

In a similar manner, 4-methylene cyclohexanones have been prepared by treatment of 1-methoxy-4-trimethylsilylmethyl-1,4-cyclohexadienes with HCl in THF and methanol. Protodesilylation of the allylic trimethylsilane and hydrolysis of the methyl enol ether occurs simultaneously [3].



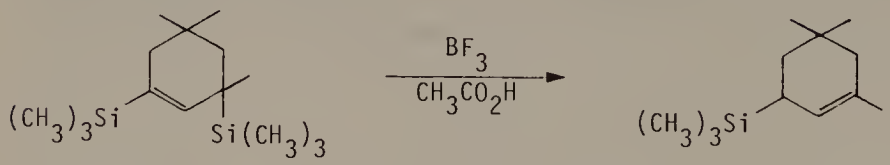
(11.4)

Protodesilylation of 2-methyl-1,4-*bis*-(trimethylsilyl)-2-butene with HCl yields 2-methyl-4-trimethylsilyl butene. This selectivity results from protonation of the C–C double bond to yield the more stable tertiary carbocation intermediate [4]. Boron trifluoride/acetic acid has proved highly effective for protodesilylation of allylic trimethysilanes [5].



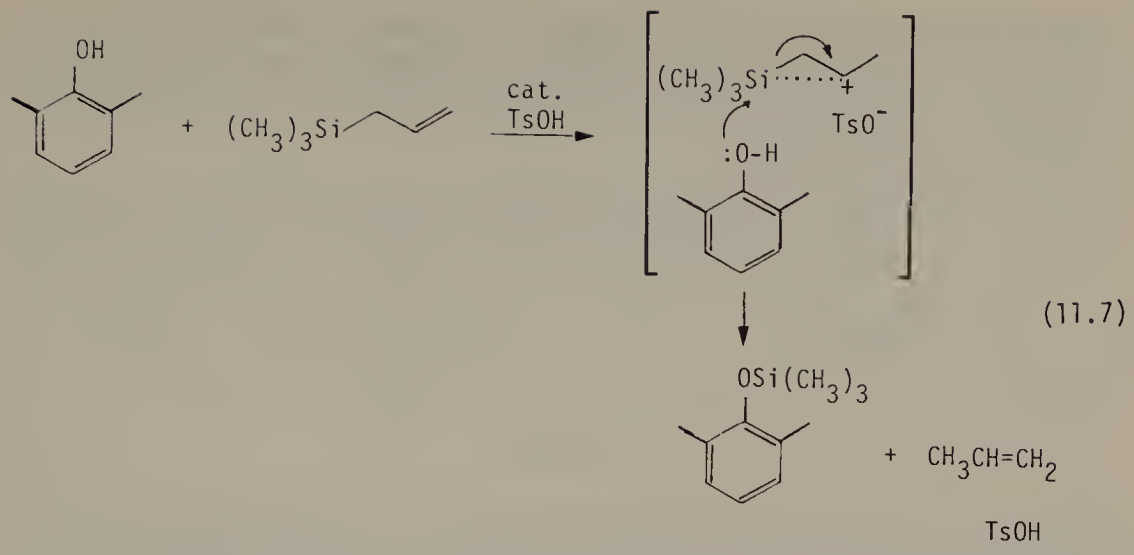
(11.5)

Protodesilylation of 1,3-*bis*-(trimethylsilyl)-1-alkenes yields allylic trimethylsilanes. This selectivity results from the preferential reaction of the allylic trimethylsilane functionality [6].



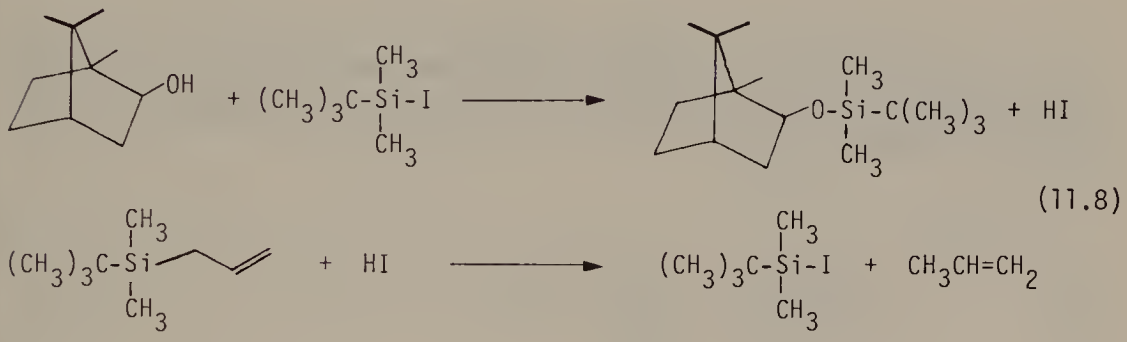
(11.6)

Allyltrimethylsilane reacts with alcohols and a catalytic amount of TsOH to yield trimethylsilyl ethers and propene as outlined [7].



(11.7)

Allyltrimethylsilane and allyl-*t*-butyldimethylsilane react with primary or secondary alcohols under catalysis by HI to yield trimethylsilyl or *t*-butyldimethylsilyl ethers, respectively. Trimethylsilyl iodide or *t*-butyldimethylsilyl iodide are intermediates [8]. This provides a method to silylate alcohols under acidic conditions.



(11.8)

B. Halogens

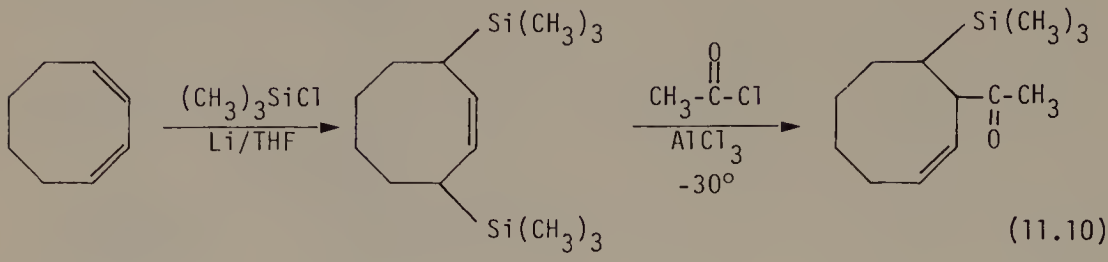
Allyltrimethylsilane reacts with bromine to yield allyl bromide and TMS-Br [1]. This reaction has been used to prepare 1-bromo-indene, a previously poorly characterized compound [9, 10]. In a similar manner, allyltrimethylsilane reacts with iodine to yield allyl iodide and TMS-I [11].

(11.9)

C. Acid Chlorides

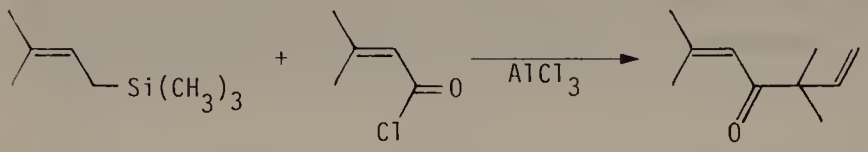
Allylic trimethylsilanes react with acid chlorides in the presence of Lewis acids to yield rearranged allylic ketones. For example, pivaloyl chloride reacts

with allyltrimethylsilane in the presence of gallium trichloride, indium trichloride or $AlCl_3$ to yield allyl *t*-butyl ketone. While 1,4-*bis*-(trimethylsilyl)-2-cyclooctene, reacts with acetyl chloride and $AlCl_3$ to yield 3-acetyl-4-trimethylsilyl cyclooctene [12].



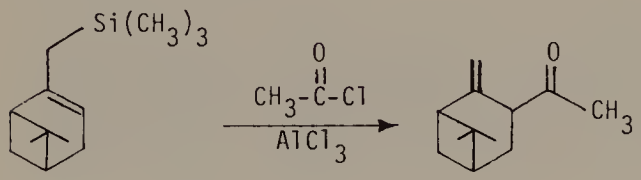
(11.10)

Reaction of γ,γ-dimethylallyltrimethylsilane with γ,γ-dimethylacryloyl chloride and $AlCl_3$ provides an efficient synthesis of L'Artemisia ketone [13].



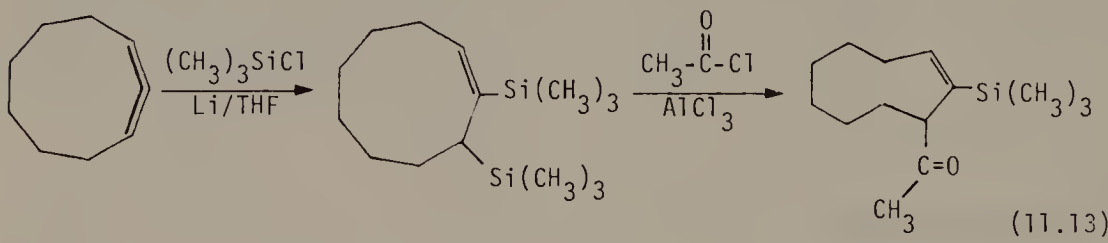
(11.11)

The observation that α-pinenyltrimethylsilane reacts with acetyl chloride in the presence of $AlCl_3$ to yield acetyl-β-pinene [14], attests to the mild reaction conditions.



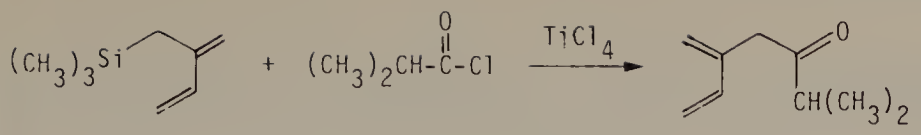
(11.12)

Similar regiospecific reactions of allylic trimethylsilanes with acid chlorides have been reported [5, 15]. 2,3-*bis*(Trimethylsilyl)cycloalkenes possess both allylic and vinylic trimethylsilane functionalities. Preferential electrophilic desilylation of the allylic trimethylsilane occurs with acetyl chloride and $AlCl_3$ [16].



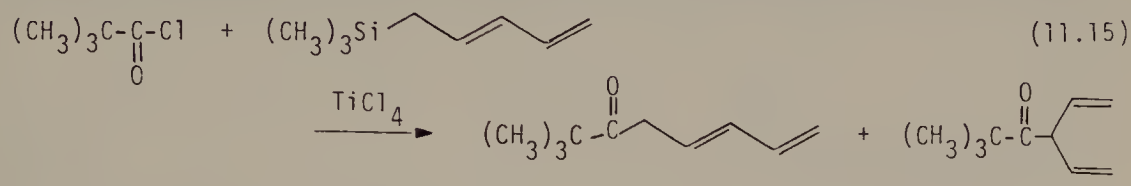
(11.13)

Reaction of 2-trimethylsilylmethyl-1,3-butadiene with acid chlorides and $TiCl_4$ yields isopropenyl ketones [17].



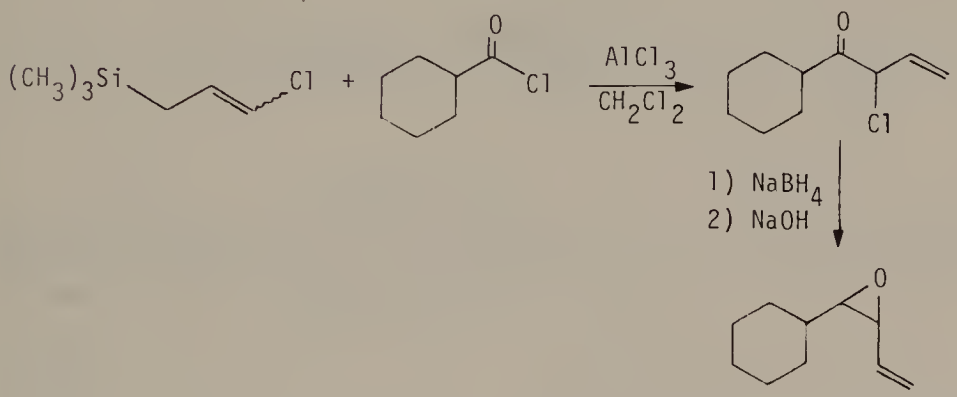
(11.14)

A similar reaction of 5-trimethylsilyl-1,3-pentadiene with pivaloyl chloride leads to a mixture of products formed by electrophilic attack by the acylium ion on both the 1 and 3 carbons of the pentadienyl system [18].



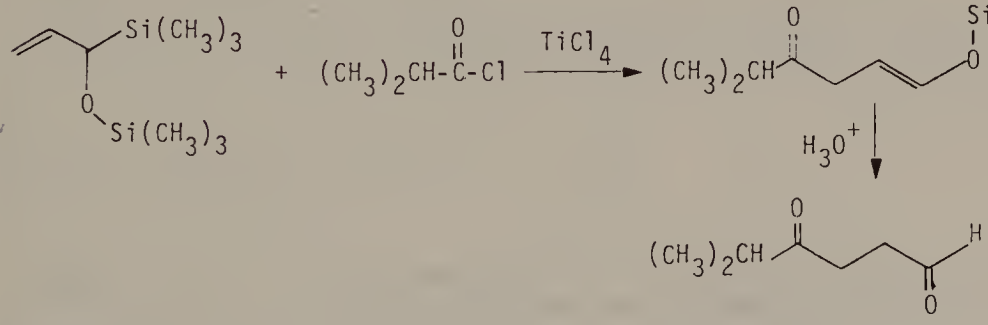
(11.15)

The reaction of 1-chloro-3-trimethylsilyl propene with acid chlorides catalyzed by $AlCl_3$ provides an efficient route to α-chloro-β,γ-unsaturated ketones. Reduction of these with $NaBH_4$ or $LiAlH_4$ followed by cyclization of the chlorohydrin product with sodium hydroxide gives vinyl substituted epoxides [19].



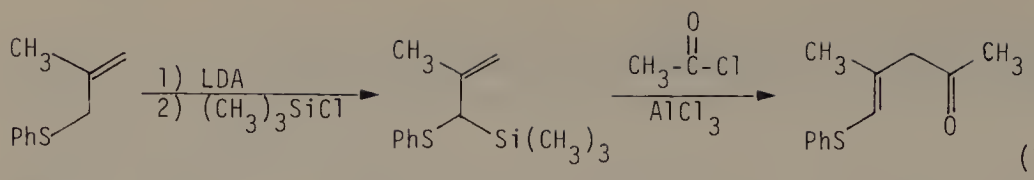
(11.16)

1-Trimethylsilyloxyallyltrimethylsilane reacts with acid chlorides under the influence of $TiCl_4$ to yield 4-keto trimethylsilyl enol ethers. These can be hydrolyzed to yield 4-keto aldehydes [20].



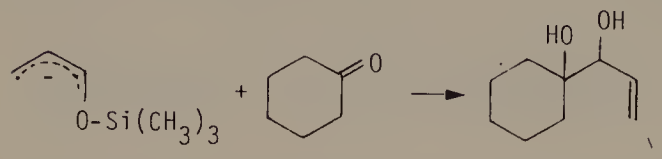
(11.17)

α-Trimethylsilylallyl phenyl sulfides undergo regiospecific acylation with acid chlorides and $AlCl_3$ to yield γ-phenylthio β,γ-unsaturated ketones [21].



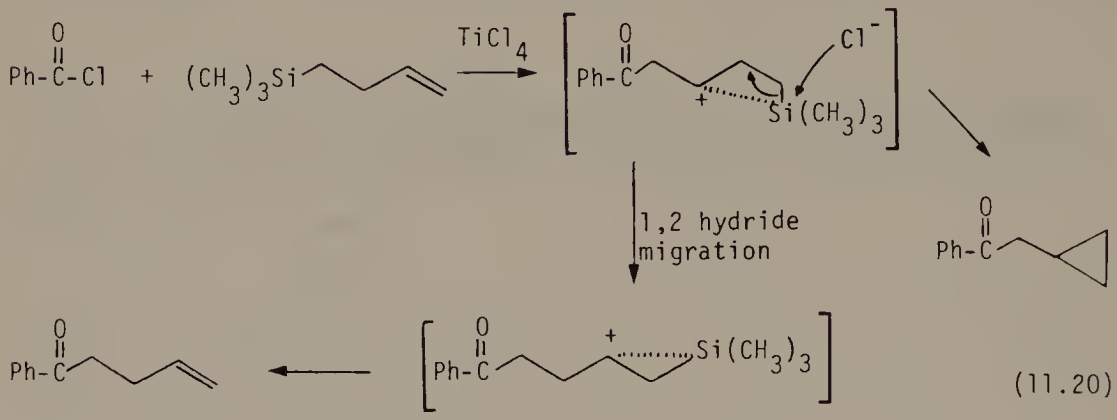
(11.18)

Metallation of allyloxytrimethylsilane yields an organo-lithium reagent which reacts regiospecifically with ketones to yield 1,2-dihydroxy-3-alkenes [22].



(11.19)

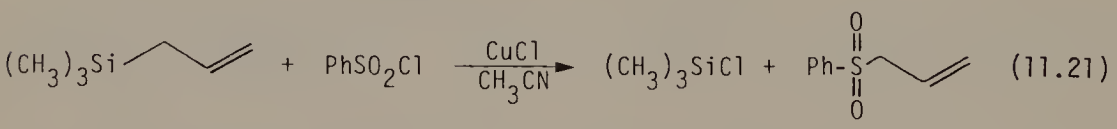
Homoallylic trimethylsilanes react with acid chlorides under the influence of $TiCl_4$ to yield mixtures of β-chloro ketones, cyclopropyl carbinyl ketones, and homoallylic ketones. The β-chloro ketones result from secondary reaction of the cyclopropyl carbinyl ketones with $TiCl_4$ [23].



(11.20)

D. Sulfonyl Chlorides

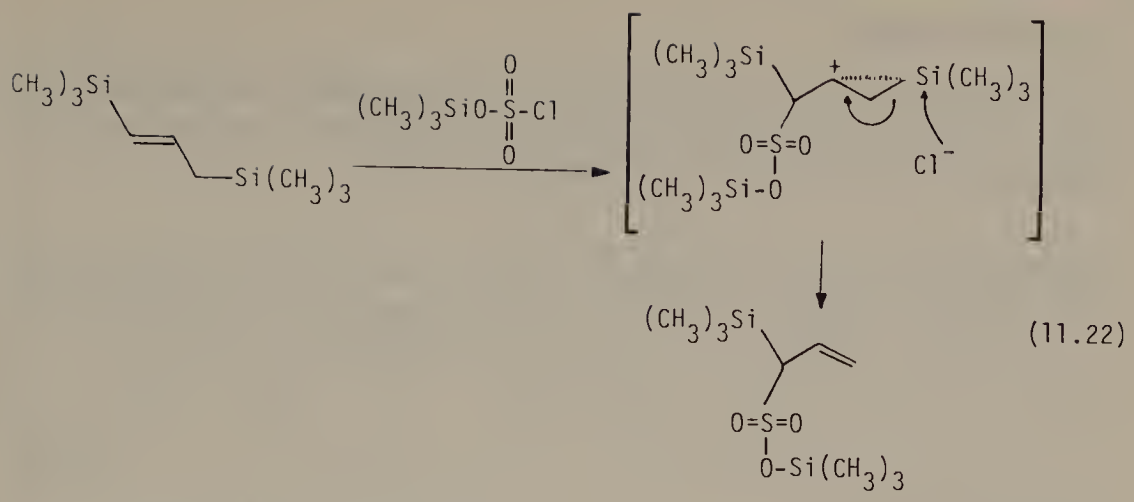
Under catalysis by cuprous chloride, allyltrimethylsilane reacts with benzene sulfonyl chloride or methane sulfonyl chloride to yield TMS-Cl and allyl phenyl sulfone or allyl methyl sulfone, respectively.



(11.21)

In a similar manner, trimethylsilyl chlorosulfonate reacts with allylic silanes to yield trimethylsilyl allylsulfonates and TMS-Cl [25].

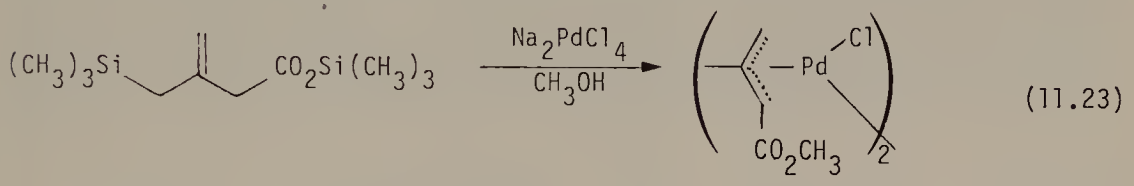
Reaction of trimethylsilyl chlorosulfonate with 1,3-*bis*-(trimethylsilyl) propene yields trimethylsilyl 1-trimethylsilylallylsulfonate. The product results from preferential electrophilic attack on the allylic silane [25].



(11.22)

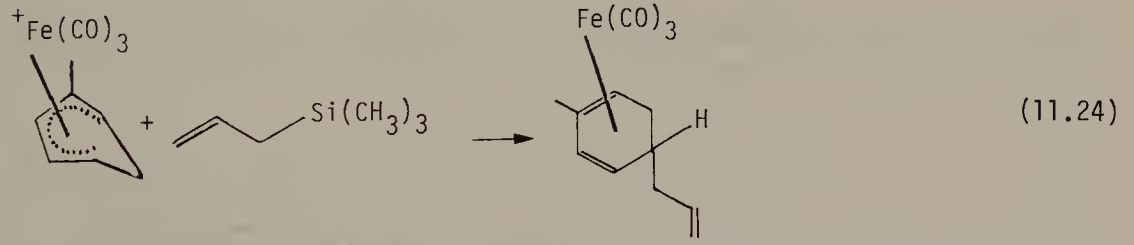
E. Transition Metal Complexes

Allylic trimethylsilanes undergo electrophilic substitution reactions with certain transition metal complexes. For example, trimethylsilyl 3-trimethylsilylmethyl-3-butenoate reacts with palladium chloride in methanol to yield the 1-carbomethoxy-2-methyl-π-allyl palladium chloride dimer [26].



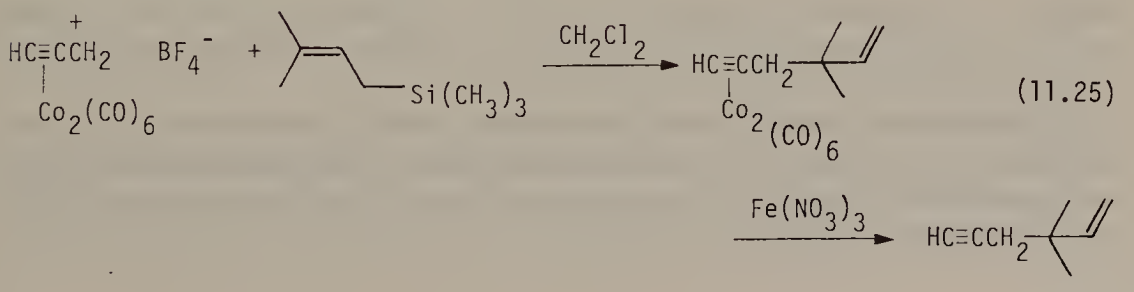
(11.23)

Cyclohexadienyl iron tricarbonyl cations react with allylic trimethylsilanes regiospecifically at the least hindered end to yield an allyl substituted cyclohexadiene iron tricarbonyl complexes [27].



(11.24)

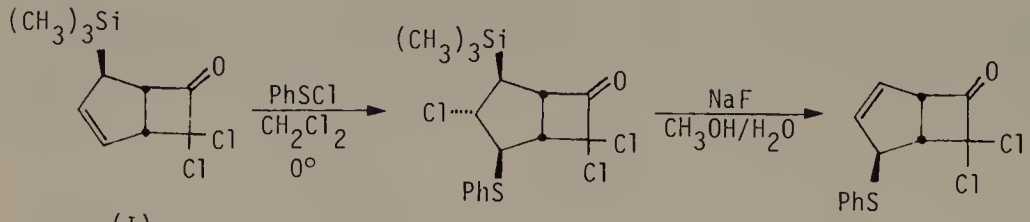
Propargyl $Co_2(CO)_6$ cations react with allylic trimethylsilanes to yield hex-1-en-5-yne $Co_2(CO)_6$ complexes. Removal of the $Co_2(CO)_6$ protecting group by oxidation with ferric nitrate yields hex-1-en-5-ynes [28]. No isomeric allenic by-products are formed.



(11.25)

F. Sulfenyl Halides

Low temperature reaction of benzene sulfenyl chloride with allylsilane (I) gives an addition product which undergoes fluoride induced elimination to yield the rearranged allyl phenyl sulfide [2, 10, 29].

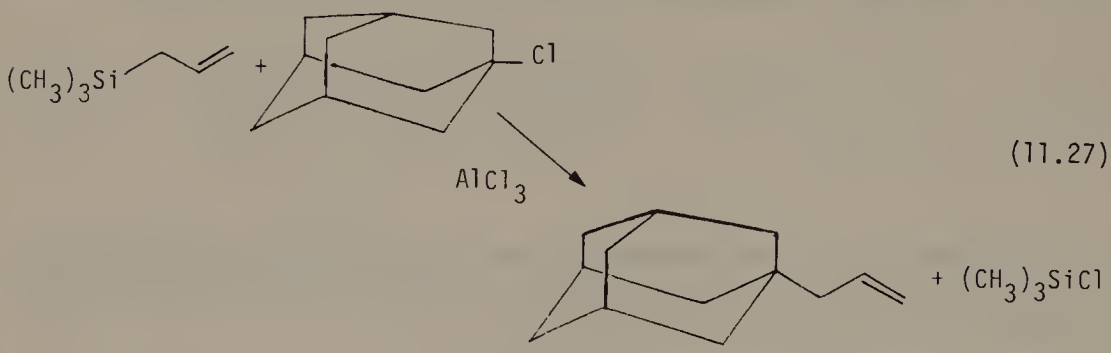


(I)

(11.26)

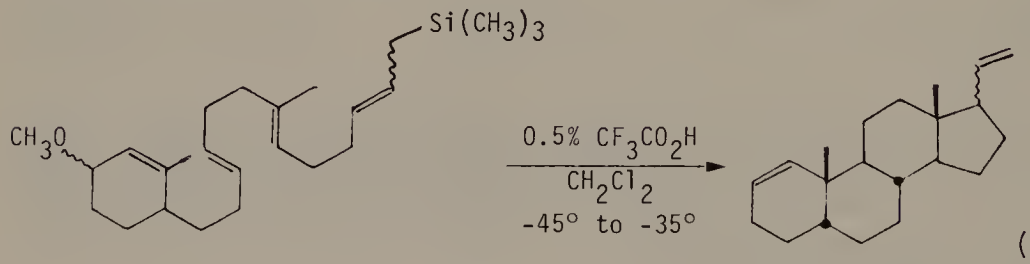
G. Carbocations

Carbocations react with allylic trimethylsilanes to yield rearranged allyl substituted alkanes. Thus adamantyl chloride reacts with allylic trimethylsilanes to yield 1-allyl adamantane derivatives [5, 30, 31].



(11.27)

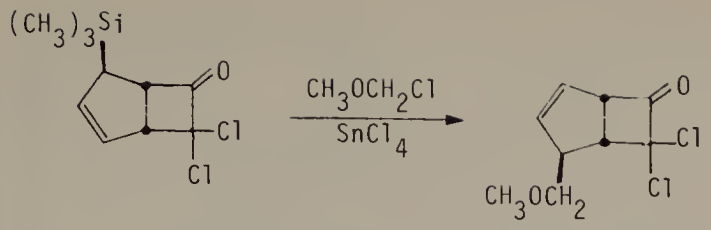
The use of allyl trimethylsilanes as terminators in biomimetic polyene cyclizations has been explored.



(11.28)

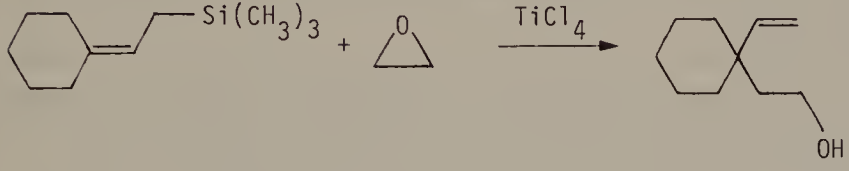
Mixtures of epimeric products at C-17 were obtained. The stability of the allylic trimethylsilane towards a variety of reaction conditions, permits its incorporation into complex molecutes [32].

Chloromethyl methyl ether reacts with allylic trimethylsilanes under $SnCl_4$ catalysis to yield rearranged homoallylic methyl ethers [10, 29]. This reaction has been used as a key step in the preparation of a precursor [33] to prostaglandin A and F.



(11.29)

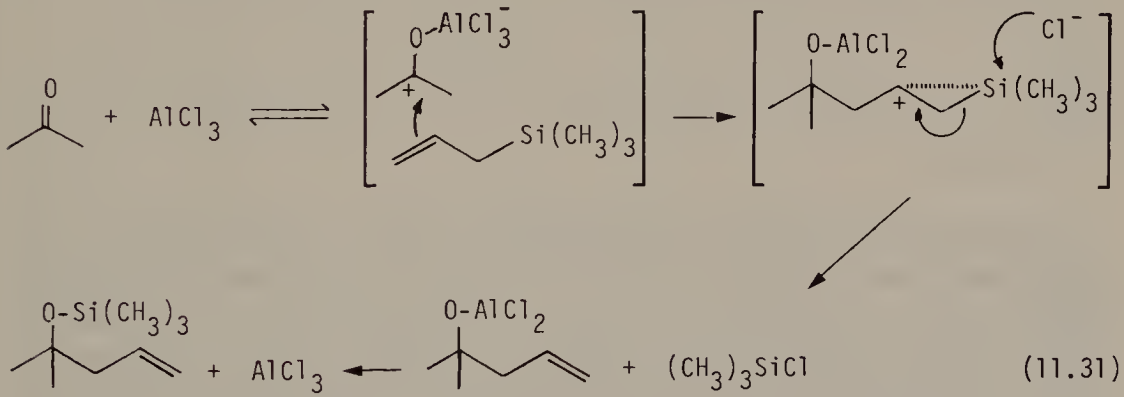
The reaction of allyl trimethylsilanes with ethylene oxide under the influence of $TiCl_4$ provides an efficient route to 4-penten-1-ols [5].



(11.30)

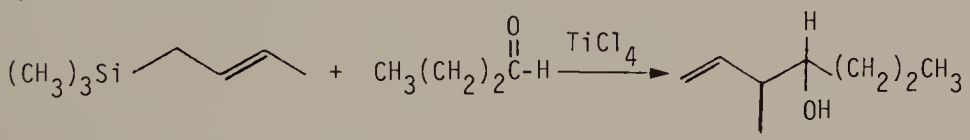
H. Ketones, Aldehydes, Acetals, and Ketals

With $AlCl_3$ or gallium trichloride, allylic trimethylsilanes undergo regiospecific reaction with aldehydes or ketones to yield rearranged homoallylic alcohols [34–37]. These reactions probably proceed by coordination of the Lewis acid to the carbonyl oxygen rendering the carbonyl carbon sufficiently electrophilic to attack the nucleophilic C–C double bond of the allylic silane.



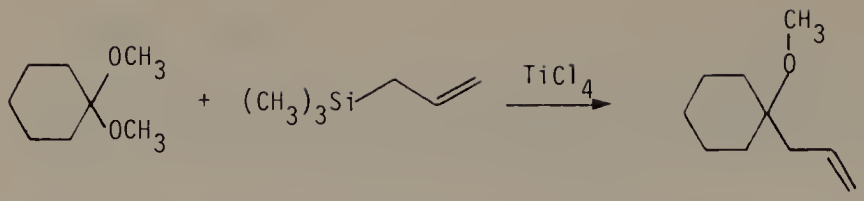
(11.31)

When an equivalent amount of $TiCl_4$ was used as Lewis acid in these reactions, significantly higher yields of homoallylic alcohols were obtained at lower temperatures [38].



(11.32)

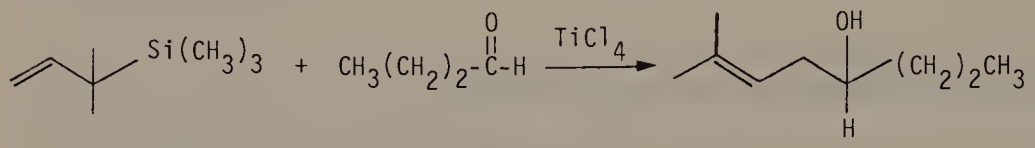
Allylic trimethylsilanes also react with acetals or ketals under Lewis acid activation by $TiCl_4$ to yield homoallylic ethers [39]. Higher yields have often been obtained from comparable reactions of an allylic trimethylsilane with an acetal or ketal rather the corresponding aldehyde or ketone.



(11.33)

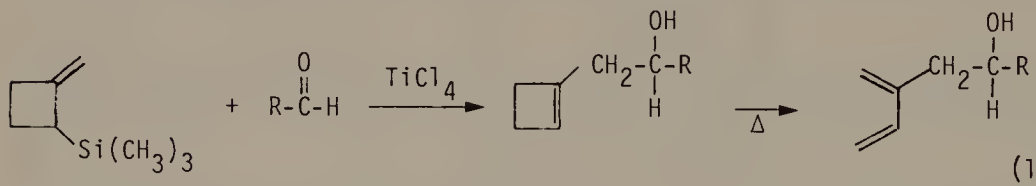
This reaction probably involves Lewis acid assisted heterolysis of a C–O bond of the ketal or acetal to yield an alkoxy stabilized carbocation which attacks the C–C double bond of the allylic trimethylsilane. A wide variety of ketones, aldehydes, acetals, or ketals react with allylic trimethylsilanes under these conditions [15].

Rearrangement of the allylic group occurs during the reaction. Thus α,α-dimethylallyltrimethylsilane reacts with aldehydes under Lewis acid catalysis by $TiCl_4$ to yield γ,γ-dimethylallyl (prenyl) carbinols [40].



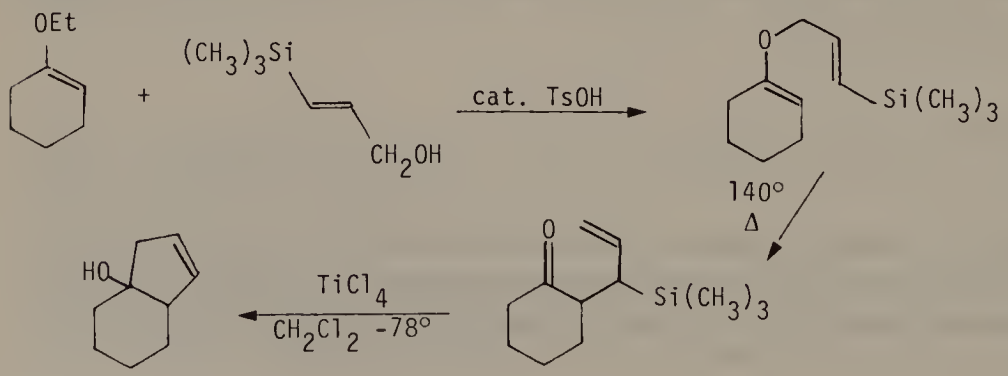
(11.34)

In a similar manner, 2-trimethylsilyl methylene cyclobutane reacts with aldehydes, or ketones and $TiCl_4$ to yield cyclobutenylmethyl carbinols. The cyclobutene ring of such alcohols will undergo a thermally allowed electrocyclic conrotatory opening to yield isopropenyl substituted carbinols [41].



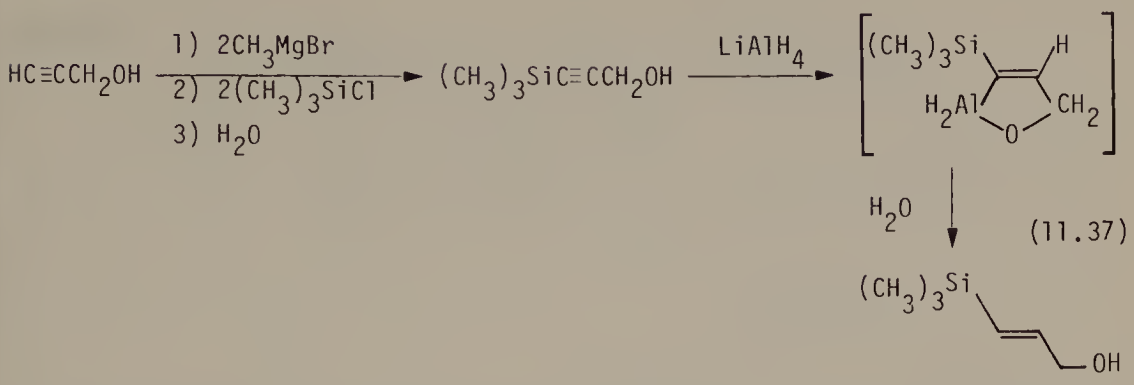
(11.35)

Intramolecular reactions of aldehydes or ketones with allylic silanes under Lewis acid catalysis yields cyclic homoallylic alcohols. 3-Trimethylsilylallyl alcohol undergoes acid catalyzed exchange with ethyl vinyl ethers to yield 3-trimethylsilylallyl vinyl ethers. On heating, Claisen rearrangement occurs to yield α-(1-trimethylsilylallyl) ketones. These undergo electrophilic cyclization/desilylation on treatment with $TiCl_4$ to yield cyclopent-3-en-1-ols [42].



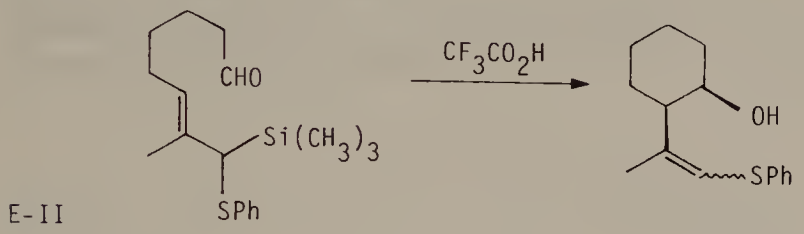
(11.36)

3-Trimethylsilylallyl alcohol has been prepared from propargyl alcohol as outlined [42].

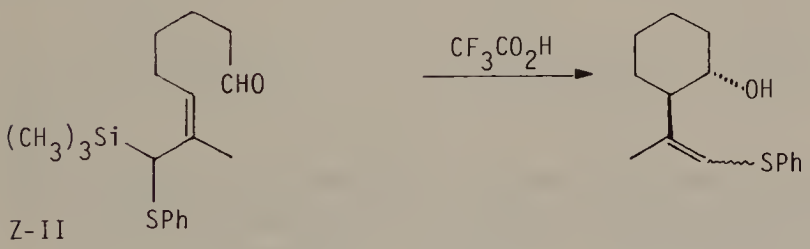


(11.37)

Intramolecular cyclization reactions of 7-methyl-8-phenylthio-8-trimethylsilyl oct-6-en-1-al (II) have been carried out with $SnCl_4$, $BF_3 \cdot OEt_2$ or TBAF catalysis. With these catalysts both *Z* and *E* isomers of II yield mixtures of stereoisomeric 2-(3′-phenylthio-propenyl)cyclohexanols. On the other hand, stereospecific cyclization occurs with trifluoroacetic acid. *E*-II yields *cis*-2-(3′-phenylthio propenyl) cyclohexanol while the corresponding *Z*-II yields *trans*-2-(3′-phenylthio propenyl) cyclohexanol [43].

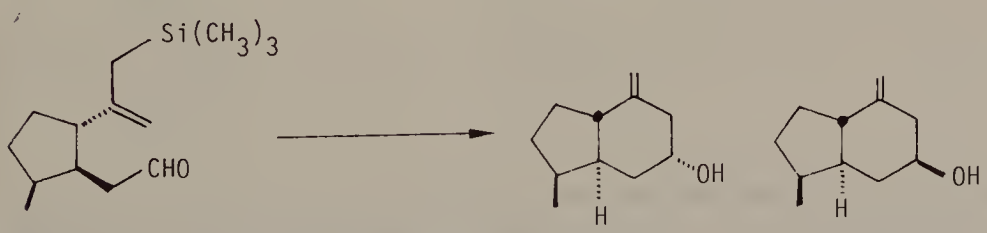


(11.38)



(11.39)

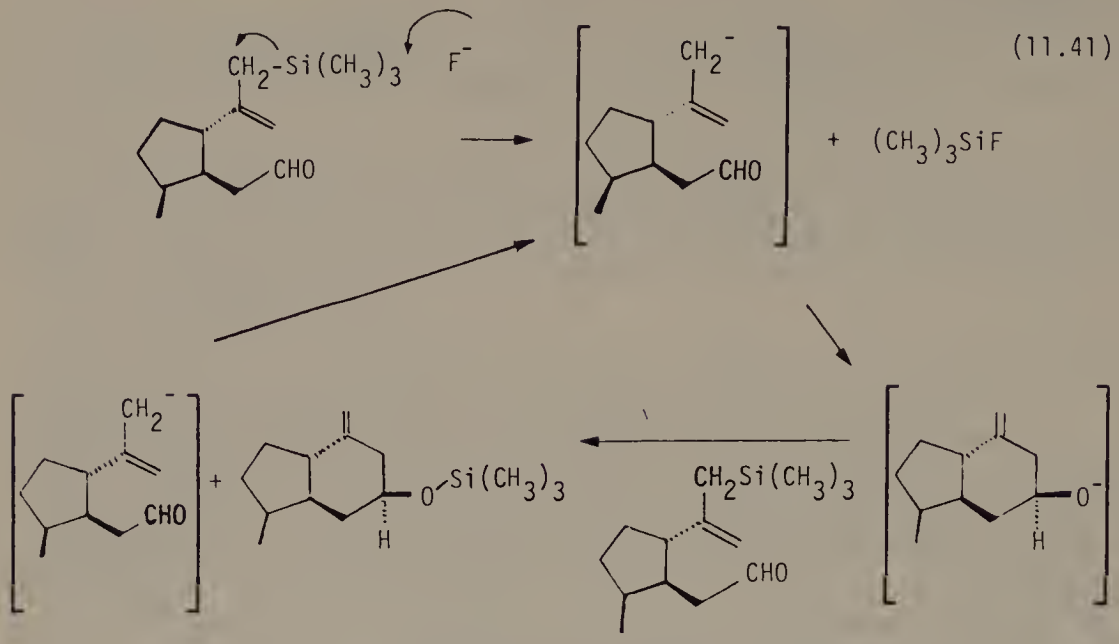
Lewis acid facilitated intramolecular reactions of 5-trimethylsilylmethyl-hex-5-en-1-als provide an efficient route to 3-methylene cyclohexanols. The ratio of axial to equitorial alcohols depends on the catalyst [44].



$BF_3 \cdot OEt_2/CH_2Cl_2$	85%	15%
TBAF/THF	18%	82%

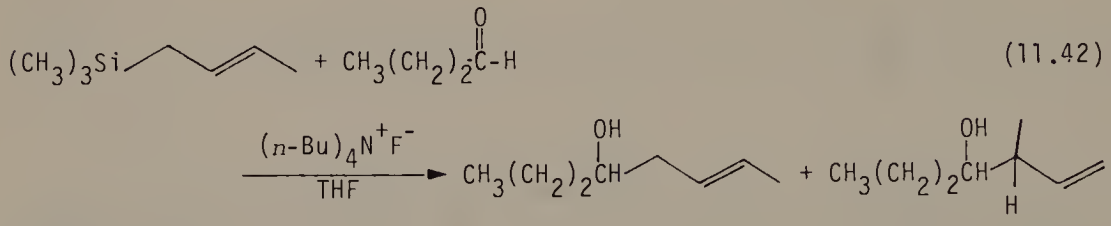
(11.40)

Catalysis by TBAF may occur as outlined below. The TBAF catalyzed



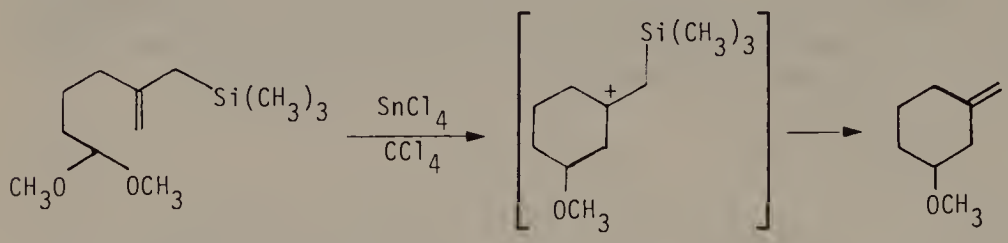
(11.41)

reaction of allylic trimethylsilanes with aldehydes or ketones to yield homoallylic alcohols is not regiospecific [45]. This reaction is probably related to the isomerization of allylic trimethylsilanes with this catalyst system [92].



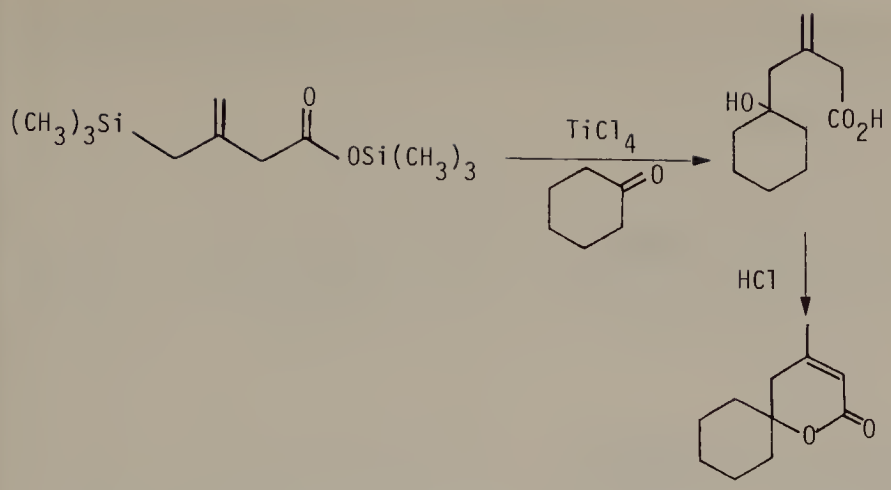
(11.42)

Dimethylacetals of 5-trimethylsilylmethyl 5-hexen-als also undergo Lewis acid cyclization to yield 3-methylene-1-methoxy cyclohexane [46, 107].



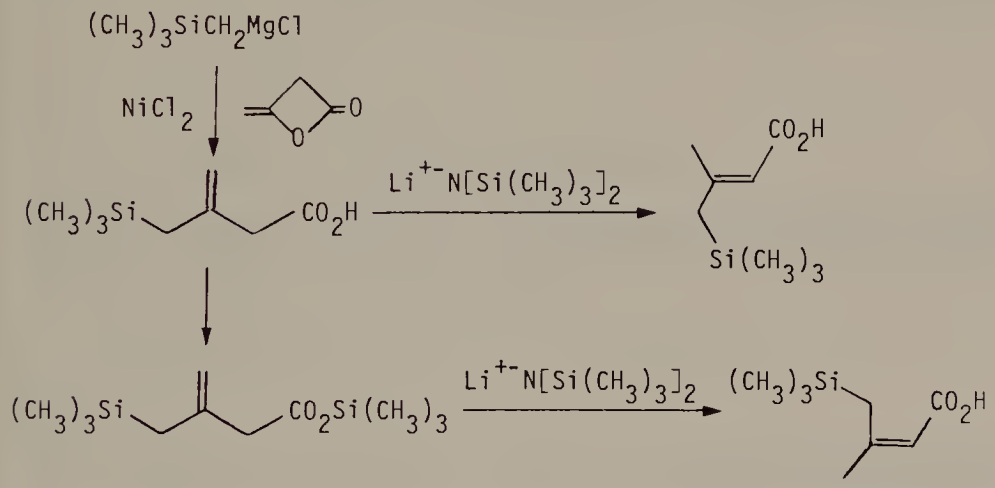
(11.43)

Trimethylsilyl-3-trimethylsilylmethyl-3-butenoate reacts with ketones under the influence of $TiCl_4$ to yield 5-hydroxy-3-methylene carboxylic acids. These can be cyclized to yield α,β-unsaturated-δ-lactones on treatment with HCl [47].



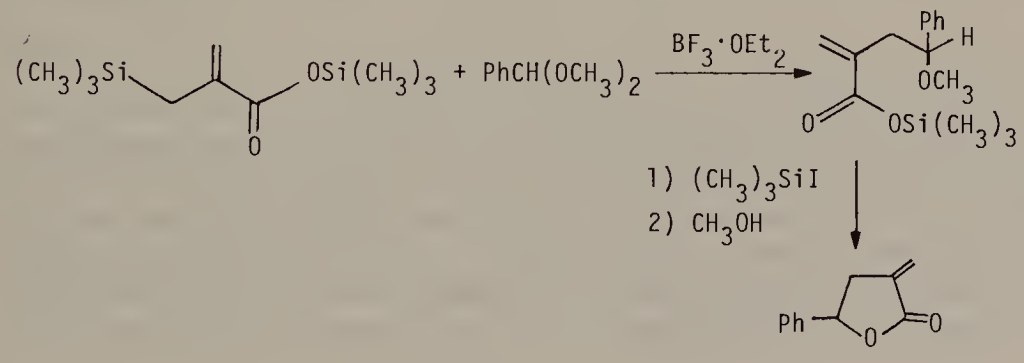
(11.44)

3-Trimethylsilylmethyl-3-butenoic acid has been prepared by a nickel chloride catalyzed addition of trimethylsilylmethyl magnesium chloride to diketene. Base catalyzed isomerization of this acid with lithium *bis*(trimethylsilyl) amide in TMEDA stereospecifically yields *E*-3-methyl-4-trimethylsilyl-2-butenoic acid. On the other hand, isomerization of trimethylsilyl ester with the same base yields predominantly *Z*-3-methyl-4-trimethylsilyl-2-butenoic acid after hydrolysis [48].



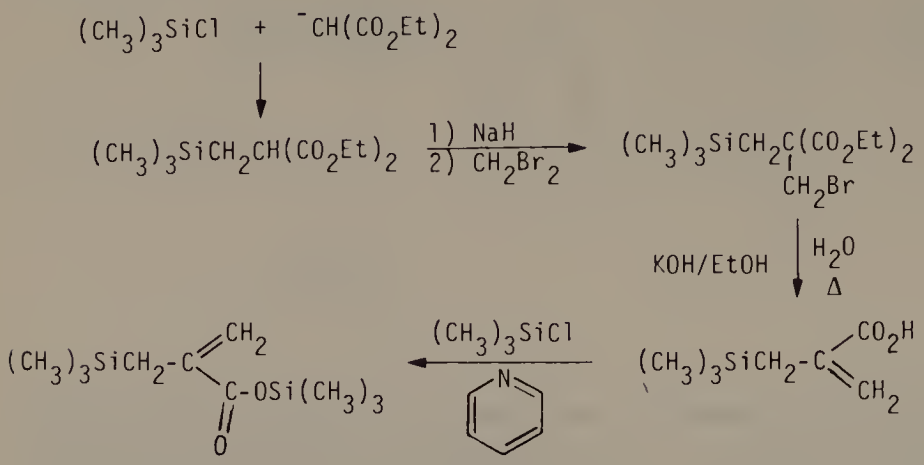
(11.45)

Lewis acid catalyzed reaction of trimethylsilyl-α-trimethylsilylmethyl acrylate with dimethyl acetals yields the corresponding γ-methoxy-α-methylene esters. These react with TMS-I to yield α-methylene-γ-lactones [49].



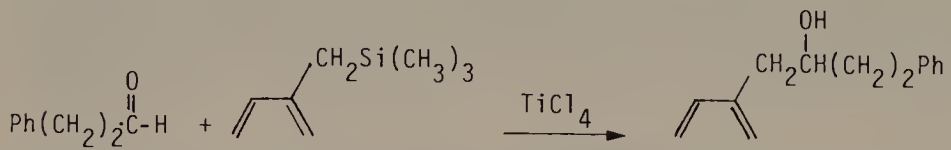
(11.46)

The necessary trimethylsilyl-α-trimethylsilylmethyl acrylate was prepared as outlined below.



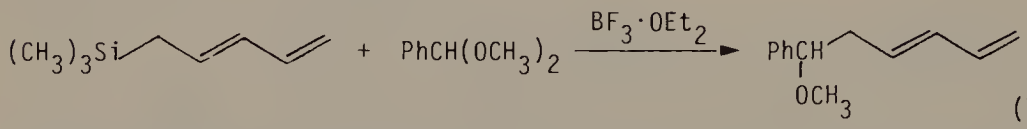
(11.47)

Isopropenyltrimethylsilane reacts with aldehydes or dimethylacetals under the influence of $TiCl_4$ to yield isopropenyl substituted carbinols or the corresponding methyl ethers, respectively (Eq. 11.48) [17]. Isopropenyltrimethylsilane has been prepared by a nickel catalyzed coupling of 2-chloro-1,3-butadiene with trimethylsilylmethyl magnesium chloride.



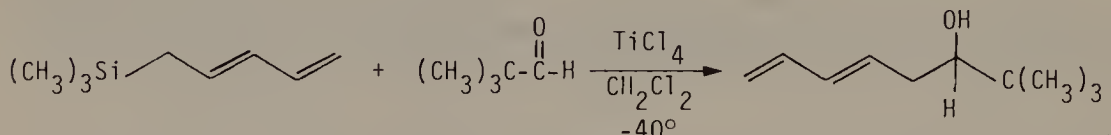
(11.48)

5-Trimethylsilyl-1,3-pentadiene reacts with dimethyl acetals under catalysis by $BF_3 \cdot OEt_2$ or $TiCl_4$ as outlined [50, 51].



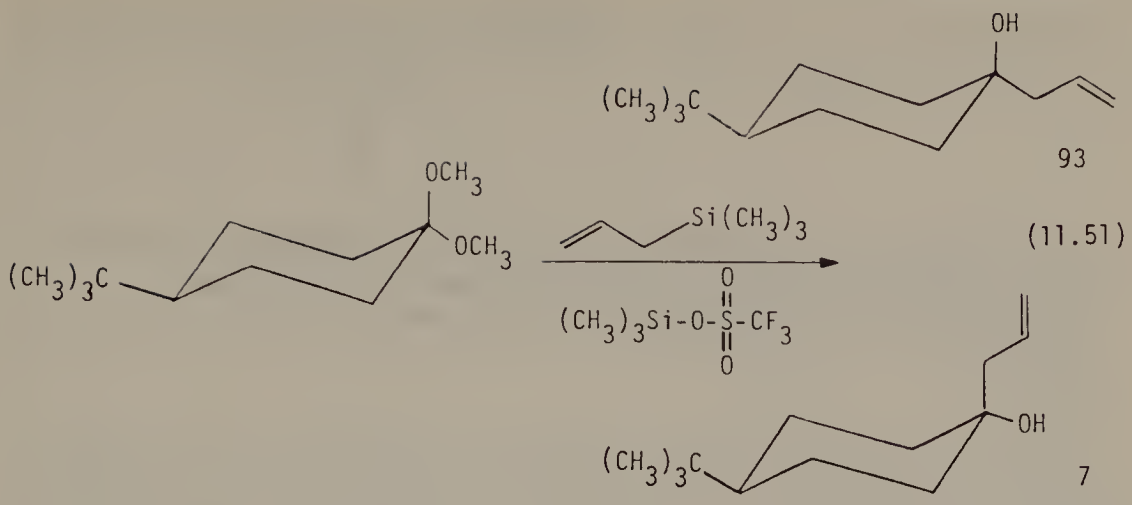
(11.49)

Similar reactions with aldehydes or ketones [52] under catalysis by $TiCl_4$ yield 1,3-pentadienylic carbinols.

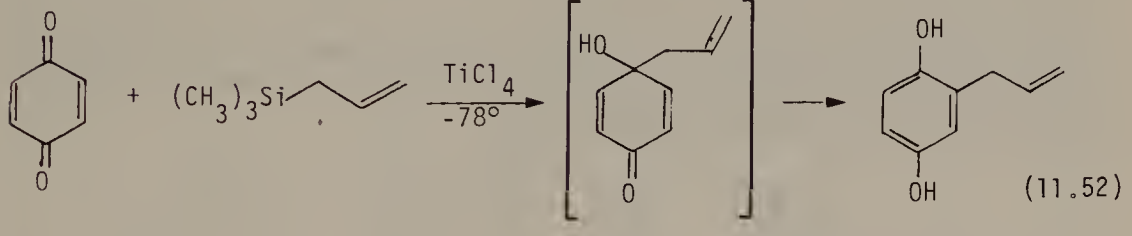


(11.50)

The reaction of allylic trimethylsilanes with acetals as usually carried out requires a stoichiometric amount of $TiCl_4$. Recently, two new procedures have been reported which only require a catalytic amount of Lewis acid. Both trimethylsilyl trifluoromethanesulfonate [106] and TMS-I [53] have proved effective catalysts for such reactions. TMS-I is particularly convenient since it can be generated *in-situ* by addition of a small amount of iodine to a slight excess of the allylic trimethylsilane.

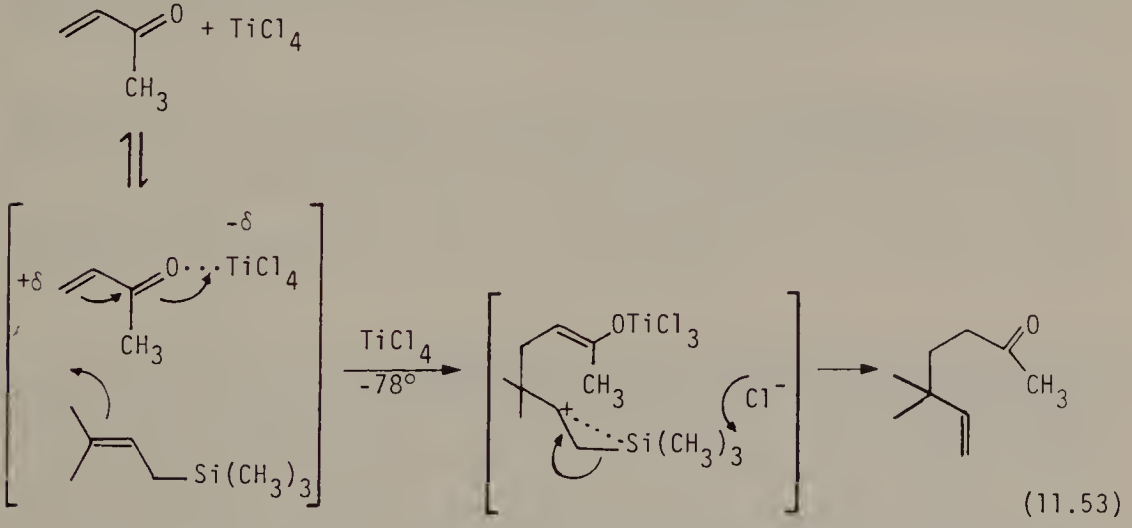


Allyltrimethylsilane reacts with *p*-quinone and $TiCl_4$ to yield 2-allyl hydroquinones. Allyl *p*-quinol is a probable intermediate [54].

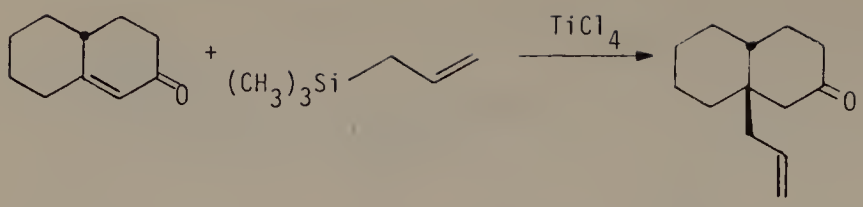


I. α,β-Unsaturated Ketones and Aldehydes

Allylic trimethylsilanes react with α,β-unsaturated ketones and $TiCl_4$ to yield δ,ε-enones as outlined in Eq. 11.53. This is equivalent to a Michael addition of the rearranged allyl group.



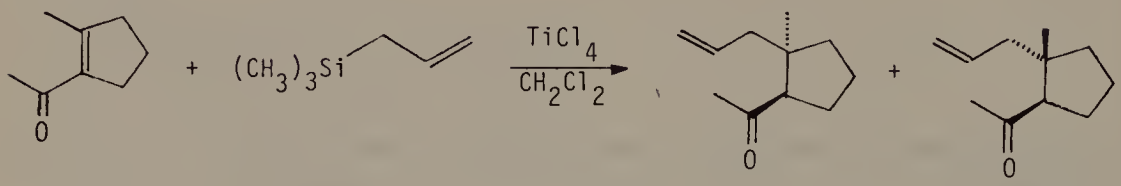
This reaction permits the introduction of an allyl group at the angular position of a fused cyclic α,β-unsaturated enone [11, 55].



(11.54)

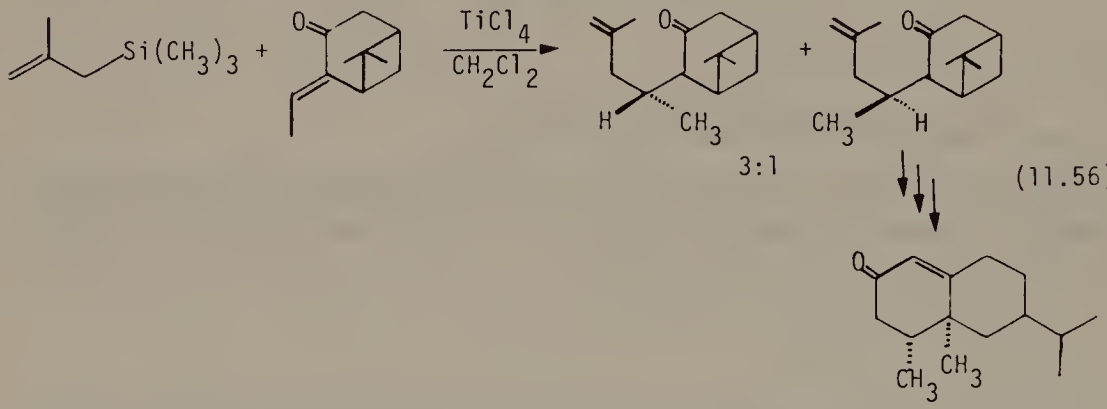
1-Acetyl-2-methyl cyclopentene reacts with allytrimethylsilane and $TiCl_4$ to give a 6:4 mixture of *Z*:*E* 1-acetyl-2-allyl-2-methyl cyclopentanes.

[56] However, reaction with acetyl cyclohexene proved to be more complicated [52].



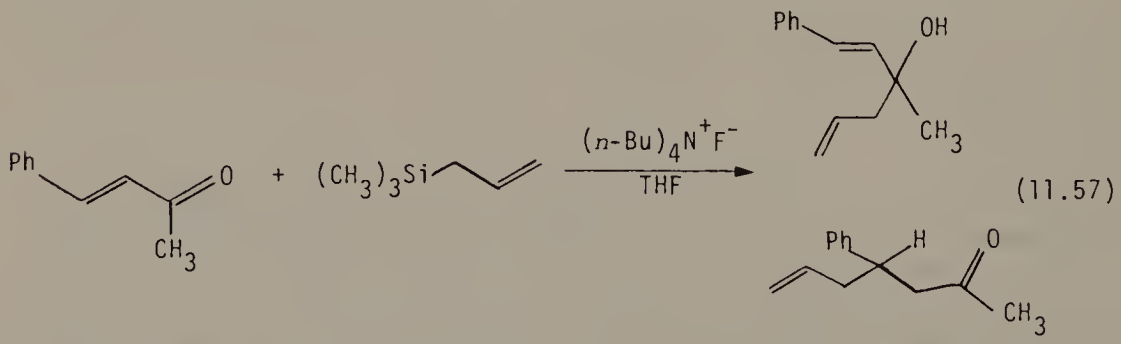
(11.55)

This regiospecific Michael addition of allylic groups to α,β-unsaturated ketones has been utilized in the synthesis of (+) Nootkatone [57, 58]. The key allylation step is outlined in Eq. 11.56.



(11.56)

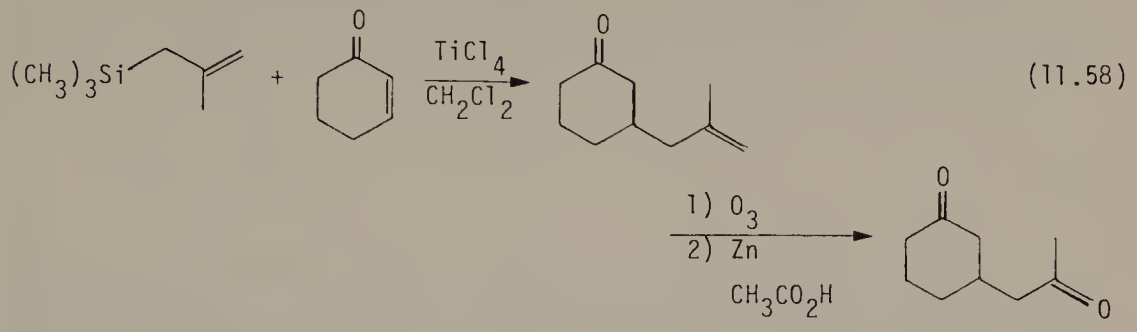
Allylic trimethylsilanes also react with α,β-unsaturated ketones under catalysis by TBAF to yield both 1,2- and 1,4-addition products [45].



(11.57)

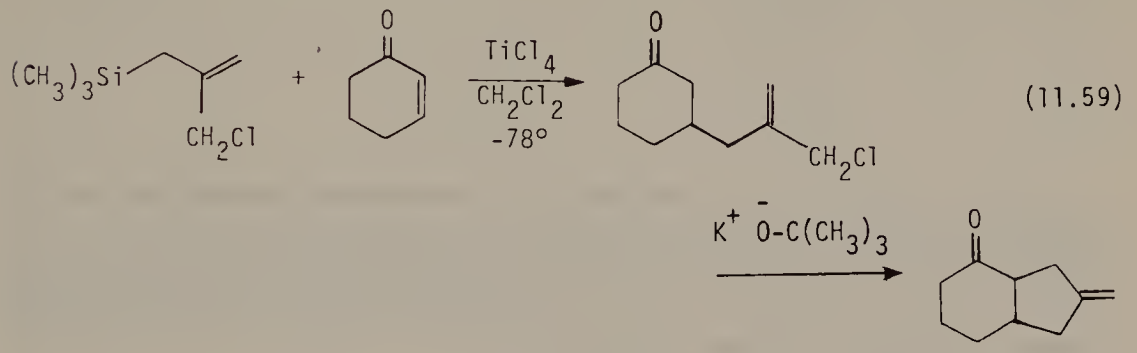
Reaction of 2-methylallyltrimethylsilane with α,β-unsaturated ketones which are activated by $TiCl_4$ or $BF_3 \cdot OEt_2$ yields δ,ε-enones. The C–C double

bond of these can be cleaved with ozone, followed by a reductive work-up to yield 1,5-dicarbonyl compounds [59].



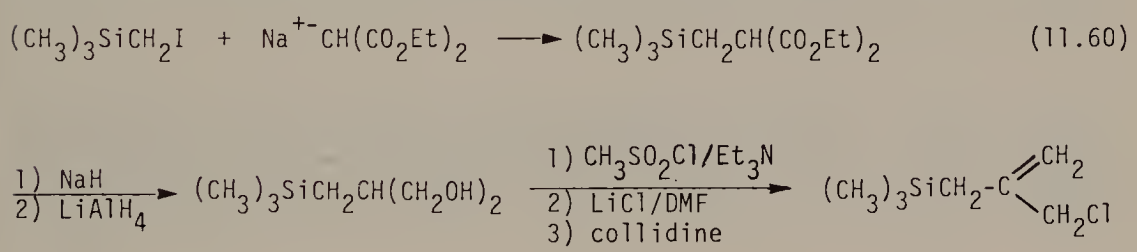
(11.58)

2-Chloromethyl-allyltrimethylsilane undergoes $TiCl_4$ induced reaction with cyclohexenone to yield β-(2-chloromethyl allyl) cyclohexanone. Treatment of this with strong base results in an intramolecular C-alkylation of the ketone enolate by the allylic chloride. This sequence permits the [3 + 2] annulation of a five membered ring onto the C–C double bond of cyclic α,β-unsaturated ketones [60].



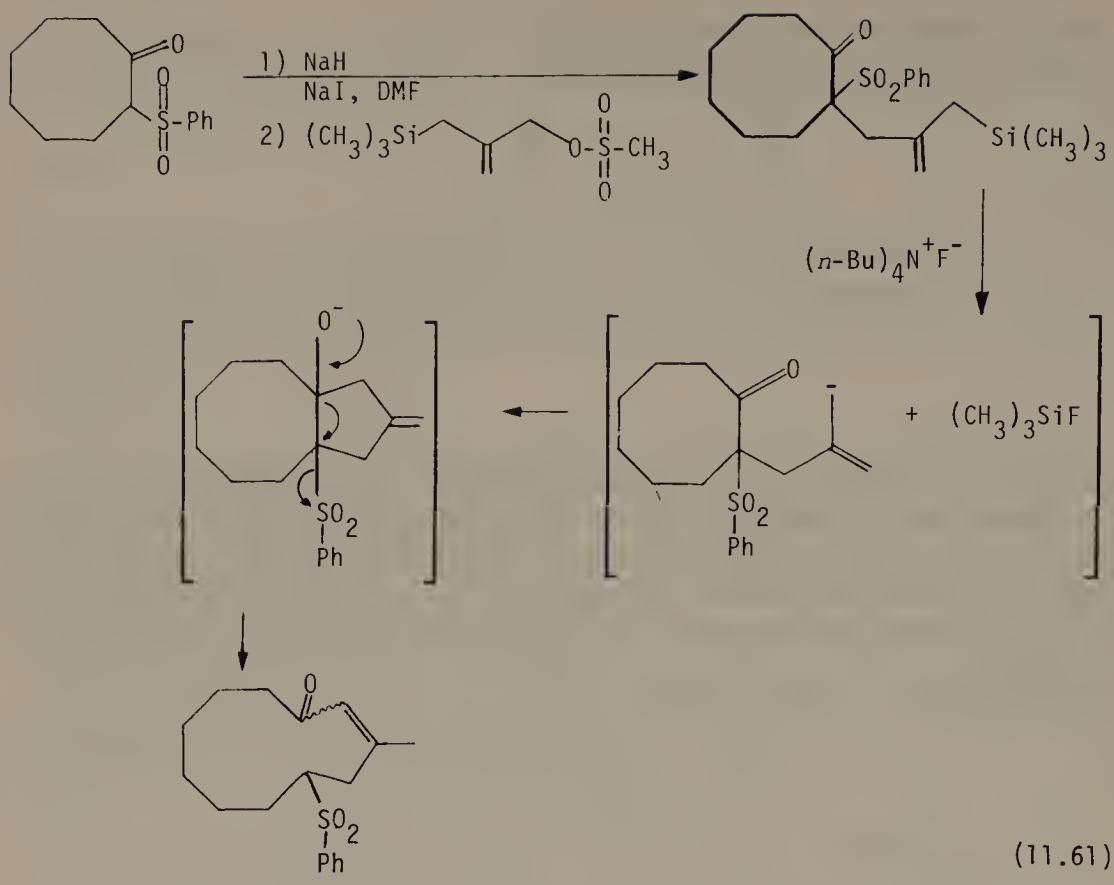
(11.59)

The necessary reagent, 2-chloromethyl-allyltrimethylsilane has been prepared from iodomethyltrimethylsilane as outlined in Eq. 11.60.



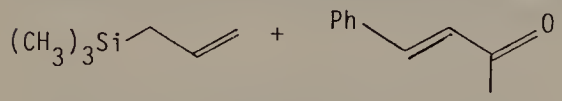
(11.60)

[2+3] Annulation of a five membered ring onto ketones has also been achieved by use of allylic silane reagents. The reaction of the enolate anion of cyclic-β-keto sulfones with 2-trimethylsilylmethyl prop-2-enyl methanesulfonate yields α-phenylsulfonyl-α-(2-trimethylsilylmethylpropenyl) ketones. Treatment of these with TBAF in THF results in cyclization. This involves an allylic anion intermediate formed by fluoride ion attack on the silyl center [108]. The initial product often undergoes fragmentation under these conditions to yield a three carbon ring expanded product.

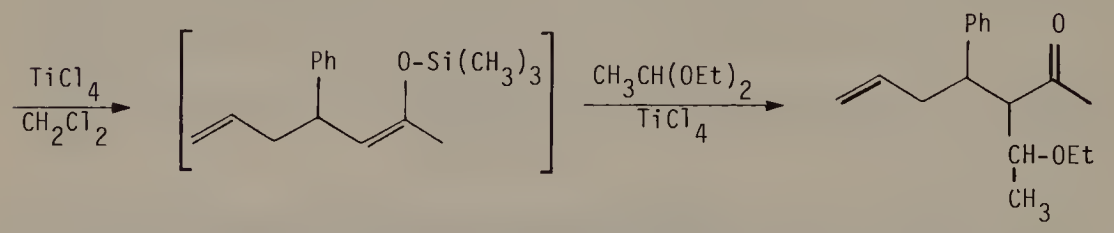


(11.61)

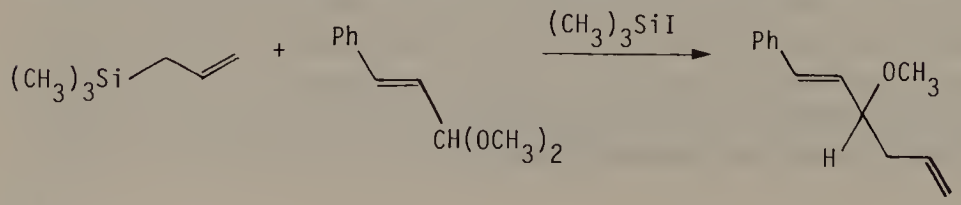
Allylic trimethylsilanes react with α,β-unsaturated ketones under the influence of $TiCl_4$ to yield δ,ε-unsaturated trimethylsilyl enol ether or δ,ε-unsaturated titanium trichloride enolates as the initial reaction products. These can be utilized synthetically, since such enol ethers react with electrophiles (acetals, aldehydes, or ketones) un the presence of $TiCl_4$ to yield α substituted δ,ε-unsaturated ketones [61] (see Chapter 12).



(11.62)

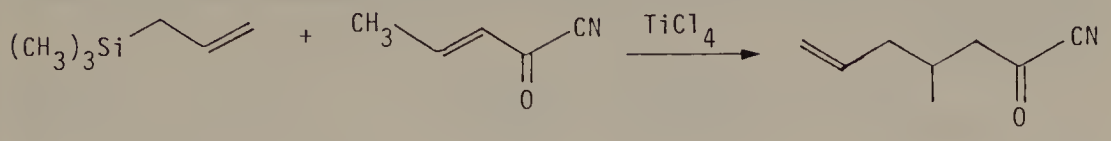


By comparison, α,β-unsaturated dimethylacetals react at the acetal carbon with allylic trimethylsilanes under the influence of TMS-I [53].



(11.63)

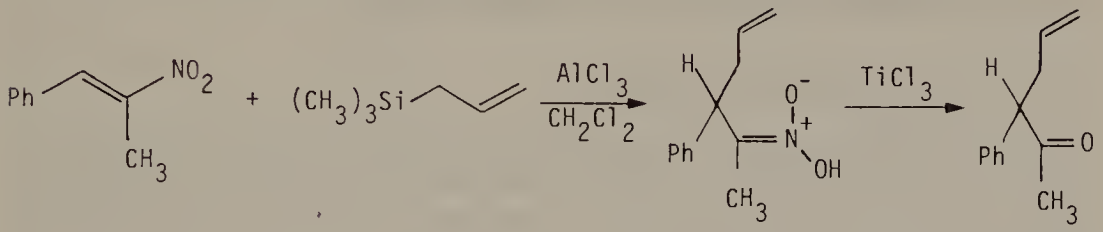
α,β-Unsaturated acyl cyanides undergo reactions with allylic trimethylsilane and $TiCl_4$ to yield δ,ε-unsaturated acyl cyanides [62].



(11.64)

J. α-Nitro Alkenes

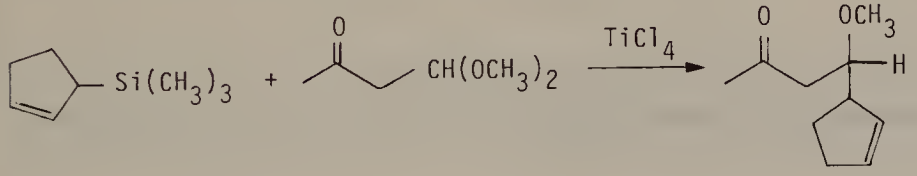
In the presence of $AlCl_3$, allylic trimethylsilanes undergo a Michael reaction with α-nitro olefins to yield reactive γ,δ-unsaturated nitronic acids. Treatment of these with titanium trichloride yields γ,δ-unsaturated ketones [63].



(11.65)

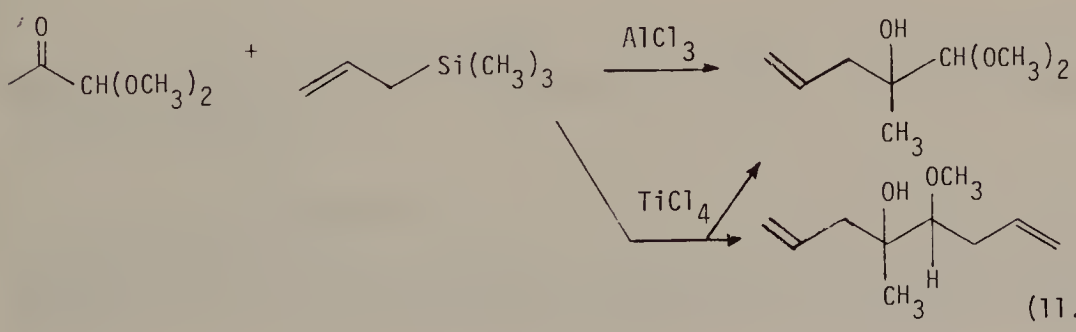
K. α- and β-Keto Acetals and α-Keto Esters

Reaction of allylic trimethylsilanes with β-keto acetals and $TiCl_4$ occurs preferentially at the acetal carbon [64].



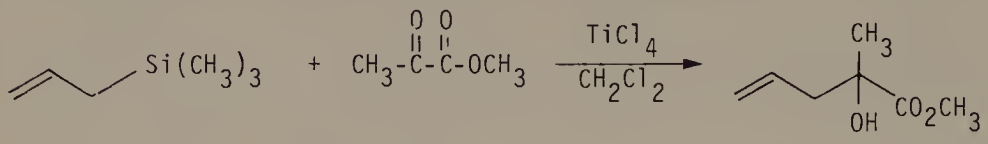
(11.66)

With α-keto acetals the site of reaction is determined by the particular Lewis acid chosen. Thus, with $AlCl_3$ reaction occurs exclusively at the carbonyl carbon, while with $TiCl_4$ reaction occurs at both the carbonyl carbon and the acetal carbon [64].



(11.67)

Allyltrimethylsilane reacts with the ketone carbonyl of pyruvate esters in the presence of $TiCl_4$ to yield γ,δ-unsaturated-α-hydroxyvalerates [65]. 3-Trimethylsilyl cyclopentene reacts similarly with ethyl pyruvate and ethyl phenyl glyoxalate [15].



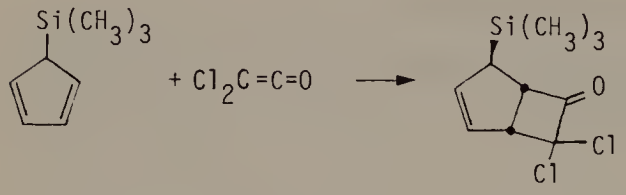
(11.68)

(−)Menthyl pyruvate reacts with allyltrimethylsilane at −75°C to yield (−)menthyl 2-hydroxy-2-methyl-pent-4-enoate. Asymmetric induction results in a 55% e.e. (S) at the new chiral center [65].

11.3 Cycloaddition Reactions of Allylic Silanes

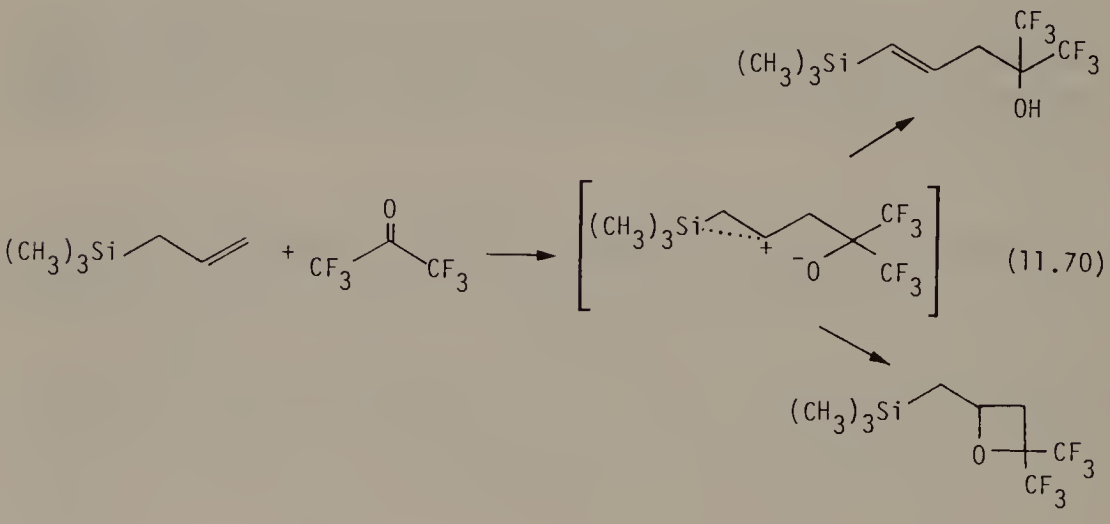
A. [2 + 2] Cycloaddition Reactions

[2 + 2] Cycloaddition reaction of 5-trimethylsilylcyclopentadiene with dichloroketene yield exclusively 7,7-dichloro-4-exo-trimethylsilylbicyclo[3,2,0]hept-2-en-6-one (Eq. 11.69) [10, 29]. On the other hand, TCNE reacts with allyltrimethylsilane to yield a mixture of 1,1,2,2-tetracyano-3-trimethylsilylmethyl cyclobutane and 1,1,2,2-tetracyano-4-pentene [66].



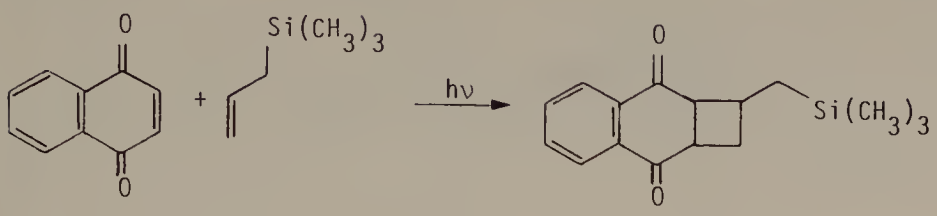
(11.69)

Hexafluoroacetone reacts with allyltrimethylsilane to yield a mixture of 2,2-*bis*-(trifluoromethyl)-4-trimethylsilylmethyloxetane and 1,1-*bis*-(trifluoromethyl)-4-trimethylsilyl-3-buten-1-ol [34].



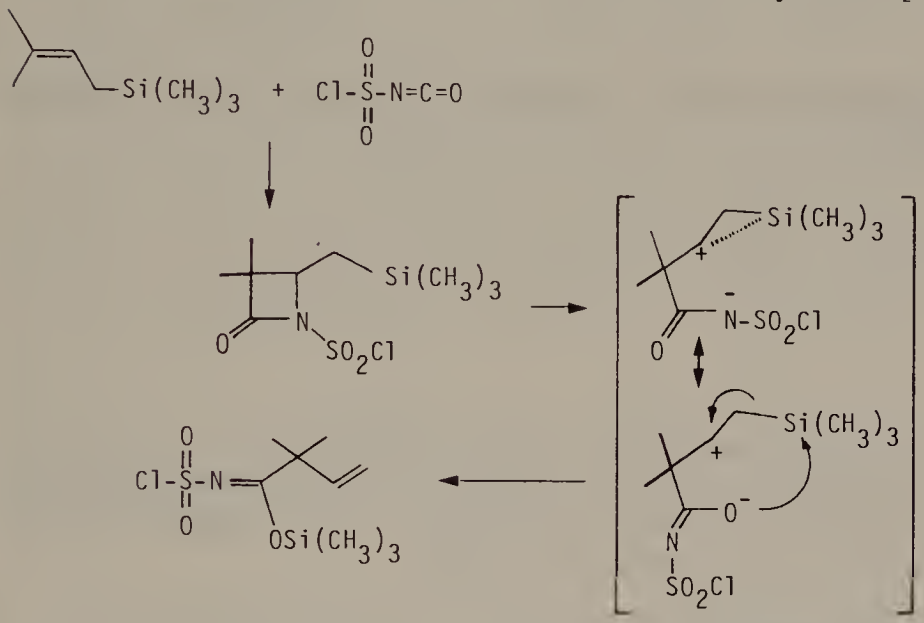
(11.70)

Allyltrimethylsilane undergoes [2 + 2] photocycloaddition with naphthoquinone [67].



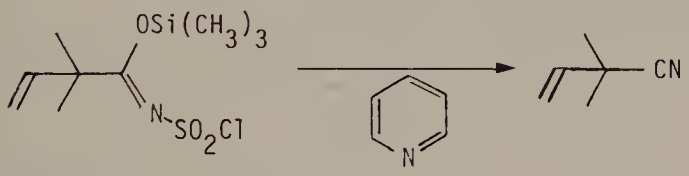
(11.71)

Chlorosulfonyl isocyanate undergoes a [2 + 2] cycloaddition reaction with γ,γ-dimethylallyltrimethylsilane at 0° to yield 4,4-dimethyl-3-trimethylsilylmethyl-N-chlorosulfonyl β lactam. At 25° this compound rapidly rearranges to α,α-dimethylallyl trimethylsilyloxy-N-chlorosulfonyl imine [68].



(11.72)

Treatment of these adducts with pyridine yields the corresponding nitriles [68].



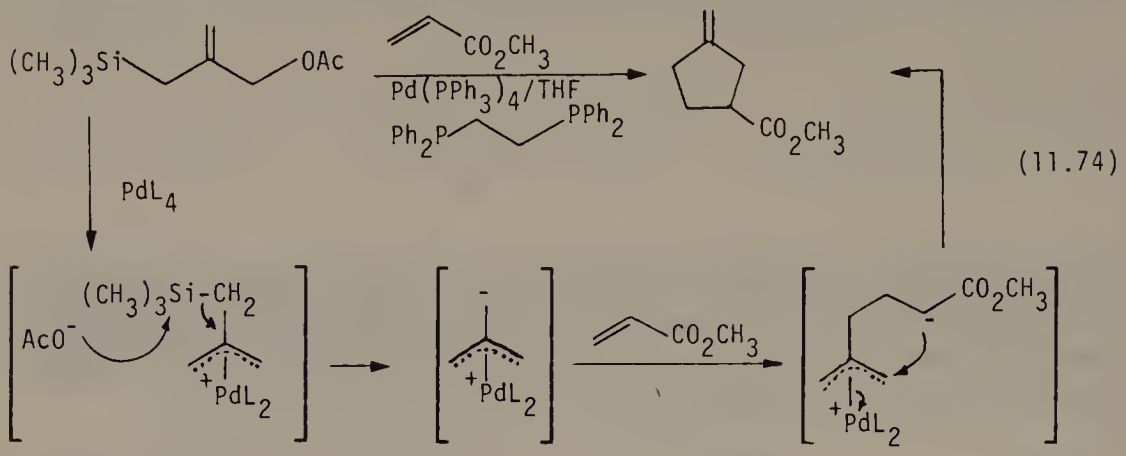
(11.73)

Such allylic trimethylsilyloxy-N-chlorosulfonyl imines can also be converted to allylic esters [69].

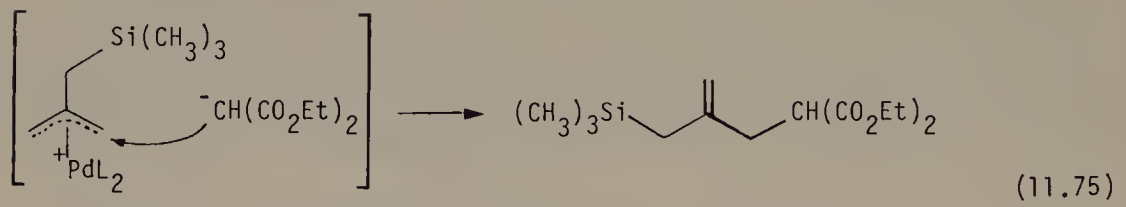
B. [3 + 2] Cycloadditions

2-Acetoxymethyl-3-allyltrimethylsilane undergoes Pd(O) catalyzed reaction with alkenes substituted with electron withdrawing groups to yield methylene

cyclopentane derivatives. These reactions may involve formation of a trimethylene methane palladium complex as an intermediate [70].



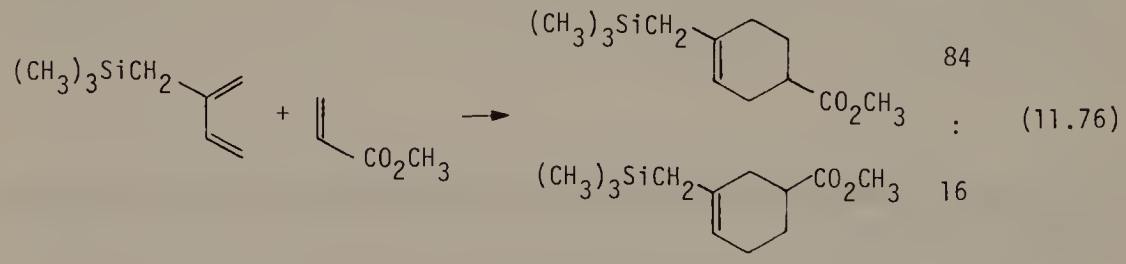
2-Trimethylsilylmethyl π-allyl palladium L_2^+ complexes, can be trapped by nucleophiles [71].



2-Acetoxymethyl-3-allyltrimethylsilane can be prepared from α-methylallyl alcohol by metallation with two equivalents of *n*-butyl lithium/TMEDA followed by the addition of TMS-Cl. Hydrolysis of the trimethylsilyl ether, followed by acetylation gives the desired reagent.

C. Diels-Alder Reactions

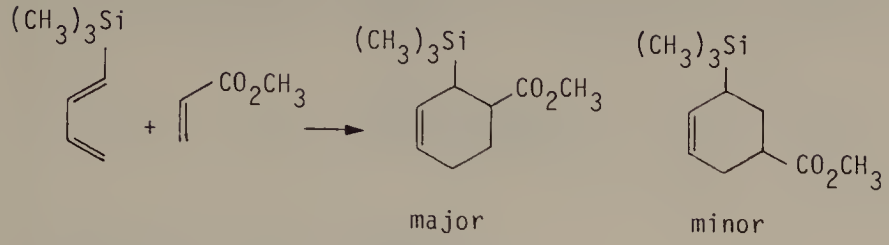
Isopropenyltrimethylsilane undergoes Diels-Alder reactions with various dienophiles to yield 1-trimethylsilylmethyl cyclohexenes [41, 72].



Isopropenyltrimethylsilane has been prepared by thermally allowed conrotatory electrocyclic ring opening of—trimethylsilylmethyl cyclobutene [17, 41, 73].

1-Trimethylsilylbutadiene undergoes Diels-Alder reactions with dienophiles

to give mixtures of regioisomers. The *ortho* adducts are usually predominant [74].

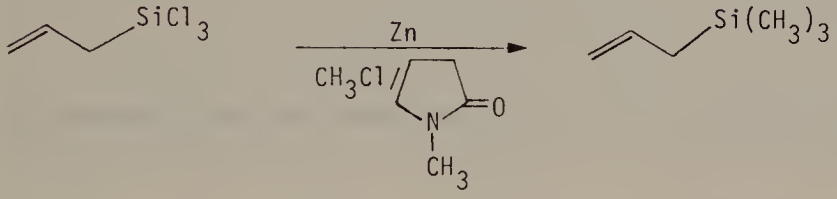


(11.77)

11.4 Preparation

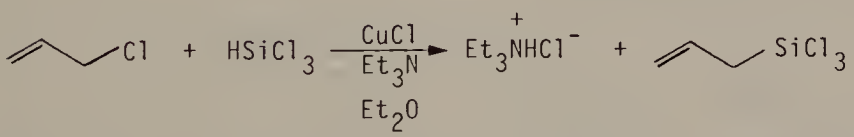
A. Direct Synthesis

Allyltrichlorosilane has been prepared by the direct synthesis. Thus reaction of allyl chloride with copper-silicon powder (10:90) at 250° yields a mixture of allyldichlorosilane, diallyldichlorosilane, and allyltrichlorosilane in which the latter product is predominant [75]. Allylic trichlorosilanes can be converted to allylic trimethylsilanes by reaction with an excess of methyl magnesium bromide [75] or by reaction with methyl chloride and zinc in N-methyl pyrrolidone [76].



(11.78)

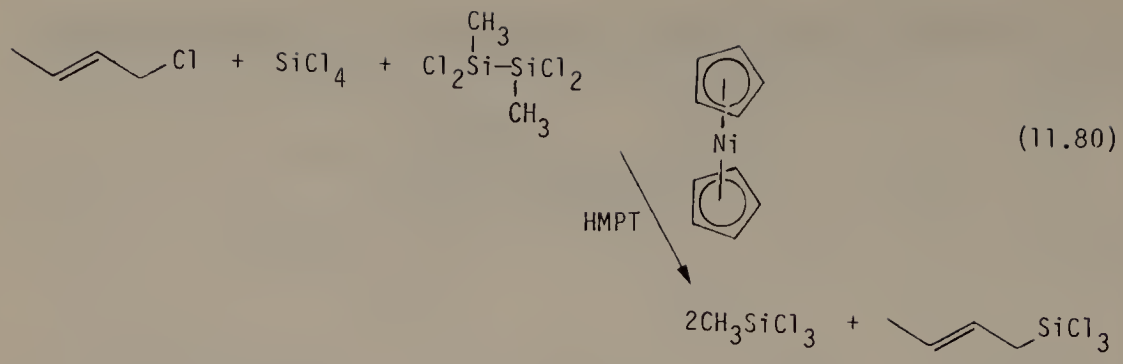
A more practical laboratory synthesis of allyltrichlorosilane involves the room temperature reaction of trichlorosilane with allyl chloride and triethylamine catalyzed by cuprous chloride [77].



(11.79)

B. Catalytic Reactions of Disilanes

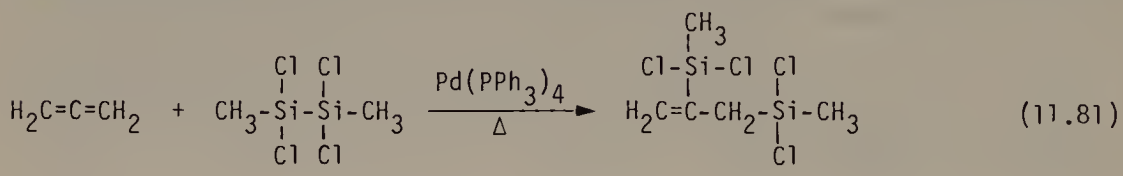
Nickelocene catalyzes the reaction of allylic chlorides, silicon tetrachloride and a mixture of *sym*-tetrachlorodimethyldisilane and 1,1,2-trichloro-1,2,2-trimethyldisilane to yield methyltrichlorosilane and allylic trichlorosilanes [78]. Unfortunately the reaction is not regiospecific. Both γ,γ-dimethylallylchloride and α,α-dimethylallylchloride yield γ,γ-dimethylallyltrichlorosilane.



(11.80)

Hexamethyldisilane, *sym*-dichlorotetramethyldisilane or *sym*-tetrachlorodimethyldisilane react with allyl chloride under catalysis by *tetrakis*-(triphenylphosphine) palladium (O) to yield allyltrimethylsilane, allyldimethylchlorosilane, or allylmethyldichlorosilane, respectively [79].

Hexamethyldisilane, as well as methoxy and chloro substituted disilanes undergo palladium (O) catalyzed addition to allene to yield 2,3-*bis*(silyl)-propene [80].



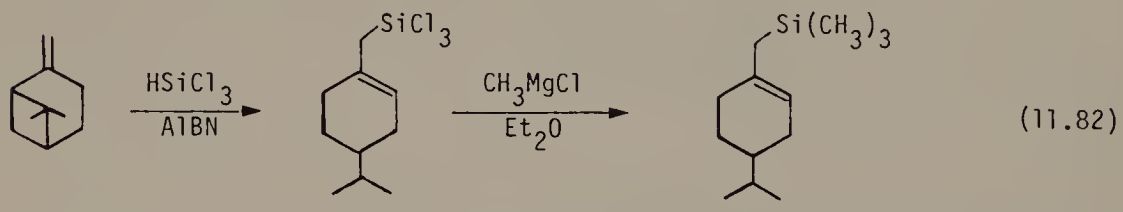
(11.81)

C. Pyrolysis

Allyltrimethylsilane has been prepared by the flash vacuum pyrolysis of cyclopropyltrimethylsilane [81].

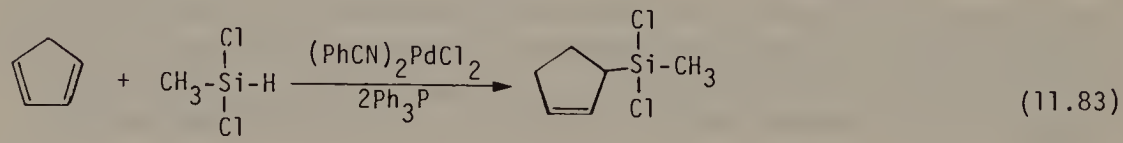
D. Hydrosilation Reactions

Hydrosilation of alkenes usually yields alkyl silanes. However, free radical catalyzed hydrosilation of β-pinene with trichlorosilane yields 4-isopropyl-1-trichlorosilylmethyl cyclohexene [14].



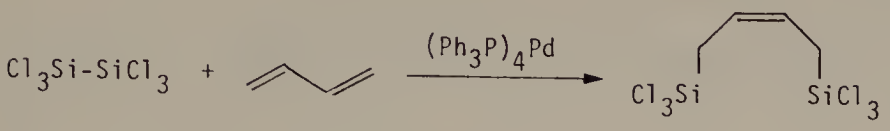
(11.82)

Transition metal catalyzed hydrosilations of 1,3-dienes occurs predominantly in a 1,4-manner to yield allylic silanes [15].



(11.83)

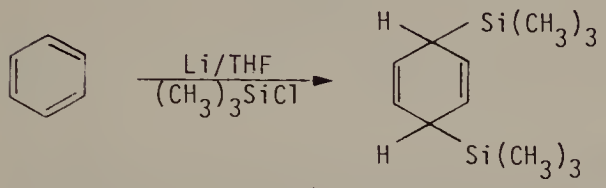
Under the catalytic influence of *tetrakis*-(triphenylphosphine) palladium(o), chloro substituted disilanes react with alicyclic 1,3-dienes to yield *Z*-1,4-*bis*-(silyl)-2-butenes [82].



(11.84)

E. Dissolving Metal Reductions

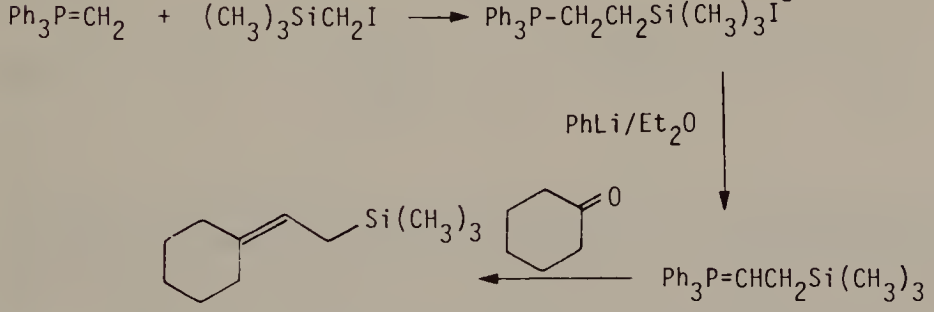
Dissolving metal reductions of aromatic hydrocarbons [83], 1,3- [4] and 1,2-dienes [16], allylic methyl ethers [84, 85], allylic trimethylsilyl sulfides [14, 86] α,β-unsaturated ethylene thioacetals or ketals [6] with TMS-Cl have proved useful for the synthesis of allylic trimethylsilanes (see Chapter 19).



(11.85)

F. Wittig Reactions

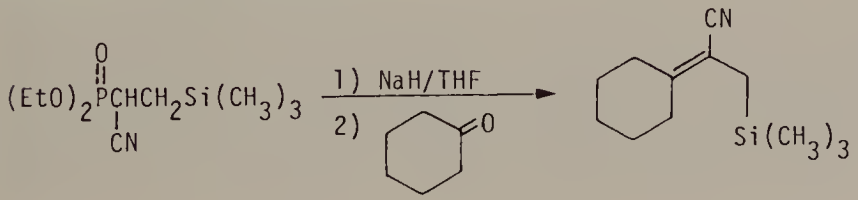
The Wittig reaction of 2-trimethylsilylethylidene triphenylphosphorane with aldehydes or ketones [5, 87] regiospecifically yields allylic trimethylsilanes. The precursor phosphonium salt, 2-trimethylsilylethyl triphenylphosphononium iodide, is prepared by reaction of iodomethyltrimethylsilane 88–90] with methylene triphenylphosphorane.



(11.86)

With sterically hindered ketones better yields are obtained with 2-dimethylsilylethylidene triphenylphosphorane [87].

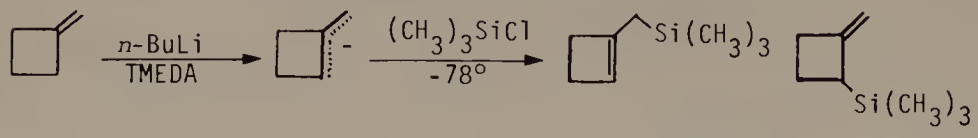
2-Cyano-3-trimethylsilyl alkenes have been prepared by a Wittig-Horner-Emmons reaction [91].



(11.87)

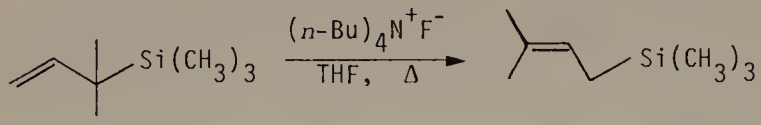
G. Allylic Organometallics

Generally, unsymmetrical allylic organometallic reagents react with TMS-Cl to yield both possible isomeric allylic trimethylsilanes [41].



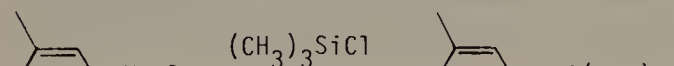
(11.88)

Treatment of isomeric mixtures of allylic trimethylsilanes with a catalytic amount of TBAF in THF at reflux results in isomerization of the mixture to the more thermodynamically stable isomer. Allylic anions may be intermediates in this equilibration [92].

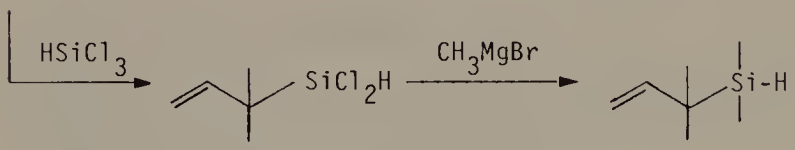


(11.89)

In certain cases, the regiospecificity of reaction of allylic organometallic reagents with chlorosilanes can be determined by the choice of the chlorosilane. For example, 3-methylbut-2-enyl magnesium chloride reacts with TMS-Cl to yield γ,γ-dimethylallyltrimethylsilane (Eq. 11.90), while it reacts with trichlorosilane to yield α,α-dimethylallyldichlorosilane (Eq. 11.91). This latter product can be converted to α,α-dimethyallyltrimethylsilane [40].

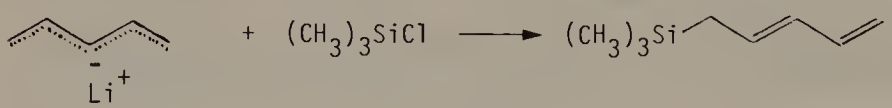


(11.90)

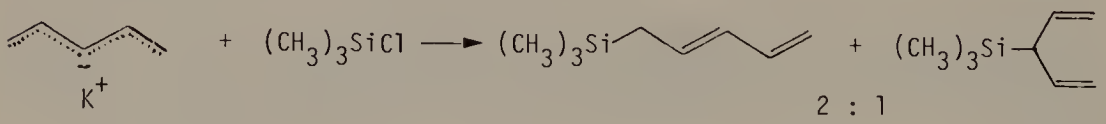


(11.91)

The particular metal cation associated with an allylic anion may also determine the regiospecificity of coupling with TMS-Cl. Pentadienyl lithium, reacts with TMS-Cl to yield 5-trimethylsilyl-1,3-pentadiene [52]. On the other hand, pentadienyl potassium reacts with TMS-Cl to yield a mixture of 5-trimethylsilyl-1,3-pentadiene and 3-trimethylsilyl-1,4-pentadiene [18].

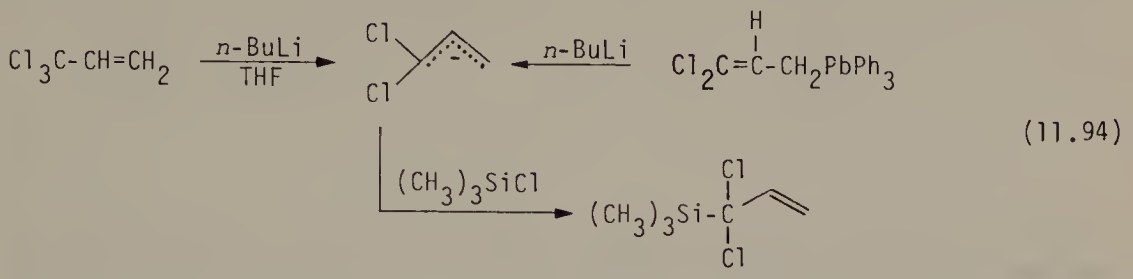


(11.92)



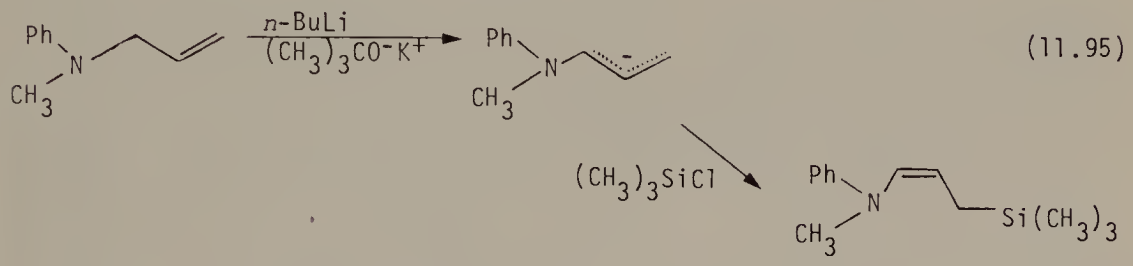
(11.93)

Substituted allylic anions may react regiospecifically with TMS-Cl. For example, α,α-dichloroallyl lithium reacts with TMS-Cl to yield 1,1-dichloro-1-trimethylsilyl-2-propene [93].



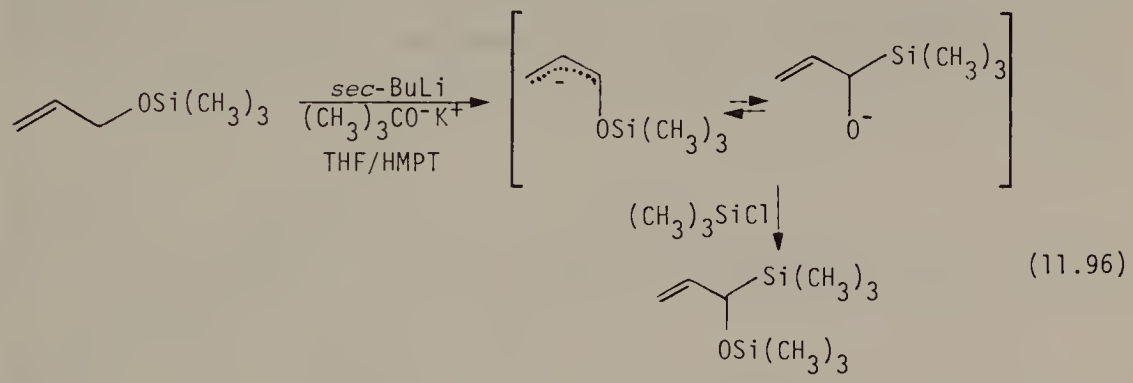
(11.94)

α-(N-methyl-N-phenylamino) allyl anion reacts with TMS-Cl to give 3-trimethylsilylpropenyl-N-methyl aniline [94].



(11.95)

Metallation of allyloxytrimethylsilane with *sec*-butyl lithium in THF/HMPT yields α-trimethylsilyloxyallyl lithium. This undergoes a Brook rearrangement where the trimethylsilyl group migrates from oxygen to the adjacent carbon. This rearrangement converts the allyl anion to an alkoxide anion. Quenching the reaction with TMS-Cl yields α-trimethylsilyloxyallyl trimethylsilane [20].



(11.96)

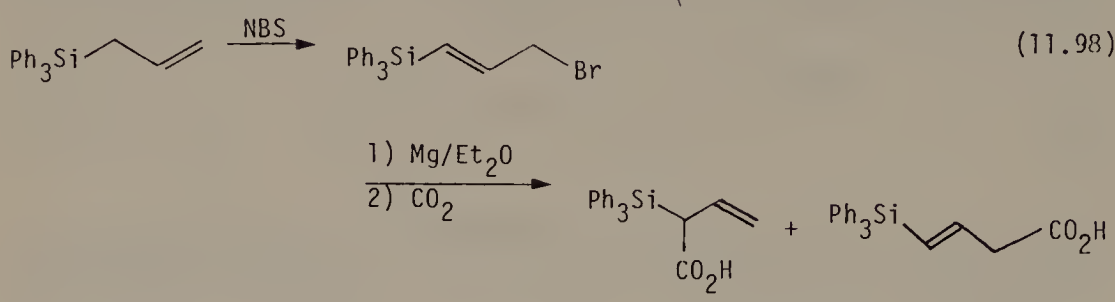
11.5 Silyl Substituted Allylic Anions

The regiospecificity of reactions of silyl substituted allylic anions is influenced by the associated cation. α-Triphenylsilylallyl lithium reacts regiospecifically at the γ position with aldehydes [95, 96], ketones [76–78], methyl iodide [76, 77], or TMS-Cl (Eq. 11.97) [95–97]. However, it reacts at both the α and γ position with carbon dioxide, ethylene oxide, or water [95, 96].

Similar regiospecificity has been observed in the reactions of α-trimethylsilylallyl lithium with ketones [98, 99].

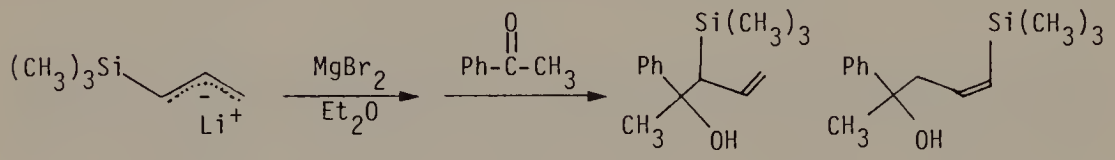
(11.97)

α-Triphenylsilylallyl Grignard reagent reacts with either carbon dioxide or ethylene oxide, predominantly at the α-position but with either benzophenone or TMS-Cl at the γ position.



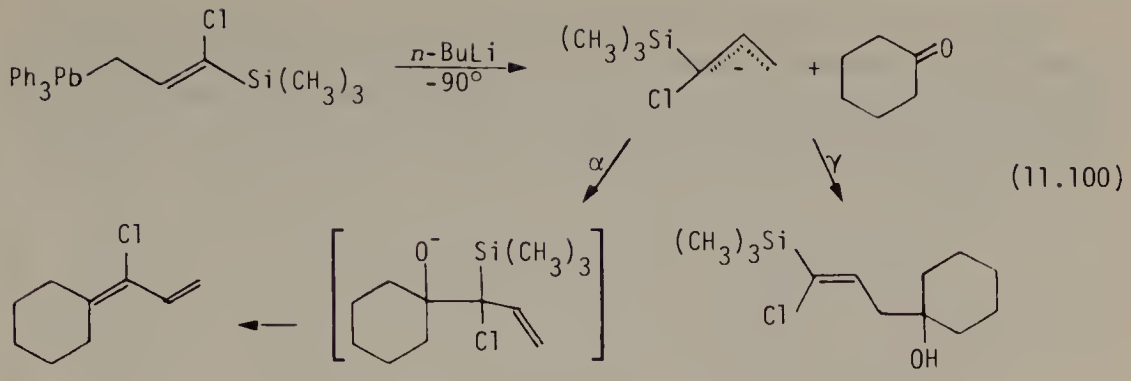
(11.98)

Addition of magnesium bromide to α-trimethylsilylallyl lithium prior to reaction with ketones or aldehydes at −78° alters the regiospecificity of this reagent. The predominant reaction at the α position occurs with ketones to yield 2-trimethylsilylbut-3-en-1-ols. These can be converted to 1,3-dienes by reaction with thionyl chloride. 1,3-Dienes also result from treatment of the corresponding acetate with fluoride ion [100].



(11.99)

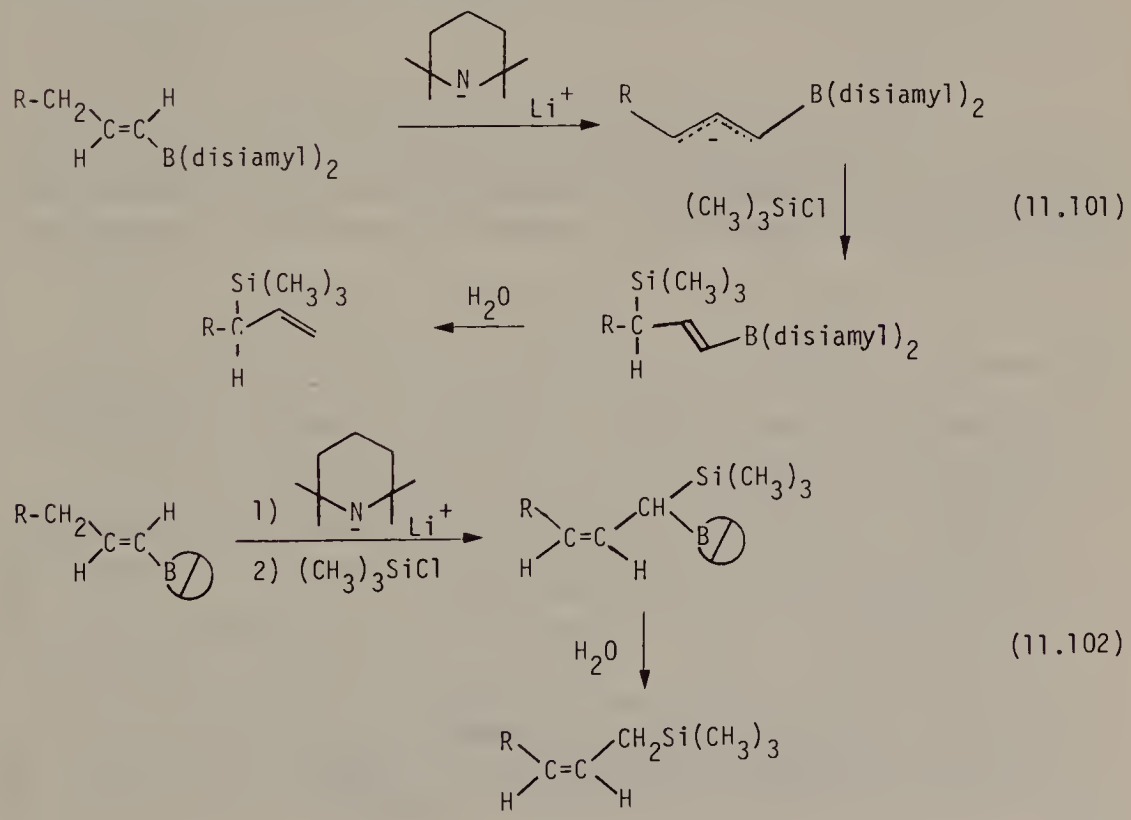
α-Chloro-α-trimethylsilylallyl lithium shows a delicate balance between α and γ reactivity with various substrates. It reacts with methyl iodide at both the α and γ positions to yield a mixture of 2-chloro-2-trimethylsilyl-3-butene and 1-chloro-1-trimethylsilyl-1-butene (4:1). Likewise, it reacts with ketones or aldehydes to yield a mixture of products. Reaction at the α-position yields 2-chloro-1,3-dienes via a Peterson reaction, while reaction at the γ-position yields 4-chloro-4-trimethylsilyl-but-3-en-1-ols [101].



(11.100)

11.6 Boron Substituted Allylic Silanes

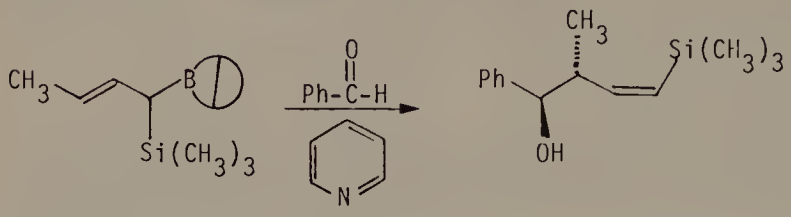
1 Alkynes can be converted specifically either to 3-trimethylsilyl-1-alkenes or to *Z*-2-alkenyltrimethylsilanes. Hydroboration of 1-alkynes with disiamyl borane yields a vinyl borane which can be metallated with lithium 2,2,6,6-tetramethyl-piperidide. This boron stabilized allylic anion reacts regiospecifically with TMS-Cl at the γ-position. This may be due to steric hinderance at the α-position from the bulky disiamyl group (Eq. 11.101) [102]. Likewise, hydroboration of 1-alkynes with 9-BBN yields a vinyl borane. This can be metallated as above to give a boron stabilized allylic anion which reacts specifically with TMS-Cl at the α position, possibly due to the smaller steric size of 9-BBN group (Eq. 11.102) [103]. These vinyl boron bonds can be cleaved by hydrolysis to give allylic silane regiospecifically.



(11.101)

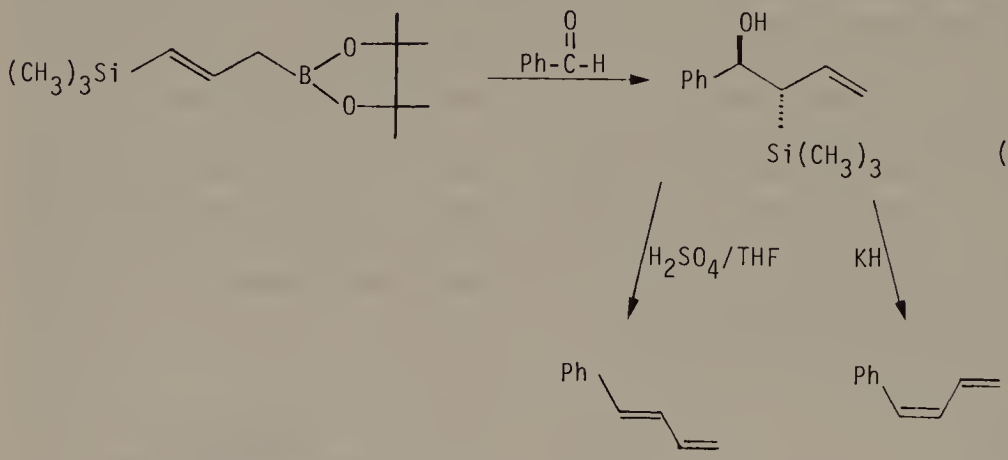
(11.102)

α-Trimethylsilyl crotyl 9-BBN reacts with aldehydes under the influence of pyridine or *n*-butyl lithium to yield homoallylic alcohols in which the stereochemistry of the four consecutive carbon atoms is controlled. This may result from the favored geometry of the six membered cyclic transition state [104].



(11.103)

Alternatively, reaction of pinacol-*E*-1-trimethylsilyl-1-propenyl boronate with aldehydes diastereoselectively yields (±)-(R*, S*) 3-trimethylsilyl 4-hydroxy-1-alkenes. These can be converted selectively to *Z* or *E* dienes [105].



(11.104)

Dimethyl *E*-1-trimethylsilyl-1-propenyl-3-boronate was prepared by reaction of α-trimethylsilylallyl lithium with trimethylborate at −78°. This was converted to pinacol-*E*-1-trimethylsilyl-1-propenyl-3-boronate by treatment with pinacol hydrate.

References

1. Sommer, L.H., Tyler, L.J., Whitmore, F.C.: J. Am. Chem. Soc. *70*, 2872 (1948)
2. Carter, M.J., Fleming, I.: J. Chem. Soc. Chem. Commun. 679 (1976)
3. Coughlin, D.J., Salomon, R.G.: J. Org. Chem. *44*, 3784 (1979)
4. Dunoguès, J., Arréguy, B., Biran, C., Calas, R., Pisciotti, F.: J. Organometal. Chem. *63*, 119 (1973)
5. Fleming, I., Paterson, I.: Synthesis, 446 (1979)
6. Pandy-Szekeres, D., Déléris, G., Picard, J.P., Pillot, J.P., Calas, R.: Tetrahedron Lett. 4267 (1980)
7. Moritz, T., Okamoto, Y., Sakurai, H.: Tetrahedron Lett. 835 (1980)
8. Hosomi, A., Sakurai, H.: Chem. Lett. 85 (1981)
9. Woell, J.B., Boudjouk, P.: J. Org. Chem. *45*, 5213 (1980)
10. Fleming, I., Au-Yeung, B.W.: Tetrahedron, *37*, 13 (1981)

11. Jung, M.E., Blumenkopf, T.A.: Tetrahedron Lett. 3657 (1978)
12. Calas, R., Dunoguès, J., Pillot, J.P., Biran, C., Pisciotti, F., Arréguy, R.: J. Organometal. Chem. *85*, 149 (1975)
13. Pillot, J.P., Dunoguès, J., Calas, R.: Tetrahedron Lett. 1871 (1976)
14. Pillot, J.P., Déléris, G., Dunoguès, J., Calas, R.: J. Org. Chem. *44*, 3397 (1979)
15. Ojima, I., Kumagai, M., Miyazawa, Y.: Tetrahedron Lett. 1385 (1980)
16. Laguerre, M., Dunoguès, J., Calas, R.: Tetrahedron Lett. 57 (1978)
17. Hosomi, A., Saito, M., Sakurai, H.: Tetrahedron Lett. 429 (1979)
18. Hosomi, A., Saito, M., Sakurai, H.: Tetrahedron Lett. 3783 (1980)
19. Ochiai, M., Fujita, E.: Tetrahedron Lett. 4369 (1980)
20. Hosomi, A., Hashimoto, H., Sakurai, H.: J. Org. Chem. *43*, 2551 (1978)
21. Hiroi, K., Chen, L.M.: J. Chem. Soc. Chem. Commun. 377 (1981)
22. Still, W.C., MacDonald, T.L.: J. Org. Chem. *41*, 3620 (1976)
23. Sakurai, H., Imai, T., Hosomi, A.: Tetrahedron Lett. 4045 (1977)
24. Pillot, J.P., Dunoguès, J., Calas, R.: Synthesis, 469 (1977)
25. Grignon-Dubois, M., Pillot, J.P., Dunoguès, J., Duffaut, N., Calas, R.: J. Organometal. Chem. *124*, 135 (1977)
26. Itoh, K., Fukui, M., Kurachi, Y.: J. Chem. Soc. Chem. Commun. 500 (1977)
27. Kelly, L.F., Narula, A.S., Birch, A.J.: Tetrahedron Lett. 871 (1980)
28. O'Boyle, J.E., Nicholas, K.M.: Tetrahedron Lett. 1595 (1980)
29. Au-Yeung, B.W., Fleming, I.: J. Chem. Soc. Chem. Commun. 81 (1977)
30. Sasaki, T., Usuki, A., Ohno, M.: Tetrahedron Lett. 4925 (1978)
31. Sasaki, T., Usuki, A., Ohno, M.: J. Org. Chem. *45*, 3559 (1980)
32. Hughes, L.R., Schmid, R., Johnson, W.S.: Bioorganic Chem. *8*, 513 (1979)
33. Raganathan, S., Raganathan, D., Mehrotra, A.K.: J. Am. Chem. Soc. *96*, 5261 (1974)
34. Abel, E.W., Rowley, R.J.: J. Organometal. Chem. *84*, 199 (1975)
35. Déléris, G., Dunoguès, J., Calas, R.: J. Organometal. Chem. *93*, 43 (1975)
36. Calas, R., Dunoguès, J., Déléris, G., Pisciotti, F.: J. Organometal. Chem. *69*, C15 (1974)
37. Déléris, G., Dunoguès, J., Calas, R.: Tetrahedron Lett. 2449 (1976)
38. Hosomi, A., Sakurai, M.: Tetrahedron Lett. 1295 (1976)
39. Hosomi, A., Endo, M., Sakurai, H.: Chem. Lett. 941 (1976)
40. Hosomi, A., Sakurai, H.: Tetrahedron Lett. 2589 (1978)
41. Wilson, S.R., Phillips, L.R., Natalie, Jr., K.J.: J. Am. Chem. Soc. *101*, 3340 (1979)
42. Kuwajima, I., Tanaka, T., Atsumi, K.: Chem. Lett. 779 (1979)
43. Itoh, A., Oshima, K., Nozaki, M.: Tetrahedron Lett. 1783 (1979)
44. Sarkar, T.K., Andersen, N.H.: Tetrahedron Lett. 3513 (1978)
45. Hosomi, A., Shirahata, A., Sakurai, H.: Tetrahedron Lett. 3043 (1978)
46. Fleming, I., Pearce, A., Snowden, R.L.: J. Chem. Soc. Chem. Commun. 182 (1976)
47. Itoh, K., Fukui, M., Kurachi, Y.: J. Chem. Soc. Chem. Commun. 500 (1977)
48. Itoh, K., Yogo, T., Ishii, Y.: Chem. Lett. 103 (1977)
49. Hosomi, A., Hashimoto, H., Sakurai, H.: Tetrahedron Lett. 951 (1980)
50. Hosomi, A., Saito, M., Sakurai, M.: Tetrahedron Lett. 3783 (1980)
51. Pornet, J.: Tetrahedron Lett. 2049 (1980)
52. Seyferth, D., Pornet, J.: J. Org. Chem. *45*, 1721 (1980)
53. Sakurai, H., Sasaki, K., Hosomi, A.: Tetrahedron Lett. 745 (1981)
54. Hosomi, A., Sakurai, H.: Tetrahedron Lett. 4041 (1977)
55. Hosomi, A., Sakurai, H.: J. Am. Chem. Soc. *99*, 1673 (1977)
56. Pardo, R., Zahra, J.P., Santelli, M.: Tetrahedron Lett. 4557 (1979)

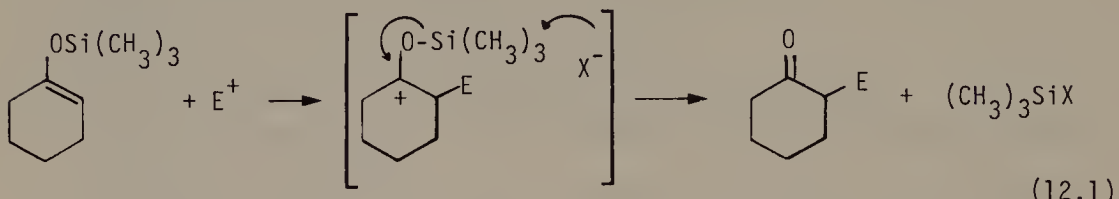
57. Yanami, T., Miyashita, M., Yoshikoshi, A.: J. Chem. Soc. Chem. Commun. 525 (1979)
58. Yanami, T., Miyashita, M., Yoshikoshi, A.: J. Org. Chem. *45*, 607 (1980)
59. Hosomi, A., Kobayashi, M., Sakurai, H.: Tetrahedron Lett. 955 (1980)
60. Knapp, S., O'Connor, U., Mobilio, D.: Tetrahedron Lett. 4557 (1980)
61. Hosomi, A., Hashimoto, H., Sakurai, H.: Chem. Lett. 245 (1979)
62. Jellal, A., Santelli, M.: Tetrahedron Lett. 4487 (1980)
63. Ochiai, M., Arimoto, M., Fujita, E.: Tetrahedron Lett. 1115 (1981)
64. Ojima, I., Kumagai, M.: Chem. Lett. 575 (1978)
65. Ojima, I., Miyazawa, Y., Kumagai, M.: J. Chem. Soc. Chem. Commun. 927 (1976)
66. Hartman, G.D., Traylor, T.G.: Tetrahedron Lett. 939 (1975)
67. Ochiai, M., Arimoto, M., Fujita, E.: J. Chem. Soc. Chem. Commun. 460 (1981)
68. Déléris, G., Dunoguès, J., Calas, R.: J. Organometal. Chem. *116*, C45 (1976)
69. Au-Yeung, B.W., Fleming, I.: J. Chem. Soc. Chem. Commun. 81 (1977)
70. Trost, B.M., Chan, D.M.T.: J. Am. Chem. Soc. *101*, 6429 (1979)
71. Trost, B.M., Chan, D.M.T.: J. Am. Chem. Soc. *101*, 6432 (1979)
72. Hosomi, A., Saito, M., Sakurai, H.: Tetrahedron Lett. 355 (1980)
73. Slutsky, J., Kwart, H.: J. Am. Chem. Soc. *95*, 8678 (1973)
74. Fleming, I., Percival, A.: J. Chem. Soc. Chem. Commun. 681 (1976)
75. Hurd, D.T.: J. Am. Chem. Soc. *67*, 1813 (1945)
76. Rhone-Poulenc, French Patent 2,051,903 (1969)
77. Furuya, N., Sukawa, T.: J. Organometal. Chem. *96*, C-1 (1975)
78. Lefort, M., Simmonet, C., Birot, M., Déléris, G., Dunoguès, J., Calas, R.: Tetrahedron Lett. 1857 (1980)
79. Matsumoto, H., Yako, T., Nagashima, S., Motegi, T., Nagai, Y.: J. Organometal. Chem. *148*, 97 (1978)
80. Watanabe, H., Saito, M., Sutou, N., Nagai, Y.: J. Chem. Soc. Chem. Commun. 617 (1981)
81. Sakurai, H., Hosomi, A., Kumada, M.: Tetrahedron Lett. 2469 (1968)
82. Matsumoto, H., Shono, K., Wada, A., Matsubara, I., Watanabe, H., Nagai, Y.: J. Organometal. Chem. *199*, 185 (1980)
83. Laguerre, M., Dunoguès, J., Calas, R., Duffaut, N.: J. Organometal. Chem. *112*, 49 (1976)
84. Biran, C., Duffaut, N., Dunoguès, J., Calas, R.: J. Organometal. Chem. *91*, 279 (1975)
85. Tzeng, D.J., Weber, W.P.: J. Org. Chem. *46*, 281 (1981)
86. Déléris, G., Kowalski, J., Dunoguès, J., Calas, R.: Tetrahedron Lett. 4211 (1977)
87. Seyferth, D., Wursthorn, K.R., Lim, T.F.O., Sepelak, D.J.: J. Organometal. Chem. *181*, 293 (1979)
88. Whitmore, F.C., Sommer, L.H.: J. Am. Chem. Soc. *68*, 481 (1946)
89. Cooper, G.D., Prober, M.: J. Am. Chem. Soc. *76*, 3943 (1954)
90. Eaborn, C., Jeffrey, J.C.: J. Chem. Soc. 4266 (1954)
91. Gopalan, A., Moerck, R., Magnus, P.: J. Chem. Soc. Chem. Commun. 548 (1979)
92. Hosomi, A., Shirahata, A., Sakurai, H.: Chem. Lett. 901 (1978)
93. Seyferth, D., Murphy, G.J., Woodruff, R.A.: J. Organometal. Chem. *141*, 71 (1977)
94. Ahlbrecht, H., Eichler, J.: Synthesis, 672 (1974)
95. Corriu, R.J.P., Massé, J., Samate, D.: J. Organometal. Chem. *93*, 71 (1975)
96. Corriu, R.J.P., Massé, J.: J. Organometal. Chem. *57*, C5 (1973)

97. Corriu, R.J.P., Lanneau, G.F., Leclercq, D., Samate, D.: J. Organometal. Chem. *144*, 155 (1978)
98. Ayalon-Chass, D., Ehlinger, E., Magnus, P.: J. Chem. Soc. Chem. Commun. 772 (1977)
99. Ehlinger, E., Magnus, P.: Tetrahedron Lett. 11 (1980)
100. Lau, P.W.K., Chan, T.H.: Tetrahedron Lett. 2383 (1978)
101. Seyferth, D., Mammarella, R.E.: J. Organometal. Chem. *156*, 279 (1978)
102. Kow, R., Rathke, M.W.: J. Am. Chem. Soc. *95*, 2715 (1973)
103. Yatagi, H., Yamamoto, Y., Maruyama, K.: J. Am. Chem. Soc. *102*, 4548 (1980)
104. Yamamoto, Y., Yatagai, H., Maruyama, K.: J. Am. Chem. Soc. *103*, 3229 (1981)
105. Tsai, D.J.S., Matteson, D.S.: Tetrahedron Lett. 2751 (1981)
106. Tsunoda, T., Suzuki, M., Noyori, R.: Tetrahedron Lett. 71 (1980)
107. Fleming, I., Pearce, A.: J. Chem. Soc. Perkin *I*, 251 (1981)
108. Trost, B.M., Vincent, J.E.: J. Am. Chem. Soc. *102*, 5680 (1980)

12 Electrophilic Reactions of Silyl Enol Ethers

12.1 Introduction

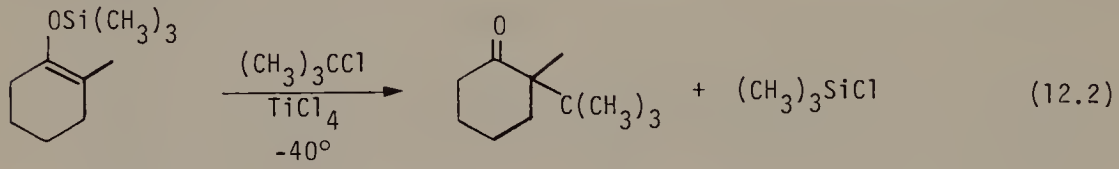
The electron rich C–C double bond of silyl enol ethers is extremely susceptible to attack by electrophiles. Electrophiles regiospecifically attack the C–C double bond of trimethylsilyl enol ethers to yield a trimethylsilyloxy stabilized carbocation. Usually, the nucleophilic anion associated with the electrophile attacks the silyl center of this intermediate to yield a substituted ketone in which the electrophile is bonded to the α position.



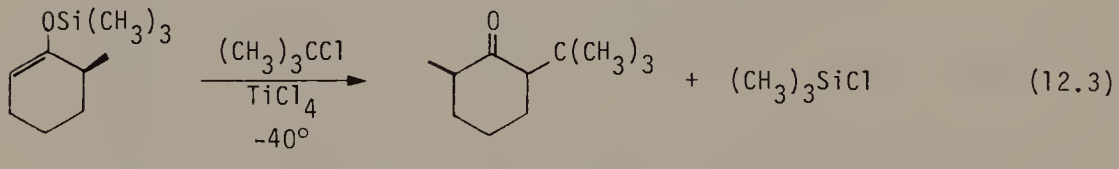
(12.1)

12.2 Carbocations

Tertiary alkyl halides which ionize to carbocations on treatment with a Lewis acid, such as $TiCl_4$, react regiospecifically with trimethylsilyl enol ethers to yield α-*t*-alkyl ketones and TMS-X [1].



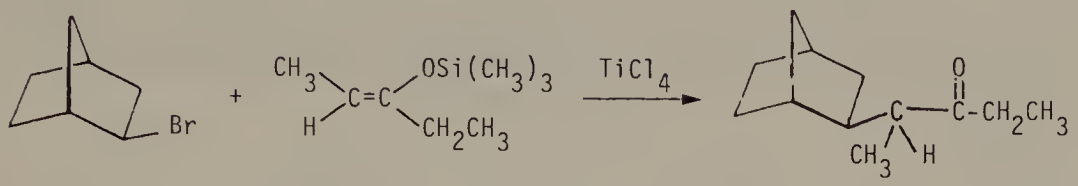
(12.2)



(12.3)

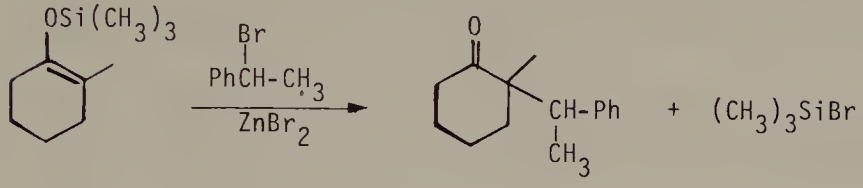
If one considers the problems associated with alkylation α to a carbonyl group, trimethylsilyl enol ethers and enolate anions compliment each other. Enolate anions react efficiently with primary alkyl halides whereas trimethyl-

silyl enol ethers react with tertiary alkyl halides [2, 3, 4]. Enolate anions usually react with alkyl halide by an S_n2 process and hence yield products with inversion of configuration. By comparison, reactive alkyl halides, which are known to solvolyze stereoselectively by S_n1 processes due to anchimeric assistance, react with silyl enol ethers in the presence of $TiCl_4$ with retention of configuration [5].



(12.4)

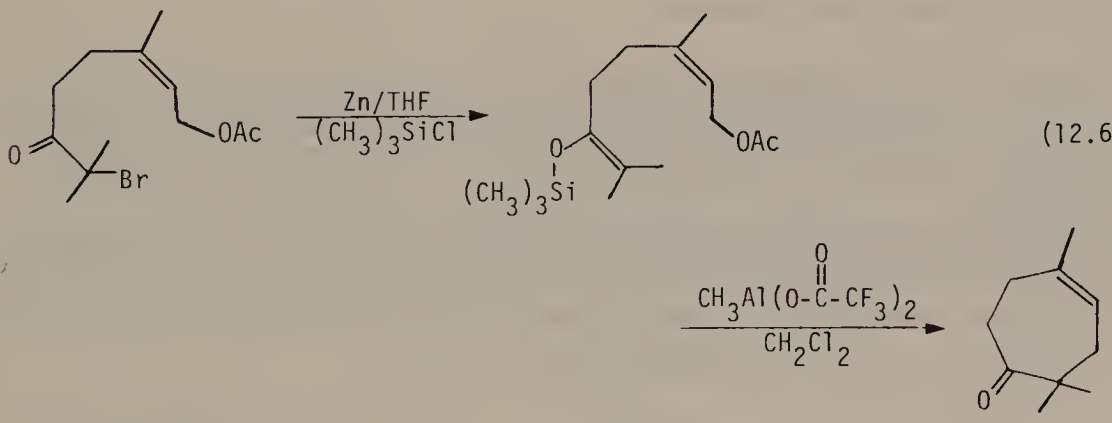
Secondary benzylic and allylic halides react with trimethylsilyl enol ethers in the presence of zinc bromide [6].



(12.5)

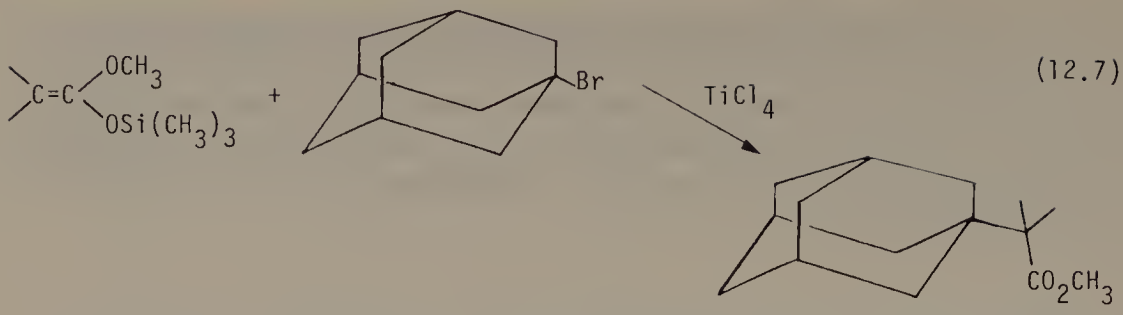
Cumyl chloride and trimethylsilyl enol ethers react in the presence of zinc chloride to yield α-cumyl ketones [7].

The formation of 2,2,5-trimethylcyclohept-4-en-1-one by intramolecular electrophilic cyclization of an allylic carbocation with a trimethylsilyl enol ether is an interesting example. The trimethylsilyl enol ether was generated regiospecifically by reduction of the corresponding α- bromo ketone with zinc dust in the presence of TMS-Cl [8].



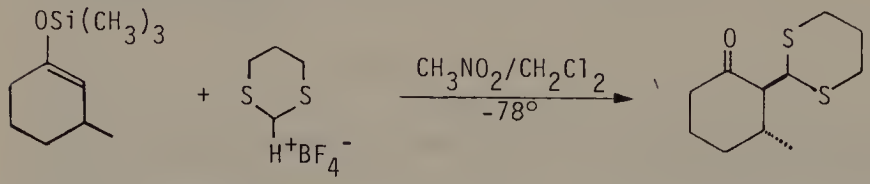
(12.6)

Alkyl trimethylsilyl ketene acetals also react with tertiary alkyl halides in the presence of $TiCl_4$ to yield α-*t*-alkyl esters [9, 10].



(12.7)

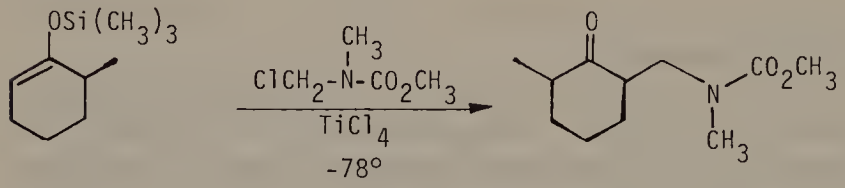
Trimethylsilyl enol ethers react regiospecifically with 1,3-dithienium tetrafluoroborate to yield α-(1,3-dithianyl) ketones [19].



(12.8)

The 1,3-Dithienium cation also reacts with 1-trimethylsilyloxy-1,3-dienes or 1-alkoxy-1-trimethylsilyloxy-1,3-dienes predominantly at the 4-position. This procedure permits the introduction of a masked carbonyl functional group [20].

Regiospecific uriedoalkylation of ketones has been achieved by reaction of methyl (N-chloromethyl, N-methyl) carbamate with trimethylsilyl enol ethers in the presence of $TiCl_4$ [21].

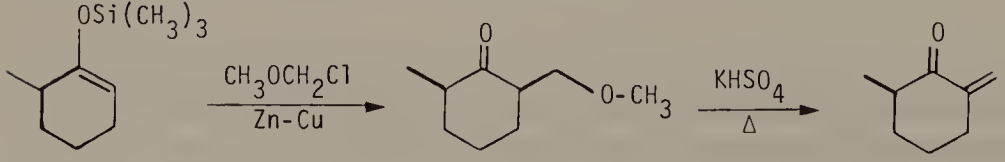


(12.9)

12.3 α-Methylene Ketones

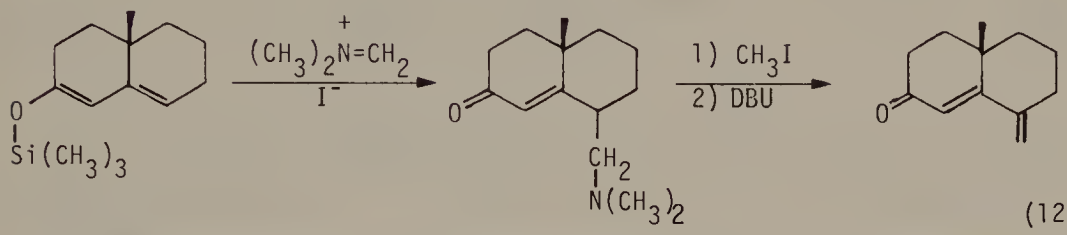
There has been considerable interest in the preparation of α-methylene carbonyl compounds since many of these have high biological activity. Three methods to prepare such compounds based on silyl enol ethers have been reported.

Electrophilic attack by chloromethyl methyl ether, in the presence of an activated zinc couple (Zu−Cu) [11] or $TiCl_4$ [6], on trimethylsilyl enol ethers yields the corresponding α-methoxymethyl ketone. Pyrolysis of these with $KHSO_4$ at 160–180°C gives the α methylene ketone.



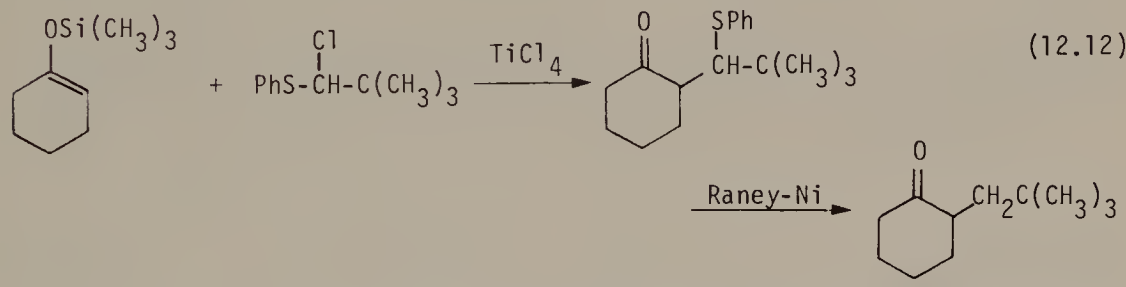
(12.10)

Likewise, trimethylsilyl enol ethers react regiospecifically with dimethyl(methylene)ammonium iodide [12] to yield α-dimethylaminomethyl ketones [13, 14]. Similar results have been obtained by treating silyl enol ethers with a combination of chloroiodomethane and N,N,N′,N′-tetraethyldiaminomethane in DMSO [15]. Further reaction with methyl iodide converts the tertiary amine to an alkyl trimethylammonium iodide which undergoes elimination on treatment with DBU to yield the desired α-methylene ketone [14]. 1-Trimethylsilyloxy-1,3-dienes react regiospecifically with dimethyl(methylene)ammonium iodide at the γ rather than the α position.



(12.11)

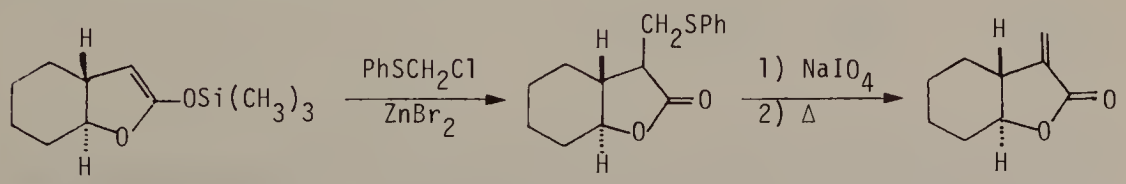
We have previously compared enolate anions, which react readily with primary alkyl halides by S_n2 displacement reactions, with trimethylsilyl enol ethers, which react easily with benzylic, allylic and tertiary alkyl halides. The use of α-chloroalkyl phenyl sulfides overcomes this limitation of trimethylsilyl enol ethers. α-Chloroalkyl phenyl sulfide reacts with trimethylsilyl enol ethers, in the presence of $TiCl_4$ or zinc bromide, to yield α-(α′-phenylthioalkyl) ketones. Raney nickel desulfurization removes the phenylthio group to yield an α-alkyl ketone [16, 17].



(12.12)

Oxidation of these with sodium periodate yields a sulfoxide which undergoes facile elimination on heating to yield α-alkylidene ketones [16, 17].

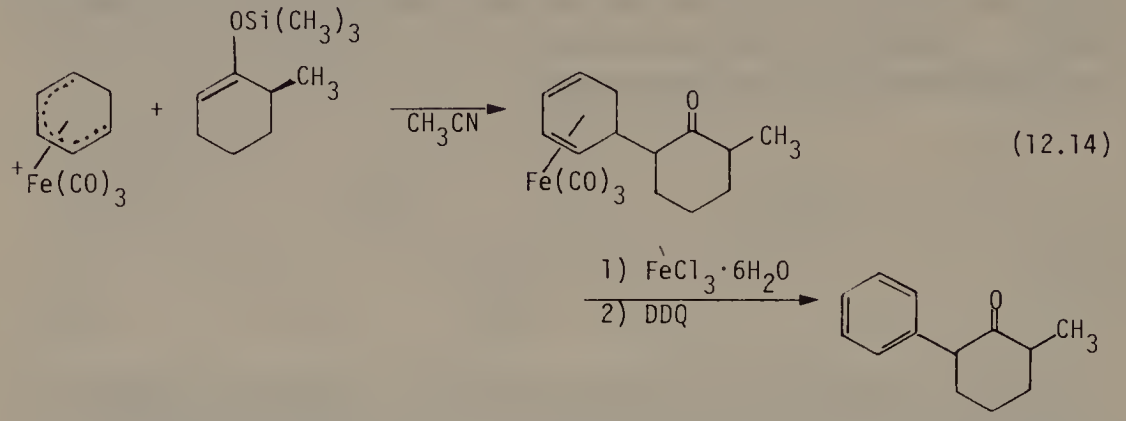
α-Methylene lactones are a key feature in many cytotoxic sesquiterpenes. Trimethylsilyl ketene acetals of lactones can be prepared by treatment of lactones with LDA followed by addition of TMS-Cl. Chloromethyl phenyl sulfide and zinc bromide react with lactone trimethylsilyl ketene acetals to yield α-phenylthiomethyl lactones [18].



(12.13)

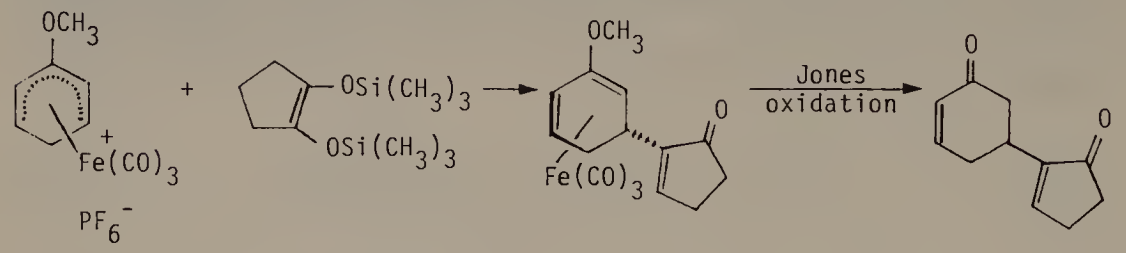
12.4 Cationic Iron Tricarbonyl Complexes

Trimethylsilyl enol ethers react with cationic cyclohexadienyl iron tricarbonyl iron complexes as outlined below. Removal of the iron tricarbonyl group by treatment with ferric chloride and dehydrogenation with DDQ gives α-aryl ketones [22].



(12.14)

1,2 *bis*(Trimethylsilyloxy) cyclopentene reacts with the cationic 3-methoxy-cyclohexa-2,4-dien-1-yl iron tricarbonyl hexafluorophosphate complex to yield after oxidation 5-(2′-cyclopentenone) cyclohex-2-enone [23].



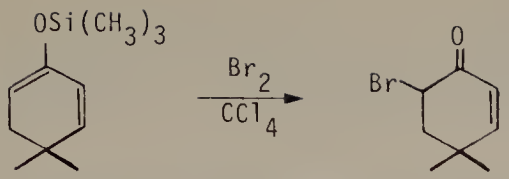
(12.15)

12.5 Halogens

Halogens react regiospecifically with trimethylsilyl enol ethers to yield α-halo ketones and TMS-X. Trimethylsilyloxycyclohexene reacts with chlorine, [24, 25] anhydrous cupric chloride or ferric chloride [26] to yield α-chloro cyclohexanone. Bromine [24, 25], cyanogen bromide [24], or NBS [27, 28] reacts with trimethylsilyloxycyclohexene to yield α-bromo cyclohexanone.

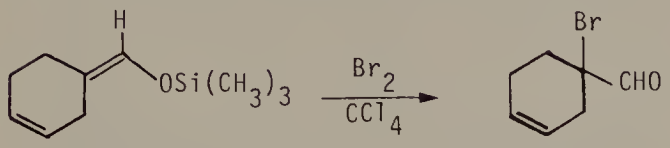
(12.16)

2-Trimethylsilyloxy-1,3-dienes react with bromine preferentially at the C–C double bond of the trimethylsilyl enol ether [29].



(12.17)

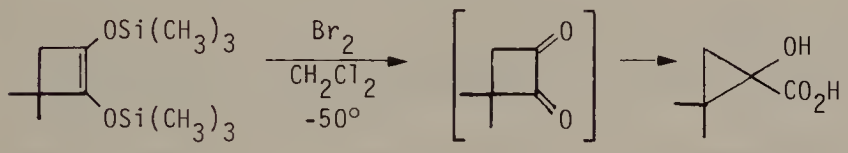
α-Bromo aldehydes can be prepared by reaction of appropriate trimethylsilyl enol ethers with bromine in CCl_4 [28, 29].



(12.18)

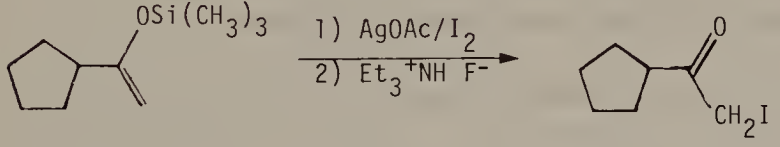
1,3-*bis*(Trimethylsilyloxy)-1-methoxy-1,3-butadiene reacts with one equivalent of bromine to yield methyl-4-bromo-3-keto butanoate. Apparently, a trimethylsilyl enol ether is more reactive than the alkyl trimethylsilyl ketene acetal [30].

Bromine reacts with 1,2-*bis*(trimethylsilyloxy)alkenes to yield 1,2-diketones [31]. 1,2-*bis*(Trimethylsilyloxy)cyclobutenes react with bromine to yield 1,2-cyclobutanediones which undergo a spontaneous benzylic acid rearrangement to give α-hydroxy cyclopropane acids [32].



(12.19)

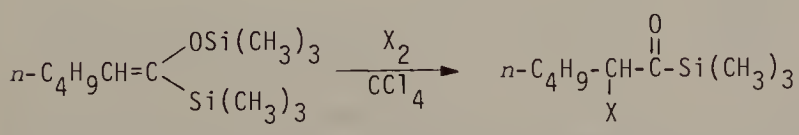
Treatment of trimethylsilyl enol ethers sequentially with silver acetate and iodine followed by triethylammonium fluoride yields α-iodo ketones. Direct reaction of trimethylsilyl enol ethers with iodine is not successful [38].



(12.20)

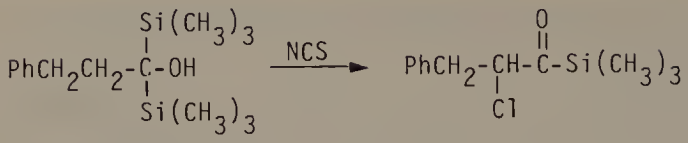
12.6 α-Halo Acyl Silanes

α-Trimethylsilyl trimethylsilyl enol ethers react with bromine or chlorine in CCl_4 to yield α-bromo or α-chloro acylsilanes respectively [33].



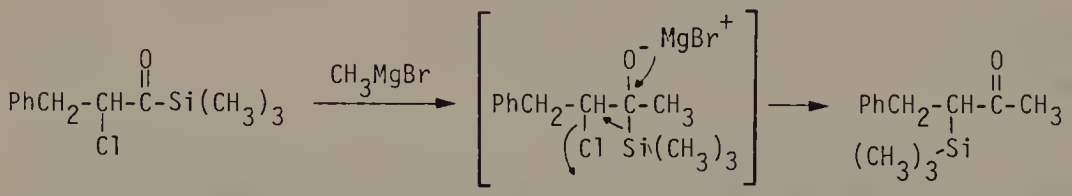
(12.21)

α-Halo acylsilanes can also be prepared by treatment of 1,1-*bis*(trimethylsilyl) alkan-1-ols with NBS or NCS [34].



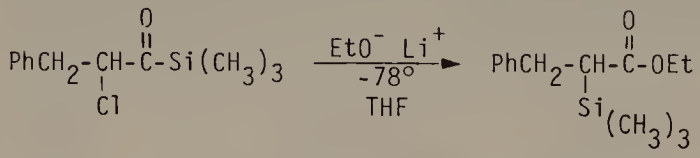
(12.22)

α-Halo acyltrimethylsilanes react with Grignard reagents to yield β-keto-alkyltrimethylsilanes. These undergo reduction to β-hydroxyalkyltrimethyl-silanes if the Grignard reagent possesses a β-hydrogen [35].



(12.23)

In a similar manner, α-halo acyltrimethylsilanes react with lithium alkoxides to yield α-trimethylsilyl esters [36].

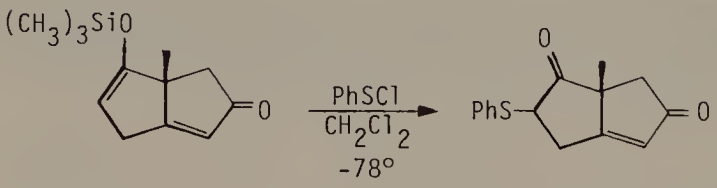


(12.24)

α-Chloro acyltrimethylsilanes react with lithium enolates of ketones to yield α-trimethylsilyl 1,3-diketones [37].

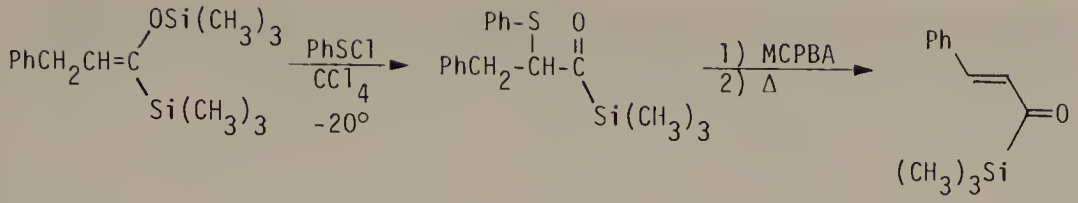
12.7 Pseudo Halogens, Sulfenyl and Selenyl Halides

A variety of pseudo halogens react with trimethylsilyl enol ethers. Thiocyanogen reacts with 3,3-dimethyl-2 trimethylsilyloxy-1-butene to yield 3,3-dimethyl-1-thiocyanoto-2-butanone [24]. Phenylsulfenyl chloride reacts with trimethylsilyl enol ethers to yield α-phenylthio ketones [39, 40].



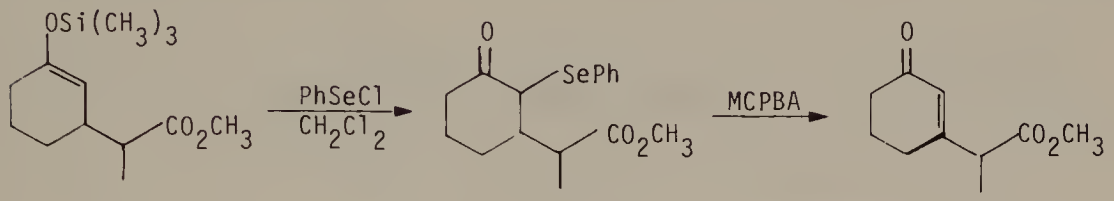
(12.25)

Phenylselenyl chloride or bromide reacts with trimethylsilyl enol ethers to ethers to yield α-phenylthio acyltrimethylsilanes. Oxidation of the sulfide to a sulfoxide with MCPBA followed by heating gives α,β-unsaturated acyltri-methylsilanes [41].



(12.26)

Phenylselenyl chloride or bromide reacts with trimethylsilyl enol ethers to yield α-phenylseleno ketones. Oxidation of the selenium to a selenoxide by MCPBA or hydrogen peroxide leads to facile *syn*-elimination of phenyl selenous acid. This converts the trimethylsilyl enol ether into an α,β-unsaturated ketone [42, 43] (see Chapter 13).

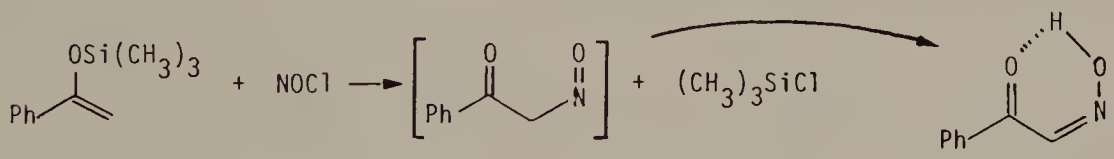


(12.27)

Carbon tetrachloride, carbon tetrabromide, trichloroacetonitrile or ethyl trichloroacetate add to trimethylsilyl enol ethers under catalysis by cuprous chloride [44].

12.8 Nitrosonium and Nitronium Cations

Nitrosyl chloride reacts with trimethylsilyl enol ethers to yield TMS-Cl and an α-nitroso carbonyl intermediate. 1,3-Tautomerization of a proton from carbon to oxygen yields α-oximino ketones. In those cases where there is no α-hydrogen, α-nitroso ketones are obtained [45].

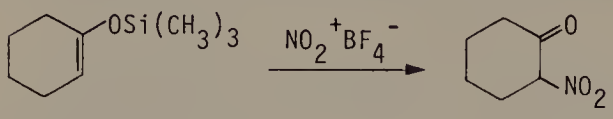


(12.28)

Alkyl trimethylsilyl ketene acetals also react with nitrosyl chloride to yield α-oximino esters which may be converted to α-amino acids.

(12.29)

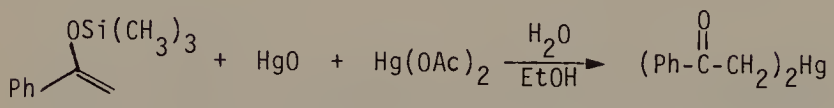
Nitronium tetrafluoroborate reacts at low temperature with trimethylsilyl enol ethers to yield α-nitroketones [46].



(12.30)

12.9 Mercuric Salts

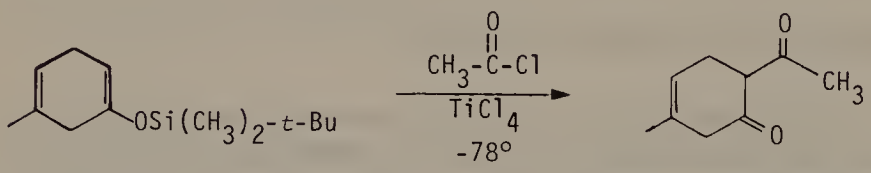
A mixture of mercuric acetate and mercuric oxide reacts with trimethyl silyl enol ethers to yield α-mercuri-ketones [47, 48].



(12.31)

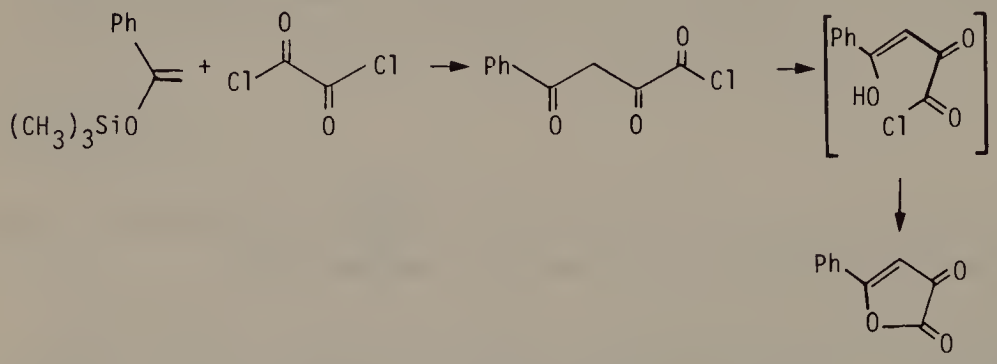
12.10 Acid Chlorides

The combination of an acid chloride and $TiCl_4$ reacts with trimethylsilyl enol ethers to yield 1,3-diketones. In some cases $TiCl_4$ is not necessary [30, 49, 50].



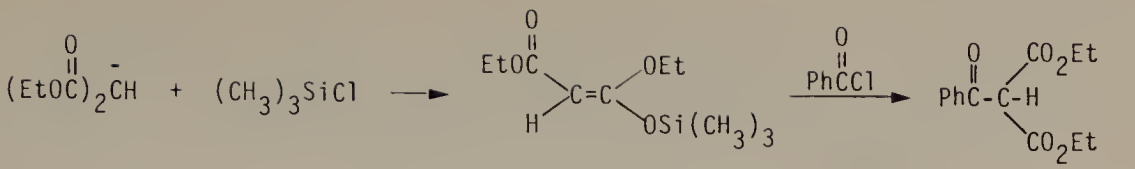
(12.32)

The reaction of trimethylsilyl enol ethers with oxalyl chloride provides the first general synthesis of 2,3-furandiones [51].



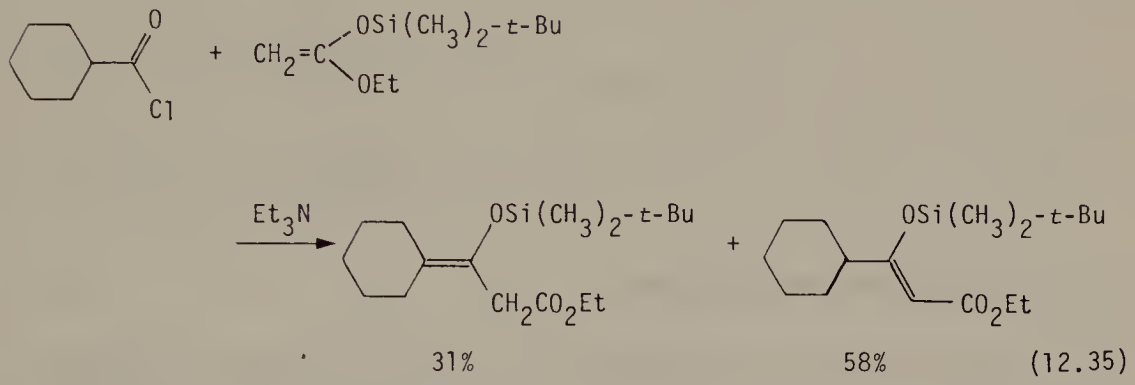
(12.33)

3-Carboethoxy-1-ethyl-1-trimethylsilyl ketene acetal reacts readily with acid chlorides to yield diethyl acul malonates [52].



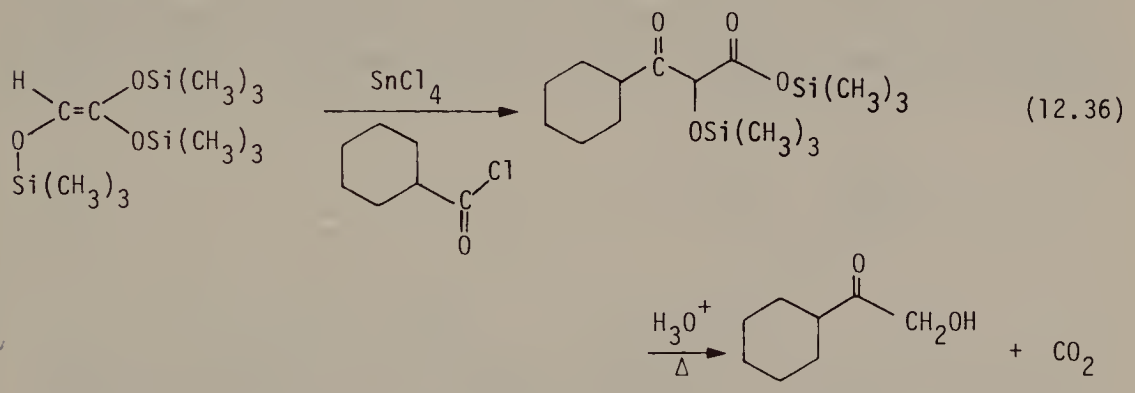
(12.34)

Ethyl *t*-butyldimethylsilyl ketene acetal reacts with acid chlorides in the presence of triethylamine to yield *t*-butyldimethylsilyl enol ethers of β-keto esters [53, 54].



(12.35)

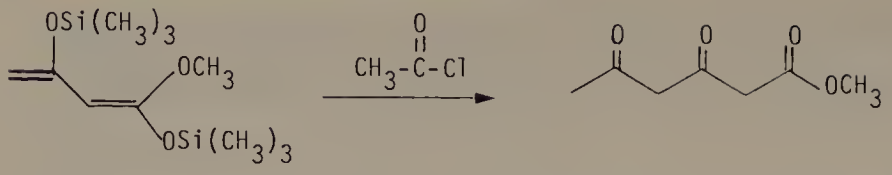
tris-(Trimethylsilyloxy)ethylene reacts with acid chlorides under $SnCl_4$ catalysis or heat to yield trimethylsilyl α-trimethylsilyloxy-β-keto esters. These can be hydrolyzed to α-hydroxy-β-keto acids which undergo decarboxylation to yield α-hydroxy ketones. This transformation has been previously carried out by reaction of acid chlorides with an excess of diazomethane. *tris*-(Trimethylsilyloxy)ethylene has been prepared from α-hydroxy acetic acid [55].



(12.36)

2-Hetero substituted *bis*(trimethylsilyl)ketene acetals react similarly with acid chlorides to yield α-hetero methyl ketones. For example, 2-methylthio-1,1-*bis*(trimethylsilyloxy)ethylene reacts with acid chlorides to yield after hydrolysis and decarboxylation, α-methylthiomethyl ketones [56].

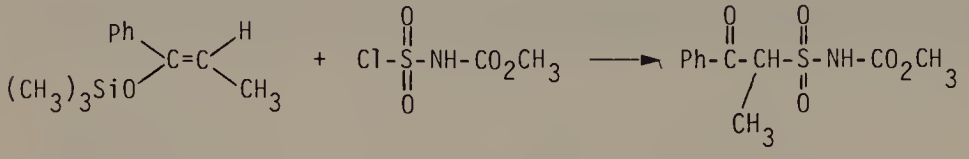
1,3-*bis*(Trimethylsilyloxy)-1-methoxy-1,3-butadiene reacts with acetyl chloride to yield methyl hexa-3,5-dionoate [30].



(12.37)

Acetyl cyanide reacts with trimethylsilyl enol ethers and $TiCl_4$ to yield β-cyano-β-hydroxy ketones [57].

Sulfonyl chlorides [58] or carbomethoxylsulfamoyl chlorides [59] react with trimethylsilyl enol ethers to yield β-keto sulfones or β-keto carbomethoxy sulfonamides, respectively.

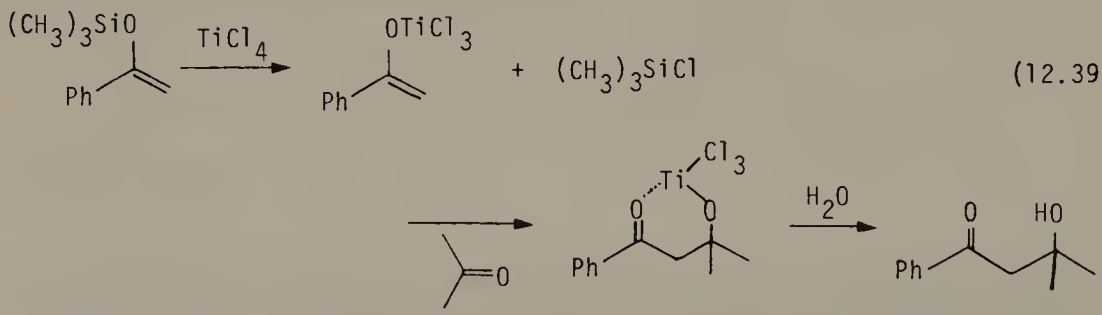


(12.38)

12.11 Aldehydes and Ketones

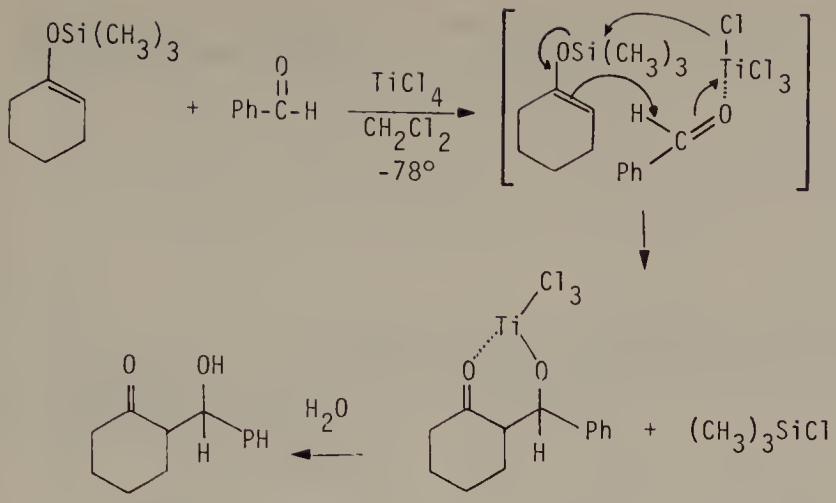
The specific cross Aldol condensation of two different aldehydes or ketones is potentially an extremely valuable synthetic reaction [60, 61]. Unfortunately, the formation of self-condensation, as well as, di- and polycondensation products frequently limits the utility of this reaction. The reaction of trimethylsilyl enol ethers with ketones or aldehydes, facilitated by $TiCl_4$ reported by Mukaiyama, provides a solution to this problem. The reaction requires a stoichiometric amount of $TiCl_4$ and methylene chloride as solvent.

Other Lewis acids, such as $SnCl_4$, $BF_3 \cdot OEt_2$, or boron trichloride, are less effective. The reaction proceeds extremely rapidly with aldehydes at $-78°$, whereas with ketones the reaction is best run at $0°$. This reaction may occur by interaction of $TiCl_4$ with the silyl enol ether to yield TMS-Cl and a trichloro titanium enol ether, which in turn reacts with the ketone or aldehyde to give the cross Aldol product [62].



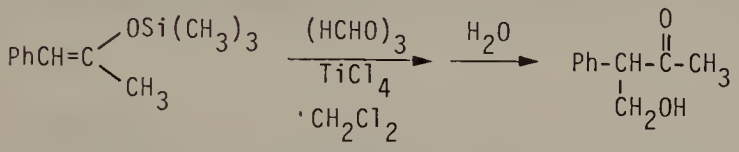
(12.39)

An alternative possibility is that $TiCl_4$ coordinates to the carbonyl oxygen of ketone or aldehyde making it highly susceptible to nucleophillic attack by the electron rich C–C double bond of the trimethylsilyl enol ether. A cyclic transition state leading directly to products has been suggested.



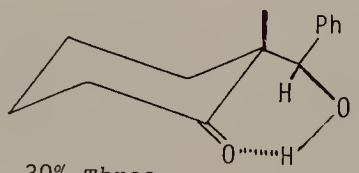
(12.40)

Cross Aldol condensation reactions between silyl enol ethers and formaldehyde (trioxane) are successful.

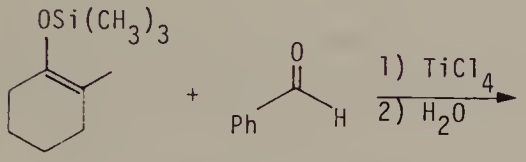


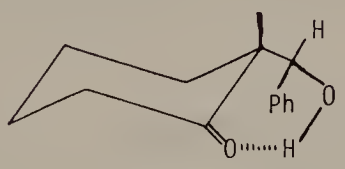
(12.41)

Isomeric trimethylsilyl enol ethers undergo regiospecific cross Aldol condensation reactions [63].



30% *Threo*



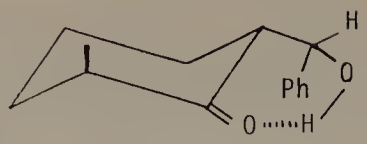


(12.42)

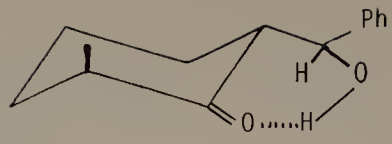
29% *Erythro*

In cross Aldol reactions zirconium enolates give a higher *erythro* to *threo* ratio of β-hydroxy ketones than do trimethylsilyl enol ethers [64].

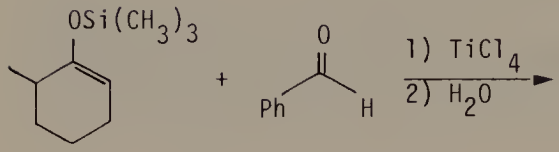
Dialkyl boron enolates also provide greater stereo and regiochemical control than do silyl enol ethers [65]. *Z*-Trimethylsilyl enol ethers react with di-*n*-butyl boranyl trifluoromethane sulfonate to yield trimethylsilyl trifluoromethane sulfonate and the corresponding di-*n*-butyl boron enolate stereospecifically. Removal of solvent and the volatile trimethylsilyl trifluoro-



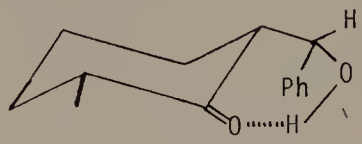
2% Axial *Erythro*



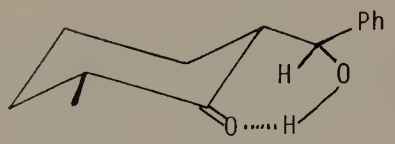
55% Axial *Threo*



(12.43)

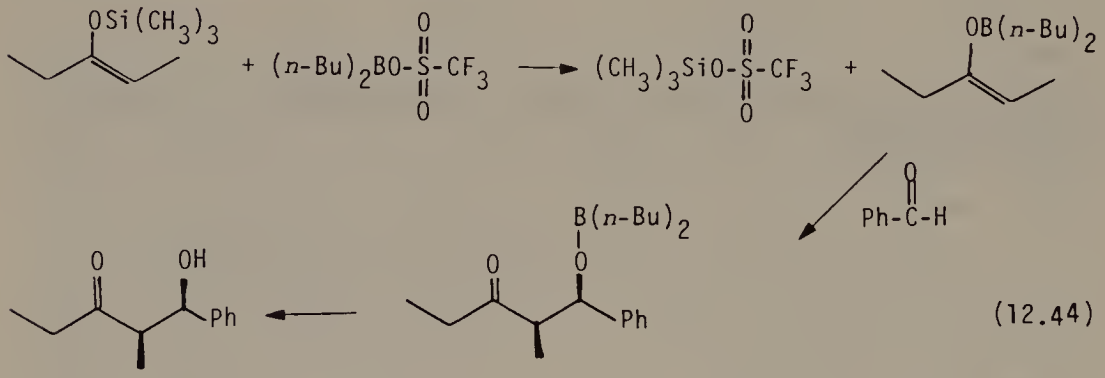


20% Equitorial *Threo*



% Equitorial *Erythro*

methane sulfonate prior to reaction of the di-*n*-butyl boron enolate with benzaldehyde at −78° yields cross Aldol products with high stereospecificity (*erythro* : *threo* 95 : 5) [66, 67].

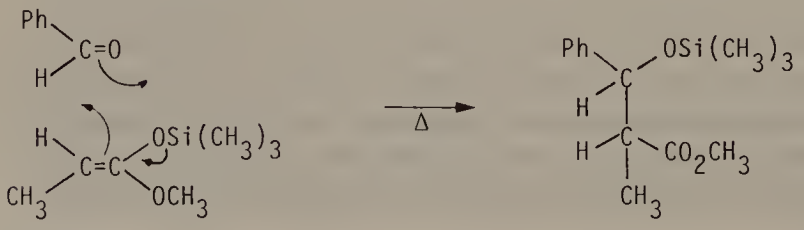


(12.44)

1-Trimethylsilyloxycyclohexene reacts with 9-bromo-9-borabicyclo [3,3,1] nonane to yield the corresponding boron enolate and TMS-Br. Such dialkyl boron enolates react with benzaldehyde to yield cross Aldol products [68].

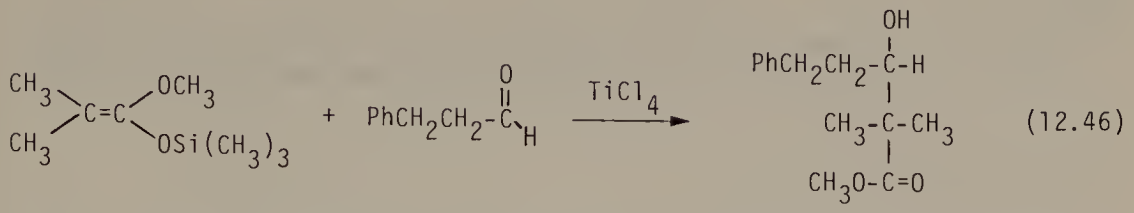
12.12 Silyl-Reformatsky

Alkyl trimethylsilyl ketene acetals and *bis*-(trimethylsilyl)ketene acetals undergo a slow thermal reaction with aromatic aldehydes to yield β-trimethylsilyloxy esters [69, 70].



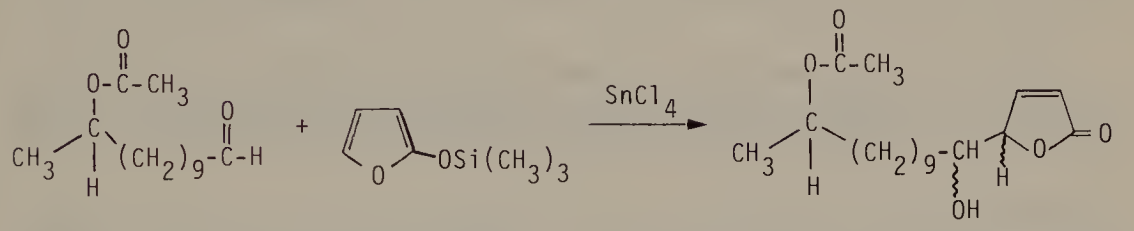
(12.45)

Silyl-Reformatsky reactions can be carried out under much milder conditions with $TiCl_4$ catalysis [71].



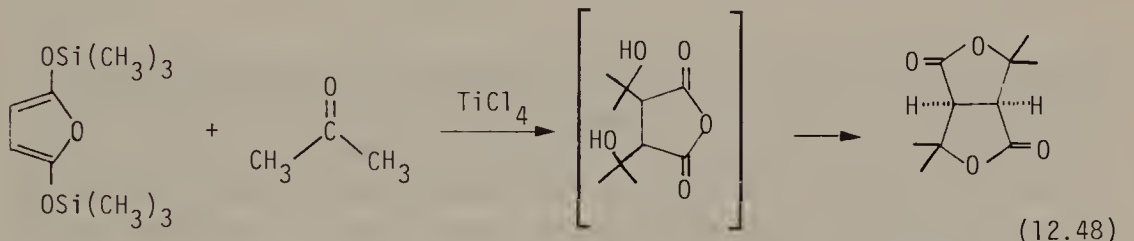
(12.46)

The reaction of 2-trimethylsilyloxy furans with aldehydes under the influence of $SnCl_4$ has been utilized in the synthesis of the macrolide antibiotic (±) -A26771B [72].



(12.47)

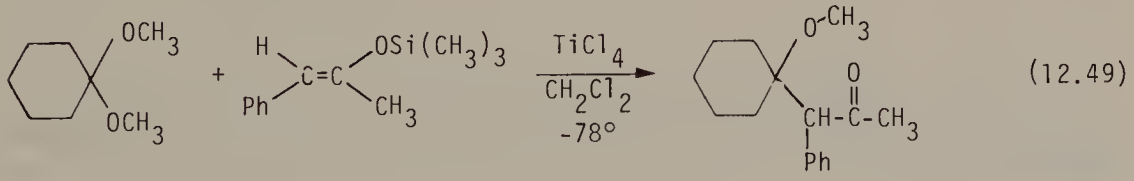
The cross Aldol reaction of 2,5-*bis*(trimethylsilyloxy) furan with ketones or aldehydes permits the facile synthesis of *bis*-lactone ligands [73].



(12.48)

12.13 Acetals and Ketals

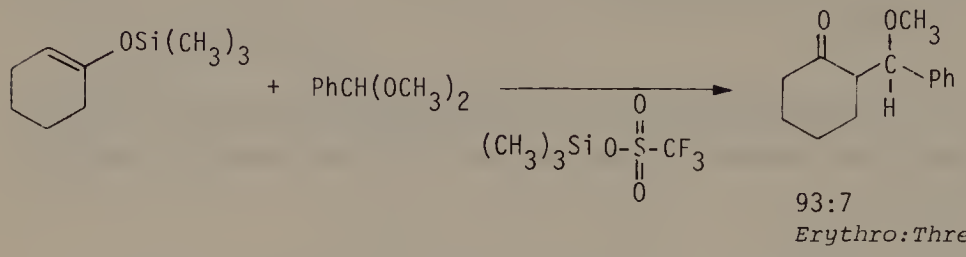
Trimethylsilyl enol ethers also undergo cross Aldol reactions with acetals, ketals, or trimethyl ortho formate activated by $TiCl_4$ to yield β-alkoxy ketones or β-keto acetals, respectively. It seems probable that these reactions proceed by $TiCl_4$ promoted ionization of a C–O bond of the acetal to yield an alkoxy stabilized carbocation which attacks the trimethylsilyl enol ether [74].



(12.49)

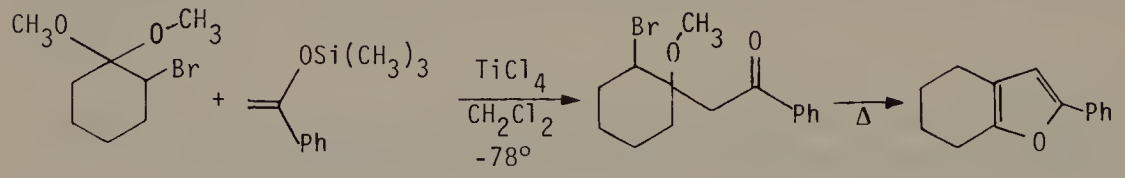
2-Trimethylsilyloxy furan reacts as a silyl enol ether with ketals or triethyl ortho acetate under Lewis acid activation to yield 4-substituted-2-buten-4-olides [75].

Similarly, reactions of trimethylsilyl enol ethers with acetals have been carried out with catalysis by trimethylsilyl trifluoromethane sulfonate [76–78].



(12.50)

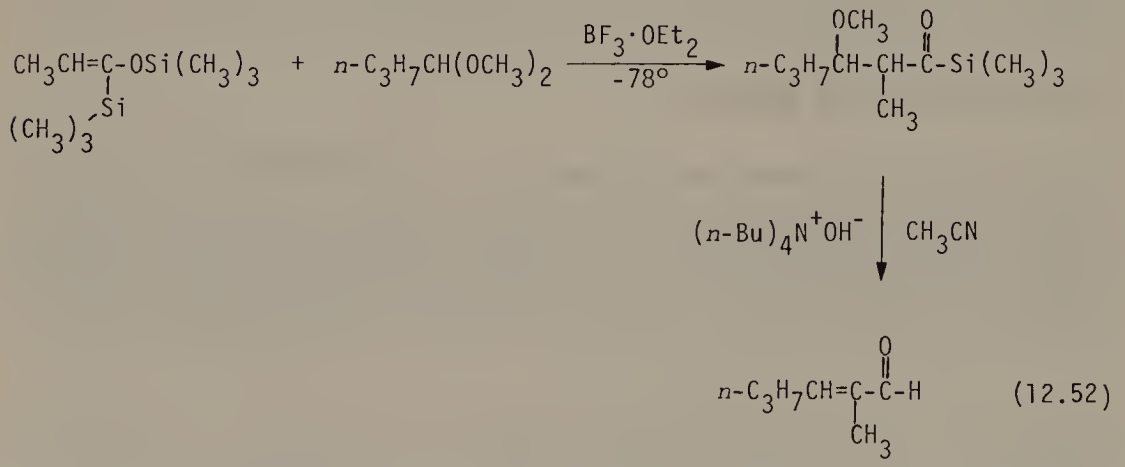
Reaction of α-bromo acetals or ketals with trimethylsilyl enol ethers promoted by $TiCl_4$ yields β-alkoxy-γ-bromo ketones. On heating, these undergo cyclization and elimination to yield furans [79, 80].



(12.51)

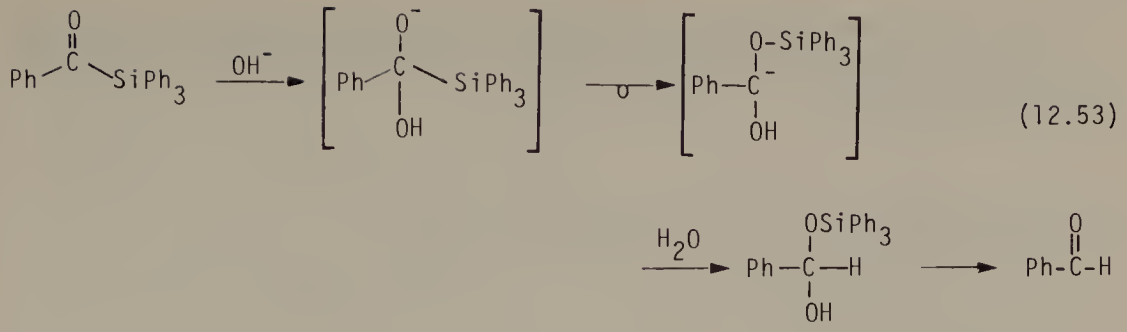
Trimethylsilyloxyallenes also react with acetals and $TiCl_4$ to yield α-(1-alkoxyalkyl) α,β-unsaturated ketones [81].

α-Trimethylsilyl trimethylsilyl enol ethers react with acetals and $BF_3 \cdot OEt_2$ at $-78°$ to yield β-alkoxy acylsilanes. On treatment with a catalytic amount of tetra-*n*-butylammonium hydroxide in acetonitrile these are converted to α,β-unsaturated aldehydes [82].



(12.52)

Such behavior is expected since acylsilanes yield aldehydes under mild basic conditions [83, 84].

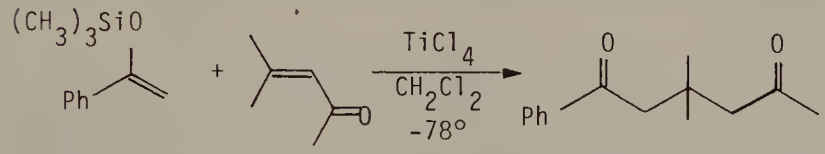


(12.53)

Cross Aldol reactions of 1-trimethylsilyloxy-1,3-butadiene [85] with acetals activated by a mixture of $TiCl_4$ and titanium tetraisopropoxide, occur exclusively at the 4-position to yield δ-alkoxy-α,β-unsaturated aldehydes [86, 87].

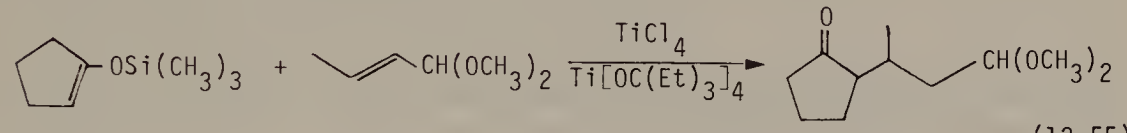
12.14 α,β-Unsaturated Ketones, Ketals and Acetals

Trimethylsilyl enol ethers undergo Michael type reactions with α,β-unsaturated ketones activated by $TiCl_4$ to yield 1,5-dicarbonyl compounds [88].



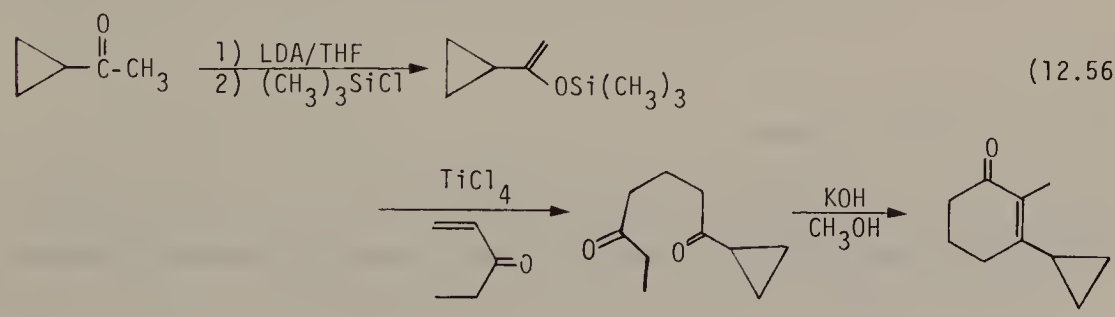
(12.54)

Trimethylsilyl enol ethers also undergo Michael reactions with α,β-unsaturated acetals or ketals on activation by $TiCl_4$ [89].



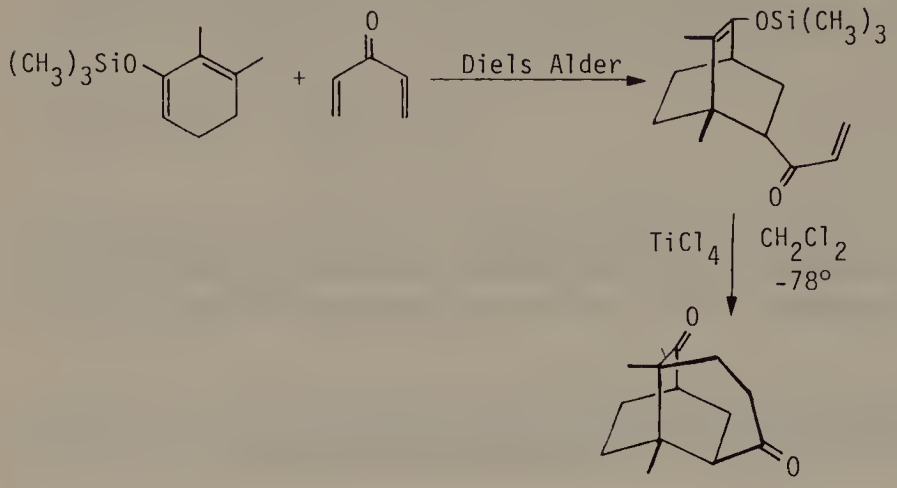
(12.55)

Michael reaction of 1-trimethylsilyloxy-1-cyclopropyl ethylene [90, 91] with α,β-unsaturated ketones activated by $TiCl_4$ yields 1-cyclopropyl-1,5-diketones. These undergo an intramolecular Aldol condensation and dehydration on treatment with potassium hydroxide in methanol to yield β-cyclopropyl α,β-unsaturated ketones.



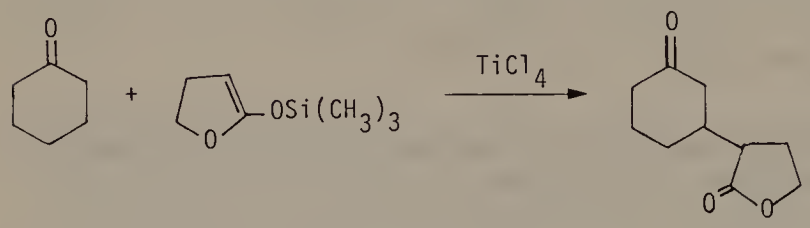
(12.56)

An intramolecular Michael reaction of a trimethylsilyl enol ether with an α,β-unsaturated ketone activated by $TiCl_4$ is a key step in an efficient synthesis of Seychellene [92].



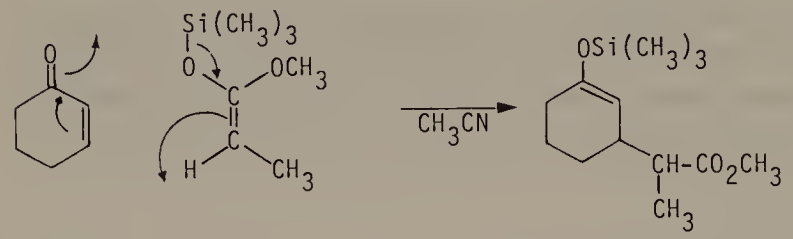
(12.57)

Alkyl trimethylsilyl ketene acetals undergo $TiCl_4$ promoted Michael reactions with α,β-unsaturated ketones to yield δ-keto esters [93].



(12.58)

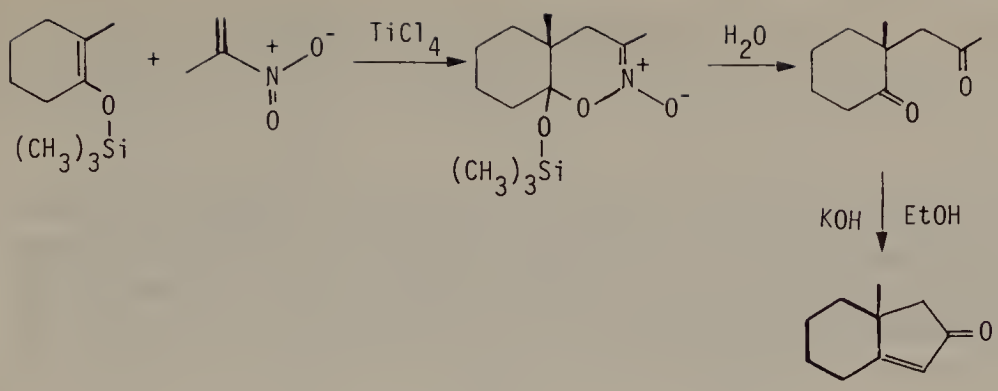
Such Michael reactions of α,β-unsaturated ketones with alkyl trimethylsilyl ketene acetals can also be carried out thermally in acetonitrile at 55° to yield the trimethylsilyl enol ether of the δ-keto esters [94].



(12.59)

12.15 α-Nitro Alkenes

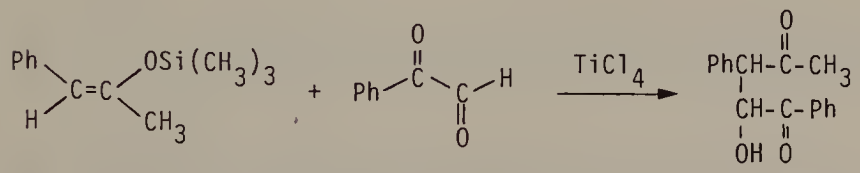
Trimethylsilyl enol ethers also undergo Michael type reactions with α-nitroalkenes under the influence of $SnCl_4$ or $TiCl_4$ to yield derivatives of nitronic acids. These can be hydrolyzed to yield 1,4-diketones [95].



(12.60)

12.16 Relative Reactivities

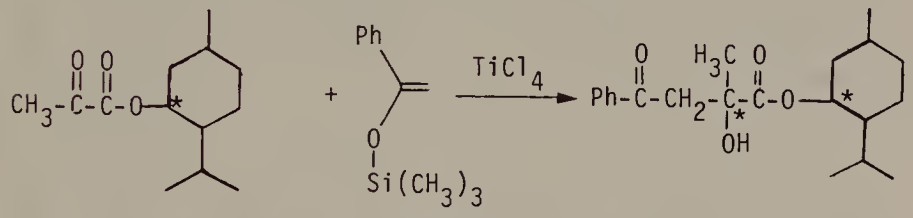
Phenyl glyoxal undergoes selective cross Aldol condensation with silyl enol ethers at the more reactive aldehyde carbonyl group.



(12.61)

Similarly, ketone carbonyl groups react in preference to ester carbonyl groups [96].

The cross Aldol reaction of trimethylsilyl enol ethers with α-keto esters of optically active alcohols such as (−)menthyl pyruvate and (−)menthyl phenylglyoxylate gives 2-hydroxy-4-oxo-butyrates. High asymmetric induction (50% e.e.) at the new chiral center is observed [97].

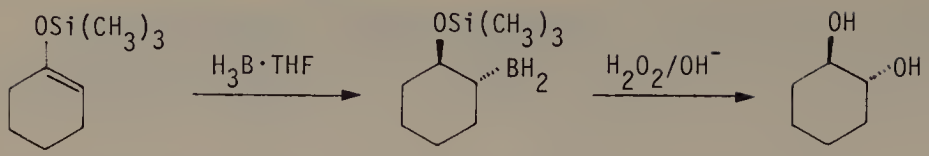


(12.62)

Alkyl trimethylsilyl ketene acetals react with the keto group of α-keto esters of optically active alcohols to yield α-hydroxy succinic acid derivatives in which the new chiral center is generated with high e.e. [98].

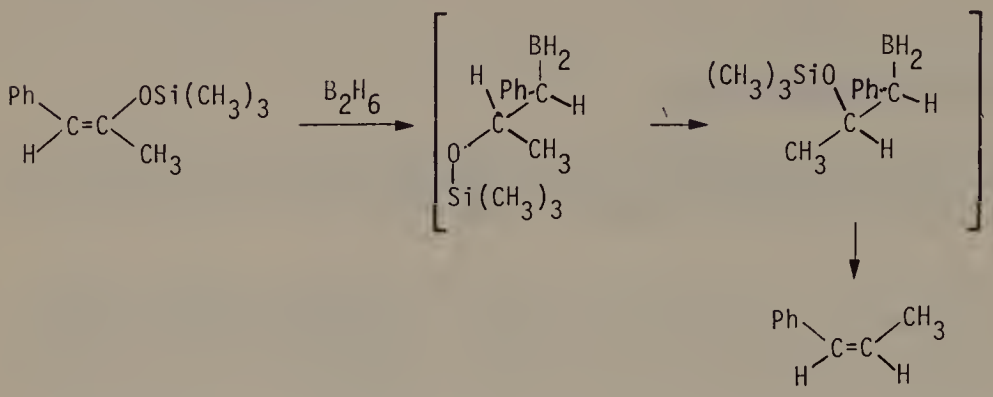
12.17 Hydroboration

Hydroboration of cyclic trimethylsilyl enol ethers leads to cyclic *trans*-β-trimethylsilyloxy organoboranes. The trimethylsilyloxy group directs the boron almost exclusively to the β carbon. Oxidation of these with alkaline hydrogen peroxide followed by hydrolysis leads to cyclic *trans*-1,2-glycols [99, 100].



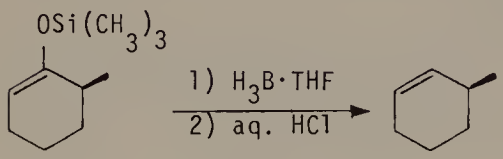
(12.63)

On the other hand, hydroboration of alicyclic trimethylsilyl enol ethers leads to β-trimethylsilyloxy organoboranes which undergo facile *syn*-elimination of trimethylsilyloxyborane to yield alkenes. Thus, an excess of *Z*-1-phenyl-2-trimethylsilyloxypropene reacts with borane to yield predominantly *z*-β-methylstyrene [100, 101].



(12.64)

Apparently, the reason cyclic *trans*-β-trimethylsilyloxy organoboranes are stable is that they cannot achieve the necessary geometry for spontaneous *syn*-elimination of trimethylsilyloxyborane. Nevertheless, cyclic-*trans*-β-trimethylsilyloxy organoboranes will undergo regiospecific elimination on treatment with acids, such as $BF_3 \cdot OEt_2$ or aq. HCl to yield specific alkenes [102].



(12.65)

References

1. Chan, T.H., Paterson, I., Pinsonnault, J.: Tetrahedron Lett. 4183 (1977)
2. Reetz, M.T., Maier, W.F.: Angew. Chem. Int. Ed. *17*, 48 (1978)
3. Reetz, M.T., Chatziiosifidis, I., Löwe, U., Maier, W.F.: Tetrahedron Lett. 1427 (1979)
4. Reetz, M.T., Maier, W.F., Chatziiosifidis, I., Giannis, A., Heimbach, H., Löwe, U.: Chem. Ber. *113*, 3741 (1980)
5. Reetz, M.T., Sauerwald, M., Walz, P.: Tetrahedron Lett. 1101 (1981)
6. Paterson, I.: Tetrahedron Lett. 1519 (1979)
7. Reetz, M.T., Hüttenhain, S.H.: Synthesis, 941 (1980)
8. Hashimoto, S., Itoh, A., Kitagawa, Y., Yamamoto, H., Nozaki, H.: J. Am. Chem. Soc. *99*, 4192 (1977)
9. Reetz, M.T., Maier, W.F., Schwellnus, K., Chatziiosifidis, I.: Angew. Chem. Int. Ed. *18*, 72 (1979)

10. Reetz, M.T., Schwellnus, K.: Tetrahedron Lett. 1455 (1978)
11. Shono, T., Nishiguchi, I., Komamura, T., Sasaki, M.: J. Am. Chem. Soc. *101*, 984 (1979)
12. Schreiber, J., Maag, H., Hashimoto, N., Eschenmoser, A.: Angew. Chem. Int. Ed. *10*, 330 (1971)
13. Danishefsky, S., Kitahara, T., McKee, R., Schuda, P.F.: J. Am. Chem. Soc. *98*, 6715 (1976)
14. Danishefsky, S., Prisbylla, M., Lipisko, B.: Tetrahedron Lett. 805 (1980)
15. Miyano, S., Hokari, H., Mori, A., Hashimoto, N.: Chem. Lett. 1213 (1980)
16. Paterson, I., Fleming, I.: Tetrahedron Lett. 995 (1979)
17. Paterson, I., Fleming, I.: Tetrahedron Lett. 2179 (1977)
18. Paterson, I., Fleming, I.: Tetrahedron Lett. 993 (1979)
19. Paterson, I., Price, L.G.: Tetrahedron Lett. 2829 (1981)
20. Paterson, I., Price, L.G.: Tetrahedron Lett. 2833 (1981)
21. Danishefsky, S., Guingant, A., Prisbylla, M.: Tetrahedron Lett. 2033 (1980)
22. Kelly, L.F., Narula, A.S., Birch, A.J.: Tetrahedron Lett. 4107 (1979)
23. Kelly, L.F., Dahler, P., Narula, A.S., Birch, A.J.: Tetrahedron Lett. 1433 (1981)
24. Lazukina, L.A., Kukhar, V.P., Pesotskaya, G.V.: Zhur. Obsh. Khim. *45*, 2100 (1975)
25. Jung, M.E., McCombs, C.A.: Tetrahedron Lett. 2935 (1976)
26. Ito, Y., Nakatsuka, M., Saegusa, T.: J. Org. Chem. *45*, 2022 (1980)
27. Nakamura, E., Murofushi, T., Shimizu, M., Kuwajima, I.: J. Am. Chem. Soc. *98*, 2346 (1976)
28. Reuss, R.H., Hassner, A.: J. Org. Chem. *39*, 1785 (1974)
29. Blanco, L., Amice, P., Conia, J.M.: Synthesis, 194 (1976)
30. Chan, T.H., Brownbridge, P.: J. Chem. Soc. Chem. Comm. 578 (1979)
31. Conia, J.M., Barnier, J.P.: Tetrahedron Lett. 4981 (1971)
32. Heine, H.G., Wendisch, D.: Liebigs Ann. Chem. 463 (1976)
33. Sato, T., Abe, T., Kuwajima, I.: Tetrahedron Lett. 259 (1978)
34. Kuwajima, I., Abe, T., Minami, N.: Chem. Lett. 993 (1976)
35. Sato, T., Abe, T., Kuwajima, I.: Tetrahedron Lett. 259 (1978)
36. Kuwajima, I., Matsumoto, K., Inoue, T.: Chem. Lett. 41 (1979)
37. Kuwajima, I., Matsumoto, K.: Tetrahedron Lett. 4095 (1979)
38. Rubottom, G.M., Mott, R.C.: J. Org. Chem. *44*, 1731 (1979)
39. Murai, S., Kuroki, Y., Hasegawa, K., Tsutsumi, S.: J. Chem. Soc. Chem. Comm. 946 (1972)
40. Trost, B.M., Curran, C.P.: J. Am. Chem. Soc. *102*, 5699 (1980)
41. Minami, N., Abe, T., Kuwajima, I.: J. Organometal. Chem. *145*, C1 (1978)
42. Ryu, I., Murai, S., Niwa, I., Sonoda, N.: Synthesis, 874 (1977)
43. Kita, Y., Segawa, J., Harata, J., Fujii, T., Tamura, Y.: Tetrahedron Lett. 3779 (1980)
44. Murai, S., Koroki, Y., Aya, T., Sonoda, N., Tsutsumi, S.: J. Chem. Soc. Chem. Comm. 741 (1972)
45. Rasmussen, J.K., Hassner, A.: J. Org. Chem. *39*, 2558 (1974)
46. Shvarts, I.S., Yarovenko, V.N., Krayushkin, M.M., Novikov, S.S., Sevost'yanova, V.V.: Izv. Akad. Nauk SSSR, Ser. Khim. 1674 (1976)
47. House, H.O., Auerbach, R.A., Gall, M., Peet, N.P.: J. Org. Chem. *38*, 514 (1973)
48. Kitching, W., Drew, G.M.: J. Org. Chem. *46*, 2695 (1981)
49. Murai, S., Koroki, Y., Hasegawa, K., Tsutsumi, S.: J. Chem. Soc. Chem. Comm. 946 (1972)
50. Donaldson, R.E., Fuchs, P.L.: J. Org. Chem. *42*, 2032 (1977)
51. Murai, S., Hasegawa, K., Sonoda, N.: Angew. Chem. Int. Ed. *14*, 636 (1975)

52. Schmidt, U., Schwochau, M.: Tetrahedron Lett. 4491 (1967)
53. Rathke, M.W., Sullivan, D.F.: Tetrahedron Lett. 1297 (1973)
54. Purlachenko, G.S., Mal'tsev, V.V., Baukov, Yu.I., Lutsenko, I.F.: Zhur. Obsh. Khim. *43*, 1724 (1973)
55. Wissner, A.: Tetrahedron Lett. 2749 (1978)
56. Wissner, A.: J. Org. Chem. *44*, 4617 (1979)
57. Kraus, G.A., Shimagaki, M.: Tetrahedron Lett. 1171 (1981)
58. Koroki, Y., Murai, S., Sonoda, N., Tsutsumi, S.: Organometal. Chem. Syn. *1*, 465 (1972)
59. Rasmussen, J.K., Hassner, A.: Tetrahedron Lett. 2783 (1973)
60. Wittig, G., Hess, A.: Org. Syn. *50*, 66 (1977)
61. House, H.O., Crumrine, O.S., Teranishi, A.Y., Olmstead, H.D.: J. Am. Chem. Soc. *95*, 3310 (1973)
62. Mukaiyama, T., Narasaka, K., Banno, K.: Chem. Lett. 1011 (1973)
63. Mukaiyama, T., Banno, K., Narasaka, K.: J. Am. Chem. Soc. *96*, 7503 (1974)
64. Yamamoto, Y., Maruyama, K.: Tetrahedron Lett. 4607 (1980)
65. Evans, D.A., Vogel, E., Nelson, J.V.: J. Am. Chem. Soc. *101*, 6120 (1979)
66. Kuwajima, I., Kato, M., Mori, A.: Tetrahedron Lett. 2745 (1980)
67. Kuwajima, I., Kato, M., Mori, A.: Tetrahedron Lett. 4291 (1980)
68. Wada, M.: Chem. Lett. 153 (1981)
69. Creger, P.L.: Tetrahedron Lett. 79 (1972)
70. Rathke, M.W., "The Reformatsky Reaction" in Organic Reactions, Vol. 22, J. Wiley, New York, New York: 1975
71. Saigo, K., Osaki, M., Mukaiyama, T.: Chem. Lett. 989 (1975)
72. Asaoka, M., Yanagida, N., Takei, H.: Tetrahedron Lett. 4611 (1980)
73. Brownbridge, P., Chan, T.H.: Tetrahedron Lett. 3427 (1980)
74. Mukaiyama, T., Hayashi, M.: Chem. Lett. 15 (1974)
75. Asaoka, M., Sugimura, N., Takei, H.: Bull. Chem. Soc. Japan, *52*, 1953 (1979)
76. Murata, S., Suzuki, M., Noyori, R.: J. Am. Chem. Soc. *102*, 3248 (1980)
77. Murata, S., Suzuki, M., Noyori, R.: Tetrahedron Lett. 2527 (1980)
78. Murata, S., Suzuki, M., Noyori, R.: Tetrahedron Lett. 2527 (1980)
79. Mukaiyama, T., Ishihara, H., Inomata, K.: Chem. Lett. 527 (1975)
80. Ishihara, H., Inomata, K., Mukaiyama, T.: Chem. Lett. 531 (1975)
81. Kuwajima, I., Kato, M.: Tetrahedron Lett. 623 (1980)
82. Sato, T., Arai, M., Kuwajima, I.: J. Am. Chem. Soc. *99*, 5827 (1977)
83. Brook, A.G.: J. Am. Chem. Soc. *79*, 4373 (1957)
84. Brook, A.G., Vandersar, T.J.D., Limburg, W.: Can. J. Chem. *56*, 1758 (1958)
85. Cazeau, P., Frainnet, E.: Bull. Soc. Chim. Fr. 1658 (1972)
86. Mukaiyama, T., Ishida, A.: Chem. Lett. 319 (1975)
87. Ishida, A., Mukaiyama, T.: Chem. Lett. 1167 (1975)
88. Narasaka, K., Soai, K., Mukaiyama, T.: Chem. Lett. 1223 (1974)
89. Narasaka, K., Soai, K., Aikawa, Y., Mukaiyama, T.: Bull. Soc. Chem. Japan, *49*, 779 (1976)
90. Fitjer, L., Conia, J.M.: Angew. Chem. Int. Ed. *12*, 332 (1972)
91. Greico, P.A., Ohfune, Y.: J. Org. Chem. *43*, 2720 (1978)
92. Jung, M.E., Pan, Y.G.: Tetrahedron Lett. 3127 (1980)
93. Saigo, K., Osaki, M., Mukaiyama, T.: Chem. Lett. 163 (1976)
94. Kita, Y., Segawa, J., Haruta, J., Fujii. T., Tamura, Y.: Tetrahedron Lett. 3779 (1980)
95. Miyashita, M., Yanami, T., Yoshikoshi, A.: J. Am. Chem. Soc. *98*, 4679 (1976)
96. Banno, K., Mukaiyama, T.: Chem. Lett. 741 (1975)
97. Ojima, I., Yoshida, K., Inaba, S.I.: Chem. Lett. 429 (1977)

98. Ojima, I., Yoshida, K., Inaba, S.I.: Chem. Lett. 429 (1979)
99. Klein, J., Levene, R., Dunkelblum, E.: Tetrahedron Lett. 2845 (1972)
100. Larson, G.L., Hernandez, D., Hernandez, A.: J. Organometal. Chem. *76*, 6 (1974)
101. Larson, G.L., Hernandez, A.: J. Organometal. Chem. *102*, 123 (1975)
102. Larson, G.L., Hernandez, E., Alonso, C., Nieves, I.: Tetrahedron Lett. 4005 (1975)

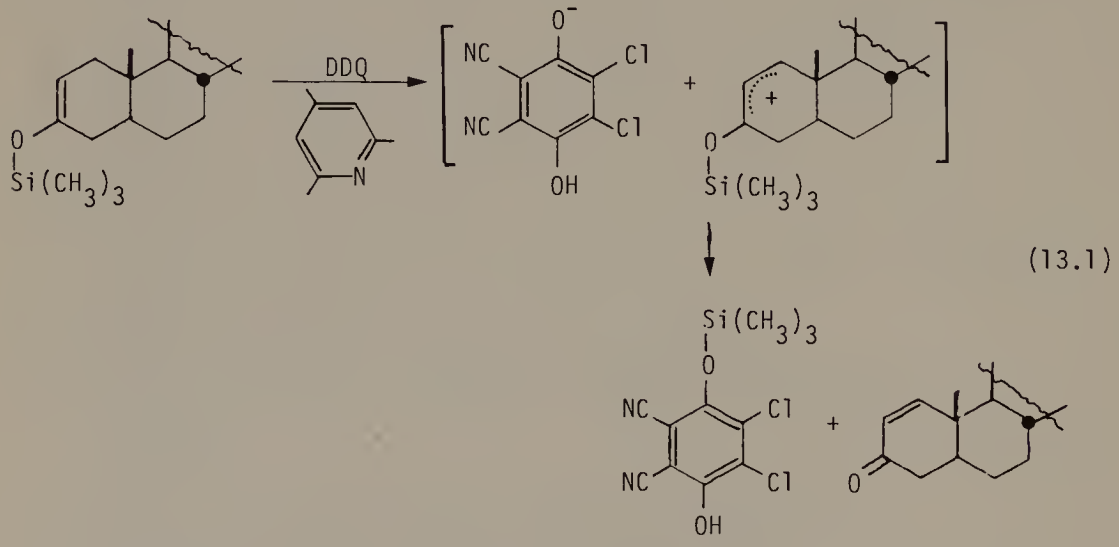
13 Oxidation of Silyl Enol Ethers

13.1 Introduction

A number of useful synthetic transformations are based on the selective oxidation of the electron rich C–C double bond of trimethylsilyl enol ethers.

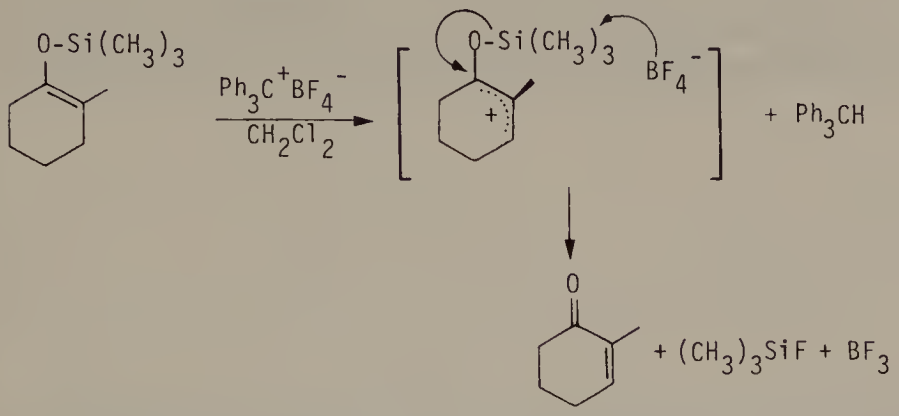
13.2 Preparation of α,β-Unsaturated Ketones

Several methods have been developed to regiospecifically convert trimethylsilyl enol ethers into α,β-unsaturated ketones. For example, treatment of trimethylsilyl enol ether with DDQ and collidine yields α,β-unsaturated ketones. This reaction may proceed by hydride abstraction from the silyl enol ether to yield a trimethylsilyloxy stabilized allylic carbocation/DDQ hydroquinone anion pair. Nucleophilic attack on the silyl center by the hydroquinone anion yields the α,β-unsaturated ketone [1, 2].



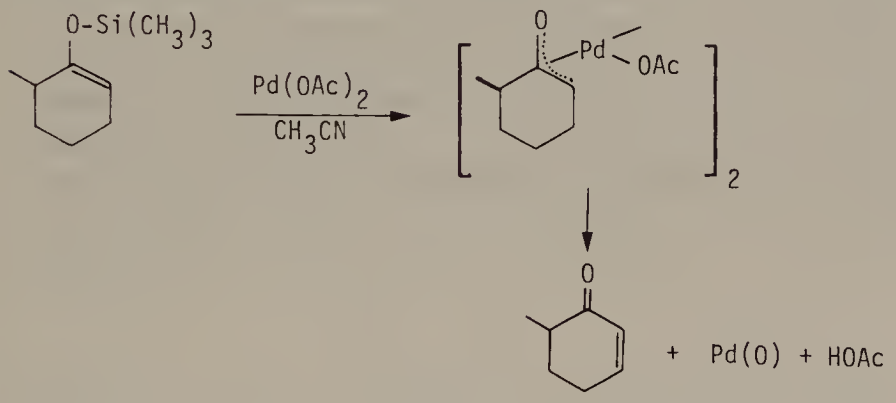
The reaction of trityl tetrafluoroborate (BF_4^-) with trimethylsilyl enol ethers to yield α,β-unsaturated ketones is mechanistically closely related. Presumably, the trityl carbocation abstracts a hydride from the trimethylsilyl enol ether to yield triphenylmethane and a trimethylsilyloxy stabilized allylic carbocation/BF_4^- pair. Nucleophilic attack by the BF_4^- ion on the silyl center

yields TMS-F, the α,β-unsaturated ketone and BF_3 [3]. Jung has used trityl BF_4^- to oxidize trimethylsilyl ethers of secondary alcohols to ketones [3, 4, 5].



(13.2)

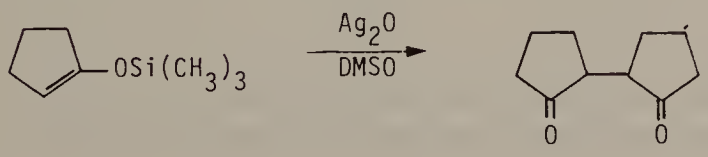
Oxidation of trimethylsilyl enol ethers with palladium acetate in acetonitrile gives high yields of α,β-unsaturated ketones [6]. The reaction may occur by formation of an intermediate oxo-π-allyl Pd(II) complex. β-Elimination of hydride from this complex yields the α,β-unsaturated ketone, Pd(O) and acetic acid. Unfortunately, reoxidation of Pd(O) to Pd(II) is a problem. The highest yields are achieved with stoichiometric amounts of palladium acetate. Conceptually, this reaction may be considered to be the reverse of the transition metal catalyzed 1,4-hydrosilation of α,β-unsaturated ketones to yield trimethylsilyl enol ethers [7].



(13.3)

13.3 Preparation of 1,4-Diketones

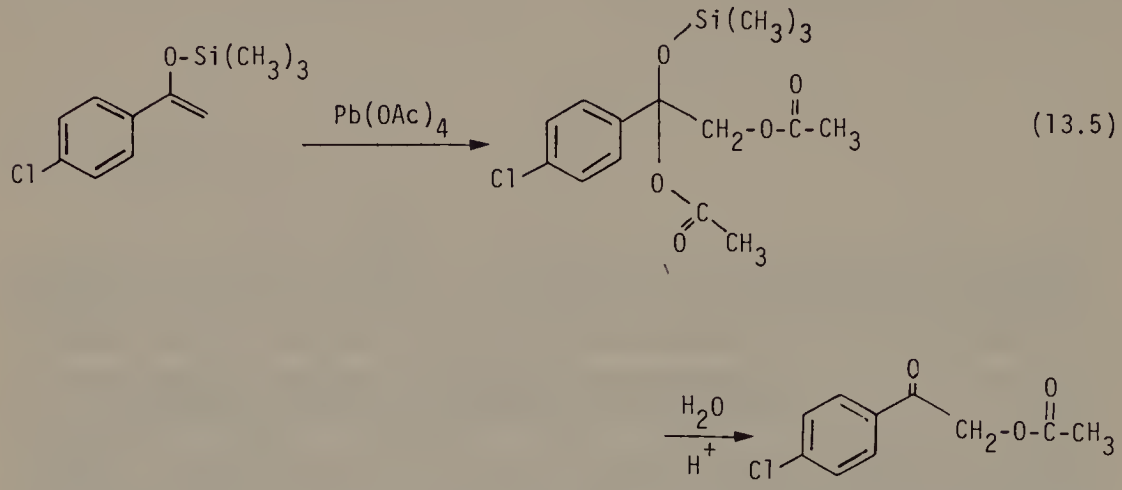
Trimethylsilyl enol ethers react with silver oxide in DMSO to yield symmetrical 1,4-diketones [8]. This reaction may involve a silver (I) enolate intermediate. One electron transfer from the enolate anion to silver (I) would lead to an enol radical and silver (O). Dimerization of such enol radicals would yield the 1,4-diketone products.



(13.4)

13.4 Preparation of α-Acyloxy and α-Hydroxy Ketones

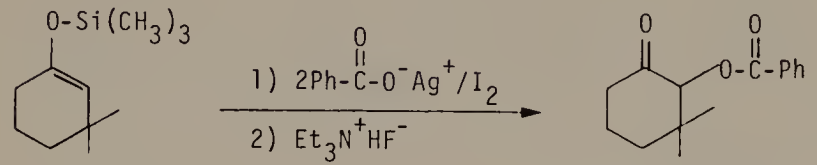
Oxidation of trimethylsilyl enol ethers with lead tetraacetate yields 1,2-diacetoxy-1-trimethylsilyloxy alkanes which hydrolyze to yield α-acetoxy ketones [9].



(13.5)

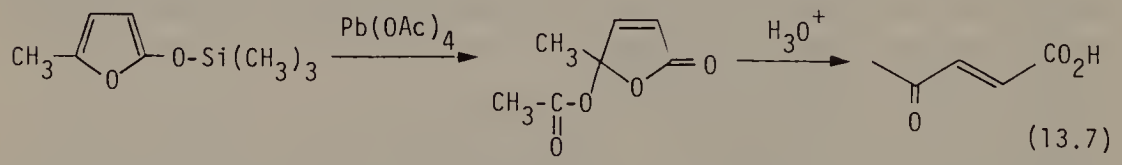
Oxidation of trimethylsilyl enol ethers with lead tetrabenzoate permits the preparation of α-benzoyloxy aldehydes, as well as α-benzoyloxy ketones. The initial 1,2-dibenzoyloxy-1-trimethylsilyloxy alkanes are converted to α-benzoyloxy aldehydes by treatment with triethylammonium fluoride [10].

Treatment of five and six-membered cyclic trimethylsilyl enol ethers with silver carboxylates and iodine in a 2 : 1 ratio, followed by addition of triethylammonium fluoride regiospecifically yields α-acyloxy ketones. With larger cyclic trimethylsilyl enol ethers the formation of 2-iodo ketones becomes important [28].



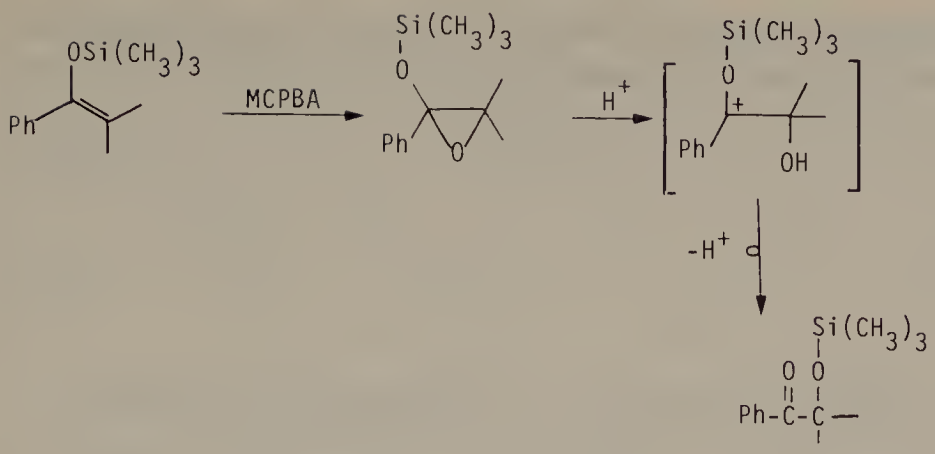
(13.6)

Oxidation of 2-methyl-5-trimethylsilyloxyfuran with lead tetraacetate yields 4-acetoxy-2-penten-4-olide which can be hydrolyzed to 4-oxo-2-pentenoic acid [11].



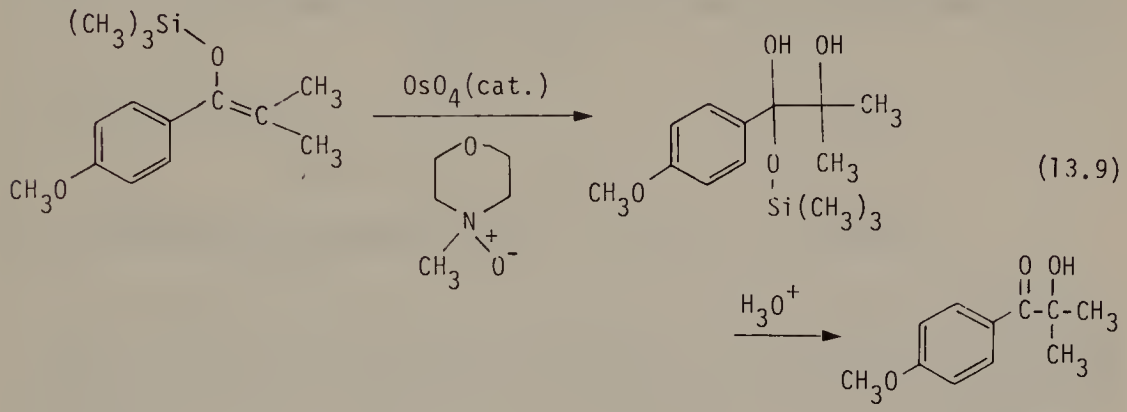
(13.7)

Oxidation of trimethylsilyl enol ethers with MCPBA yields α-trimethylsilyloxy ketones which can be hydrolyzed to α-hydroxy ketones [12–14].



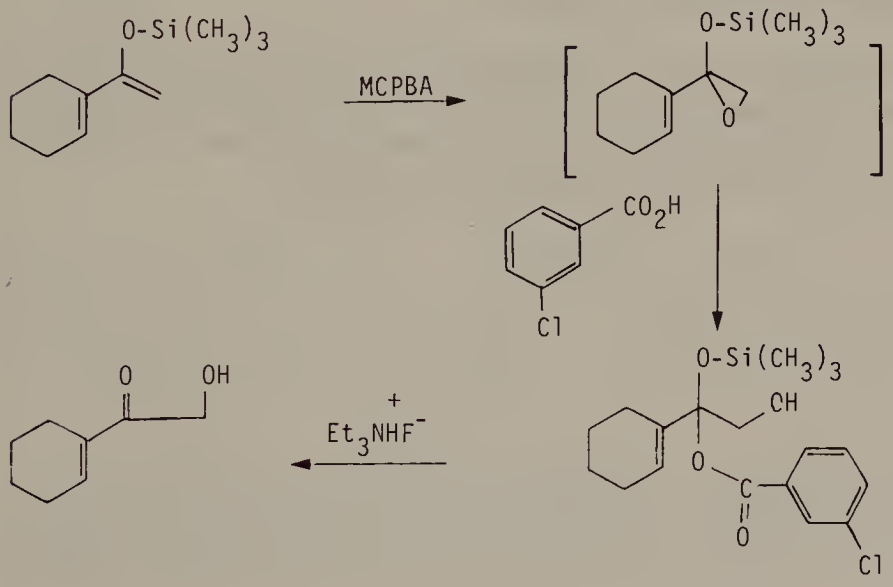
(13.8)

Oxidation of trimethylsilyl enol ethers with a catalytic amount of osmium tetraoxide with N-methyl morpholine oxide [29] as a stoichiometric reoxidant regiospecifically yields α-hydroxy ketones [30].



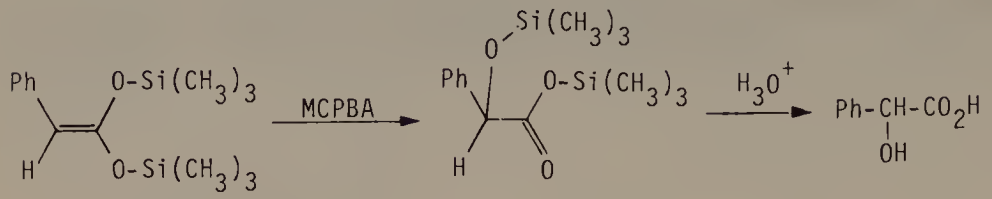
(13.9)

2-Trimethylsilyloxy-1,3-dienes are oxidized by MCPBA to yield α′-hydroxy-α,β-unsaturated ketones. This regiospecificity results from the preferential oxidation of the trimethylsilyloxy substituted C–C double bond of the diene system [15].



(13.10)

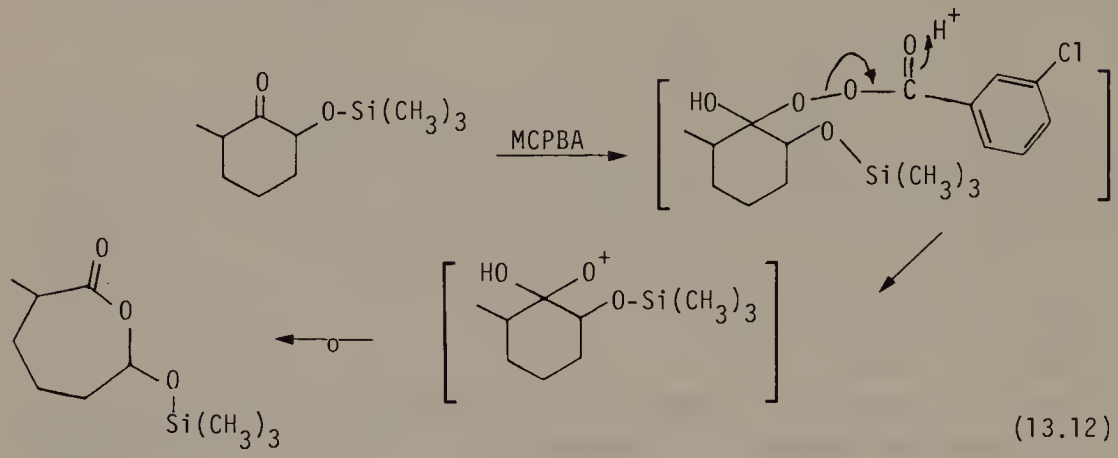
Similarly oxidation of *bis*-trimethylsilyl ketene acetals with MCPBA yields α-hydroxy carboxylic acids after hydrolysis [16].



(13.11)

13.5 Baeyer-Villiger Oxidation of α-Trimethylsilyloxy Ketones

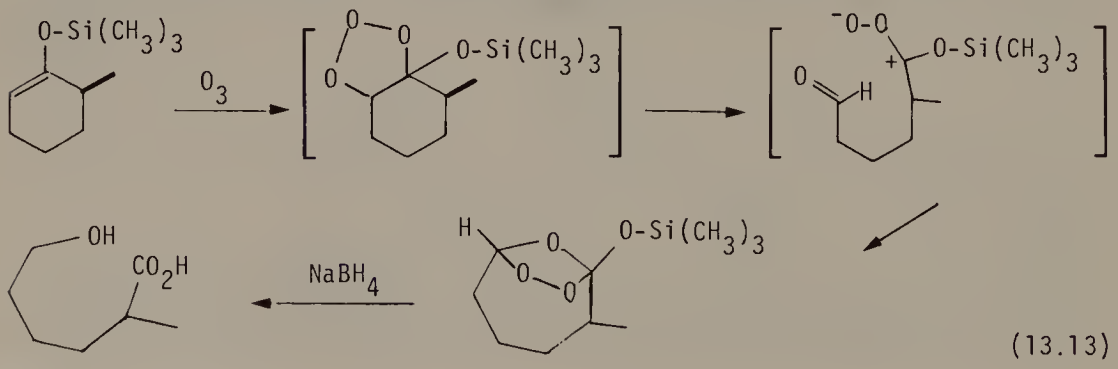
Treatment of trimethylsilyl enol ethers with two equivalents of MCPBA in ether solvent results in a Baeyer-Villiger oxidation of the initial α-trimethylsilyloxy ketone. The trimethylsilyloxy-substituted carbon selectively migrates to the electron-deficient oxygen generated in this reaction [17].



(13.12)

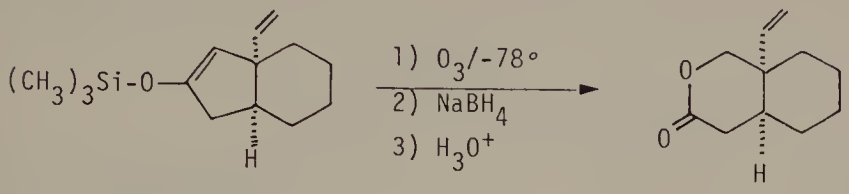
13.6 Ozonolysis of Silyl Enol Ethers

Trimethylsilyl enol ethers undergo regiospecific ozonolysis (Eq. 13.13). This can be explained if fragmentation of the primary ozonide to a ketone or aldehyde and a carbonyl ylid occurs so that the positive end of the 1,3-dipolar carbonyl ylid is stabilized by the trimethylsilyloxy group.



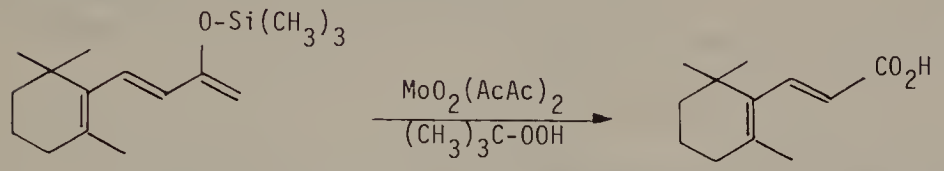
(13.13)

The high reactivity of the C–C double bond of trimethylsilyl enol ethers toward electrophilic reagents compared to other C–C double bonds has been utilized in a synthesis of Vernolepin. At −78°C, selective ozonolysis of a trimethylsilyl enol ether in the presence of a terminal vinyl group has been achieved [18–20].



(13.14)

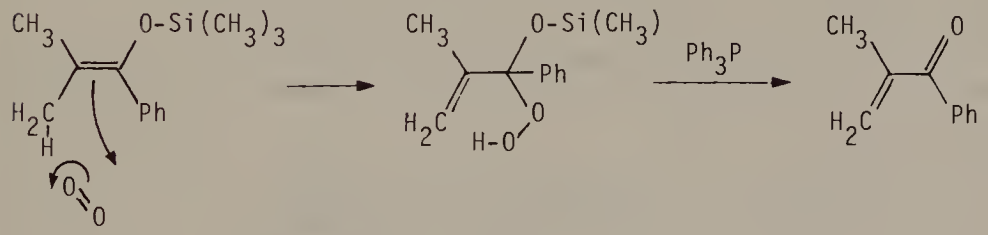
The C–C double bond of silyl enol ethers can be selectively cleaved by $MoO_2(acac)_2$ and *t*-butyl hydroperoxide [31].



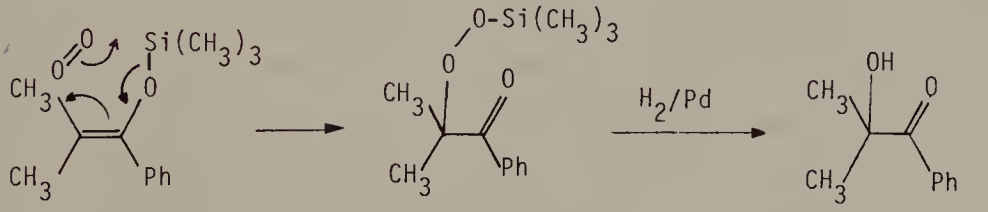
(13.15)

13.7 Reaction of Singlet Oxygen with Silyl Enol Ethers

Trimethylsilyl enol ethers react with photochemically generated singlet oxygen *via* two competing ene reactions. The first is a normal ene reaction in which an allylic hydrogen becomes bonded to oxygen to yield an allylic hydroperoxide. The other involves transfer of a trimethylsilyl group from one oxygen to another to yield an α-trimethylsilylperoxy ketone [21–23].

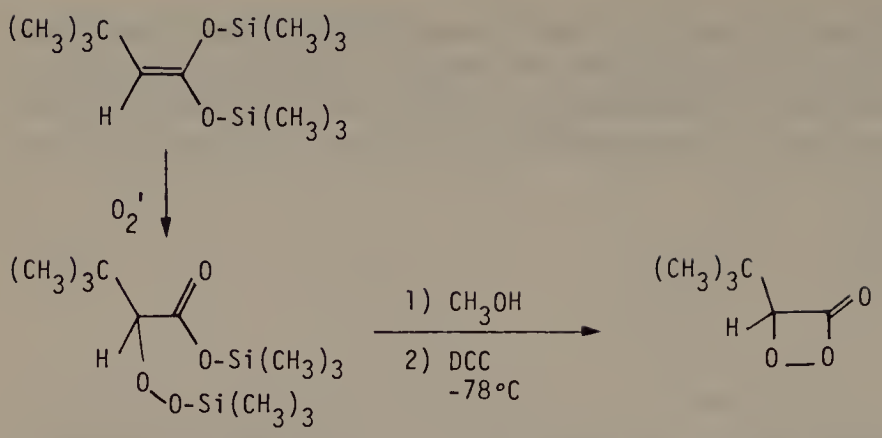


(13.16)



(13.17)

This reaction has been utilized to prepare α-peroxy-α-lactones, which are synthetically inaccessible by other routes. α-*t*-Butyl-1-peroxy-α-lactone emits light on decomposition to carbon dioxide and pivaldehyde [24–27].



(13.18)

References

1. Ryu, I., Murai, S., Hatayama, Y., Sonoda, N.: Tetrahedron Lett. 3455 (1978)
2. Fleming, I., Paterson, I.: Syn. 736 (1979)
3. Jung, M.E., Pan, Y.G., Rathke, M.W., Sullivan, D.F., Woodbury, R.P.: J. Org. Chem. *42*, 3961 (1977)
4. Jung, M.E.: J. Org. Chem. *41*, 1479 (1976)
5. Jung, M.E., Speltz, L.M.: J. Am. Chem. Soc. *98*, 7882 (1976)
6. Ito, Y., Hirao, H., Saegusa, T.: J. Org. Chem. *43*, 1011 (1978)
7. Ojima, I., Nihonyanagi, N., Kogure, T., Kumagai, M., Horiuchi, S., Nakatsugawa, N., Nagai, Y.: J. Organometal. Chem. *94*, 449 (1975)
8. Ito, Y., Konoike, T., Saegusa, T.: J. Am. Chem. Soc. *97*, 649 (1975)
9. Rubottom, G.M., Gruber, J.M., Kincaid, K.: Syn. Commun. *6*, 59 (1976)
10. Rubottom, G.M., Gruber, J.M., Mong, G.M.: J. Org. Chem. *41*, 1673 (1976)
11. Asaoka, M., Yanagida, N., Sugimura, N., Takei, H.: Bull. Chem. Soc. Japan, *53*, 1061 (1980)
12. Rubottom, G.M., Vazquez, M.A., Pelegrina, D.R.: Tetrahedron Lett. 4319 (1974)
13. Brook, A.G., MacRae, D.M.: J. Organometal. Chem. *77*, C19 (1974)
14. Hassner, A., Reuss, R.H., Pinnick, H.W.: J. Org. Chem. *40*, 3427 (1975)
15. Rubottom, G.M., Gruber, J.M.: J. Org. Chem. *43*, 1599 (1978)
16. Rubottom, G.M., Marrero, R., I. Org. Chem. *40*, 3783 (1975)
17. Rubottom, G.M., Gruber, J.M., Boeckman, Jr.R.K., Ramaiah, M., Medwid, J.B., Tetrahedron Lett. 4603 (1978)
18. Clark, R.D., Heathcock, C.H.: Tetrahedron Lett. 1713 (1974)
19. Clark, R.D., Heathcock, C.H.: Tetrahedron Lett. 2027 (1974)
20. Clark, R.D., Heathcock, C.H.: J. Org. Chem. *41*, 1396 (1976)
21. Rubottom, G.M., Nieves, M.I.L.: Tetrahedron Lett. 2423 (1972)
22. Friedrich, E., Lutz, W.: Angew. Chem. Int. Ed. *16*, 413 (1977)
23. Jefford, C.W., Rimbault, C.G.: Tetrahedron Lett. 2375 (1977)
24. Kuo, Y.N., Chen, F., Ainsworth, C., Bloomfield, J.J.: J. Chem. Sec. D, 135 (1971)
25. Adam, W., Liu, J.C.: J. Am. Chem. Soc. *94*, 2894 (1972)
26. Adam, W., Steinmetzer, H.C.: Angew. Chem. Int. Ed. *11*, 540 (1972)
27. Adam, W., Alzérreca, A., Liu, J.C., Yany, F.: J. Am. Chem. Soc. *99*, 5768 (1977)
28. Rubottom, G.M., Mott, R.C., Juve, Jr., H.D.: J. Org. Chem. *46*, 2717 (1981)
29. Van Rheenan, Kelly, R.C., Cha, D.Y.: Tetrahedron Lett. 1973 (1976)
30. McCormick, J.P., Tomasik, W., Johnson, M.W.: Tetrahedron Lett. 607 (1981)
31. Kaneda, K., Kii, N., Jitsukawa, K., Teranishi, S.: Tetrahedron Lett. 2595 (1981)

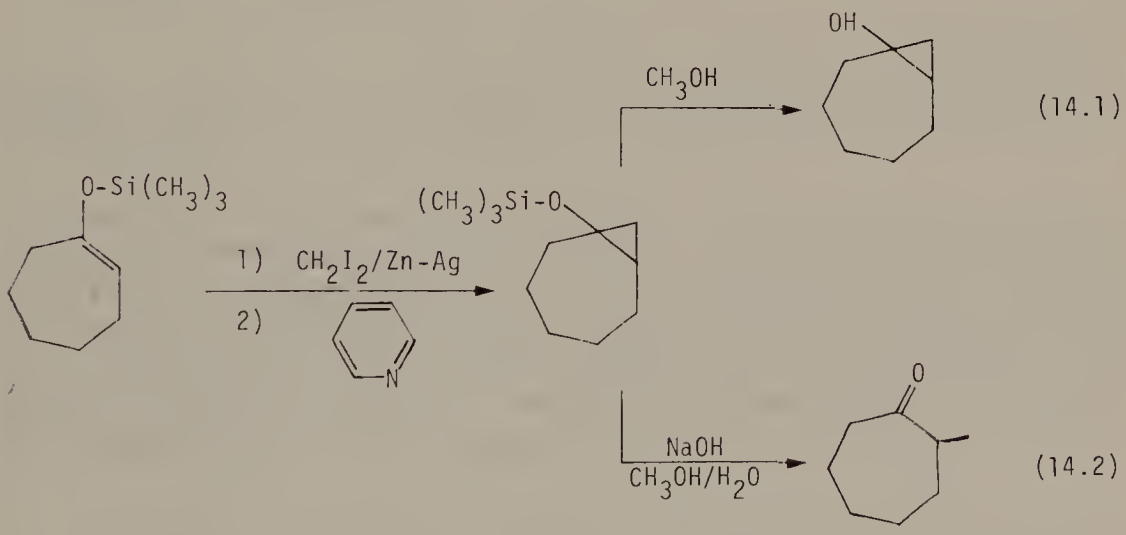
14 Cyclopropanation of Silyl Enol Ethers, Chemistry of Trimethylsilyloxycyclopropanes

14.1 Introduction

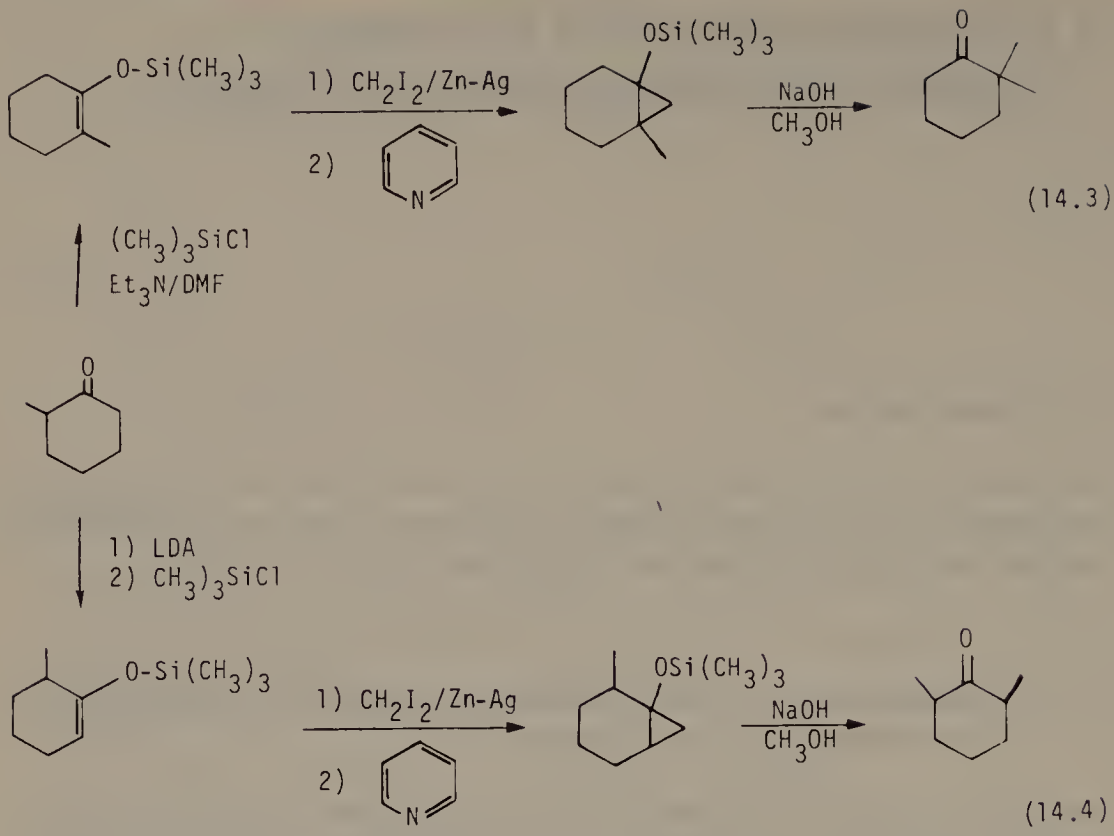
The electron rich C–C double bond of silyl enol ethers readily reacts with electrophilic carbenes to yield silyloxycyclopropanes. These are highly reactive compounds due to the cyclopropyl ring strain.

14.2 Preparation of Trimethylsilyloxycyclopropanes, Regiospecific Conversion to Methyl Ketones

The electron rich C–C double bond of trimethylsilyl enol ethers readily undergoes cyclopropanation with the Simmons-Smith reagent [CH_2I_2/Zu-Cu] [1, 2], or with methylene iodide and the more reactive zinc-silver couple in ethyl ether to yield trimethylsilyloxycyclopropane derivatives [3]. Trimethylsilyloxycyclopropanes can be hydrolyzed in acidic methanol to yield cyclopropanols (Eq. 14.1) [4, 5]. Treatment of these with methanolic sodium hydroxide yields α-methyl ketones (Eq. 14.2) [6].



The fact that trimethylsilyl enol ethers can be prepared regiospecifically from unsymmetrical ketones permits specific mono-methylation at either the α or α' position of the ketone [6].

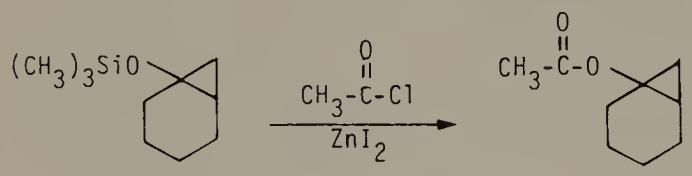


(14.3)

(14.4)

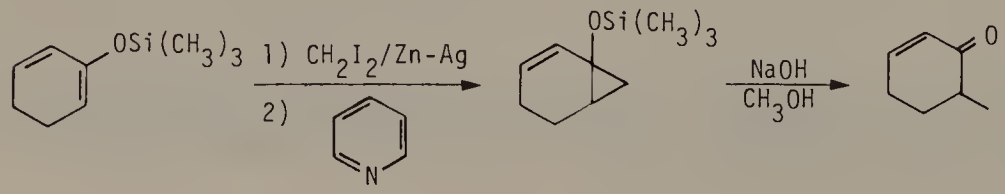
Pyridine, which is added during work-up of the reaction, precipitates the Lewis acid zinc iodide from the ethyl ether solution as a *bis*-pyridine complex.

Trimethylsilyloxycyclopropanes can be converted to the corresponding cyclopropyl acetates by reaction with acetyl chloride and zinc iodide [7].



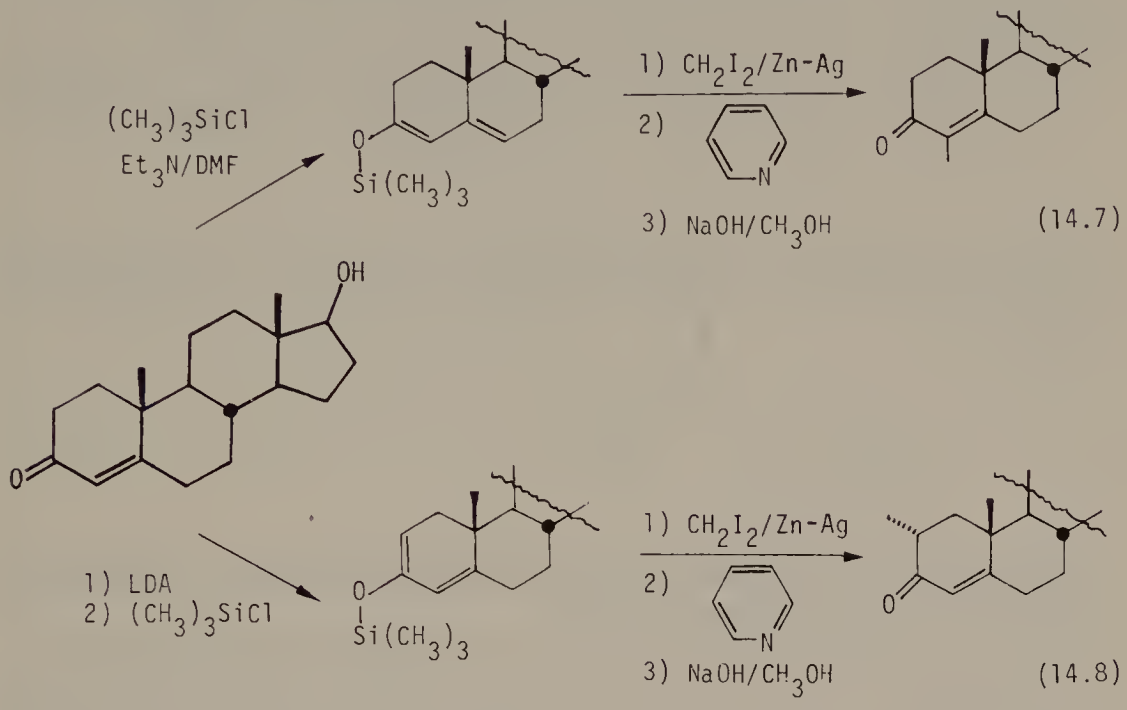
(14.5)

Trimethylsilyloxy substituted dienes can be prepared from α,β-unsaturated ketones. For example, methyl vinyl ketone can be converted to 2-trimethylsilyloxy-1,3-butadiene by treatment with TMS-Cl/triethylamine in DMF [8]. 2-Trimethylsilyloxy-1,3-cyclohexadiene can be prepared from 2-cyclohexenone by treatment with LDA followed by TMS-Cl. The trimethylsilyloxy substituted C–C double bond of these dienes is much more nucleophilic than the other C–C double bond and hence undergoes selective cyclopropanation [9].



(14.6)

Treatment of testosterone with TMS-Cl/triethylamine in DMF yields a 3-trimethylsilyloxy-3,5-diene derivative, whereas treatment with LDA and TMS-Cl yields a 3-trimethylsilyloxy-2,4-diene derivative. Cyclopropanation of both derivatives occurs from the less hindered α face of the steroid nucleus. Subsequent treatment with methanolic sodium hydroxide yields 4-methyltestosterone and 2-α-methyltestosterone, respectively [9].

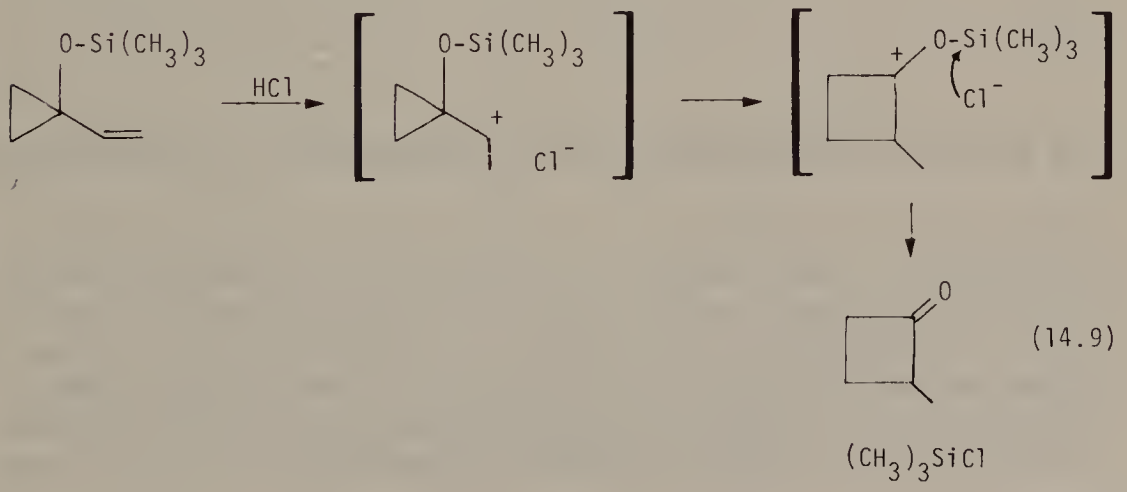


(14.7)

(14.8)

14.3 Acid Catalyzed Rearrangement of 1-Vinyl-1-trimethylsilyloxycyclopropanes

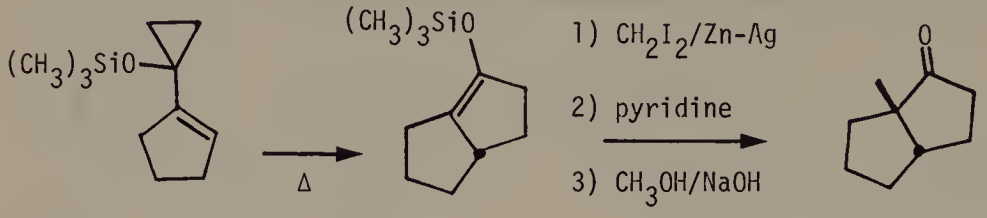
1-Vinyl-1-trimethylsilyloxycyclopropanes, formed by cyclopropanation of 2-trimethylsilyloxy-1,3-dienes undergo rearrangement to yield alkyl substituted cyclobutanones on treatment with HCl in THF [10, 11].



(14.9)

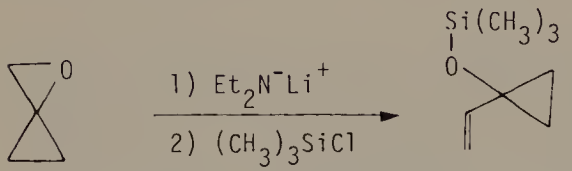
14.4 Pyrolysis of 1-Vinyl-1-trimethylsilyloxycyclopropanes

1-Vinyl-1-trimethylsilyloxycyclopropanes rearrange on pyrolysis to 1-trimethylsiloxycyclopentenes [11–13].



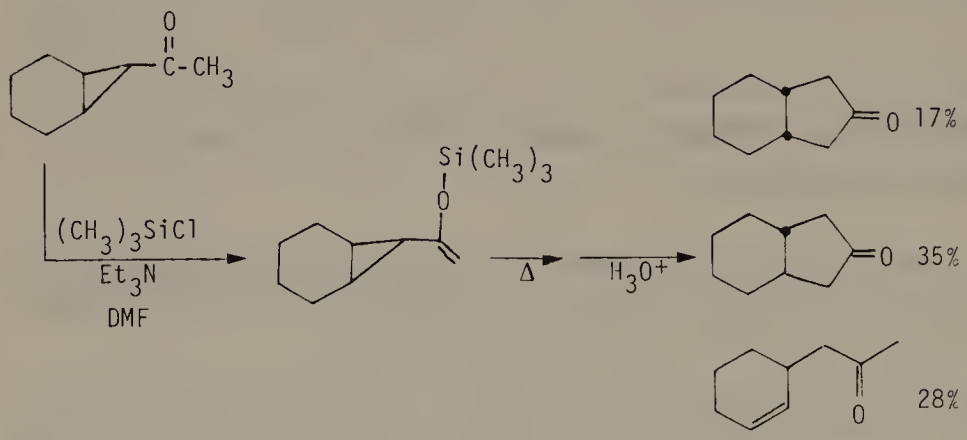
(14.10)

Alternatively, 1-vinyl-1-trimethylsilyloxycyclopropanes have been prepared by the sequential reaction of oxaspiropentanes with lithium diethylamide and TMS-Cl [11].



(14.11)

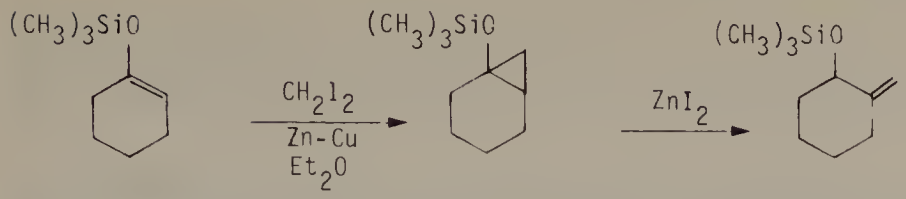
1-Cyclopropyl-1-trimethylsilyloxyethylenes undergo pyrolysis to yield, after acidic hydrolysis, cyclopentanones [14].



(14.12)

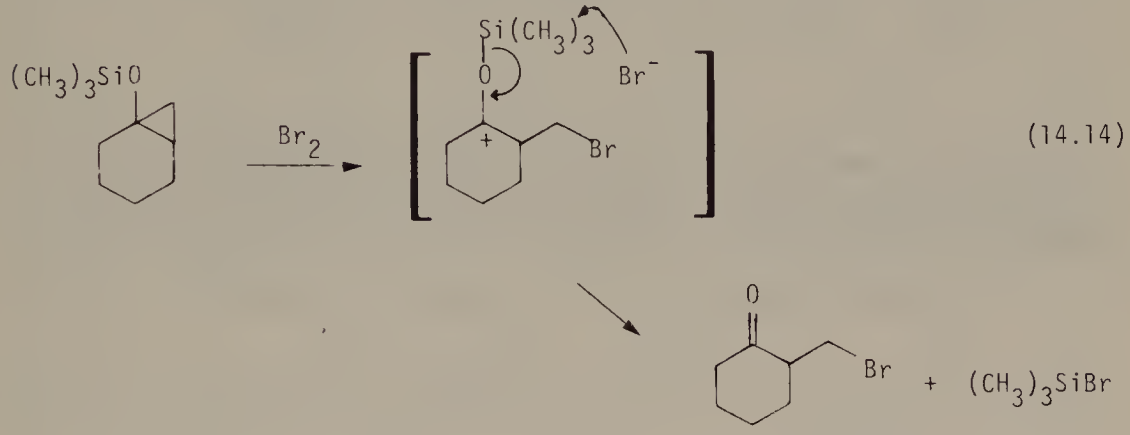
14.5 Reaction of Electrophiles with Trimethylsilyloxycyclopropanes

Trimethylsilyloxycyclopropanes are isomerized to α-methylene trimethylsilyloxyalkanes by zinc iodide [15, 16]. Diethyl zinc and methylene iodide can be used to achieve cyclopropanation of silyl enol ethers in aromatic solvents. Zinc-copper or zinc-silver couples are only effective in ether solvents. Cyclopropanation of trimethylsilyl enol ethers in benzene leads to extensive rearrangement of the initial trimethylsiloxycyclopropane due to the greater Lewis acidity of zinc iodide in hydrocarbon solvents [17].



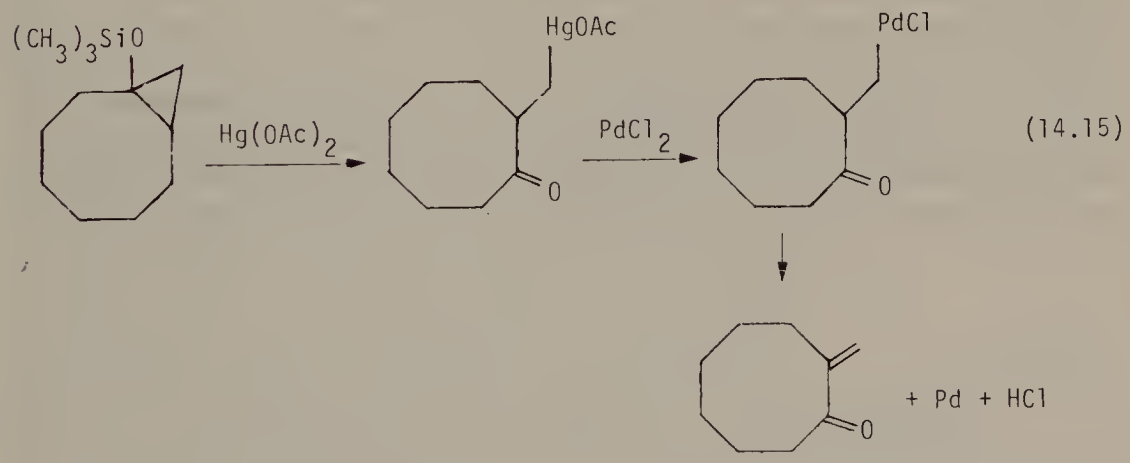
(14.13)

Trimethylsilyloxycyclopropanes react with bromine in methylene chloride at −78° to yield β-bromo ketones. Electrophilic attack by bromine on the cyclopropane ring probably leads to C-Br bond formation, cyclopropane ring opening, and formation of trimethylsilyloxy stabilized carbocation. Attack by bromide at the silyl center leads to TMS-Br and the β-bromo ketone [19].



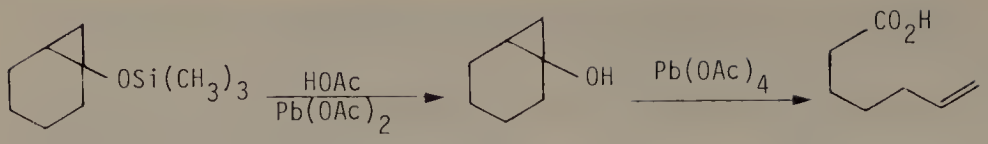
(14.14)

Trimethylsilyloxycyclopropanes react with mercuric acetate and $PdCl_2$ to yield α,β-unsaturated ketones. The following sequence of reactions may explain this result. Trimethylsilyloxycyclopropanes react with mercuric acetate to yield β-acetoxy mercuric ketones and acetoxytrimethylsilane. Metal interchange with Pd(II) gives β-palladio-ketones which undergo reductive elimination of Pd(O)/HCl to yield α,β-unsaturated ketones. The reaction can be made catalytic in Pd by reoxidation of Pd(O) to Pd(II) with cupric chloride [20].



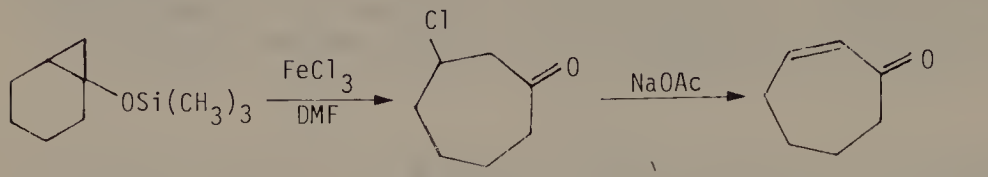
(14.15)

1-Trimethylsilyloxybicyclo[n,1,0] alkanes react with lead tetraacetate in acetic acid to yield ω-unsaturated carboxylic acids [21].



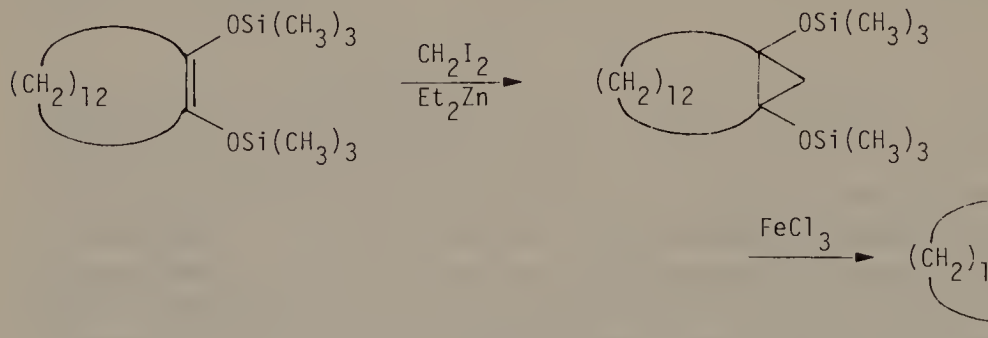
(14.16)

1-Trimethylsilyloxybicyclo[n,1,0] alkanes react with ferric chloride, by a series of one electron transfers, to yield 3-chlorocycloalkanones. These undergo dehydrohalogenation on treatment with sodium acetate to yield 2-cycloalkenones [22].



(14.17)

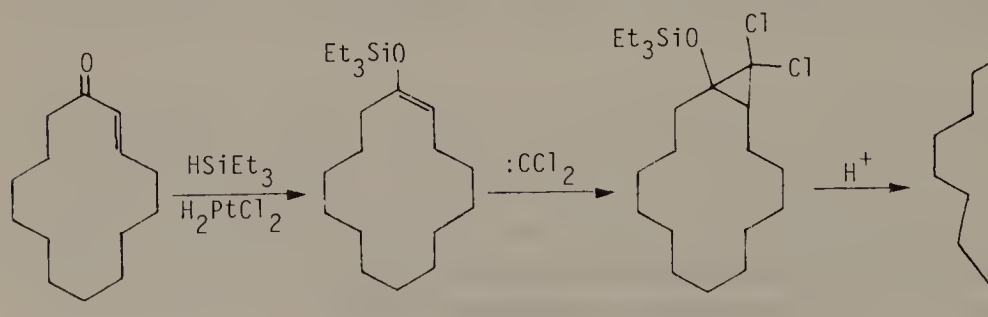
Cyclopropanation of 1,2-*bis*(trimethylsilyloxy) cyclotetradecene with diethyl zinc and methylene iodide gave 1,14-*bis*(trimethylsilyloxy) bicyclo-[12,1,0]pentadecane. Reaction of this with ferric chloride in DMF gave cyclopentadecan-1,3-dione [18].



(14.18)

14.6 Reaction of Silyl Enol Ethers with Other Carbenes

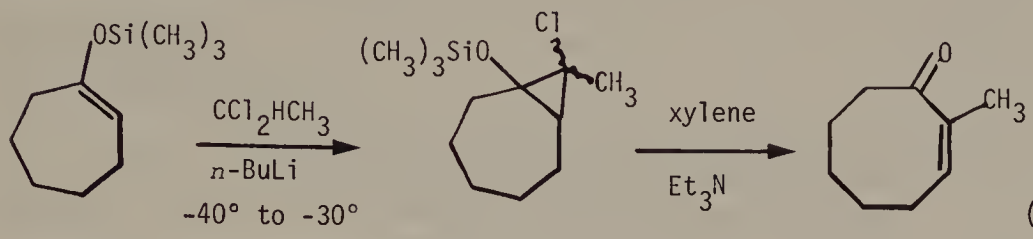
Silyl enol ethers react with other electrophilic carbenes. For example, 1-triethylsilyloxycyclotetradecene reacts with dichlorocarbene to give a 1,1-dichloro-2-triethylsilyloxycyclopropane derivative. Treatment of this with acid yields α-chlorocyclopentadecanone [23]. The precursor triethylsilyl enol ether was prepared by hydrosilation of a mixture of 2-cyclotetradecenone and 3-cyclotetradecenone. Isomerization of the β,γ-unsaturated ketone to the α,β-unsaturated ketone occurs faster than the 1,4-hydrosilation reaction.



(14.19)

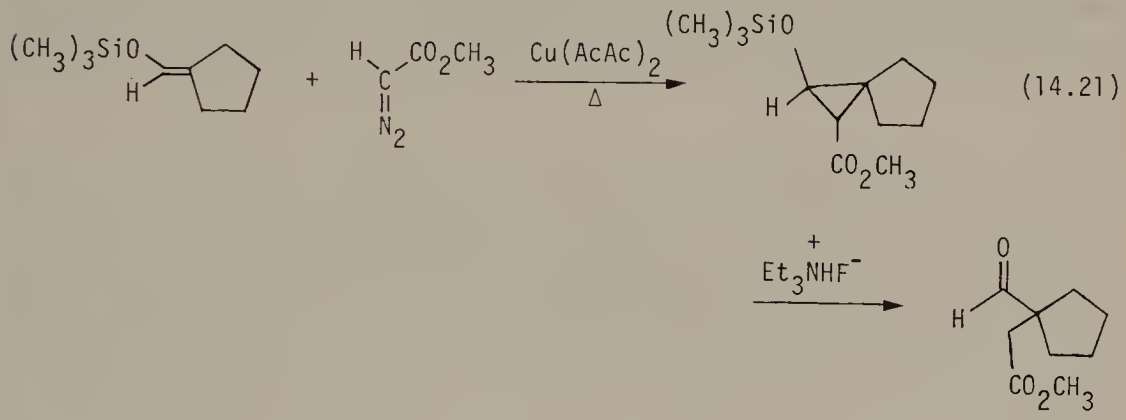
In a similar manner, dibromocarbene reacts with trimethylsilyl enol ethers to yield 1,1-dibromo-2-trimethylsilyloxycyclopropanes. These undergo reaction with methanolic HCl to yield α-bromo-α,β-unsaturated ketones or aldehydes [24].

Chloromethylcarbene adds to both cyclic [25] and alicyclic [26] trimethylsilyl enol ethers to give 1-chloro-1-methyl-2-trimethylsilyloxycyclopropanes. On heating, these lose TMS-Cl to yield α-methyl-α,β-unsaturated ketones [27].



(14.20)

Copper salts catalyze the cyclopropanation of trimethylsilyl enol ethers by methyl diazoacetate to yield 1-carbomethoxy-2-trimethylsilyloxycyclopropanes. Treatment of these with triethylammonium fluoride results in ring opening and formation of γ-keto esters, or γ-aldehydo esters [28].



(14.21)

References

1. Simmons, H.E., Smith, R.D.: J. Am. Chem. Soc. *80*, 5223 (1958)
2. Simmons, H.E., Smith, R.D.: J. Am. Chem. Soc. *81*, 4256 (1959)
3. Denis, J.M., Girard, C., Conia, J.M.: Syn. 549 (1972)
4. Murai, S., Aya, T., Sonoda, N.: J. Org. Chem. *38*, 4354 (1973)
5. Rubottom, G.M., Lopez, M.I.: J. Org. Chem. 38, 2097 (1973)
6. Conia, J.M., Girard, C.: Tetrahedron Lett. 2767 (1973)
7. Ryu, I., Murai, S., Otani, S., Sonoda, N.: Chem. Lett. 93, (1976)
8. Girard, C., Conia, J.M.: Tetrahedron Lett. 3333 (1974)
9. Girard, C., Conia, J.M.: Tetrahedron Lett. 3327 (1974)
10. Girard, C., Amice, P., Barnier, J.P., Conia, J.M.: Tetrahedron Lett. 3329 (1974)
11. Trost, B.M., Bogdanowicz, M.J.: J. Am. Chem. Soc. *95*, 5311 (1973)
12. Trost, B.M., Scudder, P.H.: J. Org. Chem. *46*, 506 (1981)
13. For a review of the rearrangement of vinyl cyclopropanes to cyclopentenes see: Rearrangements in Small Ring Compounds by Breslow, R., in Molecular Rear-

rangements (de Mayo, P., Ed.) Vol. I. pp. 234–245, New York: Interscience Publishers, 1963
14. Monti, S., Cowherd, F.G., McAninch, T.W.: J. Org. Chem. *40*, 858 (1975)
15. Ryu, I., Murai, S., Otani, S., Sonoda, N.: Tetrahedron Lett. 1995 (1977)
16. Murai, S., Aya, T., Renge, T., Ryu, I., Sonoda, N.: J. Org. Chem. *39*, 858 (1974)
17. Ryu, I., Murai, S., Sonoda, N.: Tetrahedron Lett. 4611 (1977)
18. Ito, Y., Saegusa, T.: J. Org. Chem. *42*, 2326 (1977)
19. Murai, S., Seki, Y., Sonoda, N.: J. Chem. Soc., Chem. Commun. 1032 (1974)
20. Ryu, I., Matsumoto, K., Ando, M., Murai, S., Sonoda, N.: Tetrahedron Lett. 4283 (1980)
21. Rubottom, G.M., Marrero, R., Krueger, D.S., Schreiner, J.L.: Tetrahedron Lett. 4013 (1977)
22. Ito, Y., Fujii, S., Saegusa, T.: J. Org. Chem. *41*, 2073 (1976)
23. Stork, G., MacDonald, T.L.: J. Am. Chem. Soc. *97*, 1264 (1975)
24. Amice, P., Blanco, L., Conia, J.M.: Syn. 196 (1976)
25. Blanco, L., Amice, P., Conia, J.M.: Syn. 289 (1981)
26. Blanco, L., Amice, P., Conia, J.M.: Syn. 291 (1981)
27. Blanco, L., Slougui, M., Rousseau, G., Conia, J.M.: Tetrahedron Lett. 645 (1981)
28. Reissig, H.U., Hirsch, E.: Angew. Chem. Int. Ed. *19*, 813 (1980)

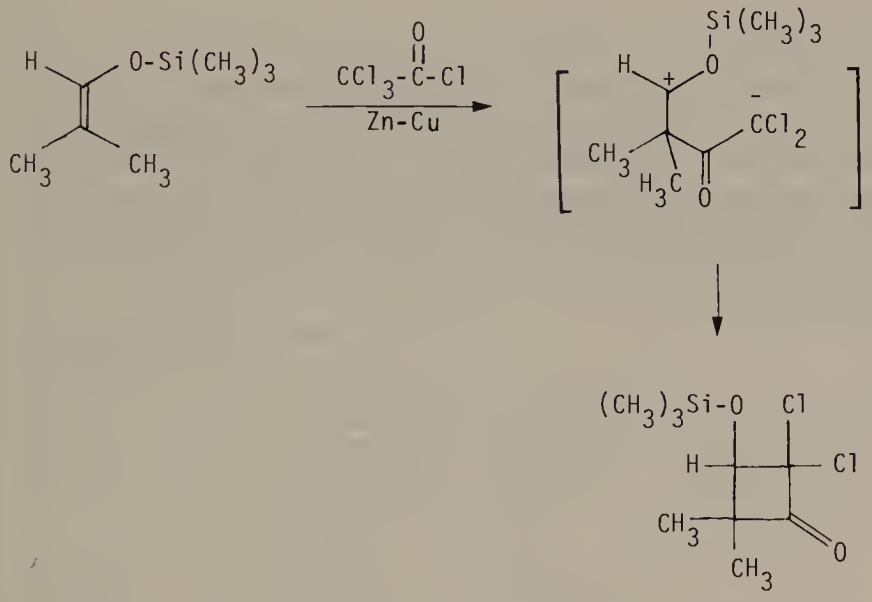
15 Cycloaddition and Electrocyclic Reactions of Silyl Enol Ethers

15.1 Introduction

The electron rich double bonds of silyl enol ethers and silyloxy dienes undergo a variety of cycloaddition and electrocyclic reactions.

15.2 [2 + 2] Cycloaddition

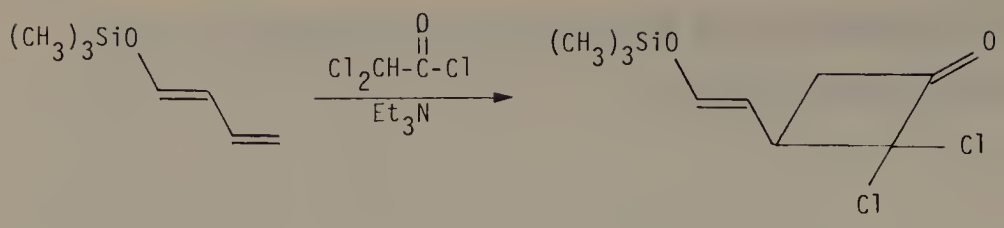
Trimethylsilyl enol ethers undergo regiospecific [2 + 2] cycloaddition with dichloroketene [1–3]. The regiospecificity results from a 1,4-zwitterionic intermediate comprised of trimethylsilyloxy stabilized carbocation and an α,α-dichloro enolate anion.



(15.1)

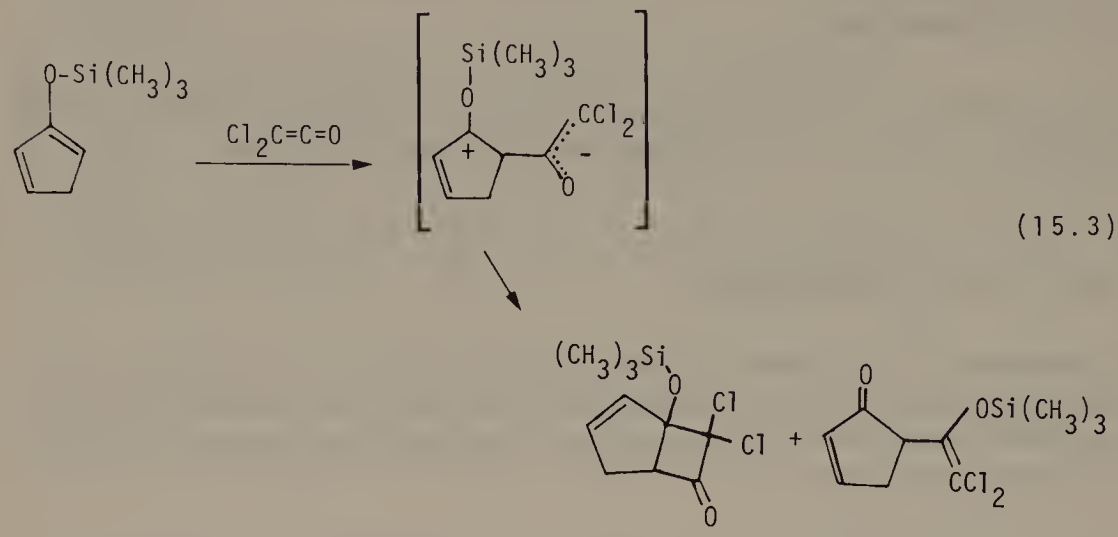
Consistent with this proposal, α-trimethylsilyloxy styrene reacts with dichloroketene to yield 1,1-dichloro-2-trimethylsilyloxy-4-phenyl-but-1-en-4-one [1].

1-Trimethylsilyloxy-1,3-butadiene undergoes regiospecific [2 + 2] cycloaddition with dichloroketene to yield 2,2-dichloro-3-[2′-(trimethylsilyloxy)-vinyl cyclobutanone [4].



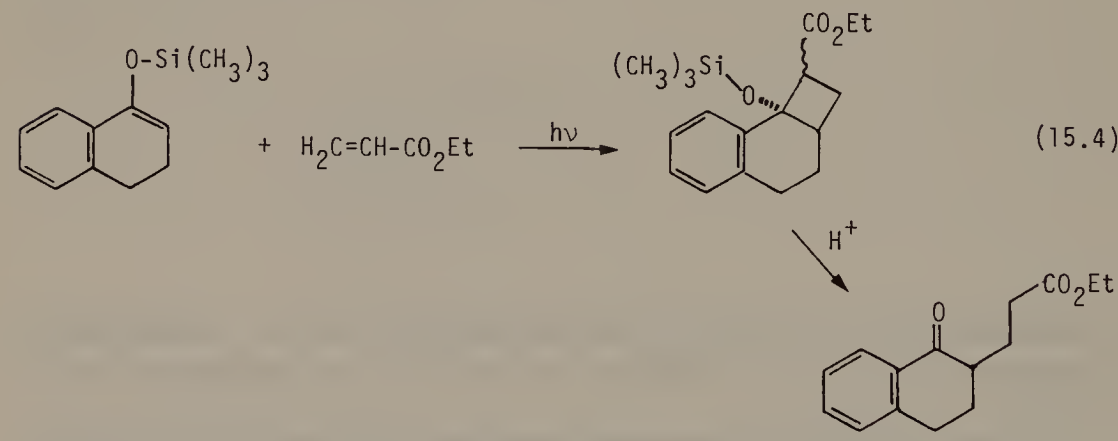
(15.2)

On the other hand, dichloroketene reacts with 2-trimethylsilyloxy-1,3-cyclopentadiene to yield two products. Both result from an initial 1,4-zwitterionic intermediate [4]. The reason for the difference between the two systems is not clear.



(15.3)

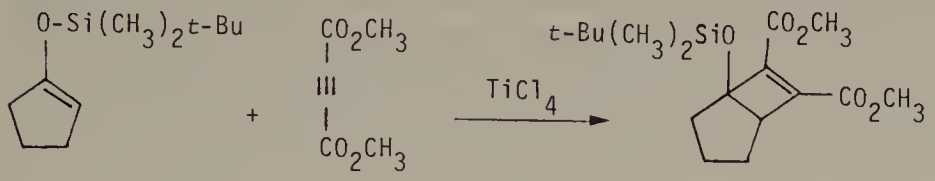
Trimethylsilyl enol ethers of α-tetralone and α-indanone undergo regiospecific triplet sensitized [2+2] photo-cycloaddition reactions with α,β-unsaturated carbonyl compounds such as ethyl acrylate, acrylonitrile and methyl vinyl ketone, to yield 1-trimethylsilyloxy-2-substituted cyclobutanes. These undergo ring opening on treatment with aq. acid to yield products of Michael addition of the trimethylsilyl enol ethers to the α,β-unsaturated carbonyl compounds [5, 41].



(15.4)

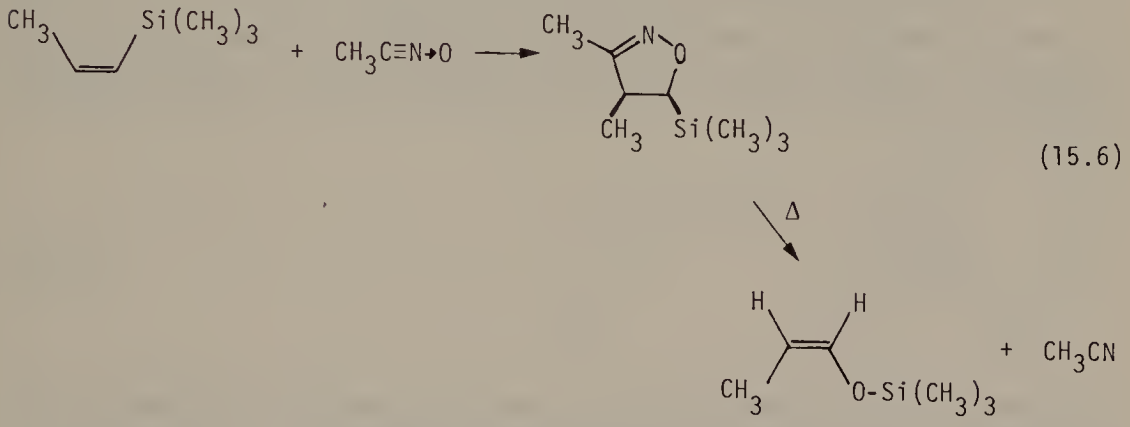
Photo-reaction of trimethylsilyl ethers of 1- and 2-naphthol with acrylonitrile yields similar results [6].

$TiCl_4$ causes silyl enol ethers to undergo [2 + 2] cycloaddition reactions with alkynes and alkenes which are substituted with electron withdrawing groups [7].



(15.5)

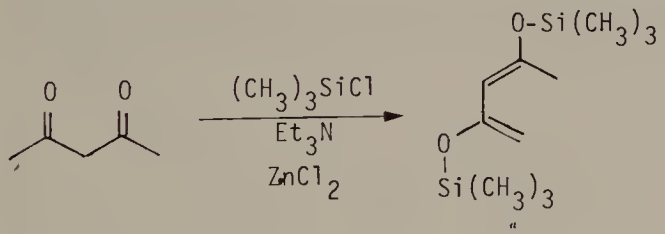
E and *Z*-1-trimethylsilyl propene undergo stereospecific [3 + 2] cycloaddition reactions with acetonitrile oxide to yield stereoisomeric 5-trimethylsilyl isoxazolines. These undergo vacuum pyrolysis with loss of acetonitrile and formation of trimethylsilyl enol ethers with retention of stereochemistry [8].



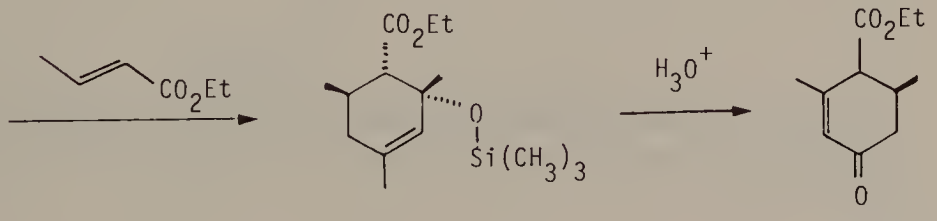
(15.6)

15.3 Diels-Alder, [4 + 2] Cycloaddition

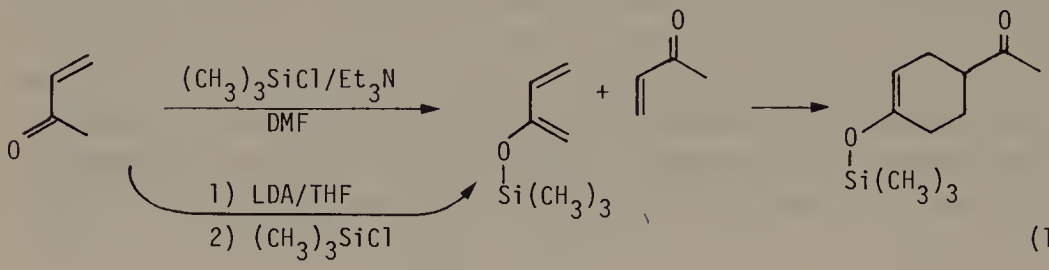
Enolizable 1,3-dicarbonyl compounds, such as acetyl acetone, are readily converted into 1,3-*bis*-(trimethylsilyloxy)-1,3-dienes by reaction with TMS-Cl and triethylamine in the presence of a catalytic amount of zinc chloride [9, 10]. Such dienes readily undergo Diels-Alder reactions with suitable dienophiles [9].



(15.7)

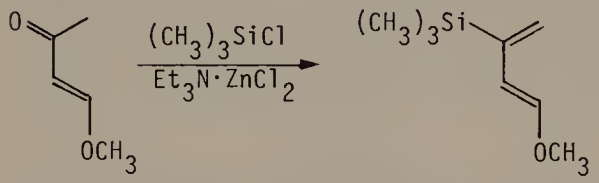


α,β-Unsaturated ketones can be converted to 2-trimethylsilyloxy-1,3-dienes by reaction with TMS-Cl and triethylamine in DMF [11], TMS-I and hexamethyldisilazane [12], or with LDA in THF, followed by addition of TMS-Cl [13]. 2-Trimethylsilyloxy-1,3-cyclohexadiene has been prepared from 2-cyclohexenone by treatment with TMS-Cl and triethylamine in DMF or with LDA and TMS-Cl in THF. These dienes have proved useful in Diels-Alder reactions [11, 13].



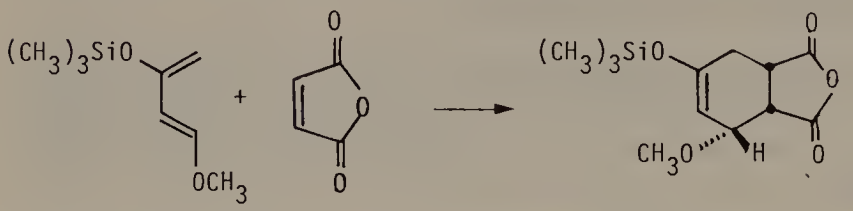
(15.8)

trans-1-Methoxy-3-trimethylsilyloxy-1,3-butadiene has been prepared by reaction of *trans*-4-methoxy but-3-en-2-one with TMS-Cl, triethylamine and zinc chloride [14].



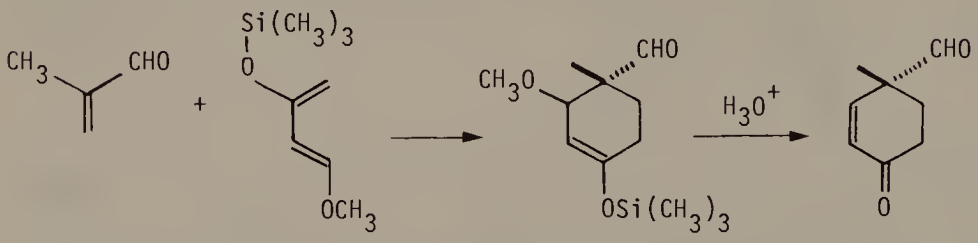
(15.9)

This diene undergoes Diels Alder reactions with a variety of dienophiles, and has been utilized in the synthesis of complex molecules.



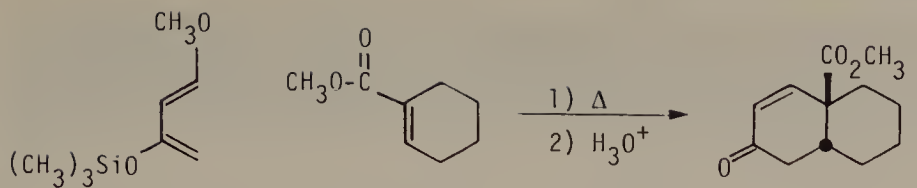
(15.10)

Reaction of this diene with methacrolein provides a one-step synthesis of 4-methyl-4-formyl cyclohex-2-en-1-one.



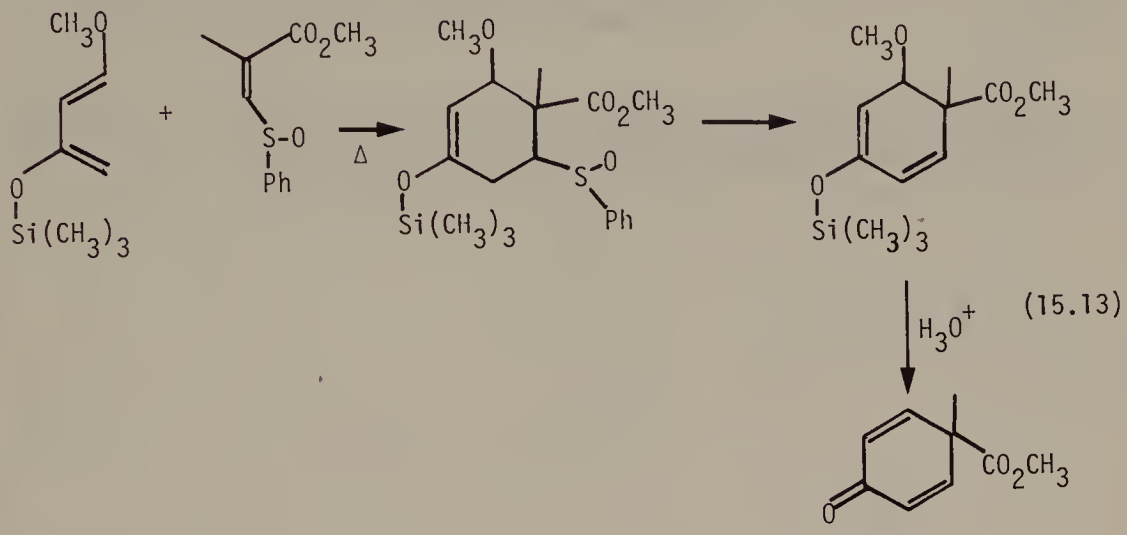
(15.11)

Reaction of *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene with methyl cyclohexene carboxylate leads to *cis*-10-carbomethoxy-1-Δ^1-3-octalone after work-up [15]



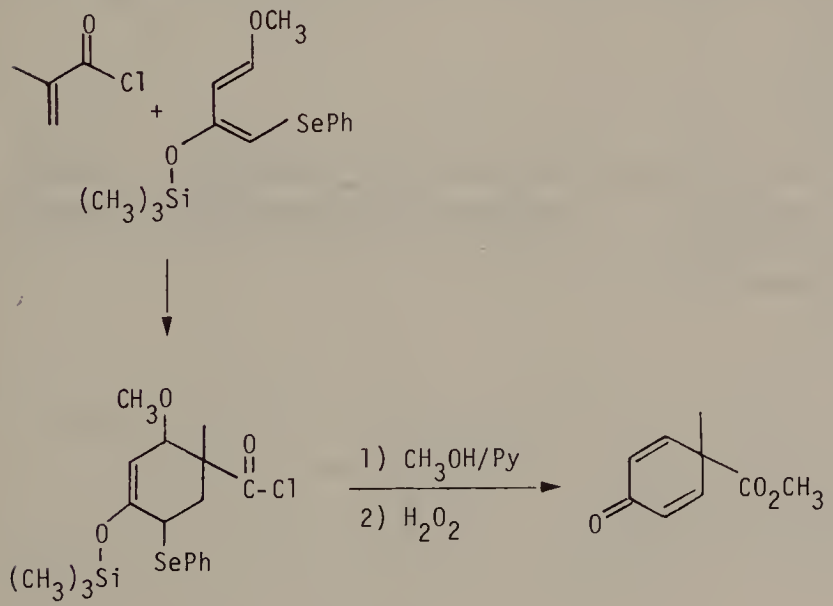
(15.12)

4-Methyl-4-carbomethoxy-2,5-cyclohexadienone has been efficiently prepared by a Diels-Alder reaction of *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene with β-phenylsulfinyl methyl methacrylate [16, 17].



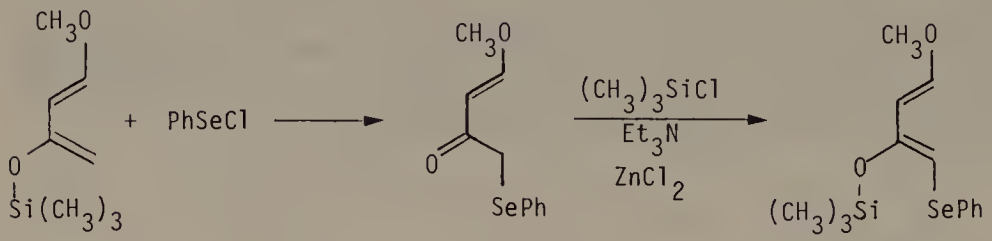
(15.13)

1-Phenylseleno-2-trimethylsilyloxy-4-methoxy-1,3-butadiene undergoes a Diels-Alder reaction with methacryloyl chloride. Treatment of the adduct with methanol in pyridine followed by oxidation with hydrogen peroxide gives 4-methyl-4-carbomethoxy-2,5-cyclohexadienone.



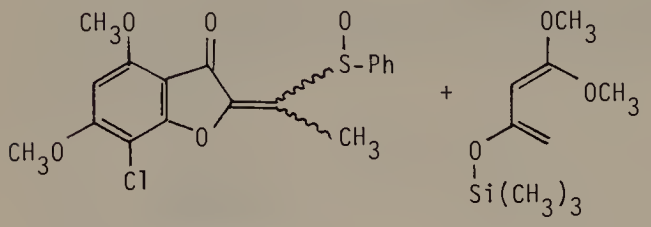
(15.14)

The necessary diene was prepared by reaction of 1-methoxy-3-trimethylsilyloxy-1,3-butadiene with phenylselenyl chloride to give 1-phenylseleno-4-methoxy-but-3-en-2-one. This was silylated by treatment with TMS-Cl, triethylamine and zinc chloride [18].

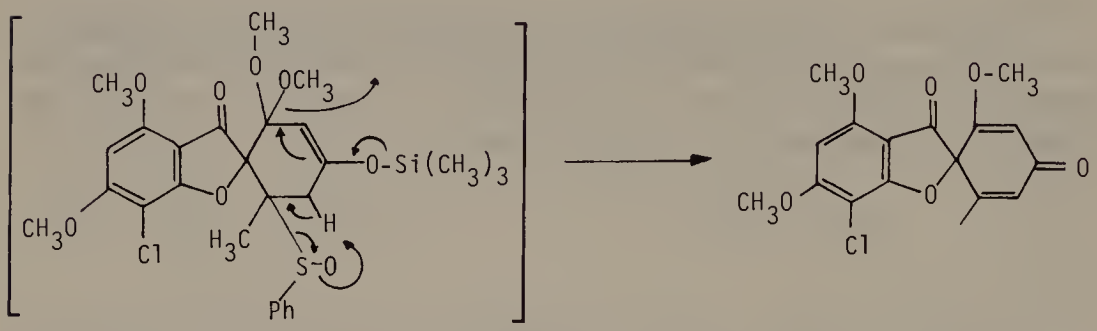


(15.15)

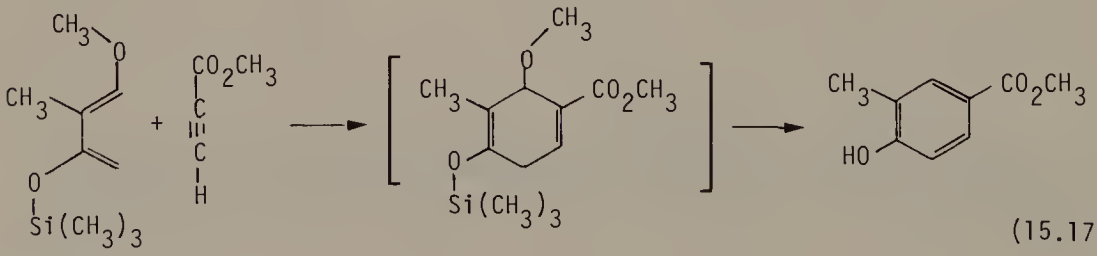
1,1-Dimethoxy-3-trimethylsilyloxy-1,3-butadiene has also proved useful as a diene for the construction of complex molecules [19, 20].



(15.16)

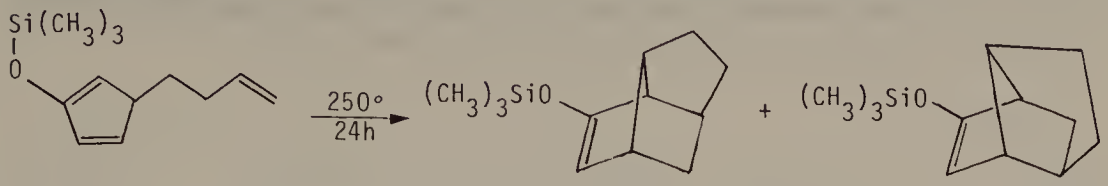


The preparation and Diels-Alder reactions of *E*-1-methoxy-2-methyl-3-trimethylsilyloxy-1,3-butadiene, *E*-1-methoxy-3-trimethylsilyloxy-1,3-pentadiene, and *E,Z-trans*-1-methoxy-3-trimethylsilyloxy-4-phenylseleno-1,3-butadiene have been described [21].



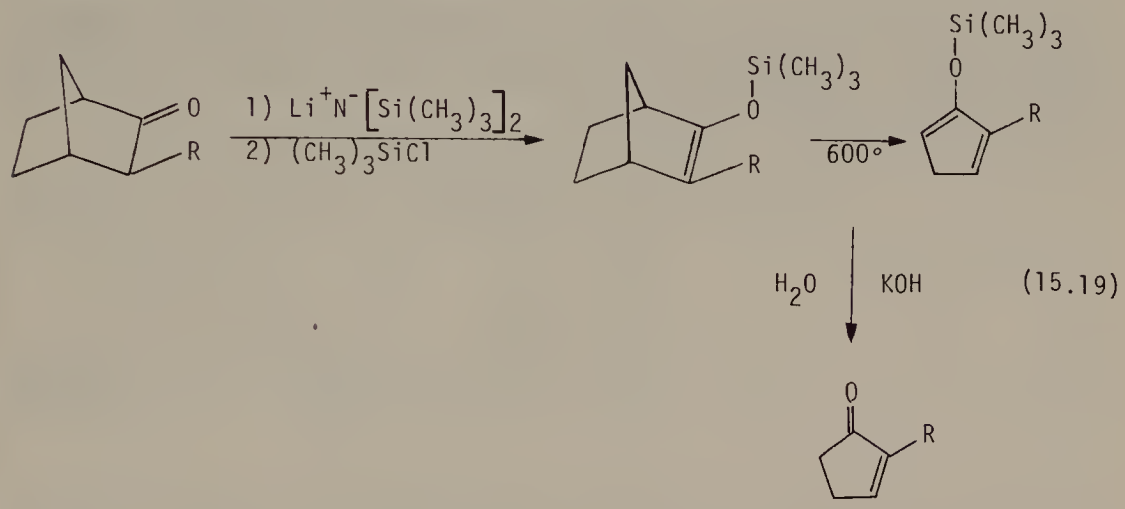
(15.17)

Intramolecular Diels-Alder reactions of 5-(3′-butenyl)-2-trimethylsilyloxycyclopentadiene and related systems have been studied [22, 23].



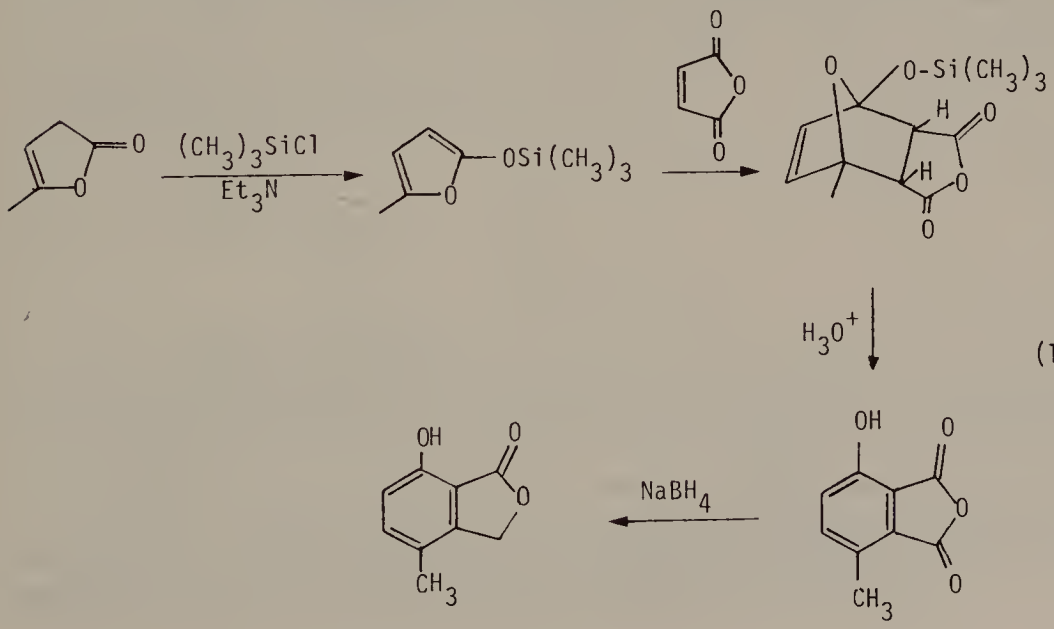
(15.18)

Retro Diels-Alder reactions of trimethylsilyl enol ethers of 2-norboranones provide an efficient route to cyclopentenones [24].



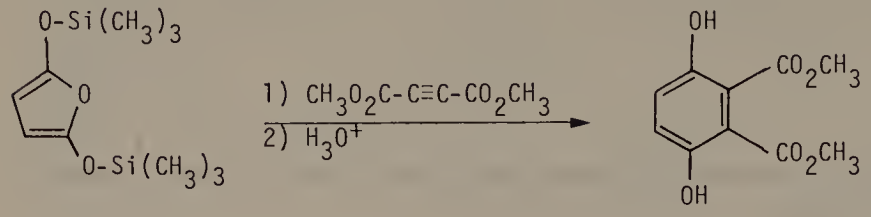
(15.19)

β,γ-Unsaturated γ-lactones can be converted into 2-trimethylsilyloxy furans by treatment with TMS-Cl and triethylamine. The Diels-Alder reaction of 5-methyl-2-trimethylsilyloxyfuran with maleic anhydride yields an adduct which can be converted regiospecifically to 7-hydroxyphthalide [26].



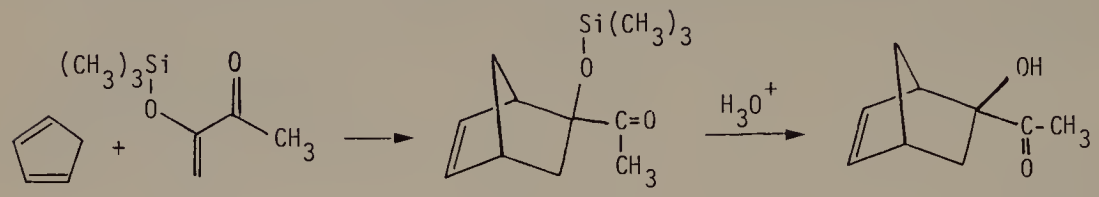
(15.21)

Succinic anhydride reacts with TMS-Cl and triethylamine in the presence of zinc chloride catalyst in acetonitrile to yield 2,5-*bis*-(trimethylsilyloxy) furan. Diels-Alder reaction of this furan with dimethylacetylene dicarboxylate yields, after hydrolysis, 3,6-dihydroxydimethylphthalate [27].



(15.22)

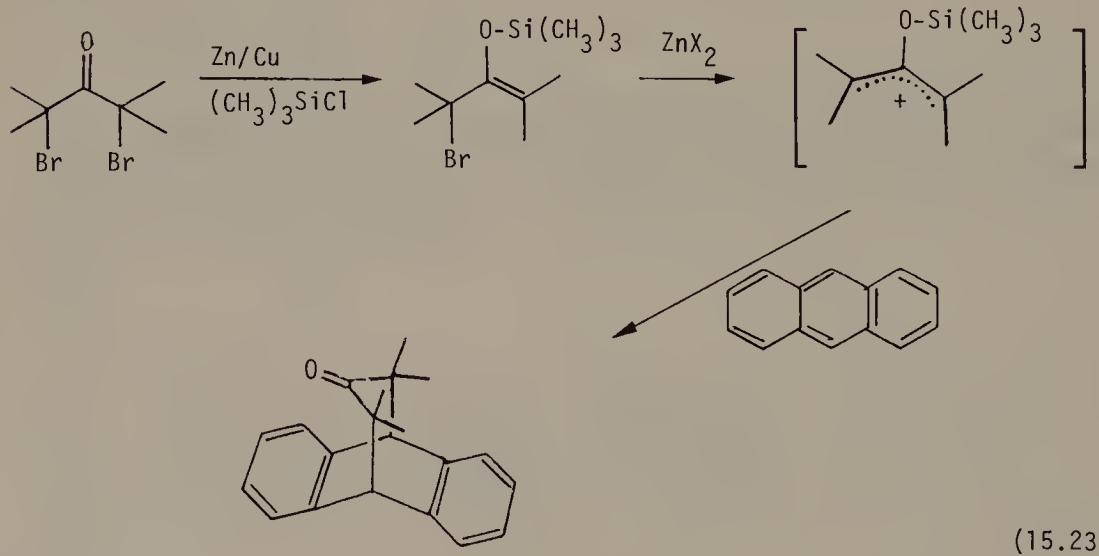
Silyl enol ethers can also serve as the dienophile component in Diels-Alder reactions. 3-Trimethylsilyloxy-3-buten-2-one undergoes Diels-Alder reactions with a number of dienes [25].



(15.20)

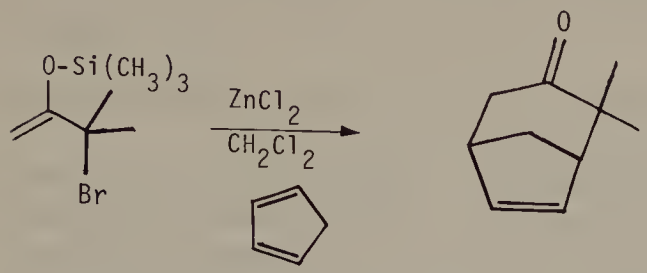
15.4 [3 + 4] and [3 + 2] Cycloaddition Reactions

Reaction of 2,4-dibromo-2,4-dimethyl-3-pentanone with a zinc-copper couple and TMS-Cl in the presence of anthracenes yields 12-oxo-9,10-propano anthracenes [28]. This reaction may occur as outlined (Eq. 15.23).



(15.23)

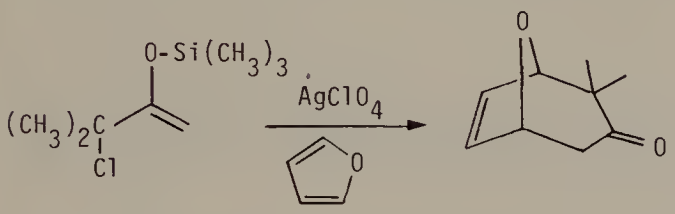
In a similar manner, 3-bromo-3-methyl-2-trimethylsilyloxy-1-butene undergoes zinc chloride assisted ionization to a 2-trimethylsilyloxy substituted allylic carbocation which reacts with 1,3-dienes [42] and α-methyl styrene [42].



(15.24)

3-Bromo-3-methyl-2-trimethylsilyloxy-1-butene was prepared by reaction of 3-bromo-3-methyl-2-butanone with LDA in THF followed by addition of TMS-Cl.

Likewise, 3-chloro-3-methyl-2-trimethylsilyloxy-1-butene undergoes silver ion assisted ionization to yield a 2-trimethylsilyloxy substituted allylic carbocation which undergoes cycloaddition with 1,3-diene [43].

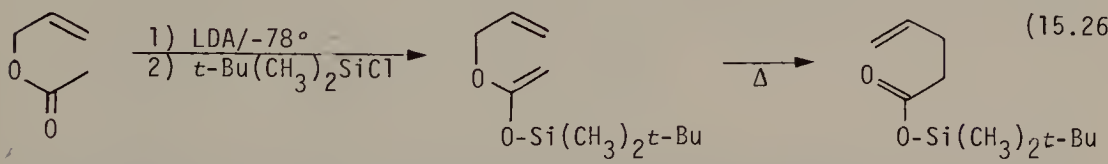


(15.25)

3-Chloro-3-methyl-2-trimethylsilyloxy-1-butene was prepared by reaction of 3-chloro-3-methyl-2-butanone with TMS-Cl and triethylamine in DMF.

15.5 Electrocyclic Reactions of Silyl Enol Ethers

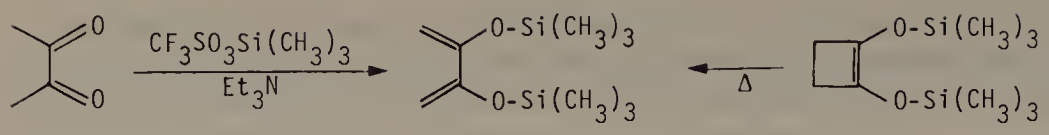
Allyl *t*-butyldimethylsilyl ketene acetals undergo Claisen [3,3]-sigmatropic rearrangement under mild conditions to yield *t*-butyldimethylsilyl γ,δ-unsaturated esters [29, 30, 31].



(15.26)

Allylic acetates can be converted to allyl *t*-butyldimethylsilyl ketene acetals by treatment with LDA at −78°C followed by addition of *t*-butyldimethylchlorosilane.

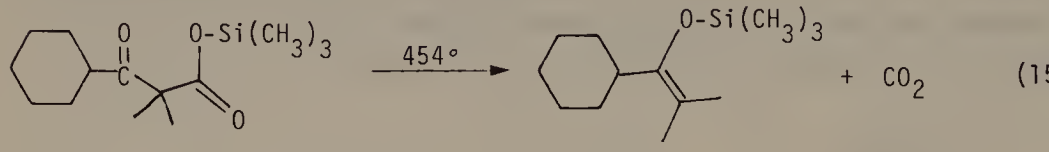
2,3-*bis*(Trimethylsilyloxy)-1,3-butadiene can be prepared by a conrotatory electrocyclic ring opening of 1,2-*bis*(trimethylsilyloxy)-cyclobutene [12]. Alternatively, this interesting diene can be prepared by treatment of 2,3-butanedione with trimethylsilyl trifluoromethane sulfonate [12].



(15.27)

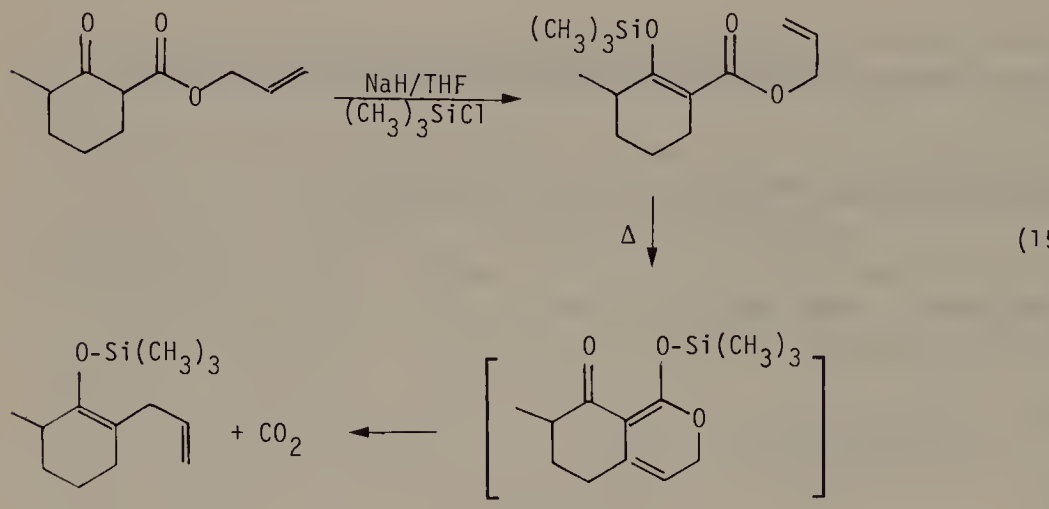
1,2-*bis*(Trimethylsilyloxy) cyclobutene is prepared by the silyl acyloin reaction with diethyl succinate [32].

There are several regiospecific methods to prepare trimethylsilyl enol ethers based on rearrangement reactions. For example trimethylsilyl β-keto carboxylates undergo pyrolysis with transfer of the trimethylsilyl group from the ester to the keto functional group with simultaneous decarboxylation to yield trimethylsilyl enol ethers [33–35]. This is analogous to the thermal decarboxylation of β-keto acids.



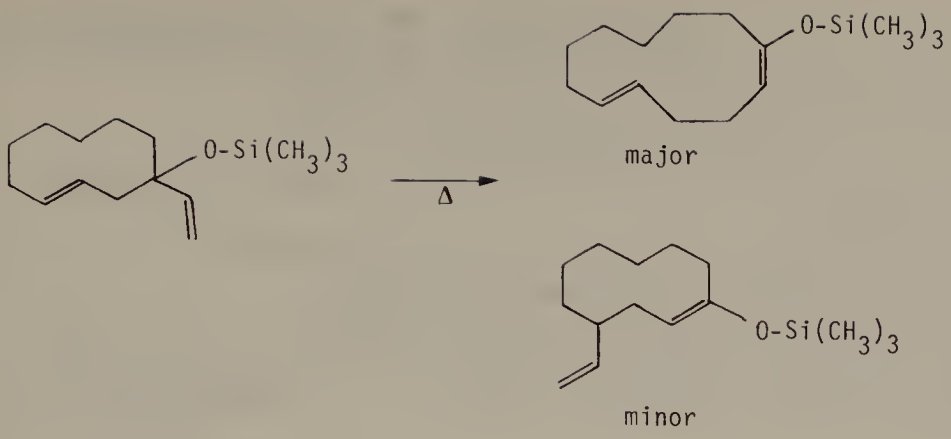
(15.28)

Trimethylsilyl enol ethers of β-keto allyl carboxylates undergo a silyl-Carrol reaction on gas phase pyrolysis to yield specific allyl substituted trimethylsilyl enol ethers and carbon dioxide [33].



(15.29)

Thies has developed a valuable two carbon ring expansion reaction based on the silyloxy-Cope rearrangement [36–40]. Cyclic β,γ-unsaturated ketones react with vinyl Grignard reagent to yield a magnesium alkoxide which reacts with TMS-Cl to give the expected trimethylsilyl ether. Pyrolysis of such compounds largely occurs via a [1,3]-sigmatropic silyloxy-Cope rearrangement to yield a cyclic trimethylsilyl enol ether which possesses two additional carbon atoms [36–40]. The competing [3,3] sigmatropic process is less important.



(15.30)

References

1. Krepski, L.R., Hassner, A.: J. Org. Chem. *43*, 3173 (1978)
2. Brady, W.T., Lloyd, R.M.: J. Org. Chem. *44*, 2560 (1979)
3. Brady, W.T., Lloyd, R.M.: J. Org. Chem. *45*, 2025 (1980)
4. Brady, W.T., Lloyd, R.M.: J. Org. Chem. *46*, 1322 (1981)
5. Mizuno, K., Okamoto, H., Pac, C., Sakurai, H., Murai, S., Sonoda, N.: Chem. Lett. 237 (1975)
6. Akhtar, I.A., McCullough, J.J.: J. Org. Chem. *46*, 1447 (1981)
7. Clark, R.D., Untch, K.G.: J. Org. Chem. *44*, 253 (1979)
8. Cunico, R.F.: J. Organometal. Chem. *212*, C51 (1981)
9. Ibuka, I., Ito, Y., Mori, Y., Anoyama, T., Inubushi, Y.: Syn. Comm. *7*, 131 (1977)
10. Hengge, E., Pletka, H.D.: Monat. für Chem. *104*, 1071 (1973)
11. Jung, M.E., McCombs, C.A.: Tetrahedron Lett. 2935 (1976)
12. Simchen, G., Kober, W.: Synthesis, 259 (1976)
13. Wunderly, S.W., Weber, W.P.: J. Org. Chem. *43*, 2277 (1978)
14. Danishefsky, S., Kitahara, T.: J. Am. Chem. Soc. *96*, 7807 (1974)
15. Danishefsky, S., Kitahara, T.: J. Org. Chem. *40*, 538 (1975)
16. Danishefsky, S., Singh, R.K., Harayama, T.: J. Am. Chem. Soc. *99*, 5810 (1977)
17. Danishefsky, S., Harayama, T., Singh, R.K.: J. Am. Chem. Soc. *101*, 7008 (1979)
18. Danishefsky, S., Yan, C.F., McCurry, Jr., P.M.: J. Org. Chem. *42*, 1819 (1977)
19. Danishefsky, S., Walker, F.J.: J. Am. Chem. Soc. *101*, 7018 (1979)
20. Danishefsky, S., Singh, R.K., Gammill, R.B.: J. Org. Chem. *43*, 379 (1978)
21. Danishefsky, S., Yan, C.F., Singh, R.K., Gammill, R.B., McCurry, Jr., P.M., Fritsch, N., Clardy, J.: J. Am. Chem. Soc. *101*, 7001 (1979)
22. Snowden, R.L.: Tetrahedron Lett. 97 (1981)
23. Snowden, R.L.: Tetrahedron Lett. 101 (1981)
24. Bloch, R.: Tetrahedron Lett. 3945 (1979)
25. Ardecky, R.J., Kerdesky, F.A.J., Cava, M.P.: J. Org. Chem. *46*, 1483 (1981)
26. Asaoka, M., Miyake, K., Takei, H.: Chem. Lett. 167 (1977)
27. Brownbridge, P., Chan, T.H.: Tetrahedron Lett. 3423 (1980)
28. Giguere, R.J., Hoffmann, H.M.R., Hursthouse, M.B., Trotter, J.: J. Org. Chem. *46*, 2868 (1981)
29. Ireland, R.E., Mueller, R.H., Willard, A.K.: J. Am. Chem. Soc. *98*, 2868 (1976)
30. Ireland, R.E., Mueller, R.H.: J. Am. Chem. Soc. *94*, 5897 (1972)
31. Katzenellenbogen, J.A., Christy, K.J.: J. Org. Chem. *39*, 3315 (1974)
32. Bloomfield, J.J.: Tetrahedron Lett. 587 (1968)

33. Coates, R.M., Sandefur, L.O., Smillie, R.D.: J. Am. Chem. Soc. *97*, 1619 (1975)
34. Bloch, R., Boivin, F., Bortolussi, M.: J. Chem. Soc. Chem. Commun. 371 (1976)
35. Bloch, R., Denis, J.M.: J. Organometal. Chem. *90*, C9 (1975)
36. Thies, R.W., Bolesta, R.W.: J. Org. Chem. *41*, 1233 (1976)
37. Thies, R.W.: J. Am. Chem. Soc. *94*, 7074 (1972)
38. Thies, R.W., Wills, M.T., Chin, A.W., Schick, L.E., Walton, E.S.: J. Am. Chem. Soc. *95*, 5281 (1973)
39. Thies, R.W., Billigmeier, J.E.: J. Am. Chem. Soc. *96*, 200 (1974)
40. Thies, R.W.: J. Chem. Soc. Chem. Commun. 237 (1971)
41. Pak, C., Okamoto, H., Sakurai, H.: Synthesis, 589 (1978)
42. Sakurai, H., Shirahata, A., Hosomi, A.: Angew. Chem. Int. Ed. *18*, 163 (1979)
43. Shimizu, N., Tsuno, Y.: Chem. Lett. 103 (1979)

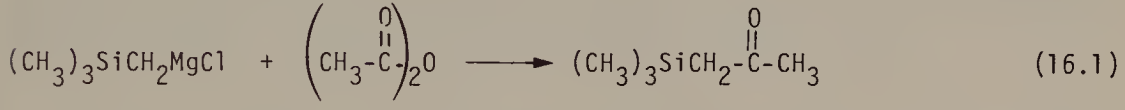
16 Preparation of Silyl Enol Ethers

16.1 Introduction

Due to the wide range of useful reactions which silyl enol ether undergo, numerous methods have been developed to prepare them. We will consider these methods in this chapter. Certain of these have been previously discussed (see Chapter 14 and 15).

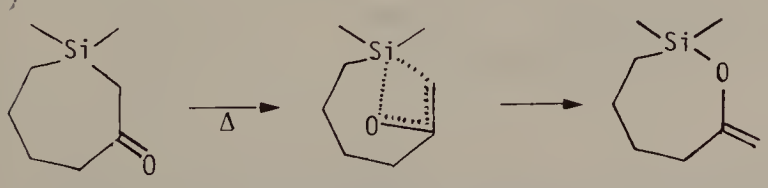
16.2 Rearrangement of β-Silyl Ketones

β-Trimethylsilyl ketones have been prepared by reaction of trimethylsilylmethyl magnesium chloride with anhydrides [1], or by reaction of diazomethane with α-silyl ketones [2].



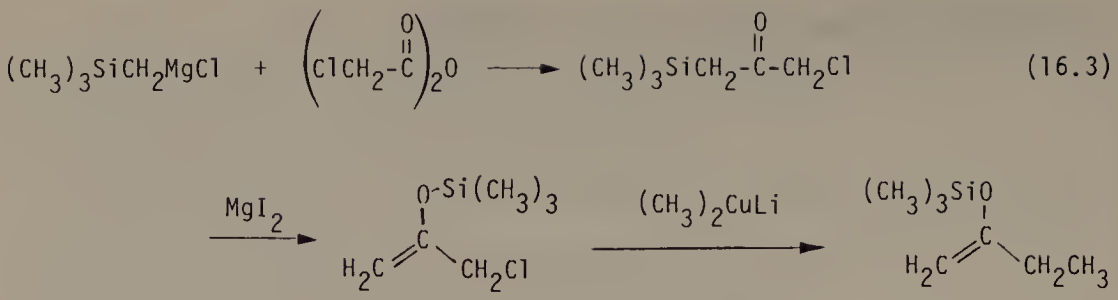
(16.1)

β-Trimethylsilyl ketones easily rearrange to the isomeric trimethylsilyl enol ethers. This rearrangement can be catalyzed by Lewis acids such as mercuric iodide or bromide. Under these conditions, the rearrangement is not completely intramolecular [3]. On the other hand, the rearrangement can also be carried out by heating β-trialkylsilyl ketones to between 160–200 °C. Under these conditions, the rearrangement is strictly intramolecular. The thermal rearrangement of an optically active β-silyl ketone to the corresponding silyl enol ether occurs with complete retention of configuration at the silyl center [4–6].



(16.2)

Lithium dialkyl cuprates undergo regiospecific S_n2' coupling with 1-chloro-2-trimethylsilyloxy propene to give trimethylsilyl enol ethers as outlined [7].

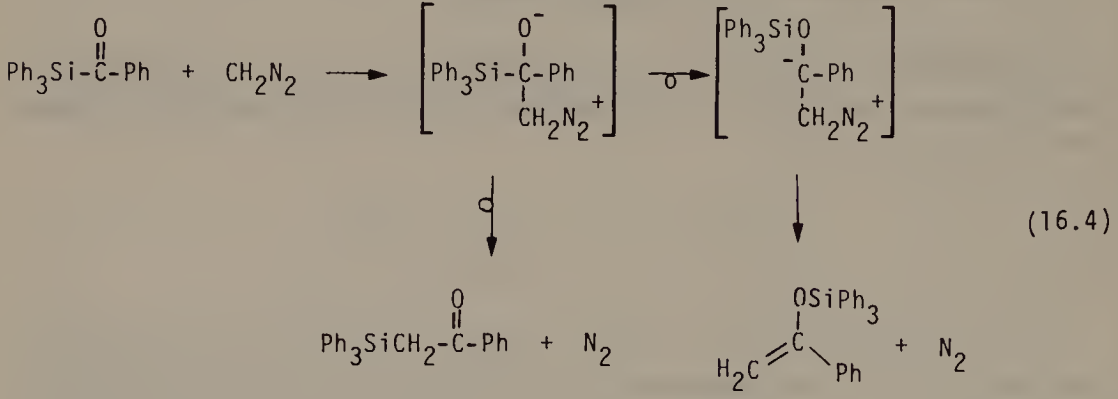


(16.3)

The reaction of β-trialkyltin ketones or esters with trialkylhalosilanes yields trialkylsilyl enol ethers or alkyl trialkylsilyl ketene acetals, respectively and trialkyltin halides [8].

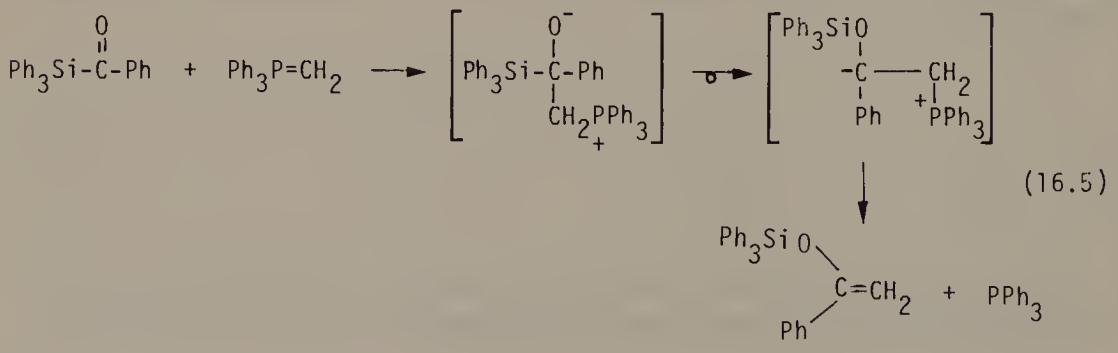
16.3 Brook Rearrangement, α-Silyl Ketones

α-Silyl ketones react with diazomethane via a 1,4-dipolar intermediate to yield mixtures of silyl enol ethers and β-silyl ketones [2]. The rearrangement of silicon from carbon to the negatively charged oxygen with formation of a carbanion is related to the Brook rearrangement [9].



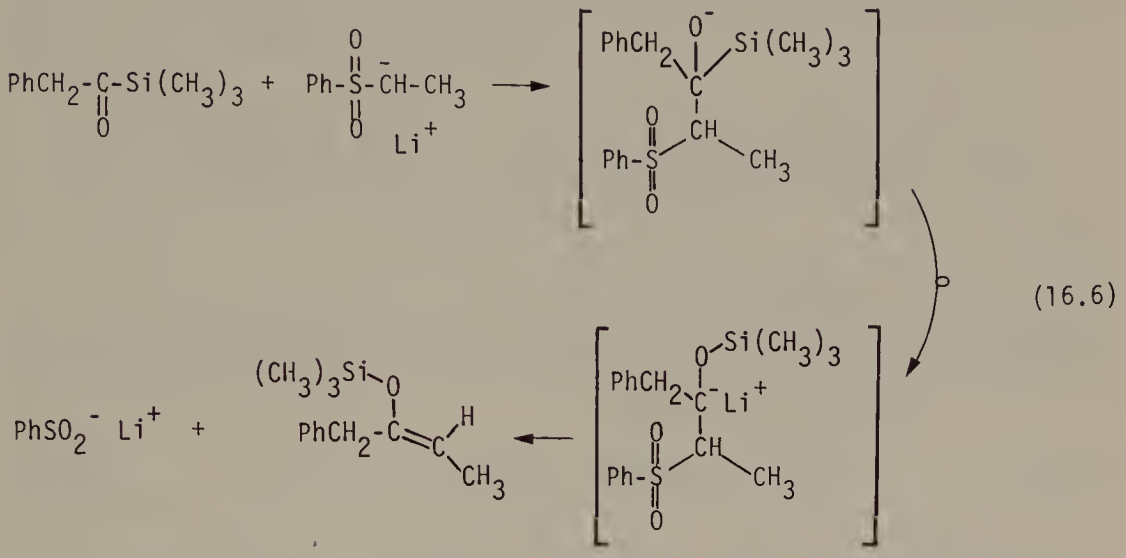
(16.4)

The addition of methylene triphenylphosphorane to α-silyl ketones yields a similar 1,4-dipolar intermediate. Aryl α-silyl ketones yield silyl enol ethers, while alkyl α-silyl ketones yield vinyl silanes via a Wittig reaction. The stabilizing effect of an aryl group on an adjacent carbanion may account for this difference [10].



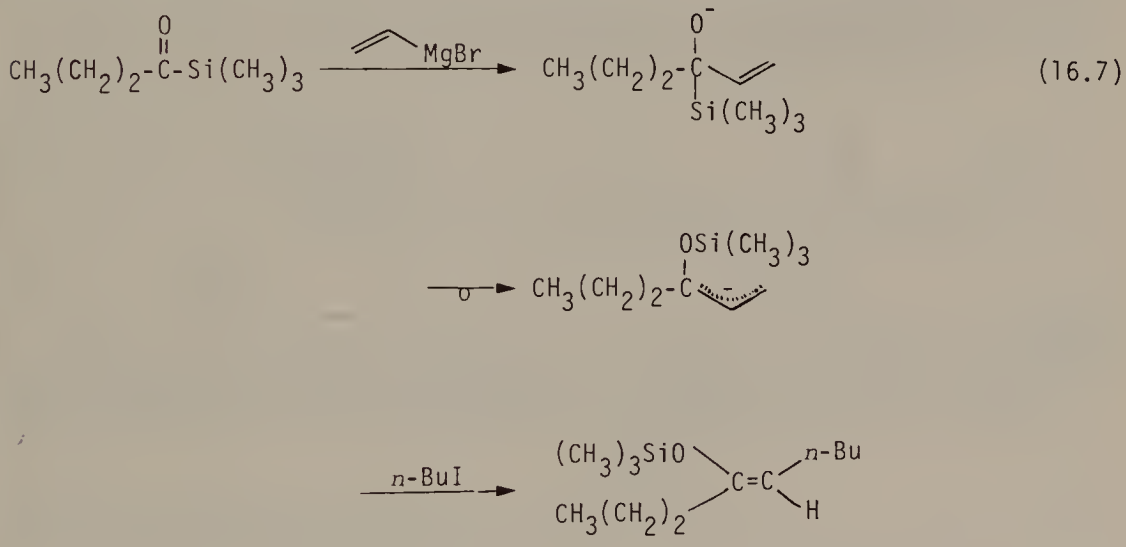
(16.5)

Benzyl-trimethylsilyl ketone reacts with α-lithioethyl phenyl sulphone to yield 1-phenyl-2-trimethylsilyloxy-2-butene and lithium phenyl sulfinate. This trimethylsilyl enol ether cannot be prepared from benzyl ethyl ketone either under the normal kinetic (LDA/TMS-Cl) or thermodynamic (TMS-Cl/Et_3N) conditions [11].



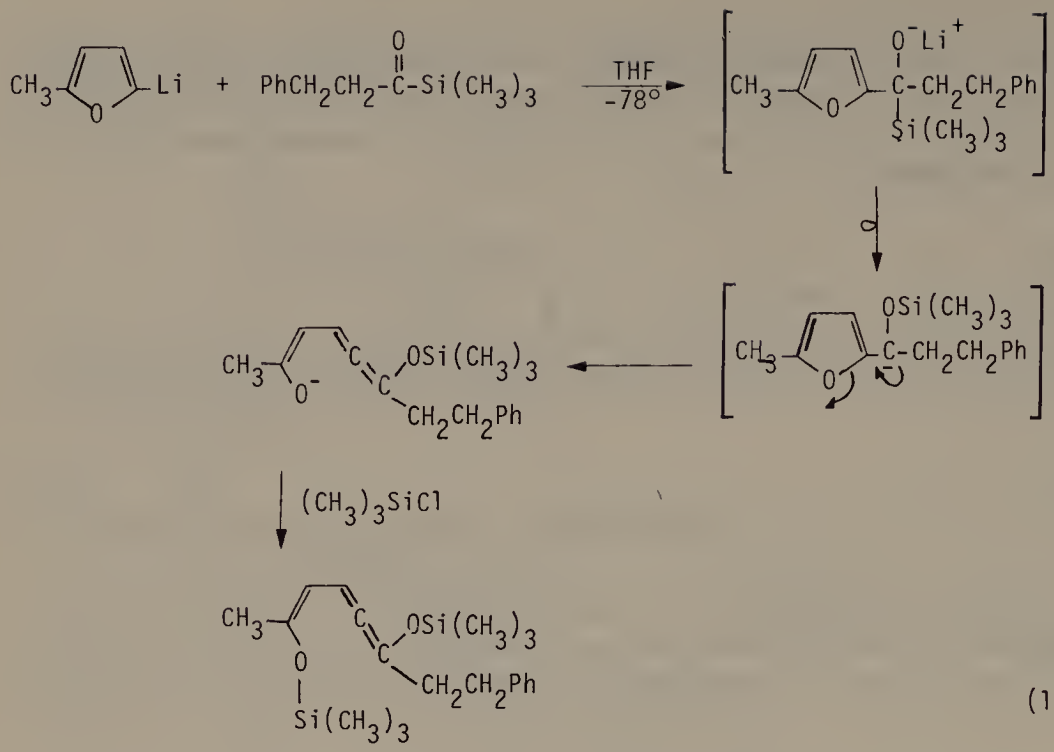
(16.6)

The addition of vinyl magnesium bromide to α-trimethylsilyl ketones yields α-trimethylsilyl allylic alcohols. The corresponding these lithium alkoxides undergo the Brook rearrangement. Reaction of these trimethylsilyloxy substituted allylic anions with alkyl iodides occurs stereo- and regiospecifically at the γ-position to yield *Z*-trimethylsilyl enol ethers [12, 13].



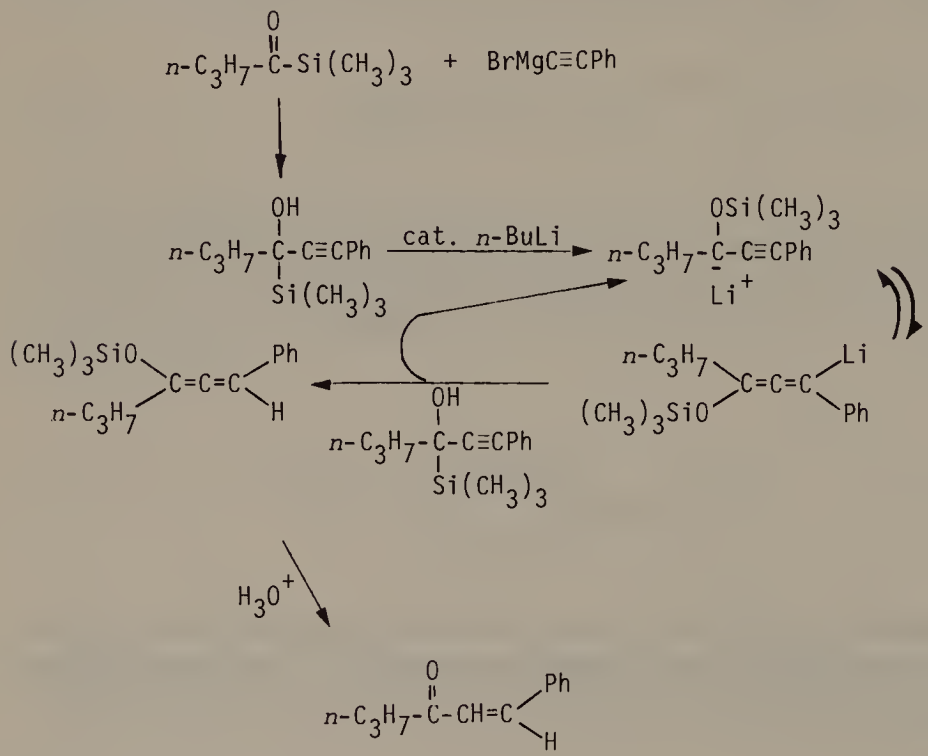
(16.7)

The addition of 2-lithio furans to α-trimethylsilyl ketones yields α-lithio-α-trimethylsilyloxy furans via a Brook rearrangement. Ring opening gives an enolate anion which reacts with TMS-Cl to give 1,5-*bis*(trimethylsilyloxy)-1,2,4-trienes [14].



(16.8)

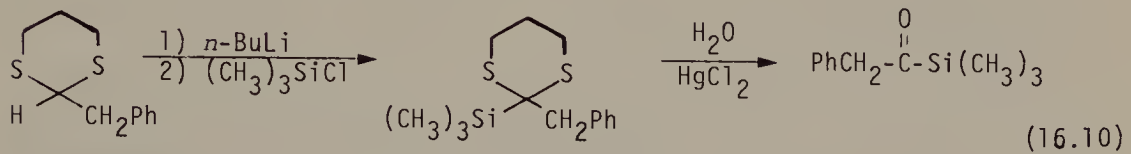
1-Trimethylsilyl propargyl alcohols undergo Brook rearrangement on treatment with a catalytic amount of *n*-butyl lithium to yield trimethylsilyloxy allenes. These undergo hydrolysis to yield α,β-unsaturated aldehydes (Eq. 16.9). If a stoichiometric amount of *n*-butyl lithium is used, 1-lithio-3-trimethylsilyloxy allenes result. These will react with alkyl iodides specifically at the 1-position [15].



(16.9)

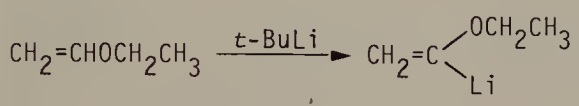
16.4 Preparation of α-Silyl Ketones

These methods obviously depend on the availability of α-silyl ketones. One of the best methods to prepare α-silyl ketones utilizes 1,3-dithiane. A major problem is hydrolysis of the 2-alkyl-2-trimethylsilyl-1,3-dithiane to the α-trimethylsilyl ketone [16, 17]. Chloramine T[3] may be a more effective hydrolysis catalyst than mercuric chloride [11].

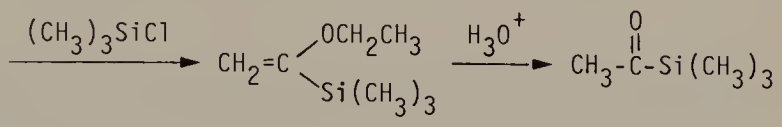


(16.10)

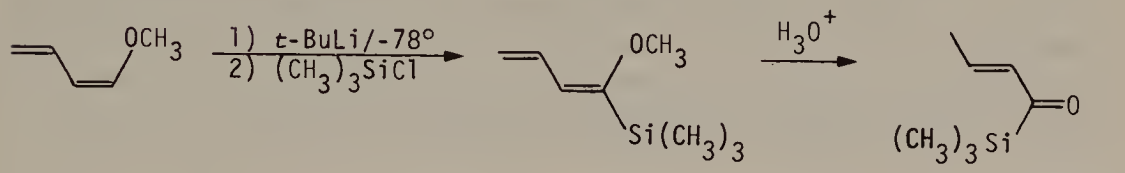
α-Silyl ketones have also been prepared by reaction of 1-ethoxyvinyl lithium with chlorosilanes. The resulting 1-ethoxyvinyl silanes are relatively easy to hydrolyze [18].



(16.11)

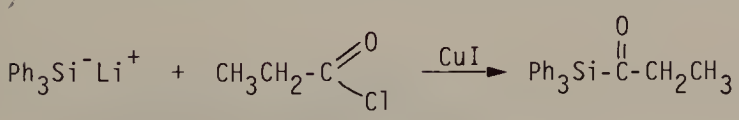


In a similar manner, α-trimethylsilyl-α′,β′-unsaturated ketones have been prepared from 1-methoxy-1,3-butadiene [75, 76], or 1-methoxy allene [77].



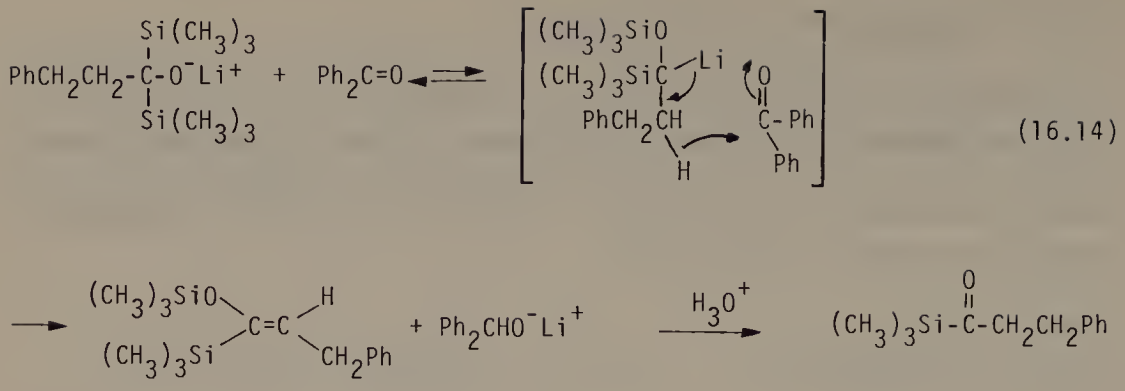
(16.12)

Triphenylsilyl lithium reacts with aliphatic acid chlorides and a stoichiometric amount of cuprous iodide to yield α-triphenylsilyl ketones [19].



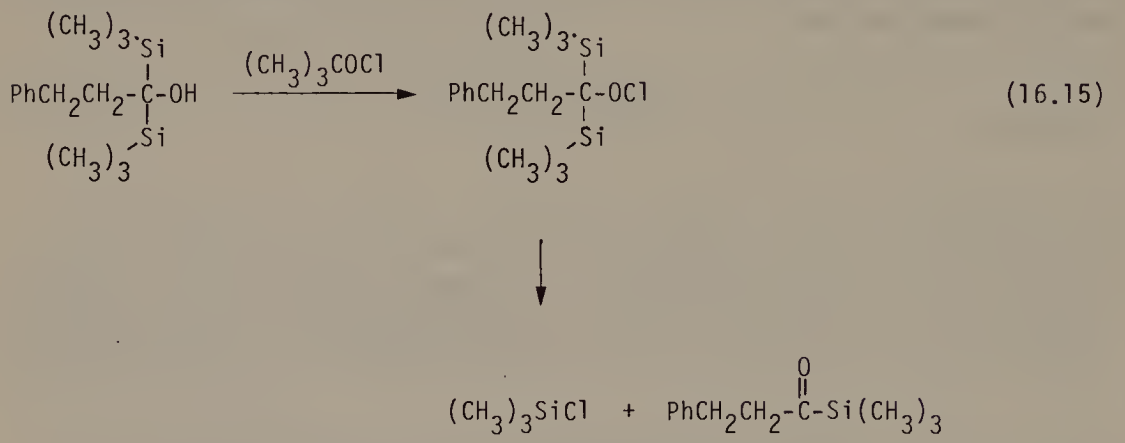
(16.13)

Lithium 1,1-*bis*(trimethylsilyl) alkoxides react with benzophenone in nonpolar solvents to yield lithium diphenylmethoxide and α-trimethylsilyl trimethylsilyl enol ethers. These can be easily hydrolyzed to α-trimethylsilyl ketones [20].



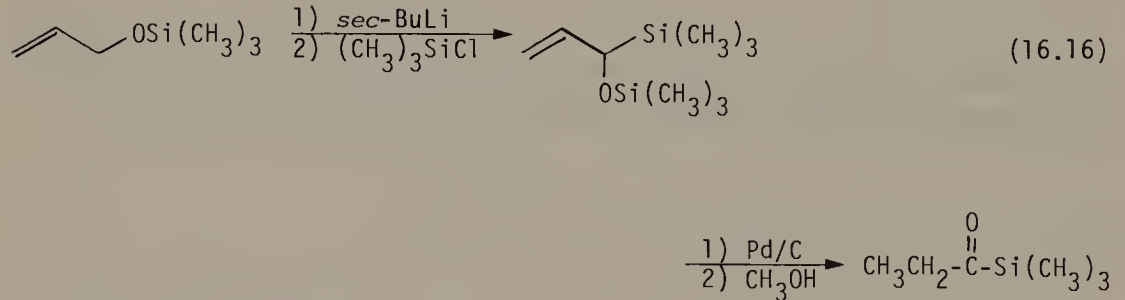
(16.14)

Oxidation of 1,1-*bis*(trimethylsilyl)alkan-1-ols with *t*-butyl hypochlorite also yields acyl silanes [21].



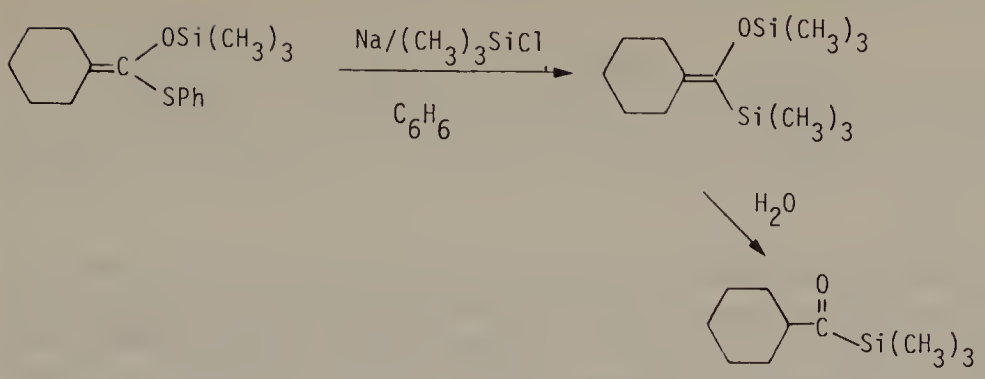
(16.15)

Acyl silanes can also be prepared from α-trimethylsilyloxy allyl silanes. These undergo Pd/C catalyzed isomeration to yield α-trimethylsilyloxy vinyl silanes. These are easily hydrolyzed to acyl silanes [22]. α-Trimethylsilyloxy allyl silanes can be prepared by metallation of trimethylsilyl allyl ethers with *sec*-butyl lithium followed by reaction with chlorosilanes [23].



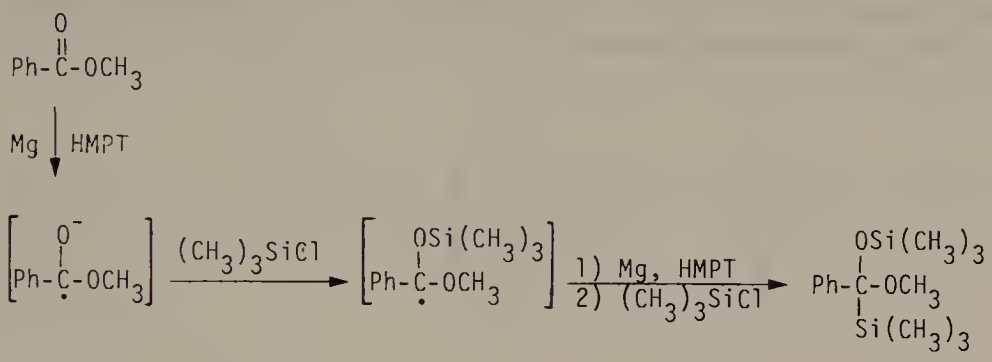
(16.16)

α-Phenylthio trimethylsilyl enol ethers undergo reductive silylation to yield α-trimethylsilyl trimethylsilyl enol ethers [24] (see Chapter 19).



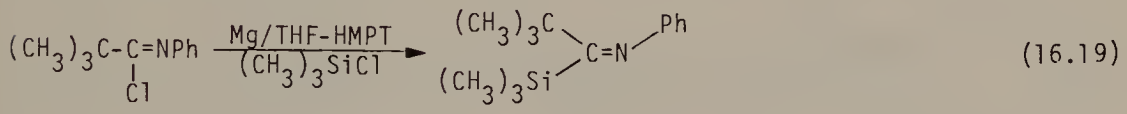
(16.17)

Methyl benzoate undergoes reductive silylation to yield α-methoxy-α-trimethylsilyl-α-trimethylsilyloxytoluene which can be hydrolyzed to yield benzoyltrimethylsilane [25] (see Chapter 19).



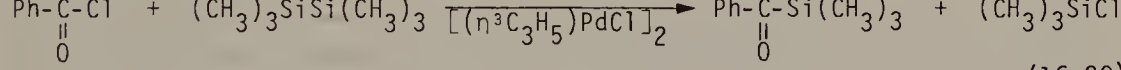
(16.18)

N-Phenyl pivalimidoyl chloride reacts with magnesium and TMS-Cl in THF/HMPT to yield the C-trimethylsilylimine. On hydrolysis this gives pivaloyltrimethylsilane [26].



(16.19)

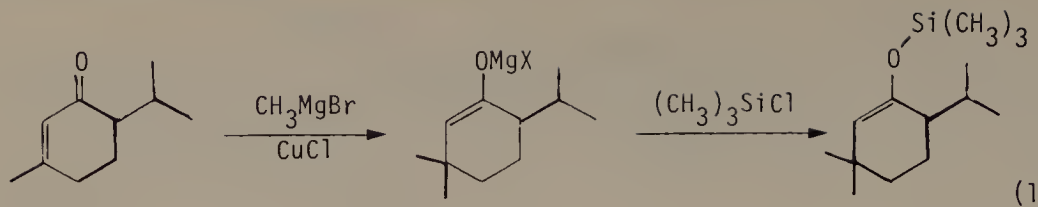
Benzoyltrimethylsilane has been prepared by reaction of benzoyl chloride with hexamethyldisilane catalyzed by a palladium complex [79].



(16.20)

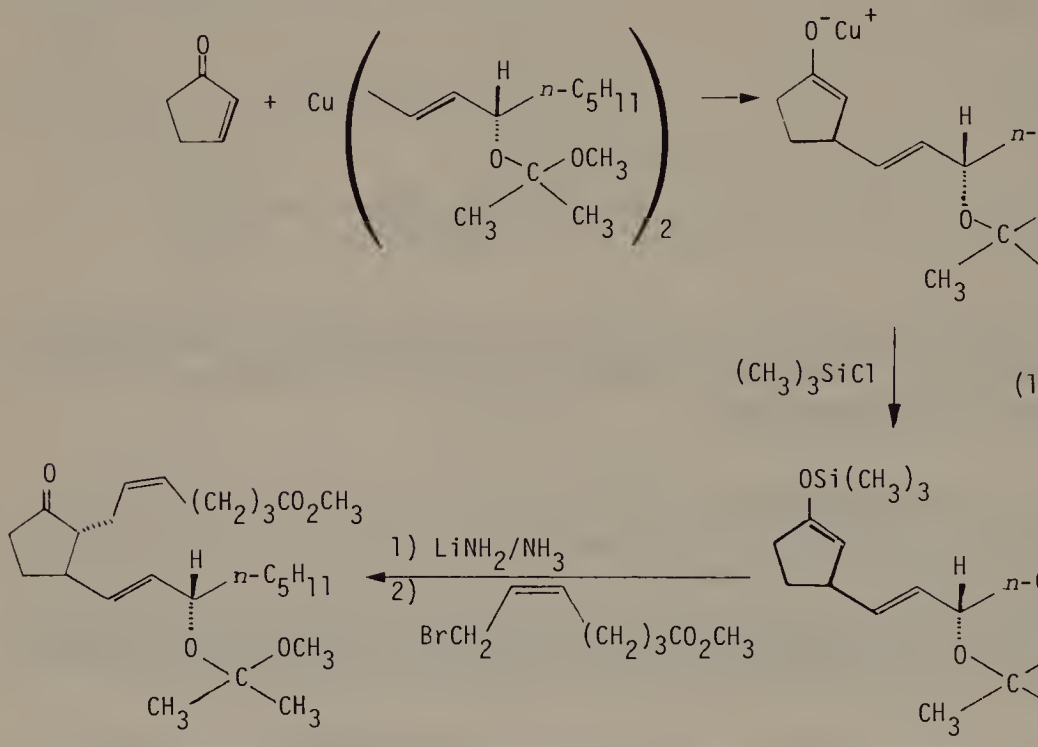
16.5 Conjugate Addition/Generation of Specific Lithium Enolates from Silyl Enol Ethers

Conjugate addition of organo cuprate reagents to α,β-unsaturated ketones yields specific enolate anions which can be quenched with TMS-Cl to give trimethylsilyl enol ethers [27, 28].



(16.21)

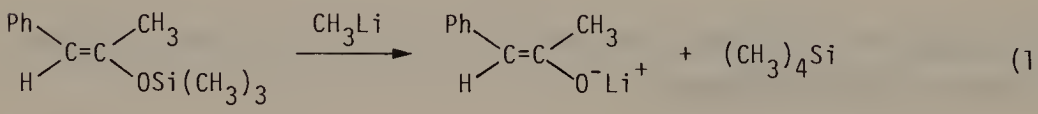
Analysis of the substitution pattern of prostaglandins suggests that such compounds might be prepared from appropriate cyclopentenone derivatives by conjugate addition of a vinyl cuprate reagent to the α,β-unsaturated ketone followed by alkylation of the enolate anion. The low reactivity of copper enolate anions in alkylation reactions constitutes a problem. However, copper enolates react with TMS-Cl to yield specific trimethylsilyl enol ethers. These can be converted to reactive lithium [29] enolates by reaction with methyl lithium or lithium amide in liquid ammonia [30, 31]. 11-Desoxyprostaglandins have been prepared by such a sequence.



(16.22)

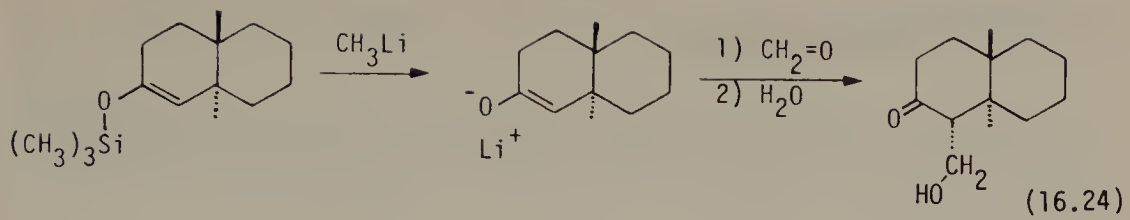
A similar sequence was used by Stork in the syntheses of lycopodine [32].

The generation of lithium enolates by reaction of methyl lithium with trimethylsilyl enol ethers has been extensively studied [33].



(16.23)

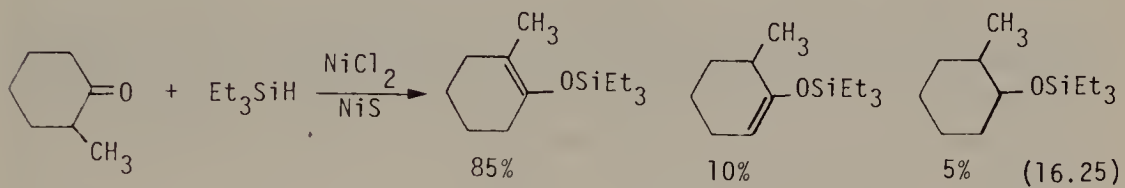
Formaldehyde has been condensed with regiospecifically generated lithium enolates formed by reaction of methyl lithium with trimethylsilyl enol ethers [34].



(16.24)

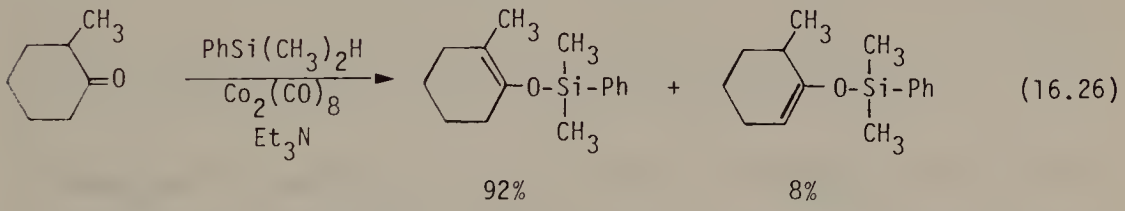
16.6 Hydrosilation of Ketones

Ketones can be catalytically hydrosilated to yield silyl ethers. (See Chapter 18.) Nevertheless, ketones and aldehydes react with silanes in the presence of certain catalysts to yield silyl enol ethers and hydrogen rather than silyl ethers. Ketones [35] and aldehydes [36] react with triethylsilane and a catalyst prepared from nickel chloride and diethyl sulfide or nickel sulfide to give a mixture of triethylsilyl enol ether and alkyl triethylsilyl ether.



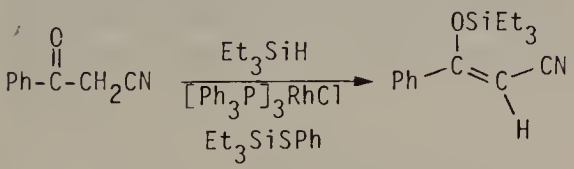
(16.25)

Similarly, ketones react with phenyldimethylsilane in the presence of a catalytic amount of $Co_2(CO)_8$ and triethylamine or other bases to yield an equilibrium mixture [27] of phenyldimethylsilyl enol ethers [37].



(16.26)

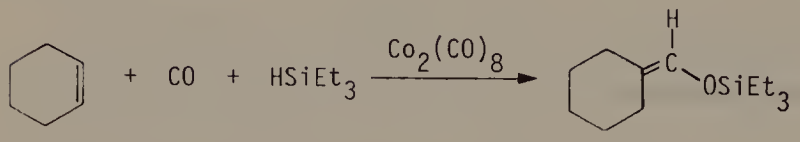
β-Keto esters or β-keto nitriles react with triethylsilane under catalysis by $[Ph_3P]_3RhCl$ and a small amount of phenylthiotriethylsilane to yield the corresponding triethylsilyl enol ethers and hydrogen [38].



(16.27)

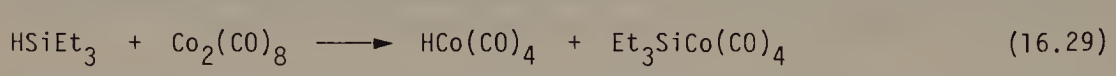
16.7 Silyl-Hydroformylation

The silyl-hydroformylation reaction of cycloalkenes with CO and triethylsilane catalyzed by $Co_2(CO)_8$ yields triethylsilyloxymethylene cycloalkanes [39, 40].



(16.28)

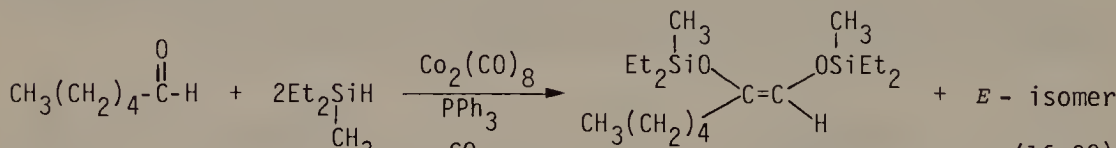
While all the steps in this catalytic reaction are not certain, it is well known that trialkylsilanes react with $Co_2(CO)_8$ to yield tetracarbonylcobalt hydride and trialkylsilylcobalt tetracarbonyl [41].



(16.29)

The catalytic reaction of 1-alkenes, CO, and diethylmethylsilane unfortunately yields mixtures of isomeric silyl enol ethers [42]. Similar product mixtures are obtained with $Co_2(CO)_8$ and triphenylphosphine or with $(Ph_3P]_2RhCl$ and triethylamine as catalysts.

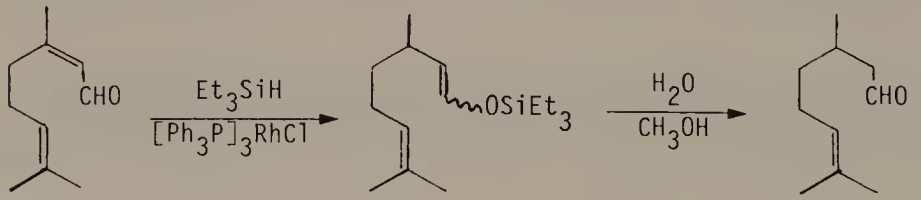
$Co_2(CO)_8$ catalyzes the reaction of aldehydes with diethylmethylsilane and CO to yield mixtures of *E* and *Z* 1,2-*bis*(diethylmethylsilyloxy)-1-alkenes [43].



(16.30)

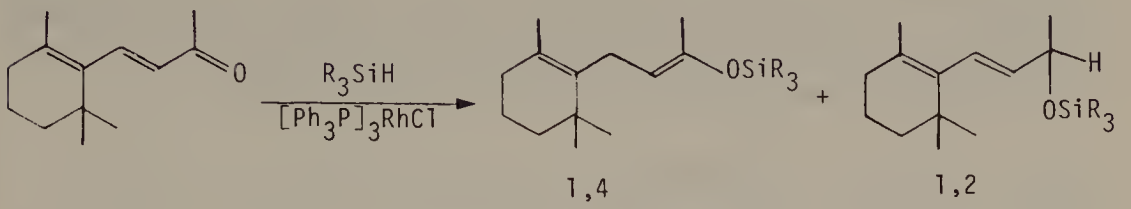
16.8 1,4-Hydrosilation of α,β-Unsaturated Carbonyl Compounds

A particularly useful method to prepare specific silyl enol ethers is the catalytic 1,4-hydrosilation of α,β-unsaturated ketones or aldehydes. *bis*(Cyclooctadienyl)nickel, $[Ph_3P]_3RhCl$ as well as a diplatinum complex are effective catalysts. The 1,4-hydrosilation of citral is outlined below. Hydrolysis of the triethylsilyl enol ether gives an aldehyde [44–46]. In this sense, the reaction is not only a synthesis of silyl enol ethers but also a selective reduction procedure.



(16.31)

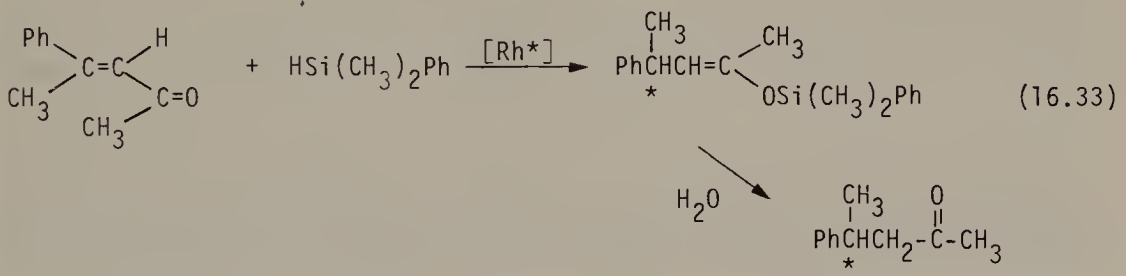
With certain α,β-unsaturated ketones, both 1,2-and 1,4-hydrosilation are observed. The ratio of these two processes depends on the particular silane [44–46].



(16.32)

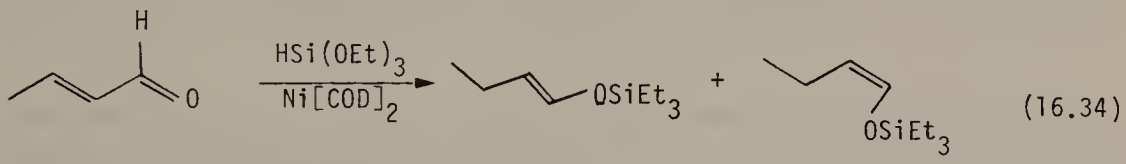
R_3SiH	1,4	1,2
$Ph(CH_3)_2SiH$	91	9
Et_3SiH	44	56
Et_2SiH_2	0	100

Hydrosilation of α,β-unsaturated ketones with a chiral cationic rhodium complex-Rh[(R)-benzylmethylphenylphosphine]$_2H_2S_2^+$ ClO_4^- yields after hydrolysis ketones which possess a chiral beta carbon. Only moderate asymmetric induction is observed (e.e. 15% or less) [78].



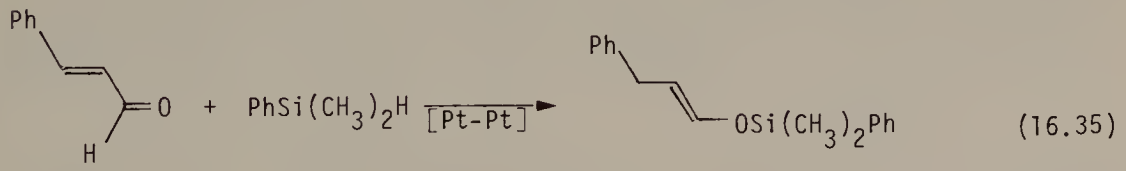
(16.33)

bis-(Cyclooctadienyl) nickel is particulary effective for the 1,4-hydrosilation of α,β-unsaturated aldehydes with trialkoxysilanes [47].



(16.34)

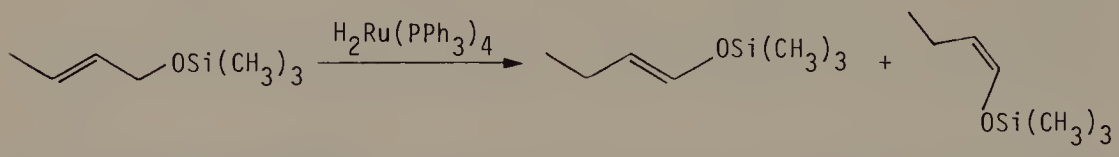
bis-Platinium complexes catalyze the 1,4-hydrosilation of α,β-unsaturated ketones or aldehydes. No competing 1,2-addition is observed [48].



(16.35)

16.9 Catalytic Isomerization of Allyloxyltrimethylsilanes

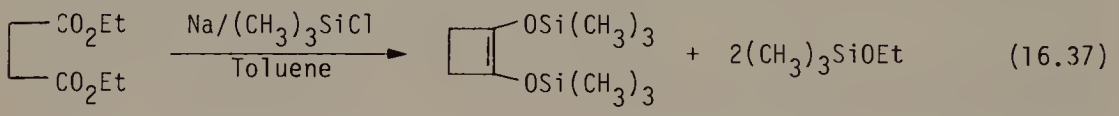
Allyloxytrimethylsilanes may be prepared by the reaction of allylic alcohols with TMS-Cl in the presence of pyridine. Both Pd/C [49] and ruthenium complexes, such as $H_2Ru(PPh_3)_4$, [50] are effective for the catalytic isomerization of allyloxytrimethylsilanes to trimethylsilyl enol ethers.



(16.36)

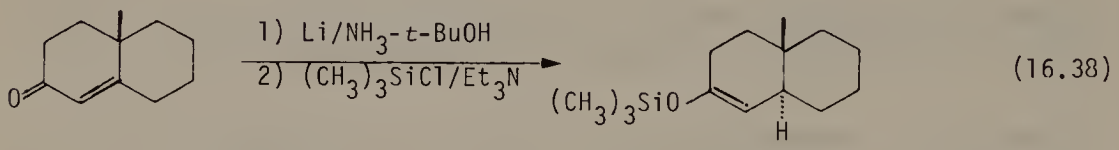
16.10 Dissolving Metal Reduction (see Chapter 19)

Dissolving metal reductions are useful for the preparation of silyl enol ethers. Esters are reduced with TMS-Cl and sodium in toluene to yield alkoxyltrimethylsilanes and 1,2-*bis*(trimethylsilyloxy)alkenes [51].



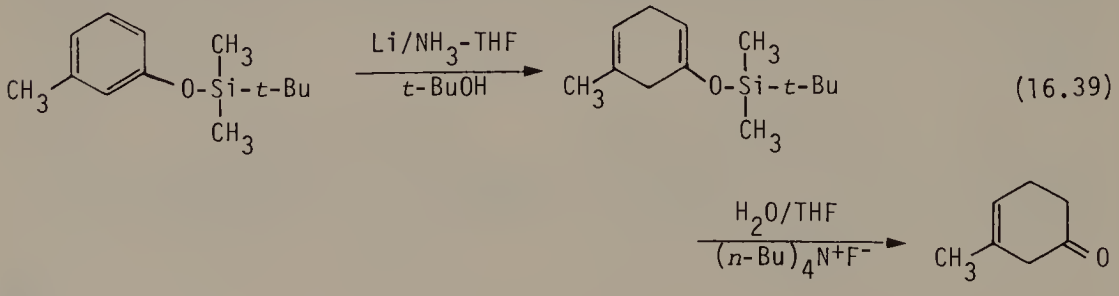
(16.37)

Dissolving metal reduction of α,β-unsaturated ketones with lithium in ammonia and *t*-butanol yields specific lithium enolates which can be quenched with TMS-Cl and triethylamine to generate trimethylsilyl enol ethers [52].



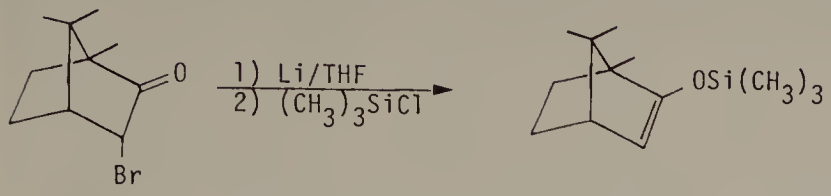
(16.38)

Birch reduction of dimethylisopropylphenoxysilanes or *t*-butyldimethylphenoxysilanes with lithium in liquid ammonia, THF, and *t*-butanol yields the corresponding isopropyl or *t*-butyldimethylsilyloxy-1,4-cyclohexadienes. Hydrolysis of these with THF and TBAF gives the corresponding cyclohex-3-en-1-ones [53].



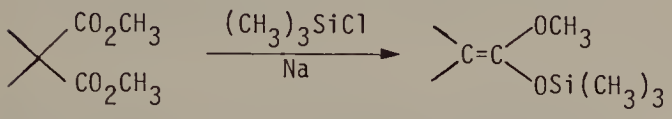
(16.39)

Dissolving metal reduction of α-bromo ketones yields specific enolate anions which react with TMS-Cl to give trimethylsilyl enol ethers [54, 55].



(16.40)

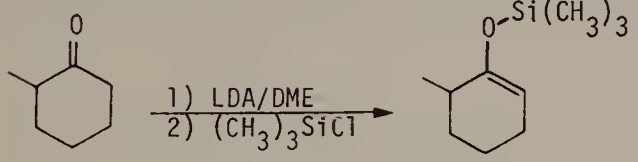
Reduction of dialkyl disubstituted malonates in the presence of TMS-Cl yields alkyl trimethylsilyl ketene acetals and CO [56].



(16.41)

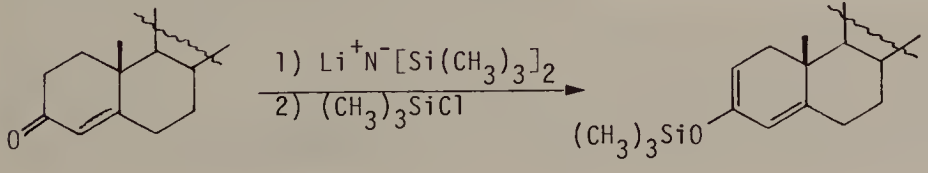
16.11 Non-Nucleophilic Bases

Trimethylsilyl enol ethers can be prepared by the treatment of ketones with strong non-nucleophilic bases to generate the corresponding enolate anions which can be quenched with TMS-Cl. In order to prevent Aldol condensations, the ketone must be instantaneously converted to its enolate anion. This is achieved by the slow addition of the ketone to a solution of strong base. Sodium *bis*(trimethylsilyl)amide [57] or LDA in DME, have been frequently used. Kinetic trimethylsilyl enol ethers are formed in this way. Treatment of 2-methylcyclohexanone with LDA followed by TMS-Cl yields exclusively 1-trimethylsilyloxy-6-methylcyclohexene [58]. Similar results can be achieved by reaction of 2,6-dibromocyclohexanone with lithium dialkyl cuprates followed by addition of TMS-Cl [59]. Reaction of 1-trimethylsilyloxy-6-methylcyclohexene with TMS-Cl and triethylamine in DMF [58], or with a catalytic amount of TsOH [27] yields a 4:1 mixture of 1-trimethylsilyloxy-2-methylcyclohexene and 1-trimethylsilyloxy-6-methylcyclohexene.



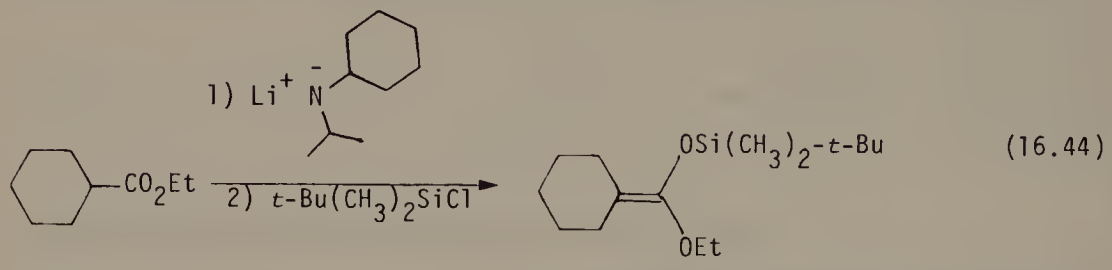
(16.42)

When 4-testosterone-17-tetrahydropyrannyl ether is treated with lithium *bis*(trimethylsilyl)amide, a 2,4-dienolate anion is formed which can be trapped by TMS-Cl [60]



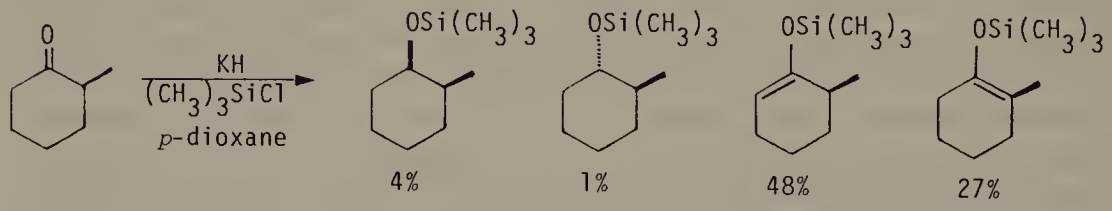
(16.43)

Non-nucleophilic strong bases, such as lithium cyclohexylisopropylamide, have been used to generate ester enolates which subsequently react with chlorosilanes to yield alkyl silyl ketene acetals. A significant problem is that C-silylation can occur in competition with the desired O-silylation. For example, reaction of methyl acetate with lithium cyclohexylisopropylamide at −78° followed by addition of TMS-Cl yields methyl trimethylsilyl ketene acetal (65%) and methyl trimethylsilylacetate (35%). Selectivity for O-silylation can be achieved by use of *t*-butyldimethylchlorosilane and a mixed solvent system of THF and HMPT [61].



(16.44)

Treatment of ketones with sodium or potassium hydride in *p*-dioxane [62] or potassium hydride in THF [63] and TMS-Cl yields predominantly trimethylsilyl enol ethers.



(16.45)

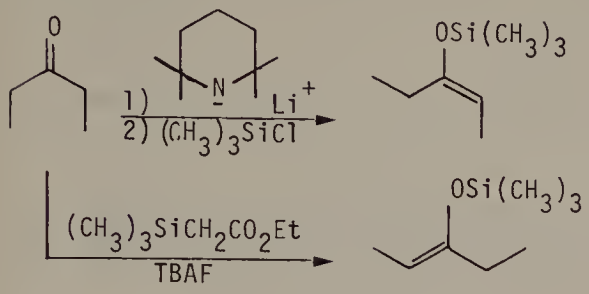
The reaction of ethyl trimethylsilylacetate with ketones catalyzed by TBAF yields trimethylsilyl enol ethers and ethyl acetate as outlined below. This procedure can be carried out at −78°C in which case, the kinetic trimethylsilyl enol ether is obtained. This method is extremely convenient since the by-product, ethyl acetate, is highly volatile [64]. Ethyl trimethylsilylacetate can be easily prepared by reaction of ethyl bromoacetate with TMS-Cl and zinc [65]

$$(CH_3)_3SiCH_2CO_2Et + (n\text{-}Bu)_4N^+F^- \longrightarrow (CH_3)_3SiF + [^-CH_2CO_2Et]\ ^+N(n\text{-}Bu)_4$$

$$(CH_3)_2CH\text{-}\overset{O}{\overset{\|}{C}}\text{-}CH_3 + [^-CH_2CO_2Et] \longrightarrow CH_3CO_2Et + [(CH_3)_2C\overset{O^-}{\overset{|}{C}}{=}CH_2] \quad (16.46)$$

$$[(CH_3)_2CH\text{-}\overset{O^-}{\overset{|}{C}}{=}CH_2] + (CH_3)_3SiCH_2CO_2Et \longrightarrow (CH_3)_3CH\text{-}\underset{OSi(CH_3)_3}{\overset{|}{C}}{=}CH_2 + [^-CH_2CO_2Et]$$

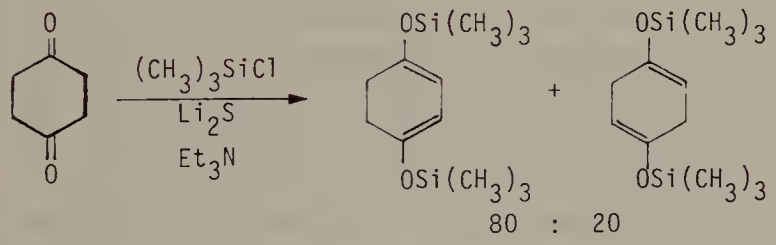
E-trimethylsilyl enol ethers may be obtained by treatment of ketones with non-nucleophilic amide bases followed by TMS-Cl, while yields *Z*-trimethylsilyl and ethers the reaction of ketones with ethyl trimethylsilylacetate and TBAF [66].



(16.47)

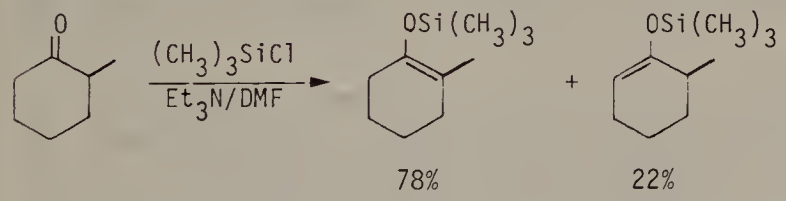
16.12 TMS-Cl/Triethylamine/DMF and Related Systems

Perhaps the most widely used method to prepare trimethylsilyl enol ethers is the reaction of ketones with TMS-Cl and triethylamine in DMF. Under these conditions, mixtures which approach the thermodynamic equilibrium of silyl enol ethers are formed [27, 58, 67]. *t*-Butyldimethylsilyl enol ethers, which are hydrolytically more stable than trimethylsilyl enol ethers can be prepared in this manner [27].



(16.48)

The combination of TMS-Cl, lithium sulfide and triethylamine is particularly effective [68].

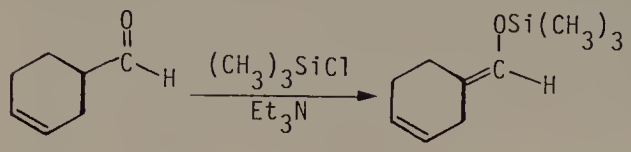


(16.49)

Treatment of ketones with TMS-I and hexamethyldisilazane directly yields the thermodynamic equilibrium mixture of trimethylsilyl enol ethers [69].
Reaction of dimethylaminotrimethylsilane with ketones yields the corresponding trimethylsilyl enol ethers [73].
α-Trimethylsilyl epoxides can also be converted to trimethylsilyl enol ethers [74].

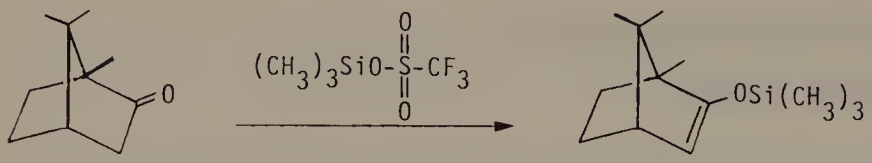
Trimethylsilyl enol ethers of aldehydes can be prepared by reaction with TMS-Cl and triethylamine [70] or TMS-I and hexamethyldisilazane [69].

While TMS-Cl and triethylamine fail to convert camphor to its trimethylsilyl enol ether [54], trimethylsilyl trifluoromethane sulfonate and triethylamine are effective [55].



(16.50)

Esters and S-alkyl thioesters react with trimethylsilyl trifluoromethane sulfonate and triethylamine to yield alkyl trimethylsilyl ketene acetals [71] and 1-alkylmercapto-1-trimethylsilyloxy alkenes [72], respectively.



(16.51)

References

1. Hauser, C.R., Hance, C.R.: J. Am. Chem. Soc. *71*, 5091 (1952)
2. Brook, A.G., Limburg, W.W., MacRae, D.M., Fieldhouse, S.A.: J. Am. Chem. Soc. *89*, 704 (1967)
3. Lutsenko, I.F., Baukov, Y.I., Dudukina, O.V., Kramarova, E.N.: J. Organometal. Chem. *11*, 35 (1968)
4. Brook, A.G., Fieldhouse, S.A.: J. Organometal. Chem. *10*, 235 (1967)
5. Brook, A.G., MacRae, D.M., Bassindale, A.R.: J. Organometal. Chem. *86*, 185 (1975)
6. Larson, G.L., Fernandez, Y.V.: J. Organometal. Chem. *86*, 193 (1975)
7. Sakurai, H., Shirahata, A., Araki, Y., Hosomi, A.: Tetrahedron Lett. 2325 (1980)
8. Baukov, J.I., Burlachenko, G.S., Lutsenko, I.F.: J. Organometal. Chem. *3*, 478 (1965)
9. Brook, A.G.: Accounts of Chem. Research, *7*, 77 (1974)
10. Brook, A.G., Fieldhouse, S.A.: J. Organometal. Chem. *10*, 235 (1967)
11. Reich, H.J., Rusek, J.J., Olson, R.E.: J. Am. Chem. Soc. *101*, 2225 (1979)
12. Kuwajima, I., Kato, M.: J. Chem. Soc. Chem. Commun. 708 (1979)
13. Kuwajima, I., Kato, M., Mori, A.: Tetrahedron Lett. 2745 (1980)
14. Kuwajima, I., Atsumi, K., Tanaka, T., Inoue, T.: Chem. Lett. 1239 (1979)
15. Kuwajima, I., Kato, M.: Tetrahedron Lett. 623 (1980)
16. Brook, A.G., Duff, J.M., Jones, P.F., Davis, N.R.: J. Am. Chem. Soc. *89*, 431 (1967)
17. Corey, E.J., Seebach, D., Freedman, R.: J. Am. Chem. Soc. *89*, 434 (1967)
18. Dexheimer, E.M., Spialter, L.: J. Organometal. Chem. *107*, 229 (1976)
19. Duffant, N., Dunoguès, J., Biran, C., Calas, R., Gerval, J.: J. Organometal. Chem. *101*, C23 (1978)
20. Kuwajima, I., Arai, M., Sato, T.: J. Am. Chem. Soc. *99*, 4181 (1977)

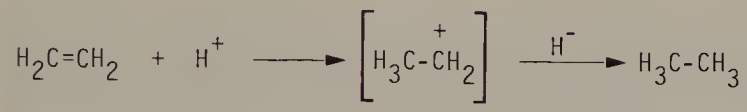
21. Kuwajima, I., Abe, T., Minami, N.: Chem. Lett. 993 (1976)
22. Hosomi, A., Hashimoto, H., Sakurai, H.: J. Organometal. Chem. *175*, C1 (1979)
23. Lau, P.W.K., Chan, T.H.: J. Organometal. Chem. *179*, C24 (1979)
24. Kuwajima, I., Kato, M., Sato, T.: J. Chem. Soc. Chem. Commun. 478 (1978)
25. Picard, J.D., Calas, R., Dunoguès, J., Duffaut, N.: J. Organometal. Chem. *26*, 183 (1971)
26. Bourgeois, P.: J. Organometal. Chem. *76*, C1 (1974)
27. Stork, G., Hudrlik, P.F.: J. Am. Chem. Soc. *90*, 4462 (1968)
28. Stotter, P.L., Hill, K.A.: J. Org. Chem. *38*, 2576 (1973)
29. Tanaka, T., Kurozumi, S., Toru, T., Kobayashi, M., Miuri, S., Ishimoto, S.: Tetrahedron Lett. 1535 (1975)
30. Kluge, A.F., Untch, K.G., Fried, J.H.: J. Am. Chem. Soc. *94*, 2827 (1972)
31. Patterson, Jr., J.W., Fried, J.H.: J. Org. Chem. *39*, 2506 (1974)
32. Stork, G.: Pure and Applied. Chem. *17*, 383 (1968)
33. House, H.O., Auerbach, R.A., Gall, M., Peet, N.P.: J. Org. Chem. *38*, 514 (1973)
34. Stork, G., d'Angelo, J.: J. Am. Chem. Soc. *96*, 7114 (1974)
35. Frainnet, E., Martel-Siegfried, V., Brousse, E., Dedier, J.: J. Organometal. Chem. *85*, 297 (1975)
36. Frainnet, E., Bourhis, R.: J. Organometal. Chem. *93*, 309 (1975)
37. Sakurai, H., Miyoshi, K., Nakadaira, Y.: Tetrahedron Lett. 2671 (1977)
38. Ojima, I., Nagai, Y.: J. Organometal. Chem. *57*, C42 (1973)
39. Seki, Y., Hadaka, A., Murai, S., Sonoda, N.: Angew. Chem. Int. Ed. *16*, 174 (1977)
40. Seki, Y., Hidaka, A., Makino, S., Murai, S., Sonoda, N.: J. Organometal. Chem. *140*, 361 (1977)
41. Chalk, A.J., Harrod, J.F.: J. Am. Chem. Soc. *89*, 1640 (1967)
42. Seki, Y., Murai, S., Hidaka, A., Sonoda, N.: Angew. Chem. Int. Ed. *16*, 881 (1977)
43. Seki, Y., Murai, S., Sonoda, N.: Angew. Chem. Int. Ed. *17*, 119 (1978)
44. Ojima, I., Kogure, T., Nagai, Y.: Tetrahedron Lett. 5085 (1972)
45. Ojima, I., Nihonyanagi, M., Kogure, T., Kumagai, M., Horiuchi, S., Nakatsugama, K.: J. Organometal. Chem. *94*, 449 (1975)
46. Ojima, I., Kogure, T., Nihonyanagi, M., Nagai, Y.: Bull. Chem. Soc. Japan, *45*, 3506 (1972)
47. Lappert, M.F., Nile, T.A.: J. Organometal. Chem. *102*, 543 (1975)
48. Barlow, A.P., Boag, N.M., Stone, F.G.A.: J. Organometal. Chem. *191*, 39 (1980)
49. Bourhis, R., Frainnet, E.: J. Organometal. Chem. *28*, C11 (1971)
50. Suzuki, H., Koyama, Y., Moro-Oka, Y., Ikawa, T.: Tetrahedron Lett. 1415 (1979)
51. Bloomfield, J.J.: Tetrahedron Lett. 587 (1968).
52. Stork, G., Singh, J.: J. Am. Chem. Soc. *96*, 6181 (1974)
53. Donaldson, R.E., Fuchs, P.L.: J. Org. Chem. *42*, 2032 (1977)
54. Pande, G.C., Pande, L.M.: Synthesis, 450 (1975)
55. Hashimoto, S., Itoh, A., Kitagawa, Y., Yamamoto, H., Nozaki, H.: J. Am. Chem. Soc. *99*, 4192 (1977)
56. Kuo, Y.N., Chen, J., Ainsworth, C., Bloomfield, J.J.: J. Chem. Soc. Chem. Commun. 136 (1971)
57. Krüger, C.R., Rochow, E.G.: J. Organometal. Chem. *1*, 476 (1964)
58. House, H.O., Czuba, L.J., Gall, M., Olmstead, H.D.: J. Org. Chem. *34*, 2324 (1969)
59. Posner, G.H., Sterling, J.J., Whitten, C.E., Lentz, C.M., Brunelle, D.J.: J. Am. Chem. Soc. *97*, 107 (1975)

60. Tanabe, M., Crowe, D.F.: J. Chem. Soc. Chem. Commun. 564 (1973)
61. Rathke, M.W., Sullivan, D.F.: Syn. Commun. *3*, 67 (1973)
62. Hudrlik, P.F., Takacs, J.M.: J. Org. Chem. *43*, 3861 (1978)
63. Brown, C.A.: J. Org. Chem. *39*, 1324 (1974)
64. Nakamura, E., Murofushi, T., Shimizu, M., Kuwajima, I.: J. Am. Chem. Soc. *98*, 2346 (1976)
65. Fessenden, R.J., Fessenden, J.S.: J. Org. Chem. *32*, 3535 (1967)
66. Nakamura, E., Hashimoto, K., Kuwajima, I.: Tetrahedron Lett. 2079 (1978)
67. House, H.O., Gall, M., Olmstead, H.D.: J. Org. Chem. *36*, 2361 (1971)
68. Olah, G.A., Gupta, B.G.B., Narang, S.C., Malhotra, R.: J. Org. Chem. *44*, 4272 (1979)
69. Miller, R.D., McKean, D.R.: Synthesis, 730 (1979)
70. Reuss, R.H., Hassner, A.: J. Org. Chem. *39*, 1785 (1974)
71. Simchen, G., Kober, W.: Synthesis, 259 (1976)
72. Simchen, G., West, W.: Synthesis, 247 (1977)
73. Hellberg, L.H., Juarez, A.: Tetrahedron Lett. 3553 (1974)
74. Hudrlik, P.F., Schwartz, R.H., Kulkarni, A.K.: Tetrahedron Lett. 2233 (1979)
75. Soderquist, J.A., Hassner, A.: J. Am. Chem. Soc. *102*, 1577 (1980)
76. Soderquist, J.A., Hassner, A.: J. Org. Chem. *45*, 451 (1980)
77. Clinet, J.C., Linstrumelle, G.: Tetrahedron Lett. 3987 (1980)
78. Hayashi, T., Yamamoto, K., Kumada, M.: Tetrahedron Lett. 3 (1975)
79. Yamamoto, K., Suzuki, S., Tsuji, J.: Tetrahedron Lett. 1653 (1980)

17 Ionic Hydrogenations

17.1 Introduction

Many reactions of silicon reagents may be classified as reductions. In this Chapter we will consider reactions in which hydrogen is added to an unsaturated functional group stepwise as a proton and a hydride ion. Major contributions to our understanding of this reaction have been made by Kursanov's group.

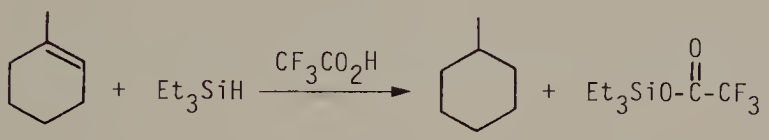


$$H_2C{=}CH_2 + H^+ \longrightarrow [H_3C{-}\overset{+}{C}H_2] \xrightarrow{H^-} H_3C{-}CH_3 \qquad (17.1)$$

It should be noted that the hydrosilation reaction of alkenes and alkynes which bears a strong analogy to catalytic hydrogenation has been previously considered (see Chapters 7 and 10).

17.2 Ionic Hydrogenation of Alkenes – Reduction of Carbocations

The reaction of methylcyclohexene, trifluoroacetic acid and triethylsilane in methylene chloride to yield methylcyclohexane and trifluoroacetoxytriethylsilane is an example of an ionic hydrogenation [1].

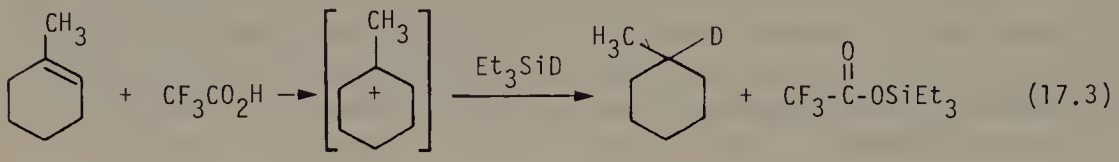


$$+ \; Et_3SiH \xrightarrow{CF_3CO_2H} \; + \; Et_3SiO{-}\overset{O}{\overset{\|}{C}}{-}CF_3 \qquad (17.2)$$

Similarly, methylcyclopentene, 2-methyl-2-butene, 2-methyl-1-butene, 2-methyl-1-pentene [2], $\Delta^{9,10}$ octalin and 3-methyl-2-chloestene [3] are reduced under these conditions. Whereas, cyclohexene, 1-hexene, and 2-hexene are not. The reaction is a two-step process. The first step is the formation of a carbocation center. This can be accomplished by protonation of a substituted alkene by trifluoroacetic acid. The stability of triethylsilane to acid limits the reaction conditions. Triethylsilane is stable to trifluoroacetic acid, ($H_0 = -3.15$) but not to stronger mineral acids such as sulfuric, or conc. HCl. Hence the reaction is limited to alkenes which can be protonated to yield carbocations by

trifluoroacetic acid. Substituted alkenes which yield tertiary carbocations on protonation are reduced, whereas alkenes which yield secondary carbocations ions are, in general, not. Alternatively, the carbocation center can be generated by ionization of a covalent precursor. The second step involves transfer of a hydride from a silane, usually triethylsilane, to the carbocation center [4]. This affects the addition of a molecule of hydrogen to a C–C double bond, as a proton and a hydride ion. The anion associated with the carbocation ion, often trifluoroacetate becomes covalently bonded to silicon.

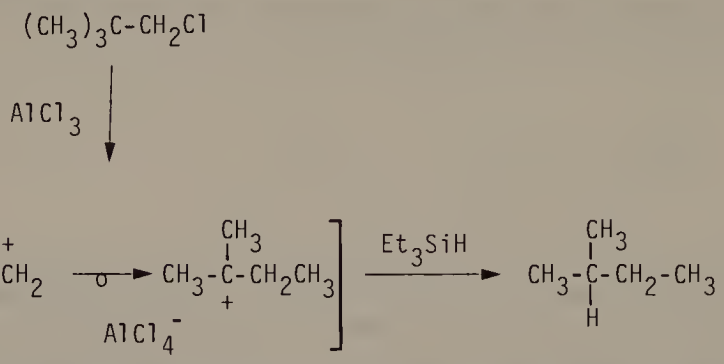
Ionic hydrogenation permits the facile specific mono or di-deuteration of alkenes, by the use of either triethylsilane-d_1, or trifluoroacetic acid-d_1 or a combination of these reagents [5, 6].



(17.3)

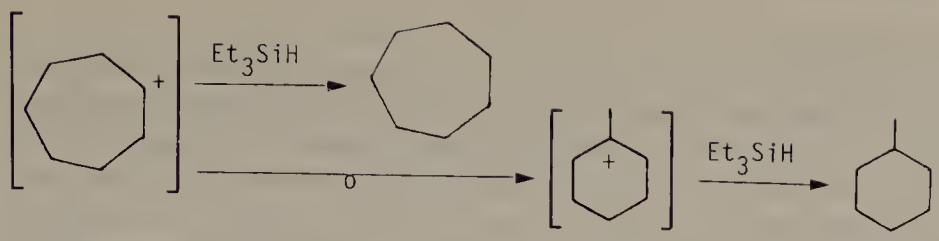
The thermodynamic driving force for the transfer of a hydride from a silane to a carbocation results not only from the greater strength of the C–H bond formed compared to the Si–H bond broken [7] but also from the formation of a strong Si–O bond [8]. The reaction of trimethylsilane with *t*-butyl carbocation is exothermic by 8 kcal/mol on the basis of appearance potential data [7].

The first examples of transfer of hydride from a silane to a carbocation were reported by Whitmore over thirty years ago. He found that when *n*-hexyl chloride was treated with triethylsilane and a catalytic amount of $AlCl_3$, *n*-hexane and triethylchlorosilane were formed. The fact that neopentyl chloride gave isopentane under these conditions provides additional evidence that carbocation intermediates are involved [9].



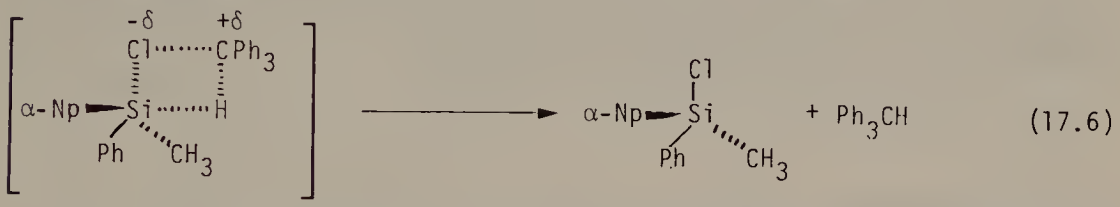
(17.4)

Reduction of secondary carbocations by silanes is competitive with their rearrangement to tertiary carbocations. Thus reaction of cycloheptyl bromide with triethylsilane and a catalytic amount of $AlCl_3$ yields a mixture of cycloheptane and methylcyclohexane. A similar reaction with the less reactive *n*-butylsilane yields methylcyclohexane and only a trace of unrearranged cycloheptane [10].



(17.5)

Alkyl halides which ionize to carbocation/halide ion pairs are reduced by silanes in the absence of $AlCl_3$. Thus, triphenylmethyl chloride is reduced by either triphenylsilane or triethylsilane to triphenylmethane in methylene chloride, a solvent in which triphenylmethyl chloride dissociates to a triphenylmethyl carbocation/chloride ion pair. On the other hand, the reduction does not occur in solvents such as benzene or cyclohexane in which triphenylmethyl chloride does not dissociate. The rate of this reaction depends to the first order on both the concentration of the silane and triphenylmethyl chloride [11]. Although a four-center transition state in which the triphenylmethyl carbocation/chloride ion pair reacts with a silane to simultaneously form new Si–Cl and C–H bonds is attractive, careful study with optically active α-naphthylphenylmethylsilane does not support this suggestion. Retention of configuration at the chiral silicon center is predicted for such a four-center transition state. However, in a variety of solvents significant racemization of α-naphthylphenylmethylchlorosilane is observed [12, 13].

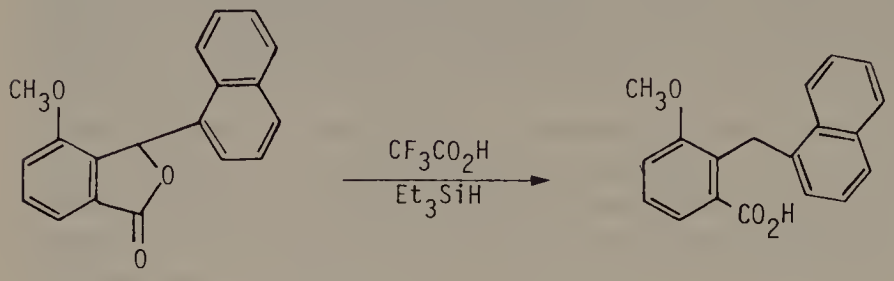


(17.6)

Prochiral carbocations are reduced by chiral silanes to optically active alkanes (2–3% e.e.). For example, the 2-phenyl-2-butyl carbocation, generated from either R, or S-2-phenyl-2-butanol or from 2-phenyl-1-butene by treatment with trifluoroacetic acid, is reduced by R-α-naphthylphenylmethylsilane to optically active 2-phenylbutane (2–3% e.e. R). Likewise, this carbocation is reduced by S-α-naphthylphenylmethylsilane to optically active 2-phenylbutane (2–3% e.e. S). This is consistent with a tight transition state for transfer of hydride from the chiral silane to the symmetrical prochiral carbocation [14, 15].

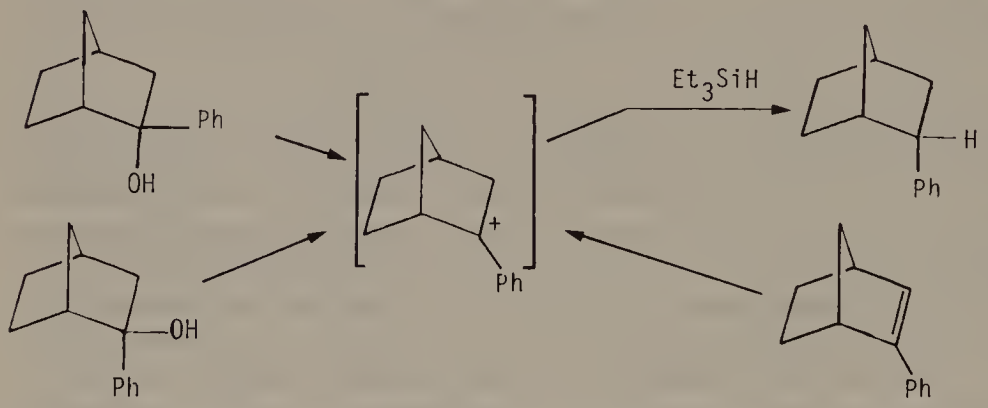
Carey has studied the reduction, by triethylsilane, of a wide range of triarylmethyl, diphenylmethyl and benzyl carbocations. These have been generated by treatment of the corresponding alcohols with trifluoroacetic acid. Carbocations whose stability is between that of *tris*-(2,6-dimethoxyphenyl)methyl carbocation (pK_R 6.5) and 2,4,6-trimethylbenzyl carbocation (pK_R– 17.4) are reduced. The rate of these reductios depends on the concentration of both the silane and the carbocation. As might be expected, triarylsilanes substituted with electron donating groups are more reactive reducing agents than those substituted with electron withdrawing groups [$Ar_3Si–H$, $p = -1.84$, $Ar(CH_3)_2Si–H$, $p = -1.01$]. The small isotope effect

observed for breaking the Si–H bond (Ph_3Si-H/Ph_3Si-D = 1.5 to 1.89) in these reactions [16] is consistant with a non-linear transition state [17]. While benzyl and cinnamyl alcohols are not reduced under these conditions [18], compounds which ionize to form secondary benzylic carbocations are reduced. Thus treatment of 1-trifluoroacetoxy-1-phenylethane with trifluoroacetic and triethylsilane leads to phenylethane [19, 20]. The triethylsilane reduction of a diphenylmethyl carbocation formed by ionization of a phthalide ester has been recently reported [21].



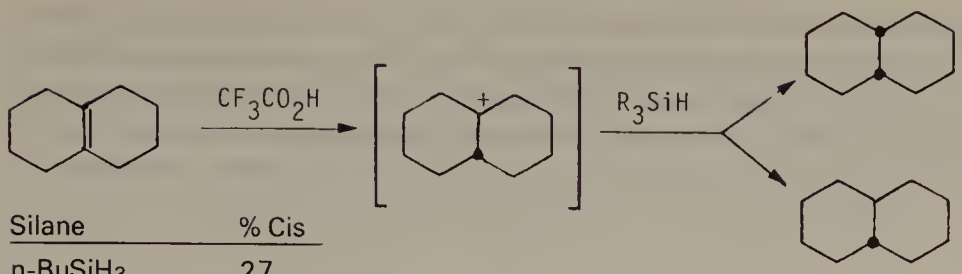
(17.7)

In the case of ionic hydrogenation of alkenes in which two stereoisomeric products can be formed, the product or ratio of products obtained does not depend on the stereochemistry of the precursor. For example, *exo* and *endo* 2-phenyl-2-norbornanol as well as 2-phenyl norbornene yield *endo*-2-phenyl norbornane on treatment with trifluoroacetic acid and triethylsilane in methylene chloride. Apparently, *exo* addition of hydride to the 2-phenyl norbornyl carbocation ($pK_R = -13$) is highly favored [22].



(17.8)

This is consistent with a reaction which involves a common carbocation intermediate. On the other hand, the stereochemistry of the product or the ratio of stereoisomers produced depends on the nature of the silane reducing agent, in particular on its steric bulk. For example, reduction of the 4-*t*-butyl-1-phenylcyclohexyl carbocation (generated from either *cis* or *trans*-4-*t*-butyl-1-phenylcyclohexanol or 4-*t*-butyl-1-phenylcyclohexene) gives a mixture of *cis* and *trans*-4-*t*-butyl-1-phenylcyclohexane which depends on the silane reducing agent. The ratio of *trans* to *cis* is 2 for triethylsilane while it is 4.5 for diethylsilane [23]. The steric effect of a series of alkyl silanes on a ratio of *cis* to *trans* decalin produced by ionic hydrogenation of $\Delta^{9,10}$ octalin has been studied. Sterically hindered trialkylsilanes favor formation of *cis*-decalin [24].

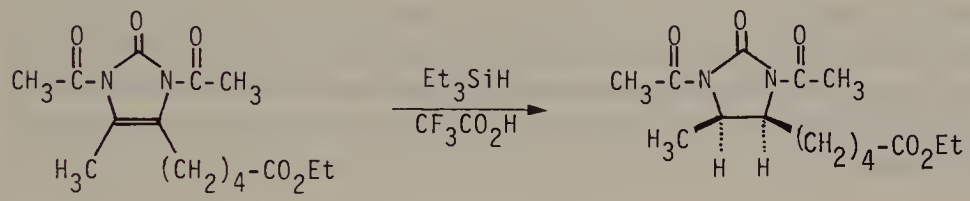


(17.9)

Silane	% Cis
n-BuSiH3	27
Et3SiH	42
(sec-Bu)3SiH	72
(t-Bu)3SiH	93

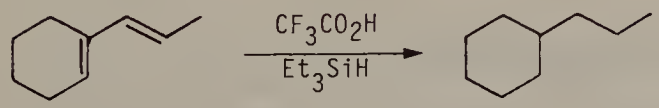
17.3 Stability of Functional Groups to Ionic Hydrogenation

Ionic hydrogenation tolerates a variety of functional groups. Carboxylic acids, esters, amides, nitriles, nitro groups, sulfonic esters, as well as most aromatic nuclei are not reduced under ionic hydrogenation conditions [4]. This permits the selective reduction of substituted C–C double bonds in the presence of a variety of functional groups [6, 25, 26].

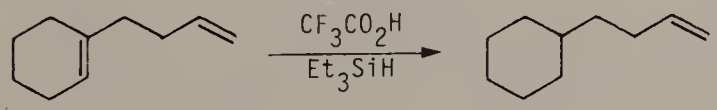


(17.10)

While both C–C double bonds of alkyl substituted conjugated 1,3-dienes are reduced under ionic hydrogenation conditions, it is possible to selectively reduce a non-conjugated tri-substituted alkene in the presence of a mono-substituted alkene [27].



(17.11)

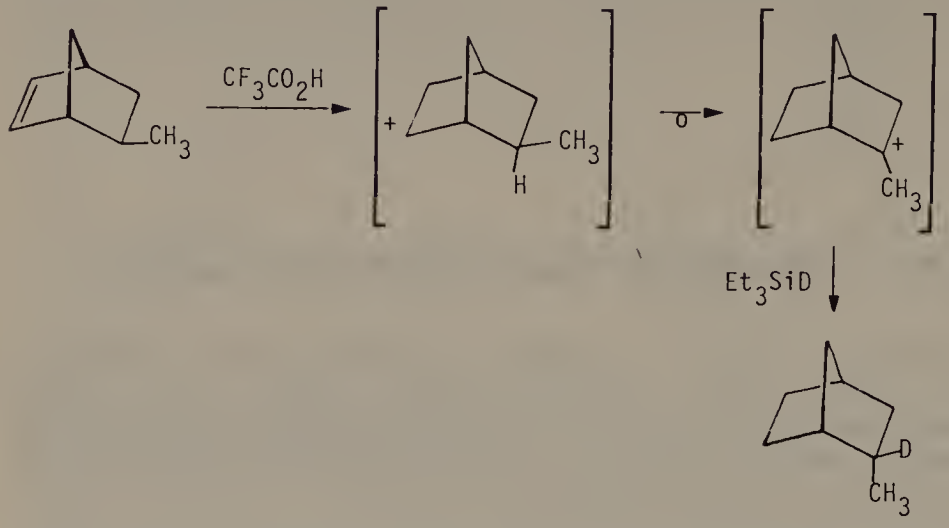


(17.12)

17.4 Ionic Hydrogenation – Reduction of Non-Classical Carbocations

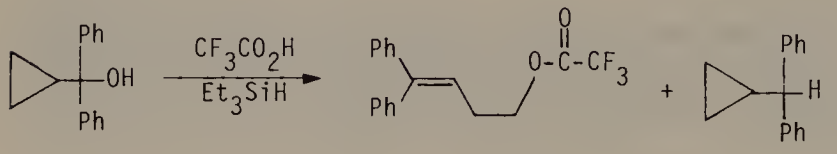
2-Norbornene is reduced, albeit, in poor yield (3.5%) on treatment with triethylsilane and trifluoroacetic acid. This probably results from the unusual stability of the 2-norboryl carbocation. Treatment of *exo*-6-methyl-2-norbor-

nene with trifluoroacetic acid gave *endo*-2-methylnorbornane. Deuterium labeling was used to determine the nature of the carbocation reduced. Treatment of *exo*-6-methyl-2-norbornene with triethylsilane-d_1, gave *endo*-2-methylnorbornane-2-d_1. Clearly, the initial secondary carbocation is converted to a tertiary carbocation, probably by a 1,6-hydride shift prior to reduction [28].



(17.13)

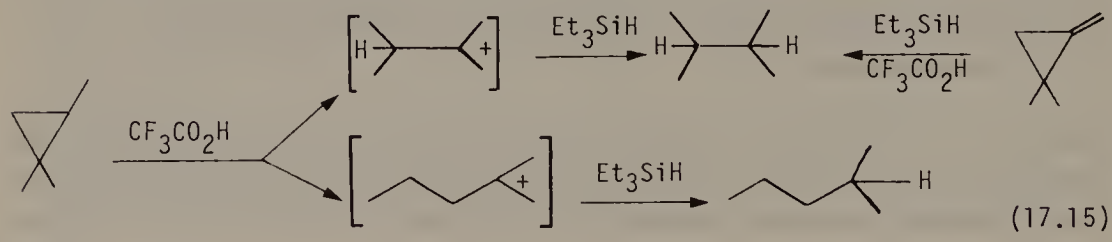
The unusual stability of the cyclopropyl carbinyl carbocation permits the reduction of vinyl cyclopropane under ionic hydrogenation conditions to yield ethylcyclopropane [29, 30]. Ring opened products have been observed only with cyclopropyl carbinyl carbocations which possess multiple carbocation stabilizing groups [31].



(17.14)

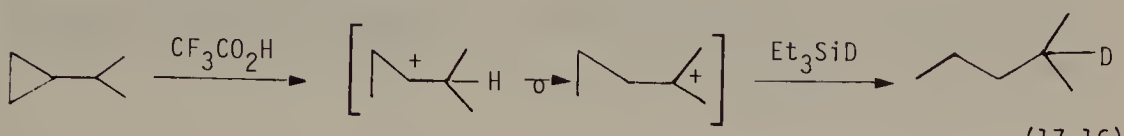
17.5 Ionic Hydrogenation of Sigma Bonds

There are a few types of sigma bonds which are protonated by trifluoroacetic acid. These undergo heterolysis to yield carbocations which are reduced under the conditions of ionic hydrogenation. For example, alkyl substituted cyclopropanes which can open on protonation to yield tertiary carbocations are reduced on treatment with trifluoroacetic acid and triethylsilane [32, 33].



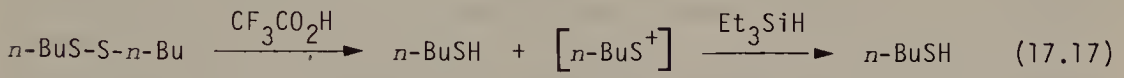
(17.15)

Ethylcyclopropane is not, however, reduced under these conditions since it can only form secondary carbocations on protonation and ring opening [34]. Isopropylcyclopropane, however, undergoes reduction to yield 2-methylpentane. Reduction with triethylsilane-d_1 has served to clarify this apparent contradiction. With triethylsilane-d_1, 2-methylpentane-2-d_1 is formed exclusively. Opening of the cyclopropane ring and 1,2-hydride migration to form a tertiary carbocation may occur simultaneously [35–37].



(17.16)

Aliphatic and many aromatic disulfides can be reduced to the corresponding thiols under ionic hydrogenation conditions. The reaction may proceed by initial protonation of one of the sulfur atoms. Cleavage of the S–S sigma bond then yields a thiol and a sulfenium cation which is reduced by hydride transfer from triethylsilane [38].



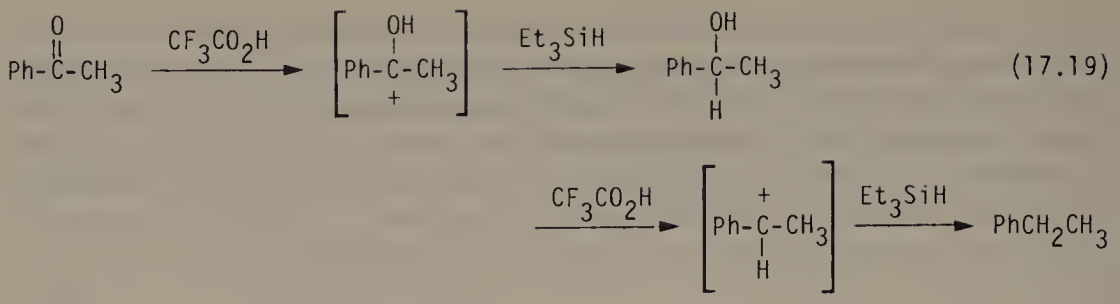
(17.17)

Similarly, ethers, which on protonation of oxygen, can undergo C–O bond heterolysis to yield stable carbocations, undergo reduction. For example, *t*-butyl ethyl ether reacts with trifluoroacetic acid and triethylsilane to yield isobutane and ethanol. *bis*-Diphenylmethyl ether is reduced to diphenylmethane [39, 40].

17.6 Reduction of Ketones

Kursanov's also reported the ionic hydrogenation of ketones [2, 41]. Thus cyclohexanone reacts with triethylsilane in the presence of trifluoroacetic acid to yield trifluoroacetoxycyclohexane. The reaction most probably proceeds by initial protonation of the oxygen of the carbonyl group to yield a hydroxy stabilized carbocation which reacts with triethylsilane to yield cyclohexanol. Cyclohexanol does not undergo further reduction. On the other hand, acetophenone and benzophenone are reduced initially to 1-phenylethanol and diphenylmethanol, respectively. These undergo further reduction under the reaction conditions to phenylethane and diphenylmethane [41, 42].

(17.18)

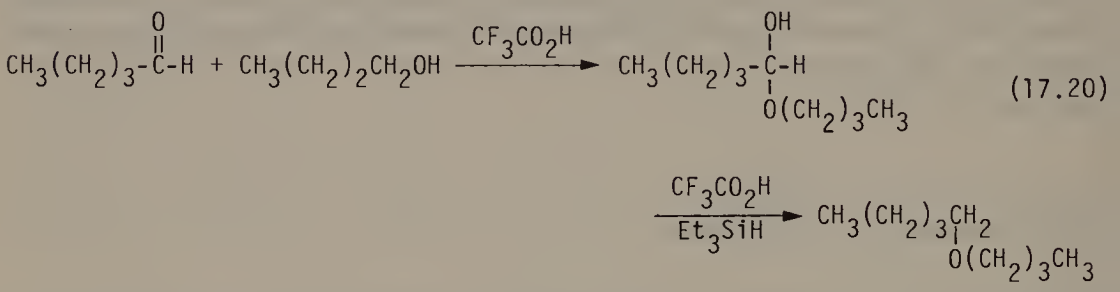


(17.19)

The reduction of 1,1-dibenzoylethane to 2-methyl-1,3-diphenyl propane, however, proved complicated [43].

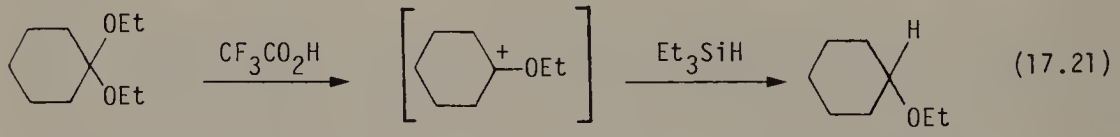
17.7 Reduction of Aldehydes

Treatment of aldehydes with triethylsilane and trifluoroacetic acid yields a mixture of alcohols and symmetrical ethers. For example, benzaldehyde yields dibenzyl ether. The formation of ethers occurs by reaction of the initially formed alcohol with additional aldehyde to yield a hemi-acetal. Protonation of the hemi-acetal leads to loss of water and formation of a stabilized carbocation which is reduced by triethylsilane, to yield the ether. Consistent with this hypothesis, treatment of a mixture of *n*-pentanal and *n*-butanol with trifluoroacetic acid and triethylsilane yields *n*-amyl *n*-butyl ether [44, 45].



(17.20)

The diethylketal of cyclohexanone undergoes reduction with triethylsilane in trifluoroacetic acid to yield cyclohexyl ethyl ether [46].

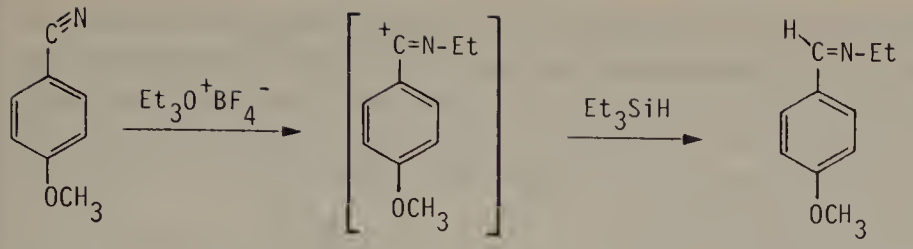


(17.21)

Ketals and acetals can also be reduced to ethers by treatment with trimethylsilane and a catalytic amount of trimethylsilyl triflate [47].

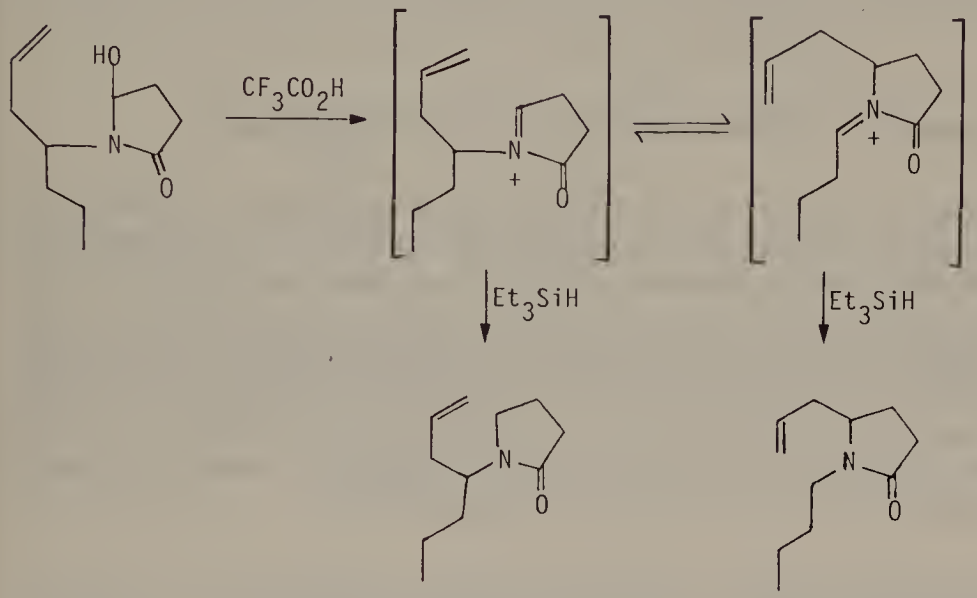
17.8 Reduction of N-Alkyl Nitrilium and N-Acyliminium Salts

N-Alkyl nitrilium ions are reduced by triethylsilane to yield N-alkylaldimines which can be hydrolyzed to aldehydes [48, 49].



(17.22)

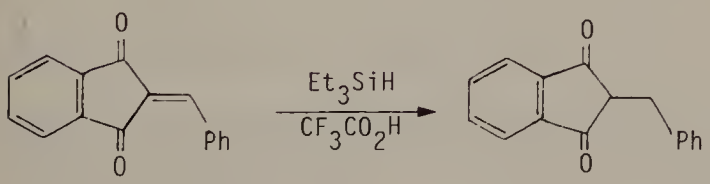
Evidence for the intermediacy of N-acyliminium ions in a 2-aza Cope rearrangement has been obtained by their reduction *in-situ* with triethylsilane and trifluoroacetic acid [50].



(17.23)

17.9 Reduction of α,β-Unsaturated Ketones

Ionic hydrogenation of α,β-unsaturated ketones and aldehydes results in preferential reduction of the C−C double bond. Reaction of methyl vinyl ketone or benzalacetophenone with one equivalent of triethylsilane in the presence of a large excess of trifluoroacetic acid yields 2-butanone or 1,3-diphenyl-1-propanone, respectively [51]. Likewise, 2-benzylidene -1,3-indanediones are reduced to 2-benzyl-1,3-indanediones on treatment with triethylsilane and trifluoroacetic acid [52].

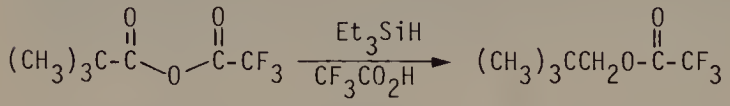


(17.24)

With excess triethylsilane, α,β-unsaturated ketones under further reduction to saturated alcohols. For example, mesityl oxide is reduced to 4-methyl-2-pentanol while benzalacetophenone yields 1,3-diphenylpropane [53].

The reduction of quinones is related to the ionic hydrogenation of α,β-unsaturated ketones. Treatment of benzoquinone with triethylsilane and trifluoroacetic acid yields hydroquinone. On the other hand, naphthoquinone and 9,10-anthraquinone are reduced to tetralin and 9,10-hydroanthracene, respectively [54]. The extent of reduction may depend on the stability of the initially formed hydroquinones.

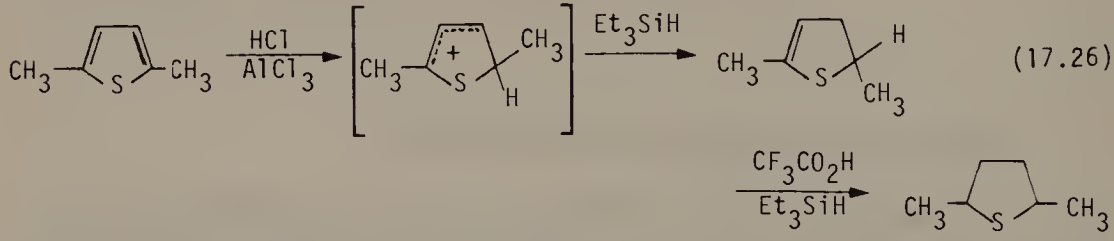
The ionic hydrogenation of mixed carboxylic trifluoroacetic anhydrides yields trifluoroacetoxyalkanes [55].



(17.25)

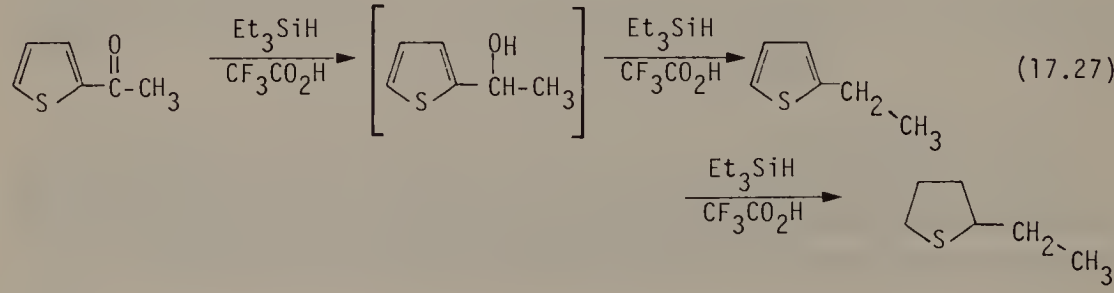
17.10 Reduction of Heteroaromatic Nuclei-Thiophenes

While aromatic nuclei are not *in general* reduced under ionic hydrogenation conditions, certain heterocyclic aromatic nuclei are reduced. The reduction of substituted thiophenes is important. Thiophenes cannot be reduced to tetrahydrothiophenes or thiophanes under usual catalytic hydrogenation conditions because the product sulfide poisons the Nobel catalyst. The reduction may occur by initial protonation of the thiophene ring at the two or the five positions. The delocalized allylic carbocation thus produced is reduced by hydride transfer from triethylsilane. The product, a 2,3-dihydrothiophene, then undergoes further reduction to the thiophane [56].



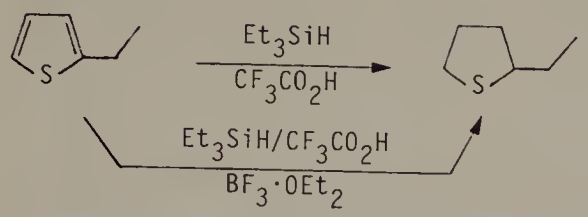
(17.26)

A number of phenyl substituted thiophenes have been reduced under ionic hydrogenation conditions to phenyl substituted tetrahydrothiophanes [57]. 2,2′-*bis*-Thiophene [1] has been reduced to 2,2′-octahydro-*bis*-thiophane [1] on treatment with triethylsilane and trifluoroacetic acid [58], while 2-acetyl thiophene yields 2-ethyltetrahydrothiophane [59].



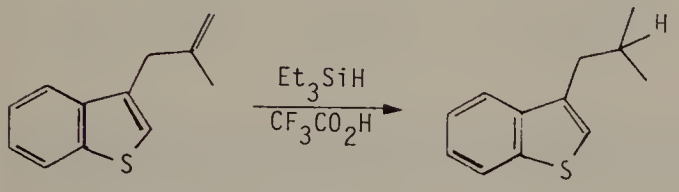
(17.27)

The reduction of thiophenes under the usual ionic hydrogenation conditions is quite slow. The addition of a catalytic amount of $BF_3 \cdot OEt_2$ accelerates the reaction [59–61].



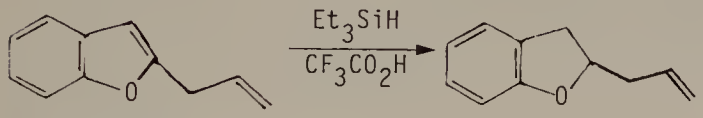
(17.28)

Reduction of the C–C double bond of 3-(β-methylallyl) benzothiophene occurs in preference to reduction of the thiophene nucleus.



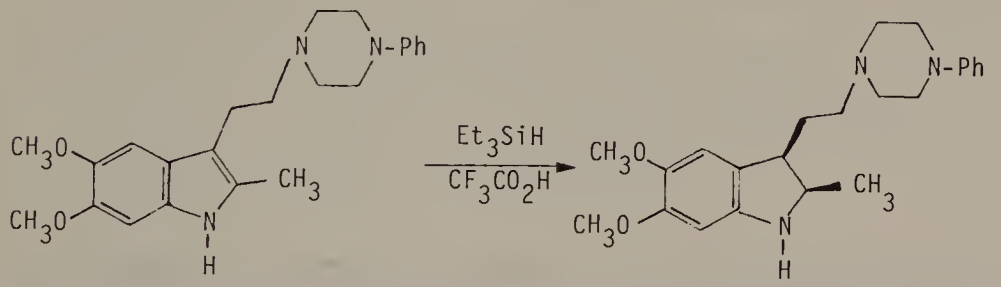
(17.29)

On the other hand, the thiophene nucleus of 2-allyl-benzothiophene and the furan nucleus of 2-allyl-benzofuran are preferentially reduced [62].



(17.30)

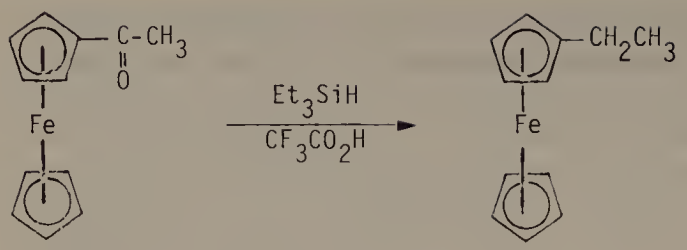
In a similar manner, the pyrrole nucleus of indole is selectively reduced under ionic hydrogenation conditions [63, 64].



(17.31)

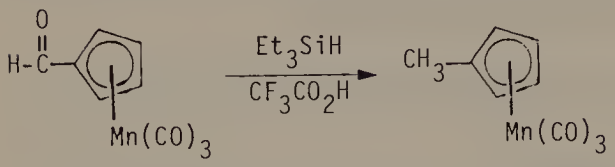
17.11 Reduction of Organometallic Complexes

Ionic hydrogenation has been utilized to reduce a number of transition metal organometallic complexes. α-Ferrocenyl alcohols, acetyl ferrocenes and vinyl ferrocenes are reduced under ionic hydrogenation conditions to yield alkyl substituted ferrocene derivatives. The rate of these reduction depends on the concentrations of both the α-ferrocenyl carbocation and triethylsilane [65–68].



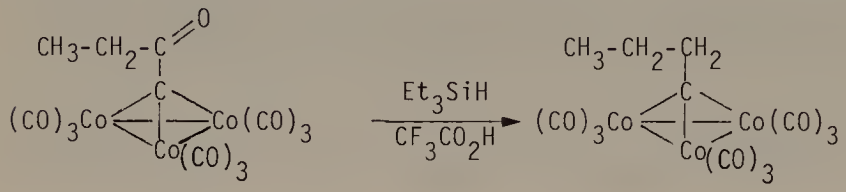
(17.32)

In a similar manner, acetyl, benzoyl, and formyl cyclopentadienyl manganese tricarbonyl complexes are reduced respectively to ethyl, benzyl, and methyl cyclopentadienyl manganese tricarbonyl complexes [69].



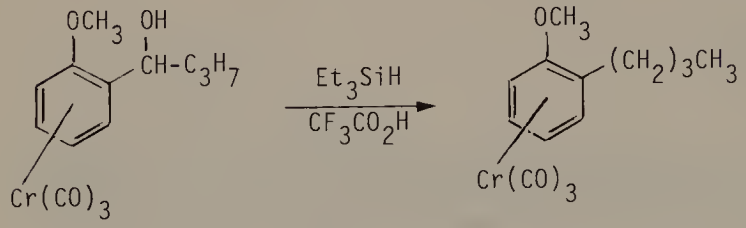
(17.33)

Acylidynetricobalt nonacarbonyl complexes are reduced under ionic hydrogenation conditions to alkyltricobalt nona carbonyl complexes [70, 71].



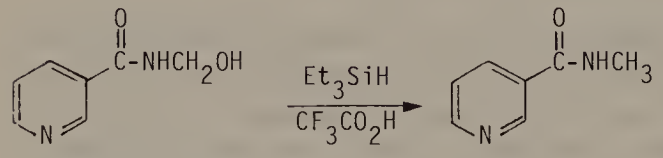
(17.34)

A benzylic alcohol π-anisole chronium tricarbonyl complex has been reduced to an alkyl π-anisole chronium tricarbonyl complex [72].



(17.35)

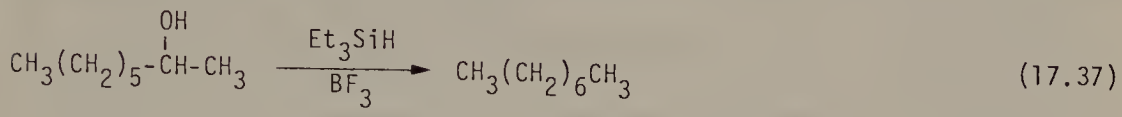
With the exception of the formyl manganese tricarbonyl complex just discussed, primary alcohols are not reduced under ionic hydrogenation conditions. However, N-hydroxymethyl groups are reduced on treatment with trifluoroacetic acid and triethylsilane to N-methyl groups [73].



(17.36)

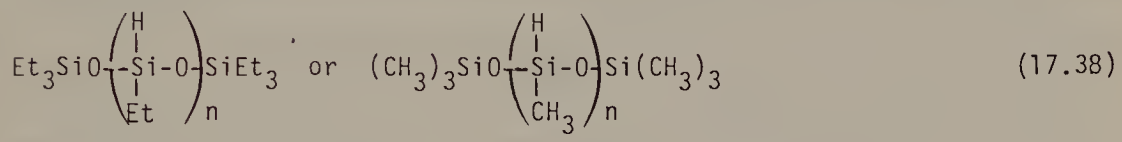
17.12 Improved Procedures

The rate accelerating effect of $BF_3 \cdot OEt_2$ on ionic hydrogenation of thiophene has been mentioned. It has been reported that $BF_3 \cdot H_2O$ can be substituted for trifluoroacetic acid to yield a more powerful reducing system. The acidity of $BF_3 \cdot H_2O$ may comparable to anhydrous sulfuric acid. Ketones such as 2-admantanone are reduced to adamantane, while polycyclic aromatic hydrocarbons such as anthracene are reduced to 9,10-dihydroanthracene by this new system [74]. The use of BF_3 in place of trifluoroacetic acid permits the reduction of aromatic [75] as well as aliphatic ketones [75], and secondary alcohols [76] to the corresponding alkanes.



$$CH_3(CH_2)_5\text{-}\underset{\displaystyle OH}{\underset{|}{CH}}\text{-}CH_3 \xrightarrow[BF_3]{Et_3SiH} CH_3(CH_2)_6CH_3 \qquad (17.37)$$

Another practical improvement involves the use of polymethylsiloxane or polyethylsiloxane in place of triethylsilane. This may facilitate separation of the product [77].



$$Et_3SiO\left(\begin{array}{c} H \\ | \\ Si\text{-}O \\ | \\ Et \end{array}\right)_n SiEt_3 \quad \text{or} \quad (CH_3)_3SiO\left(\begin{array}{c} H \\ | \\ Si\text{-}O \\ | \\ CH_3 \end{array}\right)_n Si(CH_3)_3 \qquad (17.38)$$

References

1. Parnes, Z.N., Zdanovich, V.I., Kugucheva, E.E., Basova, G.I., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *166*, 122 (1966)
2. Kursanov, D.N., Parnes, Z.N., Bassova, G.I., Loim, N.M., Zdanovich, V.I.: Tetrahedron, *23*, 2235 (1967)
3. Carey, F.A., Tremper, H.S.: J. Org. Chem. *36*, 758 (1971)
4. Kursanov, D.N., Parnes, Z.N., Loim, N.M.: Synthesis, 633 (1974)
5. Parnes, Z.N., Khotimskaya, G.A., Lyakhovestskii, Y.I., Petrovskii, P.V.: Izv. Akad. Nauk. SSSR Ser. Khim. 1562 (1972)
6. Guillerm, G., Frappier, F., Tabet, J.C., Marquet, A.: J. Org. Chem. *42*, 3776 (1977)
7. Hess, G.G., Lampe, F.W., Sommer, L.H.: J. Am. Chem. Soc. *87*, 5327 (1965)
8. Ebsworth, E.A.V., Physical Basis of the Chemistry of the Group IV Elements in Organometallic Compounds of the Group IV Elements, (MacDiarmid, A.G., Ed.), p. 46, New York: M. Dekker, 1968
9. Whitmore, F.C., Pietrusza, E.W., Sommer, L.H.: J. Am. Chem. Soc. *69*, 2108 (1947)
10. Doyle, M.P., McOsker, C.C., West, C.T.: J. Org. Chem. *41*, 1393 (1976)
11. Corey, J.Y., West, R.: J. Am. Chem. Soc. *85*, 2430 (1963)
12. Austin, J.D., Eaborn, C.: J. Chem. Soc. 2279 (1964)
13. Sommer, L.H., Bauman, D.L.: J. Am. Chem. Soc. *91*, 7076 (1969)
14. Fry, J.L.: J. Am. Chem. Soc. *93*, 3558 (1971)
15. Fry, J.L., Adlington, M.G.: J. Am. Chem. Soc. *100*, 7641 (1978)
16. Carey, F.A., Hsu, C.L.W.: J. Organometal. Chem. *19*, 29 (1969)

17. Lewis, E.S., Grinstein, R.H.: J. Am. Chem. Soc. *84*, 1158 (1962)
18. Carey, F.A., Tremper, H.S.: J. Am. Chem. Soc. *90*, 2578 (1968)
19. Parnes, Z.N., Kalinkin, M.I., Tsyryapkin, V.A., Khamitova, R.F., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *203*, 600 (1972)
20. Serebryakova, T.A., Parnes, Z.N., Zakharychev, A.V., Ananchenko, S.N., Torgov, I.V.: Izv. Akad. Nauk. SSSR Ser. Khim. 725 (1969)
21. Newman, M.S., Kanakarajan, K.: J. Org. Chem. *45*, 2301 (1980)
22. Carey, F.A., Tremper, H.S.: J. Org. Chem. *34*, 4 (1969)
23. Carey, F.A., Tremper, H.S.: J. Am. Chem. Soc. *90*, 2578 (1968)
24. Doyle, M.P., McOsker, C.C.: J. Org. Chem. *43*, 693 (1978)
25. Kursanov, D.N., Kalinkin, M.I., Gridchin, S.A., Shatalov, G.V., Parnes, Z.N.: Izv. Akad. Nauk. SSSR Ser. Khim. 803 (1979)
26. Akhrem, A.A., Moiseenkov, A.M., Krivoruchko, V.A.: Izv. Akad. Nauk. SSSR, 1800 (1973)
27. Kursanov, D.N., Parnes, Z.N., Bolestova, G.I.: Dokl. Akad. Nauk. SSSR, *181*, 1132 (1968)
28. Bolestova, G.I., Parnes, Z.N., Belikova, N.A., Kursanov, Z.D.: Izv. Akad. Nauk. SSSR Ser. Khim. 798 (1979)
29. Parnes, Z.N., Khotimskaya, G.A., Lukina, N.Y., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *178*, 620 (1968)
30. Mazur, R.H., White, W.N., Semenow, D.A., Lee, C.C., Silver, M.S., Roberts, J.D.: J. Am. Chem. Soc. *81*, 4390 (1959)
31. Carey, F.A., Tremper, H.S.: J. Am. Chem. Soc. *91*, 2967 (1969)
32. Parnes, Z.N., Khotimskaya, G.A., Lukina, N.Y., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *178*, 620 (1968)
33. Parnes, Z.N., Khotimskaya, G.A., Kudryavtsev, R.V., Kursanov, D.N.: Izv. Akad. Nauk. SSSR Ser. Khim. 901 (1972)
34. Khotimskaya, G.A., Kudryavtsev, R.V., Mil'vitskaya, E.M., Plate, A.F., Parnes, Z.N.: Izv. Akad. Nauk. SSSR Ser. Khim. 1989 (1972)
35. Parnes, Z.N., Khotimskaya, G.A., Lukina, M.Y., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *178*, 620 (1968)
36. Parnes, Z.N., Khotimskaya, G.A., Kudryavtsev, R.V., Lukina, N.Y., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *184*, 615 (1969)
37. Kursanov, D.N., Khotimskaya, G.A., Fedin, E.I., Lukina, M.Y., Parnes, Z.N.: Izv. Akad. Nauk. SSSR, Ser. Khim., 746 (1969)
38. Kalinkin, M.I., Parnes, Z.N., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *180*, 1370 (1968)
39. Zdanovich, V.I., Kudryavtsev, R.V., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *182*, 593 (1968)
40. Verheyden, J.P.H., Richardson, A.C., Bhatt, R.S., Grant, B.D., Fitch, W.L., Moffatt, J.G.: Pure and Applied Chem. *50*, 1363 (1978)
41. Kursanov, D.N., Parnes, Z.N., Loim, N.M.: Izv. Akad. Nauk. SSSR Ser. Khim. 1289 (1966)
42. West, C.T., Donnelly, S.J., Kooistra, D.A., Doyle, M.P.: J. Org. Chem. *38*, 2675 (1973)
43. Mozhaev, G.M., Parnes, Z.N., Zalukaeva, L.P., Kursanov, D.N.: Zhur. Org. Khim. *14*, 1657 (1978)
44. Kursanov, D.N., Parnes, Z.N., Loim, N.M., Bakalova, G.V.: Dokl. Akad. Nauk. SSSR, *179*, 1106 (1968)
45. Loim, N.M., Parnes, Z.N., Vasil'eva, S.P., Kursanov, D.N.: Zhur. Org. Khim. *8*, 896 (1972)
46. Doyle, M.P., DeBruyn, D.J., Kooistra, D.A.: J. Am. Chem. Soc. *94*, 3659 (1972)

47. Tsunoda, T., Suzuki, M., Noyori, R.: Tetrahedron Lett. 4679 (1979)
48. Fry, J.L., Ott, R.A.: J. Org. Chem. *46*, 602 (1981)
49. Meerwein, H., Laasch, P., Mersch, R., Spille, J.: Chem. Ber. *89*, 209 (1956)
50. Hart, D.J., Tsai, Y.M.: Tetrahedron Lett. 1567 (1981)
51. Kursanov, D.N., Loim, N.M., Baranova, V.A., Moiseeva, L.V., Zalukaev, L.P., Parnes, Z.N.: Synthesis, 420 (1973)
52. Loim, N.M., Baranova, V.A., Moiseeva, L.V., Zalukaev, L.P., Parnes, Z.N., Kursanov, D.N.: Izv. Akad. Nauk. SSSR Ser. Khim. 843 (1974)
53. Parnes, Z.N., Loim, N.M., Baranova, V.A., Kursanov, D.N.: Zhur. Org. Khim. *7*, 2066 (1971)
54. Loim, N.M., Parnes, Z.N., Brunovlenskaya, I.I., Kursanov, D.N.: Dokl. Akad. Nauk. SSSR, *196*, 1361 (1971)
55. Kalinkin, M.I., Kolomnikova, G.D., Parnes, Z.N., Kursanov, D.N.: Izv. Akad. Nauk. SSSR Ser. Khim. 1902 (1976)
56. Parnes, Z.N., Lyakhovetsky, Y.I., Kalinkin, M.I., Kursanov, D.N., Belenkii, L.I.: Tetrahedron, *34*, 1703 (1978)
57. Parnes, Z.N., Bolestova, G.I., Dolgova, S.P., Udre, V.E., Voronkov, M.G., Kursanov, D.N.: Izv. Akad. Nauk. SSSR Ser. Khim. 1834 (1974)
58. Rudakov, E.S., Parnes, Z.N., Osipov, A.M., Lyakhovetskii, Y.I., Kursanov, D.N.: Izv. Akad. Nauk. SSSR Ser. Khim. 1173 (1976)
59. Kursanov, D.N., Parnes, Z.N., Bolestova, G.I., Belenkii, L.I.: Tetrahedron, *31*, 311 (1975)
60. Parnes, Z.N., Bolestova, G.I., Kursanov, D.N.: Izv. Akad. Nauk. SSSR, 478 (1976)
61. Parnes, Z.N., Bolestova, G.I., Kursanov, D.N.: Zhur. Org. Khim. *13*, 476 (1977)
62. Anisimov, A.V., Luzikov, Y.N., Nikolaeva, V.M., Viktorova, E.A.: Zhur. Org. Khim. *15*, 172 (1979)
63. Parnes, Z.N., Budylin, V.A., Beilinson, E.Y., Kost, A.N.: Zhur. Org. Khim. *8*, 2564 (1972)
64. Lanzilotti, A.E., Littell, R., Fanshawe, W.J., McKenszie, T.C., Lovell, F.M.: J. Org. Chem. *44*, 4809 (1979)
65. Kazakova, L.I., Loim, N.M., Perevalova, E.G., Parnes, Z.N.: Zhur. Obsh. Khim. *43*, 2306 (1973)
66. Nesmeyanov, A.N., Rybinskaya, M.I., Shul'pin, G.B., Tolstaya, M.V.: Dokl. Akad. Nauk. SSSR, *229*, 1124 (1976)
67. Nesmeyanov, A.N., Shul'pin, G.B., Rybinskaya, M.I.: Izv. Akad. Nauk. SSSR Ser. Khim. 2824 (1975)
68. Kazakova, L.I., Loim, N.M., Parnes, Z.N.: Zhur. Obsh. Khim. *43*, 1577 (1973)
69. Kursanov, D.N., Anisimov, K.N., Parnes, Z.N., Loim, N.M., Zlotina, I.B., Valueva, Z.P.: Izv. Akad. Nauk. SSSR Ser. Khim. 713 (1972)
70. Seyferth, D., Hung, P.L.K., Hallgren, J.E.: J. Organometal. Chem. *44*, C66 (1972)
71. Seyferth, D., Williams, G.H., Eschbach, C.S., Nestle, M.O., Merola, J.S., Hallgren, J.E.: J. Am. Chem. Soc. *101*, 4867 (1979)
72. Semmelhack, M.F., Bisaha, J., Czarny, M.: J. Am. Chem. Soc. *101*, 768 (1979)
73. Auerbach, J., Zamore, M., Weinreb, S.M.: J. Org. Chem. *41*, 725 (1976)
74. Larson, J.W., Chang, L.W.: J. Org. Chem. *44*, 1168 (1979)
75. Fry, J.L., Orfanopoulos, M., Adlington, M.G., Dittman, Jr., W.R., Silverman, S.B.: J. Org. Chem. *43*, 374 (1978)
76. Adlington, M.G., Orfanopoulos, M., Fry, J.L.: Tetrahedron Lett. 2955 (1976)
77. Parnes, Z.N., Bolestova, G.I., Intyakova, E.I., Kursanov, D.N.: Zhur. Org. Khim. *9*, 1704 (1973)

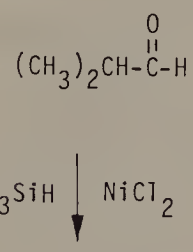
18 Reduction of Polar Multiple Bonds by Hydrosilation

18.1 Introduction

The reduction of ketones to alcohols by heterogeneous catalytic hydrogenation over noble metal catalysts is well-known. The discovery that olefins could be hydrogenated in the presence of the homogeneous catalyst $[Ph_3P]_3RhCl$, stimulated the search for similar catalysts which would permit the reduction of ketones [1]. While homogeneous catalytic hydrogenation of ketones has not developed, the homogeneous catalytic hydrosilation of ketones to yield alkyl silyl ethers has blossomed. These can be easily hydrolyzed to alcohols.

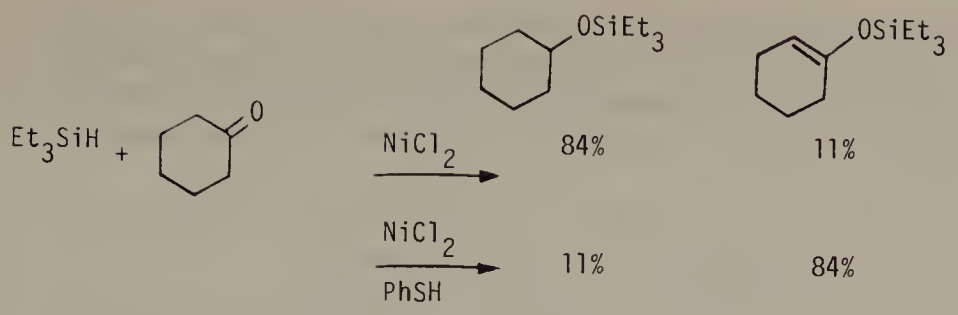
18.2 Hydrosilation of Ketones and Aldehydes

Platinum, ruthenium, rhodium, and nickel catalysts have all proved effective for the hydrosilation of ketones and aldehydes. A catalyst formed by reaction of nickel (II) chloride and triethylsilane facilitates the hydrosilation of aliphatic aldehydes. A mixture of alkyl triethylsilyl ethers, dialkyl ethers, and hexaethyldisiloxane is obtained [2].



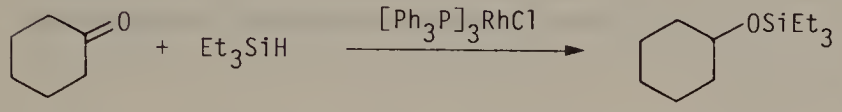
$$(CH_3)_2CH\text{-}CH_2OSiEt_3 \;+\; (CH_3)_2CHOCH(CH_3)_2 \;+\; Et_3SiOSiEt_3 \qquad (18.1)$$

The ratio of triethylsilane to aldehyde as well as the reaction temperature effects the ratio of products. Hydrosilation of ketones with triethylsilane with this catalyst yields predominantly alkyl triethylsilyl ethers. Modification of the catalyst by addition of phenyl thiol yields principally triethylsilyl enol ethers [3].



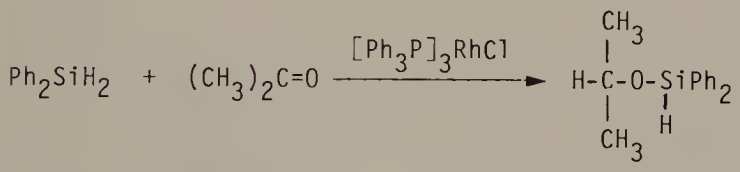
(18.2)

Wilkinson's catalyst, $[Ph_3P]_3RhCl$, has proved exceptionally active for the hydrosilation of aliphatic ketones with triethylsilane. The reaction is complete in minutes at 0 °C. Hydrosilation of alkyl aryl ketones is slower, acetophenone requires heating at 60 °C for 15 minutes [4].



(18.3)

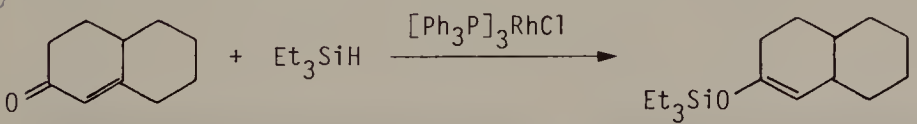
The reaction is fast with dihydro- and trihydrosilanes. Thus, the reaction of diethylsilane with acetophenone is exothermic at 0 °C [5, 6]. In the hydrosilation reaction of aldehydes or ketones, the analogous ruthenium complex $RuCl_2(PPh_3)_2$ is less active than Wilkinson's catalyst [7, 8]. With Wilkinson's catalyst, dihydrosilanes such as diphenylsilane, or α-naphthylphenylsilane yield only diarylalkoxysilanes [7].



(18.4)

A yellow complex, $(Ph_3P)_2RhHCl(SiEt_3)$ is formed on mixing triethylsilane and $[Ph_3P]_3RhCl$. This may result from oxidative addition of triethylsilane to coordinately unsaturated *bis*(triphenylphosphine)rhodium chloride formed by dissociation of a bulky triphenylphosphine ligand in solution [4, 6]. This complex has been suggested to be critical in the catalytic reaction sequence.

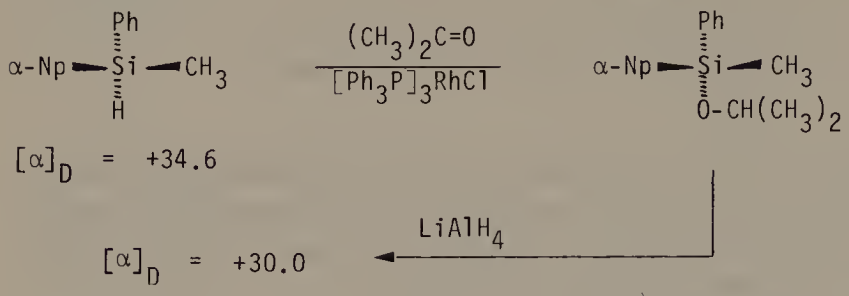
$[Ph_3P]_3RhCl$ catalyzes the 1,4-hydrosilation of α,β-unsaturated ketones and aldehydes to yield silyl enol ethers. These undergo hydrolysis with methanolic potassium hydroxide to the corresponding ketones (see 16.8).



(18.5)

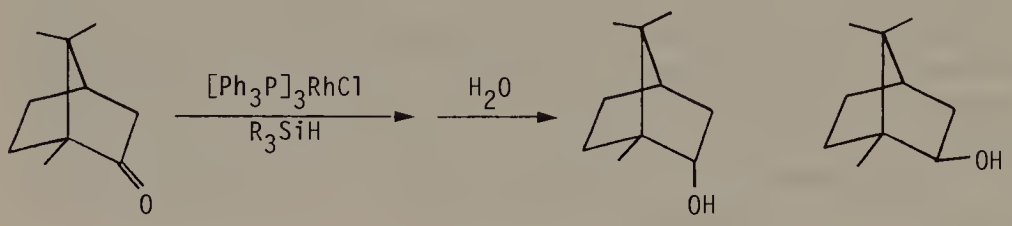
A number of studies have been done to elucidate the mechanism of hydrosilation of ketones by $[Ph_3P]_3RhCl$. Hydrosilation of acetone with optically active α-naphthylphenylmethylsilane catalyzed by $[Ph_3P]_3RhCl$ gave optically active isopropoxy-α-naphthylphenylmethylsilane. This was reduced with

$LiAlH_4$ to yield α-naphthylphenylmethylsilane of almost identical rotation to that of starting silane. Since $LiAlH_4$ reduction of alkoxysilanes is known to proceed with retention of configuration, the rhodium catalyzed hydrosilation of ketones must also proceed largely with retention of configuration at the silyl center [9].



(18.6)

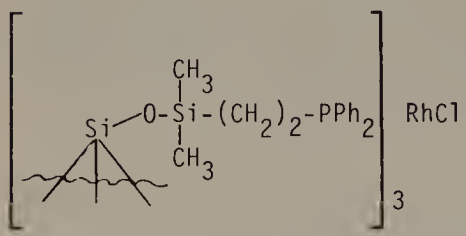
The steric requirements of the transition state have been explored by hydrosilation of stereochemically rigid ketones such as camphor and menthone. The ratio of diastereomeric alkyl silyl ethers formed in these reactions depends on the silane used [10].



(18.7)

R_3SiH			
Et_2SiH_2	91	:	9
$PhCH_3SiH_2$	75	:	25
Et_3SiH	30	:	70

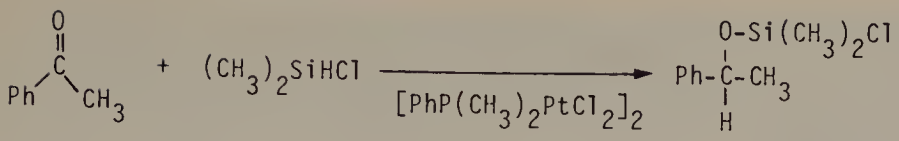
Hydrosilation of alkyl substituted cyclohexanones has been studied with $[Ph_3P]_3RhCl$ and an analogus heterogeneous rhodium catalyst [11].



(18.8)

Similar stereoselectivities were observed with both heterogeneous and homogeneous catalysts [11].

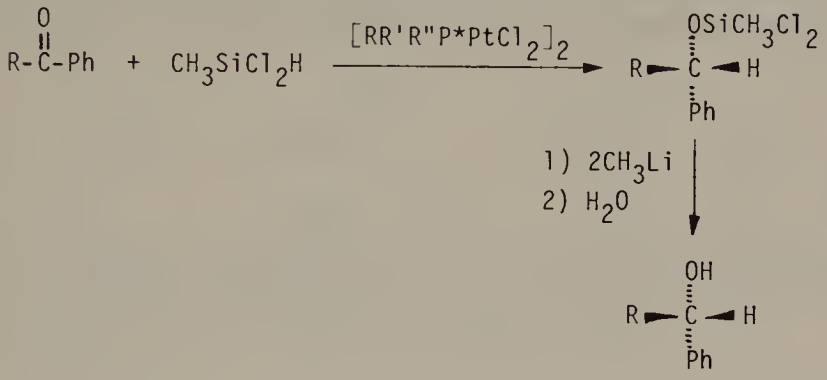
Dichloro-*bis*(dimethylphenylphosphino) di-μ-chloro diplatinum is also effective for the hydrosilation of alkyl aryl ketones with methyldichlorosilane or dimethylchlorosilane [12, 13].



(18.9)

18.3 Catalytic Asymmetric Hydrosilation of Aldehydes and Ketones

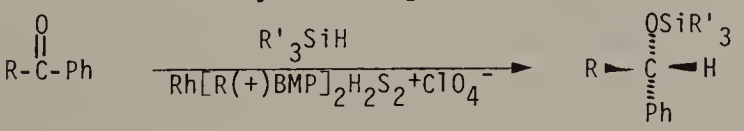
A variety of transition metal complexes with chiral tertiary phosphine ligands have proved effective for the catalytic asymmetric hydrosilation of prochiral ketones. These reactions permit the preparation of chiral alcohols. Kumada, found that both dichloro *bis* [R(+)benzylmethylphenylphosphine]-di-μ-chloro diplatinum [R(+)BMPPt] and dichloro *bis*[R(−)methyl-*n*-propylphenylphosphine] di-μ-chloro diplatinum [R(−)MPPPt] were effect asymmetric hydrosilation catalysts for alkyl aryl ketones. However, the optical yields (e.e.) of the product alcohols were relatively low [12, 13].



(18.10)

R	Catalyst	Chemical Yield	Optical Yield	Configuration
CH_3	R(+)BMPPt	81	7.6	S
t-Bu	R(+)BMPPt	33	18.6	S
CH_3	R(−)MPPPt	71	5.5	R

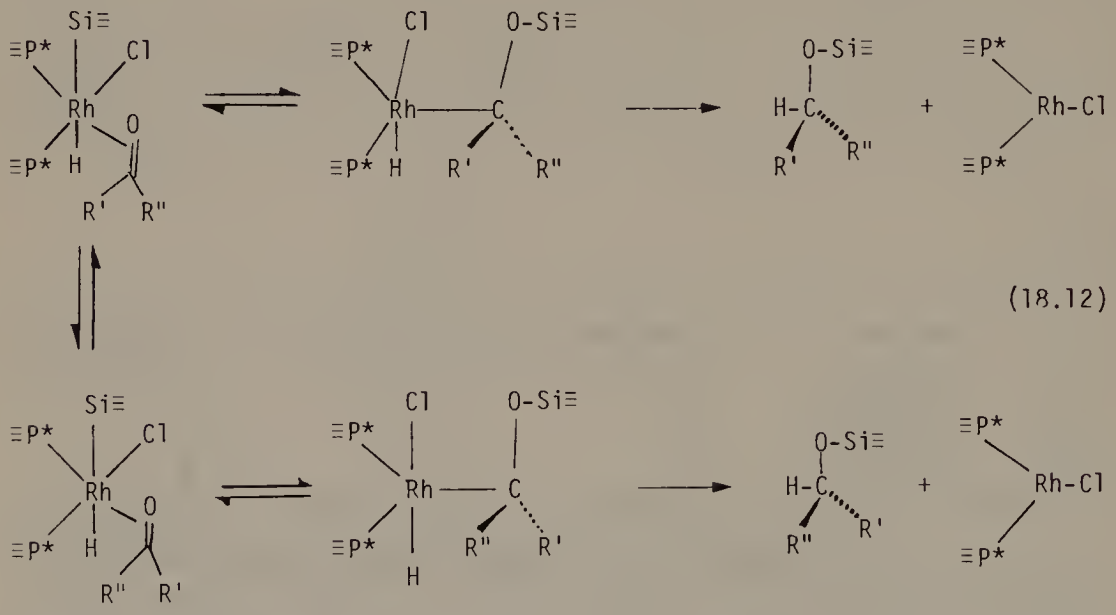
A chiral cationic rhodium complex prepared from optically active R(+)benzylmethylphenylphosphine R(+)BMP is effective for the asymmetric hydrosilation of prochiral ketones with dialkyl or trialkylsilanes [14]. The extent of the asymmetric induction as well as the configuration of the predominant alcohol produced are dependent not only on the structure of the prochiral ketone but also on the particular silane used. The different alkyl groups of the silane may effect the asymmetric reduction process due to differences in stability of the two diastereomeric α-silyloxyalkyl rhodium intermediates. Reductive elimination by transfer of hydrogen from rhodium to carbon in this intermediate yields the product [15].

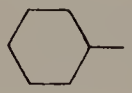


(18.11)

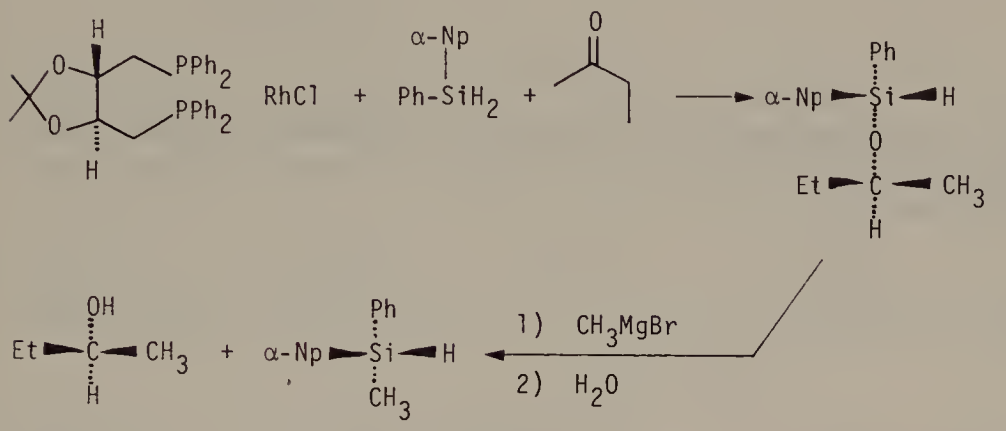
R	Silane	Chemical Yield	Optical Yield	Configuration
CH_3-	$PhSi(CH_3)_2H$	97	31.6	S
$(CH_3)_3C-$	$PhSi(CH_3)_2H$	84	61.8	S
CH_3-	$(CH_3)_3SiH$	100	5.1	S
$(CH_3)_3C-$	$(CH_3)_3SiH$	70	28.0	R

Chiral rhodium (I) complexes related to Wilkinson's catalyst have also proved effective. These have been prepared by substitution of R(+)benzylmethylphenylphosphine R(+)BMP or S(−)benzylmethylphenylphosphine S(−)BMP for triphenylphosphine. The optical yield and configuration of the product alcohol are dependent on the structure of the prochiral ketone as well as on the silane utilized. Prochiral dialkyl ketones as well as alkyl aryl ketones undergo asymmetric reduction. Analysis of the relative size of the various groups in the diastereomeric α-silyloxyalkyl rhodium intermediates permits prediction of the configuration of the predominant silyl ether product [16–18].



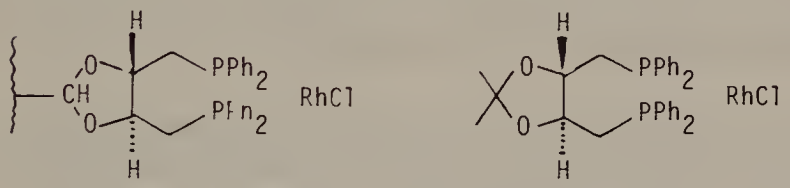
Catalyst	R′	R″	Silane	Chemical Yield	Opt. Yield	Config.
S(−)BMP	Ph	CH_3	$PhSi(CH_3)_2H$	92	44	R
	Ph	$(CH_3)_2CH$		95	56	R
	Ph	$(CH_3)_2CH$	Et_2SiH_2	98	23	S
R(+)BMP	Ph	$(CH_3)_3C$	$EtSi(CH_3)_2H$	97	56	R
	Ph	$(CH_3)_3C$	$PhSi(CH_3)_2H$	92	54	S
	Ph		$PhSi(CH_3)_2H$	90	58	S

Catalytic asymmetric hydrosilation reactions have also been carried out with chiral rhodium complexes prepared from (−) or (+) 2,3-O-isopropylidene-2,3-dihydroxy-1,4-*bis*(diphenylphosphino)butane, (−) or (+) DIOP. Hydrosilation of unsymmetrical ketones with prochiral silanes leads to asymmetric induction at both carbon and silicon of the alkoxysilane product. Hydrosilation of methyl ethyl ketone with α-naphthylphenylsilane catalyzed by a (−) DIOP rhodium complex leads to a chiral alkoxysilane. Reaction of this alkoxy silane with methyl Grignard yields both optically active (−) α-naphthylphenylmethylsilane (40% e.e.) and (−) 2-butanol (42% e.e.) [19, 20].



(18.13)

Both soluble chiral DIOP rhodium complexes and the analogous polymer bound chiral DIOP rhodium complexes yield similar results in catalytic asymmetric hydrosilation reactions of prochiral ketones [21, 22].

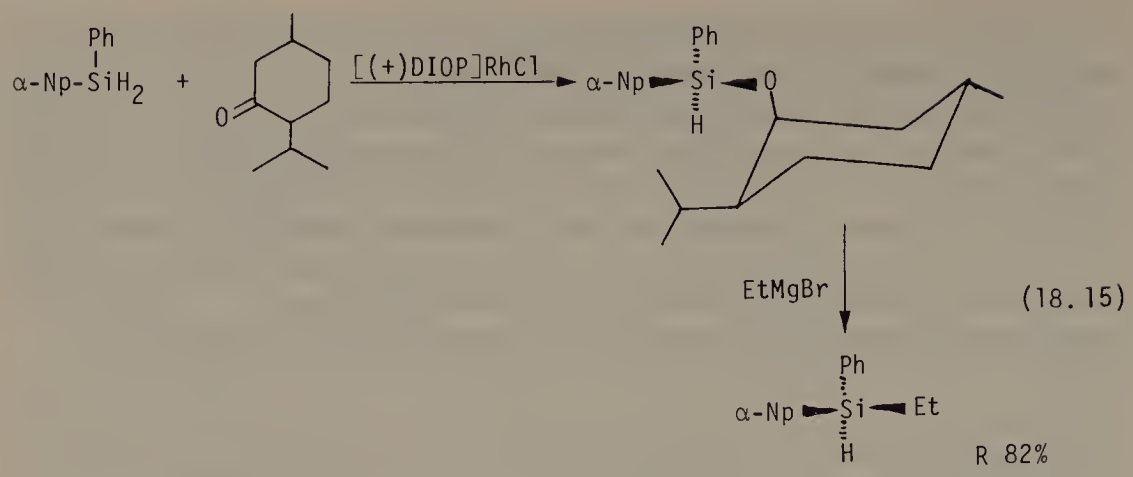


(18.14)

polymer bound soluble

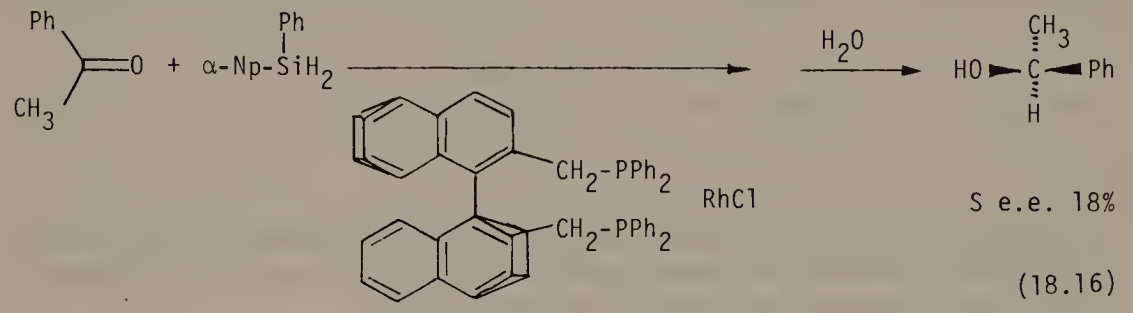
Catalyst	Silane	Ketone	Chemical Yield	Optical Yield
polymer	H_2SiPh_2	$Ph-C-CH_3$ ‖ O	90	29% S(−)
soluble	H_2SiPh_2		100	28% S(−)
soluble	H_2Si-Ph α−Np		76	53% S(−)

Catalytic hydrosilation of optically active ketones [(+) camphor and (−) menthone] with prochiral dihydrosilane such as α-naphthylphenylsilane has been studied. Both chiral and achiral rhodium complexes have been used as catalysts. The optically active diarylalkoxysilanes products were reacted with Grignard reagents to yield chiral silanes in up to 80% optical purity [23].



(18.15)

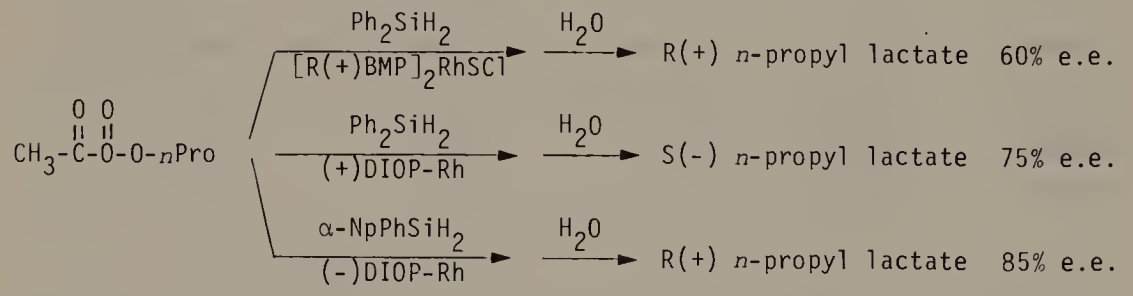
Chiral 2,2′-*bis*(diphenylphosphinomethyl)-1,1′-binaphthyl rhodium (I) complexes have also proved effective in the catalytic asymmetric hydrosilation of prochiral ketones [24].



(18.16)

18.4 Asymmetric Hydrosilation of α-Keto Esters

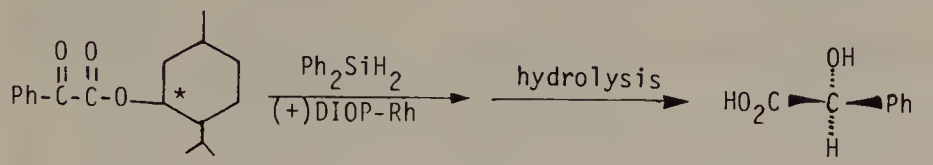
Catalytic asymmetric hydrosilation of α-keto esters such as *n*-propyl pyruvate or ethyl phenylglyoxylate, have been carried out with chiral rhodium complexes. The keto carbonyl group is preferentially reduced to yield chiral α-hydroxy esters. High asymmetric induction is observed [25].



(18.17)

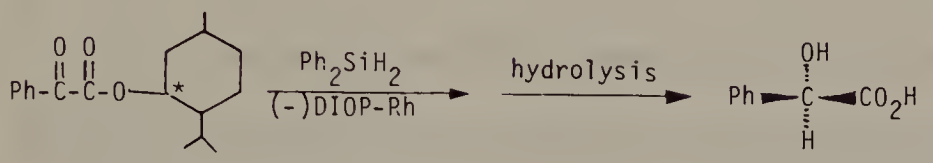
Catalytic asymmetric hydrosilation of (−) menthyl benzoylformate with chiral rhodium catalysts yields chiral α-hydroxy menthyl esters (Eq. 18.18 and 18.19). The asymmetric induction results from both the chiral rhodium

complex and the chiral menthyl group. To estimate the contribution of each, two experiments were done. First chiral menthyl α-keto esters were hydrosilated with Wilkinson's catalyst (Eq. 18.20). Second hydrosilation of cyclohexyl benzoylformate was catalyzed by the chiral rhodium complex (Eq. 18.21) [26, 27].



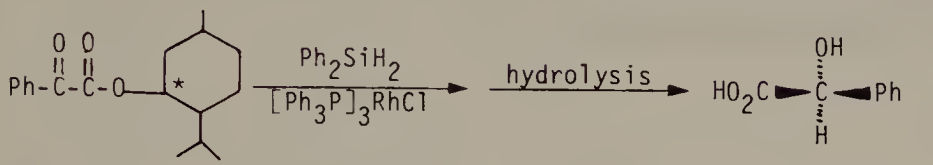
60% e.e. S

(18.18)



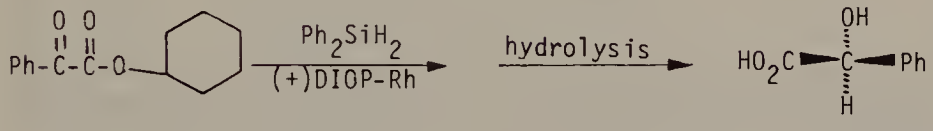
37% e.e. R

(18.19)



32% e.e. S

(18.20)



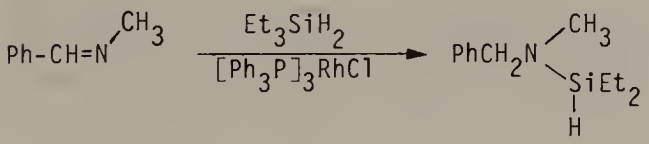
42.5% e.e. S

(18.21)

While the rationalization of these results is complex, nevertheless, catalytic asymmetric hydrosilation of α keto ester provides a new method to prepare chiral α-hydroxy acids.

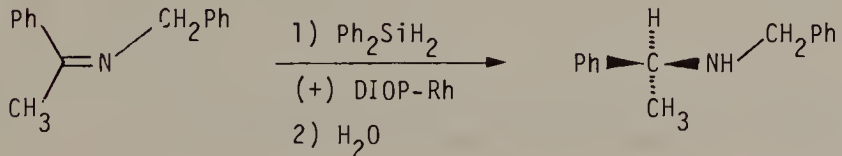
18.5 Hydrosilation of Imines and Pyridines

Imines can also be reduced to *N*-silyl amines by catalytic hydrosilation. $[Ph_3P]_3RhCl$ is most effective with dihydrosilanes, while $PdCl_2$ works well with trimethylsilane [28].



(18.22)

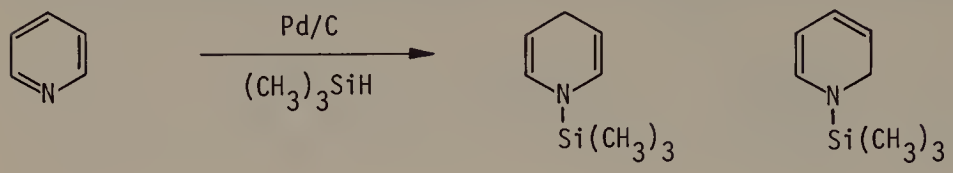
Catalytic hydrosilation of prochiral imines with chiral rhodium complexes such as (+) DIOP Rh(I) yields after hydrolysis chiral secondary amines [29].



S 50% e.e.

(18.23)

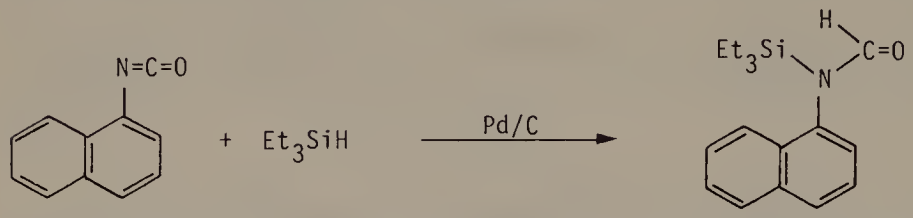
Trimethylsilane adds to pyridine in the presence of Pd/C to yield a mixture of N-trimethylsilyl-1,2 and 1,4-dihydropyridines and N,N'-*bis*(trimethylsilyl)-1,1-dihydro-4,4'-bipyridine. The ratio of products is dependent on time and other reaction conditions [37, 38].



(18.24)

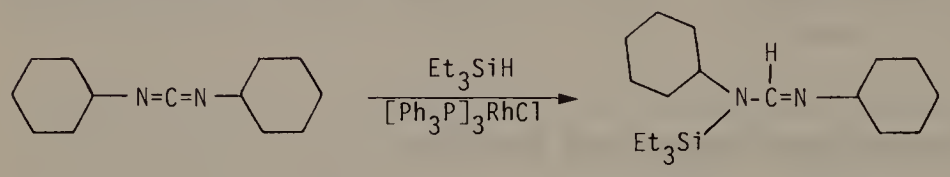
18.6 Hydrosilation of Isocyanates and Carbodiimides

Catalytic hydrosilation of aryl isocyanates with triethylsilane over Pd/C or with $PdCl_2$ gives N-α-aryl-α-silyl formamides. The opposite regiospecificity is observed with aliphatic isocyanates.



(18.25)

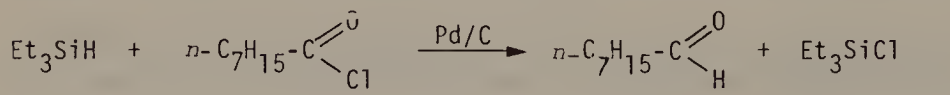
Both products react with methanol to yield formamides or with acetyl chloride to give N-acetyl formamides [30, 31]. Similar catalytic hydrosilation of dialkyl carbodiimides by $PdCl_2$ or $[Ph_3P]_3RhCl$ gives N,N'-dialkyl-N-silyl formamidines [32].



(18.26)

18.7 Silyl-Rosenmund Reduction

Like the Rosenmund reduction of acid chlorides by hydrogen over Pd [33], silanes react with acid chlorides over Pd/C [34] or in the presence of rhodium (I) complexes [35] to yield aldehydes and chlorosilanes. Yields are often higher than are obtained with lithium aluminum tri-*t*-butoxy hydride [36].



(18.27)

References

1. Schrock, R.R., Osborn, J.A.: J. Chem. Soc. Chem. Commun. 567 (1970)
2. Bourhis, R., Frainnet, E.: J. Organometal. Chem. *86*, 205 (1975)

3. Frainnet, E., Martel-Siegfried, V., Brousse, E., Dedier, J.: J. Organometal. Chem. *85*, 297 (1975)
4. Ojima, I., Nihonyanagi, M., Nagai, Y.: J. Chem. Soc. Chem. Commun. 938 (1972)
5. Ojima, I., Kogure, T., Nihonyanagi, M., Nagai, Y.: Bull. Chem. Soc. Japan, *45*, 3506 (1972)
6. Ojima, I., Nihonyanagi, M., Kogure, T., Kumagai, M., Horiuchi, S., Nakatsugama, K.: J. Organometal. Chem. *94*, 449 (1975)
7. Corriu, R.J.P., Moreau, J.J.E.: J. Chem. Soc. Chem. Commun. 38 (1973)
8. Eaborn, C., Odell, K., Pidcock, A.: J. Organometal. Chem. *63*, 93 (1973)
9. Corriu, R.J.P., Moreau, J.J.E.: J. Organometal. Chem. *85*, 19 (1975)
10. Ojima, I., Nihonyanagi, M., Nagai, Y.: Bull. Chem. Soc. Japan, *45*, 3722 (1972)
11. Ishiyama, J.I., Senda, Y., Shinoda, I., Imaizumi, S.: Bull. Chem. Soc. Japan, *52*, 2353 (1979)
12. Yamamoto, K., Hayashi, T., Kumada, M.: J. Organometal. Chem. *46*, C65 (1972)
13. Hayashi, T., Yamamoto, K., Kumada, M.: J. Organometal. Chem. *112*, 253 (1976)
14. Yamamoto, K., Hayashi, T., Kumada, M.: J. Organometal. Chem. *54*, C45 (1973)
15. Hayashi, T., Yamamoto, K., Kasuga, K., Omizu, H., Kumada, M.: J. Organometal. Chem. *113*, 127 (1976)
16. Ojima, I., Kogure, T., Nagai, Y.: Chem. Lett. 541 (1973)
17. Ojima, I., Nagai, Y.: Chem. Lett. 223 (1974)
18. Ojima, I., Kogure, T., Kumagai, M., Horiuchi, S., Sato, T.: J. Organometal. Chem. *122*, 83 (1976)
19. Corriu, R.J.P., Moreau, J.J.E.: J. Organometal. Chem. *64*, C51 (1974)
20. Corriu, R.J.P., Moreau, J.J.E.: J. Organometal. Chem. *85*, 19 (1975)
21. Poulin, J.C., Dumont, W., Dang, T.P., Kagan, H.B.: Compt. Rend. Acad. Sci. Paris, *277*, C41 (1973)
22. Dumont, W., Poulin, J.C., Dang, T.P., Kagan, H.B.: J. Am. Chem. Soc. *95*, 8295 (1973)
23. Corriu, R.J.P., Moreau, J.J.E.: Nouv. J. de Chim. *1*, 71 (1977)
24. Tamao, K., Yamamoto, H., Matsumoto, H., Miyake, N., Hayashi, T., Kumada, M.: Tetrahedron Lett. 1389 (1977)
25. Ojima, I., Kogure, T., Nagai, Y.: Tetrahedron Lett. 1889 (1974)
26. Ojima, I., Nagai, Y.: Chem. Lett. 191 (1975)
27. Ojima, I., Kogure, T., Kumagai, M.: J. Org. Chem. *42*, 1671 (1977)
28. Ojima, I., Kogure, T., Nagai, Y.: Tetrahedron Lett. 2475 (1973)
29. Langlois, N., Dang, T.P., Kagan, H.B.: Tetrahedron Lett. 4865 (1973)
30. Ojima, I., Inaba, S.I.: Tetrahedron Lett. 4363 (1973)
31. Ojima, I., Inaba, S.I.: J. Organometal. Chem. *140*, 97 (1977)
32. Ojima, I., Inaba, S.I., Nagai, Y.: J. Organometal. Chem. *72*, C11 (1974)
33. The Rosenmund Reduction of Acid Chlorides to Aldehydes by Mosettig, E., Mozingo, R.: in Organic Reactions IV.
34. Citron, J.D.: J. Org. Chem. *34*, 1977 (1969)
35. Coutis, B., Dent, S.P., Eaborn, C., Pidock, A.: J. Chem. Soc. Dalton, 2460 (1975)
36. Brown, H.C., Subba Rao, B.C.: J. Am. Chem. Soc. *80*, 5377 (1958)
37. Cook, N.C., and Lyons, J.E.: J. Am. Chem. Soc. *87*, 3283 (1963)
38. Cook, N.C., and Lyons, J.E.: J. Am. Chem. Soc. *88*, 3396 (1966)

19 Dissolving Metal Reductions

19.1 Introduction

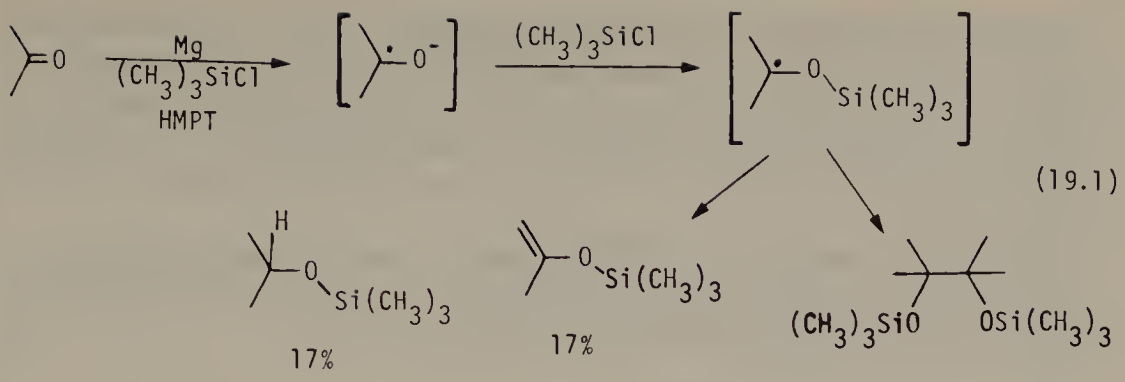
The products formed in dissolving metal reductions are often determined by the presence or absence of a proton source, as well as by other experimental conditions such as the particular metal and solvents used [1–3]. These differences may result from protonation of the initial anion radicals to yield radical intermediates, as well as from the ability of the proton source to limit the basicity of the media. Based on the analogy between a trimethylsilyl group and a proton, it is not surprising that TMS-Cl is able to influence the course of dissolving metal reductions.

This chapter will be organized by functional groups. Often several different combinations of reagents and solvents have been applied to reduce a single functional group. These may lead to diverse results. Solvent, metal, temperature, as well as the ratio of substrate to TMS-Cl influence the course of these reductions. Despite this number of variables, a coherent picture of these reductions may be possible.

French workers have made major contributions to our knowledge of dissolving metal reductions of unsaturated functional groups in the presence of TMS-Cl. They have utilized TMS-Cl with either lithium in THF (A) or magnesium in HMPT (B) as reduction systems.

19.2 Ketones and Aldehydes

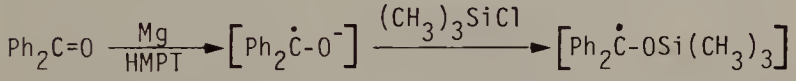
Ketones and aldehydes undergo dissolving metal reduction in the presence of a proton source to yield alcohols, while in the absence of a proton source pinacol dimers are the usual products [4]. Reduction of ketones which have α-hydrogens with magnesium in HMPT or TMU and TMS-Cl leads to a mixture of products: *bis*-1,2-(trimethylsilyloxy)alkanes, and equal amounts of alkoxytrimethylsilanes and trimethylsilyl enol ethers. Formation of these products can be accounted for as follows. Initial electron transfer to the ketone forms a ketyl (anion radical) which reacts with TMS-Cl to yield a α-trimethylsilyloxyalkyl radical. Dimerization of such radicals yields *bis*-1,2-(trimethylsilyloxy)alkanes, while radical disproportionation results in equal amounts of alkoxytrimethylsilanes and trimethylsilyl enol ethers [5].



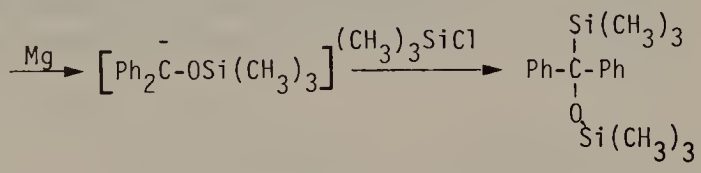
(19.1)

With cyclohexanone only the disproportionation products, cyclohexanoxytrimethylsilane and trimethylsilyloxycyclohexene are found [5].

On the other hand, benzophenone and *t*-butyl phenyl ketone react with B to yield diphenyl trimethylsilyl trimethylsilyloxymethane and *t*-butyl phenyl trimethylsilyl trimethylsilyloxymethane, respectively. These products result from a second electron transfer to the initial diphenyltrimethylsilyloxymethyl or *t*-butyltrimethylsilyloxybenzyl radicals to yield the corresponding carbanions which react with a second equivalent of TMS-Cl. Carbanion formation is probably favored by the phenyl groups. Dimerization of these radicals to form pinacol products may also be disfavored due to steric hinderance [6, 7].

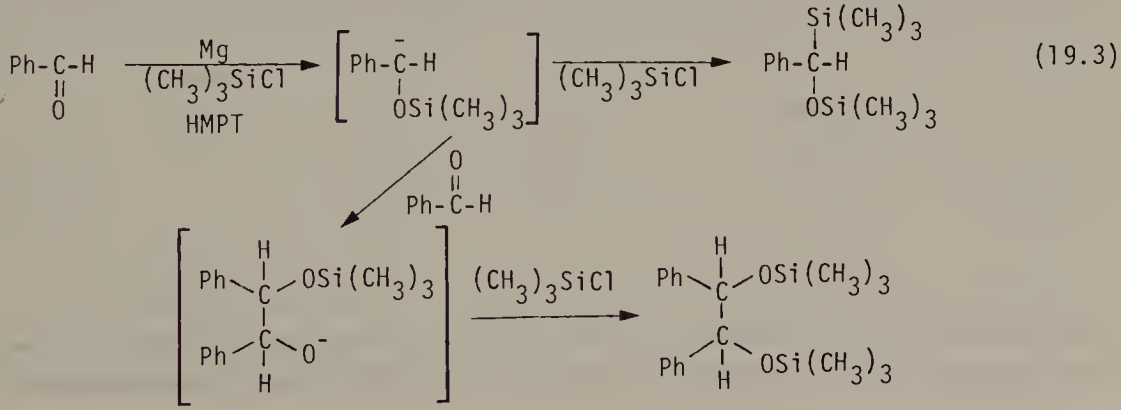


(19.2)



Addition of THF to the HMPT or TMU solvent favors formation of pinacol products with benzophenone. Electron transfer to the silyloxy radicals may be slower in THF due to its decreased cation solvating ability [8].

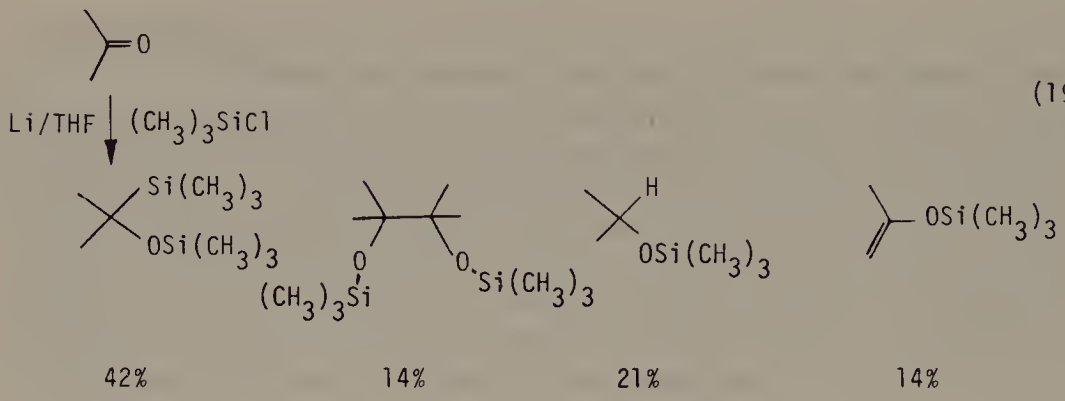
With the reduction system (B), the ratio of benzaldehyde to TMS-Cl influences the distribution of products. A 1 : 1 ratio favors 1,2-diphenyl-1,2-*bis*(trimethylsilyloxy)ethane whereas a 2 : 1 ratio of TMS-Cl to benzaldehyde favors formation of α-trimethylsilyl-α-trimethylsilyloxytoluene [9].



(19.3)

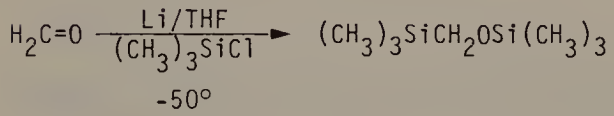
Chloral reacts with B to yield predominantly 1-chloro-1-trimethylsilyl-2-trimethylsilyloxy ethylene. Electron transfer to the trichloromethyltrimethylsilyloxy methyl radical may yield a carbanion which loses chloride to give 1,1-dichloro-2-trimethylsilyloxy ethylene as an intermediate. Under similar conditions hexachloroacetone gives 1,1,3,3,3-pentachloro-2-trimethylsilyloxy propene [10].

Reduction of ketones or aldehydes with A yields a mixture of 1,2-*bis*-(trimethylsilyloxy) alkanes, alkoxytrimethylsilanes, trimethylsilyl enol ethers, and α-trimethylsilyl-α-trimethylsilyloxy alkanes [11–13].



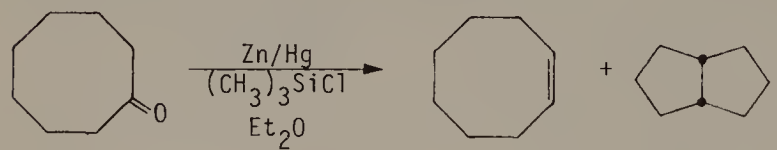
(19.4)

Apparently lithium in THF is a more powerful reducing agent than magnesium in HMPT. Reduction of the α-trimethylsilyloxy radical yields a carbanion which reacts with TMS-Cl to give C-silylated product. Formaldehyde is reduced by A at −50° to yield trimethylsilyloxytrimethylsilylmethane [14].



(19.5)

The Clemmensen reduction of ketones to alkanes utilizes zinc-amalgam and HCl. Based on the analogy between a proton and a trimethylsilyl group, it is not surprising that the combination of TMS-Cl and zinc amalgam in ether reduce aliphatic cyclic ketones to cyclic alkenes. Cyclohexanone gave cyclohexene, while cyclooctanone gave cyclooctene and bicyclo [3.3.0] octane [15]. This latter product may indicate that a carbene intermediate is involved.

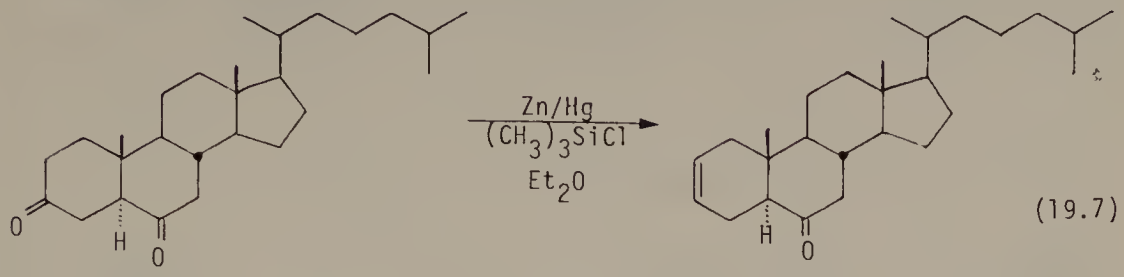


(19.6)

2:1

The reaction is quite selective, 3-keto groups are reduced in preference to keto groups in other positions of steroid nuclei [16]. Thus 5-α-cholestan-3-

one was reduced to 5-α-cholest-2-ene, while 5-α-cholestan-3,6-dione gave 5-α-cholest-2-en-6-one under these conditions.

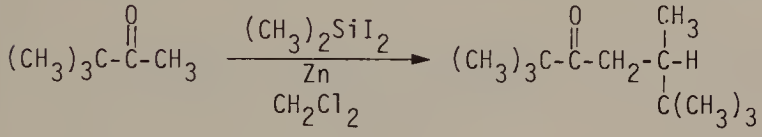


(19.7)

On the other hand, aromatic ketones, such as acetophenone, gave *bis*(trimethylsilyl) ethers of the pinacol dimers [15].

A zinc-copper couple and dimethyldichlorosilane react with ketones to yield products which may arise from carbene intermediates. For example, benzaldehyde gives benzyl phenyl ketone and diphenylacetaldehyde. These products may result from zinc chloride catalyzed rearrangement of stilbene oxide, formed by reaction of phenyl carbene with benzaldehyde. Evidence in favor of this intriguing proposal is the observation that reaction of benzaldehyde with these reagents in the presence of cyclohexene yields phenylnorcarane [17]. Carbene intermediates have been previously proposed in the Clemmensen reduction of ketones to hydrocarbons [18].

Aliphatic ketones undergo reductive condensation in the presence of dimethyldiiodosilane and zinc in methylene chloride [19].

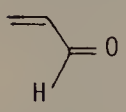
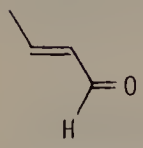
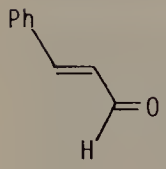
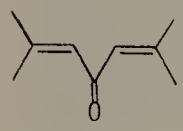
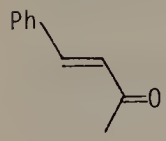
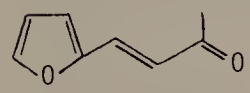
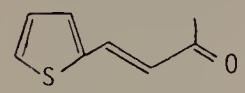
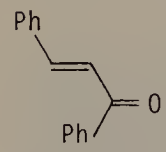
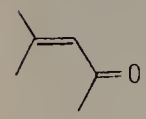
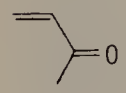
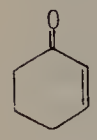


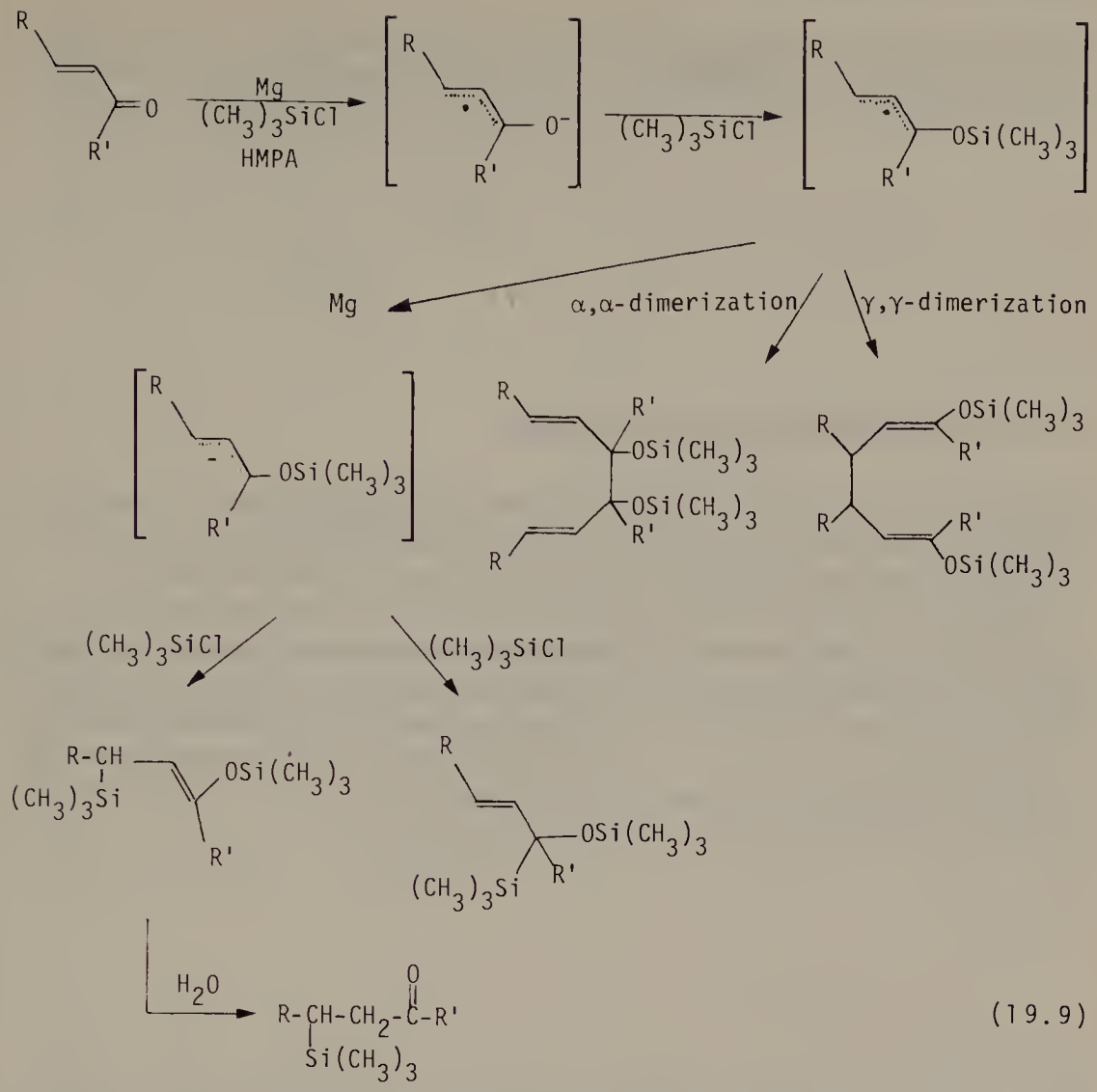
(19.8)

19.3 α,β-Unsaturated Ketones and Aldehydes

α,β-Unsaturated ketones or aldehydes undergo reduction by A or B to yield mixtures of products. Initial electron transfer to the α,β-unsaturated carbonyl compound yields an anion radical which reacts with TMS-Cl to give an α-trimethylsilyloxyallylic radical. This can undergo symmetrical dimerization at the α position to yield 3,4-*bis*(trimethylsilyloxy)-1,5-dienes (pinacol dimer). Symmetrical dimerization of the α-trimethylsilyloxy allylic radical at the γ-position gives 1,6-*bis*(trimethylsilyloxy)-1,5-dienes (3,3-dimer). Surprisingly no unsymmetrical dimer products have been detected. Further reduction of the α-trimethylsilyloxyallylic radical yields an α-trimethylsilyloxyallylic anion which reacts with TMS-Cl to yield predominantly 1-trimethylsilyloxy-3-trimethylsilyl-1-alkenes (1,4 product) and 1-trimethylsilyloxy-1-trimethylsilyl-2-alkenes (1,2 product). Product distribution data for reduction of a number of α,β-unsaturated ketones and aldehydes is given in Table 1. In these examples pinacol dimers are not found.

Table 1.

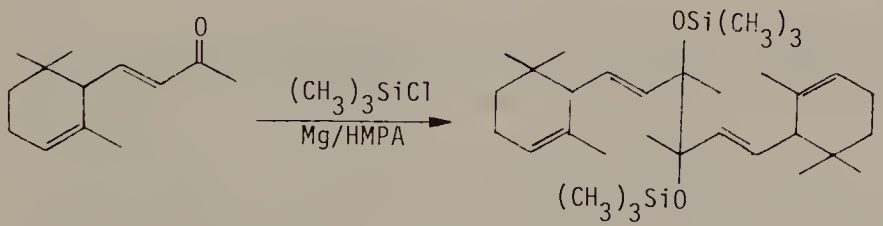
α,β-Unsaturated Ketone or Aldehyde	1,4	1,2	Pinacol Dimer	3,3-Dimer	Reduction System	Reference
	70%				A	13, 21
	20%	21%			A	13, 21
	65%				B	20, 22
	60%				B	24
	86%			5%	B	20, 22
	48%			25%	B	23
	70%			15%	B	23
	55%			30%	B	22
	33%	38%			A	12
	60%				A	12
	60%				A	12



(19.9)

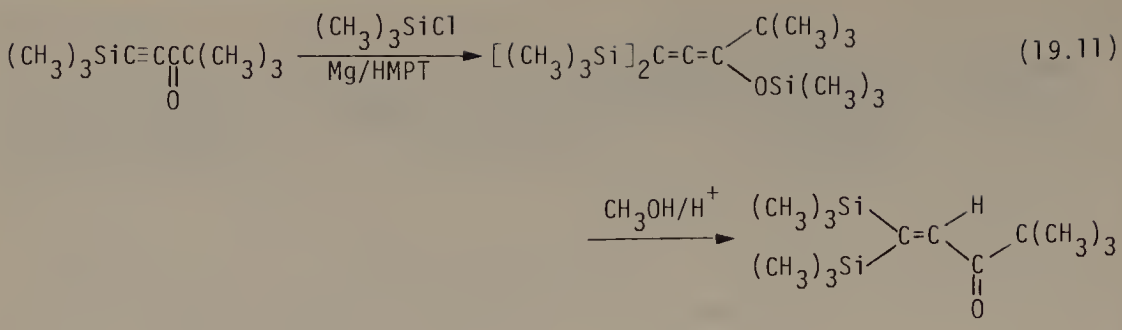
Hydrolysis of 1-trimethylsilyloxy-3-trimethylsilyl-1-alkenes yields β-trimethylsilyl substituted ketones or aldehydes.

α- and β-Ionone both give unusual product distributions on reductive silylation. Reduction of α-ionone with B gives a 50% yield of pinacol dimer, while with β-ionone the 1,4-reduction product is predominant [20, 25].



(19.10)

In a similar manner, 2-alkynones undergo reduction by B to yield 1-trimethylsilyl-3-trimethylsilyloxy-allenes as the major products. These undergo hydrolysis to yield β-trimethylsilyl α,β-unsaturated ketones [26, 27].

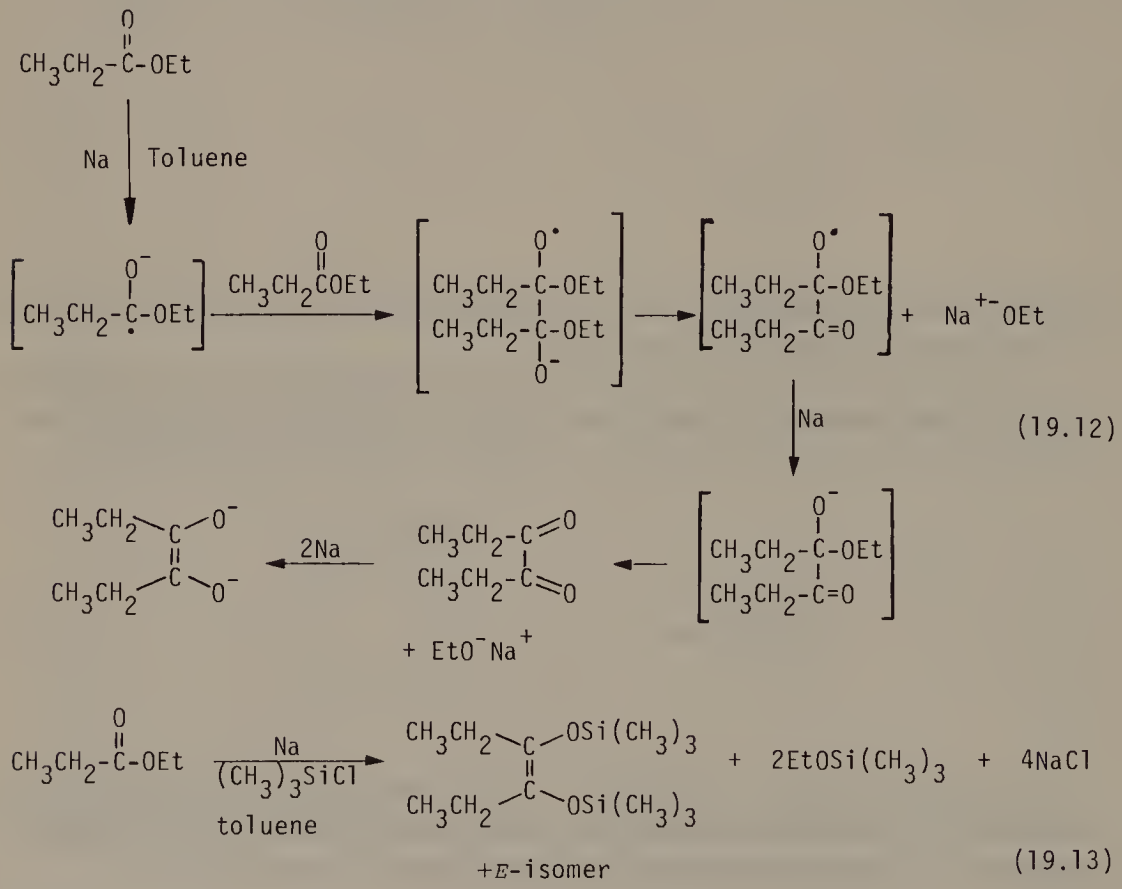


(19.11)

19.4 Esters/Silyl-Acyloin Reactions

Esters are reduced with TMS-Cl and sodium in toluene to yield alkoxytrimethylsilanes and 1,2-*bis*(trimethylsilyloxy) alkenes [28, 29]. These latter compounds undergo hydrolysis to yield α-hydroxy ketones (acyloins).

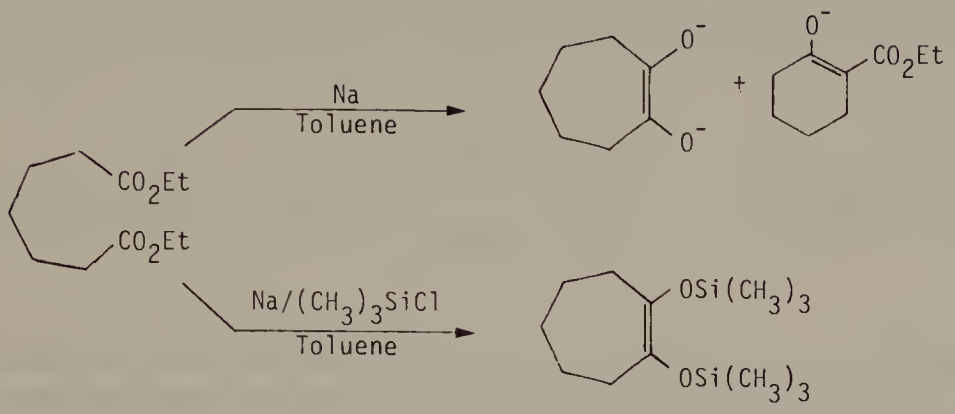
There are a number of advantages to the silyl acyloin reaction compared to the usual acyloin reaction. In the conventional acyloin reaction the media becomes increasingly basic as the reaction progresses due to formation of sodium alkoxides (Eq. 19.12). This permits competitive Claisen and Dieckman condensations to occur. In the silyl acyloin reaction, on the other hand, the reaction media remains neutral. Alkoxytrimethylsilanes and sodium chloride are formed instead of sodium alkoxides (Eq. 19.13).



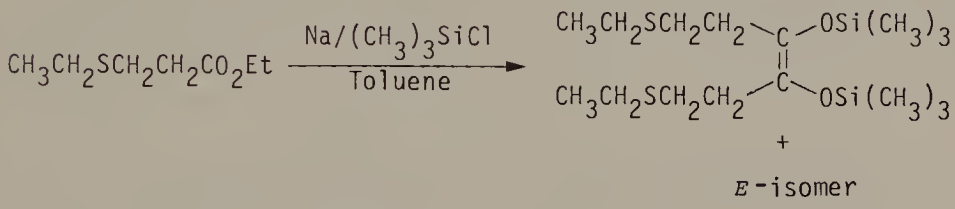
(19.12)

(19.13)

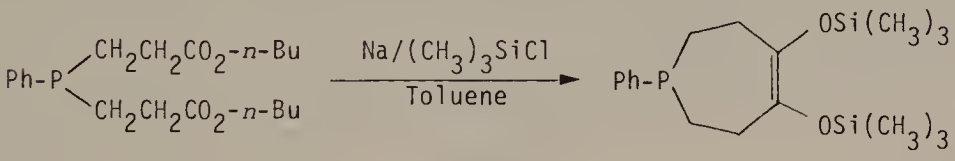
For example, treatment of diethyl pimelate with sodium under conventional acyloin conditions gives a mixture of Dieckman and acyloin products (Eq. 19.14). Whereas, under silyl acyloin conditions only 1,2-*bis*(trimethylsilyloxy)cycloheptene is formed (Eq. 19.15) [30].



The silyl acyloin reduction conditions eliminate competitive β-elimination reactions. β-Alkoxy, β-alkylmercapto and β-dialkylamino esters undergo the silyl acyloin reaction successfully [31].

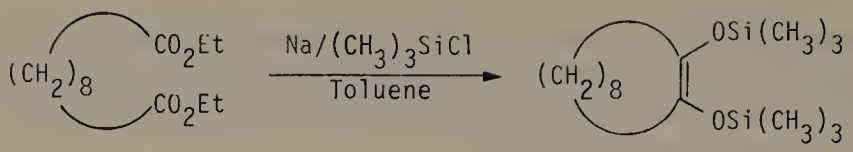


Medium sized 1,2-*bis*-trimethylsilyloxy alkenes possessing β heteroatoms such as oxygen, sulfur, nitrogen, or phosphorous can be prepared. The normal acyloin reaction fails in these cases [32].



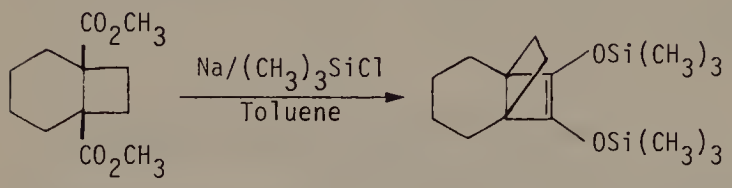
However, with ethyl β-chloropropionate reduction of the C–Cl bond apparently occurs preferentially. This leads to 1-ethoxy-1-trimethylsilyloxycyclopropane [29].

The neutral conditions of the silyl acyloin reaction permit successful reaction with ethyl phenylacetate [29]. In general the silyl acyloin reaction provides higher yields with alicyclic esters than the conventional acyloin reaction [33, 34]. With α,ω-diesters higher yields of cyclic products are obtained in the silyl acyloin reaction [28]. This is particularly useful for the preparation of medium and large sized cyclic compounds.



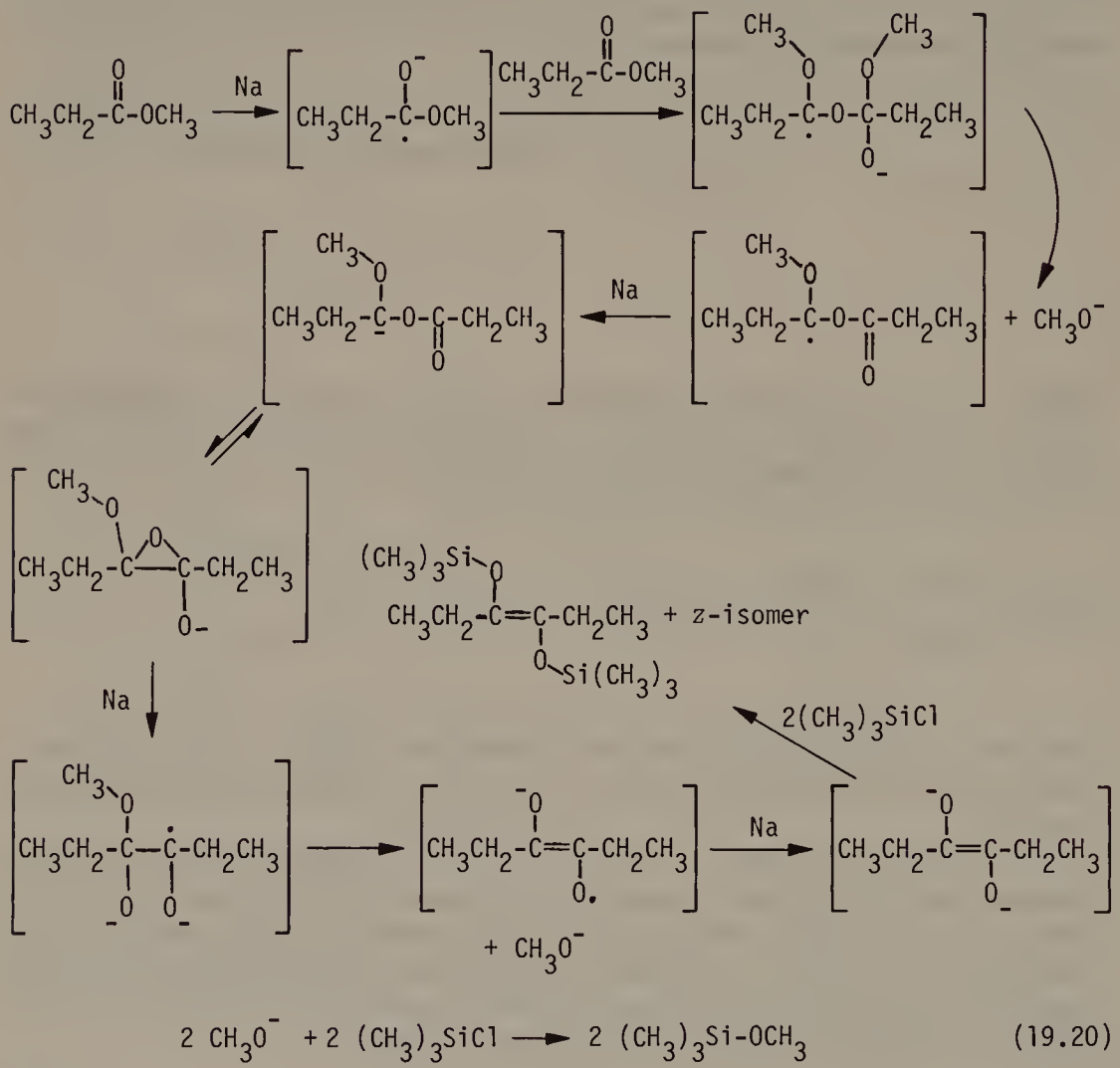
(19.18)

The silyl acyloin reaction has also proved useful for the preparation of 1,2-*bis*(trimethylsilyloxy) cyclobutenes [30, 35, 36].



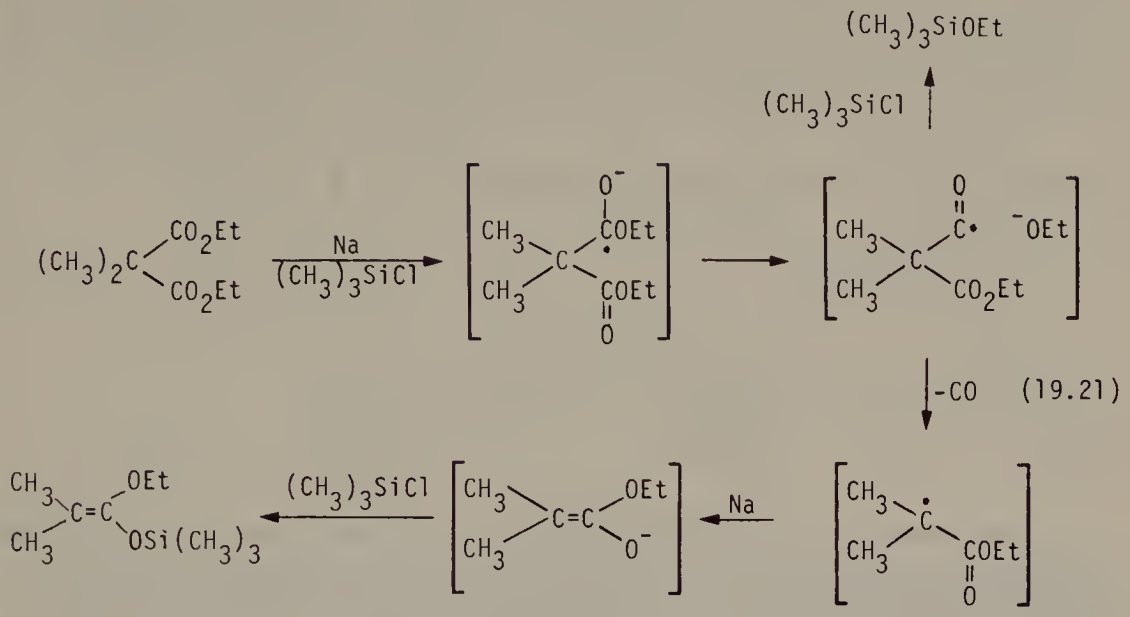
(19.19)

The sequence of reactions, proposed by Bloomfield, outlined below accounts for most of the experimental results. Of particular note, this sequence does not involve an α-diketone intermediate [37].

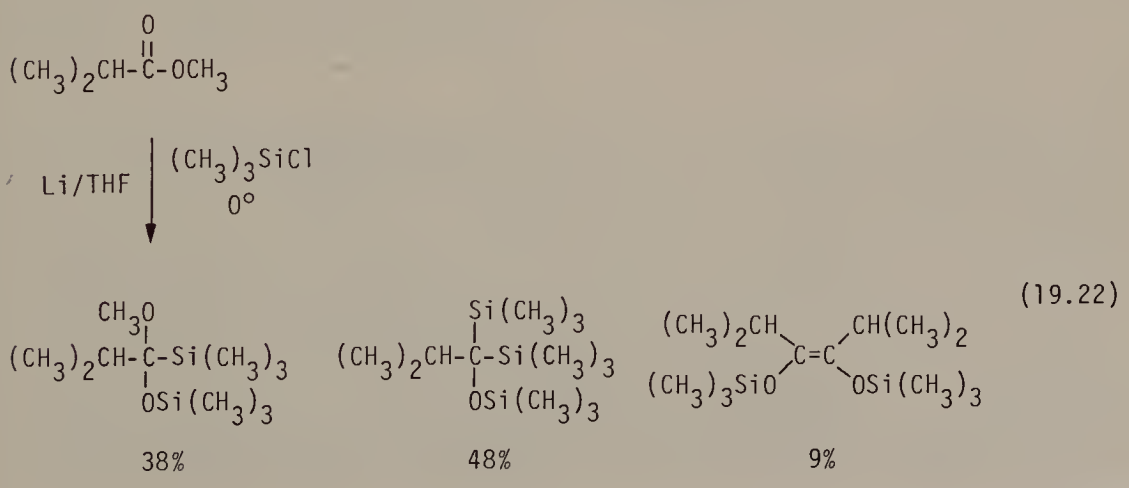


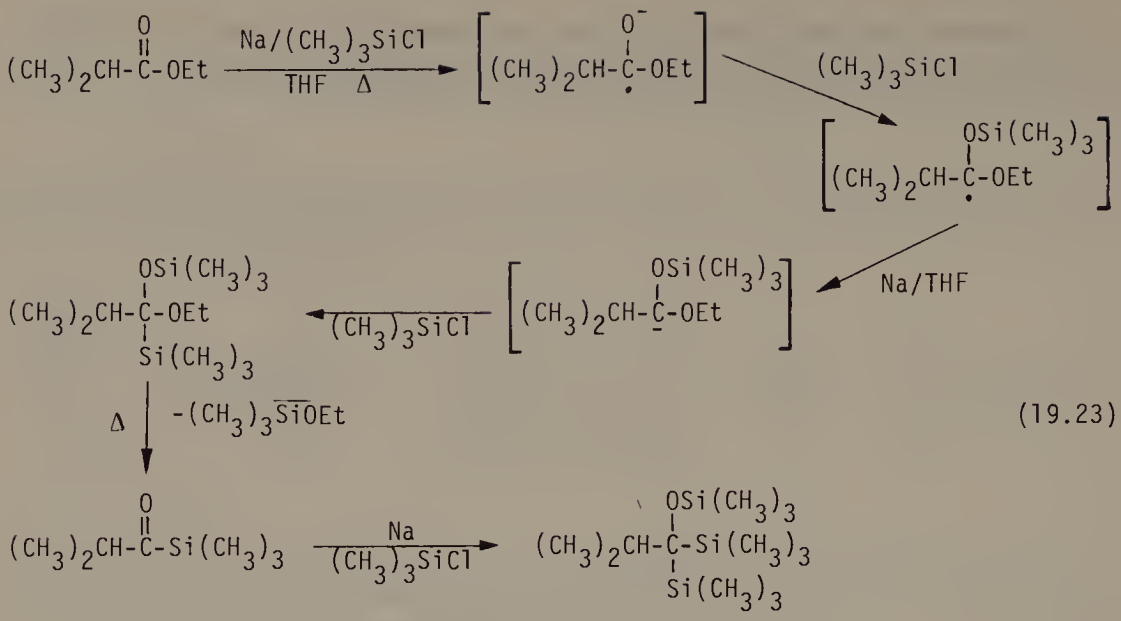
$$2\ CH_3O^- + 2\ (CH_3)_3SiCl \longrightarrow 2\ (CH_3)_3Si\text{-}OCH_3 \qquad (19.20)$$

Treatment of diethyl disubstituted malonates with sodium and TMS-Cl yields alkyl trimethylsilyl ketene acetals as outlined below [38].



On the other hand, in solvents like THF or DME, the reduction of esters with lithium or sodium and TMS-Cl yields 1-trimethylsilyloxy-1,1-*bis*(trimethylsilyl) alkanes [13, 39, 40]. This has been attributed to reaction of the initial ester anion radical with TMS-Cl rather than another molecule of ester. TMS-Cl reacts more efficiently with ketyls in more polar solvents. The α-alkoxy-α-trimethylsilyloxy alkyl radical undergoes further reduction to the corresponding anion which then reacts with TMS-Cl to yield 1-alkoxy-1-trimethylsilyl-1-trimethylsilyloxy alkanes. At low temperature these are relatively stable (Eq. 19.22) [13]. However, at higher temperature (refluxing THF), they undergo loss of alkoxytrimethylsilane and formation of acyltrimethylsilanes. These undergo further reductive silylation to yield 1-trimethylsilyloxy-1,1-*bis*(trimethylsilyl) alkanes (Eq. 19.23) [39, 40].

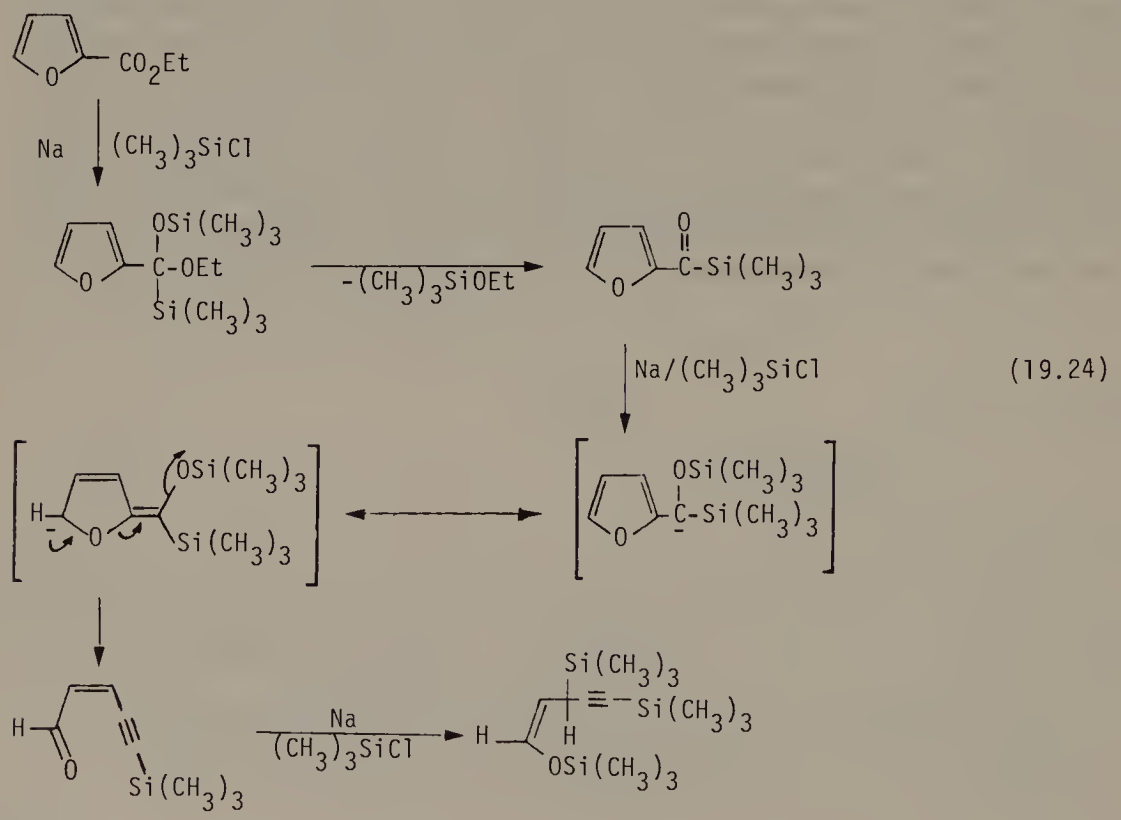




(19.23)

Consistent with this proposed mechanism, acyltrimethylsilanes are reduced under these conditions to 1-trimethylsilyloxy-1,1-*bis*(trimethylsilyl) alkanes [41]. These can be hydrolyzed to 1,1-*bis*(trimethylsilyl) alkanols. Alkoxides of these sterically hindered tertiary alcohols have proved to be highly selective bases (see Chapter 24).

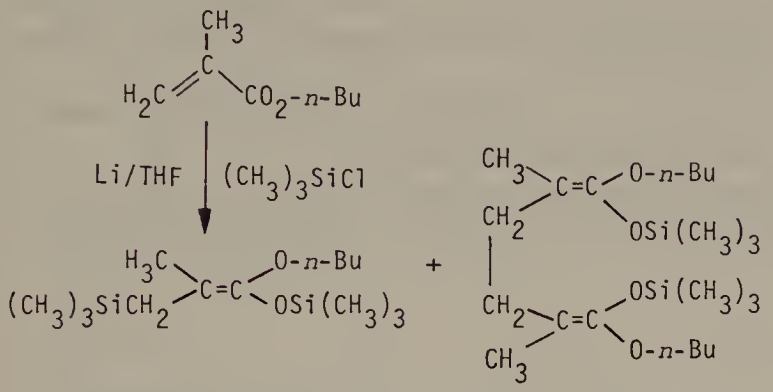
Reductive silylation of ethyl-2-furoate by sodium and TMS-Cl in THF yields 1-trimethylsilyloxy-3,5-*bis*(trimethylsilyl) pent-4-yn-1-ene as outlined below [42].



(19.24)

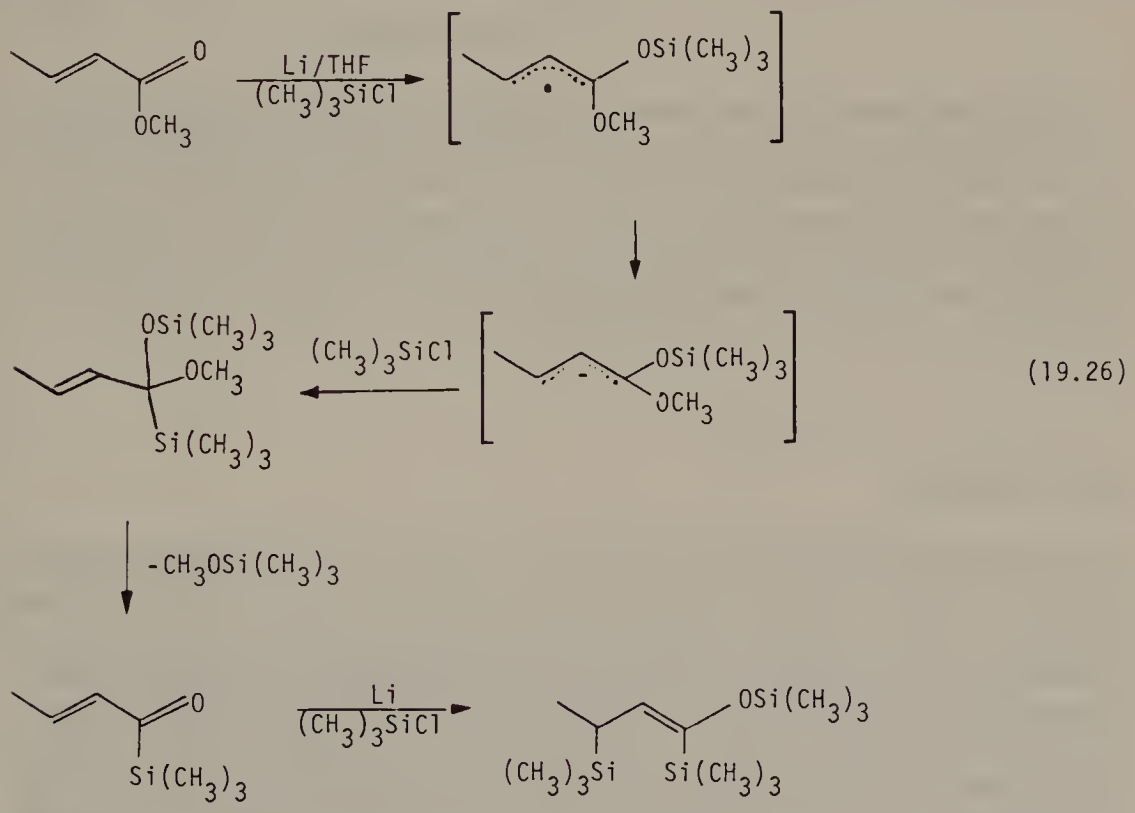
19.5 α,β-Unsaturated Esters, Amides, and Acid Chlorides

α,β-Unsaturated esters undergo reduction with B [20, 43, 44] or A [45] to give 1-alkoxy-1-trimethylsilyloxy-3-trimethylsilyl-1-alkenes and 1,6-dialkoxy-1,6-*bis*(trimethylsilyloxy)-1,5-hexadienes. These dimers result from combination of the α-alkoxy-α-trimethylsilyloxy allylic radicals at the sterically less congested γ-end.



(19.25)

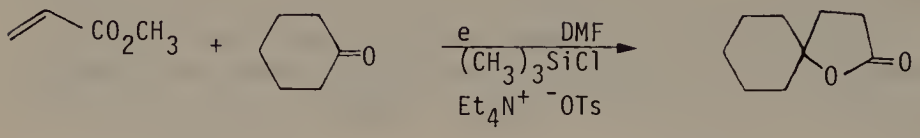
The ratio of these products formed with A depends on reaction temperature. Dimer products are favored by higher temperatures [46]. Methyl crotonate, on the other hand, is reduced by A to yield 1,3-*bis*(trimethylsilyl)-1-trimethylsilyloxy-1-butene [45].



(19.26)

The electrochemical reduction of α,β-unsaturated esters in the presence

of aliphatic ketones or aldehydes and TMS-Cl leads to formation of γ-lactones [47].

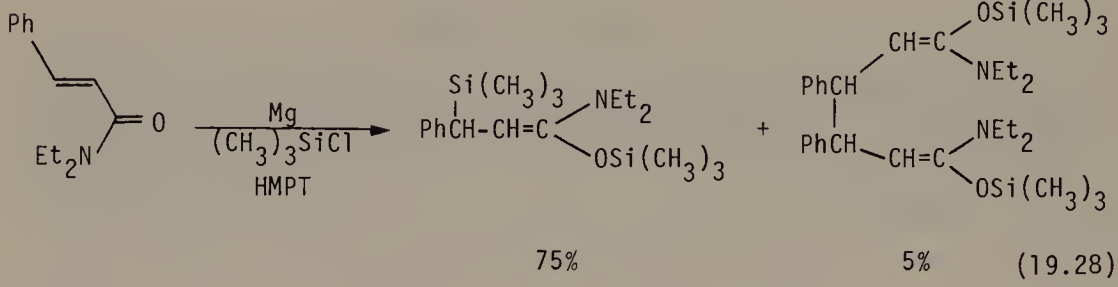


(19.27)

The presence of TMS-Cl is essential for the reaction although its exact role is not clear. Similar reactions occur with α,β-unsaturated nitriles to yield γ-hydroxynitriles.

The reductions of *n*-butanoic anhydride, dimethyl carbonate and methyl cyclopropanecarboxylate with B have been studied [46].

N,N-Dialkyl α,β-unsaturated amides undergo reduction by B to yield 1-dialkyl-amino-1-trimethylsilyloxy-3-trimethylsilyl-1-alkenes as major products [20, 48].

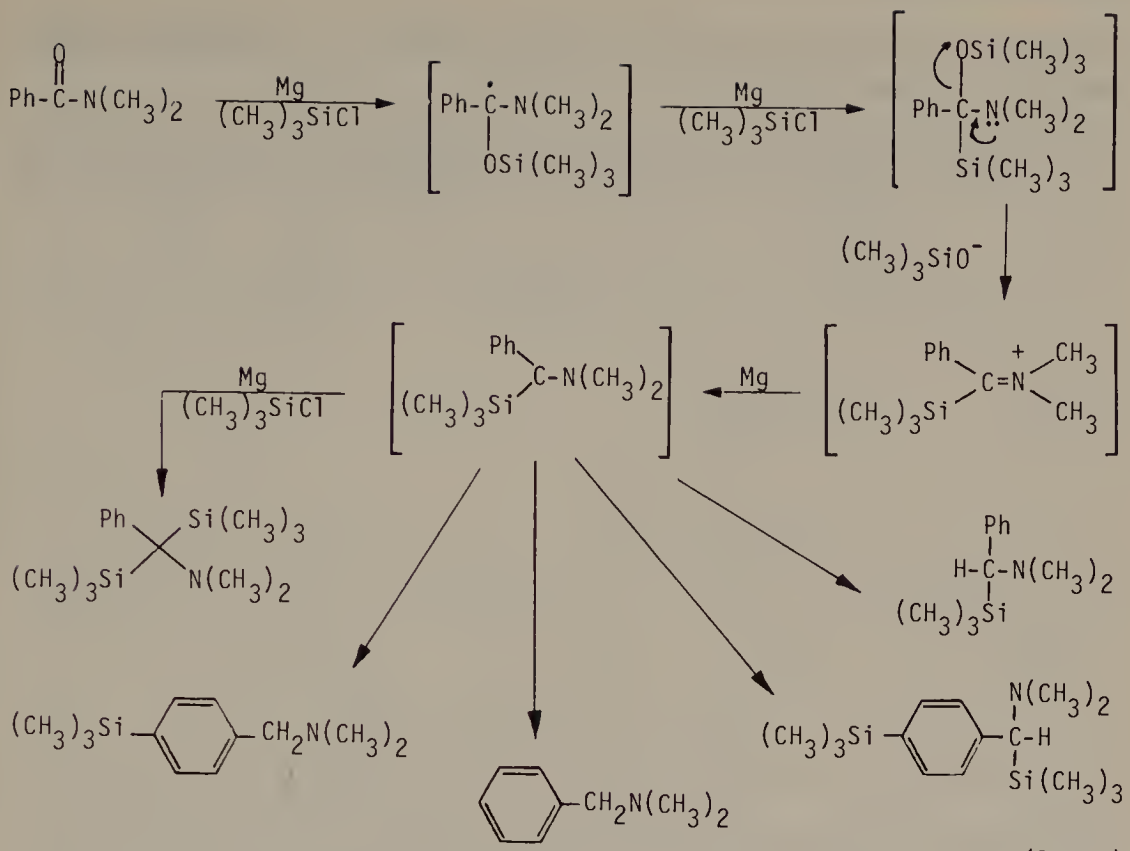


75% 5% (19.28)

α,β-Unsaturated acid chlorides react with B to yield 1,3-*bis*(trimethylsilyl)-1-trimethylsilyloxy-1-alkenes. An α,β-unsaturated acyltrimethylsilane may be involved as an intermediate which undergoes further reduction [49, 50]. As predicted, the reaction requires three equivalents of TMS-Cl and two of magnesium for every mole of α,β-unsaturated acid chloride reduced. Such 1,3-*bis*-trimethylsilyl-1-trimethylsilyloxy-1-alkenes undergo hydrolysis to β-trimethylsilyl acyltrimethylsilanes [20].

19.6 Amides

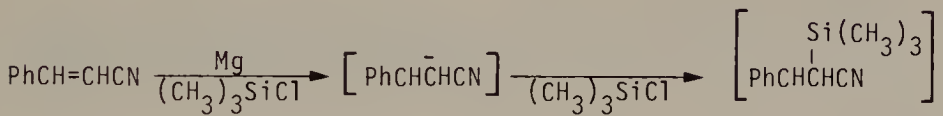
N,N-Dimethylbenzamide reacts with B to yield a mixture of deoxygenated products. The ratio of these products varies with solvent. HMPT, TMU, and THF have been studied. Initial electron transfer yields an anion radical which reacts with TMS-Cl to give the α-dimethylamino α-trimethylsilyloxybenzyl radical. Further electron transfer to this radical yields the anion which reacts with TMS-Cl to yield α-dimethylamino α-trimethylsilyloxybenzyltrimethylsilane. This undergoes fragmentation to a trimethylsilanoate anion/iminium cation pair. All products may arise from further reduction of the iminium cation [51].



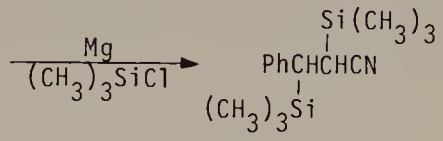
(19.29)

19.7 α,β-Unsaturated Nitriles

α,β-Unsaturated nitriles are reduced by B [50, 52] or A [46] to yield 1,2-*bis*(trimethylsilyl)alkylnitriles.



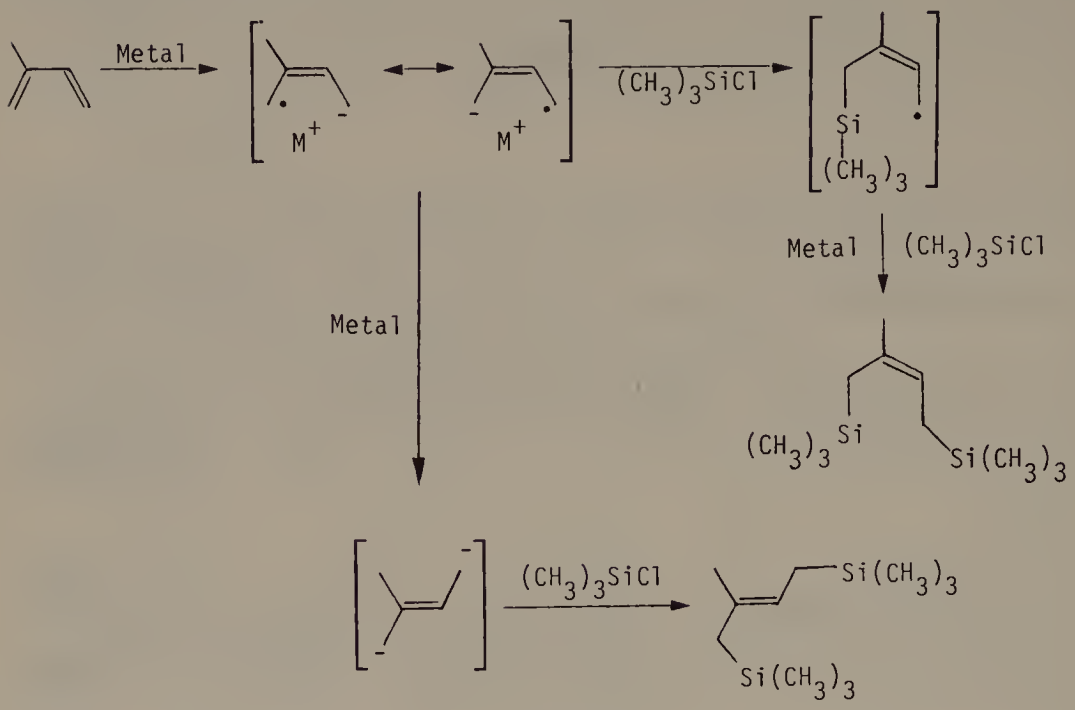
(19.30)

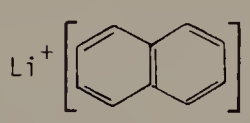


19.8 1,3-Dienes

1,3-Dienes undergo dissolving metal reductions with alkali metal and TMS-Cl in THF to yield 1,4-*bis*(trimethylsilyl)-2-butenes. The ratio of $Z:E$ products is determined by the particular alkali metal. Lithium leads predominantly to the E isomer whereas sodium or lithium naphthalide gives predominantly the Z isomer. These results have been accounted for in terms of two competing reaction pathways. An allylic anion radical prefers a cisoid conformation due to tight ion pairing and leads to Z isomer. Whereas an allylic dianion

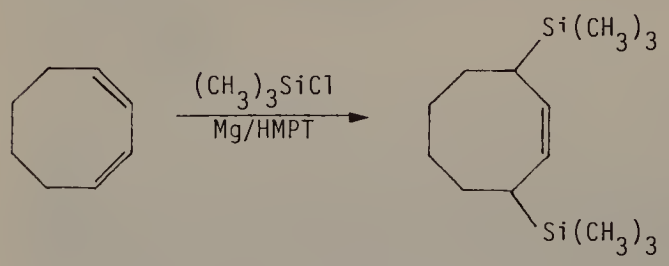
adopts a conformation to minimize repulsion between the two negative charges and gives *E* isomer [53].



	Metal	%*Z* 1,4	%*E* 1,4
Isoprene	Na	95	5
	Li	15	85
		81	19

(19.31)

Similar reduction of 1,3-dienes with B leads to both *Z* and *E* 1,4-*bis*(trimethylsilyl)-2-butenes in a 60:40 ratio [54]. Cyclic 1,3-dienes have also been reduced with B [55].

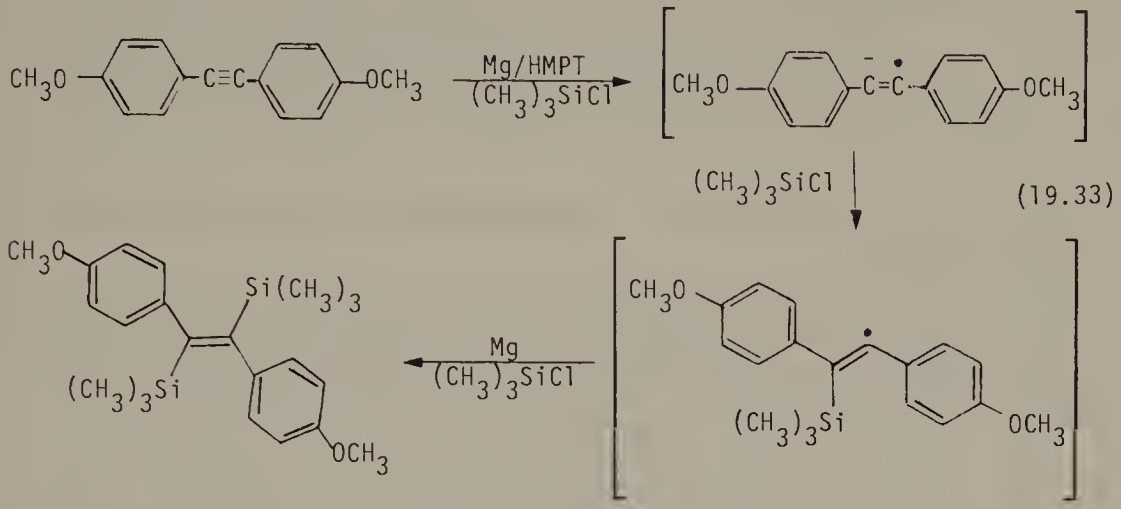


(19.32)

Dissolving metal reduction of cyclic allenes with A yields 2,3-*bis*(trimethylsilyl) cycloalkenes [56].

19.9 Acetylenes

Aryl acetylenes are reduced by B to *E*-1,2-*bis*(trimethylsilyl) alkenes. A silicon analogue of diethyl stilbesterol was prepared by treatment of *bis*(*p*-methoxyphenyl)acetylene with B [57].

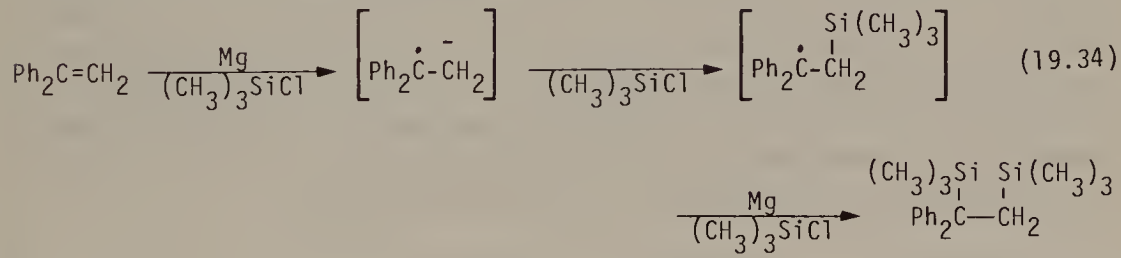


1-Phenyl-2-trimethylsilyl acetylene was reduced, in a similar manner, to yield 1-phenyl-1,2,2-*tris*(trimethylsilyl)ethylene [58].

On the other hand, treatment of aryl acetylenes with lithium in THF without TMS-Cl leads to dimerization of the initial anion radical intermediate to give 1,4-dilithio-1,3-butadienes [59].

19.10 Styrenes

Aryl substituted alkenes undergo reduction with B to yield aryl substituted 1,2-*bis*(trimethylsilyl) alkanes [60].

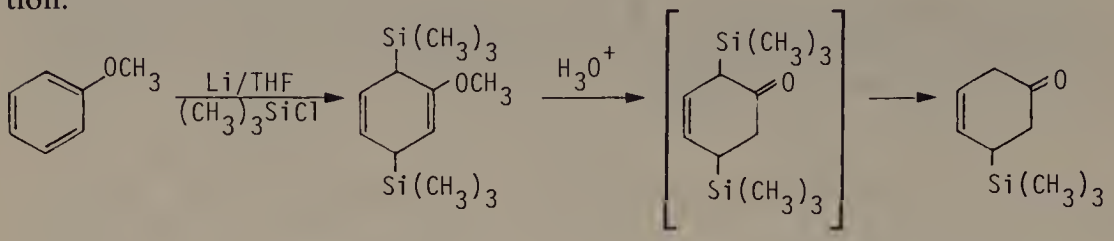


In the absence of TMS-Cl, aryl substituted alkenes undergo reductive dimerization to yield 1,4-diaryl-1,4-dilithio butanes [61].

19.11 Aromatics-Silyl Birch Reduction

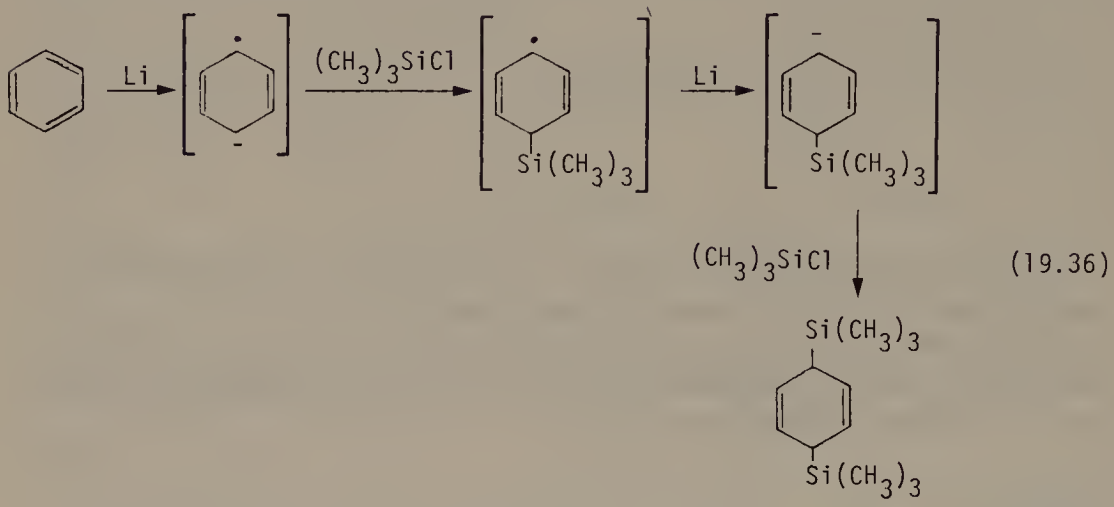
Reduction of anisole with A gives 1-methoxy-3,6-*bis*(trimethylsilyl)-1,4-cyclohexadiene. On hydrolysis, this gives 5-trimethylsilyl-cyclohex-3-enone [62, 63].

The trimethylsilyl group adjacent to a carbonyl group is easily lost under either acidic or basic conditions by processes related to enol or enolate anion formation.



(19.35)

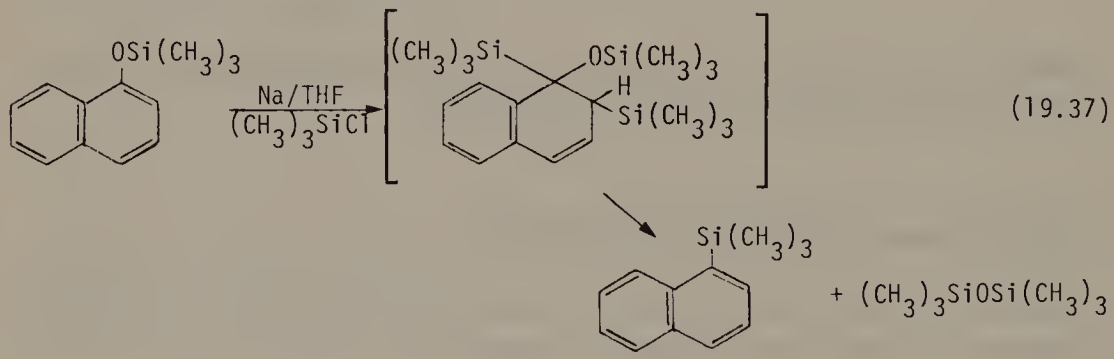
Reductions of benzene with A slowly yields 3,6-*bis*(trimethylsilyl)-1,4-cyclohexadiene [64].



(19.36)

Similar reductions of benzene [65], toluene [66], xylene isomers [66] or tetralin [67] have been reported.

Dissolving metal reduction of naphthalene with sodium and TMS-Cl occurs more rapidly to yield a mixture of 1,2-*bis*(trimethylsilyl)-1,2-dihydronaphthalene and 1,4-*bis*(trimethylsilyl)-1,4-dihydronaphthalene [68, 69]. Similar reduction of 1-trimethylsilyloxynaphthalene and 2-trimethylsilyloxynaphthalene yields 1-trimethylsilylnaphthalene and 2-trimethylsilylnaphthalene, respectively. The formation of 1-trimethylsilylnaphthalene may involve 1,2-*bis*(trimethylsilyl)-1-trimethylsilyloxy-1,2-dihydronaphthalene as an intermediate which loses hexamethyldisiloxane to yield the product [70].



(19.37)

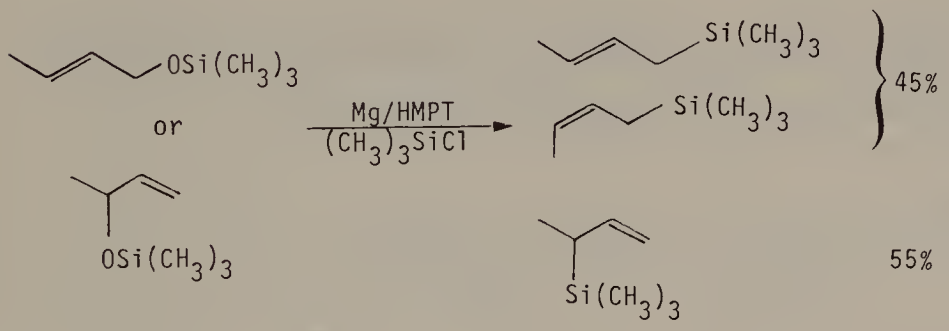
Similarly, 1,5-*bis*(trimethylsilyl)naphthalene has been prepared by reduction of 1,5-*bis*(trimethylsilyloxy)naphthalene [71].

Treatment of acenaphthylene with B gives 1,2-dihydro-1,2-*bis*(trimethylsilyl)acenaphthylene [72]. Oxidation of this with DDQ yields 1-trimethylsilylacenaphthylene. While treatment of this compound with *n*-butyl lithium/TMEDA yields a dianion which can be oxidized with cadmium chloride [73, 74] to give 1,2-*bis*(trimethylsilyl)acenaphthylene (see 8.11).

Dissolving metal reduction of aryl nitriles with B appears to involve simultaneous reduction of the nitrile and the aromatic system [15, 76].

19.12 Allylic and Benzylic Ethers

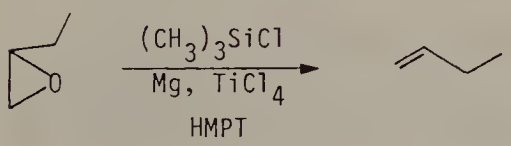
Benzylic and allylic trimethylsilyl ethers undergo dissolving metal reduction with B or sodium, TMS-Cl/toluene to yield benzylic or allylic trimethylsilanes. With B, transition metal salt ($TiCl_4$, $FeCl_3$) catalysis may be necessary. Allylic trimethylsilyl ethers are also reduced by A to allylic trimethylsilanes. Reductive silylation is favored by $TiCl_4$ or dicyclopentadienyl titanium dichloride catalysis. The reaction probably occurs by initial electron transfer to the benzylic or allylic trimethylsilyl ether resulting in scission of a C–O bond to yield a benzylic or ailylic radical and a trimethylsilanoate anion. Trimethylsilanoate anions react with TMS-Cl to yield hexamethyldisiloxane. Subsequent electron transfer to the benzylic or allylic radical yields the corresponding anion which reacts with TMS-Cl to yield product. Consistent with this mechanism, both α- or γ-methylallyl trimethylsilyl ethers yield similar mixtures of *E*- and *Z*-γ-methylallyltrimethylsilanes and α-methylallyltrimethylsilane [77–81].



(19.38)

19.13 Epoxides

Epoxides undergo deoxygenation on treatment with B to yield alkenes [82].

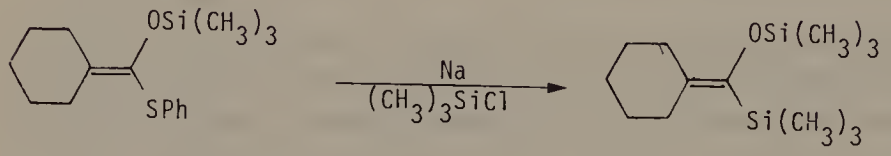


(19.39)

Styrene oxide yields 1-phenyl-1,2-*bis*(trimethylsilyl)ethane under these conditions. This product may result from initial deoxygenation to styrene which then is further reduced [60].

19.14 Carbon-Sulfur Bonds

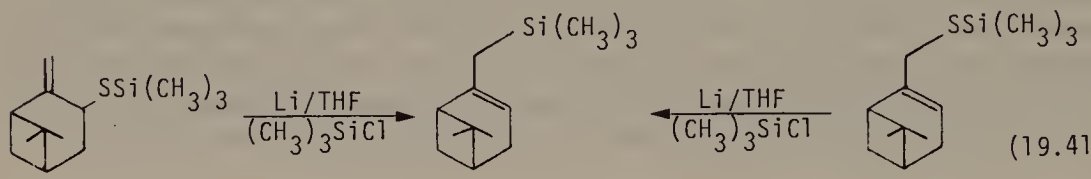
Scission of C–S bonds under dissolving metal reduction conditions is well-known. α-Phenylthio trimethylsilyl enol ethers undergo dissolving metal reduction with sodium and TMS-Cl in benzene to yield α-trimethylsilyl trimethylsilyl enol ethers [83].



(19.40)

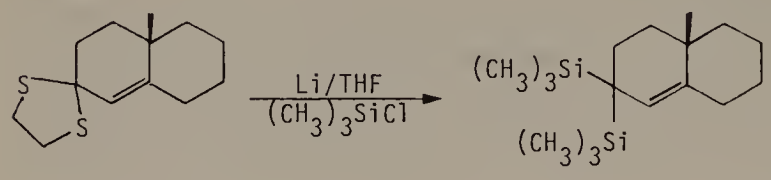
These undergo facile hydrolysis to acyltrimethylsilanes.

Allylic trimethylsilyl sulfides undergo reductive silylation on treatment with A to yield allylic trimethylsilanes [84, 85].

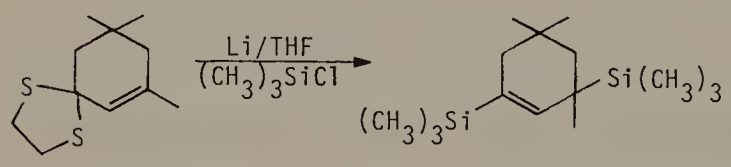


(19.41)

α,β-Unsaturated ethylene thioacetals or ketals undergo reductive silylation to yield mixtures of 3,3-*bis*(trimethylsilyl)-1-alkenes and 1,3-*bis*(trimethylsilyl) alkenes [86]. In certain cases selectivity is observed.

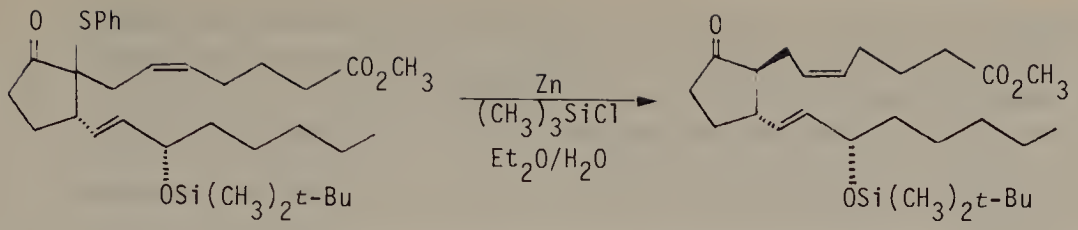


(19.42)



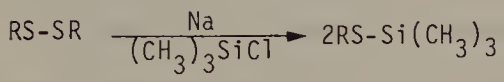
(19.43)

The combination of TMS-Cl and zinc in *moist* ether has been used to remove α-phenylthio groups from ketones. Apparently the phenylthio group is more easily reduced than the ketone carbonyl under these conditions [87].



(19.44)

Reduction of disulfides with sodium in the presence of TMS-Cl yields alkylthiotrimethylsilanes [88].



(19.45)

19.15 α-Nitroalkenes and Oximes

Steroidal nitroalkenes and oximes are converted to the corresponding ketones by reaction with zinc and TMS-Cl in ether [89].

References

1. Benkeser, R.A., Robinson, R.E., Sauve, D.M., Thomas, O.H.: J. Am. Chem. Soc. *77*, 3230 (1955)
2. Benkeser, R.A., Burrous, M.L., Hazdra, J.J., Kaiser, E.M.: J. Org. Chem. *28*, 1094 (1963)
3. Benkeser, R.A., Agnihotri, R.K., Burrous, M.L., Kaiser, E.M., Mallan, J.M., Ryan, P.W.: J. Org. Chem. *29*, 1313 (1964)
4. House, H.O., Modern Synthetic Reactions, 2nd Edition, Benjamin, W.A., Inc. 1972, p. 145–227.
5. Calas, R., Dunoguès, J., Duffaut, N., Biran, C.: C. R. Acad. Sci. *C, 267,* 494 (1968)
6. Calas, R., Dunoguès, J., Pillot, J.P., Biran, C., Duffaut, N.: J. Organometal. Chem. *25,* 43 (1970)
7. Calas, R., Biran, C., Dunoguès, J., Duffaut, N.: C. R. Acad. Sci. *C, 269,* 412 (1969)
8. Calas, R., Duffaut, N., Biran, C., Bourgeois, P., Pisciotti, F., Dunoguès, J.: C. R. Acad. Sci. *C, 267,* 322 (1968)
9. Chan, T.H., Vinokur, E.: Tetrahedron Lett. 75 (1972)
10. Dunoguès, J., Jousseaume, E., Pillot, J.P., Calas, R.: J. Organometal. Chem. *52,* C11 (1973)
11. Dunoguès, J., Calas, R., Duffaut, N., Lapouyade, P.: J. Organometal. Chem. *49,* C9 (1973)
12. Dunoguès, J., Ekouya, A., Calas, R., Duffaut, N.: J. Organometal. Chem. *87,* 151 (1975)
13. Picard, J.P., Ekouya, A., Dunoguès, J., Duffaut, N., Calas, R.: J. Organometal. Chem. *93,* 51 (1972)
14. Ekouya, A., Dunoguès, J., Duffaut, N., Calas, R.: J. Organometal. Chem. *142,* C35 (1977)
15. Motherwell, W.B.: J. Chem. Soc. Chem. Commun. 935 (1973)
16. Hodge, P., Khan, M.N.: J. Chem. Soc. Perkin, *1,* 809 (1975)

17. Smith, C.L., Arnett, J., Ezike, J.: J. Chem. Soc. Chem. Commun. 653 (1980)
18. Elphimoff-Felin, I., Sanda, P.: J. Chem. Soc. Chem. Commun. 1065 (1969)
19. Ando, W., Ikeno, M.: Chem. Lett. 1255 (1980)
20. Dunoguès, J., Calas, R., Bolourtchian, M., Biran, C., Duffaut, N., Barbe, B.: J. Organometal. Chem. *57,* 55 (1973)
21. Dunoguès, J., Ekouya, A., Duffaut, N., Calas, R.: J. Organometal. Chem. *66,* C36 (1974)
22. Calas, R., Dunoguès, J., Bolourtchian, M.: J. Organometal. Chem. *26,* 195 (1971)
23. Bolourtchian, M., Saednya, A.: Bull. Chim. Soc. Fr. II 170 (1978)
24. Calas, R., Dunoguès, J.: C. R. Acad. Sci. *C, 270,* 855 (1970)
25. Calas, R., Bolourtchian, M., Dunoguès, J., Duffaut, N., Barbe, B.: J. Organometal. Chem. *34,* 269 (1972)
26. Merault, G., Picard, J.P., Bourgeois, P., Dunoguès, J., Duffaut, N.: J. Organometal. Chem. *42,* C80 (1972)
27. Merault, G., Bourgeois, P., Dunoguès, J., Duffaut, N.: J. Organometal. Chem. *76,* 17 (1974)
28. Schräpler, U., Rühlmann, K.: Chem. Ber. *97,* 1383 (1964)
29. Rühlmann, K.: Syn. 236 (1971)
30. Bloomfield, J.J.: Tetrahedron Lett. 591 (1968)
31. Rühlmann, K., Seefluth, M., Becker, M.: Chem. Ber. *100,* 3820 (1967)
32. Von Reijenden, J.W., Baardmam, F.: Tetrahedron Lett. 5181 (1972)
33. Schräpler, U., Rühlmann, K.: Chem. Ber. *96,* 2780 (1963)
34. Cookson, C.M., Whitman, H.: J. Chem. Soc. Perkin, *1,* 806 (1975)
35. Bloomfield, J.J.: Tetrahedron Lett. 587 (1968)
36. Bloomfield, J.J., Martin, R.A., Nelke, J.M.: J. Chem. Soc. Chem. Commun. 96 (1972)
37. Bloomfield, J.J., Owsley, D.C., Ainsworth, C., Robertson, R.E.: J. Org. Chem. *40,* 393 (1975)
38. Kuo, Y.N., Chen, F., Ainsworth, C., Bloomfield, J.J.: J. Chem. Soc. Chem. Commun. 136 (1971)
39. Kuwajima, I., Sato, T., Minami, N., Abe, T.: Tetrahedron Lett. 1591 (1976)
40. Kuwajima, I., Minami, N., Abe, T., Sato, T.: Bull. Chem. Soc. Japan, *51,* 2391 (1978)
41. Picard, J.P., Calas, R., Dunoguès, J., Duffaut, N.: J. Organometal Chem. *26,* 183 (1971)
42. Kuwajima, I., Atsumi, K., Azegami, I.: J. Chem. Soc. Chem. Commun. 76 (1977)
43. Picard, J.P.: J. Organometal. Chem. *34,* 279 (1972)
44. Picard, J.P., Dunoguès, J., Calas, R.: J. Organometal. Chem. *77,* 167 (1974)
45. Dunoguès, J., Ekouya, A., Calas, R., Picard, J.P., Duffaut, N.: J. Organometal. Chem. *66,* C39 (1974)
46. Picard, J.P., Ekouya, A., Dunoguès, J., Duffaut, N., Calas, R.: J. Organometal. Chem. *93,* 51 (1972)
47. Shono, T., Ohmizu, M., Kawakami, S., Sugiyama, M.: Tetrahedron Lett. 5029 (1980)
48. Bolourtchian, M., Bourgeois, P., Dunoguès, J., Duffaut, N., Calas, R.: J. Organometal. Chem. *43,* 139 (1972)
49. Dunoguès, J., Bolourtchian, M., Calas, R., Duffaut, N., Picard, J.P.: J. Organometal. Chem. *43,* 157 (1972)
50. Bolourtchian, M., Saednya, A.: Bull. Chim. Soc. Fr. II 170, (1978)
51. Bourgeois, P., Calas, R., Duffaut, N., Dunoguès, J.: J. Organometal. Chem. *32,* 79 (1971)

52. Bolourtchian, M., Calas, R., Dunoguès, J., Duffaut, N.: J. Organometal. Chem. *33*, 303 (1971)
53. Weyenberg, D.R., Toporcer, L.H., Nelson, L.E.: J. Org. Chem. *33*, 1975 (1968)
54. Dunoguès, J., Arréguy, B., Biran, C., Calas, R., Pisciotti, F.: J. Organometal. Chem. *63*, 119 (1973)
55. Dunoguès, J., Calas, R., Dedier, J., Pisciotti, F., Lapouyade, P.: J. Organometal. Chem. *25*, 51 (1970)
56. Laguerre, M., Dunoguès, J., Calas, R.: Tetrahedron Lett. 57 (1978)
57. Calas, R., Bourgeois, P.: C. R. Acad. Sci. *C, 275*, 1117 (1972)
58. Dunoguès, J., Bourgeois, P., Pillot, J.P., Merault, G., Calas, R., Lapouyade, P.: J. Organometal. Chem. *87*, 169 (1975)
59. Nakadaira, Y., Sakurai, H.: J. Organometal. Chem. *47*, 61 (1973)
60. Dunoguès, J., Calas, R., Duffaut, N., Lapouyade, P., Gerval, J.: J. Organometal. Chem. *20*, P20 (1969)
61. Weyenberg, D.R., Toporcer, L.H., Bey, A.E.: J. Org. Chem. *30*, 4096 (1965)
62. Laguerre, M., Dunoguès, J., Calas, R., Duffaut, N.: J. Organometal. Chem. *93*, C17 (1975)
63. Laguerre, M., Dunoguès, J., Duffaut, N., Calas, R.: J. Organometal. Chem. *149*, 49 (1978)
64. Weyenberg, D.R., Toporcer, L.H.: J. Am. Chem. Soc. *84*, 2843 (1960)
65. Dunoguès, J., Calas, R., Ardoin, N.: J. Organometal. Chem. *43*, 127 (1972)
66. Laguerre, M., Dunoguès, J., Calas, R., Duffaut, N.: J. Organometal. Chem. *112*, 49 (1976)
67. Calas, R., Dunoguès, J., Pillot, J.P., Ardoin, N.: J. Organometal. Chem. *73*, 211 (1974)
68. Birkofer, L., Ramadan, N.: Chem. Ber. *104*, 138 (1971)
69. Weyenberg, D.R., Toporcer, L.H.: J. Org. Chem. *30*, 943 (1965)
70. Birkofer, L., Ramadan, N.: J. Organometal. Chem. *44*, C41 (1972)
71. Birkofer, L., Ramadan, N.: J. Organometal. Chem. *92*, C41 (1975)
72. Laguerre, M., Felix, G., Dunoguès, J., Calas, R.: J. Organometal. Chem. *44*, 4275 (1979)
73. Harvey, R.G., Cho, H.: J. Am. Chem. Soc. *96*, 2434 (1974)
74. Harvey, R.C., Cho, H.: J. Org. Chem. *40*, 3097 (1976)
75. Biran, C., Calas, R., Dunoguès, J., Duffaut, N.: J. Organometal. Chem. *22*, 557 (1970)
76. Biran, C., Dédier, J., Dunoguès, J., Calas, R., Duffaut, N., Gerval, J.: J. Organometal. Chem. *35*, 263 (1972)
77. Calas, R., Dunoguès, J., Biran, C., Duffaut, N., Pisciotti, F., Lapouyade, P.: J. Organometal. Chem. 20, P22 (1969)
78. Duffaut, N., Biran, C., Dunoguès, J., Calas, R., Lapouyade, P.: J. Organometal. Chem. *24*, C51 (1970)
79. Biran, C., Duffaut, N., Dunoguès, J., Calas, R.: J. Organometal. Chem. *91*, 279 (1975)
80. Tzeng, D., Weber, W.P.: J. Org. Chem. *46*, 265 (1981)
81. Biran, C., Dunoguès, J., Calas, R., Garvel, J., Tskhorrebachvili, T.: Syn. 220 (1981)
82. Dunoguès, J., Calas, R., Duffaut, N., Picard, J.P.: J. Organometal. Chem. 26, C13 (1971)
83. Kuwajima, I., Kato, M., Sato, T.: J. Chem. Soc. Chem. Commun. 478 (1978)
84. Pillot, J.P., Déléris, G., Dunoguès, J., Calas, R.: J. Organometal. Chem. *44*, 3397 (1979)
85. Déléris, G., Kowalski, J., Dunoguès, J., Calas, R.: Tetrahedron Lett. 4211 (1977)

86. Pandy-Szekers, D., Déléris, G., Picard, J.P., Pillot, J.P., Calas, R.: Tetrahedron Lett. 4267
87. Kurozumi, S., Toru, T., Kobayashi, M., Ishimoto, S.: Syn. Commun. *7,* 427 (1977)
88. Kuwajima, I., Abe, T.: Bull. Chem. Soc. Japan, *51,* 2183 (1978)
89. Husain, M., Khan, N.H.: Syn. Commun. *11,* 185 (1981)

20 Miscellaneous Reductions

20.1 Introduction

In addition to ionic hydrogenations, dissolving metal reductions and hydrosilation reactions which we have previously considered, there are a number of reduction reactions which utilize organosilicon reagents. These have been divided into seven sections: 1) tin hydride mediated reductions, 2) reductions which utilize silyl radicals, 3) reductions with trichlorosilane (Cl_3SiH)/tertiary amines, 4) reductions of phosphine oxides, 5) reductions of sulfoxides, 6) reductions of amine oxides, and 7) reductions of α-halo ketones. The organizing principle of the first three sections is the combination of reagents used or the reactive intermediates involved. The latter four sections are concerned with reductions of specific functional groups.

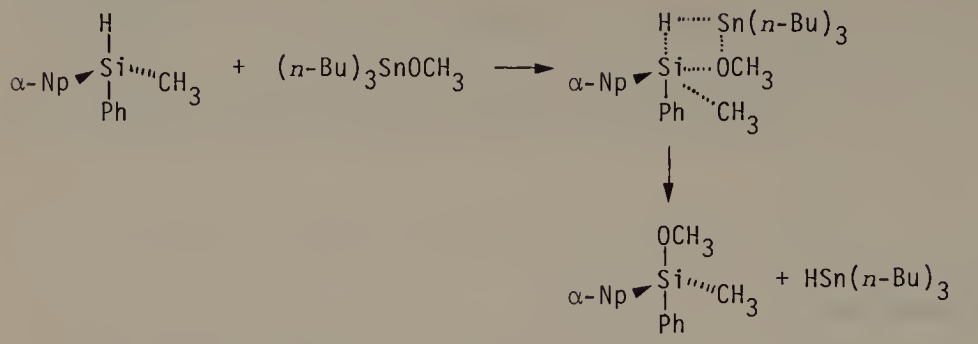
20.2 Tin-Hydride Mediated Reductions

Trialkyltin hydrides, such as tri-*n*-butyltin hydride have been utilized to carry out a number of reduction reactions [1]. Tri-*n*-butyltin hydride has been prepared by treatment of tri-*n*-butyltin chloride or *bis*(tri-*n*-butyltin) oxide with $LiAlH_4$ [2]. One of the problems is that tin hydrides are air sensitive and hence difficult to store. Polymethylsiloxane will reduce *bis*(tri-*n*-butyltin)oxide as well as polymeric di-*n*-butyltin oxide to yield tri-*n*-butyltin hydride and di-*n*-butyltin dihydride, respectively (IR: Sn–H 1814 cm^{-1}) [3]. Monomeric silanes will also reduce tri-*n*-butyltin alkoxides [4].

$$Ph_3SiH + (n\text{-}Bu)_3SnOCH_3 \longrightarrow Ph_3SiOCH_3 + (n\text{-}Bu)_3SnH \qquad (20.1)$$

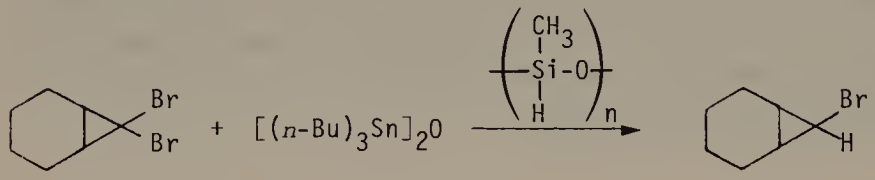
The mechanism of this reaction has been studied. Optically active α-naphthylphenylmethylsilane reacts with tri-*n*-butyltin methoxide to give tri-*n*-butyltin hydride and optically active α-naphthylphenylmethylmethoxysilane with 99% retention of configuration at the silyl center. Further, the rate of reaction depends on the concentration of both the silane and the tin alkoxide. The effect of isotopic substitution of a Si–D bond for Si–H bond on the reaction rate was determined by use of triphenylsilane-d_1 in place of triphenylsilane: $k_H/k_D = 1.64 \pm 0.08$ at 25 °C [5–8]. These facts as well as the activation parameters for the reaction: $\Delta H^{+} = 16.2$ kcal/mol

and $\Delta S^{\neq} = -32 \pm 3.6$ e.u. are consistent with a four-center S_N1-Si reaction mechanism.



(20.2)

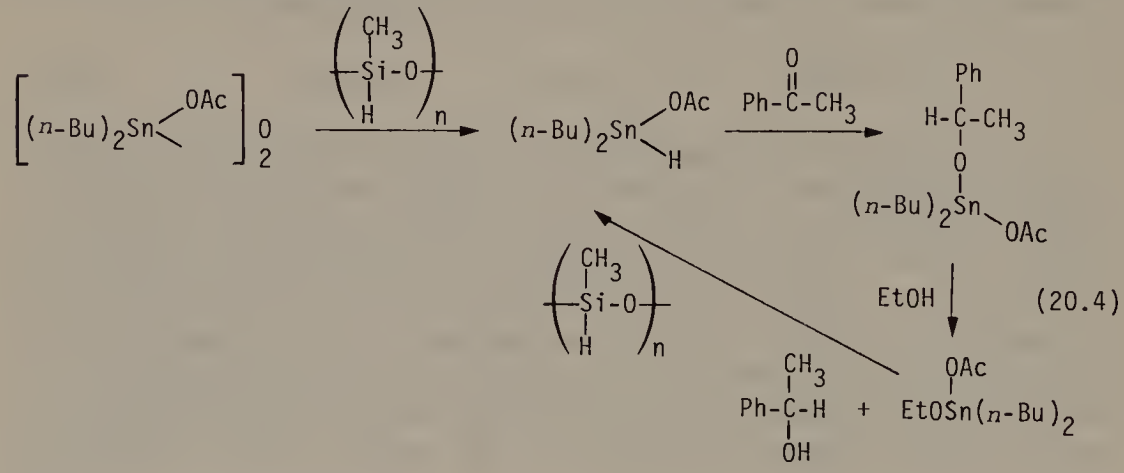
The combination of polymethylsiloxane and *bis*(tri-*n*-butyltin)oxide is effective for the reduction of alkyl or aryl bromides to the corresponding hydrocarbons. *n*-Heptyl bromide yields *n*-heptane, while *ortho*-bromotoluene gives toluene. 1,1-Dibromocyclopropanes are reduced to bromocyclopropanes [9], while 1-chloro-1-nitroethane is reduced to nitroethane [10]. These reactions can be carried out thermally or photochemically [9].



(20.3)

Polymethylsiloxane reacts with *bis*(tri-*n*-butyltin)oxide to yield tri-*n*-butyltin hydride which in turn is involved in reducing the carbon-halogen bonds.

Lipowitz and Bowman have utilized a polymethylsiloxane to generate tin hydrides by *in-situ*-reduction of tin oxides. They found that *bis*(dibutylacetoxytin)oxide was reduced in protic solvents. The tin hydride thus formed reduces ketones or aldehydes to the corresponding alcohols [11]. 4-Methylcyclohexanone was reduced to a 3:1 mixture of *cis* and *trans*-4-methylcyclohexanol [9]. Only a catalytic amount (2%) of *bis*(dibutylacetoxytin)oxide is needed since a tin alkoxide which can be reduced again by polymethylsiloxane is formed in the reaction.



(20.4)

On the other hand, nitrobenzene, benzonitrile, benzyl chloride, ethyl acetate, δ-butyrolactone, 2-ethyl hexanoic acid, and DMF were not reduced under these conditions [11].

The combination of *bis*(tri-*n*-butyltin) oxide and polymethylsiloxane reacts with propargyl sulfides to yield allenic tin compounds [12].

20.3 Silyl Radicals

Silyl radicals have often been generated by homolytic cleavage of Si–H bonds. This can be accomplished by photolysis, gamma radiation or hydrogen abstraction from silanes by alkoxy radicals such as *t*-butoxy radicals [13]. Industrially, the free radical hydrosilation of alkenes is an extremely valuable method to form C–Si bonds. The free radical catalyzed addition of Cl_3SiH to styrene is outlined below.

$$Cl_3SiH + In\cdot \longrightarrow Cl_3Si\cdot + InH$$
$$Cl_3Si\cdot + CH_2{=}CHPh \longrightarrow Cl_3SiCH_2\dot{C}HPh \qquad (20.5)$$
$$Cl_3SiCH_2\dot{C}HPh + Cl_3SiH \longrightarrow Cl_3SiCH_2CH_2Ph + Cl_3Si\cdot$$

A. Reduction of Alkyl Halides

The high affinity of silyl radicals for halogen atoms is the basis of a number of useful reduction reactions. For example, the benzoyl peroxide catalyzed reaction of triethylsilane with CCl_4 yields chloroform and triethylchlorosilane [14]. Silyl radicals abstract chlorine from sp^2 as well as sp^3 hybridized carbons. For example, triphenylsilyl radicals react with chlorobenzene to yield triphenylchlorosilane and biphenyl [15]. A detailed kinetic study of such reactions in the gas phase indicates that abstraction of chlorine from the alkyl chloride by a silyl radical is the rate limiting step [16, 17].

Considerable selectivity is observed in the reduction of alkyl halides by silyl radicals. The ease of reduction of alkyl halides: RBr > RCl > RF is consistent with increasing C–X bond energies. The order of reduction $-CCl_3 > CHCl_2 > -CH_2Cl$ results from the known stabilizing effect of chlorine atoms on carbon radical centers to which they are bonded [18].

$$ClCH_2CHCl_2 \xrightarrow[\text{benzoyl peroxide}]{Et_3SiH} ClCH_2CH_2Cl \qquad 100\% \qquad (20.6)$$

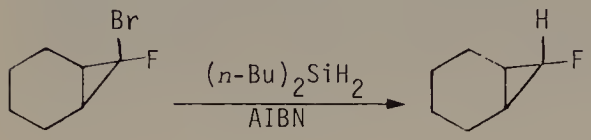
$$Cl_2HCCCl_3 \xrightarrow[\text{benzoyl peroxide}]{Et_3SiH} CHCl_2CHCl_2 + CH_2ClCCl_3$$
$$98\% : 2\% \qquad (20.7)$$

$$FCl_2CCF_2Cl \xrightarrow[\text{benzoyl peroxide}]{PhSi(CH_3)_2H} FClHCCF_2Cl \qquad 100\% \qquad (20.8)$$

$$Br(CH_2)_4Cl \xrightarrow[\text{benzoyl peroxide}]{PhSi(CH_3)_2H} CH_3(CH_2)_4Cl + CH_3(CH_2)_4Br \qquad (20.9)$$

98% : 2%

This selectivity permits the reduction of 1-bromo-1-fluorocyclopropanes to the corresponding fluorocyclopropanes. With di-*n*-butylsilane complete retention of configuration is observed.

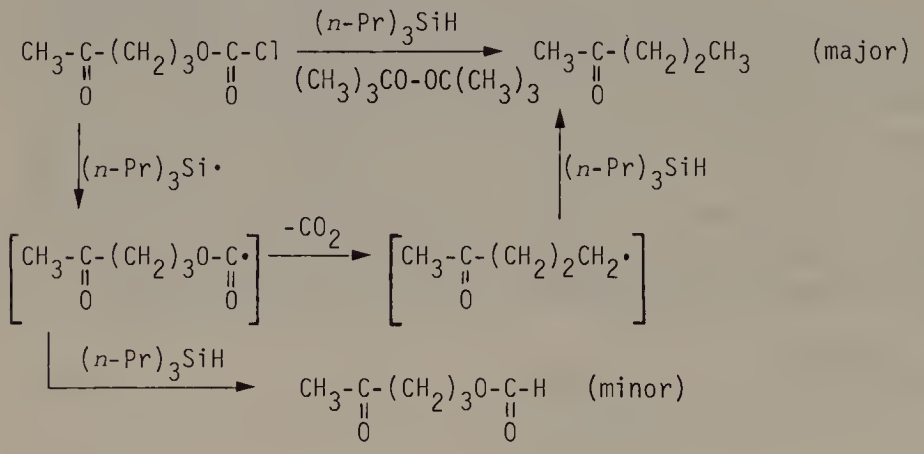


(20.10)

Apparently the rate of hydrogen abstraction from di-*n*-butylsilane is fast relative to inversion of the cyclopropyl radical [19].

B. Reduction of Chloroformates

Primary and secondary chloroformates are reduced to alkanes by reaction with tri-*n*-propylsilane and a catalytic amount of di-*t*-butyl peroxide at 140 °C. Since primary and secondary chloroformates are readily prepared by reaction of corresponding alcohols with phosgene, this reaction provides a method to reduce these alcohols to the corresponding alkanes. The reaction may occur as outlined below [20].

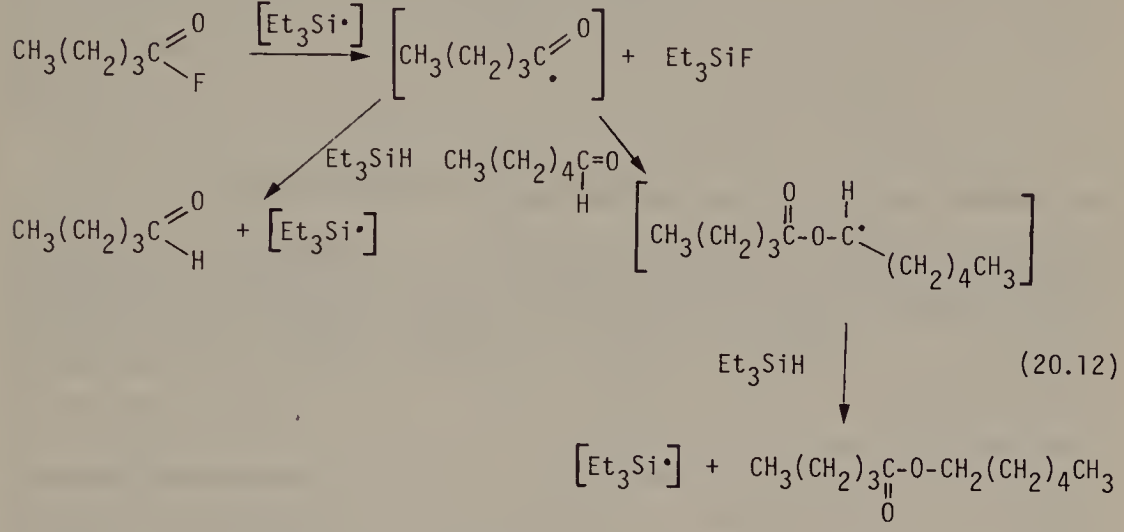


(20.11)

C. Reduction of Acyl Fluorides

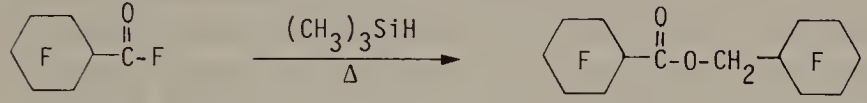
The reduction of acyl fluorides to esters with triethylsilane catalyzed by the radical initiator AIBN may result from the following sequence of reac-

tions. A triethylsilyl radical abstracts a fluorine atom from the acyl fluoride to yield triethylfluorosilane and an acyl radical. This reacts with triethylsilane to yield an aldehyde and regenerate the triethylsilyl radical. After sufficient aldehyde has been formed, the acyl radical reacts competitively with it to yield a carbon radical, which abstracts a hydrogen atom from triethylsilane to yield the ester product and regenerate the silyl radical. Consistent with this proposal, a mixture of pentanoyl fluoride and hexanal are reduced by triethylsilane to yield *n*-hexyl pentanoate [21].



(20.12)

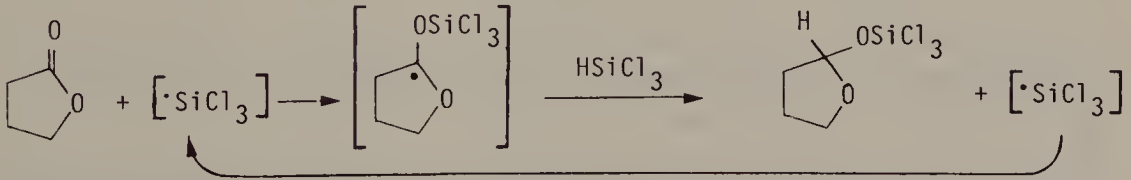
Reduction of perfluoroacyl fluorides with trimethylsilane gives 1,1-dihydroperfluoroalkyl perfluorocarboxylates [95].



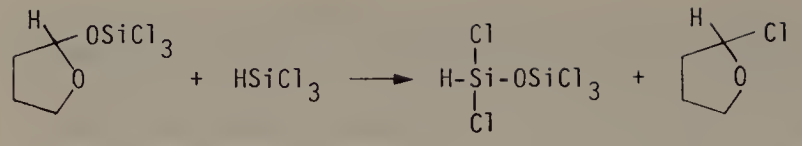
(20.13)

D. Reduction of Esters and Lactones

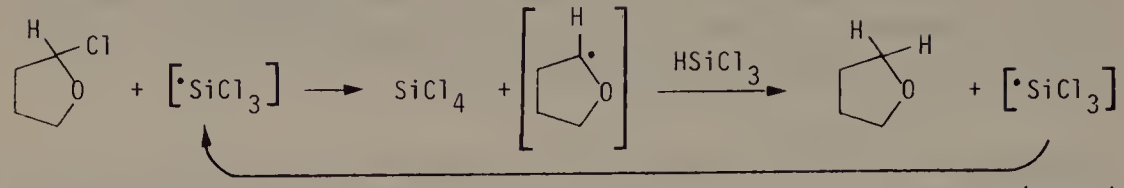
Esters and lactones are reduced to ethers by Cl_3SiH. This free radical reaction can be initiated by gamma, UV irradiation or di-*t*-butyl peroxide. The overall reaction involves two radical chain processes (Eq. 20.14 and 20.16) and a thermal exchange reaction (Eq. 20.15). Alkyl trichlorosilyl acetals undergo exchange with Cl_3SiH to yield pentachlorodisiloxane and α-chloro ethers (Eq. 20.15) [22–24].



(20.14)



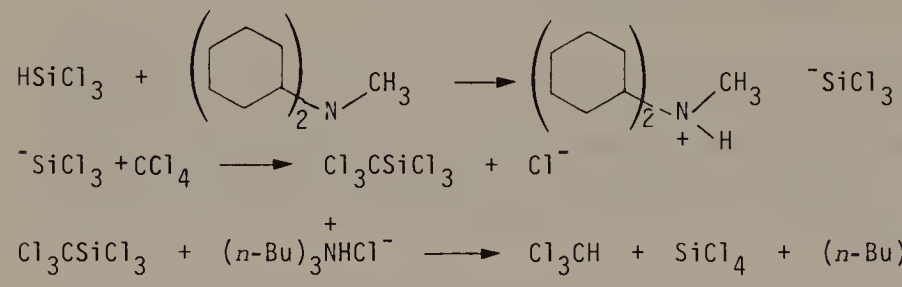
(20.15)



(20.16)

20.4 Reduction with Trichlorosilane and Tertiary Amines

Benkeser's work [25] has elucidated much of the chemistry of Cl_3SiH and tertiary aliphatic amines. Polyhalogenated alkanes are selectively reduced on treatment with Cl_3SiH in the presence of tertiary aliphatic amines, such as triethylamine. For example, CCl_4 is reduced to chloroform while methyl trichloroacetate yields methyl dichloroacetate [26]. The related reaction of *sym*-tetrachlorodimethyldisilane with CCl_4 has been reported [27]. When the reduction of CCl_4 with Cl_3SiH was carried out with dicyclohexylmethylamine, trichloromethyltrichlorosilane was obtained along with dicyclohexylmethylammonium chloride. Trichloromethyltrichlorosilane reacts with tri-*n*-butylammonium chloride to yield chloroform and tetrachlorosilane. These results led to the proposal that the reaction involves deprotonation of Cl_3SiH by the tertiary amine to form a trichlorosilyl anion/trialkylammonium cation pair. Nucleophilic attack by the trichlorosilyl anion, on CCl_4 yields trichloromethyltrichlorosilane and chloride ion. Chloride attack on the silyl center of trichloromethyltrichlorosilane yields silicon tetrachloride and a trichloromethyl anion which is protonated by the trialkylammonium ions to give chloroform and regenerate the tertiary amine.



(20.17)

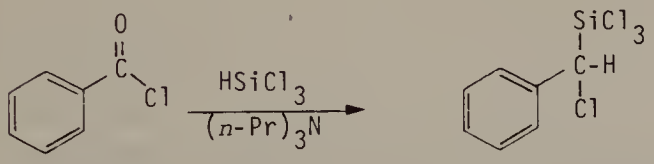
This combination of reagents reacts with benzylic chlorides to yield benzylic trichlorosilanes and trialkylammonium chlorides. Benzyl chloride gives benzyltrichlorosilane while benzal chloride gives *α,α-bis*(trichlorosilyl) toluene [28].

Tertiary amine/chlorosilane complexes are well-known [29]. Spectroscopic evidence in support of the intermediacy of the trichlorosilyl anion in these

reactions has been obtained. Thus the ^1H nmr resonance of Cl_3SiH occurs at δ 6.25 in acetonitrile. On addition of tri-*n*-propylamine, this resonance disappears, and a new resonance at δ 11.03, consistent with a N−H resonance of the tri-*n*-propylammonium cation grows in. In the presence of excess Cl_3SiH, rapid exchange between the Si−H of Cl_3SiH and the N−H of tri-*n*-propylammonium cation occurs. Consistent with the intermediacy of the trichlorosilyl anion, Cl_3SiH undergoes isotopic exchange of Si−H for Si−D in the presence of tri-*n*-propylammonium-N-d_1 chloride [30, 31].

Cl_3SiH and tertiary aliphatic amines have been utilized to reduce germanium tetrachloride to tertiary amine complexes of germanium trichloride. These exist as trichlorogermanyl anion trialkylammonium cation pairs. These react with primary alkyl halides to yield alkyltrichlorogermanium compounds. This constitutes a valuable Ge−C bond-forming reaction [32, 33].

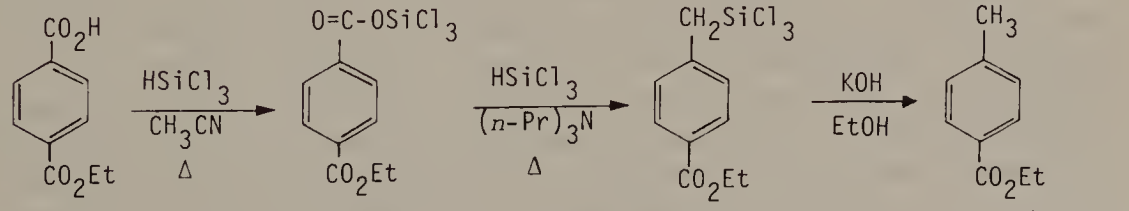
Of more general synthetic interest, aromatic ketones, aldehydes, and acid chlorides react with Cl_3SiH and aliphatic tertiary amines to yield deoxygenated products. A hydrogen and a trichlorosilyl group are bonded to the carbon in place of the double bonded oxygen of the starting material. Reaction of benzophenone with this pair of reagents yields diphenylmethyltrichlorosilane [34]. N,N-dialkyl benzamides are also reduced [35].



(20.18)

C−Si bonds of such benzylic-trichlorosilanes are readily cleaved by aq. alcoholic base [36]. Thus treatment of α-(N,N-dimethylamino)benzyltrichlorosilane with ethanolic potassium hydroxide yields N,N-dimethylbenzylamine [35].

The reduction of aromatic carboxylic acids to methyl aromatics is a general reaction. The first step involves reaction of the aromatic carboxylic acid with Cl_3SiH to yield a silyl ester. Treatment of the ester with additional Cl_3SiH and an aliphatic tertiary amine yields a benzylic trichlorosilane [37]. Finally, cleavage of the benzylic C−Si bond with base yields a methyl-substituted aromatic. This one-pot reaction sequence constitutes a unique procedure to convert aromatic carboxylic acids to methyl groups [38].



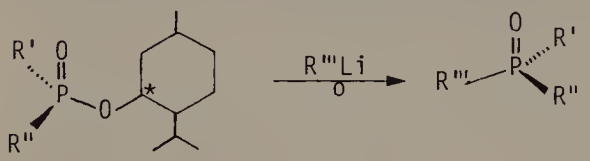
(20.19)

Consistent with this reaction sequence, alkyl benzoates are not reduced, whereas trimethylsilyl benzoates are reduced [39]. The reaction tolerates

ether, aliphatic esters, and dimethylamino functional groups [39]. A number of methyl substituted aromatic compounds have been prepared by this method: 4-methylfluorene [40], 2-fluoro-8-methylnaphthalene [41], 1-fluoro-5-methylnaphthalene [42], and 2-methylnaphtho [1,2,b] thiophene [43].

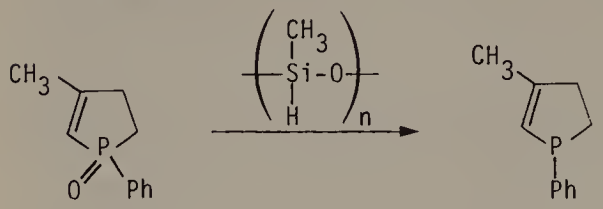
20.5 Reduction of Phosphine Oxides

Optically active tertiary phosphines are important not only for mechanistic studies but also as chiral ligands for catalytic asymmetric reactions. Optically active tertiary phosphine oxides can be prepared by reaction of Grignard or organolithium reagents with optically active dialkyl menthyl phosphinates [44]. The critical step in the preparation of chiral tertiary phosphines is the stereospecific reduction of the corresponding chiral tertiary phosphine oxides. Several silicon reagents are effective for the reduction of tertiary phosphine oxides to tertiary phosphines. By the appropriate choice of silane these reductions can be carried out stereoselectively either with retention or inversion of configuration at phosphorous.



(20.20)

Fritzsche showed that a variety of triaryl phosphine oxides, trialkyl phosphine oxides, and cyclic phosphine oxides could be reduced to the corresponding tertiary phosphines by treatment with polymethylsiloxane or phenylsilane [45].

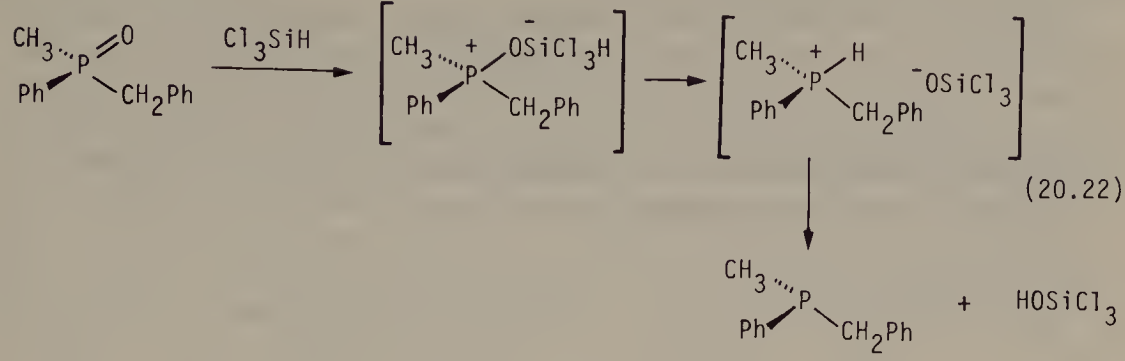


(20.21)

A. Trichlorosilane-tertiary amines/hexachlorodisilane

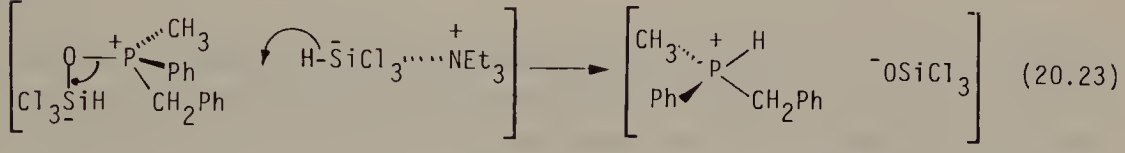
The combination of Cl_3SiH and triethylamine reduces optically active acyclic tertiary phosphine oxides to the corresponding tertiary phosphines with net inversion of configuration. On the other hand, Cl_3SiH and pyridine or N,N-dimethylaniline reduces optically active tertiary phosphine oxides to tertiary phosphines with net retention of configuration [46]. These results were explained in terms of initial coordination of the Cl_3SiH to the oxygen of the phosphine oxide to yield a 1,3-zwitterionic species. In the presence of weak bases such as pyridine, this zwitterion undergoes an intramolecular transfer of hydride from silicon to the phosphonium center with simultaneous scission of the P–O bond to yield a trichlorosilyloxy anion/tertiary phosphonium cation

pair. Proton transfer from the phosphonium cation to the silyloxy anion is the final step.



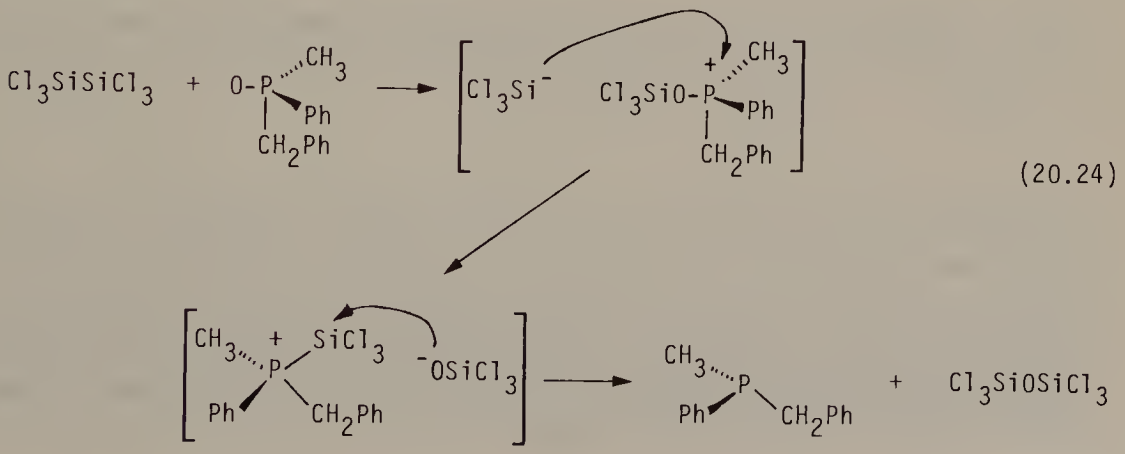
(20.22)

In the presence of triethylamine, backside attack by hydride on the initial 1,3-zwitterionic complex occurs. This causes inversion at phosphorous.



(20.23)

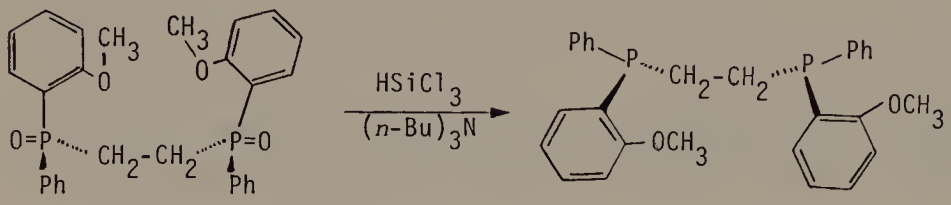
The mechanism of these reductions with Cl_3SiH was studied in detail by Mislow. He found that with strong tertiary nitrogen bases ($pK_b \leqq 5$) inversion of configuration at phosphorous occurs. Whereas with weaker tertiary amine bases ($pK_b > 7$), retention at phosphorous was observed. In the presence of triethylamine, Cl_3SiH undergoes equilibration to form perchloropolysilanes. These were proposed to be the active reducing agents [47]. In support of this proposal, Mislow found that hexachlorodisilane and octachlorotrisilane reduce chiral tertiary phosphine oxides with complete inversion of configuration. The reduction may occur by the following reaction sequence. Attack by the oxygen of the phosphine oxide on hexachlorodisilane yields a trichlorosilyl anion/trichlorosilyloxy-substituted phosphonium cation pair. Nucleophilic backside attack by the trichlorosilyl anion on the phosphonium cation leads to inversion at phosphorous and formation of trichlorosilyloxy anion/trichlorosilyl-substituted phosphonium cation. Attack by the trichlorosilyloxy anion on the silyl center yields hexachlorodisiloxane and the inverted tertiary phosphine [48].



(20.24)

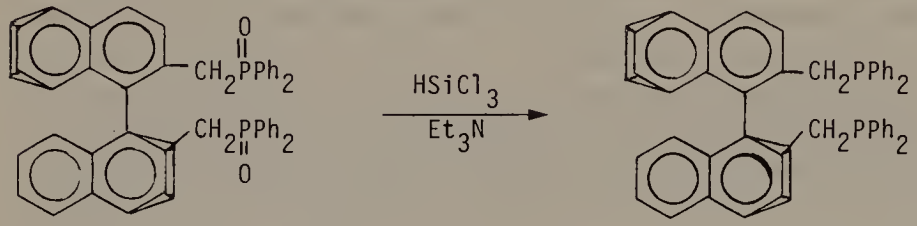
By comparison, hexachlorodisilane reduces chiral tertiary phosphine sulfides with retention of configuration [67].

Optically active *bis*(*o*-anisyl phenylphosphinyl) ethane has been reduced with Cl_3SiH and tri-*n*-butylamine in acetonitrile solvent to give the chiral *bis*-tertiary phosphine. Inversion at both asymmetric phosphorous atoms occurs during reduction [49]. This chiral ligand has been used in rhodium catalyzed asymmetric hydrogenation of α-acylamido acrylic acids. Commercially this chemistry is critical to the synthesis of L-Dopa.



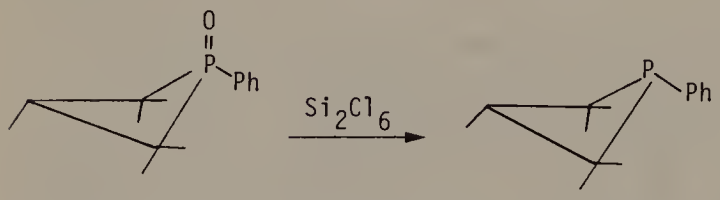
(20.25)

Optically active 2,2′*bis*(diphenylphosphinomethyl)-1,1′-binaphthyl, a chiral tertiary phosphine possessing an axial element of chirality [50] has been prepared by reduction of the corresponding *bis*-phosphine oxide with Cl_3SiH and triethylamine.



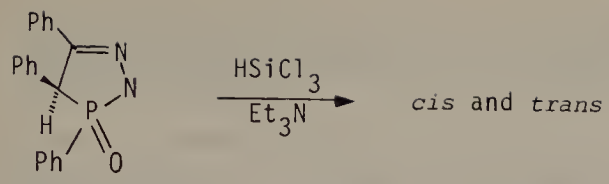
(20.26)

However, Cl_3SiH and triethylamine or hexachlorodisilane reduce four membered cyclic phosphine oxides to cyclic phosphines with retention of configuration at phosphorous. This may be consistent with Mislow's mechanistic proposals, since S_n2 displacement at phosphorous in a four membered ring is expected to be disfavored by angle strain [51, 52].



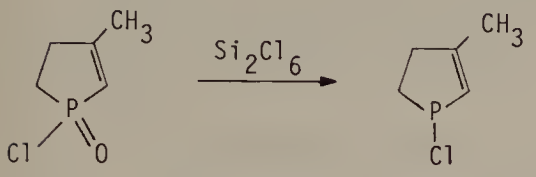
(20.27)

On the other hand, phenylphosphahomocubane oxide, a compound in which phosphorous is in five membered rings, is reduced by hexachlorosilane or Cl_3SiH and triethylamine to phenylphosphahomocubane with inversion at phosphorous [53–55]. Reduction of diazaphospholene oxide with Cl_3SiH and triethylamine is not stereospecific. This results from stereomutation of the starting material by hexachlorodisiloxane [56].



(20.28)

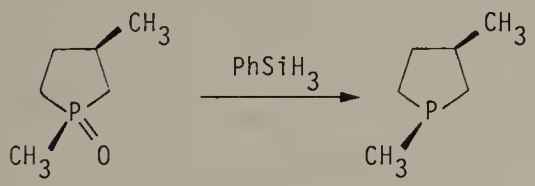
A series of macrocyclic *bis*-phosphine oxides were reduced by treatment with Cl_3SiH. *cis-bis*-Phosphine oxides were reduced to *cis-bis*-phosphines while *trans-bis*-phosphine oxides gave the corresponding *trans-bis*-phosphines [57]. Hexachlorodisilane reduces 1-halophospholene oxides to the corresponding 1-halophospholenes [58].



(20.29)

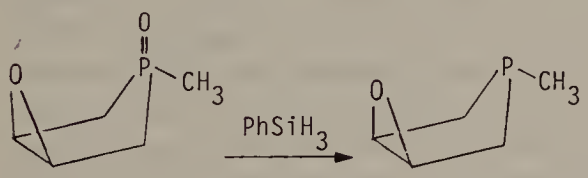
B. Phenylsilane

While hexachlorodisilane is an excellent reagent, it is rather expensive. Some racemization occurs on reduction of cyclic chiral tertiary phosphine oxides with Cl_3SiH and triethylamine. On the other hand, such cyclic chiral tertiary phosphine oxides are reduced by phenylsilane to the corresponding tertiary phosphines with complete retention of configuration [59–62]. In only one case has racemization been reported [63].



(20.30)

Phenylsilane permits the selective reduction of 3,4-epoxyphospholane oxides to the corresponding 3,4-epoxyphospholanes [64, 65].

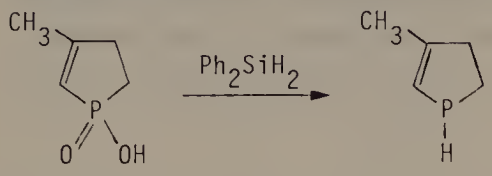


(20.31)

Despite the fact that little mechanistic work has appeared concerning reductions of tertiary phosphine oxides with phenylsilane, it is probably the reagent of choice. Phenylsilane may be prepared by treatment of phenyltrichlorosilane with $LiAlH_4$ [66]. After filtration to remove excess $LiAlH_4$, it is critical that

the ether or THF solution of phenylsilane be extracted with water prior to distillation. If this is not done, vigorous decomposition during distillation will ensue.

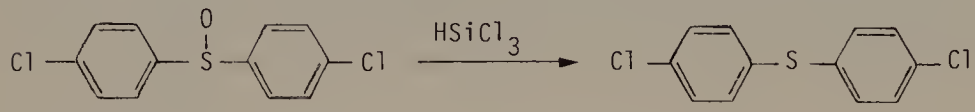
Phenylsilane, diphenylsilane, and polymethylsiloxane reduce a variety of phosphorous oxygen functional groups to P–H bonds. For example, diethyl *n*-butylphosphonate has been reduced by polymethylsiloxane to yield *n*-butylphosphine [68].



(20.32)

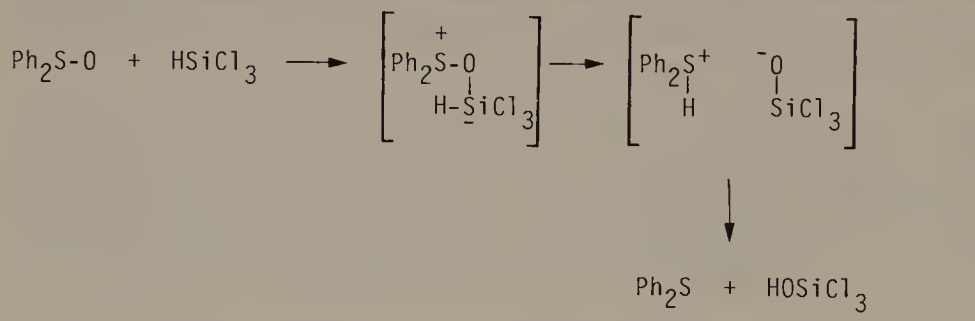
20.6 Reduction of Sulfoxides

Cl_3SiH reduces diaryl sulfoxides to the corresponding sulfides [69].



(20.33)

The mechanism of this reaction has been studied [70]. The first order dependence of the reaction rate on the concentration of both the diaryl sulfoxide and Cl_3SiH, the large negative entropy of activations ($\Delta S^{\neq} = 31$ e.u.) as well as the small isotope effects $k_H/k_D = 2.1–2.4$ are all consistent with a four-center transition state [70].

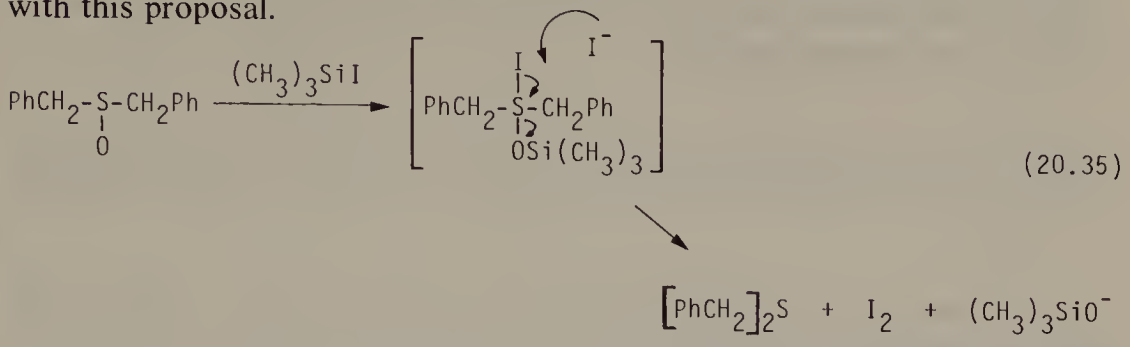


(20.34)

The reduction of dibenzyl sulfoxide with Cl_3SiH results in a mixture of dibenzyl sulfide and the benzyl mercaptal of benzaldehyde [69].

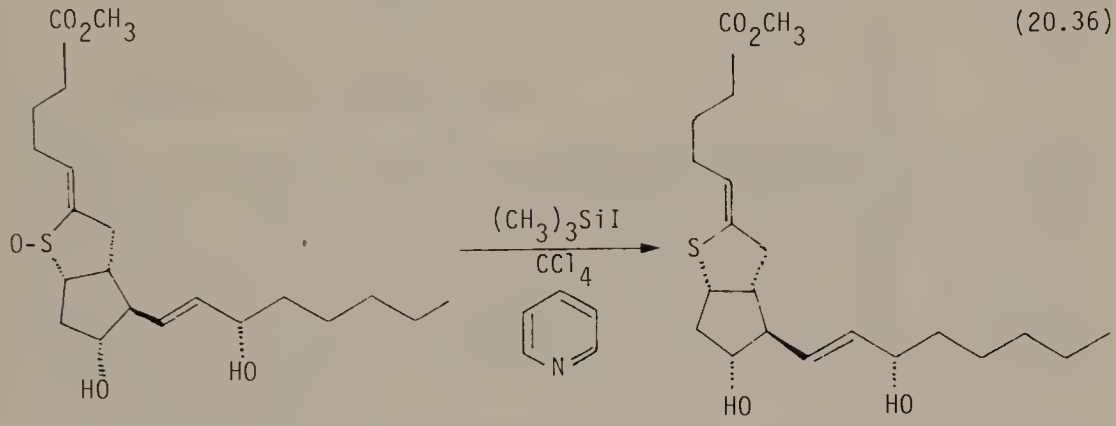
TMS-I has also proved useful for the reduction of sulfoxide to sulfides [71, 72]. Dibenzyl sulfoxide is reduced to dibenzyl sulfide in high yield. TMS-1 may be generated *in-situ* by reaction of trimethylphenylsilane [72] or hexamethyldisilane with iodine [72] or by reaction of TMS-Cl with sodium iodide in acetonitrile solvent [73]. The latter method is faster, possibly due to a combination of a favorable solvent effect and iodide ion catalysis. The following mechanism has been proposed. Nucleophilic attack by the sulfoxide oxygen on the silyl center of TMS-I leads to a dialkyl trimethylsilyloxy sulfonium cation/iodide ion pair. This may collapse to an intermediate which possess a tetra-coordinate sulfur atom (sulfurane). Iodide ion attack on the iodine

atom bonded to sulfur leads to the products. Catalysis by iodide and other soft anions such as cyanide, methyl thiolate, and thiocyanate is consistent with this proposal.



(20.35)

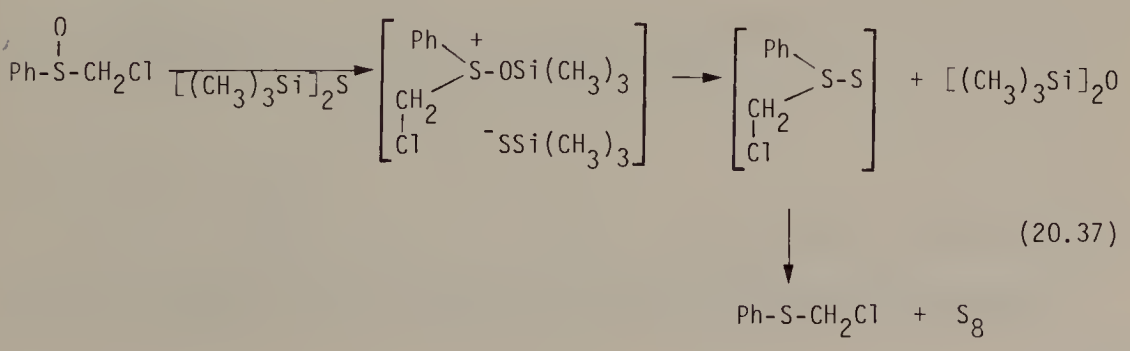
TMS-I has been utilized to reduce a sulfoxide to a sulfide in the synthesis of PGI_2 a prostacyclic analog [74].



(20.36)

TMS-Br also reduces sulfoxides to sulfides. However, with diphenyl sulfoxide ring brominated diphenyl sulfides are isolated [72]. TMS-Br generated *in-situ* by reaction of TMS-Cl with sodium bromide in acetonitrile also reduces sulfoxides to sulfides. With ethylene present as a halogen scavenger, the problem of aromatic bromination can be eliminated [75]. Diphenyldichlorosilane reacts with DMSO to yield hexaphenylcyclotrisiloxane and dimethyl sulfide. The generality of this reaction has not been explored [76]. Aliphatic and aromatic sulfoxides are readily reduced to the corresponding sulfides by TMS-Cl and zinc in THF [77].

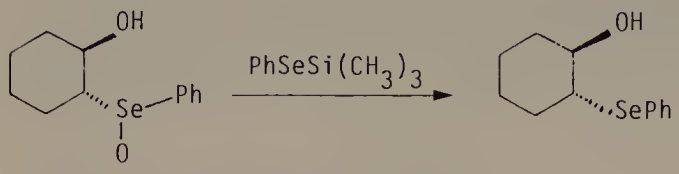
Diaryl, alkyl aryl, and dialkyl sulfoxides are reduced by disilthianes to yield sulfides, siloxanes, and elemental sulfur [78]. This reaction may occur as outlined below.



(20.37)

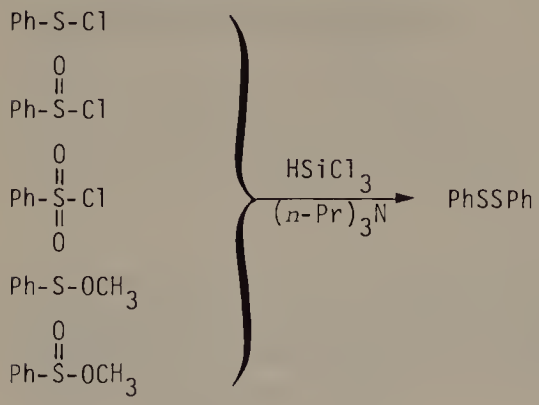
The combination of TMS-Cl and benzene thiol reduces sulfoxides to sulfides. In the process, benzene thiol is oxidized to diphenyl disulfide [79].

Phenylselenotrimethylsilane is also high effective for the reduction of sulfoxides and selenoxides [80].



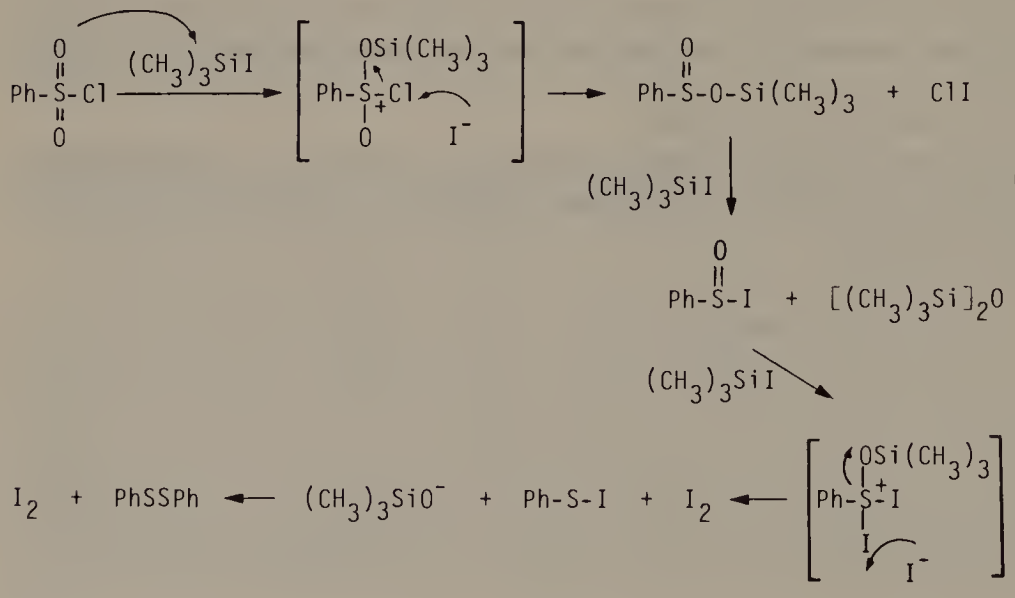
(20.38)

The combination of Cl_3SiH and tri-*n*-propyl amine reduces sulfenyl, sulfinyl, and sulfonyl chlorides as well as sulfenate and sulfinate esters to the corresponding disulfides [81].



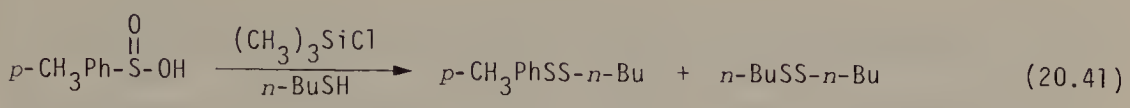
(20.39)

Trimethylsilyl iodide also reduces sulfonyl chlorides and bromides to disulfides [82]. The fact that alkyl sulfinate esters, sulfinyl chlorides and sulfenyl chlorides are reduced by TMS-I to disulfides is consistent with reaction sequence proposed.



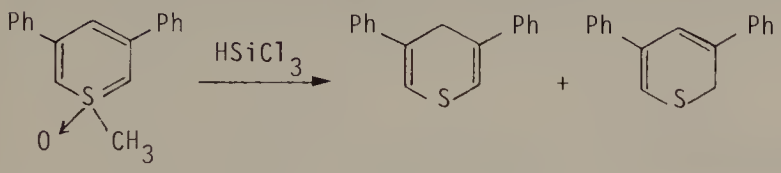
(20.40)

Sulfinic acids are also reduced to disulfides by the combination of thiols and TMS-Cl [83].



(20.41)

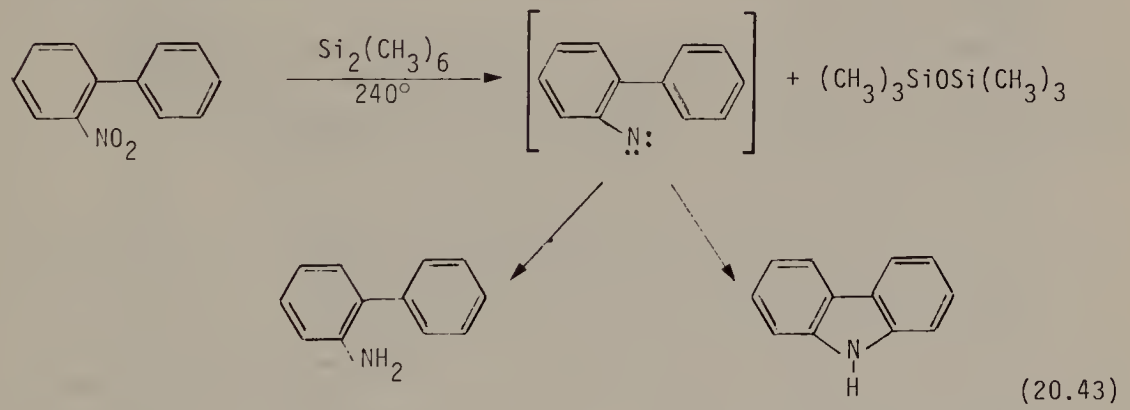
Thiabenzene-1-oxides are reduced by Cl_3SiH. 1-Methyl-3,5-diphenylthiabenzene-1-oxide gives a mixture of 2H- and 4H-3,5-diphenylthiopyrans [84].



(20.42)

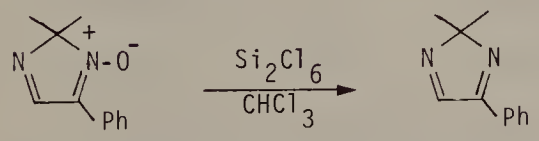
20.7 Reduction of Amine Oxides

Both the combination of Cl_3SiH and tertiary aliphatic amines, as well as, hexachlorodisilane reduce a variety of N–O bonds. Tertiary amine oxides are reduced by hexachlorodisilane to the corresponding tertiary amines [47]. The combination of Cl_3SiH and triethylamine has proved effective for reduction of nitrobenzene to aniline [32]. Thermal reaction (250 °C) of 2-nitrobiphenyl with hexamethyldisilane leads to carbazole, 2-amino biphenyl, and hexamethyldisiloxane [85]. The formation of carbazole may implicate a nitrene intermediate [86].



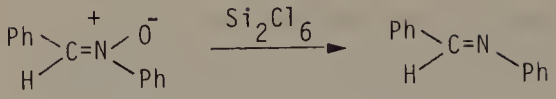
(20.43)

A number of aromatic heterocyclic N-oxides have been effectively reduced by treatment with hexachlorodisilane [87].



(20.44)

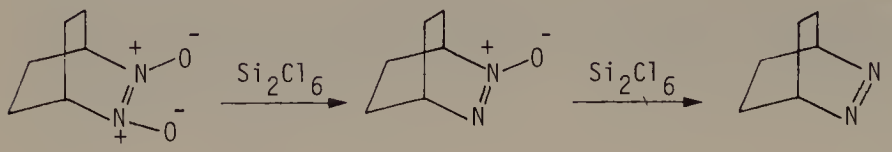
Nitrones are reduced by hexachlorodisilane to the corresponding imines.



(20.45)

Pyridine-N-oxides have been reduced by reaction with phenoxypentamethyl disilane [88].

Hexachlorodisilane reduces cyclic *cis*-azoxy compounds to corresponding azo compounds, which often spontaneously lose nitrogen under the reduction conditions [89–91]. Hexachlorodisilane also reduces cyclic *cis*-azo dioxides, C-nitroso dimers, first to the *cis*-azoxy derivatives and then to the azo compounds [90, 92].



(20.46)

20.8 Reduction of α-Halo Ketones

TMS-I reduces α-halo ketones to ketones [93, 94].

References

1. Kuivila, H.G., Advances in Organometallic Chem., *1,* 47, New York: Academic Press 1964
2. Poller, R.C.: The Chemistry of Organotin Compounds, p. 105–107, New York: Academic Press, 1970
3. Hayashi, K., Iyoda, J., Shiihara, I.: J. Organometal. Chem. *10,* 81 (1967)
4. Bellegarde, B., Pereyre, M., Valade, J.: Bull. Soc. Chem. Fr. 3082 (1967)
5. Pereyre, M., Pijselman, J.: J. Organometal. Chem. *25,* C27 (1970)
6. Pijselman, J., Pereyre, M.: J. Organometal. Chem. *63,* 139 (1973)
7. Lewis, E.S., Grinstein, R.H.: J. Am. Chem. Soc. *84,* 1158 (1962)
8. O'Ferrall, R.A.M.: J. Chem. Soc. B, 785 (1970)
9. Grady, F.L., Kuivila, H.G.: J. Org. Chem. *34,* 2014 (1969)
10. Barnes, M.W., Patterson, J.M.: J. Org. Chem. *41,* 733 (1976)
11. Lipowitz, J., Bowman, S.A.: J. Org. Chem. *38,* 162 (1973)
12. Ueno, Y., Okawara, M.: J. Am. Chem. Soc. *101,* 1893 (1979)
13. For a Review of Silyl Radicals see Davidson, I.M.T., J. Chem. Soc. Quarterly Review, *25,* 111 (1971)
14. Nagai, Y., Yamazaki, K., Shiojima, I., Kobori, N., Hayashi, N.: J. Organometal. Chem. *9,* P21 (1967)
15. Curtice, J., Gilman, H., Hammond, G.S.: J. Am. Chem. Soc. *79,* 4754 (1957)
16. Kerr, J.A., Smith, B.J.A., Trotman-Dickenson, A.F., Young, J.C.: J. Chem. Soc. Chem. Commun. 157 (1966)
17. Kerr, J.A., Smith, B.J.A., Trotman-Dickenson, A.F., Young, J.C.: J. Chem. Soc. A, 510 (1968)
18. Nagai, Y., Yamazaki, K., Shiojima, I.: J. Organometal. Chem. *9,* P25 (1967)
19. Ando, T., Hosaka, H., Funasaka, W., Yamanaka, H.: Bull. Soc. Chem. Japan, *46,* 3513 (1973)

20. Billingham, N.C., Jackson, R.A., Malek, F.: J. Chem. Soc. Chem. Commun. 344 (1977)
21. Citron, J.D.: J. Org. Chem. *36*, 2547 (1971)
22. Nakao, R., Fukumoto, T., Tsurugi, J.: J. Org. Chem. *37*, 76 (1972)
23. Nagata, Y., Dohmaru, T., Tsurugi, J.: J. Org. Chem. *38*, 795 (1973)
24. Nakao, R., Fukumoto, T., Tsurugi, J.: J. Org. Chem. *37*, 4349 (1972)
25. Benkeser, R.A.: Accts. Chem. Res. *4*, 94 (1971)
26. Benkeser, R.A., Smith, W.E.: J. Am. Chem. Soc. *90*, 5307 (1968)
27. Matsumoto, H., Ohkawa, K., Nakano, T., Nagai, Y.: Chem. Lett. 721 (1980)
28. Benkeser, R.A., Gaul, J.M., Smith,W.E.: J. Am. Chem. Soc. *91*, 3666 (1969)
29. Burg, A.B.: J. Am. Chem. Soc. *76*, 2674 (1954)
30. Benkeser, R.A., Foley, K.M., Grutzner, J.B., Smith, W.E.: J. Am. Chem. Soc. *92*, 697 (1970)
31. Bernstein, S.C.: J. Am. Chem. Soc. *92*, 699 (1970)
32. Nametkin, N.S., Kuz'min, O.V., Korolev, V.K., Kobrakov, K.I., Patriekeev, A.V.: Izv. Akad. Nauk SSSR, 676 (1978)
33. Nametkin, N.S., Kuz'min, O.V., Korolev, V.K., Kobrakov, K.I.: Dokl. Akad. Nauk. SSSR, *234*, 340 (1977)
34. Benkeser, R.A., Smith, W.E.: J. Am. Chem. Soc. *91*, 1556 (1969)
35. Benkeser, R.A., Li, G.S., Mozdzen, E.C.: J. Organometal. Chem. *178*, 21 (1979)
36. Eaborn, C., "Organosilicon Compounds", pp. 143–146, London: Buttersworth, 1960
37. Benkeser, R.A., Gaul, J.M.: J. Am. Chem. Soc. *92*, 720 (1970)
38. Benkeser, R.A., Foley, K.M., Gaul, J.M., Li, G.S.: J. Am. Chem. Soc. *92*, 3232 (1970)
39. Benkeser, R.A., Mozdzen, E.C., Muth, C.L.: J. Org. Chem. *44*, 2185 (1979)
40. Buckle, D.R., Morgan, N.J., Alexander, R.G.: J. Chem. Soc. Perkin *I*, 3004 (1979)
41. Adcock, W., Dewar, M.J.S., Golden, R., Zeb, M.A.: J. Am. Chem. Soc. *97*, 2198 (1975)
42. Adcock, W., Alste, J., Rizui, S.Q.A., Aurangzeb, M.: J. Am. Chem. Soc. *98*, 1701 (1976)
43. Clarke, K., Gregory, D.N., Scrowston, R.M.: J. Chem. Soc. Perkin *I*, 63 (1977)
44. Korpiun, O., Lewis, R.A., Chickos, J., Mislow, K.: J. Am. Chem. Soc. *90*, 4842 (1968)
45. Fritzsche, H., Hasserodt, U., Korte, F.: Chem. Ber. *97*, 1988 (1964)
46. Horner, L., Balzer, W.D.: Tetrahedron Lett. 1157 (1965)
47. Naumann, K., Zon, G., Mislow, K.: J. Am. Chem. Soc. *91*, 7012 (1969)
48. Naumann, K., Zon, G., Mislow, K.: J. Am. Chem. Soc. *91*, 2788 (1969)
49. Knowles, W.S., Sabacky, M.J., Vineyard, B.D., Weinkauff, D.J.: J. Am. Chem. Soc. *97*, 2567 (1975)
50. Tanao, K., Yamamoto, H., Matsumoto, H., Miyake, N., Hayashi, T., Kumada, M.: Tetrahedron Lett. 1389 (1977)
51. Cremer, S.E., Chorvat, R.J.: J. Org. Chem. *32*, 4066 (1967)
52. DeBruin, K.E., Zon, G., Naumann, K., Mislow, K.: J. Am. Chem. Soc. *91*, 7027 (1969)
53. Katz, T.J., Carnahan, Jr., J.C., Clarke, G.M., Acton, N.: J. Am. Chem. Soc. *92*, 734 (1970)
54. Turnblom, E.W., Katz, T.J.: J. Am. Chem. Soc. *93*, 4065 (1971)
55. Turnblom, E.W., Katz, T.J.: J. Am. Chem. Soc. *95*, 4292 (1973)
56. Baccolini, G., Todesco, P.E.: J. Org. Chem. *40*, 2318 (1975)
57. Chan, T.H., Ong, B.S.: J. Org. Chem. *39*, 1748 (1974)

58. Myers, D.K., Quin, L.D.: J. Org. Chem. *36*, 1285 (1971)
59. Marsi, K.L.: J. Am. Chem. Soc. *91*, 4724 (1969)
60. Egan, W., Chauviere, G., Mislow, K., Clark, R.T., Marsi, K.L.: J. Chem. Soc. Chem. Commun. 733 (1970)
61. Marsi, K.L.: J. Org. Chem. *39*, 265 (1974)
62. Marsi, K.L., Tuinstra, H.: J. Org. Chem. *40*, 1843 (1975)
63. Fisher, C., Mosher, H.S.: Tetrahedron Lett. 2487 (1977)
64. Symmes, Jr., C., Quin, L.D.: Tetrahedron Lett. 1853 (1976)
65. Quin, L.D., Symmes, Jr., C., Middlemas, E.D., Lawson, H.F.: J. Org. Chem. *45*, 4688 (1980)
66. Benkeser, R.A., Landesman, H., Foster, D.J.: J. Am. Chem. Soc. *74*, 648 (1952)
67. Zon, G., DeBruin, K.E., Naumann, K., Mislow, K.: J. Am. Chem. Soc. *91*, 7023 (1969)
68. Fritzsche, H., Hasserodt, U., Korte, F.: Chem. Ber. *98*, 1681 (1965)
69. Chan, T.H., Melnyk, A., Harpp, D.N.: Tetrahedron Lett. 201 (1969)
70. Chan, T.H., Melnyk, A.: J. Am. Chem. Soc. *92*, 3718 (1970)
71. Olah, G.A., Narang, S.C., Gupta, B.G.B., Malhotra, R.: Synthesis, 61 (1979)
72. Olah, G.A., Gupta, B.G.B., Narang, S.C.: Synthesis, 583 (1977)
73. Olah, G.A., Narang, S.C., Gupta, B.G.B., Malhotra, R.: Angew. Chem. Int. Ed. *18*, 612 (1979)
74. Nicolaou, K.C., Barnette, W.E., Magolda, R.L.: J. Am. Chem. Soc. *100*, 2567 (1978)
75. Schmidt, A.H., Russ, M.: Chem. Ber. *114*, 1099 (1981)
76. Goossens, J.C., Fr. Pat. 1, 456, 981 (1966), CA. *67*, 54239 (1967)
77. Schmidt, A.H., Russ, M.: Chem. Ber. *114*, 822 (1981)
78. Soysa, H.S.D., Weber, W.P.: Tetrahedron Lett. 235 (1978)
79. Numata, T., Togo, H., Oae, S.: Chem. Lett. 329 (1979)
80. Detty, M.R.: J. Org. Chem. *44*, 4528 (1979)
81. Chan, T.H., Montillier, J.P., Van Horn, W.F., Harpp, D.N.: J. Am. Chem. Soc. *92*, 7224 (1970)
82. Olah, G.A., Narang, S.C., Fields, L.D., Salem, G.F.: J. Org. Chem. *44*, 4792 (1980)
83. Oae, S., Togo, H., Numata, T., Fujimori, K.: Chem. Lett. 1193 (1980)
84. Hortmann, A.G., Harris, R.L.: J. Am. Chem. Soc. *92*, 1803 (1970)
85. Tsui, F.P., Vogel, T.M., Zon, G.: J. Org. Chem. *40*, 761 (1975)
86. Cadogan, J.I.G.: J. Chem. Soc. Quarterly, Review, *22*, 222 (1968)
87. Hortmann, A.G., Koo, J.Y., Yu, C.C.: J. Org. Chem. *43*, 2289 (1978)
88. Sakurai, H., Kira, M., Kumada, M.: Bull. Chem. Soc. Japan, *44*, 1167 (1971)
89. Snyder, J.P., Lee, L., Bandurco, V.T., Yu, C.Y., Boyd, R.J.: J. Am. Chem. Soc. *94*, 3260 (1972)
90. Snyder, J.P., Heyman, M.L., Suciu, E.N.: J. Org. Chem. *40*, 1395 (1975)
91. Olsen, H., Snyder, J.P.: J. Am. Chem. Soc. *99*, 1524 (1977)
92. Greene, F.D., Gilbert, K.E.: J. Org. Chem. *40*, 1409 (1975)
93. Olah, G.A., Arvanaghi, M., Vankar, Y.D.: J. Org. Chem. *45*, 3531 (1980)
94. Ho, T.L.: Syn. Commun. *11*, 101 (1981)
95. Croft, T.S., McBrady, J.J.: J. Org. Chem. *41*, 2256 (1976)

21 Silicon-Sulfur

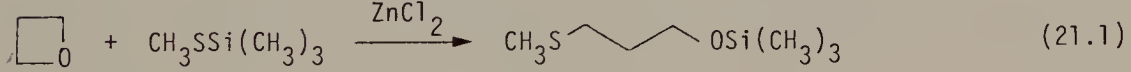
21.1 Introduction

Silicon-sulfur and selenium compounds have proved to be valuable synthetic reagents [1]. The preparation of both vinyl thio ethers [2, 3] and vinyl sulfinyl ethers [4] by the Peterson reaction has been discussed [2], as well as reductions of sulfoxides by silyl sulfide [5] and silyl selenide [6] reagents (20.6).

Methylthiotrimethylsilane may be thought of as the combination of hard acid, the trimethylsilyl group, with a soft base, the methylthio group. The relative strength of Si–S single bonds (~99 kcal/mol) [7, 8] compared to that of Si–O single bonds (~128 kcal/mol) [8] may account for the facility with which these reagents react with a variety of oxygen functional groups.

21.2 Epoxides and Oxetanes

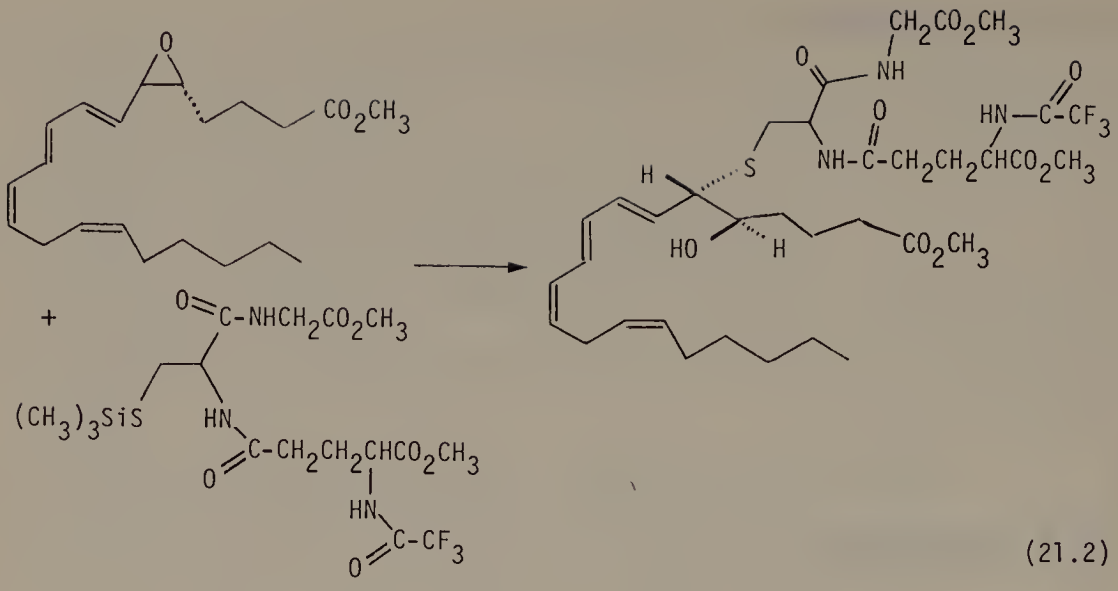
Methylthiotrimethylsilane reacts with epoxides and oxetanes under Lewis acid catalysis by zinc chloride to yield (2-methylthioethoxy)trimethylsilanes and (3-methylthiopropoxy)trimethylsilanes, respectively [9].



(21.1)

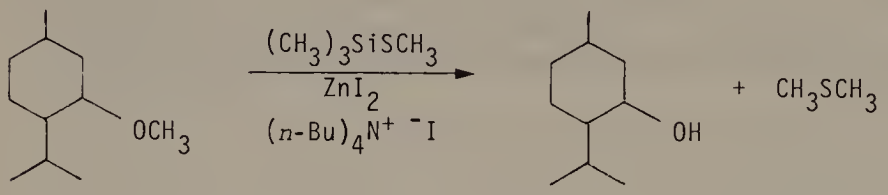
Propylene oxide reacts under these conditions to yield (1-methylthio-2-propoxy)trimethylsilane. This regiospecificity is expected if the formation of the C–S bond has the characteristic of an S_n2 nucleophilic reaction.

The regiospecific reaction of the S-trimethylsilyl derivative of glutathione with methyl-*E*-5,6-epoxy-*E,E,Z,Z*-7,9,11,14-eicosatetraenoate is a key step in the synthesis of A-leukotriene [10].



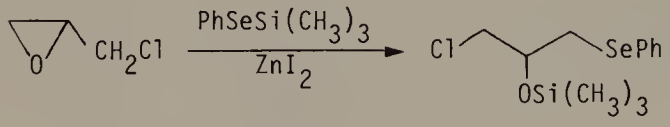
(21.2)

The combination of methylthiotrimethylsilane, zinc iodide and tetra-*n*-butylammonium iodide has proved valuable for the cleavage of methyl and benzyl ethers to yield alkoxytrimethylsilanes and dimethylsulfide or benzyl methyl sulfides, respectively [11]. Unlike TMS-I this combination of reagents results in neither competitive formation of alkyl iodides nor in cleavage of acetates or benzoates (Chapter 3).



(21.3)

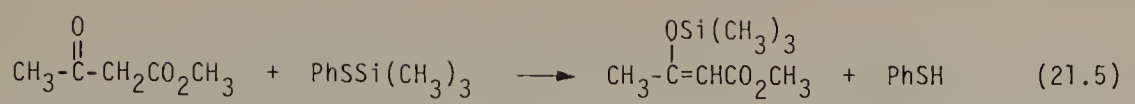
Phenylselenotrimethylsilane likewise reacts stereo- and regiospecifically with epoxides to yield *trans*-2-phenylselenoalkoxytrimethylsilanes either under Lewis acid catalysis by zinc iodide [12] or nucleophilic catalysis by potassium fluoride/18-C-6 [13].



(21.4)

21.3 Aldehydes and Ketones

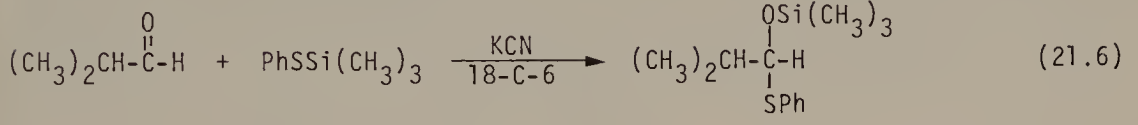
Phenylthiotrimethylsilane reacts thermally with easily enolizable ketones such as methyl acetoacetate or benzoylacetonitrile to yield trimethylsilyl enol ethers and phenylthiol [16].



(21.5)

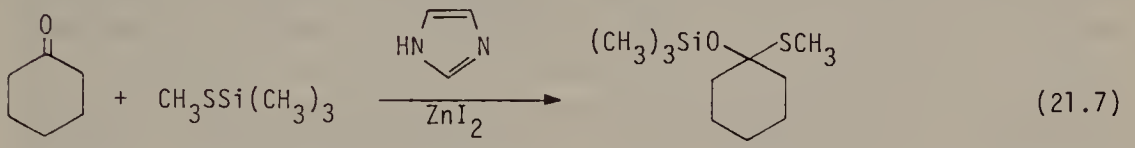
These results are related to the reaction of alkylthiotrimethylsilanes with alcohols to yield alkoxyltrimethylsilanes and thiols.

Although aldehydes undergo slow thermal reaction with methylthiotrimethylsilane, most ketones do not react. This reaction can be catalyzed by addition of Lewis acids or by anionic activation. Phenylthiotrimethylsilane or methylthiotrimethylsilane reacts readily with aldehydes in the presence of a catalytic amount of potassium cyanide/18-C-6, or tetra-*n*-butylammonium cyanide to yield O-trimethylsilyl hemithioacetals [17, 18].



(21.6)

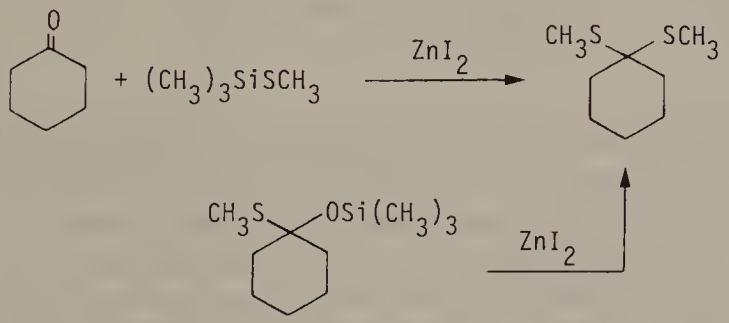
In the presence of imidazole or other weak bases and zinc iodide, methythiotrimethylsilane adds to aldehydes or ketones to yield O-trimethylsilyl hemithioacetals or ketals [18].



(21.7)

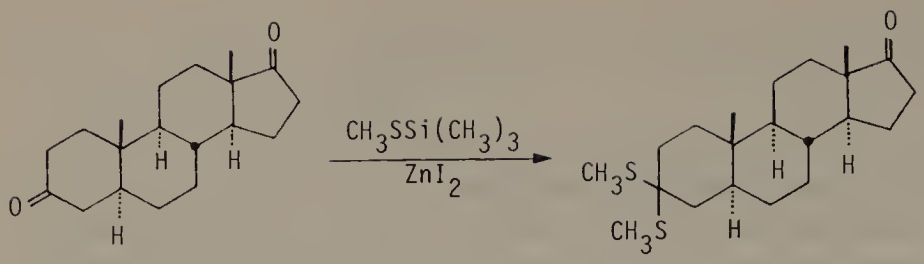
Hexafluoroacetone [14] or chloral [15] react with methylthiotrimethylsilane to yield the corresponding O-trimethylsilyl hemithioketal. No catalyst is required.

Ketones or aldehydes react with methylthiotrimethylsilane in the presence of zinc iodide to yield *bis*(methylthio) ketals or acetals directly [17, 18]. The fact that 1-trimethylsilyloxy-1-methylthiocyclohexane is converted to 1,1-*bis*(methylthio)cyclohexane on treatment with zinc iodide, supports the hypothesis that the O-trimethylsilyl hemithioketal is an intermediate in this reaction.



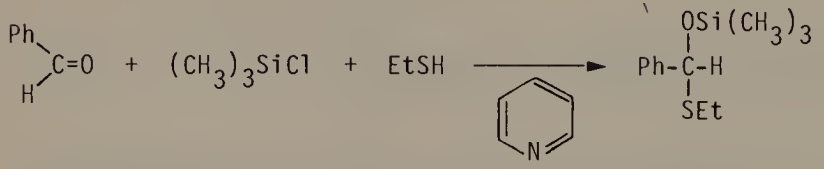
(21.8)

A high level of carbonyl differentiation is observed in these reactions. Sterically unhindered ketones are preferentially converted to thioketals [17].



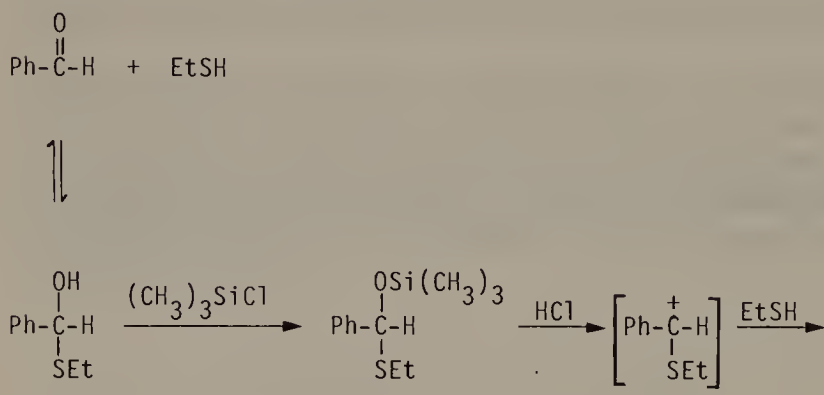
(21.9)

Prior preparation of the alkylthiotrimethylsilane is not essential. Thus addition of a thiol to a solution of an aldehyde or ketone, TMS-Cl and pyridine yields the O-trimethylsilyl hemithioketal or acetal directly [19]. The reaction apparently involves *in-situ* formation of the alkylthiotrimethylsilane [18].



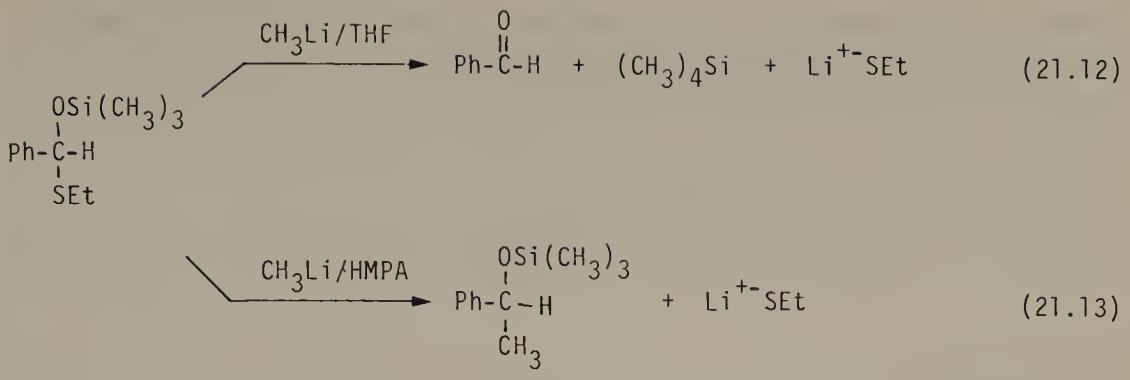
(21.10)

Similarly, reaction of thiols, benzaldehyde, hexamethyldisilazane and a catalytic amount of imidazole or potassium cyanide/18-C-6 yields the O-trimethylsilyl hemiacetals directly [20]. Aldehydes or ketones react directly with two equivalents of thiols and one equivalent of TMS-Cl to yield thioacetals or thioketals [21]. HCl generated in this reaction is critical for the conversion of the intermediate O-trimethylsilyl hemithioacetals or ketals to thioacetals or ketals. Esters, amides, and C–C double bonds are not affected by these reaction conditions.



(21.11)

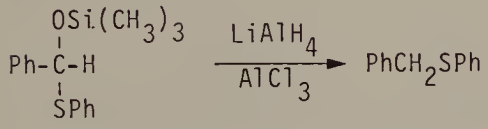
0-Trimethylsilyl hemithioketals and acetals resist hydrolysis by 5% NaOH or sodium carbonate and are stable in methanol/water, pyridine, HMPT, and other common organic solvents. They are, however, rapidly hydrolyzed to regenerate the ketone or aldehyde by dilute HCl [19]. Solvents effect the reaction of alkyl lithium reagents with 0-trimethylsilyl hemithioketals or acetals. In ether or THF alkyl lithium reagents react at the silyl center (Eq. 21.12). However, in HMPT or THF/TMEDA solvents alkyl lithium reagents react at the central carbon (Eq. 21.13).



(21.12)

(21.13)

The sensitivity of 0-trimethylsilyl hemiacetals to Lewis acids has been exploited. Reaction of 0-trimethylsilyl hemiacetals with a mixture of $LiAlH_4$/$AlCl_3$ gives sulfides [20].

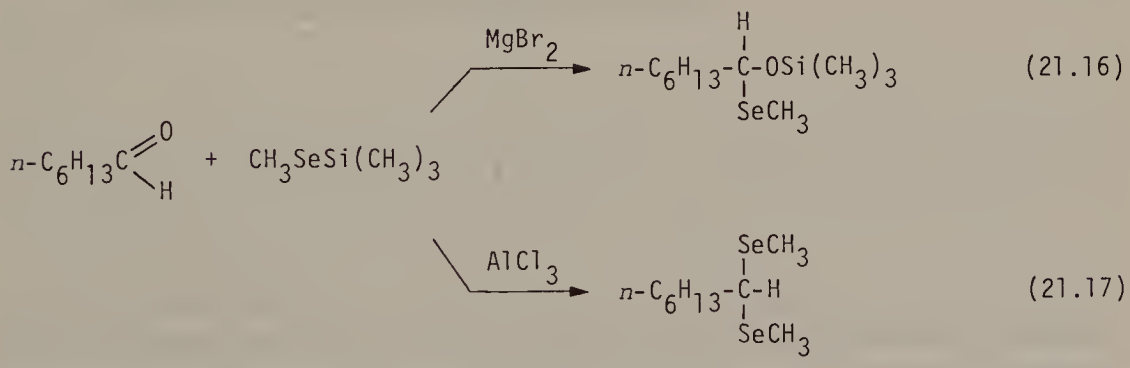


(21.14)

Alkyl or aryl trimethylsilyl sulfides react with α,β-unsaturated ketones or aldehydes in a 1,4-conjugate manner either under nucleophilic activation or electrophilic catalysis by zinc iodide [17, 18].

(21.15)

Neither methylseleno-nor phenylselenotrimethylsilane react with aldehydes at room temperature. However, in the presence of magnesium bromide, zinc chloride or zinc iodide reaction occurs to give 0-trimethylsilyl hemiselenoacetals (Eq. 21.16) [22, 23]. Use of the stronger Lewis acid, $AlCl_3$ leads to selenoacetals (Eq. 21.17). 0-Trimethylsilyl hemiselenoacetals or ketals can also be prepared directly by reaction of ketones or aldehydes with phenylselenol and TMS-Cl in pyridine [22].

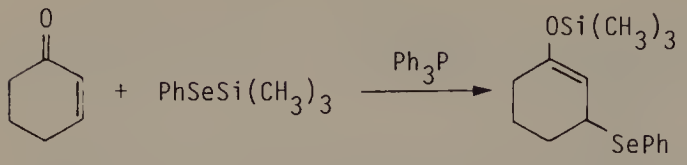


(21.16)

(21.17)

Phenylselenotrimethylsilane adds in a conjugate manner to α,β-unsaturated

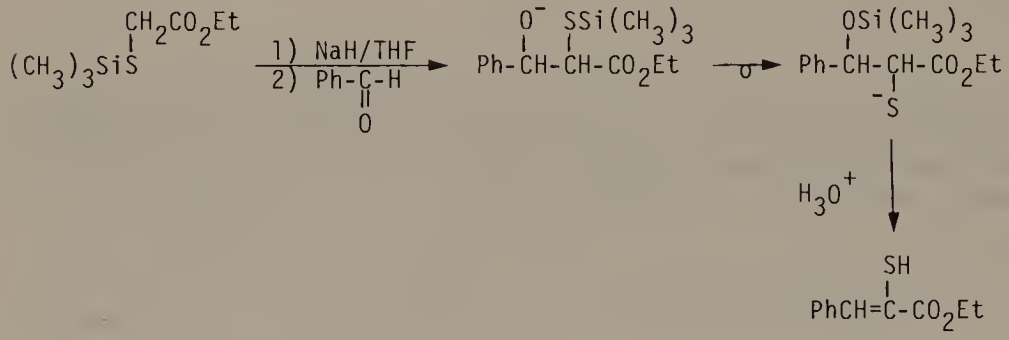
ketones or aldehydes under the catalytic influence of triphenylphosphine, zinc iodide [23] or potassium fluoride/18-C-6 [13].



(21.18)

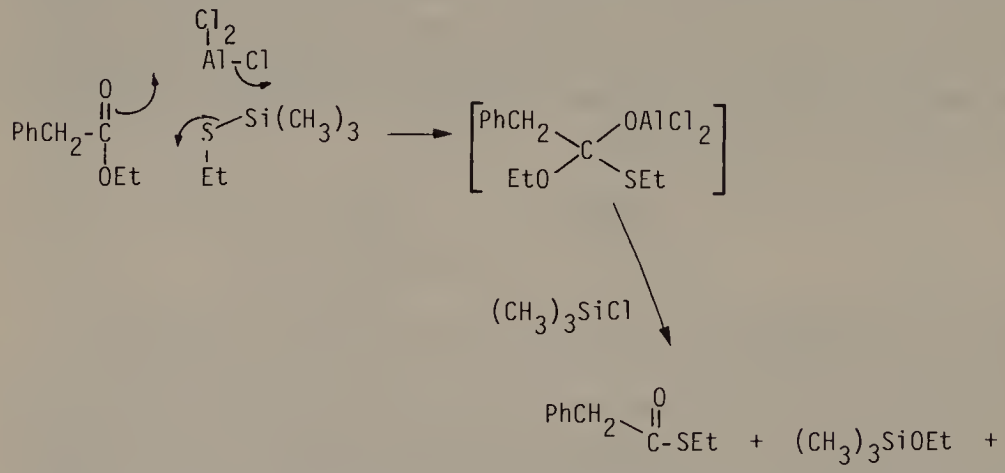
21.4 Esters

Ethyl α-mercapto cinnamates esters have been efficiently prepared by reaction of ethyl S-trimethylsilyl-thioglycolate with aromatic aldehydes and sodium hydride followed by an acidic work-up [74].



(21.19)

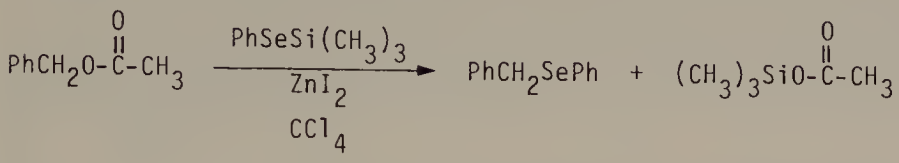
Ethylthiotrimethylsilane reacts with β-propiolactone to yield trimethylsilyl 3-ethylthiopropionate [24]. Ethylthio or phenylthiotrimethylsilane reacts with alicyclic esters under the influence of $AlCl_3$ to yield thioesters [25].



(21.20)

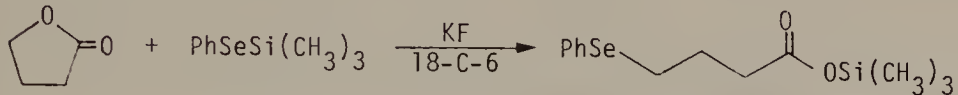
On the other hand, Breslow reports that methyl-*m*-iodobenzoate reacts with ethylthiotrimethylsilane and $AlCl_3$ to yield triethyl-*m*-iodo-*ortho*-thiobenzoate [26].

Phenylselenotrimethylsilane reacts with alkyl acetates under catalysis by zinc iodide in CCl_4 or toluene to yield alkyl phenyl selenides and acetoxytrimethylsilane. These weakly acidic reaction conditions provide a novel route to such compounds.



(21.21)

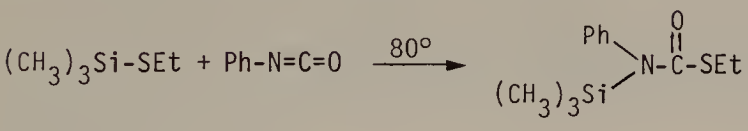
The fact that both crotyl and 1-methylallyl acetate react with phenylselenotrimethylsilane to yield crotyl phenyl selenide is suggestive of catonic intermediates [27]. δ-Butyrolactone reacts with phenylselenotrimethylsilane under catalysis by potassium fluoride/18-C-6 to yield trimethylsilyl 4-phenylselenobutyrate [13].



(21.22)

21.5 Cumulenes

Ethylthiotrimethylsilane reacts with phenyl isocyanate to yield N-phenyl-N trimethylsilyl S-ethyl thiourethane [24, 28].

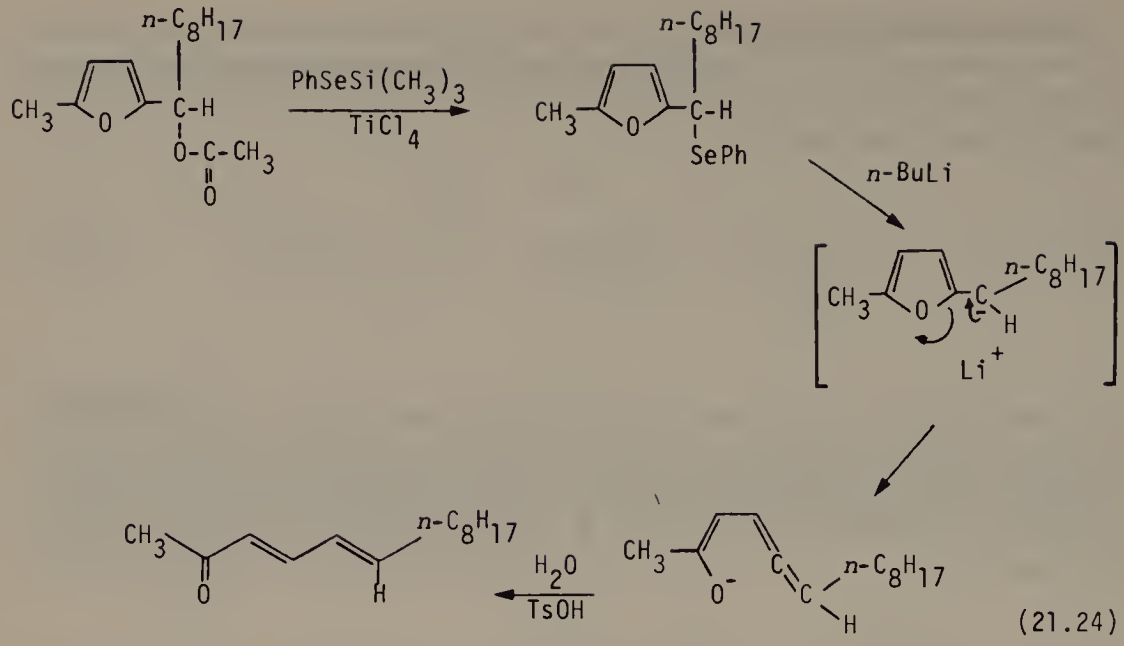


(21.23)

21.6 Allylic Acetals and Benzylic Acetates

Allylic acetals react with phenylthiotrimethylsilane or ethylthiotrimethylsilane and $AlCl_3$ to yield γ-alkoxy allyl sulfides, α,β-unsaturated thioacetals or α,β-unsaturated 0-alkyl hemithioacetals. The particular products formed are dependent on the silyl sulfide, as well as, the allylic acetal utilized [29].

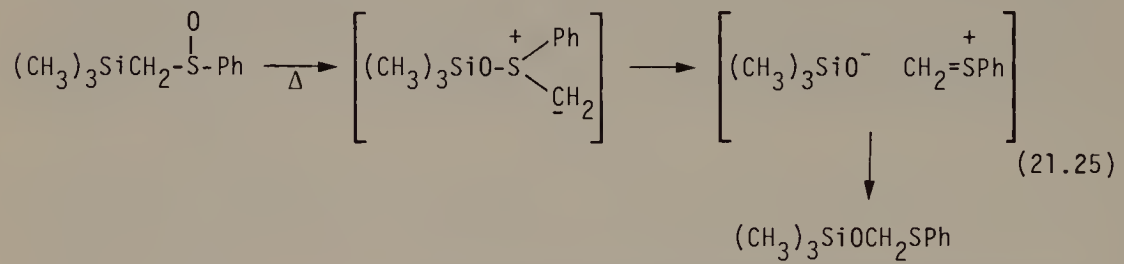
Furfuryl acetates react with phenylselenotrimethylsilane and $TiCl_4$ to yield furfuryl phenyl selenides. It seems likely that these reactions involve carbocation intermediates. Such furfuryl phenyl selenides react with *n*-butyl lithium to yield furfuryl lithium which undergoes ring opening. Acidic work-up yields *α,β,γ,δ*-dienones [30, 31] (see 6.2E).



(21.24)

21.7 Silyl-Pummerer Rearrangements

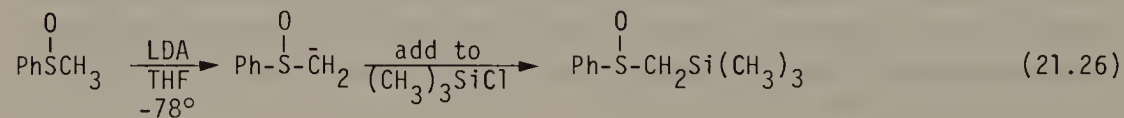
Trimethylsilylmethyl phenyl sulfoxide was shown by Brook to rearrange thermally at 60 °C to yield trimethylsilyloxymethyl phenyl sulfide. This silyl-Pummerer rearrangement may occur by migration of the trimethylsilyl group from carbon to oxygen to yield an ylid which fragments to a trimethylsilanoate/methylene phenyl sulfonium ion pair which recombine to yield the 0-trimethylsilyl hemithioacetal [32].



(21.25)

The facile acid catalyzed hydrolysis of such 0-trimethylsilyl hemithioacetals to regenerate aldehydes has been previously discussed. The silyl Pummerer rearrangement is the basis for a number of aldehyde syntheses.

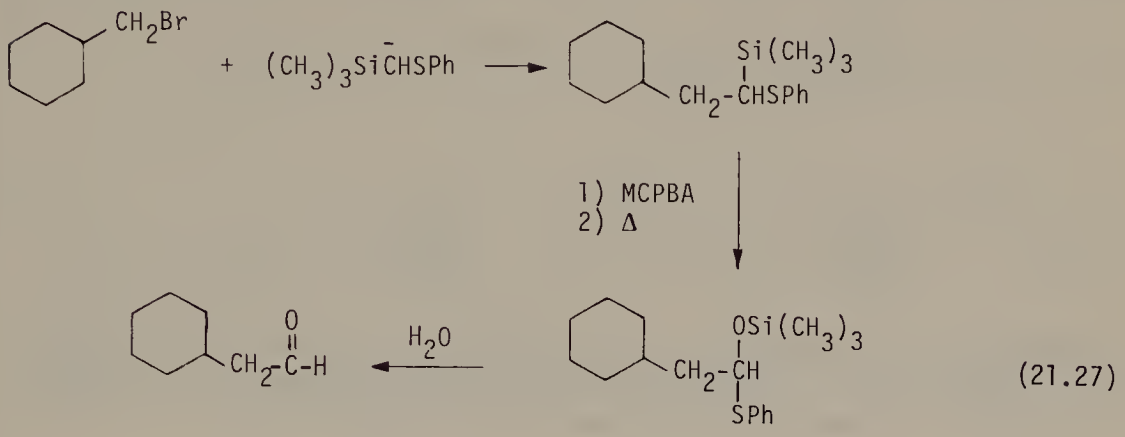
Trimethylsilylmethyl phenyl sulfoxide was initially prepared by reaction of trimethylsilylmethyl magnesium chloride with methyl benzene sulfinate [32]. Vedejas found that addition of phenylsulfinyl methyl lithium to TMS-Cl also gave trimethylsilylmethyl phenyl sulfoxide. This order of addition is critical to the success of the reaction [33].



(21.26)

A. Synthesis of Aldehydes

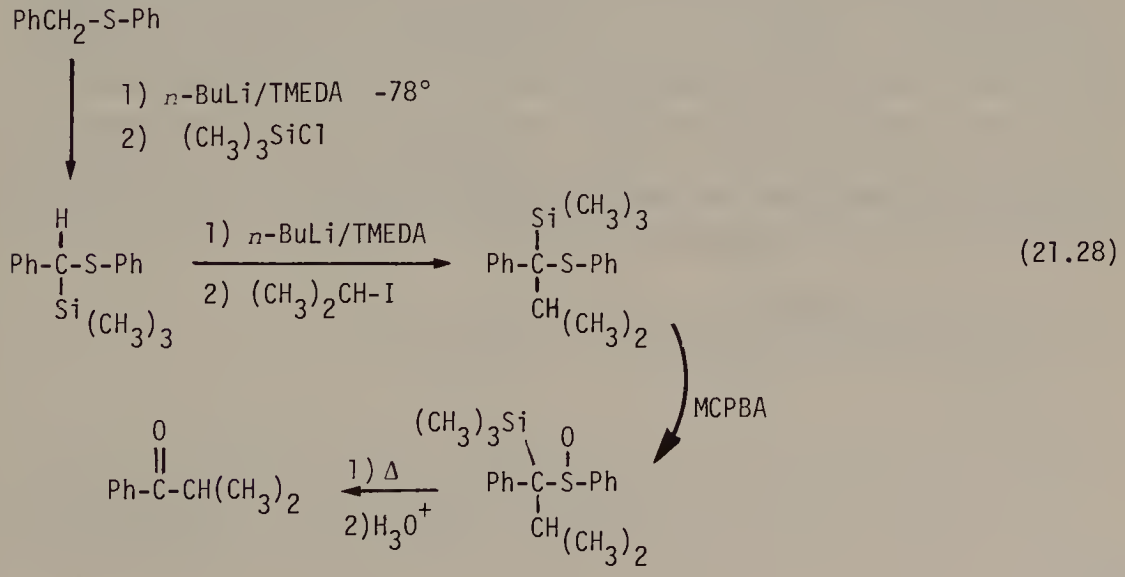
Metallation of trimethylsilylmethyl phenyl sulfide [34, 35] with *n*-butyl lithium in THF followed by alkylation with primary alkyl bromides or epoxides yields 1-phenylthioalkyltrimethylsilanes. Oxidation of the sulfide to a sulfoxide with MCPBA at −15° followed by a silyl-Pummerer rearrangement and hydrolysis of the 0-trimethylsilyl hemithioacetals gives the desired aldehydes [36, 37]. By comparison, 1,3,dithianes are often difficult to hydrolyze.



(21.27)

B. Synthesis of Ketones

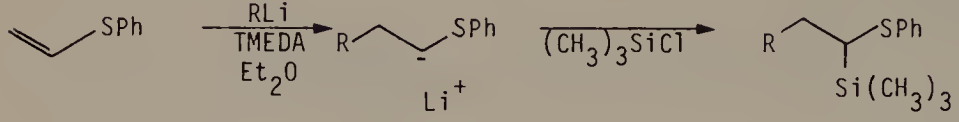
While it is possible to metallate 1-phenylthioalkyltrimethylsilanes, it has not been possible to get such anions to react with alkyl halides. Hence this methodology is not generally useful for the preparation of ketones. The preparation of alkyl phenyl ketones is an exception. Alkylation of (phenylthio)phenyl-(trimethylsilyl)methyl lithium followed by oxidation with MCPBA and silyl-Pummerer rearrangement yields 1-phenylthio-1-trimethylsilyloxy 1-phenyl-alkane which undergoes facile acid catalyzed hydrolysis to yield the alkyl phenyl ketone [38].



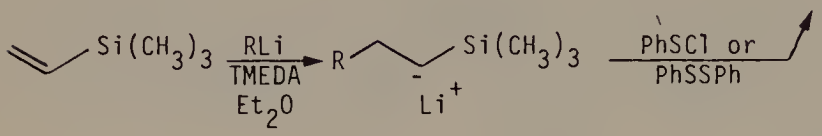
(21.28)

C. Preparation of 1-Phenylthioalkyltrimethylsilanes

Alkyl lithium reagents will add to either phenyl vinyl sulfide or vinyl trimethylsilane in ether/TMEDA to yield α-lithioalkyl phenyl sulfides or α-lithioalkyltrimethylsilanes, respectively. 1-Phenylthioalkyltrimethylsilanes result from reaction of either α-lithioalkyl phenyl sulfides with TMS-Cl (Eq. 21.29) or α-lithioalkyltrimethylsilanes with phenylsulfenyl chloride or diphenyl disulfide (Eq. 21.30) [39].

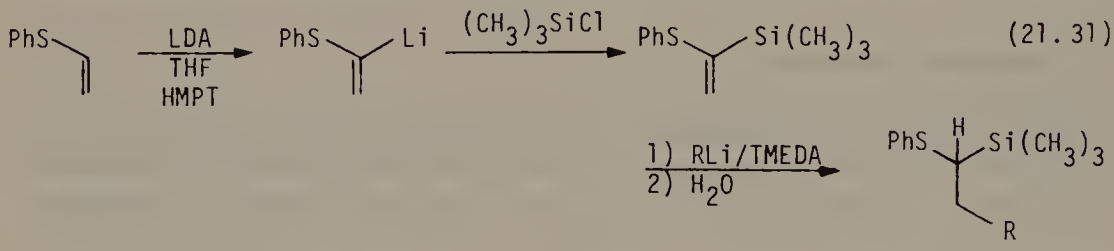


(21.29)



(21.30)

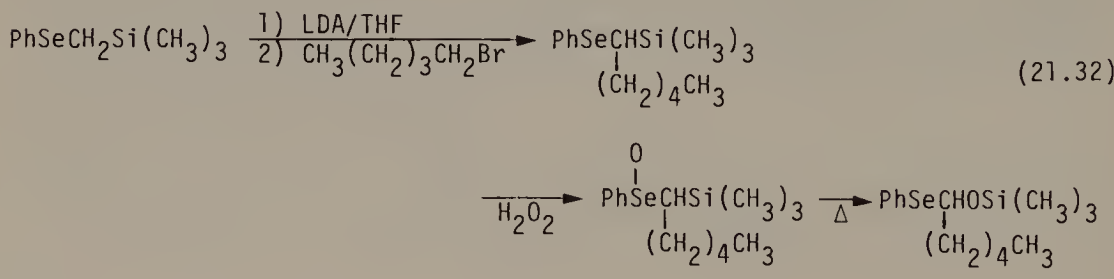
An alternative approach to 1-phenylthioalkyltrimethylsilanes utilizes phenyl vinyl sulfide [39, 41]. 1-Phenylthio-1-trimethylsilyl ethylene can be oxidized by MCPBA to 1-phenylsulfinyl-1-trimethylsilyl ethylene [40].



(21.31)

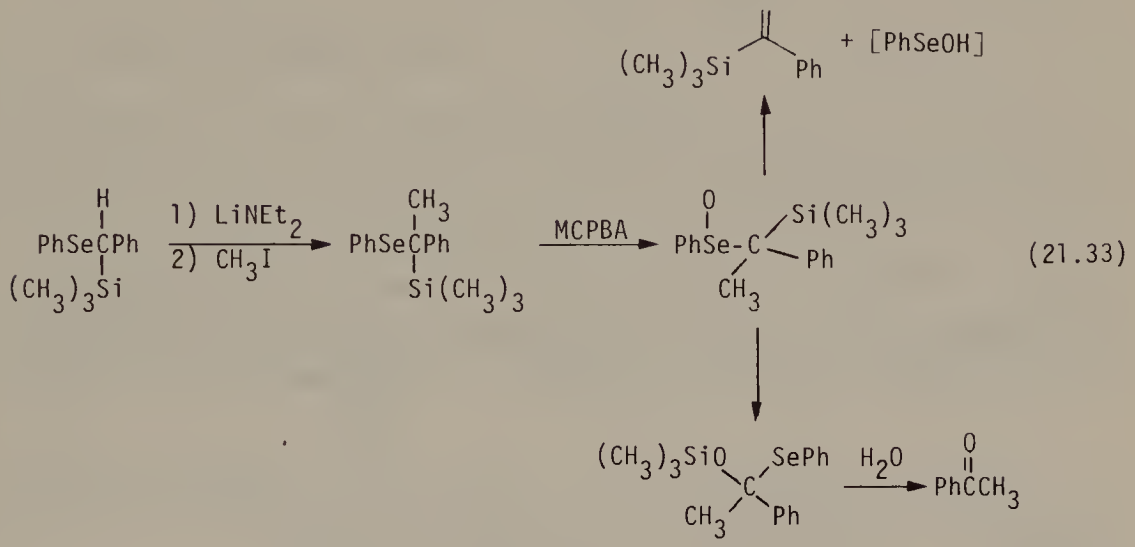
D. Synthesis of Aldehydes/Selenium-Silicon Reagents

Trimethylsilylmethyl phenyl selenide has also proved useful for the preparation of aldehydes. Metallation with LDA followed by alkylation with primary alkyl bromides or iodides yields 1-phenylselenoalkyltrimethylsilanes. Oxidation of these with 30% hydrogen peroxide gives the corresponding selenoxide which can undergo a silyl-Pummerer rearrangement to an 0-trimethylsilyl hemiselenoacetal. Hydrolysis of these compounds gives the desired aldehyde. The necessary precursor has been prepared by reaction of sodium phenyl selenide with chloromethyltrimethylsilane [42].



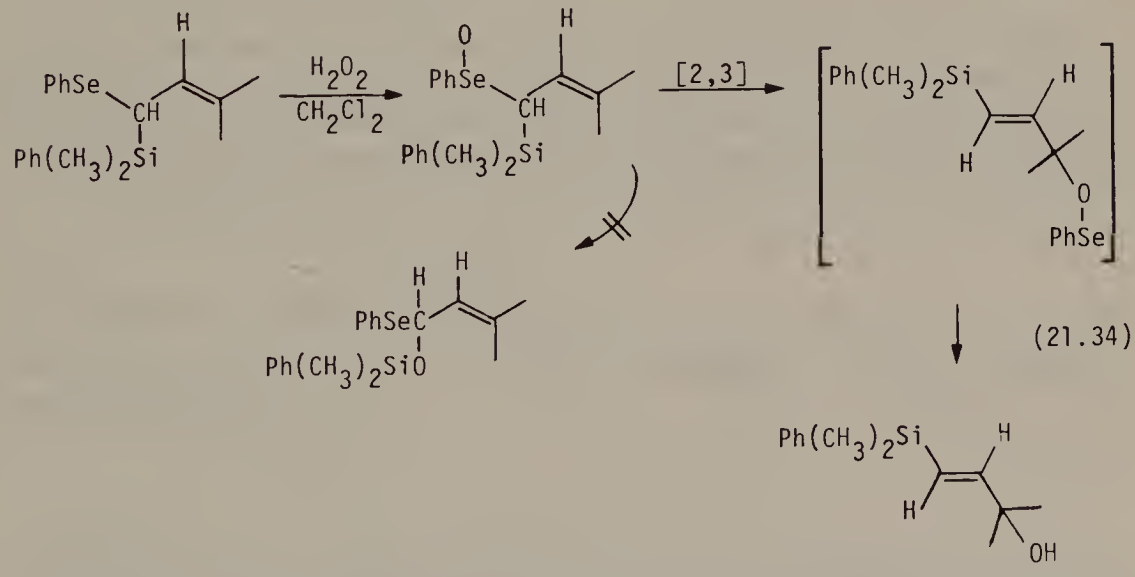
(21.32)

Attempts to prepare alkyl phenyl ketones by this procedure proved more complicated. Deprotonation of benzyl phenyl selenide with LDA followed by reaction with TMS-Cl gives α-phenylselenobenzyltrimethylsilane. Metallation of this compound followed by reaction with methyl iodide gives α-methyl-α-phenylselenobenzyltrimethylsilane. However, on oxidation with MCPBA the selenoxide undergoes not only the silyl-Pummerer rearrangement but also *syn*-elimination of phenylselenous acid. *Syn*-elimination is much more facile for selenium than for sulfur [43].



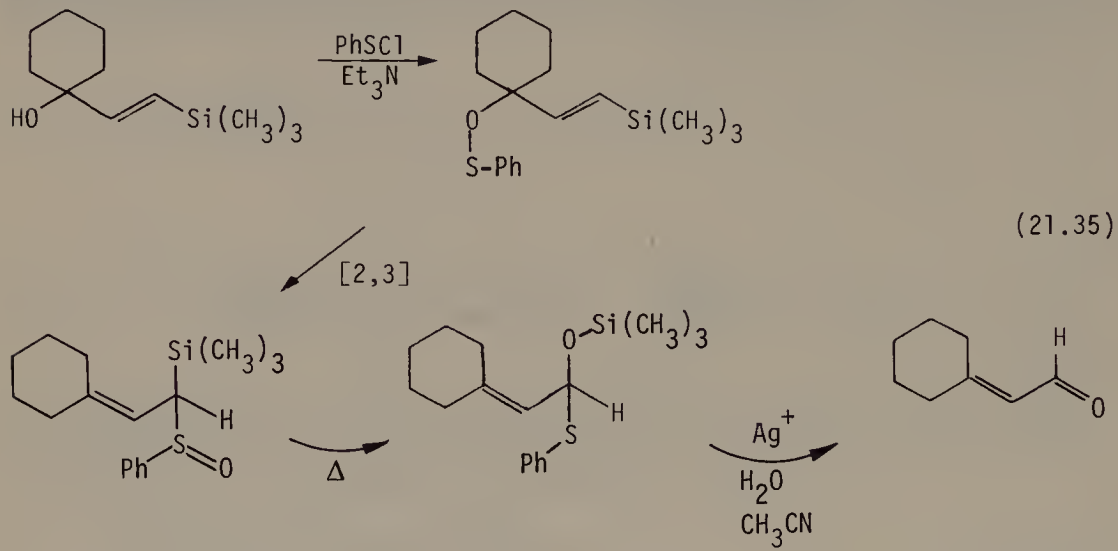
(21.33)

Oxidation of allylic systems such as 1-phenylseleno-1-dimethylphenylsilyl-3-methyl-2-butene leads to 2-methyl-4-dimethylphenylsilyl-3-buten-2-ol. Clearly the silyl-Pummerer is not competitive with the[2,3]-sigmatropic rearrangement of allylic selenoxides [44].



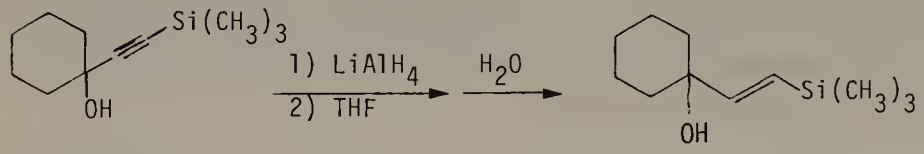
E. Synthesis of α,β-Unsaturated Aldehydes

3-Trimethylsilylallylic alcohols can be converted to α,β-unsaturated aldehydes by reaction with phenylsulfenyl chloride and triethylamine. This results from a [2,3]-sigmatropic rearrangement of the initial adduct to yield an α,β-unsaturated 0-trimethylsilyl hemiacetal [45].



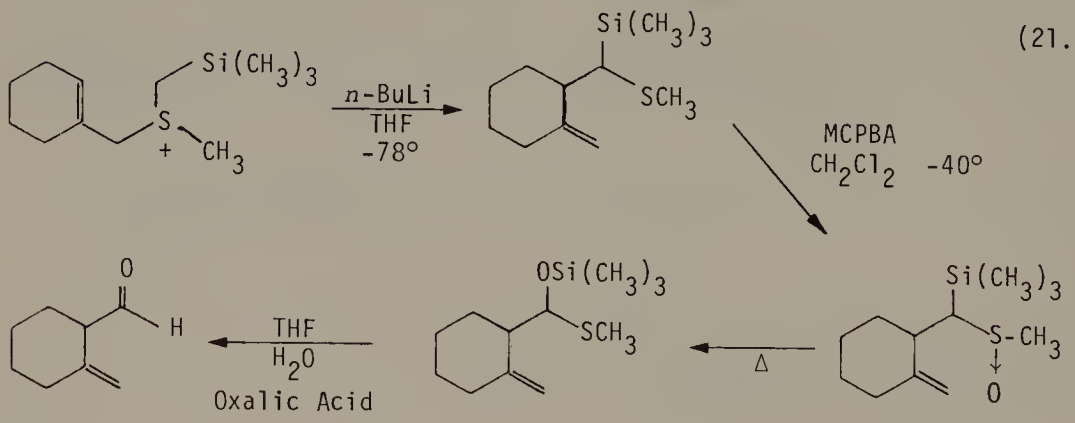
(21.35)

The required 3-trimethylsilyl allylic alcohols can be prepared by $LiAlH_4$ reduction of 1-(1'-hydroxyalkyl)-2-trimethylsilyl acetylenes.



(21.36)

Ylides formed by deprotonation of allyl methyl trimethylsilylmethyl sulfonium salts with *n*-butyl lithium, undergo [2,3] sigmatropic rearrangement to yield homoallylic α-methylthio trimethylsilanes. These can be oxidized with MCPBA to the corresponding sulfoxides which undergo silyl-Pummerer rearrangement to yield β,γ-unsaturated aldehydes after hydrolysis [46].



(21.37)

21.8 Exchange Reactions

Silyl sulfur reagents undergo exchange reactions with halogen containing substrates: such that one of the products possesses a Si–X bond while the other has a sulfur bonded to the substrate where the halogen was bonded in the starting material. The thermodynamic driving force for these reactions may, in general, be the strength of the Si–X bond which is formed (Si–Cl ~113 kcal/mol) [7].

A. Synthesis of Sulfides

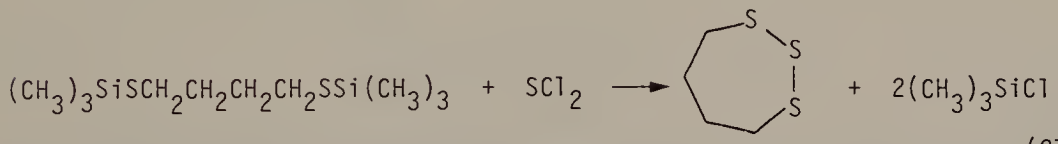
Alkyl halide react with *n*-butylthiotrimethylsilane to yield alkyl *n*-butyl sulfide and TMS–X. As expected on the basis of bond energies, primary with the following order of reactivity is observed alkyl halide RI > RBr > RCl [75].

B. Synthesis of Polysulfides

Sulfenyl chlorides react with alkylthiotrimethylsilanes to yield TMS-Cl and unsymmetrical disulfides [47].

(21.38)

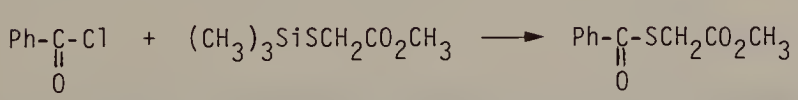
In a similar manner, 1,3-*bis*(trimethylsilylthio)propane or 2,2-dimethyl-2-sila-1,3-dithiocyclohexane [48] reacts with sulfur dichloride to yield 1,2,3-trithiocyclohexane. 1,4-*bis*(Trimethylsilylthio)butane reacts with sulfur dichloride to yield 1,2,3-trithiocycloheptane [49]. This procedure is the most direct approach to such cyclic polysulfides.



(21.39)

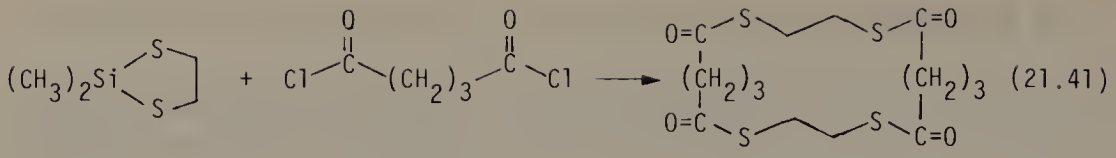
C. Synthesis of S-alkyl Thiocarboxylates

Alkylthiotrimethylsilanes react with acid chlorides to yield S-alkyl thiocarboxylates [76].



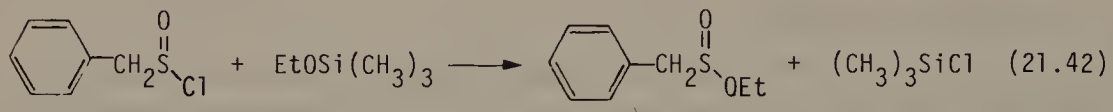
(21.40)

2,2-Dimethyl-2-sila-1,3-dithiocyclopentane [50] reacts under high dilution conditions (10^{-2} molar solutions) with α,ω-diacid chlorides to yield macrocyclic tetrathiolactones [50, 51].



(21.41)

Phenylselenotrimethylsilane reacts in an analogous manner with acid chlorides to yield Se-phenyl selenocarboxylates [52]. Sulfinyl chlorides react with alkoxytrimethylsilane to yield sulfinate esters and TMS-Cl [47].

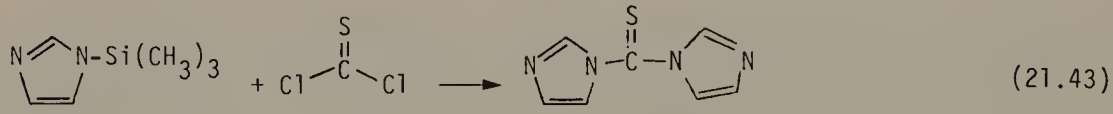


(21.42)

This reaction is analogous to the exchange reaction between carboxylic acid chlorides and alkoxytrimethylsilanes which yield esters and TMS-Cl [54]. Reactions are also observed between methyl benzene sulfenate and TMS-Cl or TMS-CN to yield methoxytrimethylsilane and benzene sulfenyl chloride or phenyl thiocyanate, respectively [47].

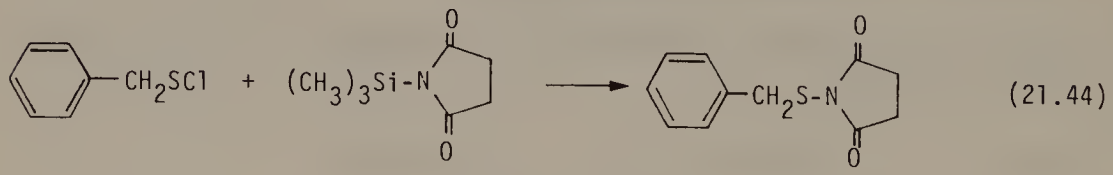
D. Sulfur Transfer Reagents

A number of useful sulfur transfer reagents have been prepared by use of organosilicon reagents. For example, 1,1-thiocarbonyl di-imidazole has been prepared by reaction of N-trimethylsilyl imidazole and thiophosgene. Related heterocyclic thiocarbonyl transfer reagents based on benzimidazole, benzotriazole and pyrazole have also been prepared [56].



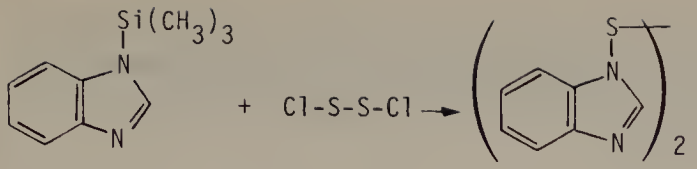
(21.43)

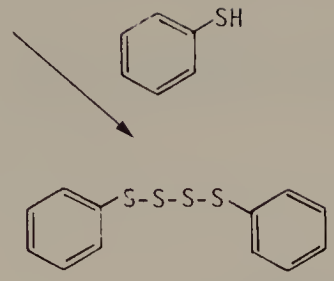
In a similar manner sulfenyl chlorides react with N-trimethylsilyl succinimide to yield N-alkylthio or N-arylthio succinimide [57].



(21.44)

N-Trimethylsilyl heterocycles react with sulfur dichloride or sulfur monochloride to yield a series of mono or disulfur transfer reagents. These react with thiols to regenerate the heterocycle and yield tri-or tetrasulfides respectively [58].



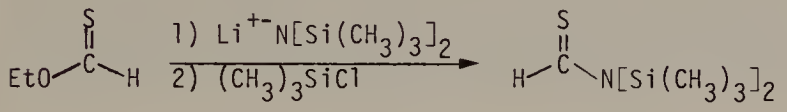


(21.45)

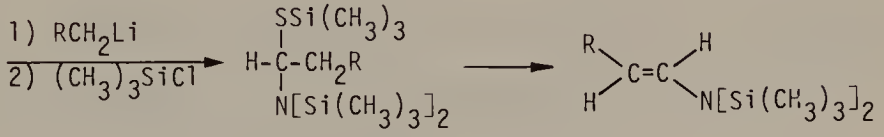
21.9 Miscellaneous

N-(Trimethylsilyl)thioformamide has been prepared by reaction of thioformamide with hexamethyldisilazane [59]. Metallation of N-alkyl thioformamides followed by reaction with TMS-Cl yields N-alkyl-N-trimethylsilyl thioformamides. These exhibit temperature dependent dynamic NMR behavior [60].

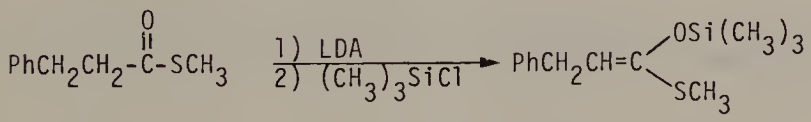
N,N-*bis*(Trimethylsilyl)thioformamide has been utilized to prepare N,N-*bis*(trimethylsilyl)enamines [61].



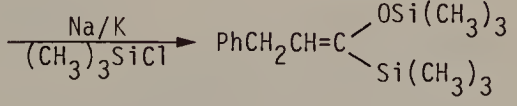
(21.46)



Reductive cleavage of the C–S bond of α-methylthio trimethylsilyl enol ethers with sodium or sodium/potassium alloy in the presence of TMS-Cl yields α-trimethylsilyl trimethylsilyl enol ethers [55]. These can be easily hydrolyzed to acyl trimethylsilanes.

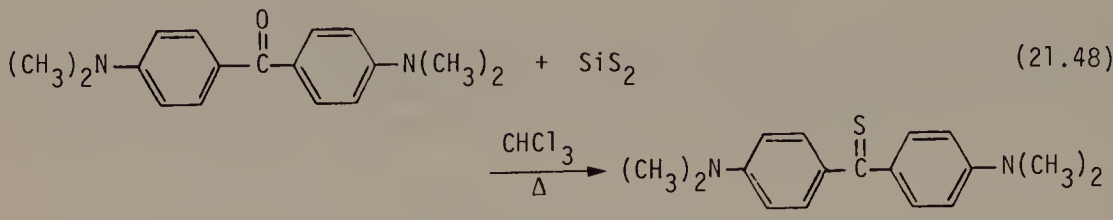


(21.47)



All of the silicon-sulfur reagents we have considered thus far have possessed organic groups on either silicon or sulfur or both. Silicon sulfide is,

in this regard, unique. It is virtually insoluble in all common organic solvents, except DMSO with which it reacts. Silicon sulfide reacts with ketones possessing electron releasing groups in refluxing chloroform to convert the carbonyl to a thiocarbonyl group [53].



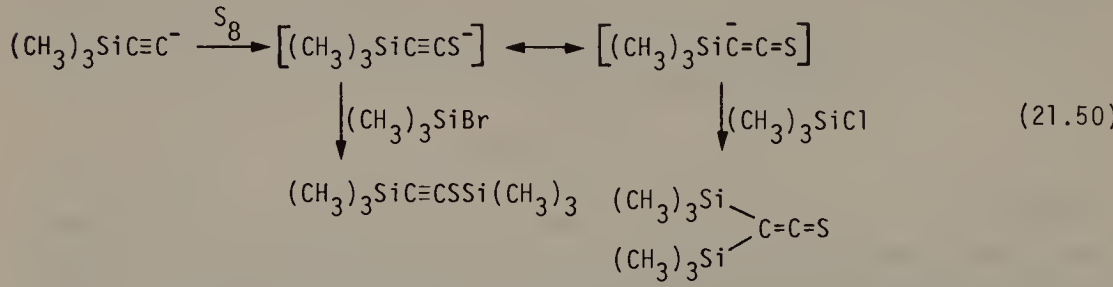
(21.48)

21.10 Preparation

Alkylthiotrimethylsilanes have been prepared by reaction of TMS-Cl with metal mercaptides [62].

$$CH_3\text{-}MgI + CH_3S\text{-}H \longrightarrow CH_3\text{-}S\text{-}MgI \xrightarrow{(CH_3)_3SiCl} CH_3S\text{-}Si(CH_3)_3 \qquad (21.49)$$

Lithium trimethylsilylacetylide reacts with sulfur to yield lithium 2-trimethylsilylethynylthiolate. This ambident anion reacts with TMS-Cl to yield *bis*(trimethylsilyl)thioketene and with TMS-Br to yield 1-trimethylsilylthio-2-trimethylsilyl acetylene. This difference may result from the hard-soft nature of the leaving groups.



(21.50)

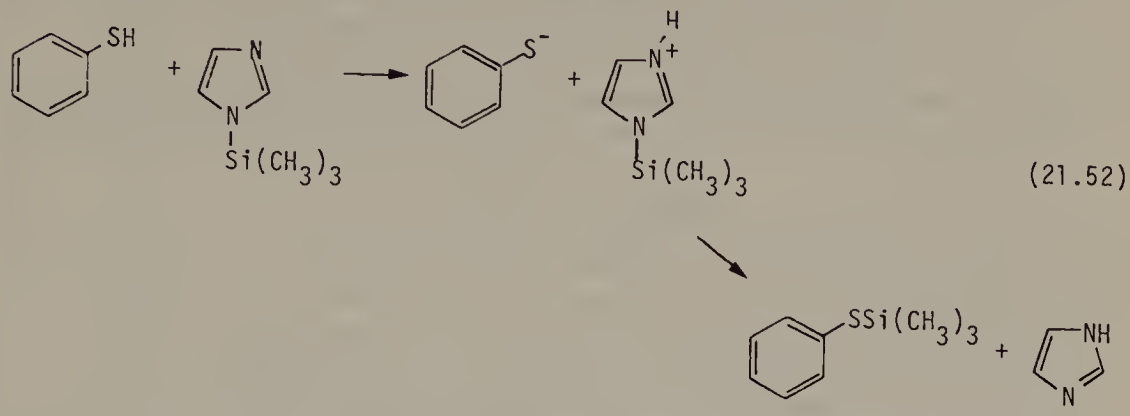
bis(Trimethylsilyl)thioketene like di-*t*-butyl thioketene does not dimerize or polymerize [63].

Sodium phenyl selenide, formed by the reduction of diphenyl diselenide with sodium in THF, reacts with TMS-Cl to yield phenylselenotrimethylsilane [64, 65].

$$PhSeSePh \xrightarrow[THF]{Na} PhSe^-Na^+ \xrightarrow{(CH_3)_3SiCl} PhSeSi(CH_3)_3 \qquad (21.51)$$

Magnesium-*p*-tolyl selenide, prepared by reaction of *p*-tolyl magnesium bromide with selenium, reacts with TMS-Cl to yield *p*-tolylselenotrimethylsilane. This approach has also been used to prepare *p*-tolyltellurotrimethylsilane [66].

The reaction of trimethylsilylamines with thiols yields alkylthio- and arylthiotrimethylsilanes [67]. Deprotonation of the thiol to yield a thiolate by N-trimethylsilyl imidazole may be an essential step in the reaction [68].



(21.52)

The reaction of hexamethyldisilazane with thiols can be catalyzed by imidazole [69].

$$[(CH_3)_3Si]_2NH + H_2S \xrightarrow[\text{Imidazole}]{} [(CH_3)_3Si]_2S + NH_3 \qquad (21.53)$$

Likewise phenylselenotrimethylsilane can be prepared by reaction of phenylselenol with TMS-Cl in the presence of trimethylamine. The preparation and purification of phenylselenol is, however, difficult [70].

Alkylthio- and arylthiotrialkylsilanes can be prepared by reaction of trialkylsilanes with thiols catalyzed by $[Ph_3P]_3RhCl$ [71, 72].

$$PhSH + Et_3SiH \xrightarrow{[Ph_3P]_3RhCl} Et_3Si\text{-}SPh \qquad (21.54)$$

Dissolving metal reduction of symmetrical disulfides in the presence of TMS-Cl yields alkylthiotrimethylsilanes [73].

References

1. For a review of silicon-sulfur Chemistry see: Abel, E.W., Armitage, D.A.: Adv. Organometal. Chem. *5,* 2 (1967)
2. Peterson, D.J.: J. Org. Chem. *33,* 780 (1968)
3. Carey, F.A., Court, A.S.: J. Org. Chem. *37,* 939 (1972)
4. Carey, F.A., Hernandez, O.: J. Org. Chem. *38,* 2670 (1973)
5. Soysa, H.S.D., Weber, W.P.: Tetrahedron Lett. 235 (1978)
6. Detty, M.R.: J. Org. Chem. *44,* 4528 (1979)
7. Walsh, R.: Accts. of Chem. Res. *14,* 246 (1981)
8. Schmeisser, M., Muller, H.: On the basis of equilibration studies, Si–S and C–S single bonds appear to be approximately equal strength: Angew. Chem. *69,* 781 (1957)
9. Abel, E.W., Walker, D.J.: J. Chem. Soc. *A,* 2338 (1968)
10. Rokach, J., Girard, Y., Guidon, Y., Atkinson, J.G., Larue, M., Young, R.N., Masson, P., Holme, G.: Tetrahedron Lett. 1485 (1980)

11. Hanessian, S., Guindon, Y.: Tetrahedron Lett. 2305 (1980)
12. Miyoshi, N., Kondo, K., Murai, S., Sonoda, N.: Chem. Lett. 909 (1979)
13. Detty, M.R.: Tetrahedron Lett. 5087 (1978)
14. Abel, E.W., Walker, D.J., Wingfield, N.J.: J. Chem. Soc. *A*, 1814 (1968)
15. Itoh, K., Matsuzaki, K., Ishii, Y.: J. Chem. Soc. *C*, 2709 (1968)
16. Ojima, I., Nagai, Y.: J. Organometal. Chem. *57*, C42 (1973)
17. Evans, D.A., Grimm, K.G., Truesdale, L.K.: J. Am. Chem. Soc. *97*, 3229 (1975)
18. Evans, D.A., Truesdale, L.K., Grimm, K.G., Nesbitt, S.L.: J. Am. Chem. Soc. *99*, 5009 (1977)
19. Chan, T.H., Ong, B.S.: Tetrahedron Lett. 319 (1976)
20. Glass, R.S.: Syn. Comm. *6*, 47 (1976)
21. Ong, B.S., Chan, T.H.: Syn. Commun. *7*, 283 (1977)
22. Dumont, W., Krief, A.: Angew. Chem. Int. Ed. *16*, 540 (1977)
23. Liotta, D., Paty, P.B., Johnston, J., Zima, G.: Tetrahedron Lett. 5091 (1978)
24. Itoh, K., Matsuzaki, K., Ishii, Y.: J. Chem. Soc. *C*, 2709 (1968)
25. Mukaiyama, T., Takeda, T., Atsumi, K.: Chem. Lett. 187 (1974)
26. Breslow, R., Pandey, P.S.: J. Org. Chem. *45*, 740 (1980)
27. Miyoshi, N., Ishii, H., Murai, S., Sonoda, N.: Chem. Lett. 873 (1979)
28. Ricci, A., Danieli, R., Pirazzini, G.: J.C.S. Perkin 1, 1069 (1977)
29. Mukaiyama, T., Takeda, T., Atsumi, K.: Chem. Lett. 1013 (1974)
30. Kuwajima, I., Hoshino, S., Tanaka, T., Shimizu, M.: Tetrahedron Lett. 3209 (1980)
31. Dumont, W., Krief, A.: Angew. Chem. Int. Ed. *15*, 161 (1976)
32. Brook, A.G., Anderson, D.G.: Can. J. Chem. *46*, 2115 (1968)
33. Vedejs, E., Mullins, M.: Tetrahedron Lett. 2017 (1975)
34. Cooper, G.D.: J. Am. Chem. Soc. *76*, 3713 (1954)
35. Corey, E.J., Seebach, D.: J. Org. Chem. *31*, 4097 (1966)
36. Kocienski, P.J.: Tetrahedron Lett. 1559 (1980)
37. Ager, D.J., Cookson, R.C.: Tetrahedron Lett. 1677 (1980)
38. Ager, D.J.: Tetrahedron Lett. 4759 (1980)
39. Ager, D.J.: Tetrahedron Lett. 587 (1981)
40. Harirchian, B., Magnus, P.: J. Chem. Soc. Chem. Commun. 522 (1977)
41. Cookson, R.C., Parsons, P.J.: J. Chem. Soc. Chem. Commun. 990 (1976)
42. Sachdev, K., Sachdev, H.S.: Tetrahedron Lett. 4223 (1976)
43. Reich, H.J., Shan, S.K.: J. Org. Chem. *42*, 1773 (1977)
44. Reich, H.J.: J. Org. Chem. *40*, 2570 (1975)
45. Cutting, I., Parsons, P.J.: Tetrahedron Lett. 2021 (1981)
46. Kocienski, P.J.: J. Chem. Soc. Chem. Commun. 1096 (1980)
47. Harpp, D.N., Friedlander, B.T., Larsen, C., Steliou, K., Stockton, A.: J. Org. Chem. *43*, 3481 (1978)
48. Wieber, M., Schmidt, M.: J. Organometal. Chem. *I*, 336 (1964)
49. Yamazaki, N., Nakahama, S., Yamaguchi, K., Yamaguchi, T.: Chem. Lett. 1355 (1980)
50. Wieber, M., Schmidt, H.: Z. Naturf. *18*, 846 (1963)
51. Shanzer, A., Schwartz, E.: Tetrahedron Lett. 5019 (1979)
52. Derkach, N.Y., Tishchenko, N.P.: Zh. Org. Khim. *13*, 100 (1977)
53. Dean, F.M., Goodchild, J., Hill, A.W.: J. Chem. Soc. *C*, 2192 (1969)
54. For a review see Klebe, J.F.: Adv. Org. Chem. *8*, 97–178 (1972)
55. Kuwajima, I., Mori, A., Kato, M.: Bull. Chem. Soc. Japan, *53*, 2634, (1980)
56. Larsen, C., Steliou, K., Harpp, D.N.: J. Org. Chem. *43*, 337 (1978)
57. Harpp, D.N., Friedlander, B.T., Mullins D., Vines, S.M.: Tetrahedron Lett. 963 (1977)

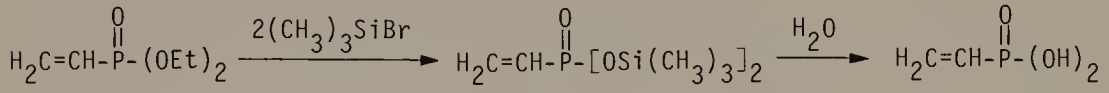
58. Harpp, D.N., Steliou, K., Chan, T.H.: J. Am. Chem. Soc. *100*, 1222, (1978)
59. Walter, W., Lüke, H.W., Voss, J.: Liebigs. Ann. Chem. 1808 (1975)
60. Walter, W., Lüke, H.W.: Angew. Chem. Int. Ed. *14*, 427 (1975)
61. Walter, W., Lüke, H.W.: Angew. Chem. Int. Ed. *16*, 535 (1977)
62. Hootan, K.A., Allred, A.L.: Inorg. Chem. *4*, 671 (1965)
63. Harris, S.J., Walton, D.R.M.: J. Chem. Soc. Chem. Commun. 1008 (1976)
64. Miyoshi, N., Ishii, H., Kondo, K., Murai, K., Sonoda, N.: Synthesis, 300 (1979)
65. Liotta, D., Markiewicz, W., Santiesteban, H.: Tetrahedron Lett. 4365 (1977)
66. Praefcke, K., Weichsel, C.: Synthesis, 216 (1980)
67. Louis, E., Urry, G.: J. Inorg. Chem. *7*, 1253 (1968)
68. Glass, R.S.: J. Organometal. Chem. *61*, 83 (1973)
69. Harpp, D.N., Steliou, K.: Synthesis, 721 (1976)
70. Derkach, N.Y., Pasmurtseva, N.A., Levchenko, E.S.: Zh. Org. Khim. *7*, 1543 (1971)
71. Ojima, I., Nihonyanagi, M., Nagai, Y.: J. Organometal. Chem. *50*, C26 (1973)
72. Sommer, L.H., Citron, J.D.: J. Org. Chem. *32*, 2470 (1967)
73. Kuwajima, I., Abe, T.: Bull. Chem. Soc. Japan, *51*, 2183 (1978)
74. Hayashi, T., Midorikawa, H.: Tetrahedron Lett. 2461 (1973)
75. Abel, E.W., Armitage, D.A., Bush, R.P.: J. Chem. Soc. 2455 (1964)
76. Rimpler, M.: Chem. Ber. *99*, 1528 (1966)

22 Silicon-Phosphorous

22.1 Introduction

A number of silicon-phosphorous compounds have proved to be useful reagents in organic synthesis. Among these are at least four major types: trimethylsilyl phosphines, $Ph_2PSi(CH_3)_3$; trimethylsilyl phosphites, $(CH_3)_3SiOP(OEt)_2$; trimethylsilyl phosphates, $[(CH_3)_3SiO]_3P{=}O$, and trimethylsilyl hypophosphites, $[(CH_3)_3SiO]_2P{-}H$. In general all four react with a single functional group in similar ways and so their chemistry will be examined together.

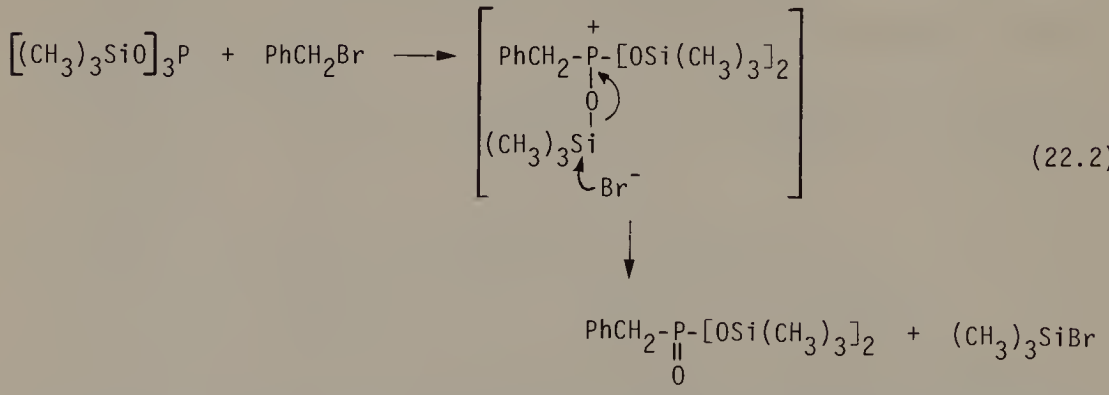
We have previously considered the preparation of vinyl phosphonates as well as the reaction of trimethylsilyl bromide with dialkylphosphonates (see 6.1 and 3.9).



(22.1)

22.2 Alkyl Halides—Arbuzov Reactions

bis(Trimethylsilyl) alkylphosphonates can be prepared by the Arbuzov reaction of primary alkyl halides with *tris*(trimethylsilyl) phosphite [1, 2].

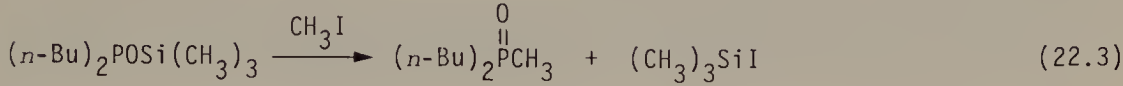


(22.2)

Arbuzov reaction of *d,l*-3-iodo-1,2-distearoyl propane with *tris*(trimethylsilyl) phosphite gives after hydrolysis *d,l*-2,3-distearoyl propylphosphonic acid

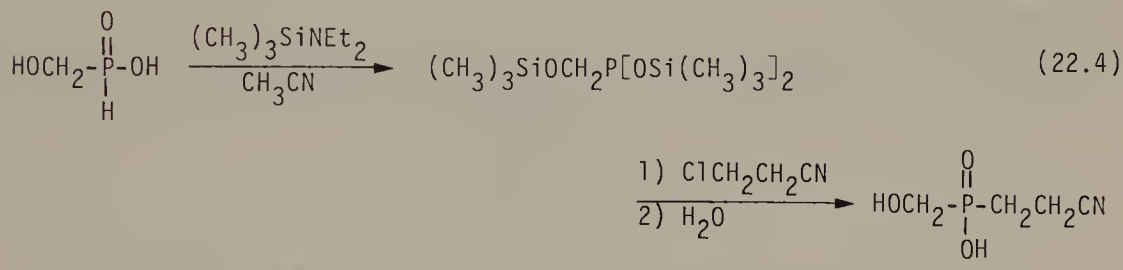
which was converted to 2,3-distearoyl propylphosphonyl choline derivatives [3, 73].

Trimethylsilyl phosphinites undergo Arbuzov reaction with alkyl iodides to yield tertiary phosphine oxides [4].



$$(n\text{-Bu})_2POSi(CH_3)_3 \xrightarrow{CH_3I} (n\text{-Bu})_2\overset{O}{\overset{\|}{P}}CH_3 + (CH_3)_3SiI \qquad (22.3)$$

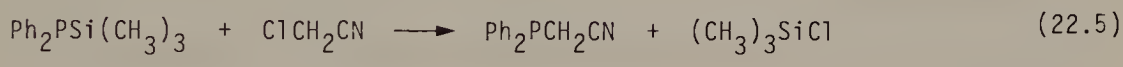
Arbuzov reaction of *bis*(trimethylsilyl) trimethylsilyloxymethyl phosphinate with 3-chloropropionitrile yields 2-cyanoethyl(hydroxymethyl)phosphinic acid after hydrolysis [5].



$$HOCH_2\overset{O}{\overset{\|}{P}}(H)OH \xrightarrow[CH_3CN]{(CH_3)_3SiNEt_2} (CH_3)_3SiOCH_2P[OSi(CH_3)_3]_2 \qquad (22.4)$$

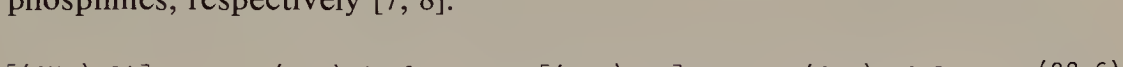
$$\xrightarrow[2)\ H_2O]{1)\ ClCH_2CH_2CN} HOCH_2\overset{O}{\overset{\|}{P}}(OH)CH_2CH_2CN$$

Trimethylsilyl phosphines react with chloroacetonitrile to yield cyanomethyl phosphines and TMS-Cl [6].



$$Ph_2PSi(CH_3)_3 + ClCH_2CN \longrightarrow Ph_2PCH_2CN + (CH_3)_3SiCl \qquad (22.5)$$

Trimethylsilyl phosphines also react with organogermanium chlorides and organotin chlorides to yield TMS-Cl and organogermanium or organotin phosphines, respectively [7, 8].

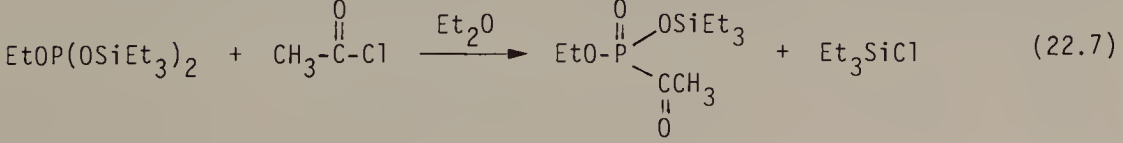


$$[(CH_3)_3Si]_3P + 3(CH_3)_3SnCl \longrightarrow [(CH_3)_3Sn]_3P + 3(CH_3)_3SiCl \qquad (22.6)$$

22.3 Acid Chlorides

A. Acyl Phosphonates

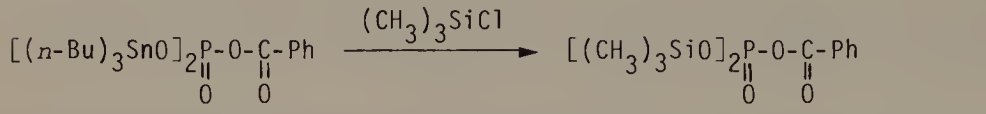
Acid chlorides react with silyl phosphites to yield acyl phosphonates. This reaction has been carried out with *tris*(triethylsilyl) phosphite, ethyl *bis*(triethylsilyl) phosphite and diethyl triethylsilyl phosphite [9].



$$EtOP(OSiEt_3)_2 + CH_3\overset{O}{\overset{\|}{C}}Cl \xrightarrow{Et_2O} EtO\text{-}\overset{O}{\overset{\|}{P}}(OSiEt_3)(CCH_3\overset{\|}{O}) + Et_3SiCl \qquad (22.7)$$

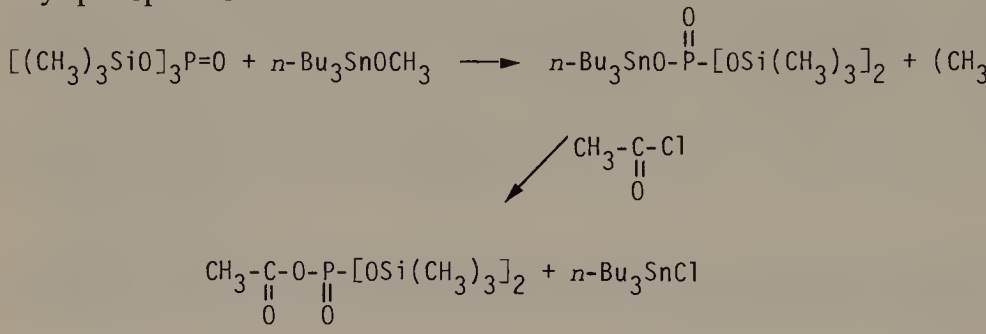
B. Acyl Phosphates

Acyl phosphates are a type of mixed anhydrides. They have been prepared in two ways. Acyl *bis*(tri-*n*-butylstannyl)phosphate reacts with TMS-Cl to yield acyl *bis*(trimethylsilyl)phosphate.



(22.8)

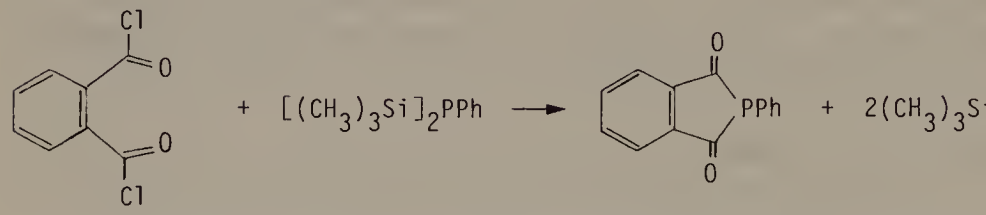
Alternatively, tri-*n*-butyltin methoxide reacts with *tris*(trimethylsilyl)phosphate to yield trimethylmethoxysilane and tri-*n*-butylstannyl *bis*(trimethylsilyl)phosphate which reacts with acid chlorides to yield acyl *bis*(trimethylsilyl)phosphates [10]. These easily undergo hydrolysis to yield the desired acyl phosphates.



(22.9)

C. Acyl Phosphines

Silyl phosphines also react with acid chlorides to yield acyl phosphines and silyl chlorides [11–13].

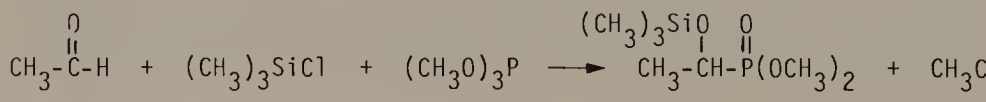


(22.10)

Silyl phosphines react with sulfonyl chlorides in a more complex manner [12].

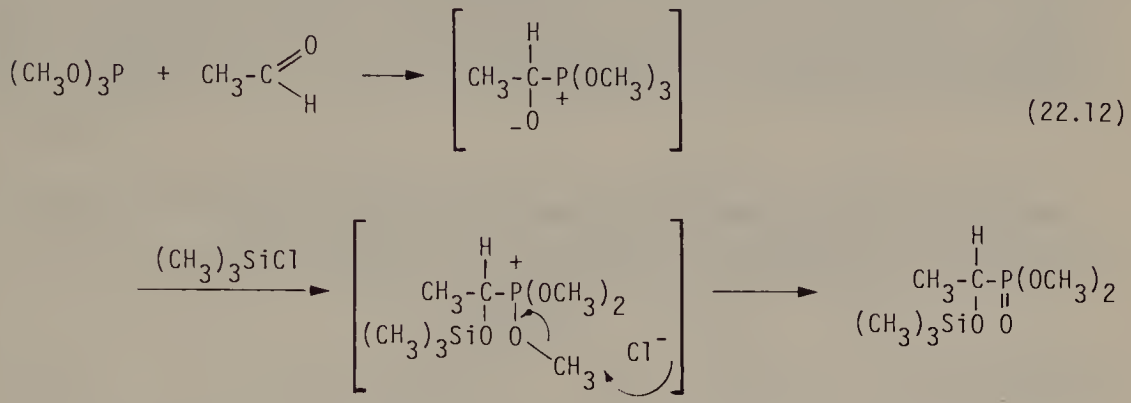
22.4 Ketones and Aldehydes

Trialkylsilyl phosphites react with ketones or aldehydes to yield 1-trialkylsilyloxyalkyl phosphonates. The reaction of acetaldehyde, TMS-Cl and trimethylphosphite also yields dimethyl (1-trimethylsilyloxyethyl)phosphonate [14].



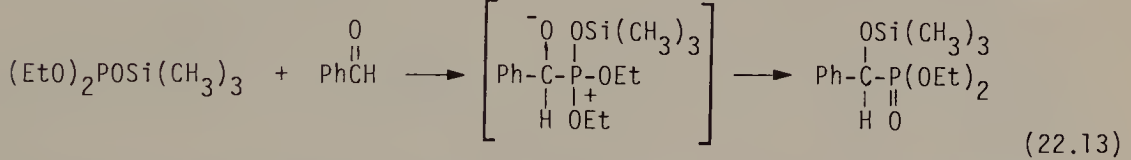
(22.11)

In a thorough study, Evans showed that this reaction does not involve prior formation of dimethyl trimethylsilyl phosphite [15]. An alternative possibility involves nucleophilic attack by phosphorous on the carbonyl carbon of acetaldehyde to yield a zwitterionic intermediate. The negatively charged alkoxide anion attacks the silicon of TMS-Cl to give a trimethoxy(1-trimethylsilyloxyethyl)phosphonium/chloride ion pair. Chloride attack on a methyl group in an Arbuzov reaction gives methyl chloride and the product.



(22.12)

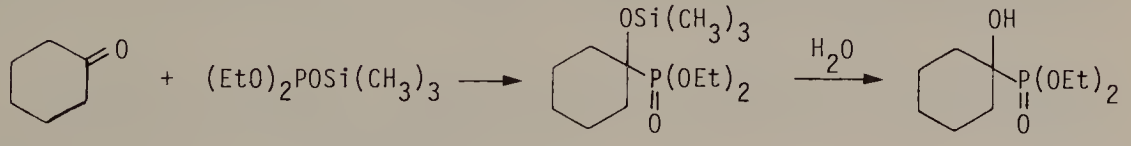
The reaction of dialkyl trimethylsilyl phosphites with ketones or aldehydes also proceeds by nucleophilic attack by phosphorous on the carbonyl carbon to yield a zwitterionic intermediate. 1,4-Intramolecular rearrangement of the trialkylsilyl group from an oxygen bonded to phosphorous to the alkoxide oxygen yields the product. Intramolecular migration of trialkylsilyl groups via front side displacement with retention of configuration at the silyl center is well-known [16].



(22.13)

As predicted by this mechanism, no crossover products were observed when diethyl trimethylsilyl phosphite, dimethyl *t*-butyldimethylsilyl phosphite and benzaldehyde were reacted in a 1:1:2 molar ratio [15].

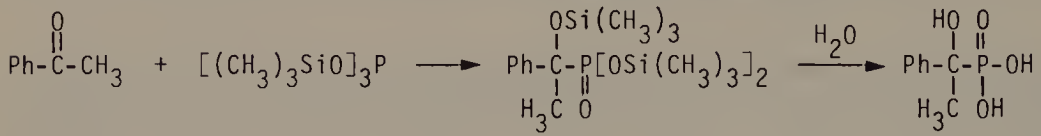
Numerous examples of this reaction have been reported. Much of the original work was done by Russian chemists. Diethyl trimethylsilyl phosphite reacts with aldehydes or ketones to yield diethyl (1-trimethylsilyloxyalkyl)-phosphonates [17, 18]. These are easily hydrolyzed to yield diethyl (1-hydroxyalkyl)phosphonates [17, 18].



(22.14)

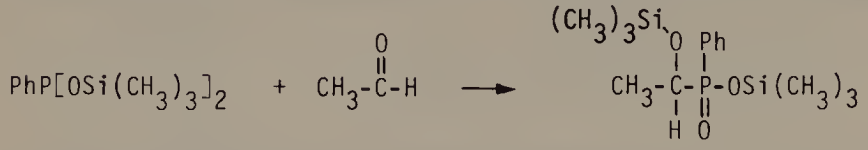
The reaction of diethyl trimethylsilyl phosphite with aromatic aldehydes has been studied [20]. The effect of substituents on reaction rate is consistent with the importance of nucleophilic attack by phosphorous on the carbonyl carbon.

tris(Trimethylsilyl) phosphite reacts with aldehydes or ketones to yield *bis*(trimethylsilyl) 1-trimethylsilyloxyalkyl phosphonates [29, 30]. These can be readily hydrolyzed to yield α-hydroxyalkyl phosphonic acids.



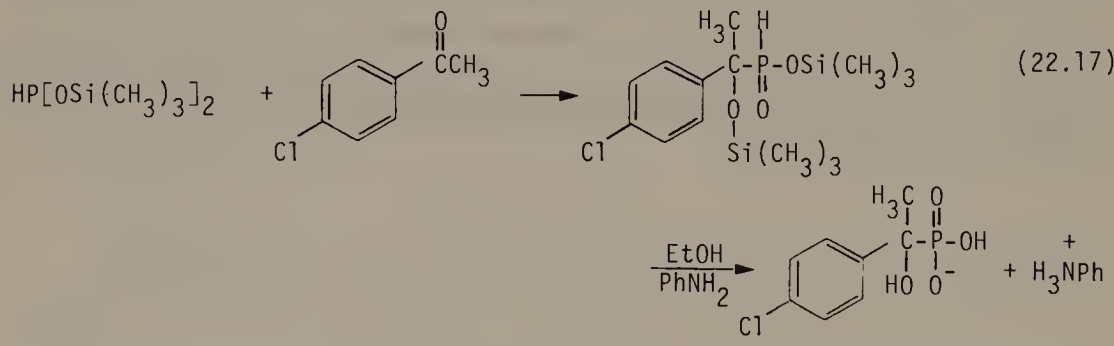
(22.15)

bis(Trimethylsilyl) phenyl phosphinate reacts with aldehydes to yield trimethylsilyl (1-trimethylsilyloxyalkyl) phenyl phosphinate [30].



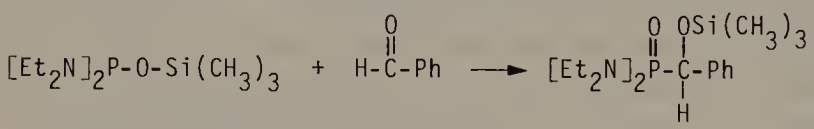
(22.16)

Likewise, *bis*(trimethylsilyl)hypophosphite reacts with aromatic aldehydes or ketones [31].



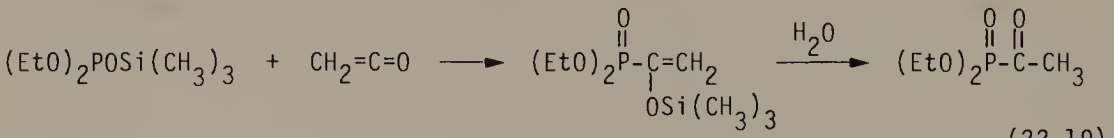
(22.17)

Trimethylsilyl-N,N,N′,N′-tetraethylphosphorodiamidite reacts with aromatic aldehydes [32] to yield the expected 1 : 1 adducts: N,N,N′N′-tetraethyl-P-[α-trimethylsilyloxybenzyl]phosphonic diamides.



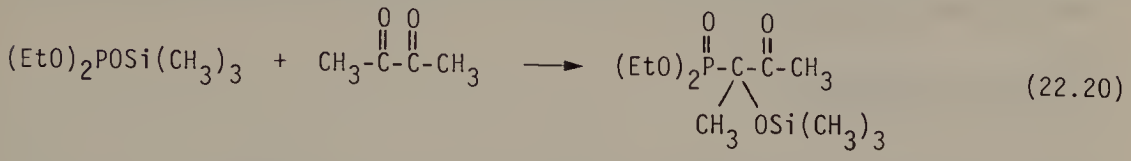
(22.18)

Diethyl trimethylsilyl phosphite reacts with ketene to yield diethyl (1-trimethylsilyloxyvinyl)phosphonate which can be hydrolyzed to yield acetyl diethyl phosphonate [17, 19] (see 22.3 A).



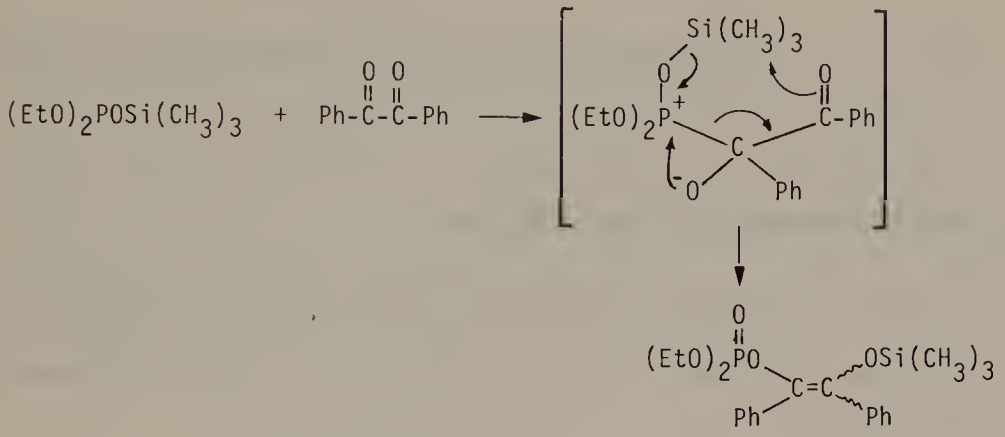
(22.19)

Reaction of diethyl trimethylsilyl phosphite with 2,3-butanedione yields diethyl (1-methyl-1-trimethylsilyloxyacetonyl)phosphonate [21].



(22.20)

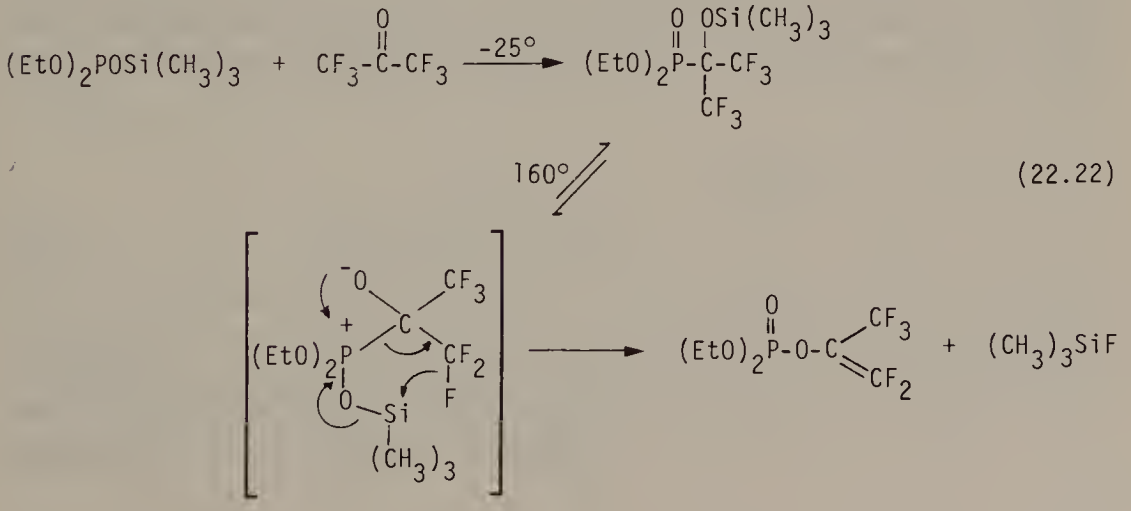
This is surprising since trialkyl phosphites react with α-diketones to yield cyclic 1 : 1 adducts [22, 23]. On the other hand, diethyl trimethylsilyl phosphite reacts with benzil to yield diethyl-[1,2-diphenyl-2-trimethylsiloxyvinyl]phosphate [20].



(22.21)

Similarly, *tris*(trimethylsilyl) phosphite reacts with 2,3-butanedione to yield *bis*(trimethylsilyl) (1,2-dimethyl-2-trimethylsilyloxyvinyl)phosphate [24]. The reason for the difference in behavior of diethyl trimethylsilyl phosphite and *tris*(trimethylsilyl)phosphite toward 2,3-butanedione is not obvious.

Diethyl trimethylsilyl phosphite reacts with both hexafluoroacetone [25, 26] and chloral [27] at low temperature to yield diethyl (1-trifluoromethyl-1-trimethylsilyloxy-2,2,2-trifluoroethyl)phosphonate and diethyl(1-trimethylsilyloxy-2,2,2-trichloroethyl)phosphonate, respectively. These rearrange on heating at 140–160 °C to yield diethyl-(2,2-difluoro-1-trifluoromethylvinyl)-phosphate and diethyl-(2,2-dichlorovinyl)phosphate [26].

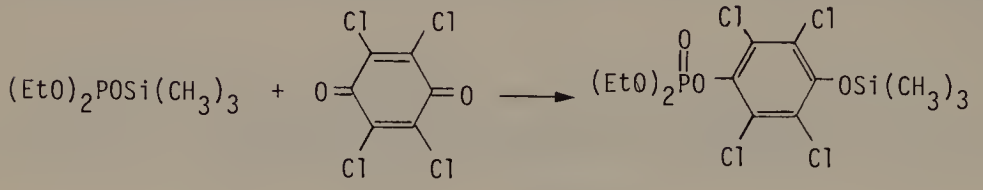


(22.22)

The thermal decomposition of dimethyl [α-methyl-α-trimethylsilyloxybenzyl]phosphonate to yield dimethyl trimethylsilyl phosphite and acetophenone is closely related [28].

22.5 Benzoquinones

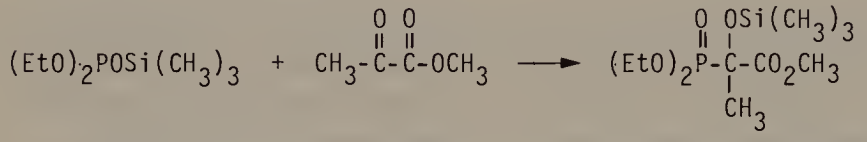
Both diethyl trimethylsilyl phosphite [20, 33] and *tris*(trimethylsilyl) phosphite [24] react with *p*-benzoquinones to yield diethyl-4-trimethylsilyloxyphenyl phosphates or *bis*(trimethylsilyl)4-trimethylsiloxyphenyl phosphates, respectively [33].



(22.23)

22.6 α-Keto Esters and α-Keto Nitriles

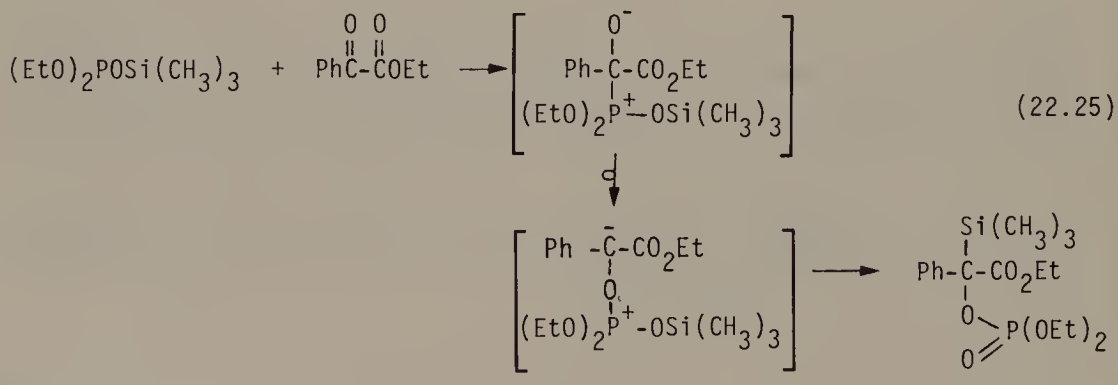
Diethyl trimethylsilyl phosphite reacts with methyl pyruvate and pyruvonitrile to yield 1 : 1 adducts: diethyl [1-carbomethoxy-1-trimethylsilyloxyethyl) phosphonate and diethyl [1-cyano-1-trimethylsilyloxyethyl] phosphonate, respectively [34].



(22.24)

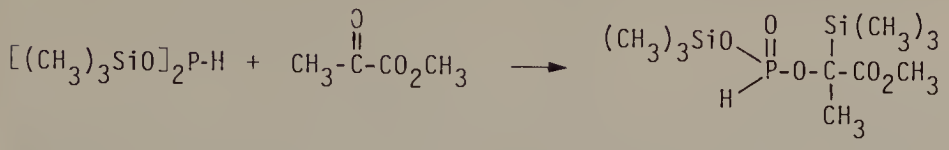
tris(Trimethylsilyl) phosphite and *bis*(trimethylsilyl) phenyl phosphinate react with pyruvonitrile in a similar manner to yield *bis*(trimethylsilyl)-[1-cyano-1-trimethylsilyloxyethyl] phosphonate and trimethylsilyl [1-cyano-1-trimethylsilyloxyethyl] phenyl phosphinate [30].

Diethyl trimethylsilyl phosphite reacts with ethyl phenylglyoxylate to yield diethyl [α-carboethoxy-α-trimethylsilylbenzyl] phosphate. Stabilization of the carbanion by adjacent ester and phenyl groups may facilitate the critical rearrangement step which converts a 1,3-phosphonium/alkoxide zwitterionic intermediate into a 1,3-phosphonium/carbanion zwitterionic intermediate [34].



(22.25)

bis(Trimethylsilyl) hypophosphite reacts in a similar manner with methyl pyruvate [35].

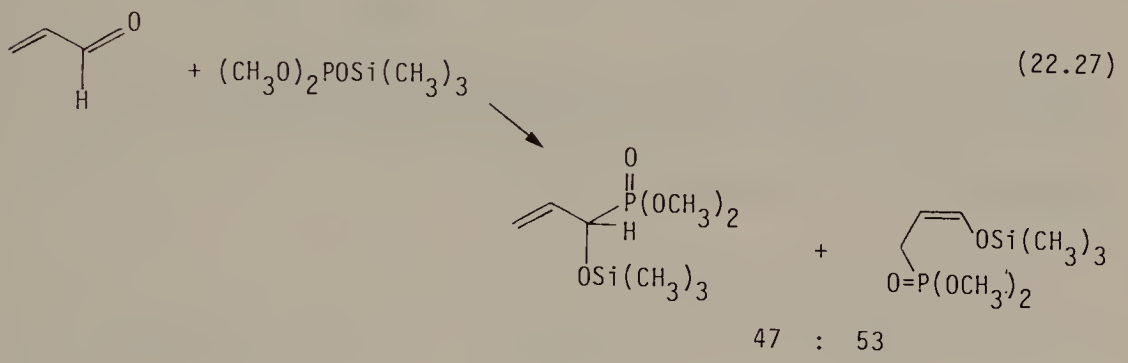


(22.26)

The reaction of *bis*(trimethylsilyl) hypophosphite with methyl 3,3-dimethyl-2-ketobutyrate is more complicated [36].

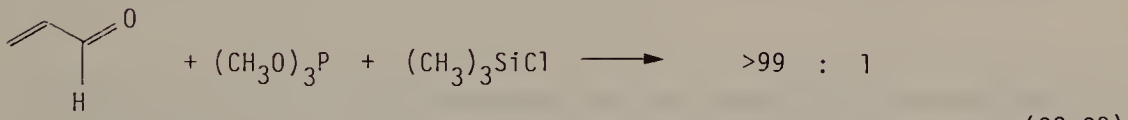
22.7 α,β-Unsaturated Carbonyl Compounds

Dimethyl trimethylsilyl phosphite reacts with α,β-unsaturated aldehydes to yield mixtures of 1,2 and 1,4-adducts (Eq. 22.27). Significantly, trimethyl phosphite and TMS-Cl [14] react regiospecifically with α,β-unsaturated aldehydes to yield only 1,2-adducts (Eq. 22.28) [15,37]. α,β-Unsaturated ketones yield only 1,4-adducts with either reagent (Eq. 22.29).

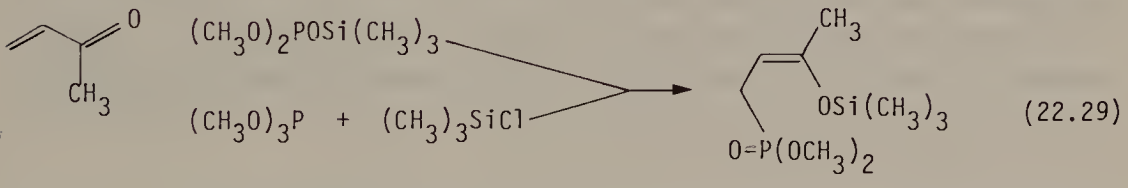


47 : 53

(22.27)

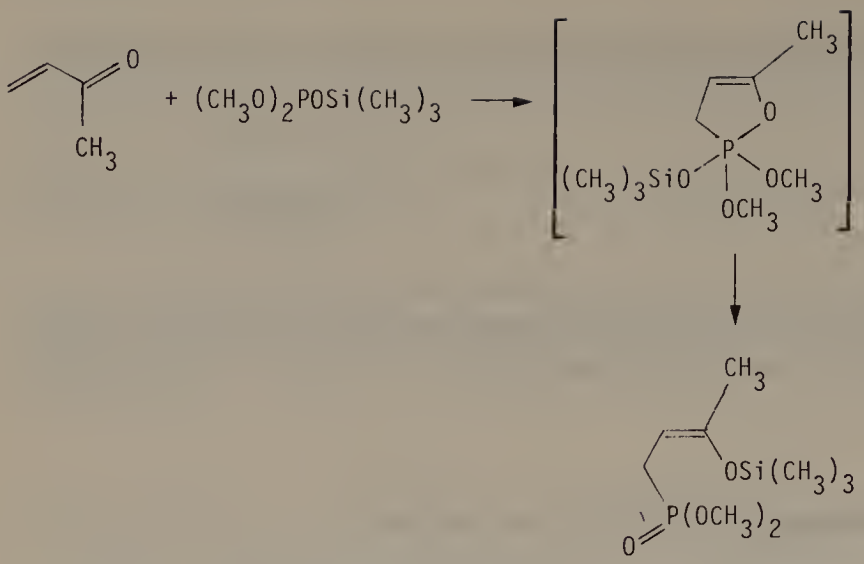


(22.28)



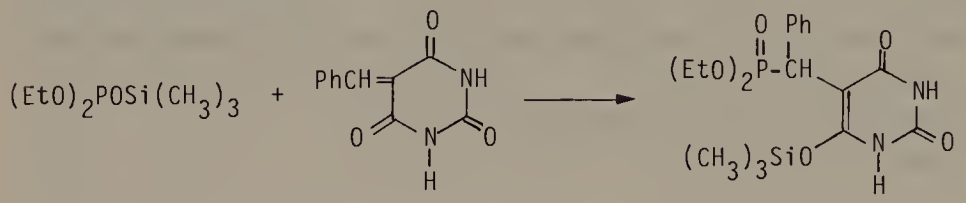
(22.29)

Based on NMR coupling constants, the stereochemistry of these 1,4-adducts has been determined to be exclusively *Z*. α,β-Unsaturated ketones which cannot adopt a cisoid geometry, such as 2-cyclohexenone do not react. These facts suggest that the 1,4-adducts may be formed via a cyclic intermediate [15]. Since 1,2 and 1,4 adducts do not interconvert thermally, the ratio of these products must be kinetically controlled.



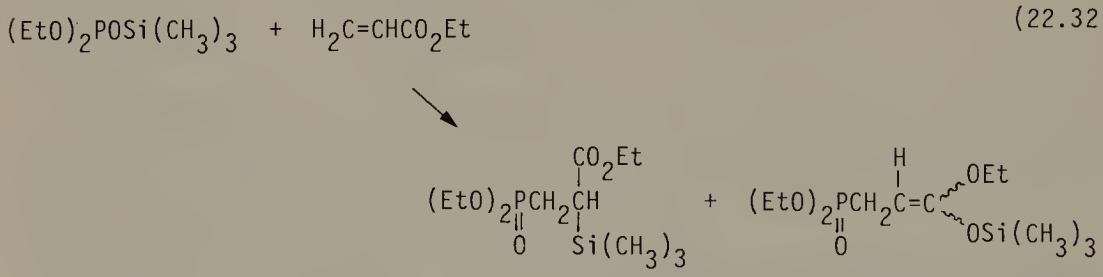
(22.30)

Diethyl trimethylsilyl phosphite reacts in a 1,4 manner with 5-benzyldiene barbituric acid [38].



(22.31)

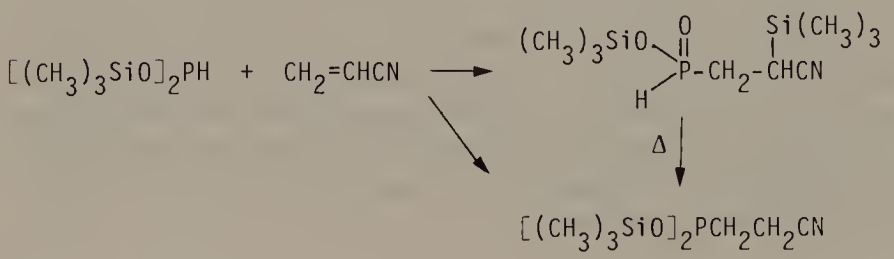
Diethyl trimethylsilyl phosphite reacts with α,β-unsaturated esters such as ethyl acrylate to yield mixtures of adducts [19].



(22.32)

tris(Trimethylsilyl) phosphite reacts regiospecifically with α,β-unsaturated aldehydes to give 1,2-adducts while it reacts with α,β-unsaturated ketones or esters to give 1,4-adducts [29].

bis-(Trimethylsilyl) hypophosphite reacts with acrylonitrile to yield a mixture of trimethylsilyl hydrogen [2-cyano-2-trimethylsilylethyl] phosphonite and *bis*(trimethylsilyl) 2-cyanoethyl phosphonite. Heating converts the mixture to the latter product exclusively [39, 40].

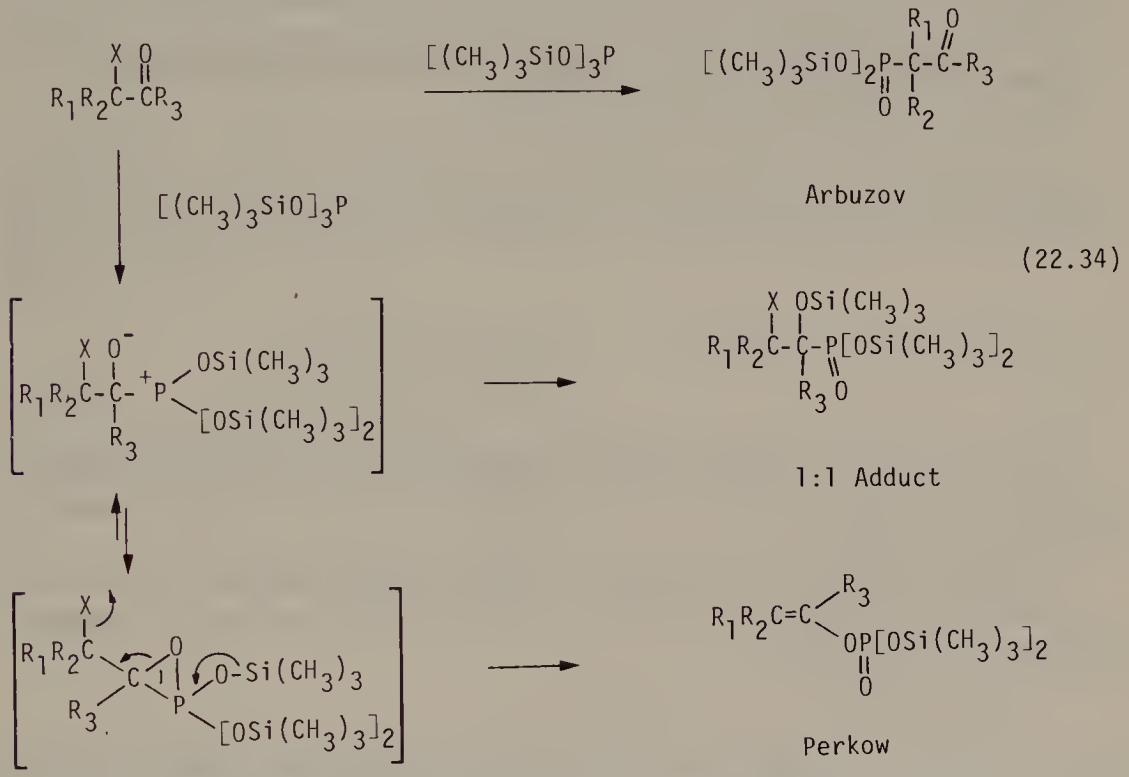


(22.33)

bis(Trimethylsilyl) hypophosphite reacts with styrene to yield *bis*(trimethylsilyl) 2-phenylethyl phosphonite [39].

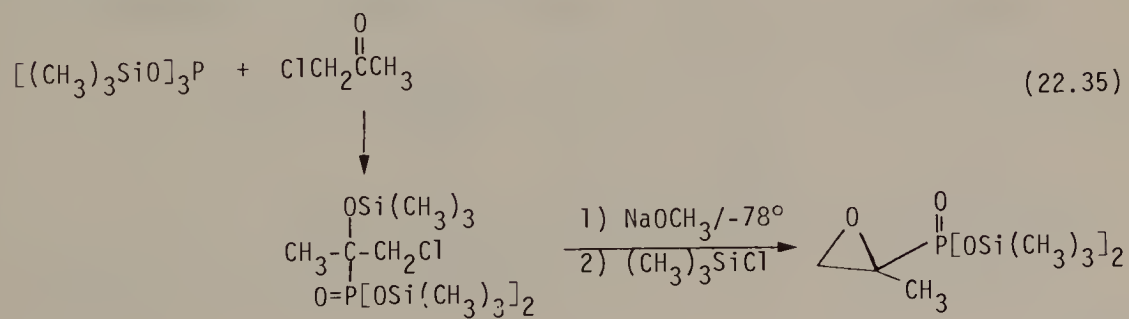
22.8 α-Haloketones

The reaction of *tris*(trimethylsilyl) phosphite with α-halo ketones occurs by three possible pathways [41]. The first is the Arbuzov reaction which yields *bis*(trimethylsilyl) 2-oxoalkyl phosphonates. Second is the formation of 1:1-adducts: *bis*(trimethylsilyl) (2-halo-1-trimethylsilyloxyalkyl) phosphonates. Third is the Perkow reaction which results in formation of *bis*(trimethylsilyl) vinyl phosphates. These latter two reactions may involve a common initial zwitterionic intermediate.



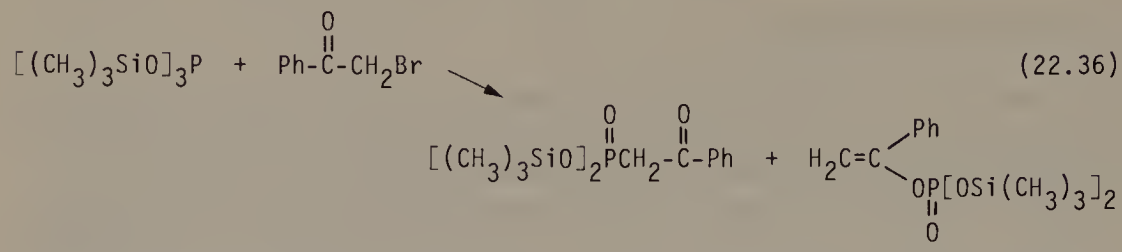
(22.34)

With aliphatic α-haloketones or aldehydes the 1 : 1 adducts predominate. Thus chloroacetone reacts with *tris*(trimethylsilyl) phosphite to give *bis*(trimethylsilyl)-(2-chloro-1-methyl-1-trimethylsilyloxyethyl) phosphonate. This compound can be converted to the corresponding epoxide which is related to the antibiotic phosphonomycin [41, 42].



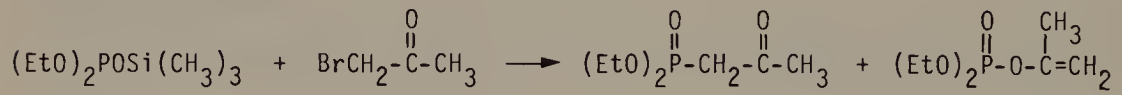
(22.35)

Phenacyl bromide reacts with *tris*(trimethylsilyl) phosphite to yield a mixture of Arbuzov (14%) and Perkow (61%) products (Eq. 22.36) [41, 43]. α-Haloesters yield exclusively Arbuzov products.



(22.36)

Diethyl trimethylsilyl phosphite reacts with bromoacetone to yield a mixture of Arbuzov (24%) and Perkow (65%) products while chloroacetone yields only 1 : 1 type adducts. This difference has been attributed to the increased nucleophilicity of the phosphorous of diethyl trimethylsilyl phosphite compared to *tris*(trimethylsilyl) phosphite and to the relative strength of a C–Br bond compared to a C–Cl bond [41].

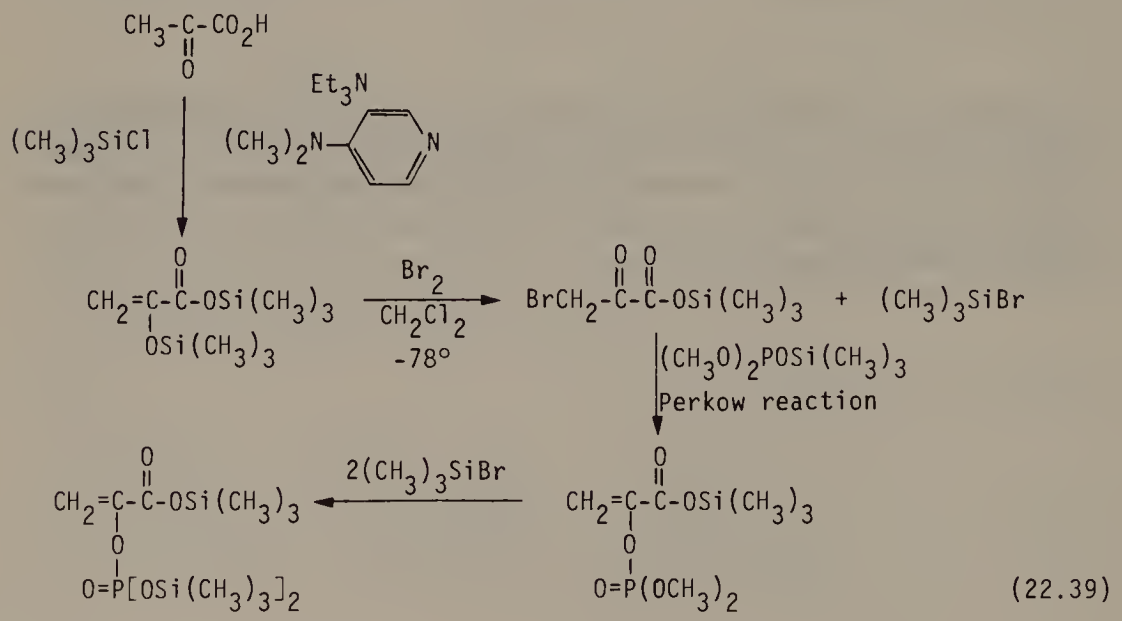


(22.37)

(22.38)

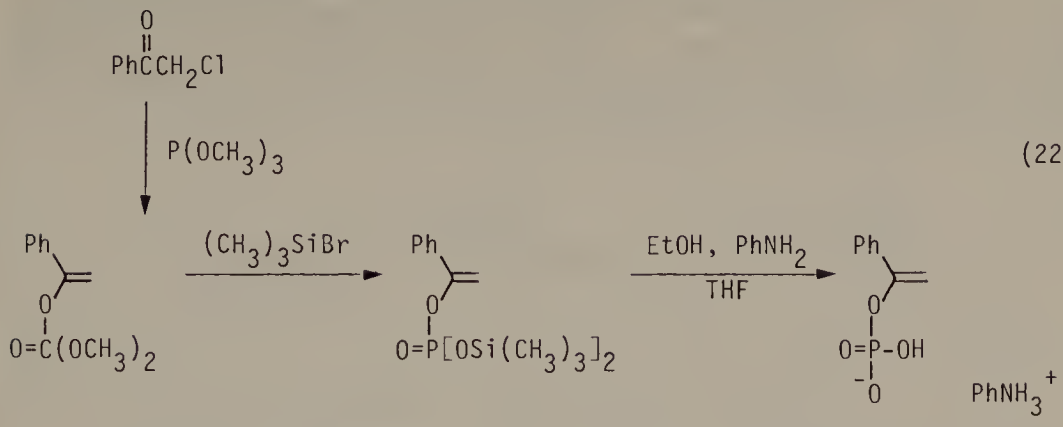
bis(Trimethylsilyl) hypophosphite reacts with chloroacetone to yield approximately equal amounts of 1:1 adduct (37,6%) and Perkow reaction product (41,5%) [44].

Phosphoenol pyruvate possesses a high energy phosphate bond, [$\Delta G^\circ = -14.8$ kcal/mole on hydrolysis]. It can be prepared in an one pot reaction sequence (Eq. 22.39) [45].



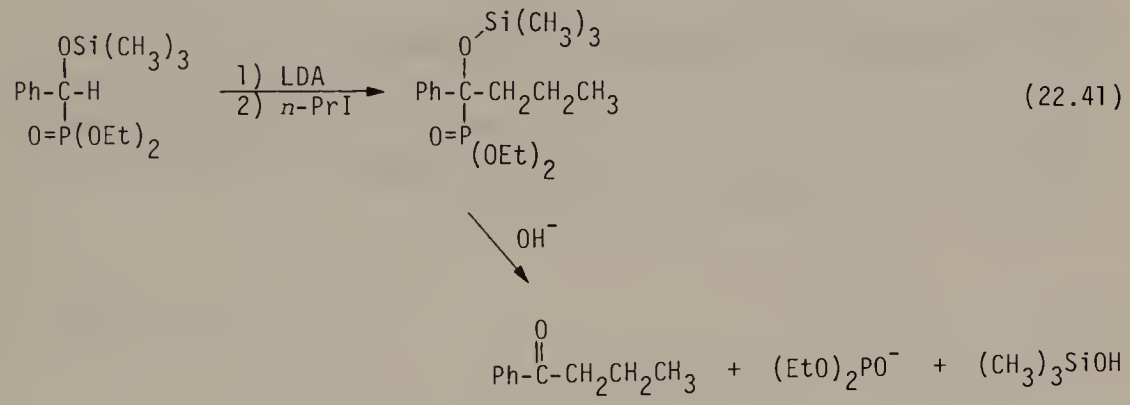
(22.39)

Enol phosphates have been prepared as outlined [46].

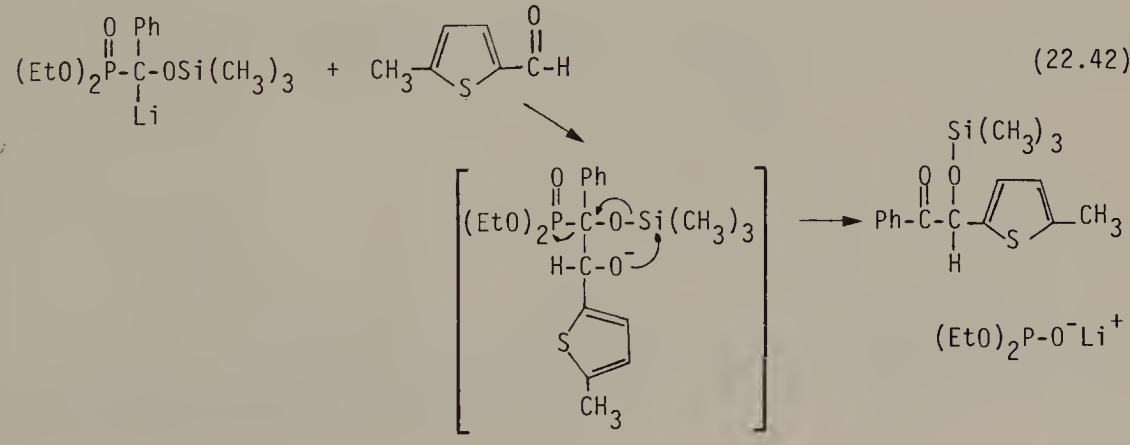


22.9 Carbon-Carbon Bond Formation/Acyl Anion Synthons

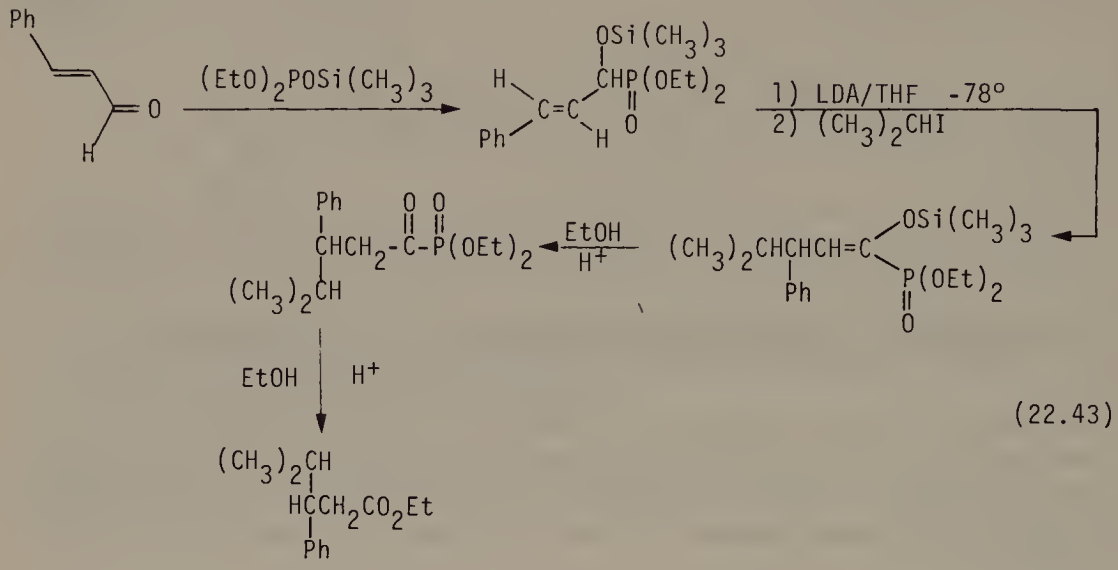
Benzaldehyde can be converted to diethyl (α-trimethylsilyloxybenzyl) phosphonates (Eq. 22.13), which can be metallated with LDA. This anion reacts with primary alkyl iodides or bromides to yield diethyl [α-alkyl-α-trimethylsilyloxybenzyl] phosphonates. Treatment of these with base gives alkyl aryl ketones [37, 47].



Diethyl [α-lithio-α-trimethylsilyloxybenzyl] phosphonate also reacts with ketones or aldehydes to yield α-hydroxy ketones [48, 49].



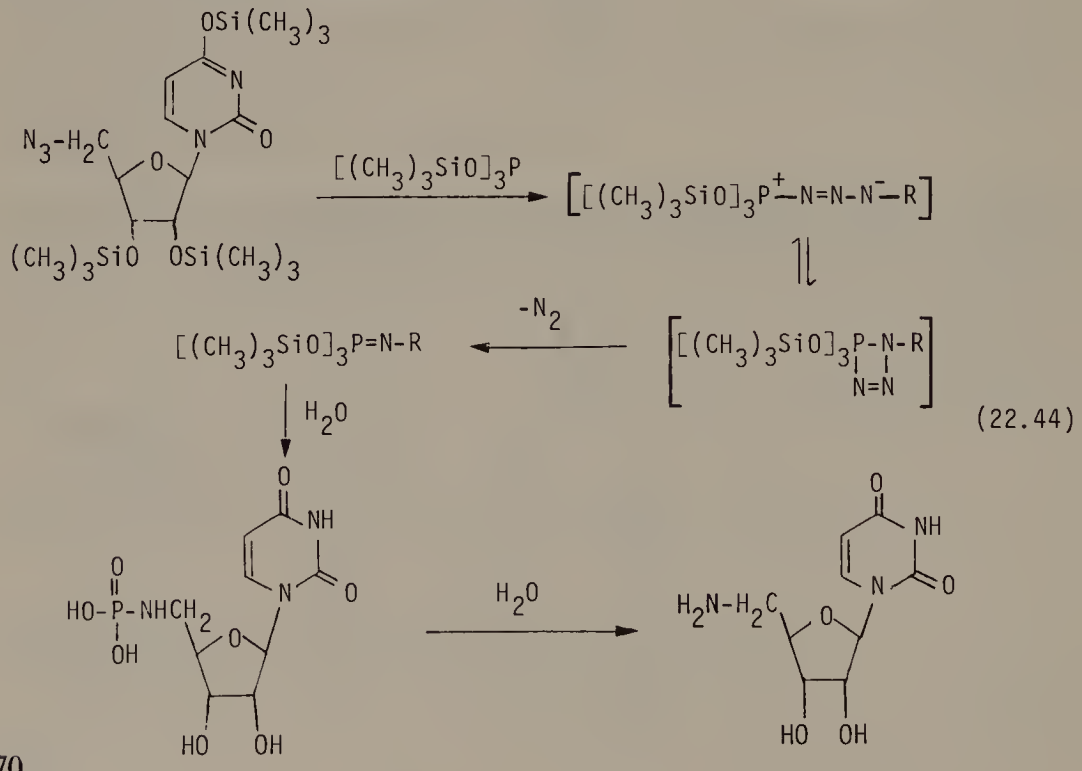
Diethyl trimethylsilyl phosphite reacts with α,β-unsaturated aldehydes to yield 1,2-adducts. Metallation of these yields allylic carbanions which react regiospecifically with primary secondary alkyl iodides at the γ-position to yield diethyl (2-alkyl-1-trimethylsilyloxyvinyl) phosphonates. These undergo acidic hydrolysis to yield esters [50].



(22.43)

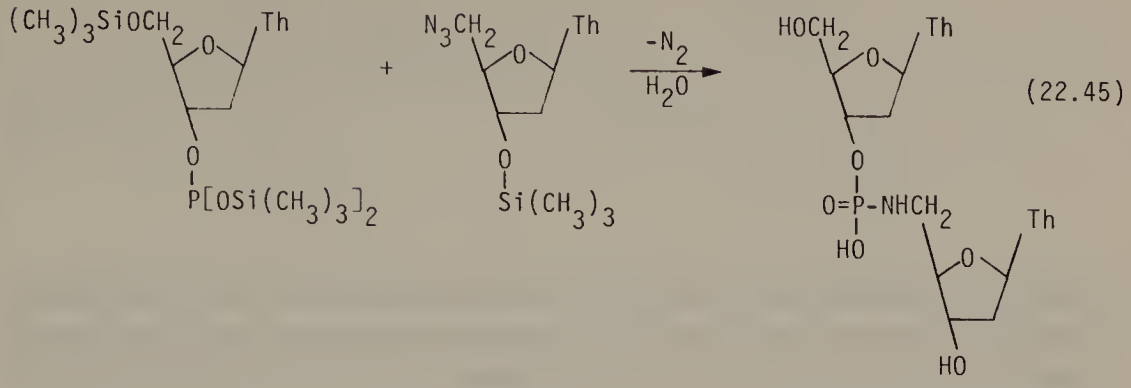
22.10. Oxidation of Trimethylsilyl Phosphites

tris(Trimethylsilyl) phosphite reduces 5′-azido-5′-deoxyribonucleosides to 5′-amino-5′-deoxyribonucleosides as outlined below. The phosphite is oxidized to a phosphoramidate in the process [51].



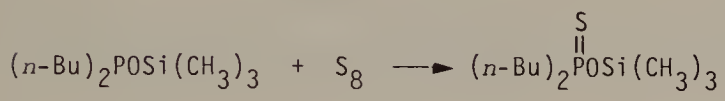
(22.44)

This procedure has been used to prepare 3′,5′-dinucleoside phosphoramidates.



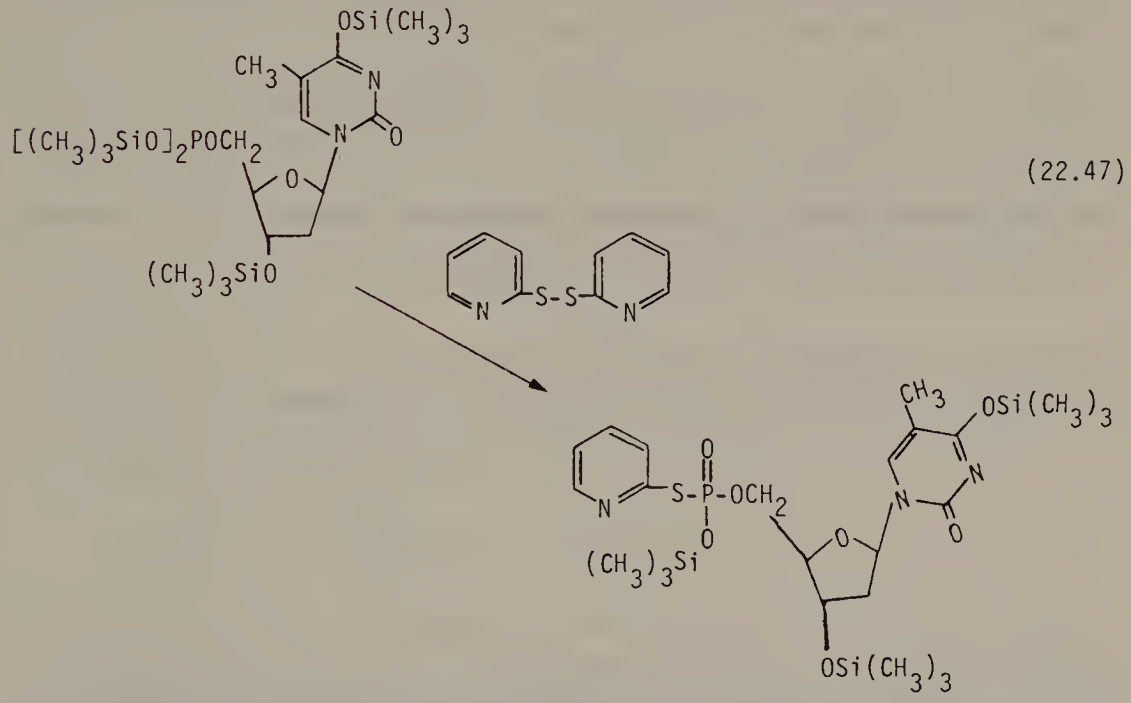
(22.45)

Trimethylsilyl phosphinites react with sulfur to yield trimethylsilylthiophosphinates [4]. *bis*(Trimethylsilyl) phenyl phosphonate reacts with sulfur to yield O,O-*bis*(trimethylsilyl) phenyl phosphonothioate [52, 53].



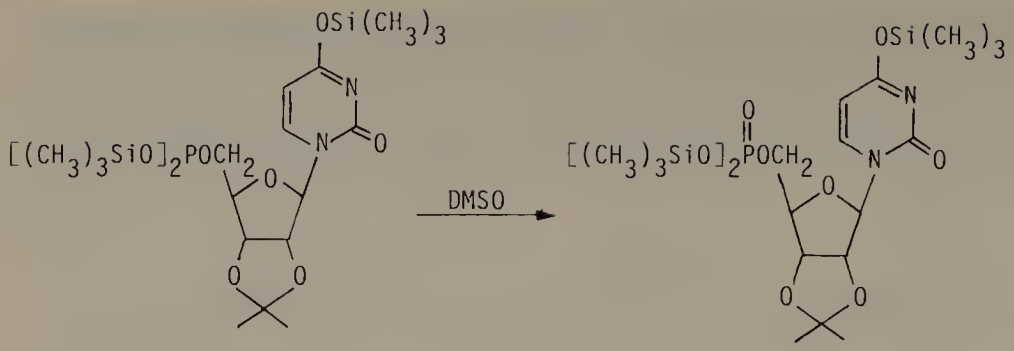
(22.46)

In a similar manner, alkyl *bis*(trimethylsilyl) phosphites react with diaryl disulfides to yield arylthiotrimethylsilanes and alkyl S-aryl trimethylsilyl thiophosphates. This methodology has proved useful for the oxidation of nucleoside phosphites [53, 54, 74].



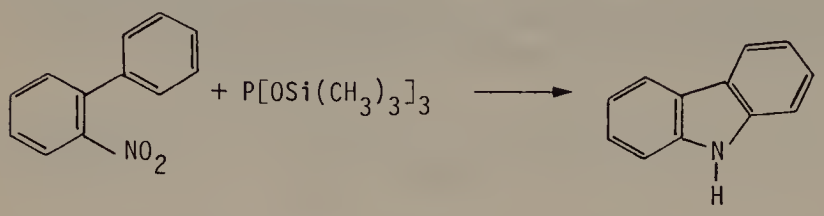
(22.47)

DMSO also oxidizes *bis*-(trimethylsilyl) nucleoside phosphites to *bis*-(trimethylsilyl) nucleoside phosphates [75].



(22.48)

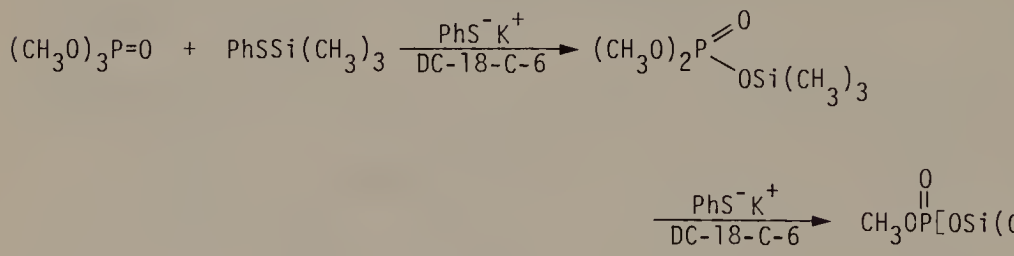
Likewise *tris*(trimethylsilyl phosphite is oxidized by methyl phenyl sulfoxide to *tris*(trimethylsilyl) phosphate [75]. On the other hand, *tris*(trimethylsilyl) phosphite reacts at 130° with 2-nitrobiphenyl to yield carbazole and *tris*-(trimethylsilyl) phosphate.



(22.49)

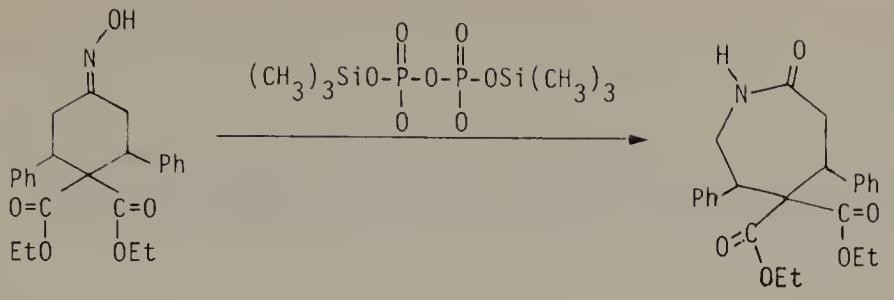
22.11 Miscellaneous Reactions

Under nucleophilic catalysis by potassium phenylthiolate/DC-18-C-6, phenylthiotrimethylsilane reacts with trimethylphosphate to yield first dimethyl trimethylsilyl phosphate and then more slowly methyl *bis*(trimethylsilyl) phosphate and finally *tris*(trimethylsilyl) phosphate. The half-life for the first exchange is significantly shorter than that for the second which in turn is shorter than the third ($t_1 = 7.5$ min, $t_2 = 55$ min, and $t_3 = 455$ min at 30 °C). This difference permits isolation of intermediate products [55]. TMS-Br, while effective for such reactions, is not selective.



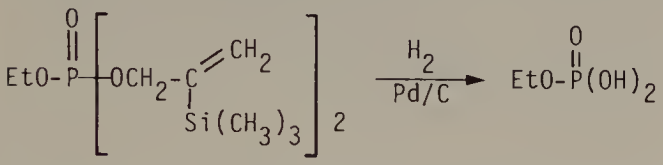
(22.50)

Trimethylsilyl polyphosphate may be prepared by addition of P_2O_5 to hexamethyldisiloxane. Unlike polyphosphoric acid, it has good solvent properties and will dissolve a number of organic substrates at room temperature [56]. It has been utilized for the Beckman rearrangement to convert oximes to amides [56, 57].



(22.51)

2-Trimethylsilylprop-2-enyl esters of phosphoric acid can be used as a protecting group since they are relatively stable to acidic and basic conditions [58]. They are, however, removed by hydrogenolysis over Pd/C or by treatment with tetraethylammonium fluoride.

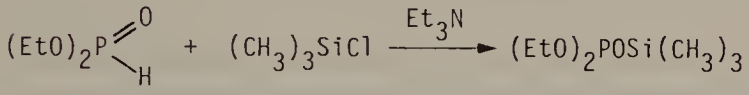


(22.52)

They may be prepared by reaction of 2-trimethylsilylprop-2-enol [59] with phosphorodichloridates in pyridine.

22.12 Preparations

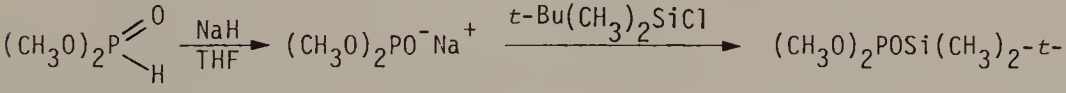
Diethyl trimethylsilyl phosphite has been prepared by reaction of diethylphosphite with TMS-Cl and triethylamine [60, 61].



(22.53)

Dimethyl trimethylsilyl phosphite [62], and dimethyl triethylsilyl phosphite [62] have been prepared by analogous reactions [62]. Dimethyl trimethylsilyl phosphite has been prepared by reaction of dimethyl phosphite with hexamethyldisilazane [63].

Dialkyl phosphites also react with dialkylaminotrialkylsilanes to yield dialkyl trialkylsilyl phosphites [64]. Dimethyl *t*-butyldimethylsilyl phosphite has been prepared by reaction of dimethylphosphite with sodium hydride and *t*-butyldimethylchlorosilane [15].



(22.54)

Detailed instructions for the preparation of *tris*(trimethylsilyl) phosphite by reaction of TMS-Cl with phosphorous acid and triethylamine have been published [41].

$$H\text{-}P(OH)_2 \xrightarrow[Et_3N]{(CH_3)_3SiCl} [(CH_3)_3SiO]_3P \qquad (22.55)$$

bis(Trimethylsilyl) hypophosphite has been prepared by reaction of hypophosphorous acid with TMS-Cl and trimethylamine or with *bis*(trimethylsilyl)acetamide. NOTE: It is inflammable and burns in air [31].

$$H_2POH + CH_3\text{-}C(OSi(CH_3)_3)=NSi(CH_3)_3 \longrightarrow HP[OSi(CH_3)_3]_2 \qquad (22.56)$$

bis(Trimethylsilyl) hypophosphite can also be prepared by reaction of hypophosphorous acid with two equivalents of dimethylaminotrimethylsilane [65].

bis(Trimethylsilyl) phenyl phosphinate has been prepared by reaction of phenyl phosphonous acid with hexamethyldisilazane [30].

$$Ph\text{-}P(=O)(OH)H + [(CH_3)_3Si]_2NH \longrightarrow PhP[OSi(CH_3)_3]_2 \qquad (22.57)$$

Phenyl phosphonous acid also reacts with triethylsilane under catalysis by nickel to yield *bis*(triethylsilyl) phenyl phosphinate [66].

Trimethylsilyl N,N,N′,N′-tetraethylphosphorodiamidite has been prepared by reaction of magnesium bromide N,N,N′,N′-tetraethylphosphorodiamidite with TMS-Cl [67].

$$[Et_2N]_2PO^-MgBr^+ + (CH_3)_3SiCl \longrightarrow [Et_3N]_2POSi(CH_3)_3 \qquad (22.58)$$

Reaction of N,N,N′,N′-tetramethylphosphorodiamido chloride with sodium triethylsilanoate yields triethylsilyl N,N,N′,N′-tetramethylphosphorodiamidite [15].

$$Et_3SiOH \xrightarrow{NaH} Et_3SiO^-Na^+ + [(CH_3)_2N]_2PCl \longrightarrow Et_3SiOP[N(CH_3)_2]_2 \qquad (22.59)$$

Secondary phosphine oxides react with alkali metals in aprotic solvents with evolution of hydrogen. The anion thus formed reacts with TMS-Cl to yield trimethylsilyl phosphinites [4].

$$Ph_2P(=O)H \xrightarrow{K} Ph_2PO^-K^+ \xrightarrow{(CH_3)_3SiCl} Ph_2POSi(CH_3)_3 \qquad (22.60)$$

tris(Trimethylsilyl) phosphate can be prepared by reaction of TMS-Cl with phosphoric acid. Triethylbromosilane also reacts with triethylphosphate to yield ethyl bromide and *tris*(triethylsilyl) phosphate [68].

tris(Trimethylsilyl) phosphine undergoes oxidation by nitrogen dioxide to yield *tris*(trimethylsilyl) phosphate [69].

$$[(CH_3)_3Si]_3P + NO_2 \longrightarrow [(CH_3)_3SiO]_3P{=}O \qquad (22.61)$$

Silyl phosphines [70] have been prepared by reaction of alkali metal phosphides and chlorosilanes [69–71].

$$PhPK_2 + 2(CH_3)_3SiCl \longrightarrow PhP[Si(CH_3)_3]_2 \qquad (22.62)$$

Trimethylsilyl diphenyl phosphine has been prepared by Wurtz type reaction of diphenylphosphinous chloride, TMS-Cl and sodium [72] or magnesium [7] in ether solvents.

tris(Trimethylsilyl) phosphine, *t*-butyl *bis*(trimethylsilyl) phosphine and di-*t*-butyl trimethylsilyl phosphine have been prepared by Wurtz type reaction of TMS-Cl and phosphorous trichloride, *t*-butyl dichloro phosphine or di-*t*-butyl phosphinous chloride respectively with magnesium in THF [8].

$$(CH_3)_3CPCl_2 + 2(CH_3)_3SiCl \xrightarrow{Mg/THF} (CH_3)_3CP[Si(CH_3)_3]_2 \qquad (22.63)$$

Experimental details of the reaction of aldehydes with TMS-Cl and trialkyl phosphites have been published [15, 49].

$$Ph\text{-}\overset{\overset{O}{\|}}{C}\text{-}H + (EtO)_3P + (CH_3)_3SiCl \longrightarrow Ph\text{-}\overset{\overset{OSi(CH_3)_3}{|}}{\underset{\underset{O=P(OEt)_2}{|}}{C}}\text{-}H \qquad (22.64)$$

References

1. Voronkov, M.G., Skorik, Y.I.: Zh. Obsh. Khim. *35,* 106 (1965)
2. Hata, T., Sekine, M., Kagawa, N.: Chem. Lett. 635 (1975)
3. Rosenthal, A.F., Vargas, L.A., Isaacson, Y.A., Bittman, R.: Tetrahedron Lett. 977 (1975)
4. Issleib, K., Walther, B.: Angew. Chem. Int. Ed. *6,* 88 (1967)
5. Rosenthal, A.F., Gringauz, A., Vargas, L.A.: J. Chem. Soc. Chem. Commun. 384 (1976)
6. Dahl, O.: Acta. Chem. Scand. *B, 30,* 799 (1976)
7. Schumann, H., duMont, W.W.: Chem. Ber. *108,* 2261 (1975)
8. Schumann, H., Rösch, L.: Chem. Ber. *107,* 854 (1974)
9. Orlov, N.F., Kaufman, B.L.: Zh. Obsh. Khim. *38,* 1842 (1968)
10. Yamaguchi, Y., Kamimura, T., Hata, T.: J. Am. Chem. Soc. *102,* 4534 (1980)
11. Becher, H.J., Fenske, D., Langer, E.: Chem. Ber. *106,* 177 (1973)
12. Kunzek, H., Braun, M., Nesener, E., Rühlmann, K.: J. Organometal. Chem. *49,* 149 (1973)
13. Fenske, D., Langer, E., Heymann, M., Becher, H.J.: Chem. Ber. *109,* 359 (1976)
14. Birum, G.H., Richardson, G.A.: U.S. Patent 3,113,139 (1963)
15. Evans, D.A., Hurst, K.M., Takacs, J.M.: J. Am. Chem. Soc. *100,* 3467 (1978)
16. Brook, A.G.: Accts. Chem. Res. *7,* 77 (1974)

17. Novikova, Z.S., Mashoshina, S.N., Sapozhnikova, T.A., Lutsenko, I.F.: Zh. Obsh. Khim. *41,* 2622 (1971)
18. Nesterov, L.V., Krepysheva, N.E., Sabirova, R.A., Romanova, G.N.: Zh. Obsh. Khim. *41,* 2449 (1971)
19. Novikova, Z.S., Lutsenko, I.F.: Zh. Obsh. Khim. *40,* 2129 (1970)
20. Pudovik, A.N., Kibardin, A.M., Pashinkin, A.P., Sudarev, Y.I., Gazizov, T.K.: Zh. Obsh. Khim. *44,* 522 (1974)
21. Gazizov, T.K., Kibardin, A.M., Pashinkin, A.P., Sudarev, Y.I., Pudovik, A.N.: Zh. Obsh. Khim. *43,* 679 (1973)
22. Ramirez, F.: Pure and Applied Chem. *9,* 337 (1964)
23. Ramirez, F., Desai, N.B.: J. Am. Chem. Soc. *85,* 3252 (1963)
24. Hata, T., Sekine, M., Ishikawa, N.: Chem. Lett. 645 (1975)
25. Pudovik, A.N., Gazizov, T.K., Kibardin, A.M.: Zh. Obsh. Khim. *44,* 1210 (1974)
26. Kibardin, A.M., Gazizov, T.K., Pudovik, A.N.: Zh. Obsh. Khim. *45,* 1982 (1975)
27. Pudovik, A.N., Gazizov, T.K., Sudarev, Y.I.: Zh. Obsh. Khim. *43,* 2086 (1973)
28. Pudovik, A.N., Gazizov, T.K., Sudarev, Y.I.: Zh. Obsh. Khim. *44,* 951
29. Sekine, M., Yamamoto, I., Hashizume, A., Hata, T.: Chem. Lett. 485 (1977)
30. Lebedev, E.P., Pudovik, A.N., Tsyganov, B.N., Nazmutdinov, R.Y., Romanov, G.V.: Zh. Obsh. Khim. *47,* 765 (1977)
31. Hata, T., Mori, H., Sekine, M.: Chem. Lett. 1431 (1977)
32. Pudovik, A.N., Batyeva, E.S., Al'fonsov, V.A.: Zh. Obsh. Khim. *45,* 939 (1975)
33. Pudovik, A.N., Batyeva, E.S., Zamaletdinova, G.U.: Zh. Obsh. Khim. *42,* 2577 (1972)
34. Konovalova, I.V., Burnaeva, L.A., Saifullina, N.S., Pudovik, A.N.: Zh. Obsh. Khim. *46,* 18 (1976)
35. Pudovik, A.N., Romanov, G.V., Nazmutdinov, R.Y., Konovalova, I.V.: Zh. Obsh. Khim. *43,* 678 (1973)
36. Pudovik, A.N., Romanov, G.V., Nazmutdinov, R.Y.: Zh. Obsh. Khim. *45,* 1896 (1975)
37. Evans, D.A., Hurst, K.M., Truesdale, L.K., Takacs, J.M.: Tetrahedron Lett. 2495 (1977)
38. Pudovik, A.N., Batyeva, E.S., Zamaletdinova, G.U.: Zh. Obsh. Khim. *43,* 947 (1973)
39. Pudovik, A.N., Romanov, G.V., Nazmutdinov, R.Y.: Zh. Obsh. Khim. *47,* 555 (1977)
40. Voronkov, M.G., Marmur, L.Z., Dolgov, O.D., Pestunovich, V.A., Pokrovskii, E.I., Popel, Y.I.: Zh. Obsh. Khim. *41,* 1987 (1971)
41. Sekine, M., Okimoto, K., Yamada, K., Hata, T.: J. Org. Chem. *46,* 2097 (1981)
42. Sekine, M., Okimoto, K., Hata, T.: J. Am. Chem. Soc. *100,* 1001 (1978)
43. Hata, T., Sekine, M., Kagawa, N.: Chem. Lett. 635 (1975)
44. Pudovik, A.N., Romanov, G.V., Nazmutdinov, R.Y.: Zh. Obsh. Khim. *44,* 221 (1974)
45. Sekine, M., Futatsugi, T., Yamada, K., Hata, T.: Tetrahedron Lett. 371 (1980)
46. Hata, T., Yamada, K., Futatsugi, T., Sekine, M.: Synthesis, 189 (1979)
47. Hata, T., Hashizume, A., Nakajima, M., Sekine, M.: Tetrahedron Lett. 363 (1978)
48. Koenigkramer, R.E., Zimmer, H.: Tetrahedron Lett. 1017 (1980)
49. Koenigkramer, R.E., Zimmer, H.: J. Org. Chem. *45,* 3994 (1980)
50. Hata, T., Nakajima, M., Sekine, M.: Tetrahedron Lett. 2047 (1979)
51. Hata, T., Yamamoto, I., Sekine, M.: Chem. Lett. 601 (1976)
52. Orlov, N.F., Belokrinitskii, M.A.: Zh. Obsh. Khim. *40,* 504 (1970)
53. Hata, T., Sekine, M.: Tetrahedron Lett. 3943 (1974)

54. Sekine, M., Hata, T.: Tetrahedron Lett. 1711 (1975)
55. Takeuchi, Y., Demachi, Y., Yoshii, E.: Tetrahedron Lett. 1231 (1979)
56. Imamoto, T., Yokoyama, H., Yokoyama, M.: Tetrahedron Lett. 1803 (1981)
57. Cava, M.P., Lakshmikanthan, M.V., Mitchell, M.J.: J. Org. Chem. *34,* 2665 (1969)
58. Chan, T.K., DiStefano, M.: J. Chem. Soc. Chem. Commun. 761 (1978)
59. Chan, T.H., Mychajlowskij, W., Ong, B.S., Harpp, D.N.: J. Org. Chem. *43,* 1526 (1978)
60. Orlov, N.F., Kaufman, B.L., Sukhi, L., Slesar, L.N., Sudakova, E.V.: Khim. Prakt. Primen. Kreminorg. Soedin, Tr. Soveshch. 111 (1966) CA *72,* 217384 (1970)
61. Orlov, N.F., Sudakova, E.V.: Zh. Obsh. Khim. *39,* 222 (1969)
62. Nesterov, L.V., Krepysheva, N.E., Sabirova, R.A., Romanova, G.N.: Zh. Obsh. Khim. *41,* 2449 (1971)
63. Chevnyshev, E.A., Bugerenko, E.F., Akat'eva, A.S., Naumov, A.D.: Zh. Obsh. Khim. *45,* 242 (1975)
64. Pudovik, M.A., Medvedeva, M.D., Pudovik, A.N.: Zh. Obsh. Khim. *45,* 700 (1975)
65. Voronkov, M.G., Marmur, L.Z., Dolgov, O.N., Pestunovich, V.A., Pokrovskii, E.I., Popel, Y.I.: Zh. Obsh. Khim. *41,* 1987 (1971)
66. Orlov, N.F., Belokrinitskii, M.A.: Zh. Obsh. Khim. *40,* 504 (1970)
67. Pudovik, A.N., Batyeva, E.S., Al'fonsov, V.A.: Zh. Obsh. Khim. *45,* 248 (1975)
68. Voronkov, M.G., Zgonnik, V.N.: Zh. Obsh. Khim. *27,* 1483 (1957)
69. Parshall, G.W., Lindsey, Jr., R.V.: J. Am. Chem. Soc. *81,* 6273 (1959)
70. For a review of the older literature concerning silyl phosphines see Fritz, G.: Angew. Chem. Int. Ed. *5,* 53 (1966)
71. Baudler, M., Zarkadas, A.: Chem. Ber. *106,* 3970 (1973)
72. Kuchen, W., Buchwald, H.: Chem. Ber. *92,* 227 (1959)
73. Deroo, P.W., Rosenthal, A.F., Isaacson, Y.A., Vargas, L.A., Bittman, R.: Chem. and Phys. of Lipids, *16,* 60 (1976)
74. Hata, T., Sekine, M.: J. Am. Chem. Soc. *96,* 7363 (1974)
75. Sekine, M., Yamagata, H., Hata, T.: Tetrahedron Lett. 375 (1979)

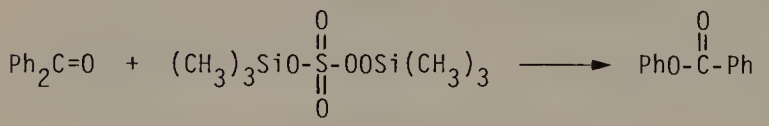
23 Silyl Oxidants

23.1 Introduction

While there are numerous silyl reduction reactions, there are just a few silicon based oxidizing reagents. Oxidation of silyl enol ethers and the modification of lead tetraacetate by TMS-N_3 have been previously considered.

23.2 *bis*(Trimethylsilyl) monoperoxysulfate

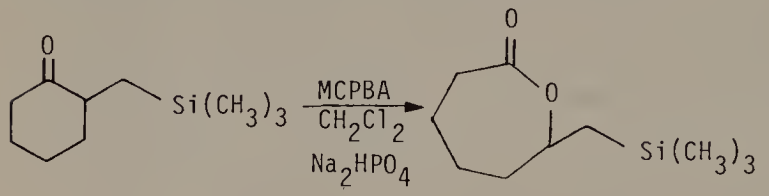
bis(Trimethylsilyl) monoperoxysulfate is a silyl derivative of Caro's acid. Soluble in aprotic non-polar solvents such as methylene chloride, it has proved useful for Baeyer-Villiger oxidation of ketones to the esters [1].



(23.1)

bis(Trimethylsilyl) monoperoxysulfate is prepared by reaction of sulfur trioxide with *bis*(trimethylsilyl) peroxide.

Baeyer-Villiger oxidations of β-trimethylsilyl ketones yield esters of β-hydroxyalkyltrimethylsilanes. Migratory aptitude in Baeyer-Villiger oxidation, may be related to the propensity of the migrating group to bear positive charge. The 2-trimethylsilylethyl group has a migratory aptitude between that of tertiary and secondary alkyl groups [2].



(23.2)

23.3 *bis*(Trimethylsilyl)peroxide and *t*-Butyl Trimethylsilyl Peroxide

bis(Trimethylsilyl)peroxide might be considered to be analogous to hydrogen peroxide. It oxidizes sulfides to sulfoxides and sulfones, phosphites to phosphates and tertiary phosphines to tertiary phosphine oxides [3, 4].

$$Ph_3P + (CH_3)_3SiOOSi(CH_3)_3 \longrightarrow Ph_3P{\rightarrow}O + (CH_3)_3SiOSi(CH_3)_3 \qquad (23.3)$$

It also reacts with Grignard and organolithium reagents to yield alkoxy- or aryloxytrimethylsilanes and trimethylsilanoate [3, 4].

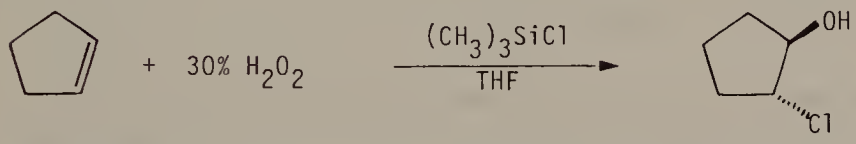
$$n\text{-BuLi} + (CH_3)_3SiOOSi(CH_3)_3 \longrightarrow n\text{-BuOSi}(CH_3)_3 + Li^+ \ ^-OSi(CH_3)_3 \qquad (23.4)$$

Si–Si and Si–H bonds have also been oxidized by *bis*(trimethylsilyl)peroxide [5]. *bis*-Trimethylsilyl)peroxide may be prepared by reaction of TMS-Cl with 90% hydrogen peroxide or by reaction of the 1,4-diazo bicyclo [2,2,2] octane/hydrogen peroxide complex with TMS-Cl [6].

t-Butyl trimethylsilyl peroxide also oxidizes tertiary phosphines to tertiary phosphine oxides and phosphites to phosphates [7]. Photolysis of *t*-butyl trimethylsilyl peroxide results in homolytic fission of the O–O bond to yield *t*-butoxy and trimethylsilyloxy radicals [8]. These are able to initiate vinyl polymerizations [9].

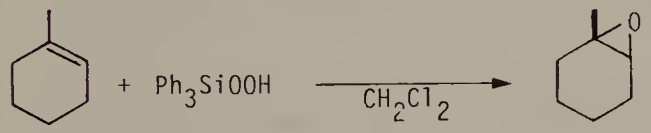
23.4 Silyl Hydroperoxides

Trimethylsilyl hydroperoxide/HCl, generated *in-situ*, by reaction of TMS-Cl with aq. hydrogen peroxide, reacts with alkenes to yield chlorohydrins. An intermediate oxirane has been proposed [10].



(23.5)

Consistent with this prosposal, triphenylsilyl hydroperoxide [11] was found to epoxidize alkenes [12].

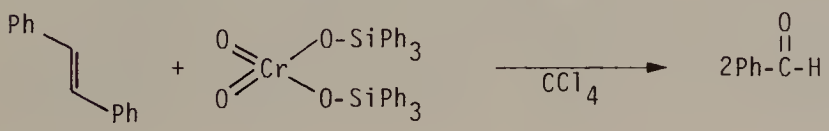


(23.6)

The older literature on silyl peroxides and hydroperoxides has been reviewed [13].

23.5 Silyl Chromate

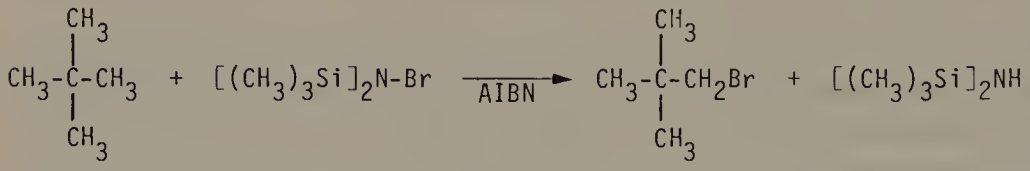
bis(Triphenylsilyl) chromate oxidizes alkenes to ketones or aldehydes in non-polar solvents such as CCl_4 or heptane [14]. It is also a useful catalyst for polymerization of ethylene [14].



(23.7)

23.6 *bis*(Silyl) Bromamine

bis(Trimethylsilyl) bromamine reacts with hydrocarbons to yield alkyl bromides and hexamethyldisilazane via a free radical mechanism. The *bis*(trimethylsilyl)aminyl radical is similar in reactivity to an alkoxy or succinimidyl radical [15].

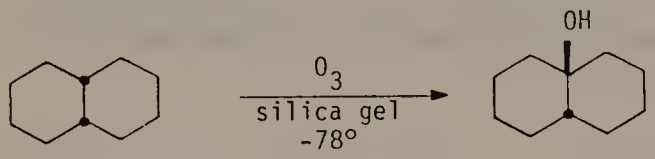


(23.8)

bis(Trimethylsilyl)bromamine has been prepared by reaction of hexamethyldisilazane with NBS [16].

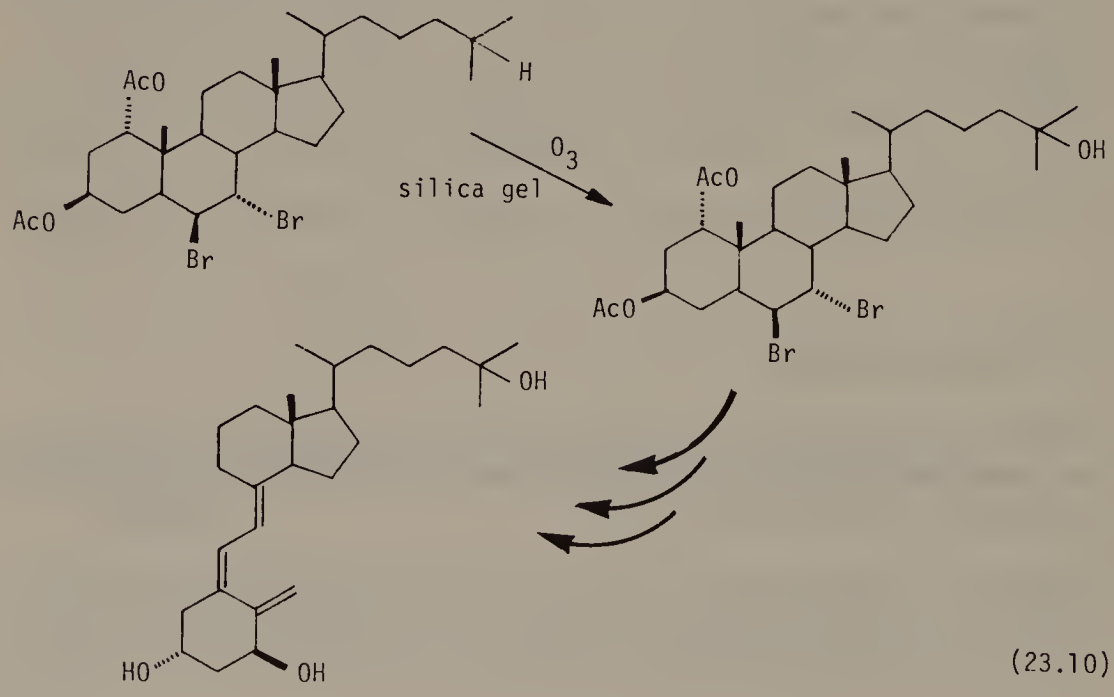
23.7 Silica Gel Mediated Oxidations

A number of selective oxidations of substrates absorbed on silica gel by ozone have been reported. Tertiary C–H bonds of hydrocarbons undergo hydroxylation by ozone under these conditions [17].



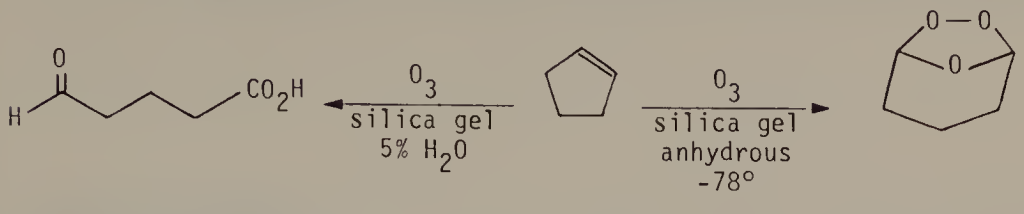
(23.9)

This procedure has been utilized in an efficient synthesis of 1-α,25-dihydroxyvitamin D_3 [18]. Treatment of steroids absorbed on silica gel with ozone results in selective hydroxylation at C-25 [19].



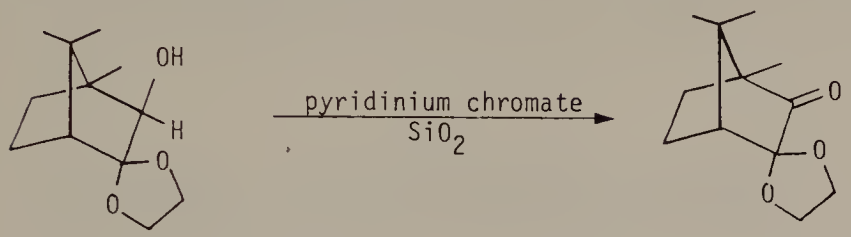
(23.10)

Primary amines are oxidized to nitro compounds under these conditions [20]. Reaction of 1,2-alkenes absorbed on silica gel with ozone results in exclusive formation of ozonides. If the silicon gel contains 5% water a 1 : 1 mixture of aldehyde and carboxylic acid is obtained [21].



(23.11)

Chromic acid adsorbed on silica gel has been found to be an effective reagent for the oxidation of primary and secondary hydroxyl groups to aldehydes and ketones, respectively [22, 23]. Pyridinium chromate adsorbed on silica gel permits selective oxidation of primary and secondary alcohols which possess acid labile functional groups, such as a cyclopropane ring or ketal protecting groups [23].



(23.12)

It would appear that much work remains to be done in the area of silyl oxidants.

References

1. Adams, W., Rodriguez, A.: J. Org. Chem. *44,* 4969 (1979)
2. Hudrlik, P.F., Hudrlik, A.M., Nagendrappa, G., Yimenu, T., Zellers, E.T., Chin, E.: J. Am. Chem. Soc. *102,* 6894 (1980)
3. Brandes, D., Blaschette, A.: J. Organometal. Chem. *49,* C6 (1973)
4. Brandes, D., Blaschette, A.: J. Organometal. Chem. *73,* 217 (1974)
5. Tamao, K., Kumada, M., Takahashi, T.: J. Organometal. Chem. *94,* 367 (1975)
6. Cookson, P.G., Davies, A.G., Fazal, N.: J. Organometal. Chem. *99,* C31 (1975)
7. Brandes, D., Blaschette, A.: J. Organometal. Chem. *99,* C33 (1975)
8. Edge, D.J., Kochi, J.K.: J. Chem. Soc. Perkin II, 182 (1973)
9. Hahn, W., Metzinger, L.: Makromol. Chem. *21,* 113 (1956)
10. Ho, T.L.: Syn. Commun. *9,* 37 (1979)
11. Dannley, R., Jalics, G.: J. Org. Chem. *30,* 2417 (1965)
12. Rebek, J., McCready, R.: Tetrahedron Lett. 4337 (1979)
13. Brandes, D., Blaschette, A.: J. Organometal. Chem. *78,* 1 (1974)
14. Baker, L.M., Carrick, W.L.: J. Org. Chem. *35,* 774 (1970)
15. Roberts, B.P., Wilson, C.: J. Chem. Soc. Chem. Commun. 752 (1978)
16. Wiberg, N., Raschig, F.: J. Organometal. Chem. *10,* 15 (1967)
17. Cohen, Z., Keinan, E., Mazur, Y., Varkony, T.H.: J. Org. Chem. *40,* 2141 (1975)
18. Cohen, Z., Keinan, E., Mazur, Y., Ulman, A.: J. Org. Chem. *41,* 2651 (1976)

19. Cohen, Z., Mazur, Y.: J. Org. Chem. *44,* 2318 (1979)
20. Keinan, E., Mazur, Y.: J. Org. Chem. *42,* 844 (1977)
21. Besten, C.E.D., Kinstle, T.H.: J. Am. Chem. Soc. *102,* 5969 (1980)
22. Santaniello, E., Ponti, F., Manzocchi, A.: Synthesis, 534 (1978)
23. Singh, R.P., Subbarao, H.N., Dev, S.: Tetrahedron, *35,* 1789 (1979)

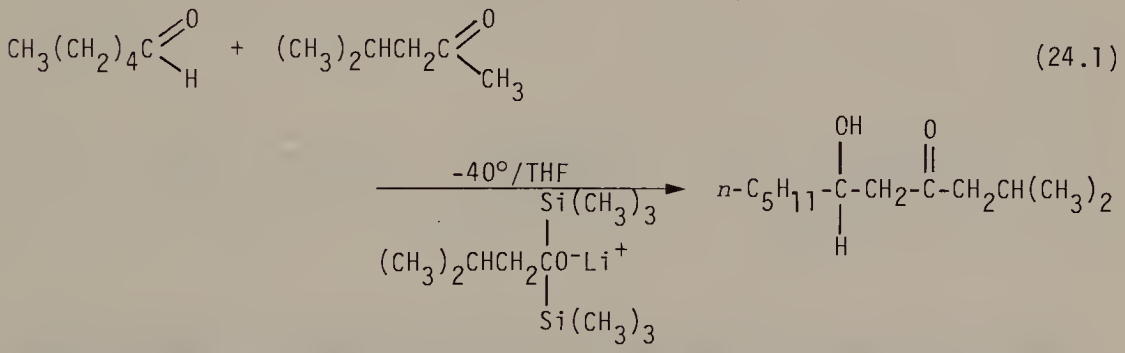
24 Silyl Bases

24.1 Introduction

Trimethylsilyl substituents affect the reactivity, solubility, and selectivity of both alkoxide and amide bases. Since this is one of the last chapters in this monograph certain examples of the use of lithium and sodium *bis*(trimethylsilyl) amide bases have been previously discussed [see: (16.11)]. This chapter is not comprehensive, rather illustrative examples will be presented.

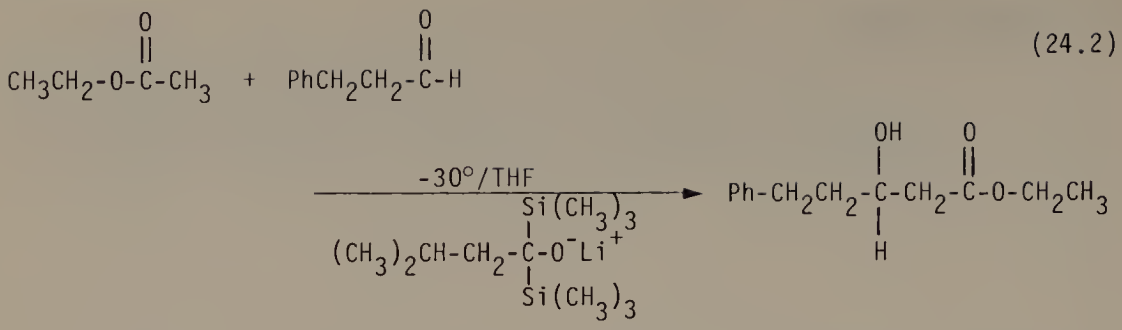
24.2 Lithium 1,1-*bis*(trimethylsilyl) alkoxides

Lithium 1,1-*bis*(trimethylsilyl) alkoxides have proved to be extremely selective bases. Their basicity is apparently intermediate between those of tertiary alkoxides and lithium amide bases. This has been attributed to the inductive electron releasing effect of the trimethylsilyl groups. Lithium 1,1-*bis*(trimethylsilyl) alkoxide bases permit the selective generation of kinetic enolate anions of methyl ketones in the presence of aldehydes. This results in the regiospecific cross-aldol reactions between methyl ketones and aldehydes [1].



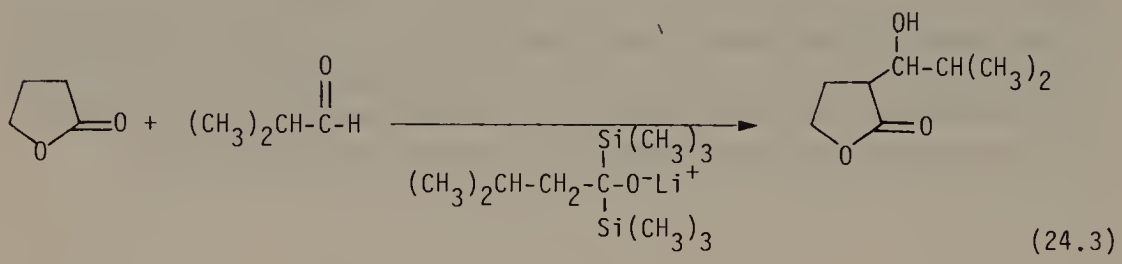
(24.1)

Lithium-1,1-*bis*(trimethylsilyl)-3-methyl-1-butoxide permits the selective generation of ester enolates in the presence of aldehydes [2]. This reaction yields β-hydroxy esters. This provides a viable alternative to the Reformatsky reaction.



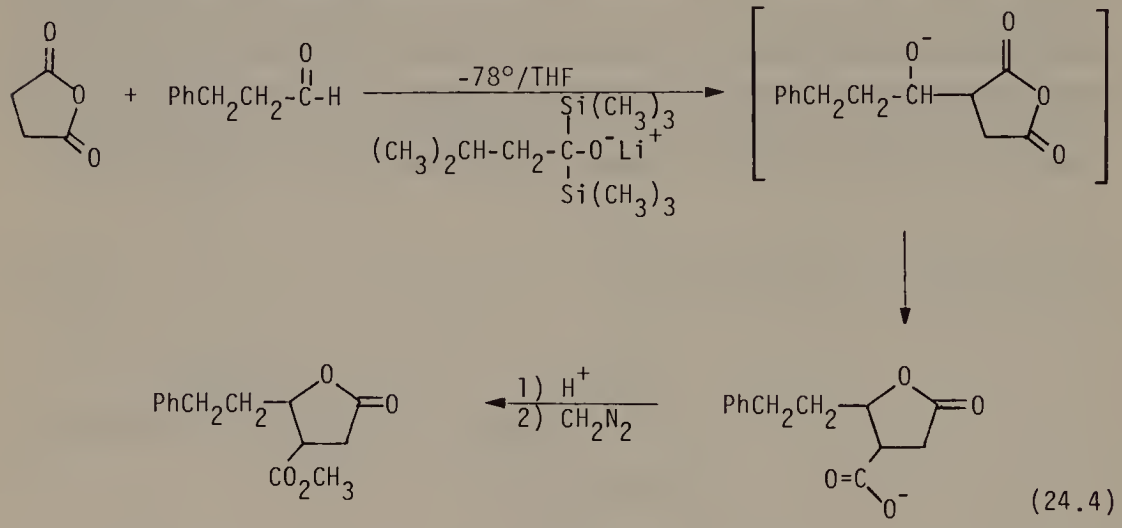
(24.2)

Lactone enolates of γ-butyrolactone and δ-valerolactone can be generated in the presence of aldehydes or ketones by use of lithium 1,1-*bis*(trimethylsilyl) alkoxide bases.



(24.3)

The enolate anion of succinic anhydride can also be generated in the presence of aldehydes or ketones by reaction with lithio-1,1-*bis*(trimethylsilyl)-3-methyl-1-butoxide. This provide a facile method to prepare β-carbomethoxy-γ-substituted-γ-butyrolactones [3].



(24.4)

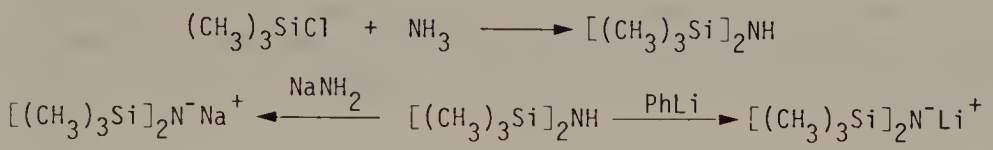
The preparation of the necessary 1,1-*bis*(trimethylsilyl) alcohols has been previously discussed in connection with dissolving metal reductions of esters (see Chapter 19).

24.3 Alkali *bis*(trimethylsilyl) Amides

The first work with sodium and lithium *bis*(trimethylsilyl) amides was reported by Wannagat and Rochow [4–9]. Both are distillable low melting solids. They are prepared as outlined below.

$[(CH_3)_3Si]_2N^-Li^+$ bp 115°/1 mm mp 70–72

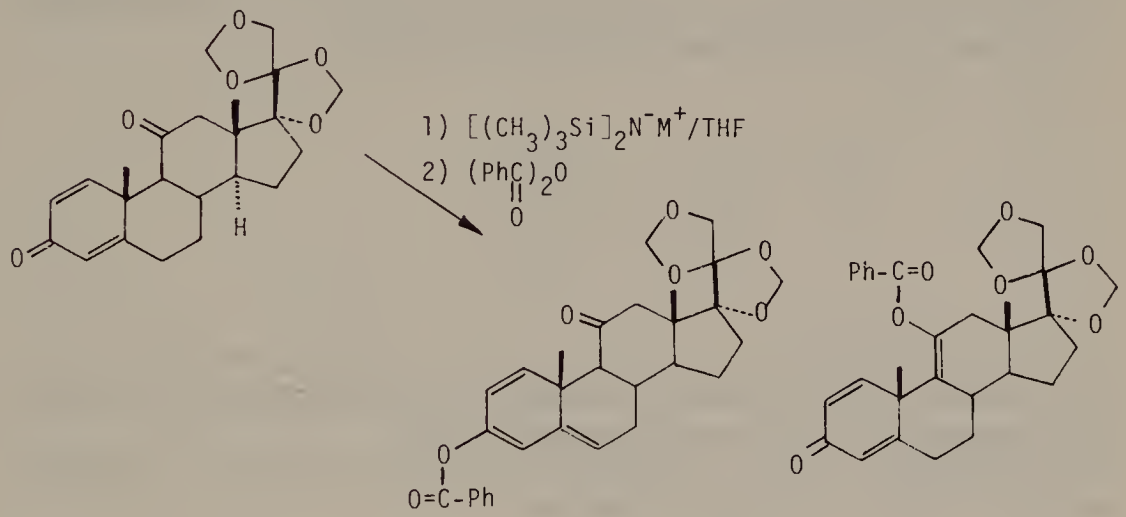
$[(CH_3)_3Si]_2N^-Na^+$ bp 170°/2 mm mp 165–167°



(24.5)

A. Ketone Enolate Anions

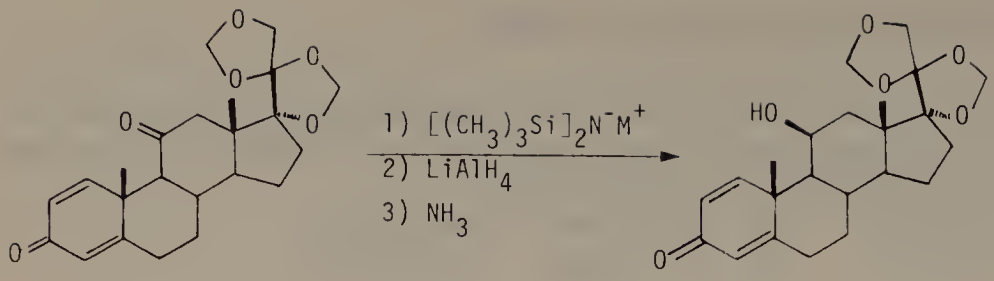
Both lithium and sodium *bis*(trimethylsilyl) amides have proved highly effective bases for the generation of kinetic enolate anions from ketones. Both are soluble in most non-polar solvents. In certain cases different ratios of enolate anions are obtained with lithium *bis*(trimethylsilyl) amide than with sodium *bis*(trimethylsilyl) amide. This results from the more facile isomerization of sodium enolates compared to lithium enolates in the presence of unionized ketone [10, 11].



Na^+	1	:	2
Li^+	100	:	0

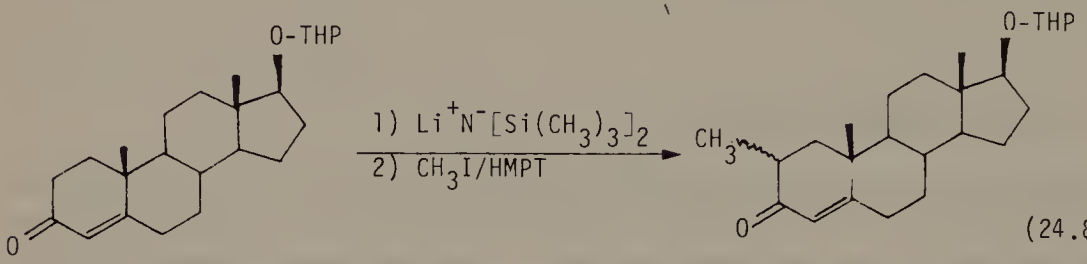
(24.6)

Alkali metal enolates of ketones generated by reaction with lithium *bis*(trimethylsilyl) amides have been utilized as ketone protecting groups during metal hydride reductions [12].



(24.7)

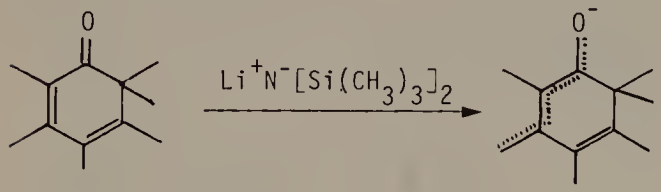
Δ^4-3-Keto steroids yield kinetic 2,4-dienolate anions on treatment with lithium *bis*(trimethylsilyl) amide. These can be alkylated by additions of methyl iodide or trapped as silyl enol ethers by addition of *t*-butyldimethylchlorosilane [13].



(24.8)

On the other hand, Δ^4-3-keto steroids undergo alkylation with potassium-*t*-butoxide in *t*-butanol and methyl iodide to give 4,4-dimethyl Δ^5-3-keto steroids. This results from alkylation of the thermodynamically more stable 3,5-dienolate anion [14].

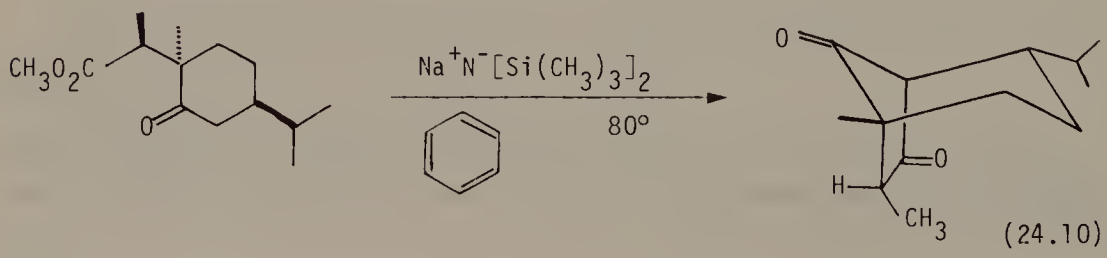
Enolate anions of hexamethyl-2,4-cyclohexadienone have been generated by treatment with lithium *bis*(trimethylsilyl) amide [15].



(24.9)

Sodium *bis*(trimethylsilyl) amide has proved a particularly effective base for intramolecular condensation reactions. This methodology has proved useful in the synthesis of sesquiterpenes [16, 17].

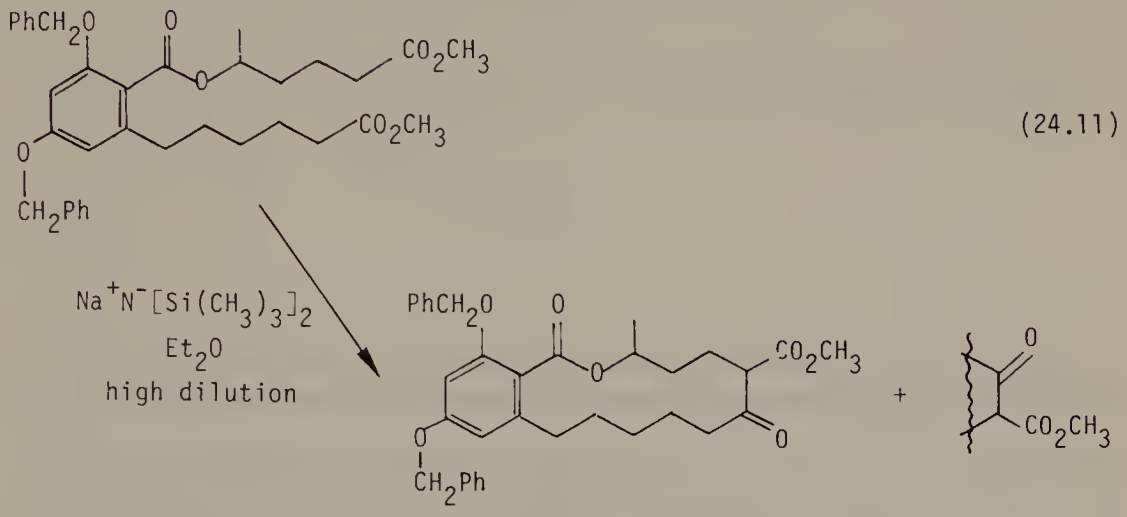
The solubility of sodium *bis*(trimethylsilyl) amide in benzene or DME is probably critical to the reaction's success.



(24.10)

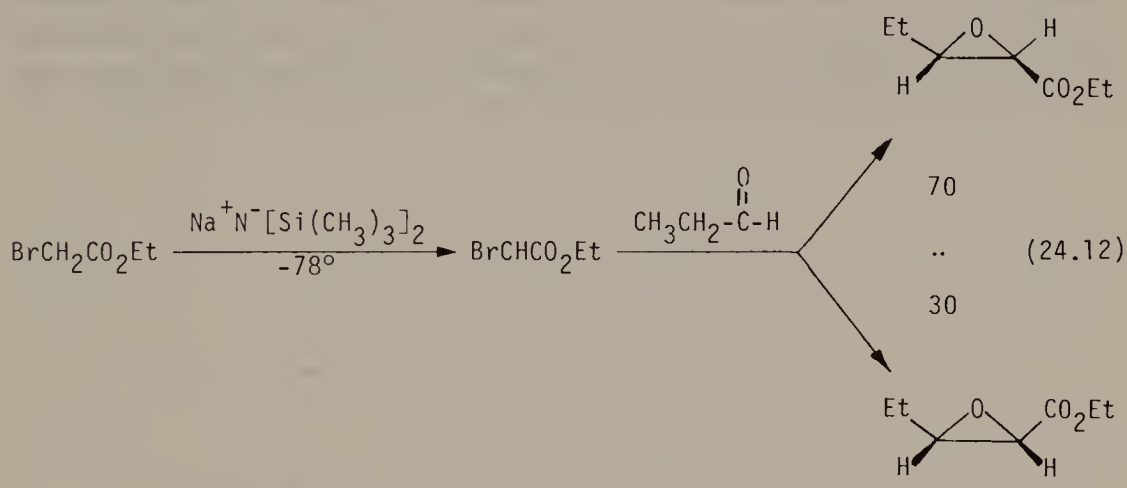
B. Ester Enolate Anions

Sodium *bis*(trimethylsilyl) amide has proved effective for the preparation of large ring ketones via Dieckman condensation. Such reactions are usually only useful for the preparation of five and six membered ring compounds [18].



(24.11)

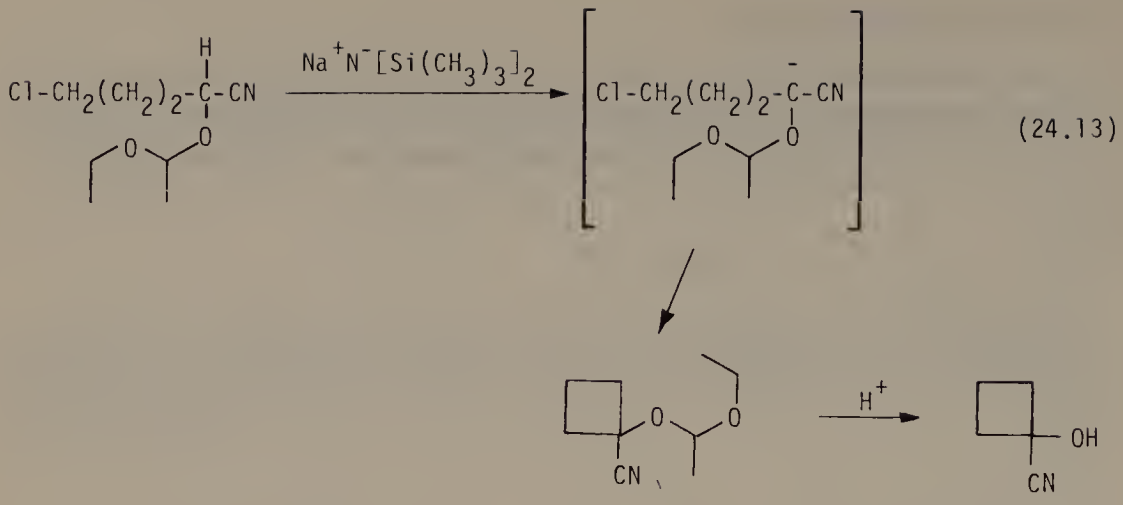
Sodium *bis*(trimethylsilyl) amide quantitatively converts α-bromo esters to the corresponding ester enolates. Addition of aldehydes or ketones to a solution of α-bromo ester enolate gives high yields of glycidic esters [18]. The Darzens condensation usually fails with aldehydes due to competing base catalyzed self-condensation reactions [19].



(24.12)

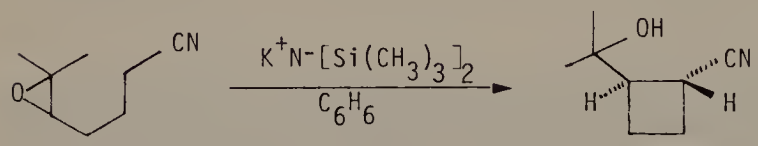
C. Cyano-Stabilized Anions

Intramolecular cyclization of protected 3-chloropropionaldehyde cyanohydrins and 4-chlorobutyraldehyde cyanohydrins by treatment with sodium *bis*(trimethylsilyl)amide yields cyanohydrins of cyclopropanones and cyclobutanones, respectively [20].



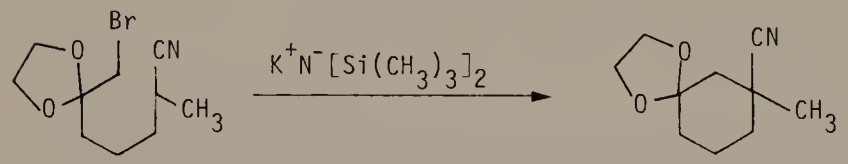
(24.13)

Epoxynitrile cyclizations leading to cyanocyclobutylcarbinols have been carried out with potassium or lithium *bis*(trimethylsilyl)amide [21].

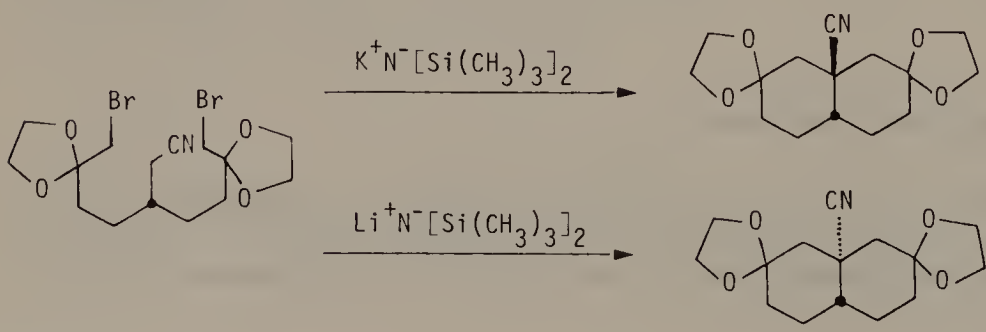


(24.14)

Intramolecular cyclization reactions of α-bromo or α-chloro ketals are successful (24.15). These involve S_n2 displacement of halide by a cyano stabilized carbanion. These anions have been generated by deprotonation with potassium or lithium *bis*(trimethylsilyl)amide in benzene [22]. The particular cation can have a dramatic effect on the stereochemistry of cyclization (24.16) [23].



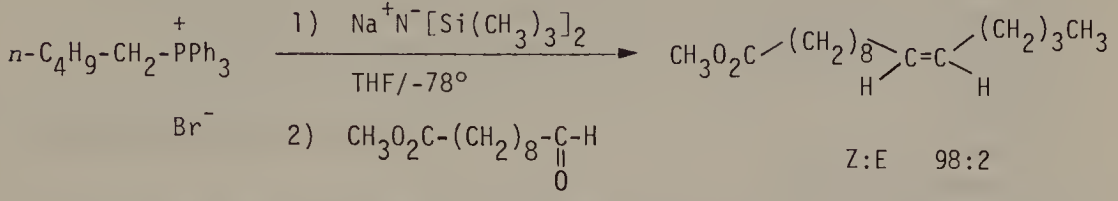
(24.15)



(24.16)

D. Ylids

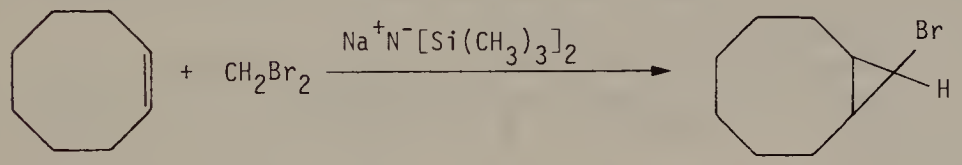
Sodium *bis*(trimethylsilyl)amide is a useful base for the generation of lithium, salt free alkylidene triphenylphosphoranes in THF or HMPT. Under these conditions, Wittig reactions with aldehydes lead stereoselectively to *Z*-alkenes [24–26].



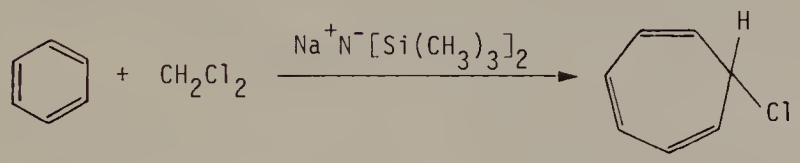
(24.17)

E. Carbenes

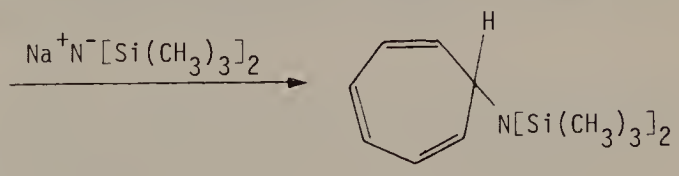
Sodium *bis*(trimethylsilyl)amide has proved useful for the *in-situ* generation of monobromo [27, 28] and monochlorocarbene [29] by deprotonation of dibromomethane and methylene chloride, respectively.



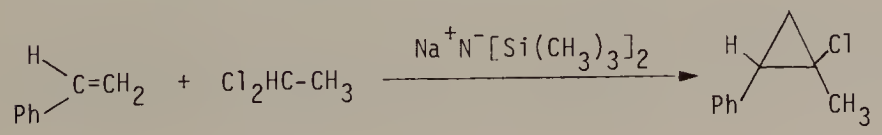
(24.18)



(24.19)



Chloromethylcarbene has been generated by deprotonation of 1,1-dichloroethane with sodium *bis*(trimethylsilyl)amide [30].



(24.20)

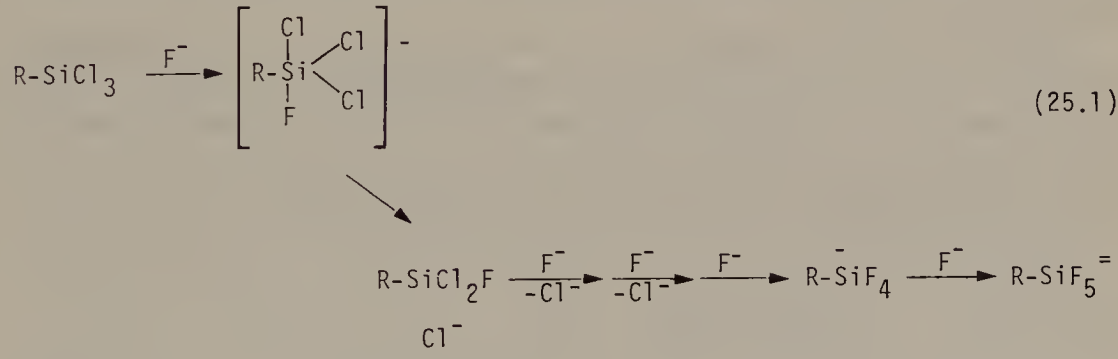
References

1. Kuwajima, I., Sato, T., Arai, M., Minami, N.: Tetrahedron Lett. 1817 (1975)
2. Kuwajima, I., Minami, N., Sato, T.: Tetrahedron Lett. 2253 (1976)
3. Minami, N., Kuwajima, I.: Tetrahedron Lett. 1423 (1977)
4. Wannagat, U., Niederprüm, H.: Chem. Ber., *94*, 1540 (1961)
5. Krüger, C.R., Rochow, E.G., Wannagat, U.: Chem. Ber. *96*, 2131 (1963)
6. Krüger, C.R., Rochow, E.G., Wannagat, U.: Chem. Ber. *96*, 2138 (1963)
7. Krüger, C.R., Rochow, E.G.: Angew. Chem. Int. Ed. *2*, 617 (1963)
8. Krüger, C.R., Rochow, E.G.: J. Organometal. Chem. *1*, 476 (1964)
9. Wannagat, U., Niederprüm, H.: Zeit für Anorg. und Allgem. Chem. *308*, 337 (1961)
10. Barton, D.H.R., Hesse, R.H., Tarzia, G., Pechet, M.M.: J. Chem. Soc. Chem. Commun. 1497 (1969)
11. Tanabe, M., Crowe, D.F.: J. Chem. Soc. Chem. Commun. 1498 (1969)
12. Barton, D.H.R., Hesse, R.H., Pechet, M.M., Wiltshire, C.: J. Chem. Soc. Chem. Commun 1017 (1972)
13. Tanabe, M., Crowe, D.F.: J. Chem. Soc. Chem. Commun. 564 (1973)
14. Woodward, R.B., Patchett, A.A., Barton, D.H.R., Ives, D.A.J., Kelly, R.B.: J. Am. Chem. Soc. *76*, 2852 (1951)
15. Hart, H., Love, G.M., Wang, I.C.: Tetrahedron Lett. 1377 (1973)
16. Piers, E., Geraghty, M.B., Kido, F., Soucy, M.: Syn. Commun. *3*, 39 (1973)
17. Piers, E., Britton, R.W., Geraghty, M.B., Keziere, R.J., Smille, R.D.: Can. J. Chem. *53*, 2827 (1975)
18. Hurd, R.M., Shah, D.M.: J. Org. Chem. *38*, 390 (1973)
19. Borch, R.F.: Tetrahedron Lett. 3761 (1972)
20. Stork, G., Depezay, J.C., d'Angelo, J.: Tetrahedron Lett. 389 (1975)
21. Stork, G., Cohen, J.F.: J. Am. Chem. Soc. *96*, 5270 (1974)
22. Stork, G., Gardner, J.O., Boeckman, Jr., R.K., Parker, K.A.: J. Am. Chem. Soc. *95*, 2014 (1973)
23. Stork, G., Boeckman, Jr., R.K.: J. Am. Chem. Soc. *95*, 2016 (1973)
24. Bestmann, H.J., Stransky, W., Vostrowsky, O.: Chem. Ber. *109*, 1694 (1976)
25. Bestmann, H.J., Brosche, T., Koschatzky, K.H., Michaelis, K., Platz, H., Vostrowsky, O.: Tetrahedron Lett. 747 (1980)
26. Schneider, M.P., Goldbach, M.: J. Am. Chem. Soc. *102*, 6114 (1980)
27. Martel, B., Hiriart, J.M.: Angew. Chem. Int. Ed. *11*, 326 (1972)
28. Martel, B., Hiriart, J.M.: Synthesis, 201 (1972)
29. Martel, B., Aly, E.: J. Organometal. Chem. *29*, 61 (1971)
30. Arora, S., Binger, P.: Synthesis, 801 (1974)

25 Silicon-Fluorine

25.1 Introduction

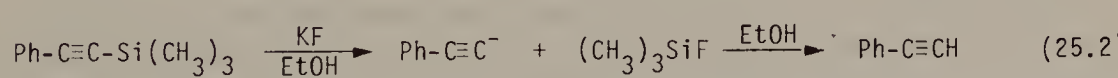
The formation of a Si–F bond (142 kcal/mol) is usually a highly exothermic process. This provides the driving force for a number of useful synthetic reactions. Since this is the last chapter, many of these have been previously considered. Reactions of fluoride ion with organosilicon compounds probably proceed by initial attack of fluoride ion on one of the empty 3d orbitals of silicon to form a pentacoordinate negatively charged species. The fate of this intermediate depends on the other groups bonded to silicon. Alkyltrichlorosilanes react with fluoride ion to form alkyl pentafluorosilicates. This results from sequential loss of chloride ion, a relatively good leaving group, and association of additional fluoride ions (see Chapter 10).



(25.1)

25.2 Generation of Carbanions and Enolate Anions

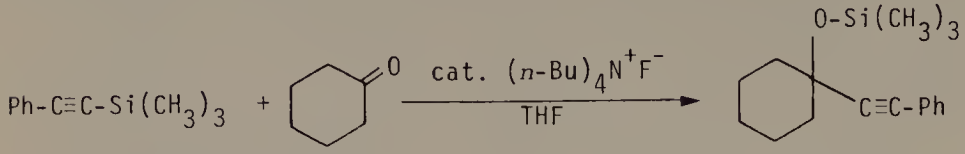
Reactions of many types of organotrimethylsilanes with fluoride ion result in formation of trimethylfluorosilane (TMS-F) and loss of the organic group as an anion. For example, 1-trimethylsilyl alkynes react with fluoride ion to yield TMS-F and relatively stable acetylide anions [1].



(25.2)

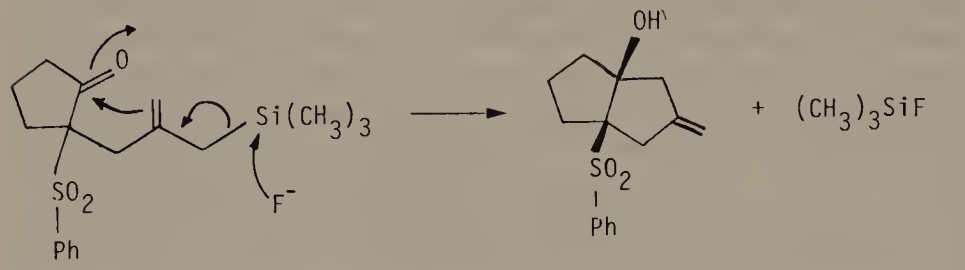
This methodology has been used to remove trimethylsilyl protecting groups from terminal acetylenes. Both potassium fluoride dihydrate in methanol [2] and TBAF in THF [3] have proved effective.

The reaction of 1-trimethylsilyl alkynes with ketones or aldehydes under nucleophilic catalysis by TBAF [4] or potassium fluoride/18-C-6 [5] to yield propargyl trimethylsilyl ethers, involves acetylide anions as intermediates (see 9.3 E).



(25.3)

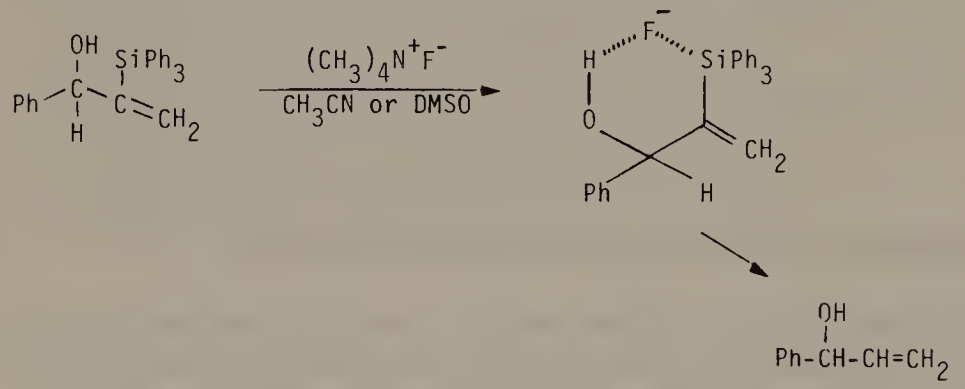
Allylic trimethylsilanes also react with fluoride ion to generate TMS-F and allylic carbanions. Fluoride ion catalyzes reaction of allylic silanes with aldehydes or ketones to yield homoallylic trimethylsilyl ethers [6–8] (see II. 2 H).



(25.4)

The reaction of aliphatic and aromatic aldehydes with propargyl trimethylsilane to yield rearranged allenic trimethylsilyl ethers is also catalyzed by TBAF [9] (see 9.3 E).

Vinylsilanes do not in general react with fluoride ion to yield fluorosilanes and vinyl carbanions [10]. However, β-hydroxy groups accelerate the rate of cleavage of Si–C sp^2 bonds by fluoride ion. A cyclic transition state has been proposed in which the fluoride ion is both hydrogen bonded to the adjacent hydroxyl group and bonded to the silyl center [10].

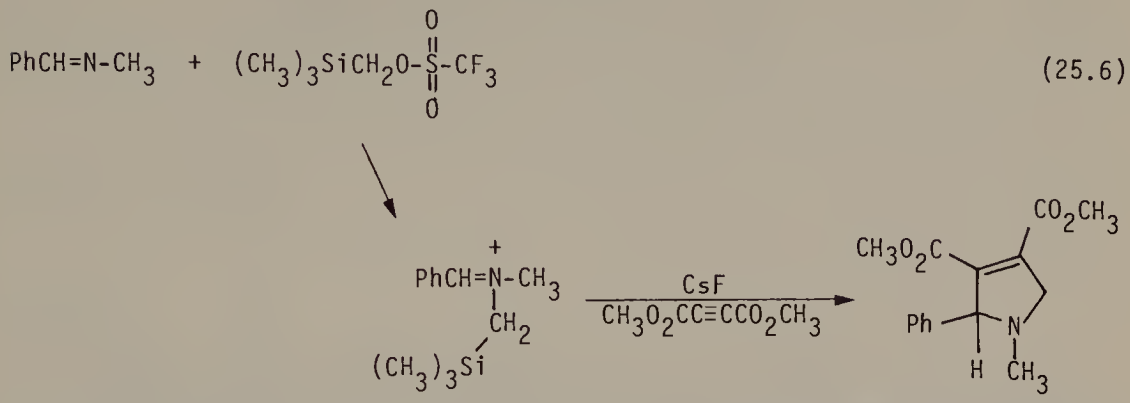


(25.5)

Adjacent hydroxy groups also accelerate the cleavage of C–Si bonds of α-silyl epoxides [11]. An oxaranyl anion has been proposed as an intermediate in this reaction. The anchimeric assistance of an adjacent hydroxyl group does not, however permit cleavage of most Si–C sp^3 bonds by fluoride ion.

Fluoride ion induced desilylation of trimethylsilylmethylsulfonium, ammonium, immonium, and phosphonium salts leads to formation of ylids [12].

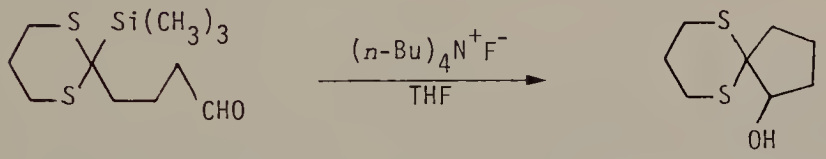
These reactions are synthetically important in cases where the molecule contains base sensitive functional groups or acidic C–H bonds. These ylids undergo their characteristic reactions. For example, the desilylation of trimethylsilylmethyl iminium salts leads to azomethine ylids which may be trapped via [3 + 2] cycloaddition reactions.



(25.6)

The necessary salts have been generated by reaction of trimethylsilylmethyl triflate with amines, imines, sulfides, or phosphines.

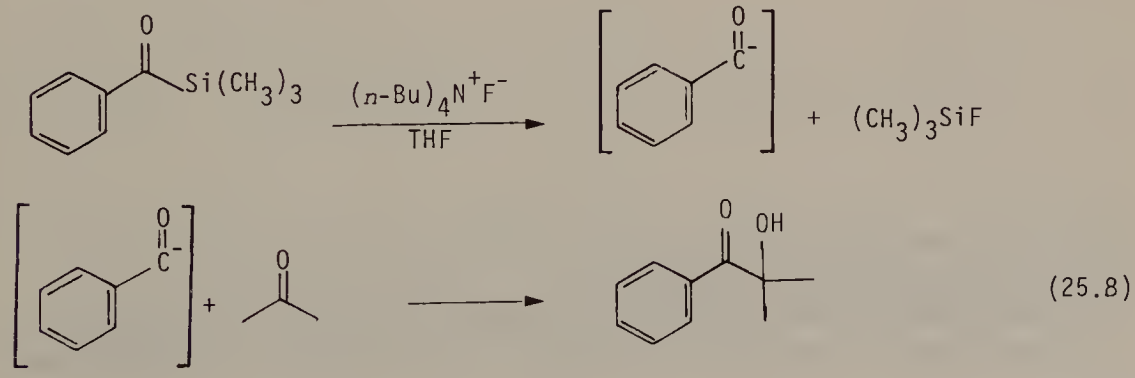
Dithianyl anions can be generated by treatment of 2-trimethylsilyl-1,3-dithianes with TBAF in THF [13]. This methodology has been used to prepare spiro alcohols by intramolecular addition of the dithianyl anion to ω-aldehyde functional groups.



(25.7)

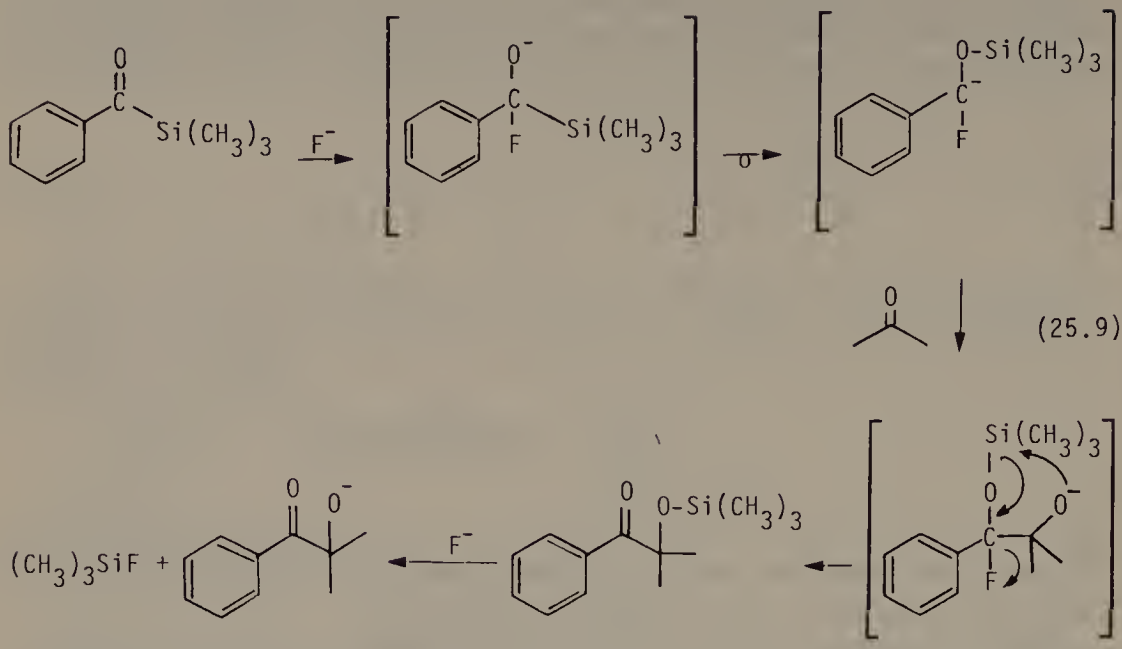
The dithianyl anion also undergoes intramolecular 1,4-conjugate addition to α,β-unsaturated ketones. Neither aldehydes nor α,β-unsaturated ketones are compatible with the usual basic conditions needed to generate dithianyl anions.

Benzoyl trimethylsilanes react with potassium fluoride in moist DMSO or HMPT or with TBAF in moist THF to yield benzaldehyde. If this reaction is carried out in the presence of alkyl halides [49] alkyl aryl ketones are formed. With ketones or aldehydes, the reaction yields α-hydroxy ketones [14]. These reactions may involve direct fluoride attack on the silyl center to form a benzoyl anion.



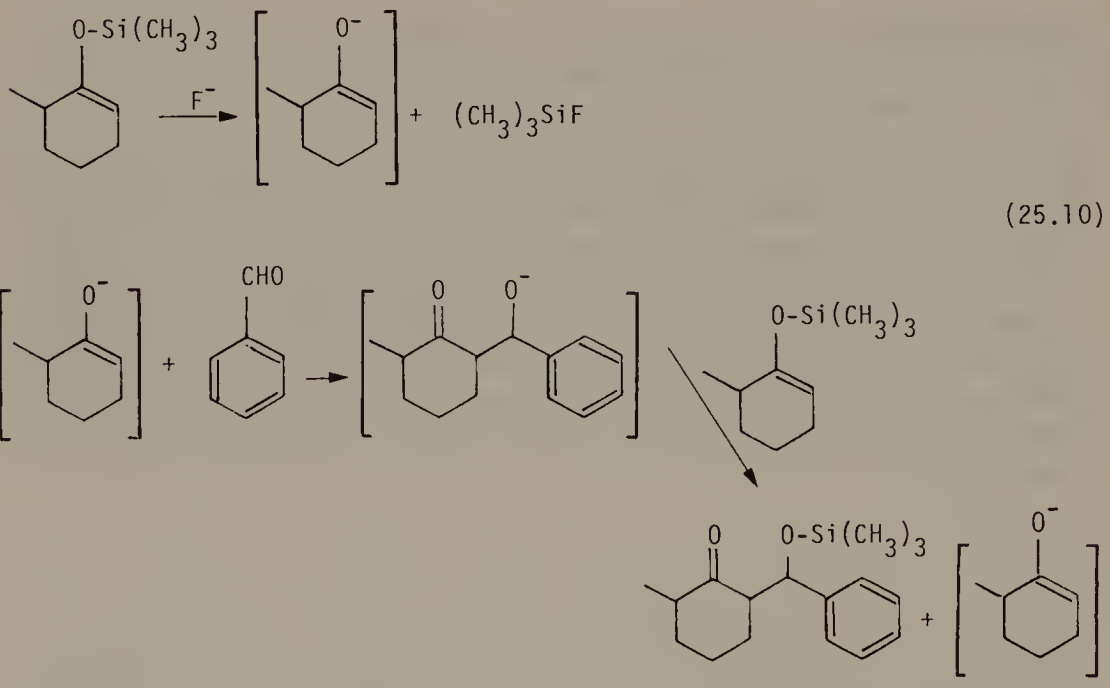
(25.8)

An alternative mechanistic possibility involves a Brook rearrangement.



(25.9)

Fluoride ion catalyzes regiospecific aldol condensations between trimethylsilyl enol ethers and aliphatic or aromatic aldehydes [15].

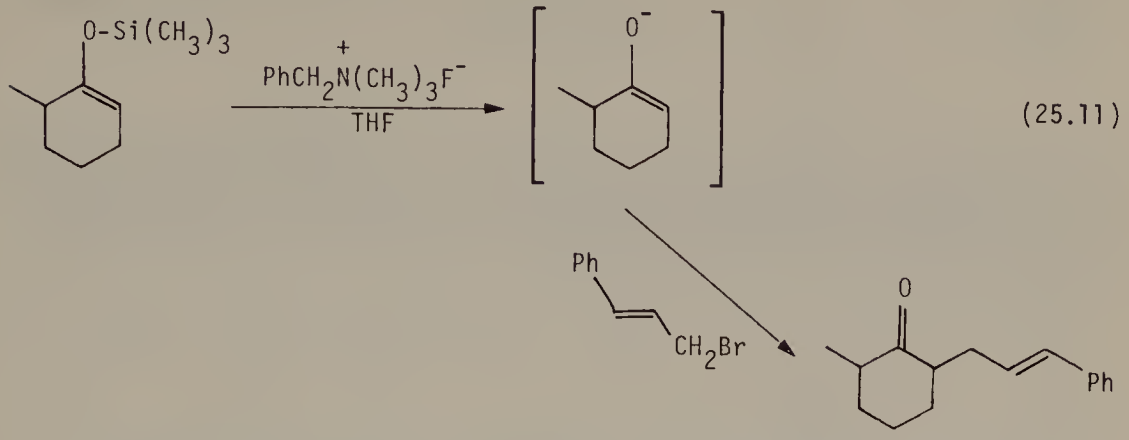


(25.10)

Nitro aldol reactions have also been carried out by reaction of silyl nitronates with fluoride ion (see 5.3) [16,17].

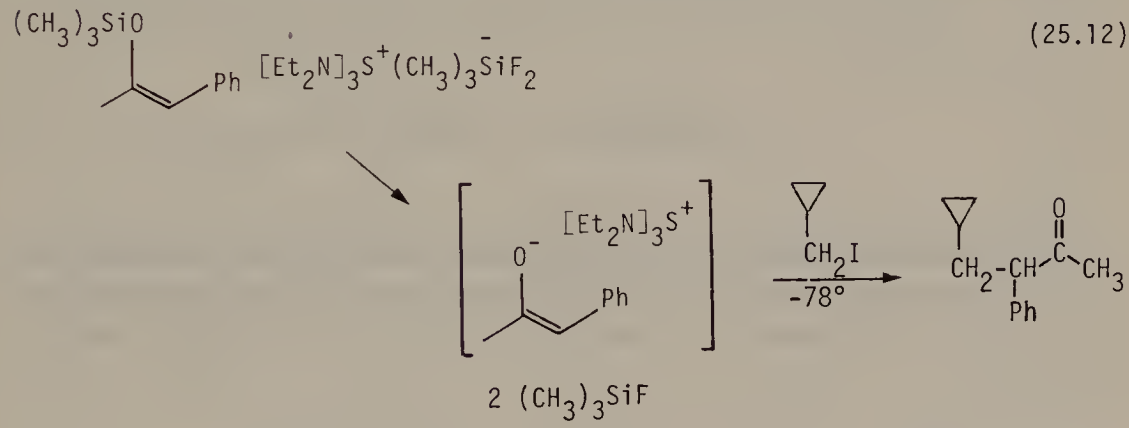
In a similar manner, tetraalkylammonium enolates have been generated regiospecifically by reaction of trimethylsilyl enol ethers with benzyltrime-

thylammonium fluoride in THF. These enolate anions may be alkylated with allylic or benzylic bromides or methyl iodide [18].



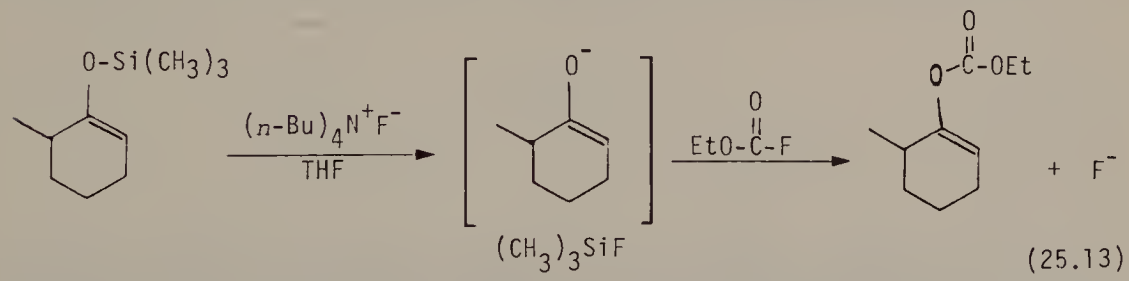
(25.11)

tris(Diethylamino)sulfonium difluorotrimethylsiliconate reacts with trimethylsilyl enol ethers to yield TMS-F and *tris*(diethylamino)sulfonium enolate ions pairs. These enolates can be C-alkylated by primary alkyl iodides, allylic or benzylic bromides or α-bromo esters [19].



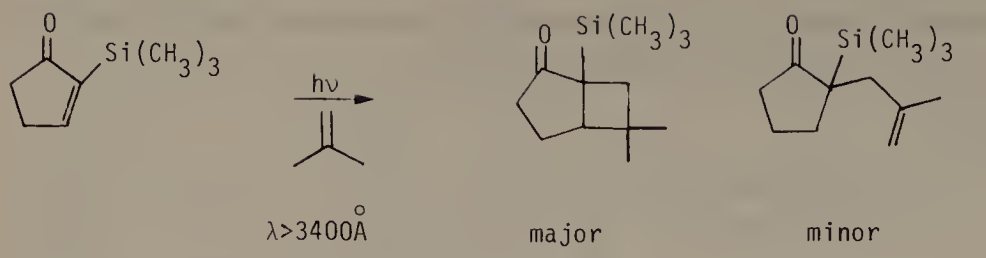
(25.12)

Ketone enolate anions generated by reaction of trimethylsilyl enol ethers with fluoride ion undergo O-acylation by ethyl fluoro formate or carbamoyl fluorides to yield enol carbonates or enol carbamates, respectively [20].



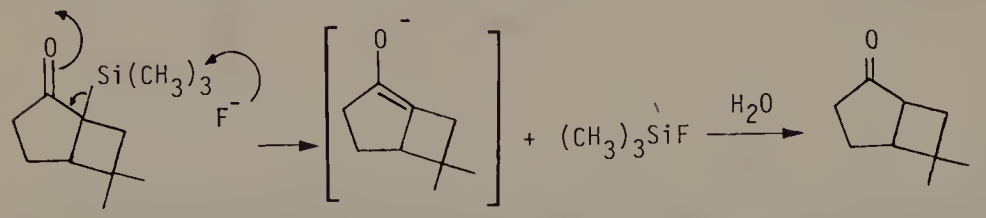
(25.13)

Photocycloaddition reactions of 2-trimethylsilylcyclopentenones with simple alkenes proceed in a highly regiospecific manner to yield head to tail cycloadducts.



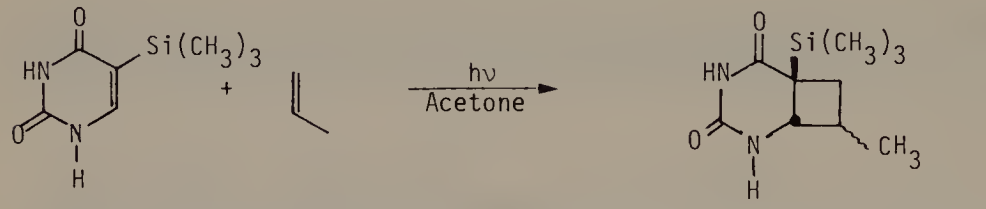
(25.14)

The trimethylsilyl group can be removed by desilylation with potassium fluoride dihydrate in DMSO. This probably involves formation of the enolate anion of the ketone and TMS-F [21, 22].



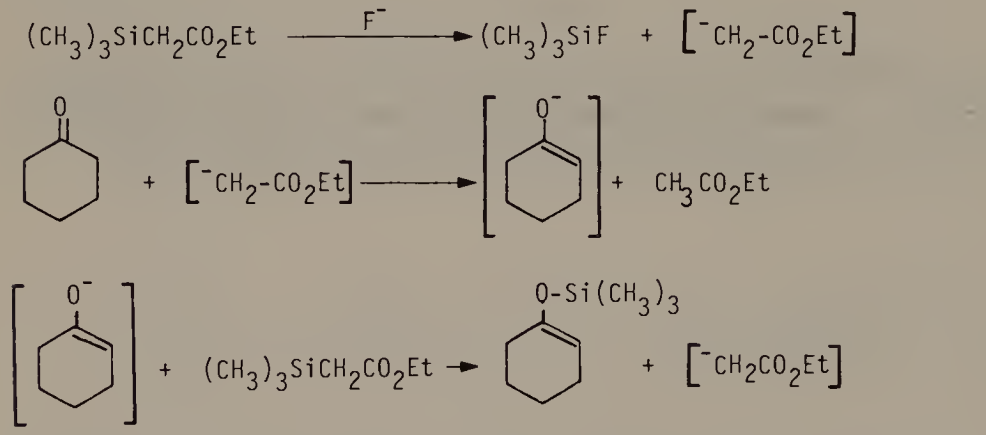
(25.15)

Similar directing effects were observed in the photocycloaddition reactions of 5-trimethylsilyl uracil with alkenes [22].



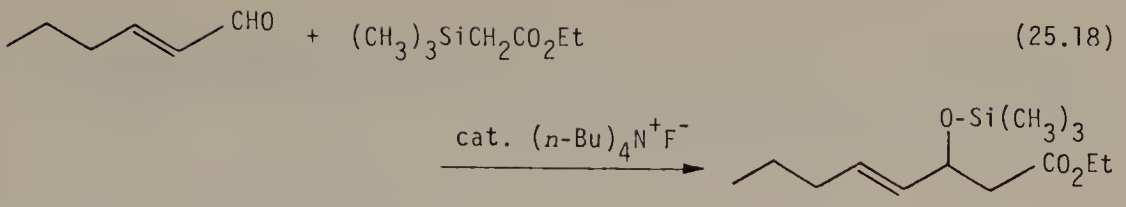
(25.16)

The conversion of ketones to trimethylsilyl enol ethers by reaction with ethyl trimethylsilylacetate and a catalytic amount of TBAF depends on the generation of ester enolates by reaction of fluoride ion with ethyl trimethylsilylacetate.



(25.17)

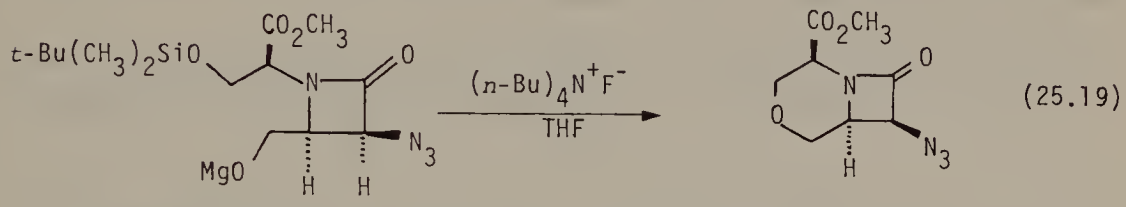
On the other hand, reactions of ethyl trimethylsilylacetate with aldehydes yields β-trimethylsilyloxy esters. This difference results from the greater reactivity of aldehydes toward nucleophilic addition. The ester enolate serves as a base towards ketones but reacts as a nucleophile with aldehydes [23].



(25.18)

Ethyl trimethylsilylacetate also reacts under fluoride ion catalysis with non-enolizable ketones or aldehydes to yield β-trimethylsilyloxy esters [24].

Intramolecular Williamson ether syntheses have been carried out under fluoride ion activation. Silyl ethers react with fluoride ion to yield reactive alkoxide ions and silyl fluorides. This procedure has proved effective for the synthesis of O-2-isocephams [25].

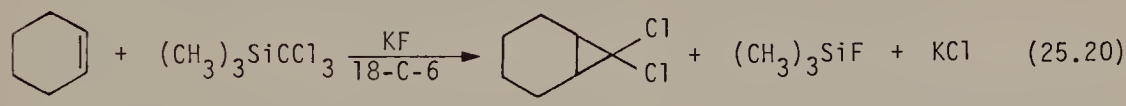


(25.19)

Potassium phenylselenide has been generated by treatment of phenyl trimethylsilyl selenide with potassium fluoride (see eq. 21.22) [26].

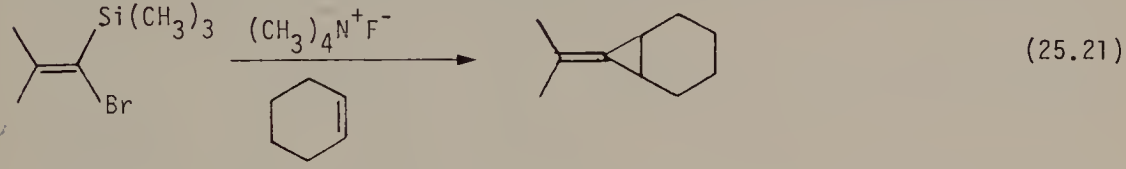
25.3. Generation of Carbenes, α-Elimination

Trihalomethyltrimethylsilanes react with potassium fluoride/18-C-6 in diglyme to yield TMS-F and potassium cation trihalomethyl anion pairs. These undergo α-elimination to yield dihalocarbenes [27].



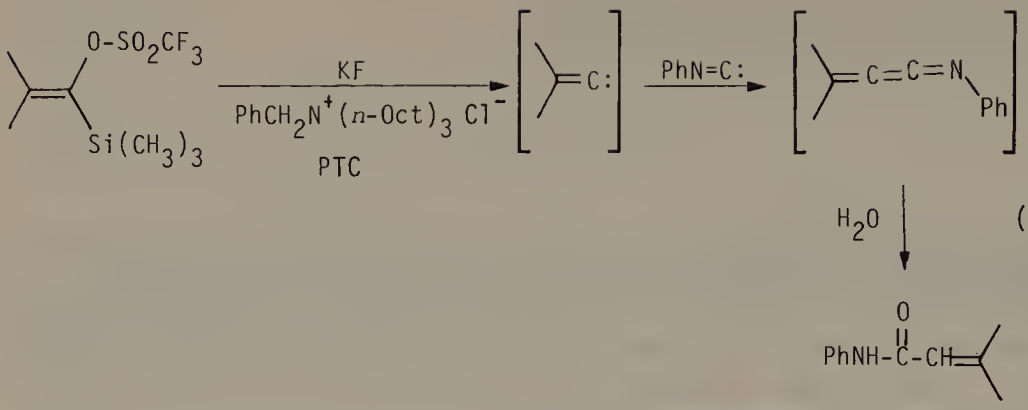
(25.20)

1-Halo-1-trimethylsilyl-2-methyl propene undergoes α-elimination on treatment with fluoride ion in diglyme to yield isopropylidene carbene. This reacts *in-situ* with olefins to yield isopropylidene cyclopropanes [28, 29].



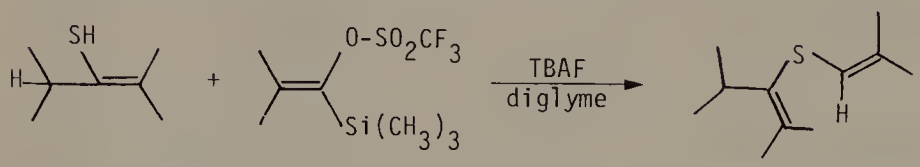
(25.21)

Similar α-eliminations occur under milder conditions (−20° to 0°) on treatment of α-trimethylsilylvinyl triflates with potassium fluoride/18-C-6 or anhydrous TBAF or by PTC. Alkylidene carbenes, generated in this way, add to C−C double bonds, to give vinylidene cyclopropanes [30]. They also undergo α-addition to the carbon of isonitriles to yield alkadienylidenamines which undergo hydrolysis to give vinylamides [31].



(25.22)

Insertion of alkylidene carbenes into the S–H single bonds of enethiols provides an efficient route to divinyl sulfides [32].

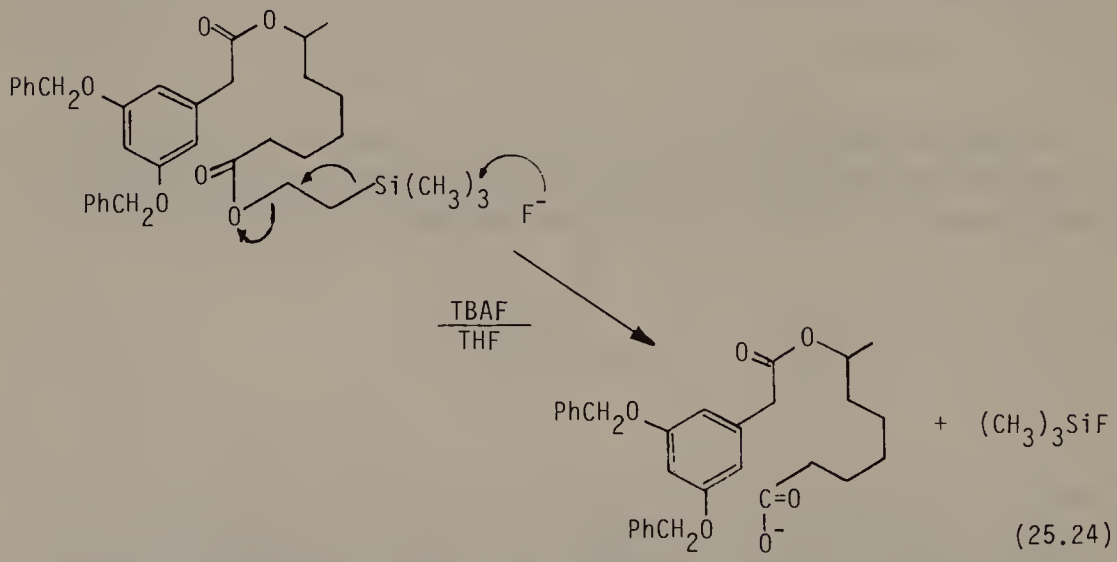


(25.23)

The necessary α-trimethylsilylvinyl triflates can be prepared by reaction of acylsilanes with triflic anhydride and pyridine in methylene chloride [30].

25.4 1,2-, 1,4- and 1,6-Elimination Reactions

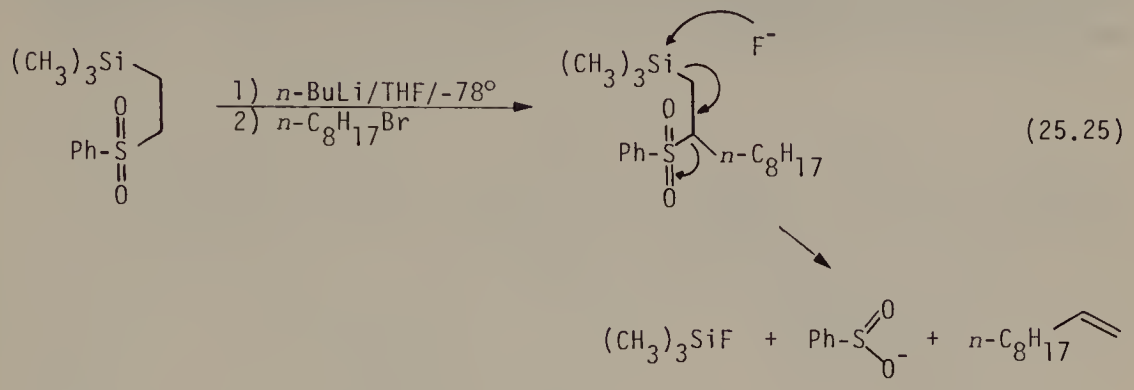
Fluoride ion also promotes 1,2-elimination reactions of alkyltrimethylsilanes if the alkyl group is substituted with a leaving group in the β-position. For example, 2-trimethylsilylethyl esters function as carboxyl protecting groups which may be selectively removed by fluoride ion [33, 34].



(25.24)

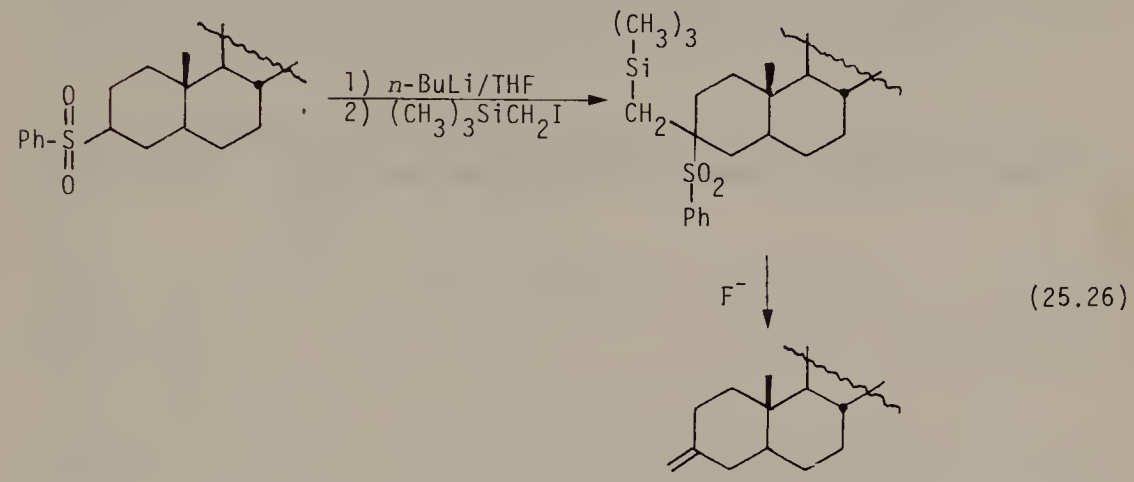
β-Trimethylsilylalkyl phenyl sulfones react with TBAF · 3 H_2O in THF to yield TMS-F, phenyl sulfinate ion and an alkene. The facile formation and alkylation of carbanions alpha to a phenylsulfonyl group combined with

this fluoride ion mediated elimination reaction provides a new method to prepare terminal olefins [35].



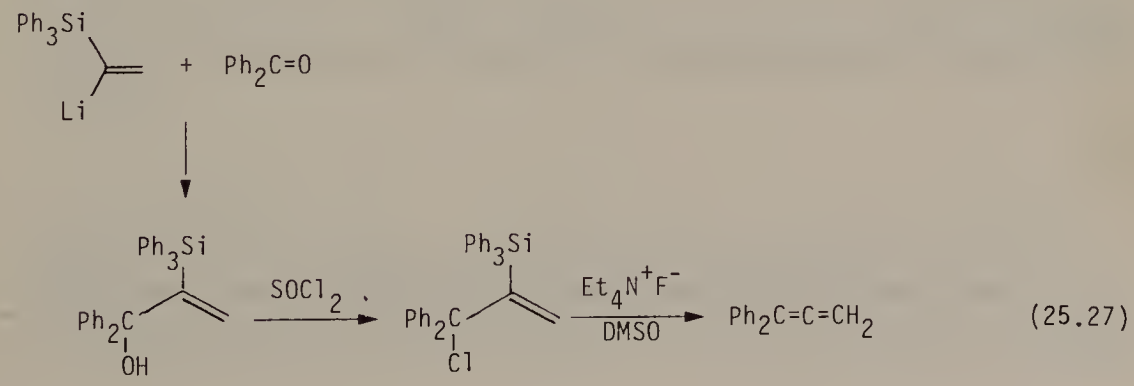
(25.25)

Such β-trimethylsilylalkyl phenyl sulfones can be prepared by reaction of iodomethyltrimethylsilane with phenylsulfonyl stabilized carbanions.



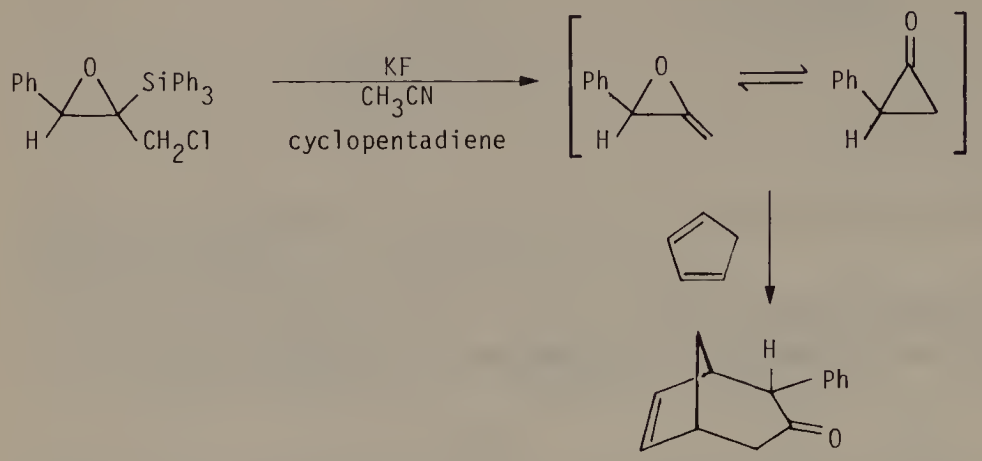
(25.26)

2-Triphenylsilyl allylic alcohols do not readily undergo elimination of triphenylsilanol or triphenylsilanoate (see 6.4 E). However, they can be converted to 2-triphenylsilyl allylic chlorides by reaction with thionyl chloride. These undergo elimination on treatment with tetraethylammonium fluoride in DMSO to yield allenes [36, 37].



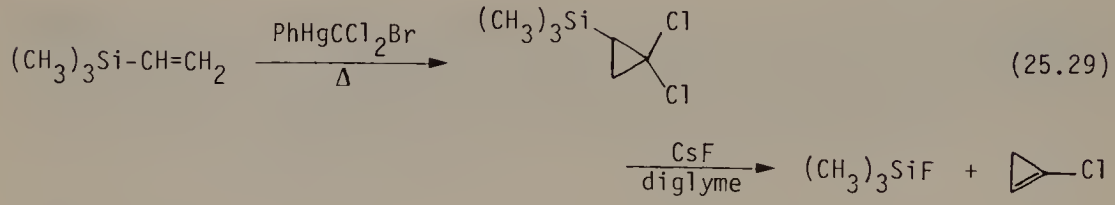
(25.27)

Allene oxides-cyclopropanones have been prepared by fluoride induced elimination from α-chloromethyl-α-silyl epoxides. These reactive intermediates have been trapped *in-situ* by cycloaddition reactions with cyclopentadiene and furan [38, 39].



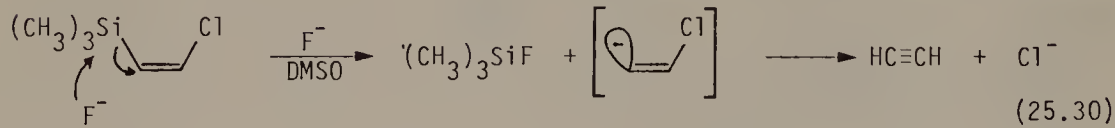
(25.28)

1-Halo-cyclopropenes have been generated by fluoride promoted β-elimination of 1,1-dihalo-2-trimethylsilyl cyclopropanes [40].



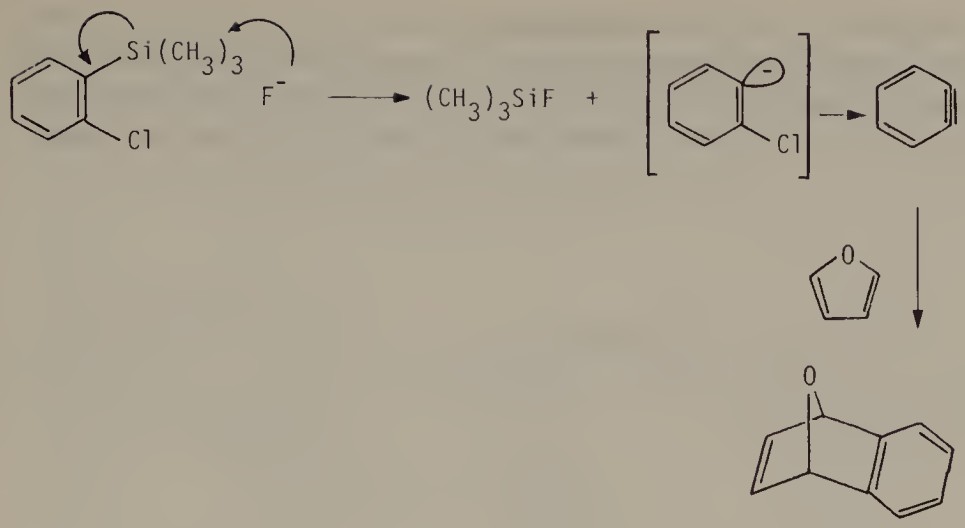
(25.29)

Fluoride ion promotes β-elimination of both *cis* and *trans* β-chlorovinyltrimethylsilanes to yield acetylene and TMS-F. As expected, the *trans* isomer reacts considerably faster than the *cis* [41].



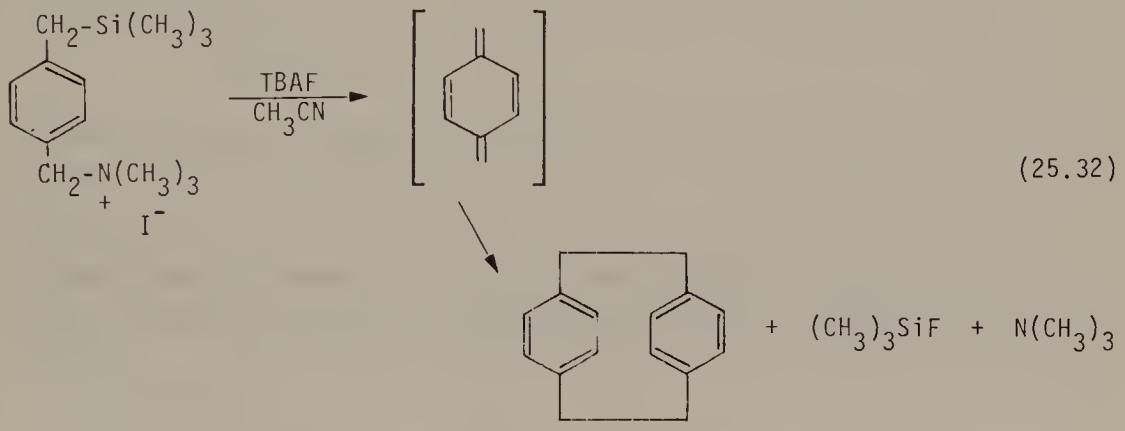
(25.30)

ortho-Halophenyltrimethylsilanes undergo loss of the elements of TMS-X on treatment with trimethylammonium fluoride or potassium-*t*-butoxide in HMPT to yield benzyne as a reactive intermediate. This may be trapped *in-situ* by reaction with furan [42].



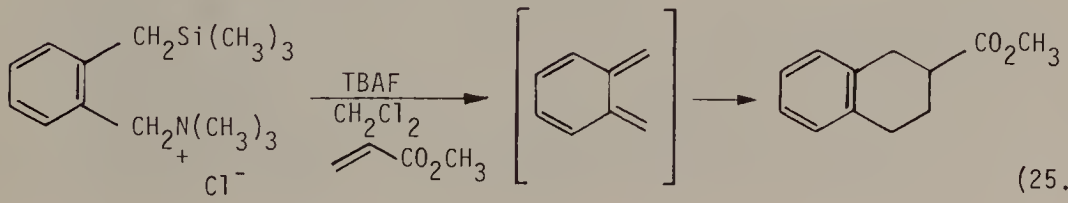
(25.31)

Fluoride ion induced 1,6-elimination of [*p*-(trimethylsilylmethyl)benzyl]-trimethylammonium iodide provides a convenient route to *p*-quinodimethane. This reactive intermediate may dimerize to yield [2,2]-paracyclophane or polymerize to poly-*p*-xylylene depending on reaction conditions [43].



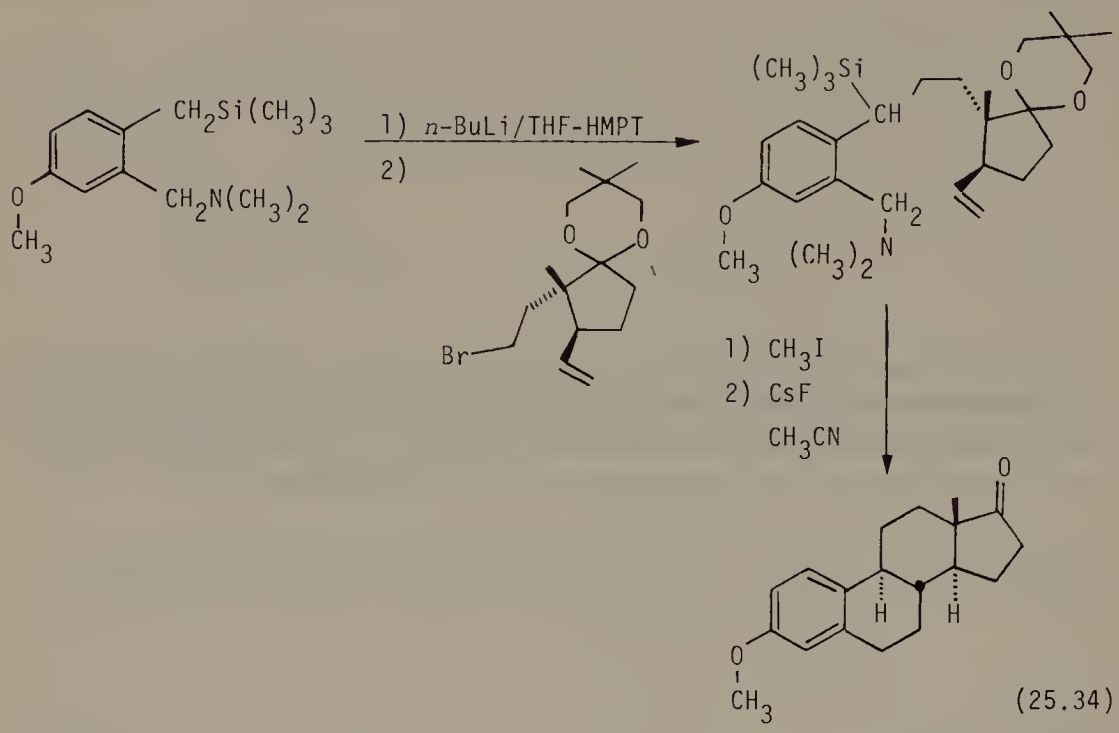
(25.32)

o-Xylylene reactive intermediates have been generated by fluoride ion induced 1,4-elimination from *ortho*-(α-trimethylsilylalkyl) benzyltrimethylammonium halides. *o*-Xylylene undergoes *in-situ* [4 + 2] cycloaddition reactions with alkenes and alkynes substituted with electron withdrawing groups to yield tetrahydronaphthalene and dihydronaphthalene derivatives, respectively [44].



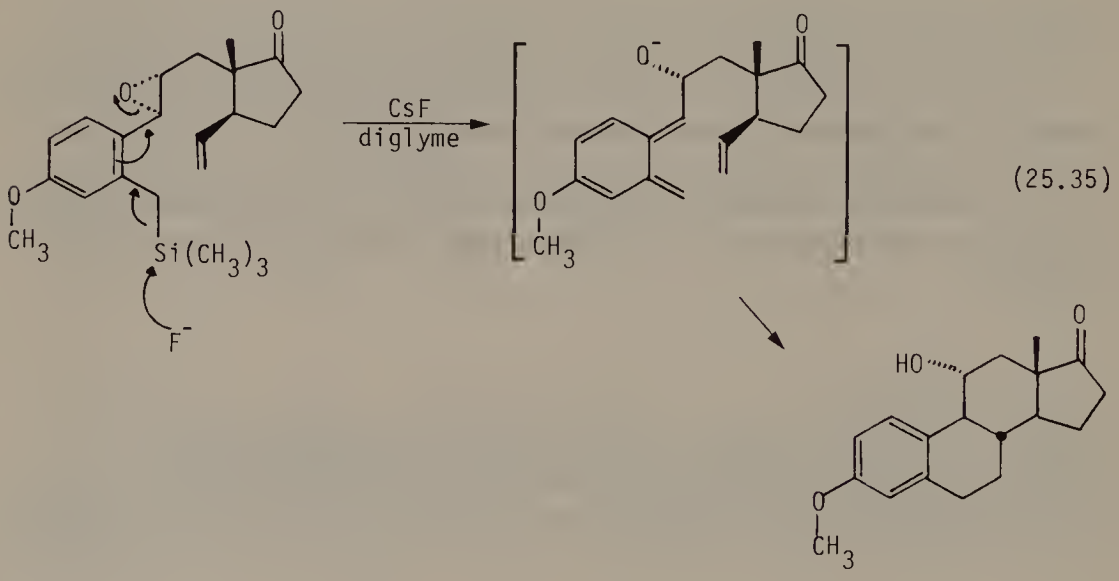
(25.33)

ortho-[Trimethylsilylmethyl]benzyldimethylamine can be converted to *ortho* [α-trimethylsilylalkyl]benzyldimethylamine by metallation with *n*-butyl lithium followed by reaction with primary alkyl iodides [44]. This methodology has been utilized in an efficient stereoselective synthesis of estrone as outlined [45].



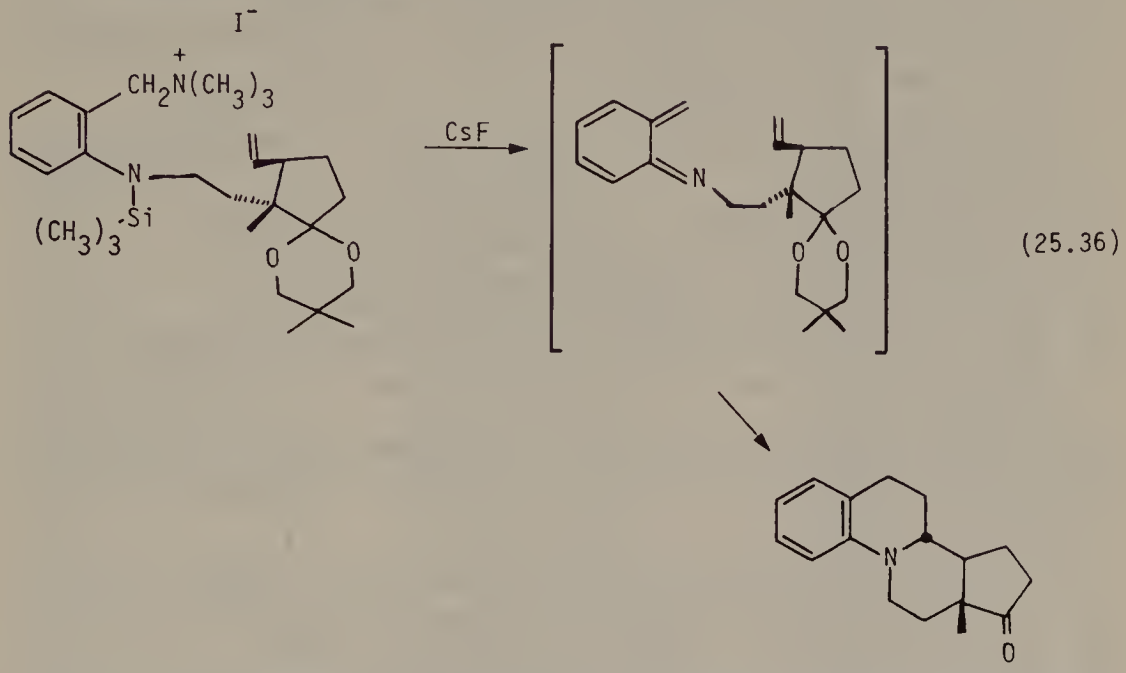
(25.34)

d,l-11-α-Hydroxyesterone methyl ether has been prepared by a closely related intramolecular cycloaddition reaction. The reactive *ortho*-quinodimethane was formed by a fluoride ion induced 1,4-elimination of a 2-trimethylsilylmethyl styrene oxide derivative as outlined below [46].



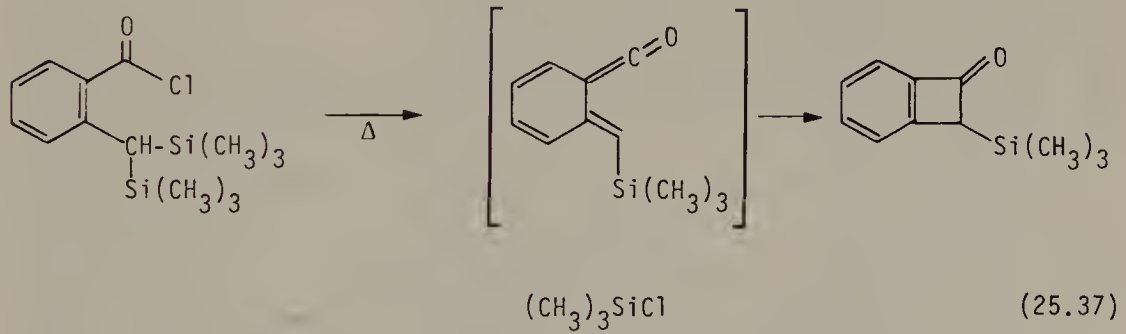
(25.35)

Recently, reactive *o*-quinone methide N-alkylimine intermediates have been generated by fluoride ion induced 1,4-elimination reactions. While intermolecular Diels-Alder reactions with dienophiles fail, they undergo intramolecular Diels-Alder electrocyclic reactions with C–C double bonds to yield nitrogen containing polycyclic molecules [47].



(25.36)

Flash vacuum pyrolysis of *o*-trimethylsilylmethyl benzoyl chlorides at 600° results in elimination of TMS-Cl and formation of benzocyclobutenones [48].



$(CH_3)_3SiCl$ (25.37)

References

1. Kraihanzel, C.S., Poist, J.E.: J. Organometal. Chem. *8,* 239 (1967)
2. Stang, P.J., Ladika, M.: Synthesis, 29 (1981)
3. Holmes, A.B., Raphel, R.A., Welland, N.K.: Tetrahedron Lett. 1539 (1976)
4. Nakamura, E., Kuwajima, I.: Angew. Chem. Int. Ed. *15,* 498 (1976)
5. Holmes, A.B., Jennings-White, C.L.D., Schulthess, A.M., Akinde, B., Walton, D.R.M.: J. Chem. Soc. Chem. Commun. 840 (1979)
6. Sarkar, T.K., Anderson, N.H.: Tetrahedron Lett. 3513 (1978)
7. Hosomi, A., Shirahata, A., Sakurai, H.: Tetrahedron Lett. 3043 (1978)

8. Trost, B.M., Vincent, J.E.: J. Am. Chem. Soc. *102,* 5680 (1980)
9. Pornet, J.: Tetrahedron Lett. 455 (1981)
10. Chan, T.H., Mychajlowskij, W.: Tetrahedron Lett. 3479 (1974)
11. Chan, T.H., Lau, P.W.K., Li, M.P.: Tetrahedron Lett. 2667 (1976)
12. Vedejs, E., Martinez, G.R.: J. Am. Chem. Soc. *101,* 6452 (1979)
13. Grotjahn, D.G., Andersen, N.H.: J. Chem. Soc. Chem. Comm. 306 (1981)
14. Schinzer, D., Heathcock, C.H.: Tetrahedron Lett. 1881 (1981)
15. Noyori, R., Yokoyama, K., Sakata, J., Kuwajima, I., Nakamura, E., Shimizu, M.: J. Am. Chem. Soc. *99,* 1265 (1977)
16. Colvin, E.W., Seebach, D.: J. Chem. Soc. Chem. Comm. 689 (1978)
17. Seebach, D., Beck, A.K., Lehr, F., Weller, T., Colvin, E.: Angew. Chem. Int. Ed. *20,* 397 (1981)
18. Kuwajima, I., Nakamura, E.: J. Am. Chem. Soc. *97,* 3257 (1975)
19. Noyori, R., Nishida, I., Sakata, J.: Tetrahedron Lett. 2085 (1980)
20. Olofson, R.A., Cuomo, J.: Tetrahedron Lett. 819 (1980)
21. Swenton, J.S., Fritzen, Jr., E.L.: Tetrahedron Lett. 1951 (1979)
22. Shih, C., Fritzen Jr., E.L., Swenton, J.S.: J. Org. Chem. *45,* 4462 (1980)
23. Nakamura, E., Murofushi, T., Shimizu, M., Kuwajima, I.: J. Am. Chem. Soc. *98,* 2346 (1976)
24. Nakamura, E., Shimizu, M., Kuwajima, I.: Tetrahedron Lett. 1699 (1976)
25. Just, G., Hakimelahi, G.H., Ugolini, A., Zamboni, R.: Synthesis Comm. *9,* 113 (1979)
26. Detty, M.R.: Tetrahedron Lett. 5087 (1978)
27. Cunico, R.F., Chou, B.B.: J. Organometal. Chem. *154,* C45 (1978)
28. Cunico, R.F., Han, Y.K.: J. Organometal. Chem. *105,* C29 (1976)
29. Cunico, R.F., Han, Y.K.: J. Organometal. Chem. *162,* 1 (1978)
30. Stang, P.J., Fox, D.P.: J. Org. Chem. *42,* 1667 (1977)
31. Stang, P.J., Bjork, J.A.: J. Chem. Soc. Chem. Comm. 1057 (1978)
32. Stang, P.J., Christensen, S.B.: J. Org. Chem. *46,* 823 (1981)
33. Gerlach, H.: Helv. Chim. Acta *60,* 3039 (1977)
34. Sieber, P.: Helv. Chim. Acta, *60,* 2711 (1977)
35. Kocienski, P.J.: Tetrahedron Lett. 2649 (1979)
36. Chan, T.H., Mychajlowskij, W.: Tetrahedron Lett. 171 (1974)
37. Chan, T.H., Mychajlowski, W., Ong, B.S., Harpp, D.N.: J. Org. Chem. *43,* 1526 (1978)
38. Chan, T.H., Li, M.P., Mychajlowskij, W., Harpp, D.N.: Tetrahedron Lett. 3511 (1974).
39. Chan, T.H., Ong, B.S.: J. Org. Chem. *43,* 2994 (1978)
40. Chan, T.H., Massuda, D.: Tetrahedron Lett. 3383 (1975)
41. Cunico, R.F., Dexheimer, E.M.: J. Am. Chem. Soc. *94,* 2868 (1972)
42. Cunico, R.F., Dexheimer, E.M.: J. Organometal. Chem. *59,* 153 (1973)
43. Ito, Y., Miyata, S., Nakatsuka, M., Saegusa, T.: J. Org. Chem. *46,* 1043 (1981)
44. Ito, Y., Nakatsuka, M., Saegusa, T.: J. Am. Chem. Soc. *102,* 863 (1980)
45. Ito, Y., Nakatsuka, M., Saegusa, T.: J. Am. Chem. Soc. *103,* 476 (1981)
46. Djuric, S., Sarkar, T., Magnus, P.: J. Am. Chem. Soc. *102,* 6885 (1980)
47. Ito, Y., Miyata, S., Nakatsuka, M., Saegusa, T.: J. Am. Chem. Soc. *103,* 5250 (1981)
48. Chenard, B.L., Slapak, C., Anderson, D.K., Swenton, J.S.: J. Chem. Soc. Chem. Commun. 179 (1981)
49. Degl'Innocenti, A., Pike, S., Walton, D.R.M., Seconi, G., Ricci, A. Fioreza, M.: J. Chem. Soc. Chem. Commun. 1201 (1980)

Author Index

Subject Index

ISBN 3-540-11675-3
ISBN 0-387-11675-3