Silicon in Organic Synthesis

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1 Introduction

The explosive growth of organosilicon chemistry over the past decade has created a growing awareness of its considerable synthetic utility to the organic chemist. It is the purpose of this review to demonstrate that such utility is, if anything, under-estimated; in scope, it discusses the use of silyl-substituted reagents and substrates to activate the substrate to reaction, to direct the course of reaction, or to protect the substrate from unwanted reaction, emphasis being placed on those sequences where silicon is absent in the final product.

Other sources recommended for consultation are an on-going annual survey,[1] a new series,[2] and a short review;[3] other reviews[4] and monographs,[5] while less timely, are of considerable value. Applications of silylation as derivatization to confer g.l.c. volatility or characterizable mass spectral fragmentation have been adequately reviewed elsewhere.[6]

2 Atomic Properties

Silicon has the outer electronic configuration $3s^23p^23d^0$, differing from carbon in its possession of vacant d-orbitals, which can be used to expand the valency, as in $SiF_6{}^{2-}$, or to allow back-bonding. The $3p$ orbitals are of too high an energy to give adequate π-overlap with $2p$ orbitals, so sila-ethanes such as (1)[7] are very unstable,[8] and stable compounds with silicon–oxygen π-bonds are unknown.

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[1] S. S. Washburne, *J. Organometallic Chem.*, 1974, **83**, 155; 1976, **123**, 1.

[2] 'New Applications of Organometallic Reagents in Organic Synthesis', ed. D. Seyferth, *J. Organometallic Chem. Library*, Vol. 1 and 2, Elsevier, Amsterdam, 1976; see, in particular, P. F. Hudrlik, Vol. 1, p. 127; see also Vol. 4, 1977.

[3] I. Fleming, *Chem. and Ind.*, 1975, 449.

[4] J. F. Klebe, *Adv. Org. Chem.*, 1972, **8**, 97; *Accounts Chem. Res.*, 1970, **3**, 299; (*b*) L. Birkofer and A. Ritter in 'Newer Methods in Preparative Organic Chemistry', ed. W. Foerst, Academic Press, New York, 1968, Vol. 5, p. 211.

[5] C. Eaborn, 'Organosilicon Compounds', Butterworths, London, 1960.

[6] A. E. Pierce, 'Silylation of Organic Compounds', Pierce Chemical Co., Rockford, Illinois, 1968; G. D. Brittain and J. E. Sullivan in 'Recent Advances in Gas Chromatography', ed. I. I. Domsky and J. A. Perry, Marcel Dekker, New York, 1971.

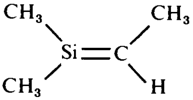
[7] O. L. Chapman, C.-C. Chang, J. Kolc, M. E. Jung, J. A. Lowe, T. J. Barton, and M. L. Tumey, *J. Amer. Chem. Soc.*, 1976, **98**, 7844; M. R. Chedekel, M. Skoglund, R. L. Kreeger, and H. Schechter, *ibid.*, p. 7486.

[8] R. E. Ballard and P. J. Wheatley, ref. 2, Vol. 2, p. 1; L. E. Gusel'nikov, N. S. Nametkin, and V. M. Vdovin, *Accounts Chem. Res.*, 1975, **8**, 18; N. Wiberg and G. Preiner, *Angew. Chem. Internat. Edn.*, 1977, **16**, 328; T. J. Barton and D. Banasiak, *J. Amer. Chem. Soc.*, 1977, **99**, 5199, describe the generation and trapping of a silabenzene.

Table 1 *Some values of bond energies*/kJ mol^{-1}

Si—F	540—570	C—F	440—465
Si—O	370—450	C—O	350—360
Si—C	230—320	C—C	347
Si—H	290—320	C—H	414

Organic compounds of silicon are normally quadricovalent, the stereochemistry and mechanism of reactions at the silicon atom having been clearly expounded.[9a]



(1)

Silicon's utility in organic synthesis derives from three main factors, as listed below.

A. Relative Bond Strengths.—From Table 1,[10] it can be seen that, whereas silicon's bonds to oxygen and fluorine are stronger than the bonds between carbon and these elements, its bonds to carbon and hydrogen are weaker. Such characteristics give rise to a wide range of thermodynamically favourable processes.

B. Vacant *d*-Orbitals.—These orbitals[9b] are of suitable energy for back-bonding with a filled $2p$ orbital on an adjacent atom of a first-row element, enabling silicon to stabilize, for example, an adjacent carbanion. They can also be involved in substitution reactions at silicon[9] or at an adjacent atom.[5]

C. Relative Electronegativity.—Silicon has a Pauling electronegativity of 1.8, and carbon a value of 2.5, making silicon–carbon bonds polarized (2), and therefore susceptible to nucleophilic attack at silicon. This leads to bond heterolysis, especially when the carbon fragment being expelled is a good leaving group, as exemplified in Scheme 1; silyl ethers behave similarly.

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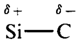
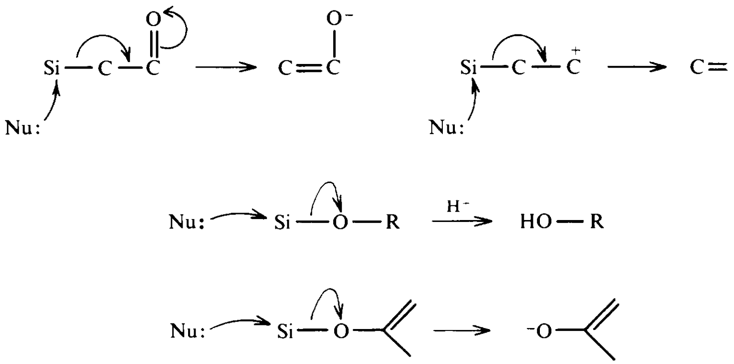
[9] (*a*) L. H. Sommer, 'Stereochemistry, Mechanism and Silicon', McGraw-Hill, New York, 1965; (*b*) H. Kwart and K. King, '*d*-Orbital Involvement in the Organo-chemistry of Silicon, Phosphorus, and Sulphur', 'Reactivity and Structure', 'Concepts in Organic Chemistry', Springer Verlag, Berlin, 1977; see also M. E. Childs and W. P. Weber, *J. Org. Chem.*, 1976, **41**, 1799.

[10] L. Pauling, 'The Nature of the Chemical Bond', Cornell University Press, Ithaca, New York, 1960, pp. 85—86; T. Cottrell, 'The Strengths of Chemical Bonds', Butterworths, London, 1958, pp. 270—280; see also E. A. V. Ebsworth, in 'Organometallic Compounds of the Group IV Elements', ed. A. G. MacDiarmid, Marcel Dekker, New York, 1968, Vol. 1, Part 1.



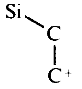
$\overset{\delta+}{\mathrm{Si}}\text{—}\overset{\delta-}{\mathrm{C}}$

(2)



Scheme 1

A further, profound, property is the ability of a silicon–carbon bond to stabilize an adjacent carbonium ion (3); this phenomenon can perhaps be compared with the hyperconjugative situation in (4).



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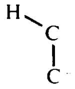

(4)

Manifestations of all the above properties will be illustrated in the succeeding reactions, which have been classified either by reaction type or by reagent type, an unavoidable but comprehensible ambiguity.

3 Directing/Stabilizing Effects of Silicon Substituents

A. Carbonium Ions.—The electropositive nature of silicon results in the observable capacity of a carbon–silicon bond to stabilize a carbonium ion β to it,[11] either by bridging[12,13] or by hyperconjugation.[14] An elegant demonstration of bridging was reported by Eaborn[12] and Jarvie;[13] re-isolation of starting material from the partial solvolysis of 2-bromo-2,2-dideuterio-1-trimethylsilylethane (5) yielded material in which the deuterium had been extensively scrambled between C-1 and C-2, consistent with a mechanism involving an

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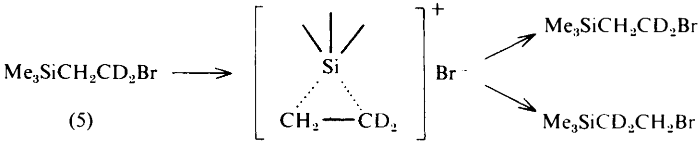
[11] A. W. P. Jarvie, *Organometallic Chem. Rev.* (*A*), 1970, **6**, 153.

[12] M. A. Cooke, C. Eaborn, and D. R. M. Walton, *J. Organometallic Chem.*, 1970, **24**, 301.

[13] A. J. Bourne and A. W. P. Jarvie, *J. Organometallic Chem.*, 1970, **24**, 335.

[14] T. G. Traylor, W. Hanstein, H. J. Berwin, N. A. Clinton, and R. S. Braun, *J. Amer. Chem. Soc.*, 1971, **93**, 5715.

anchimerically assisted ionization of the C—Br bond to give a silacyclopropenium ion (6) (Scheme 2). There also exists evidence that cations α to silicon are *destabilized.*[15] *Ab initio* SCF MO calculations on silyl-substituted alkanes, alkyl radicals, and carbonium ions show that the carbonium ion is destabilized by an α-silyl group and stabilized by a β-silyl group by comparison with the carbon analogues. These results are consistent with observations on the rates of S_N1 solvolysis of silylmethyl halides (Scheme 2).



(5)

(6)

$$R_3SiCH_2CH_2X \xrightarrow{S_N1} \text{faster than analogous C compound}$$

$$R_3SiCH_2X \xrightarrow{S_N1} \text{slower than analogous C compound}$$

Scheme 2

(i) *Silyl-arenes.* Such stabilization has been studied extensively in the aromatic series.[16,17] The Hammett electrophilic *para*-substitution constant for the Me_3SiCH_2 group is -0.66.[16] This closely approximates to the value for the MeO group, *viz.* -0.74, implying that in general terms a Me_3Si group β to a carbonium ion stabilizes that ion to about the same extent as does a MeO group α to it.

This has been put to practical use: under normal conditions of electrophilic aromatic substitution, such substitution on silyl-arenes will take place at the site of the silyl group,[18,19] even when the other ring substituents do not favour such regiospecificity[20,21] (Scheme 3); one is of course, faced with the not inconsiderable initial problem of preparing the silyl-arenes.

(ii) *Vinyl-silanes.* Similarly, the orientation of electrophilic attack on alkenes can be controlled by the introduction of a silyl substituent, as can (in appropriate cases) the stereochemistry. An example can be seen in the ability of vinyl-

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[15] C. Eaborn, F. Feichtmayr, M. Horn, and J. R. Murrell, *J. Organometallic Chem.*, 1974, **77**, 39.

[16] W. Hanstein, H. J. Berwin, and T. G. Traylor, *J. Amer. Chem. Soc.*, 1970, **92**, 829, 7476.

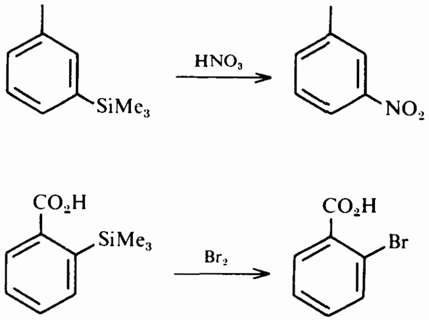
[17] C. Eaborn and K. C. Pande, *J. Chem. Soc.*, 1960, 1566.

[18] C. Eaborn, A. A. Najam, and D. R. M. Walton, *J.C.S. Perkin I*, 1972, 2481.

[19] J. B. F. Lloyd and P. A. Ongley, *Tetrahedron*, 1964, **20**, 2185.

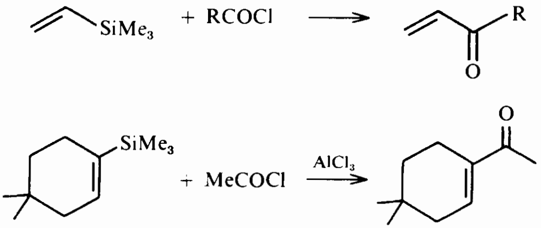
[20] V. Chvalovský and V. Bažant, *Coll. Czech. Chem. Comm.*, 1951, **16**, 580.

[21] T. Hashimodo, *J. Pharm. Soc. Japan*, 1967, **87**, 528; G. Félix, J. Dunoguès, F. Pisciotti, and R. Calas, *Angew. Chem. Internat. Edn.*, 1977, **16**, 488.



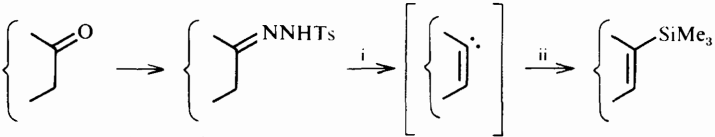
Scheme 3

silanes to transfer the vinyl group to acid chlorides (Scheme 4) in an attractive synthesis[22] of $\alpha\beta$-unsaturated ketones.



Scheme 4

The stereospecific synthesis of both isomers of vinyl-silanes has stimulated much activity, most existing methodologies[23] starting with alkynes; a recent route from ketones involves electrophilic trapping of vinyl anions (Scheme 5).[24]



Reagents: i, Bu^{n}Li; ii, Me$_3$SiCl

Scheme 5

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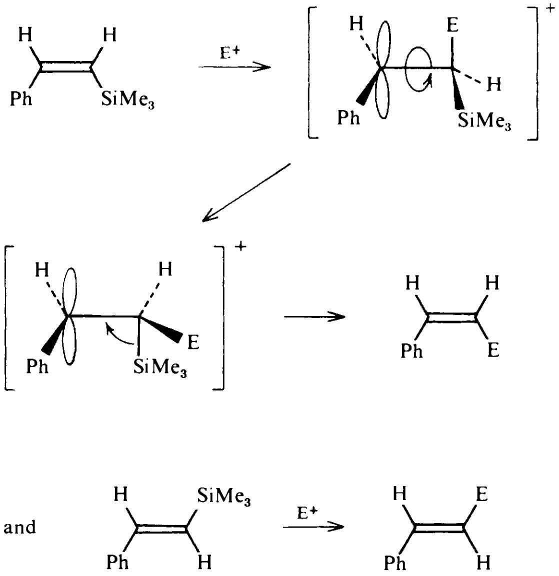
[22] J.-P. Pillot, J. Dunoguès, and R. Calas, *Compt. rend.*, 1974, **278,** *C*, 787, 789; *Bull. Soc. chim. France*, 1975, 2143; I. Fleming and A. Pearce, *J.C.S. Chem. Comm.*, 1975, 633; for a related use of cyclopropylsilanes, see M. Grignon-Dubois, J. Dunoguès, and R. Calas, *Synthesis*, 1976, 737.

[23] C. Eaborn and R. W. Bott in 'Organometallic Compounds of the Group IV Elements', ed. A. G. MacDiarmid, Marcel Dekker, New York, 1968, Vol. 1, Part 1; J. J. Eisch and G. A. Damasevitz, *J. Org. Chem.*, 1976, **41,** 2214; K. Uchida, K. Utimoto, and H. Nozaki, *ibid.*, pp. 2215, 2941; R. Köster and L. A. Hagelee, *Synthesis*, 1976, 118. For different approaches, see K. Sachdev, *Tetrahedron Letters*, 1976, 4041; H. Westmijze, J. Meijer, and P. Vermeer, *ibid.*, 1977, 1823; M. Obayashi, K. Utimoto, and H. Nozaki, *ibid.*, p. 1805.

[24] T. H. Chan, A. Baldassarre, and D. Massuda, *Synthesis*, 1976, 801; R. T. Taylor, C. R. Degenhardt, W. P. Melega, and L. A. Paquette, *Tetrahedron Letters*, 1977, 159; see also R. H. Shapiro, *Org. Reactions*, 1976, **23,** 405.

The powerful directing effect of silicon in such systems can be seen in the stereospecific reactions shown in Scheme 6. The mechanism proposed[25] is that, simultaneously with attack of the electrophile on the double bond, rotation occurs about the developing C—C single bond in such a direction as to permit the C—Si bond to stabilize the benzylic carbonium-ion centre continuously; rotation in the opposite direction would bring the C—Si bond into the nodal plane of the developing ion, and so preclude such continuity.



Scheme 6

This concept has been shown to be generally applicable,[26] mono-and di-substituted vinyl-silanes undergoing electrophile-induced desilylation with strict retention of configuration, and its utility has been extended by Chan,[27] by developing simple stereospecific routes to disubstituted vinyl-silanes (Scheme 7).

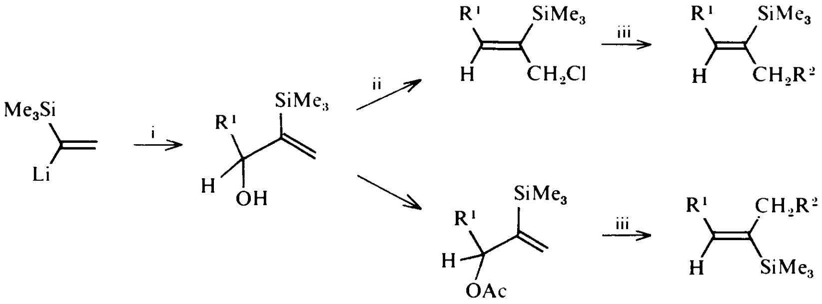
Interestingly, the treatment of vinyl-silanes with molar equivalents of chlorine or bromine results in apparent *trans*-addition. The resulting dihalides, on *anti*-periplanar elimination of the elements of trimethylsilyl halide, yield vinyl halides of *opposite* sterochemistry[28] (Scheme 8); iodination results in either

[25] K. E. Koenig and W. P. Weber, *Tetrahedron Letters*, 1973, 2533.

[26] K. Utimoto, M. Kitai, and H. Nozaki, *Tetrahedron Letters*, 1975, 2825.

[27] T. H. Chan, W. Mychajlowskij, B. S. Ong, and D. N. Harpp, *J. Organometallic Chem.*, 1976, **107**, Cl; W. Mychajlowskij and T. H. Chan, *Tetrahedron Letters*, 1976, 4439; for n.m.r. and g.c. differentiation of geometric isomers of vinylsilanes see T. H. Chan, W. Mychajlowskij, and R. Amoroux, *Tetrahedron Letters*, 1977, 1605.

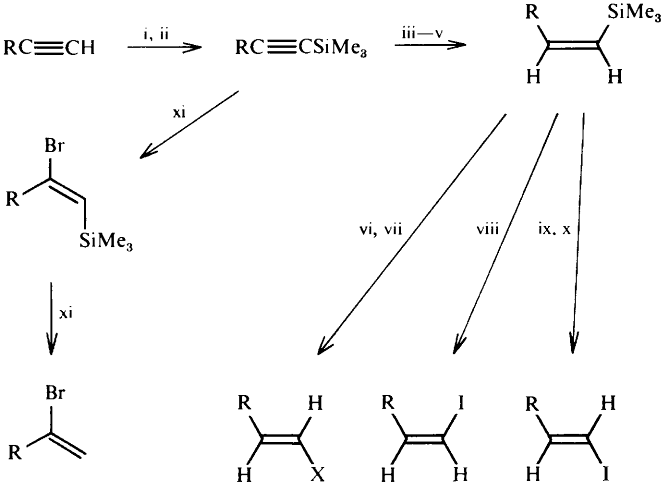
[28] R. B. Miller and T. Reichenbach, *Tetrahedron Letters*, 1974, 543.



Reagents: i, R^{1}CHO; ii, SOCl$_2$; iii, LiCuR$^2_2$ or R$^2_2$CuMgBr

Scheme 7

retention or inversion, as shown. Finally, HBr in pentane, which adds sluggishly to terminal alkynes, giving meagre yields of 2-bromoalk-1-enes, reacts smoothly[29] with trimethylsilyl-alkynes to give the desired bromides in high yield (Scheme 8).



Reagents: i, EtMgBr; ii, Me$_3$SiCl; iii, (C$_6$H$_{11}$)$_2$BH; iv, Ac$_2$O–heat; v, NaOH–H$_2$O$_2$; vi, Cl$_2$ or Br$_2$; vii, NaOMe; viii, I$_2$; ix, I$_2$–CF$_3$CO$_2$Ag; x, KF–DMSO–H$_2$O; xi, HBr

Scheme 8

(iii) *Allyl-silanes*. Allyl-silanes, as homologues of vinyl-silanes, undergo similarly controlled regiospecific electrophilic attack, the electrophile bonding to the γ-carbon atom, which results in a net shift of position of the double bond[30] (Scheme 9).

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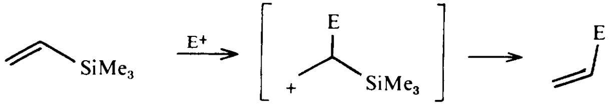
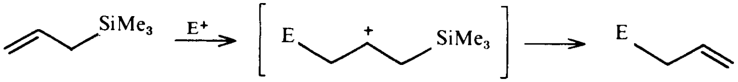
[29] R. K. Boeckman and D. M. Blum, *J. Org. Chem.*, 1974, **39**, 3307.

[30] R. Calas and E. Frainnet, *Compt. rend.*, 1955, **240**, 203; 1956, **243**, 595.

Vinyl-silanes



Allyl-silanes



Scheme 9

The allyl-silane (7) has been converted into the aglucone ethanoate (8)[31] of loganin, and, by a separate series of transformations, into the prostaglandin intermediate (9)[32] (Scheme 10). A related study[33] of the synthetic utility of 1-trimethylsilylbuta-1,3-diene (10) as a Diels–Alder dienophile has been reported.

An example of the powerful directing effect of silicon in such systems can be seen in a preparation of synthetically versatile allyl sulphides by acid-catalysed rearrangement of the more accessible β-hydroxyalkyl phenyl sulphides, when, with silicon's assistance, migration from a secondary to a tertiary cationic site is observed[34] (Scheme 11). Similarly, the allyl-silane (11) gives solely[35] the alkene (13), in contrast to (12), which gives a gross mixture of alkene isomers (Scheme 11); predictably, the rearrangement is faster with the silylated substrate.

As with vinyl-silanes, allyl-silanes can be induced to transfer the allyl group to suitable electrophiles,[36,37] leading, in one case,[38] to a ready synthesis of artemesia ketone (14) (Scheme 12).

Allyl-silanes react regiospecifically with chlorosulphonyl isocyanate to give intermediate β-lactams, which rearrange thermally to lactim ethers (15); such species can be hydrolysed to acids,[31] or, by treatment with pyridine,[39] converted into nitriles (Scheme 13).

To summarize, the two modes of interaction of a carbon–silicon bond with a

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[31] B.-W. Au-Yeung and I. Fleming, *J.C.S. Chem. Comm.*, 1977, 81.

[32] B.-W. Au-Yeung and I. Fleming, *J.C.S. Chem. Comm.*, 1977, 79.

[33] M. J. Carter and I. Fleming, *J.C.S. Chem. Comm.*, 1976, 679; I. Fleming and A. Percival, *ibid.*, p. 681.

[34] P. Brownbridge, I. Fleming, A. Pearce, and S. Warren, *J.C.S. Chem. Comm.*, 1976, 751 and references therein; P. Brownbridge and S. Warren, *J.C.S. Perkin I*, 1977, 1131.

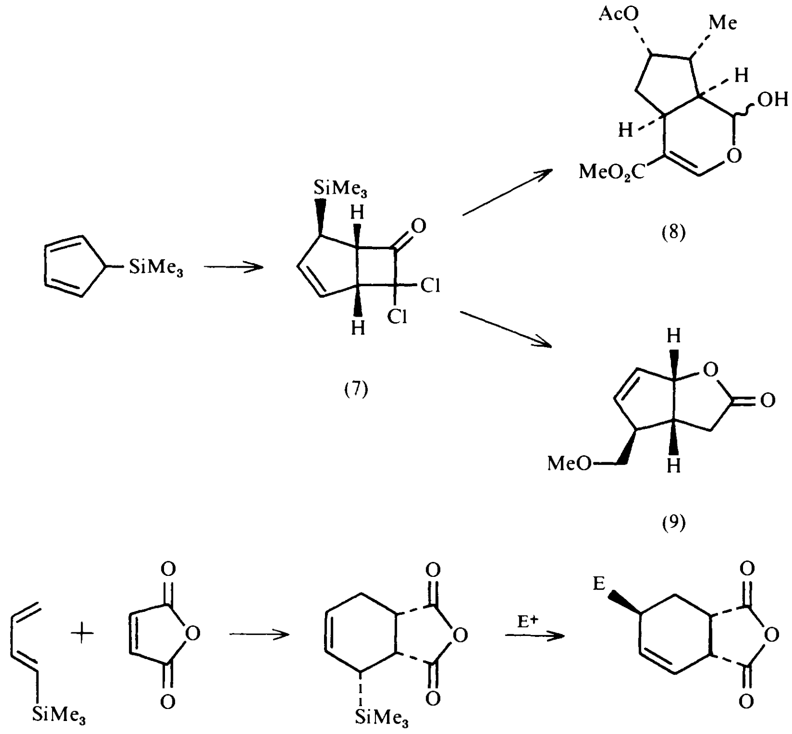
[35] I. Fleming, A. Pearce, and R. L. Snowden, *J.C.S. Chem. Comm.*, 1976, 182.

[36] A. Hosomi and H. Sakurai, *Tetrahedron Letters*, 1976, 1295; for conjugate addition to enones, see *J. Amer. Chem. Soc.*, 1977, **99**, 1673.

[37] I. Ojima, Y. Miyazawa, and M. Kumagai, *J.C.S. Chem. Comm.*, 1976, 927; for more highly functionalized allylsilanes, see I. Ojima, M. Kumagai, and Y. Miyazawa, *Tetrahedron Letters*, 1977, 1385; K. Itoh, M. Fukui, and Y. Kurachi, *J.C.S. Chem. Comm.*, 1977, 500.

[38] J.-P. Pillot, J. Dunoguès, and R. Calas, *Tetrahedron Letters*, 1976, 1871; see also G. Deleris, J. Dunoguès, and R. Calas, *ibid.*, p. 2449.

[39] G. Deleris, J. Dunoguès, and R. Calas, *J. Organometallic Chem.*, 1976, **116**, C45.



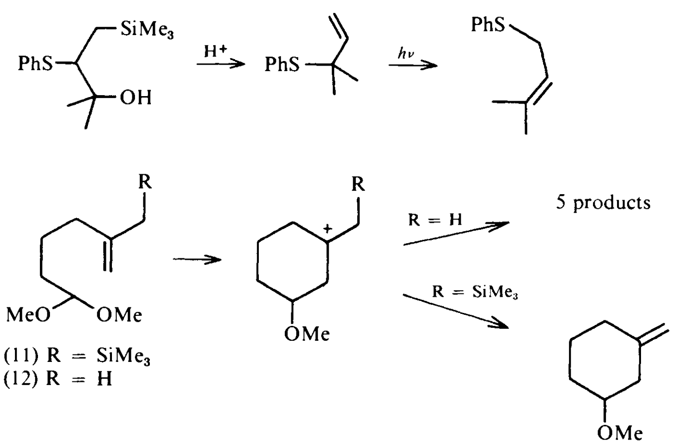
(7)

(8)

(9)

(10)

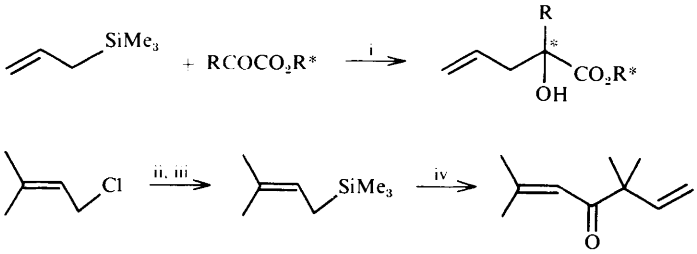
Scheme 10



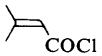
(11) $R = SiMe_3$
(12) $R = H$

(13)

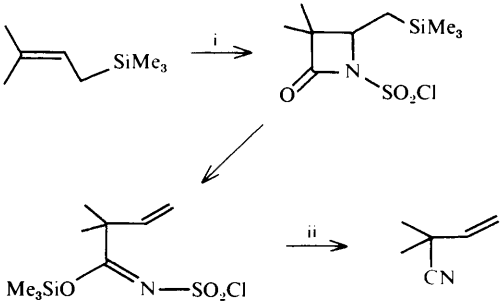
Scheme 11



(14)

Reagents: i, $TiCl_4$; ii, Mg–Et_2O; iii, Me_3SiCl; iv,  and $AlCl_3$

Scheme 12



(15)

Reagents: i, $ClSO_2NCO$; ii, pyridine

Scheme 13

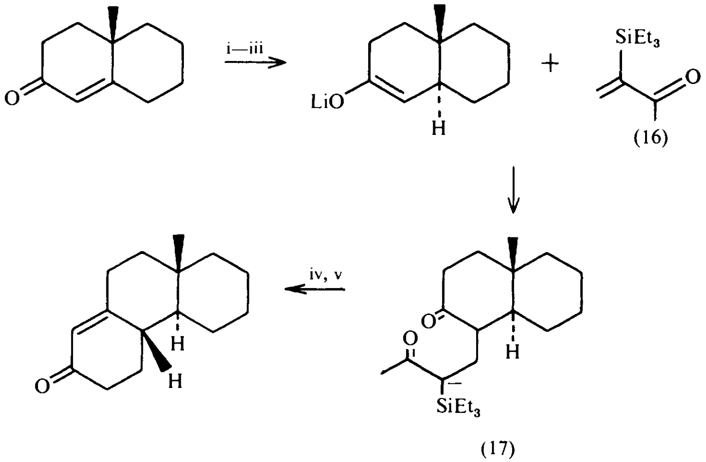
cationic centre can be represented as shown in Scheme 9. In subsequent sections, more examples of such behaviour will be illustrated.

B. Carbanions.—$(p\text{–}d)\pi$-Back-bonding between silicon and carbon, and consequent electron withdrawal from carbon, is sufficiently strong in many cases to stabilize an α-silyl carbanion. Using strong base, a proton can be removed from even tetramethylsilane.[40] In most cases, however, the carbanion is also flanked by another electron-withdrawing group; in addition, the reaction partner is normally a carbonyl compound, and the final product is an alkene: these reactions are discussed in Section 4.

Two reactions do not fall into this general class. The regiospecific addition of vinyl ketones to enolate anions (kinetically generated under aprotic conditions) is not normally practicable, owing to extensive polymerization of vinyl ketones under such conditions and relatively rapid proton transfer, resulting in

[40] D. J. Peterson, *J. Organometallic Chem.*, 1967, **9**, 373.

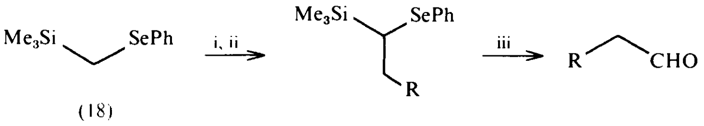
loss of enolate regiospecificity. The silylated methyl vinyl ketone (16) successfully traps[41] even readily equilibrated enolate anions (Scheme 14), with the intermediacy of the relatively stable, and hence non-basic, anion (17); the silyl group in the product, being now α-ketonic, is readily displaced by nucleophiles.



Reagents: i, Li–NH_3–Bu^tOH (1 equiv.); ii, Me_3SiCl, then isolation; iii, LiMe; iv, NH_4Cl–H_2O; v, NaOMe–MeOH.

Scheme 14

Phenylselenomethyltrimethylsilane (18) furnishes a carbanion which reacts[42] smoothly with primary alkyl bromides and iodides. The alkylated products, after treatment with hydrogen peroxide, did not produce vinyl-silanes by selenoxide elimination, but did afford the homologous aldehydes directly (Scheme 15) (see Section 5). Extension to provide a general acyl carbanion equivalent should be possible.



Reagents: i, $LiNPr^i_2$–THF, at −78 °C; ii, RCH_2X; iii, 30% H_2O_2

Scheme 15

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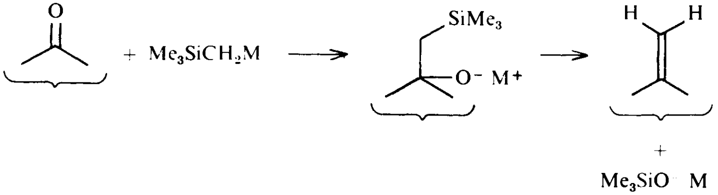
[41] (*a*) G. Stork and B. Ganem, *J. Amer. Chem. Soc.*, 1973, **95**, 6152; (*b*) R. K. Boeckman, *ibid.*, p. 6867; *J. Org. Chem.*, 1973, **38**, 4450; *J. Amer. Chem. Soc.*, 1974, **96**, 6179; (*c*) G. Stork and J. Singh, *ibid.*, p. 6181; for a related process with α-silyl propenoate esters, see S. L. Hartzell and M. W. Rathke, *Tetrahedron Letters*, 1976, 2737.

[42] K. Sachdev and H. S. Sachdev, *Tetrahedron Letters*, 1976, 4223; see also H. J. Reich and S. K. Shah, *J. Org. Chem.*, 1977, **42**, 1773.

4 β-Hydroxy-silanes as Alkene Precursors

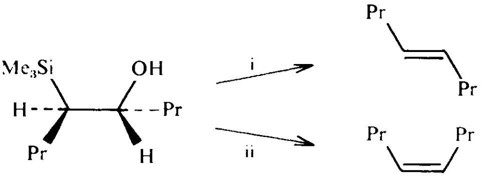
In most examples of processes involving α-silyl carbanionoids, the reaction partner is a carbonyl compound, and the β-hydroxy-silane thus formed can be converted into an alkene by thermodynamically favourable β-elimination of trimethylsilanol or its equivalent. The classic example of this process, which is analogous to the Wittig reaction and often superior to it, especially for the introduction of exomethylene units,[43] is known as Peterson olefination[44] (Scheme 16).



Scheme 16

The factors influencing the ease and stereochemical requirements of this elimination have been delineated by several groups. It has been observed that lithium and magnesium salts of β-hydroxy-silanes undergo elimination more readily[44] when the resulting alkene is non-terminal than when it is terminal. Treatment of β-hydroxy-silanes with ethanoyl chloride or thionyl chloride[45] is effective in promoting elimination.

In a study[46] of the stereochemistry of silanol elimination, the silane (19) (of unknown relative configuration, but diastereoisomerically almost pure) gave almost exclusively *E*-alkene, the expected product of *syn*-elimination from the *threo*-form, when treated with potassium hydride (Scheme 17). Boron trifluoride etherate, on the other hand, gave *Z*-alkene, the expected product of *anti*-elimination. These different elimination pathways reflect the requirement, in the former case, for *syn*-elimination to occur in order that an Si—O bond might



(19)

Reagents: i, KH; ii, BF_3, Et_2O

Scheme 17

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[43] R. K. Boeckman and S. M. Silver, *Tetrahedron Letters*, 1973, 3497.

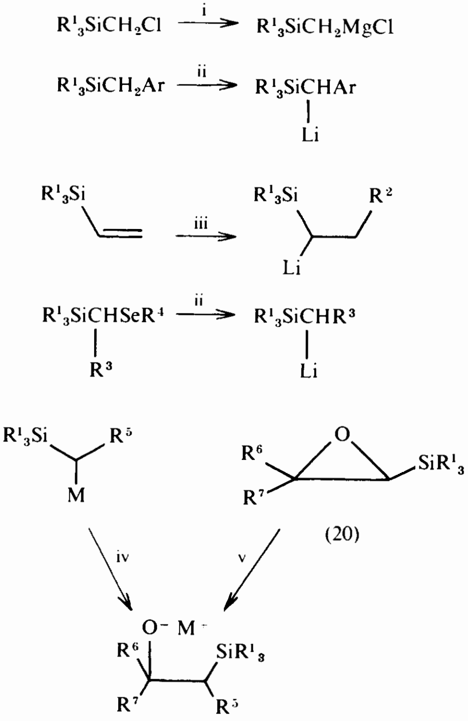
[44] D. J. Peterson, *J. Org. Chem.*, 1968, **33**, 780; see also F. A. Carey and J. R. Toler, *ibid.*, 1976, **41**, 1966.

[45] T. H. Chan and E. Chang *J. Org. Chem.*, 1974, **39**, 3264.

[46] P. F. Hudrlik and D. Peterson, *J. Amer. Chem. Soc.*, 1975, **97**, 1464.

be formed; in the latter case, an Si—F bond is formed, and the usual stereoelectronic factors determine the geometry of elimination.

This same general process can be used for the stereoselective production of trisubstituted alkenes,[47] or, by reaction with an aldehyde, 1,2-disubstituted alkenes. The requisite reagents are generated as Grignard reagents,[44] by direct lithiation of a suitably substituted silane or addition of an alkyl-lithium to a vinyl-silane,[48] or by cleavage of an α-silylmethyl selenide;[49] if the epoxy-silane (20) is readily available (see Section 5), it undergoes a regiospecific ring opening on treatment[50] with lithium dialkylcuprates, once again producing alkenes (Scheme 18).



(20)

Reagents: i, Mg; ii, Bu^nLi; iii, R^2Li; iv, R^6COR^7; v, $LiCuR^5_2$

Scheme 18

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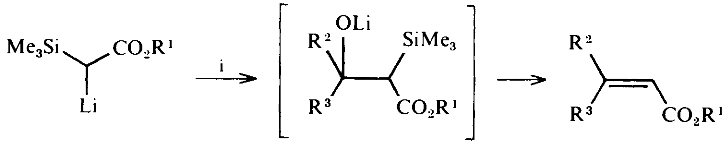
[47] K. Utimoto, M. Obayashi, and H. Nozaki, *J. Org. Chem.*, 1976, **41**, 2940.

[48] T. H. Chan, E. Chang, and E. Vinokur, *Tetrahedron Letters*, 1970, 1137; T. H. Chan and E. Chang, *J. Org. Chem.*, 1974, **39**, 3264; for the original observation, see L. F. Cason and H. G. Brooks, *ibid.*, 1954, **19**, 1278; see also P. R. Jones and T. F. O. Lim, *J. Amer. Chem. Soc.*, 1977, **99**, 2013.

[49] W. Dumont and A. Krief, *Angew. Chem. Internat. Edn.*, 1976, **15**, 161.

[50] P. F. Hudrlik, D. Peterson, and R. J. Rona, *J. Org. Chem.*, 1975, **40**, 2263.

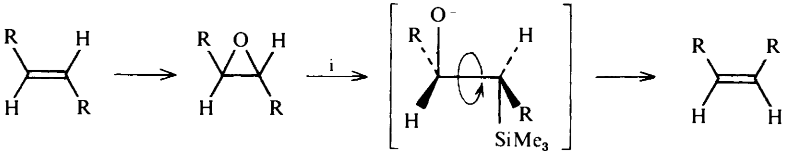
The analogous direct conversion of aldehydes or ketones into homologated $\alpha\beta$-unsaturated esters (Scheme 19) has been described.[51,52]



Reagent: i, R^2COR^3

Scheme 19

Trimethylsilylpotassium smoothly converts oxirans into alkenes, nucleophilic ring opening being followed by spontaneous β-elimination; this provides an excellent alternative[53] to the earlier Wittig-based methods[54] of geometric isomerization of alkenes (Scheme 20).



Reagents: i, $Me_3SiSiMe_3$–KOMe–HMPA

Scheme 20

The silicon- and phosphorus-substituted diazomethanes (21) and (22), as their metal salts, convert[55] some ketones and aldehydes into homologous alkynes (Scheme 21); evidence has been presented in the phosphorus case, and (by implication) in the silicon analogue also; this implies that there is initial elimination to give a diazovinyl species, which then undergoes skeletal rearrangement.

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[51] K. Shimoji, H. Taguchi, K. Oshima, H. Yamamoto, and H. Nozaki, *J. Amer. Chem. Soc.*, 1974, **96**, 1620; H. Taguchi, K. Shimoji, H. Yamamoto, and H. Nozaki, *Bull. Chem. Soc. Japan*, 1974, **47**, 2529.

[52] S. L. Hartzell, D. F. Sullivan, and M. W. Rathke, *Tetrahedron Letters*, 1974, 1403; for $\alpha\beta$-unsaturated thiol esters, see D. H. Lucast and J. Wemple, *ibid.*, 1977, 1103; for $\alpha\beta$-unsaturated acids see P. A. Grieco, C.-L. J. Wang, and J. S. Burke, *J.C.S. Chem. Comm.*, 1975, 537.

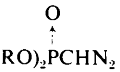
[53] P. B. Dervan and M. A. Shippey, *J. Amer. Chem. Soc.*, 1976, **98**, 1265; for the analogous use of $PhMe_2SiLi$, see M. T. Reetz and M. Plachky, *Synthesis*, 1976, 199; for other functional silyl anions, see W. C. Still, *J. Org. Chem.*, 1976, **41**, 3063; H. Watanabe, K. Higuchi, M. Kobayashi, M. Hara, Y. Koike, T. Kitahara, and Y. Nagai, *J.C.S. Chem. Comm.*, 1977, 534.

[54] E. Vedejs and P. L. Fuchs, *J. Amer. Chem. Soc.*, 1973, **95**, 822; A. J. Bridges and G. H. Whitham, *J.C.S. Chem. Comm.*, 1974, 142; see also P. E. Sonnet and J. E. Oliver, *J. Org. Chem.*, 1976, **41**, 3279.

[55] E. W. Colvin and B. J. Hamill, *J.C.S. Perkin I*, 1977, 869; see also ref. 64*c*.

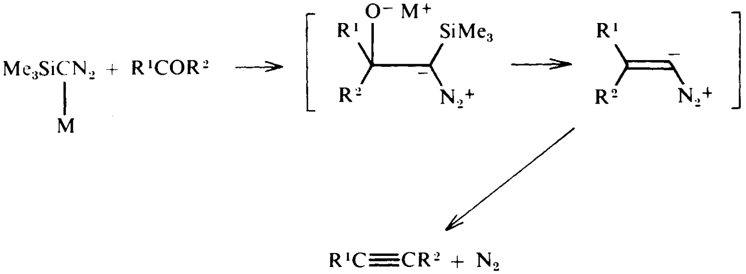
Me_3SiCHN_2

(21)



$(RO)_2\overset{O\uparrow}{P}CHN_2$

(22)



Scheme 21

A final example of the mechanistic parallel between silicon and phosphorus involves the silylated dithian anion (23), which, like the phosphorus analogue (24), converts[56] carbonyl compounds into synthetically useful keten thioacetals (Scheme 22); whereas the use of the ylide (24) is restricted to aldehydes, the lithio-salt (23) can be applied generally. Vinyl sulphoxides are obtainable[57] using the metallated species (25); the value of this method is reduced somewhat by the difficulty experienced in preparing (25).

The reaction of 1-triphenylsilylvinyl-lithium with aldehydes leads to allenes[58] (Scheme 23); in such cases, silanoxide elimination does not occur readily, and fluoride ion is used to displace the silyl moiety. It seems, however, that this reaction cannot be extended to ketones to produce 1,1-disubstituted allenes; in such cases, elimination does not occur, although the silyl group is lost.[59]

Symmetrical allenes[60] are formed by the reaction of the phosphorane (26) with aryl ketones; alkenes are formed simultaneously, by displacement of a silyl group from the phosphorane followed by a normal Wittig reaction (Scheme 24); variation of the ylide and/or the ketone leads to a range of products.

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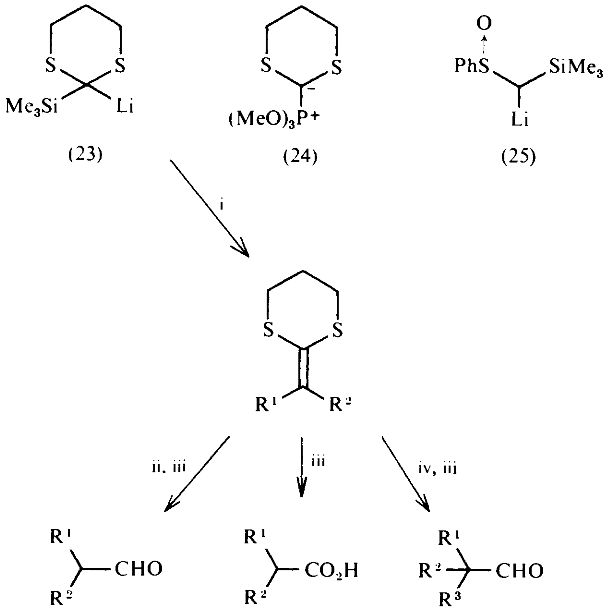
[56] F. A. Carey and A. S. Court, *J. Org. Chem.*, 1972, **37**, 1926; P. F. Jones and M. F. Lappert, *J.C.S. Chem. Comm.*, 1972, 526; D. Seebach, B.-Th. Gröbel, A. K. Beck, M. Braun, and K.-H. Geiss, *Angew. Chem. Internat. Edn.*, 1972, **11**, 443; D. Seebach, M. Kolb, and B.-Th. Gröbel, *Tetrahedron Letters*, 1974, 3171; B.-Th. Gröbel, R. Burstinghaus, and D. Seebach, *Synthesis*, 1976, 121.

[57] F. A. Carey and O. Hernandez, *J. Org. Chem.*, 1973, **38**, 2670; see also F. A. Carey and A. S. Court, *ibid.*, 1972, **37**, 939, and ref. 44.

[58] T. H. Chan and W. Mychajlowskij, *Tetrahedron Letters*, 1974, 171.

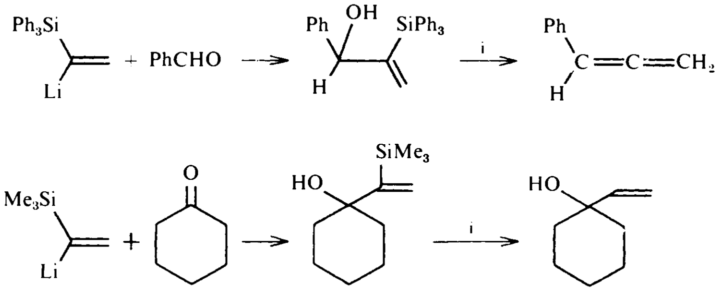
[59] T. H. Chan and W. Mychajlowskij, *Tetrahedron Letters*, 1974, 3479.

[60] H. Schmidbaur and H. Stühler, *Angew. Chem. Internat. Edn.*, 1973, **12**, 321; H. Schmidbaur, *Accounts Chem. Res.*, 1975, **8**, 62.



Reagents: i, R^1COR^2; ii, Et_3SiH-CF_3CO_2H; iii, Hg^{II}; iv, R^3Li

Scheme 22



Reagents: i, KF–DMSO

Scheme 23

The treatment of a variety of ketones with trimethylsilyl chloride and zinc produces alkenes (Scheme 25); this deoxygenation may be related to the Peterson reaction, but the available evidence[61] favours a carbenoid pathway.

5 Vinyl-silanes and αβ-Epoxy-silanes

Vinyl-silanes are readily converted into αβ-epoxy-silanes, which, by acid-catalysed nucleophilic displacement of the silyl group, efficiently give carbonyl

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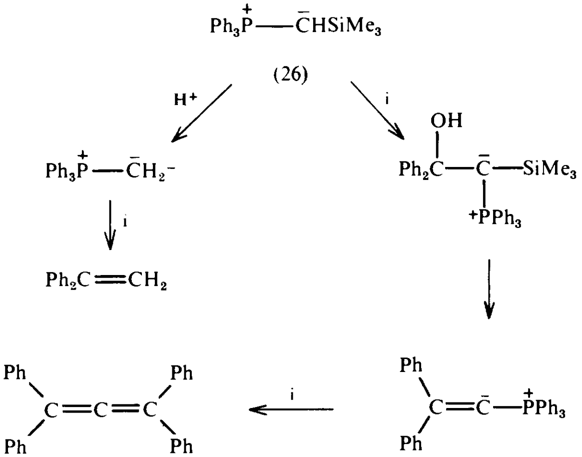
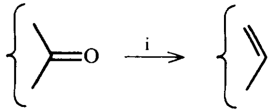
[61] W. B. Motherwell, *J.C.S. Chem. Comm.*, 1973, 935.



Reagent: i, PhCOPh

Scheme 24



Reagents: i, Zn–Me_3SiCl

Scheme 25

compounds.[62] This synthetic equivalence has found use in several general routes to carbonyl compounds, utilizing α-lithio-vinyl-silanes,[63] α-lithio-disilylmethanes,[64a] α-chloro-α-trimethylsilyl carbanions,[64b] and α-lithio-αβ-epoxy-silanes[65] (Scheme 26). Routes[66] to β-lithio-vinyl silanes have been developed, adding further scope to this process. It has also been applied in a regiospecific alternative to the Robinson annelation sequence, using allyl halides[67] such as (27); interestingly, displacement of the silyl group in such cases is easier than in simple αβ-epoxy-silanes, possibly owing to participation by the neighbouring carbonyl group (Scheme 27). Similarly, the silyl vinylcuprate (28) effects conjugate addition[68] of an ethanoyl anion equivalent.

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[62] G. Stork and E. Colvin, *J. Amer. Chem. Soc.*, 1971, **93**, 2080.

[63] B.-Th. Gröbel and D. Seebach, *Angew. Chem. Internat. Edn.*, 1974, **13**, 83; *Chem. Ber.*, 1977, **110**, 852, 867; see also K. Sachdev, *Tetrahedron Letters*, 1976, 4041.

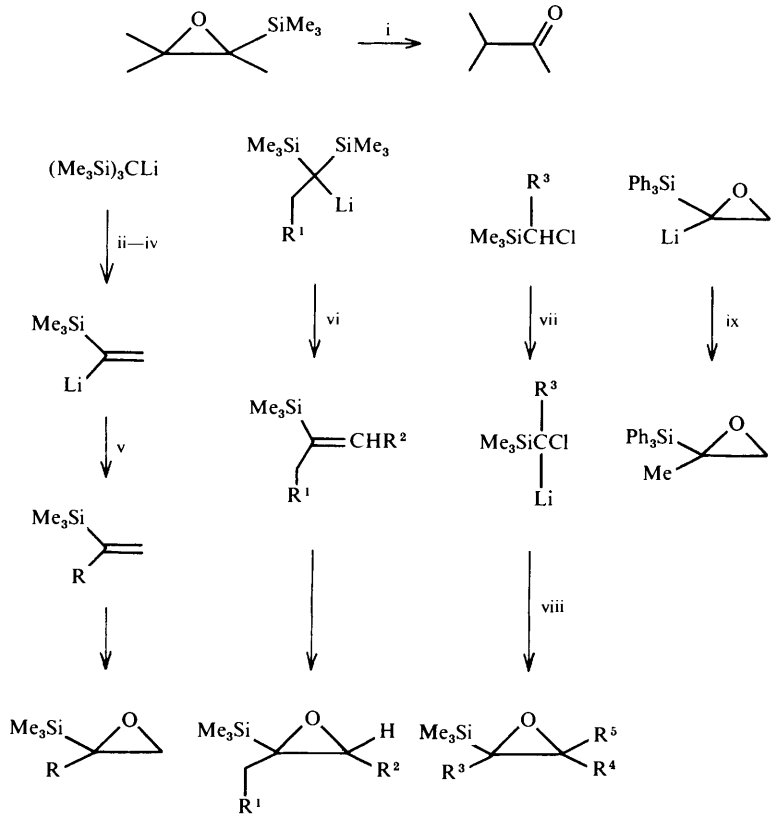
[64] (*a*) H. Sakurai, K. Nishiwaka, and M. Kira, *Tetrahedron Letters*, 1973, 4193; (*b*) C. Burford, F. Cooke, E. Ehlinger, and P. Magnus, *J. Amer. Chem. Soc.*, 1977, **99**, 4536; F. Cooke and P. Magnus, *J.C.S. Chem. Comm.*, 1977, 513; (*c*) see also U. Schöllkopf and H.-U. Scholz, *Synthesis*, 1976, 271.

[65] J. J. Eisch and J. E. Galle, *J. Amer. Chem. Soc.*, 1976, **98**, 4646.

[66] R. F. Cunico and F. J. Clayton, *J. Org. Chem.*, 1976, **41**, 1480.

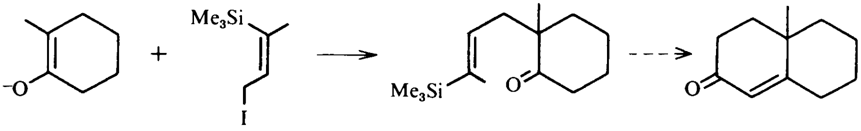
[67] G. Stork and M. E. Jung, *J. Amer. Chem. Soc.*, 1974, **96**, 3682; G. Stork, M. E. Jung, E. Colvin, and Y. Noel, *ibid.*, p. 3684.

[68] R. K. Boeckman and K. J. Bruza, *Tetrahedron Letters*, 1974, 3365.



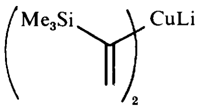
Reagents: i, H^+ Nu^-; ii, CH_2O; iii, Br_2; iv, Bu^tLi; v, RX; vi, R^2CHO; vii, Bu^sLi; viii, R^4COR^5; ix, MeI

Scheme 26



(27)

Scheme 27



(28)

$\alpha\beta$-Epoxy-silanes undergo electrophile-catalysed ring opening to give products of predominant α-cleavage.[69,70] This result is, at first sight, rather unexpected, as, although a fully developed carbonium ion may not be involved in such an opening, one would still expect β-cleavage to predominate, in view of the well-documented stability of cations β to silicon (see Section 3). However, the relative orientations of the C—Si and the β C—O bonds deviate markedly from the coplanar alignment favourable for stabilization of a developing positive charge by the C—Si bond. Indeed, the preference for α-opening in these reactions suggests that the silyl group may actually facilitate[71] bimolecular nucleophilic displacements α to silicon. In contrast, $\beta\gamma$-epoxy-silanes have no such geometric constraint, and are not only more labile, but open by exclusive β-cleavage,[72] *via* a developing β carbonium ion.

It would therefore appear that the conversion of $\alpha\beta$-epoxy-silanes into carbonyl compounds proceeds by initial solvolysis to $\alpha\beta$-dihydroxy-silanes, followed by acid-catalysed elimination; isolation[73] of the glycol (29) lends credence to this postulate, as here the trimethylsilyl groups and hydroxy-groups cannot fulfil the preferred *anti*-periplanar geometry for acid-catalysed elimination (Scheme 28). Such stability to acid suggests[74] that the standard hydrolysis conditions can be used only for those cases leading to acyclic carbonyl compounds; in principle, base-induced elimination, with its different stereochemical requirement, could be used for cyclic cases. $\alpha\beta$-Epoxy-silanes undergo thermolysis[75,76] to the isomeric silyl enol ethers; this route is unlikely to compete with the more standard methods for such compounds (see Section 7).

Simple $\alpha\beta$-epoxy-silanes undergo[77] desilylation on treatment with fluoride ion (Scheme 29) with retention of stereochemistry. Chloromethyl $\alpha\beta$-epoxy-silanes such as (30), on the other hand, give allene oxides as products of elimination;[78] this provides a reliable and easy entry into the allene oxide–oxyallyl zwitterion–cyclopropanone set of valence-bond tautomers, and has recently resulted in the isolation[79] of t-butylallene oxide (Scheme 29).

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[69] P. F. Hudrlik, R. N. Misra, G. P. Withers, A. M. Hudrlik, R. J. Rona, and J. P. Arcoleo, *Tetrahedron Letters*, 1976, 1453; see also ref. 50; for an application see M. Obayashi, K. Utimoto, and H. Nozaki, *ibid.*, 1977, 1807.

[70] J. J. Eisch and J. T. Trainor, *J. Org. Chem.*, 1963, **28**, 2870; J. J. Eisch and J. E. Galle, *ibid.*, 1976, **41**, 2615.

[71] C. Eaborn and J. C. Jeffrey, *J. Chem. Soc.*, 1954, 4266.

[72] P. F. Hudrlik and G. P. Withers, *Tetrahedron Letters*, 1976, 29.

[73] C. M. Robbins and G. H. Whitham, *J.C.S. Chem. Comm.*, 1976, 697.

[74] P. F. Hudrlik, J. P. Arcoleo, R. H. Schwartz, R. N. Misra, and R. J. Rona, *Tetrahedron Letters*, 1977, 591; for an application to produce heteroatom-substituted alkenes, see P. F. Hudrlik, A. M. Hudrlik, R. J. Rona, R. N. Misra, and G. P. Withers, *J. Amer. Chem. Soc.*, 1977, **99**, 1993.

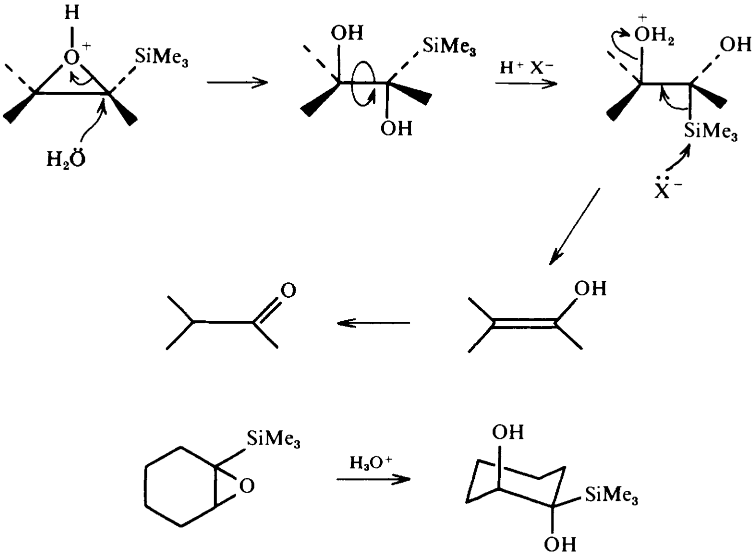
[75] P. F. Hudrlik, C.-N. Wan, and G. P. Withers, *Tetrahedron Letters*, 1976, 1449.

[76] A. R. Bassingdale, A. G. Brook, P. Chen, and J. Lennon, *J. Organometallic Chem.*, 1975, **94**, C21.

[77] T. H. Chan, P. W. K. Lau, and M. P. Li, *Tetrahedron Letters*, 1976, 2667.

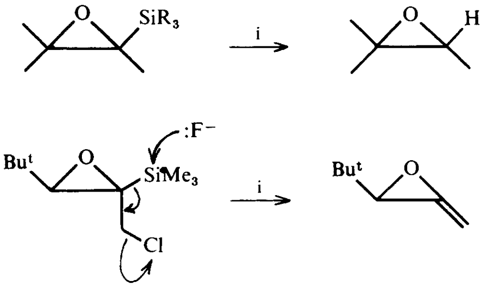
[78] T. H. Chan, M. P. Li, W. Mychajlowskij, and D. N. Harpp, *Tetrahedron Letters*, 1974, 3511.

[79] T. H. Chan, B. S. Ong, and W. Mychajlowskij, *Tetrahedron Letters*, 1976, 3253; B. S. Ong and T. H. Chan, *ibid.*, p. 3257.



(29)

Scheme 28



(30)

Reagent: i, F⁻

Scheme 29

Dihalogenocarbene addition to vinyl-silanes, followed by fluoride-ion-induced desilylation, similarly gives entry into strained halogenocyclopropenes[80] and the transient preparation of a bicyclo[2,2,2]oct-1-ene.[81]

6 Protection of Functional Groups

This section will concentrate on the protection afforded to various functional groups by their conversion into silyl derivatives, considerable emphasis being

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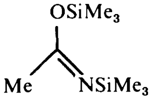
[80] T. H. Chan and D. Massuda, *Tetrahedron Letters*, 1975, 3383.
[81] T. H. Chan and D. Massuda, *J. Amer. Chem. Soc.*, 1977, **99**, 936.

placed on cases where the silyl group modifies, in a positive sense, the reactivity of the parent functional group. Specifically excluded are references to silylation as a derivatization procedure for chromatography or mass spectrometry, both fields being adequately covered elsewhere.[4,6]

A. Protection of Alcohols.—The protection of hydroxy-groups as their trimethylsilyl ethers has found use in several syntheses of natural products,[82–84] but the solvolytic lability of such ethers limits their utility. t-Butyldimethylsilyl ethers, on the other hand, are *ca.* 10^4 times less readily hydrolysed,[85] and can survive several sequential synthetic operations.[86–89] This group is stable to aqueous or alcoholic base under the conditions of ethanoate hydrolysis, and also to palladium-catalysed hydrogenolysis, and it resists mild reducing and oxidizing agents.[90] It is unaffected by hydrazine hydrate under conditions used to remove β-benzoylpropanoyl or *N*-acyl groups, but can be removed efficiently with fluoride ion or 80% ethanoic acid; iron(III) chloride in ethanoic anhydride transforms such ethers directly into the corresponding ethanoates,[91] with chiral retention. A final important advantage is that the formation of t-butyldimethylsilyl ethers does not introduce further chirality, in contrast to the use of tetrahydropyranyl ethers.

(i) *Formation.* The conversion of alcohols into their silyl ethers is normally achieved under very mild conditions, using the appropriate silyl chloride in the presence of a tertiary amine base, including the efficient combination[92] of bistrimethylsilylamine, trimethylsilyl chloride, and pyridine; silyl-transfer reagents such as (31)[93] and (32)[94] are of value. Imidazole is a most effective



(31)

$Me_3SiNHSO_3SiMe_3$

(32)

[82] E. J. Corey and B. B. Snider, *J. Amer. Chem. Soc.*, 1972, **94**, 2549.

[83] R. Wies and P. Pfaender, *Annalen*, 1973, 1269.

[84] E. Negishi, G. Lew, and T. Yoshida, *J.C.S. Chem. Comm.*, 1973, 874.

[85] Ref. 9, pp. 132, 138.

[86] E. J. Corey and A. Venkateswarlu, *J. Amer. Chem. Soc.*, 1972, **94**, 6190; see also D. A. Evans, T. C. Crawford, R. C. Thomas, and J. A. Walker, *J. Org. Chem.*, 1976, **41**, 3947.

[87] G. D. Prestwich and J. N. Labowitz, *J. Amer. Chem. Soc.*, 1974, **96**, 7103.

[88] E. J. Corey and H. S. Sachdev, *J. Amer. Chem. Soc.*, 1973, **95**, 8483.

[89] K. K. Ogilvie and D. J. Iwacha, *Tetrahedron Letters*, 1973, 317.

[90] E. W. Yankee, U. Axen, and G. L. Bundy, *J. Amer. Chem. Soc.*, 1974, **96**, 5865; see also ref. 86.

[91] B. Ganem and V. R. Small, *J. Org. Chem.*, 1974, **39**, 3728.

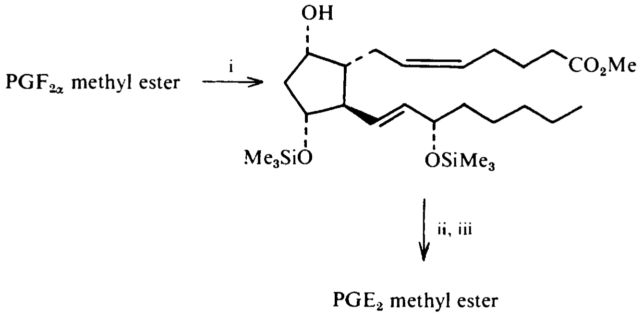
[92] C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Amer. Chem. Soc.*, 1963, **85**, 2497; H. E. Carter and R. C. Gaver, *J. Lipid Res.*, 1967, **8**, 391.

[93] J. F. Klebe, H. Finkbeiner, and D. M. White, *J. Amer. Chem. Soc.*, 1966, **88**, 3390; M. N. Galbraith, D. H. S. Horn, E. Middleton, and R. J. Hackney, *Chem. Comm.*, 1968, 466; see also L. Birkofer, A. Ritter, and F. Bentz, *Chem. Ber.*, 1964, **97**, 2196.

[94] B. E. Cooper and S. Westall, *J. Organometallic Chem.*, 1976, **118**, 135.

catalyst, finding particular utility[86] in the preparation of t-butyldimethylsilyl ethers.

Considerable regio- and stereo-selectivity is readily attained. The rates of silylation of secondary alcohols by bistrimethylsilylamine in pyridine at 25 °C vary[95] over a factor of 10^3 from *endo*-fenchol to *exo*-norborneol. t-Butyldimethylsilyl chloride reacts[96] selectively with the 3β-hydroxy-group of androst-5-ene-3β,17β-diol. Trimethylsilyldiethylamine silylates equatorial hydroxy-groups,[97] axial alcohols being unreactive under the conditions used; it selectively silylates the prostaglandin F series at the 11-, and, if secondary, the 15-position, allowing clean conversion[98] into the E series (Scheme 30). The demands made by the prostaglandins, in synthesis and interconversion, have done much to stimulate activity in studies of methods of protection that involve silyl ethers.



Reagents: i, Et_2NSiMe_3; ii, CrO_3,2py; iii, MeOH–H^+

Scheme 30

Silyl ethers have been used extensively in oligonucleotide synthesis,[99] affording selective protection to ribonucleoside hydroxy-functions.

(ii) *Cleavage*. Cleavage of silyl ethers to the parent alcohols can be achieved readily in the cases of labile ethers by treatment with nucleophiles such as methanol, often with methoxide ion as catalyst. The more stable, more useful, ethers such as t-butyldimethylsilyl are cleaved by protolysis with ethanoic acid or by fluoride ion, normally as tetra-n-butylammonium fluoride, in THF;[86] under such conditions fluoride ion is a strong base, so the appropriate care must be taken with base-labile substrates.

(iii) *Applications*. Dimethyldichlorosilane and related species convert diols

[95] H. J. Schneider and R. Hornung, *Annalen*, 1974, 1864.

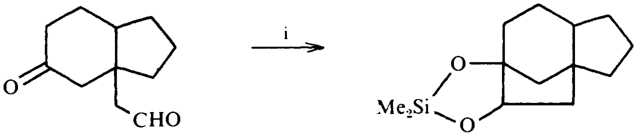
[96] H. Hosoda, D. K. Fukushima, and J. Fishman, *J. Org. Chem.*, 1973, **38**, 4209.

[97] I. Weisz, K. Felföldi, and K. Kovács, *Chem. Abs.*, 1969, **70**, 47 668.

[98] E. W. Yankee, C. H. Lin, and J. Fried, *J.C.S. Chem. Comm.*, 1972, 1120; E. W. Yankee and G. L. Bundy, *J. Amer. Chem. Soc.*, 1972, **94**, 3651.

[99] K. K. Ogilvie, E. A. Thompson, M. A. Quilliam, and J. B. Westmore, *Tetrahedron Letters*, 1974, 2865 and references therein; see also E. Lukevics, A. E. Zabotskaya, and I. I. Solomennikova, *Russ. Chem. Rev.*, 1974, **43**, 140; S. L. Beaucage and K. K. Ogilvie, *Tetrahedron Letters*, 1977, 1691.

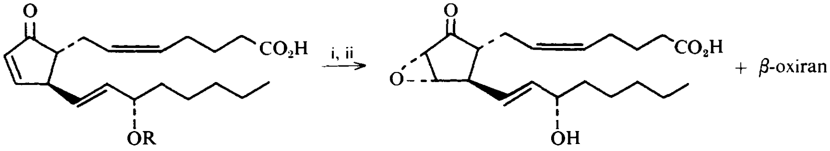
into siliconides,[100] which are analogous to acetonides; it acts as a kinetic trap[101] in the gibberellin-orientated pinacol cyclization shown (Scheme 31), a complex mixture being formed in its absence.



Reagents: i, $Mg(Hg)–Me_2SiCl_2$

Scheme 31

Trimethylsilyl ethers are oxidized to carbonyl compounds[102] by hydride abstraction with the triphenylmethyl cation; this has been extended to the selective oxidation of primary, secondary diols at the secondary position, though here the bistriphenylmethyl ethers are more suitable.[103] Epoxidation of the prostaglandin (33) with alkaline hydrogen peroxide gives a mixture of α- and β-10,11-oxirans. Attachment of a bulky 'remote controller' group to the hydroxy-group at C-15 permits stereoselective epoxidation, the highest degree[104] being attained with the tri-(*p*-xylyl)silyl derivative (34), which screens the β-face of the molecule owing to the configuration of C-12; the hydroxy-group is regenerated, in this case, by reduction with aluminium amalgam (Scheme 32).



(33) R = H
(34) R = $Si(CH_2C_6H_4Me\text{-}p)_3$

94 : 6

Reagents: i, $H_2O_2–HO^-$; ii, $Al(Hg)–MeCO_2H$

Scheme 32

Oxy-Cope and siloxy-Cope rearrangements of the diene (35) give quite different products (Scheme 33), in a rather dramatic demonstration[105] of the fact that silyl-substitution modifies the reaction course.

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[100] R. W. Kelly, *Tetrahedron Letters*, 1969, 967; *J. Chromatog.*, 1969, **43**, 229.

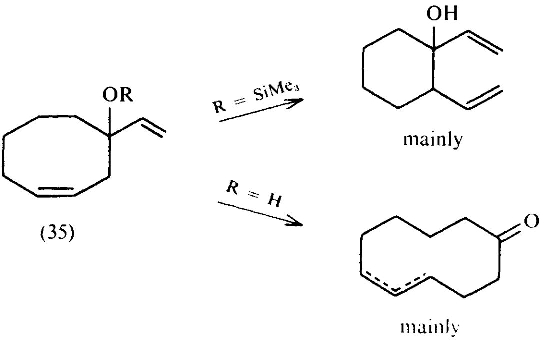
[101] E. J. Corey and R. L. Carney, *J. Amer. Chem. Soc.*, 1971, **93**, 7318; see also E. J. Corey, R. L. Danheiser, and S. Chandrasekaran, *J. Org. Chem.*, 1976, **41**, 260.

[102] M. E. Jung, *J. Org. Chem.*, 1976, **41**, 1479.

[103] M. E. Jung and L. M. Speltz, *J. Amer. Chem. Soc.*, 1976, **98**, 7882.

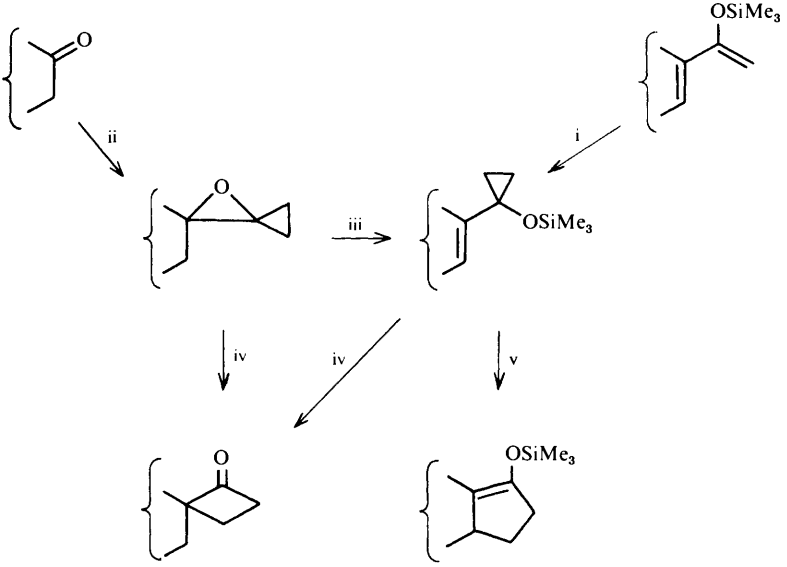
[104] E. J. Corey and H. E. Ensley, *J. Org. Chem.*, 1973, **38**, 3187.

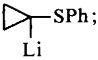
[105] R. W. Thies, M. T. Wills, A. W. Chin, L. E. Schick, and E. S. Walton, *J. Amer. Chem. Soc.*, 1973, **95**, 5281; see also R. W. Thies and R. E. Bolesta, *J. Org. Chem.*, 1976, **41**, 1233.



Scheme 33

Trimethylsilyloxycyclopropanes have been involved[106,107] in several valuable synthetic procedures, exemplified in Scheme 34.



Reagents: i, CH_2I_2–Zn–Cu; ii, ; iii, $LiNR_2$–Me_3SiCl; iv, H^+ or Lewis acid; v, heat

Scheme 34

B. Protection of Carboxylic and Sulphenic Acids.—The relative stability of silyl esters to basic and oxidizing conditions,[108] coupled with their ready cleavage on mild treatment with methanol or ethanol, makes them attractive protecting

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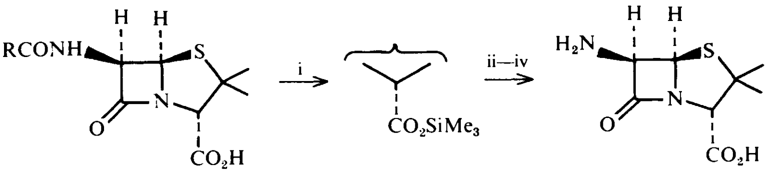
[106] B. M. Trost and M. J. Bogdanowicz, *J. Amer. Chem. Soc.*, 1973, **95**, 289, 2038; B M. Trost. and S. Kurozumi, *Tetrahedron Letters*, 1974, 1929.

[107] C. Girard, P. Amice, J. P. Barnier, and J. M. Conia, *Tetrahedron Letters*, 1974, 3329.

[108] See, for example, E. J. Corey and C. U. Kim, *J. Org. Chem.*, 1973, **38**, 1233.

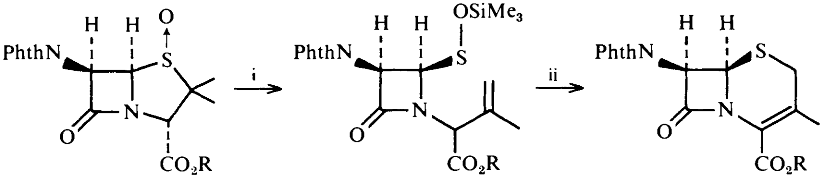
groups for carboxyl functions. Their use to protect the carboxy-group attached to C-3 in penicillins during the cleavage of side-chains represented an important achievement[109] in devising a practical route to 6-aminopenicillanic acid (Scheme 35). Similar techniques have brought significant improvements to the preparation of 7-aminocephalosporanic acid.



Reagents: i, Me_3SiCl-py; ii, PCl_5-py; iii, R^1OH; iv, $(NH_4)HCO_3$-H_2O

Scheme 35

The labile sulphenic acid partner in the reversible thermal rearrangement of penicillin sulphoxides can be trapped[110] as the silyl ester (36), which functions as a masked RS^+ species, as shown by its acid-catalysed cyclization to the cephem (37) (Scheme 36).

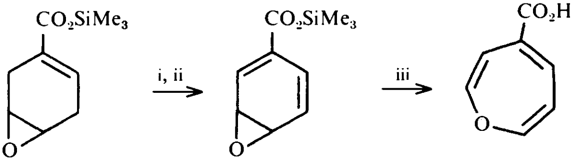


(36) (37)

Reagents: i, Me_3SiCl-heat; ii, $MeSO_3H$

Scheme 36

The protected acid (38) survived two sets of reagents before liberation with methanol to give the oxepin (39)[111] (Scheme 37).



(38) (39)

Reagents: i, *N*-Bromosuccinimide-CCl_4-$h\nu$; ii, Et_3N-Et_2O; iii, MeOH

Scheme 37

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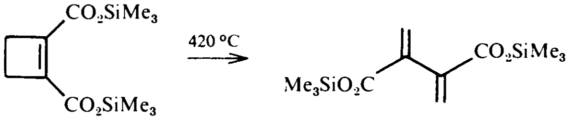
[109] F. M. Huber, R. C. Chauvette, and B. G. Jackson in 'Cephalosporins and Penicillins', ed. E. H. Flynn, Academic Press, New York, 1972, Ch. 2.

[110] T. S. Chou, *Tetrahedron Letters*, 1974, 725; T. S. Chou, J. R. Burgtorf, A. L. Ellis, S. R. Lammert, and S. Kukolja, *J. Amer. Chem. Soc.*, 1974, **96**, 1609.

[111] J. D. Richardson, T. C. Bruice, S. M. Waraskiewicz, and G. A. Berchtold, *J. Org. Chem.*, 1974, **39**, 2088.

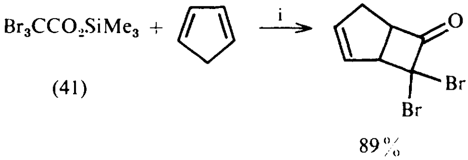
Pyrolysis of the diester (40), followed by hydrolysis, yielded[112] the hitherto elusive butadiene-2,3-dicarboxylic acid (Scheme 38).



(40)

Scheme 38

Sensitive and rather inaccessible acid chlorides such as 2-oxopropanoyl chloride can be prepared in good yield[113] by the reaction of the corresponding silyl ester with oxalyl chloride. Bistrimethylsilyl malonate[114,115] and alkyl trimethylsilyl malonates[116,117] have found predictable utility. Trimethylsilyl α-bromo-esters are recommended[118] in the Reformatsky reaction when isolation of the β-hydroxy-acid is desired. Trimethylsilyl tribromoethanoate (41) is an effective source of dibromoketen[119] (Scheme 39). The potential of the trimethylsilyloxycarbonyl function as a nitrogen-protecting group in peptide synthesis has been explored.[120]



(41)

Reagent: i, Ph_3P

Scheme 39

C. Protection of Alkynes and Ketens.—The use of the trialkylsilyl group to afford protection to terminal alkynes is a most active area, important contributions having been made by Walton[121] and co-workers, resulting in routes to

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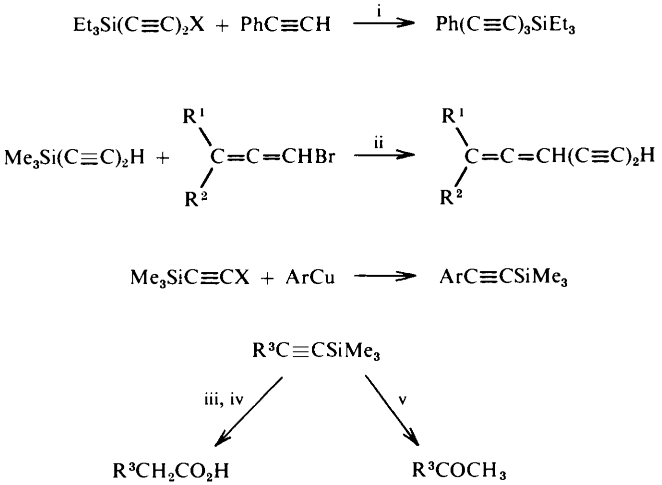
[112] P. Dowd and K. Kang, *Synthetic Comm.*, 1974, **4**, 151.
[113] J. Häusler and V. Schmidt, *Chem. Ber.*, 1974, **107**, 145.
[114] N. H. Nam, J.-P. Beaucourt, H. Hoellinger, and L. Pichat, *Bull. Soc. chim. France*, 1974, 1367; for conversion into carbon suboxide, see L. Birkofer and P. Sommer, *Chem. Ber.*, 1976, **109**, 1701.
[115] U. Schmidt and M. Schwochau, *Tetrahedron Letters*, 1967, 4491.
[116] L. Pichat and J.-P. Beaucourt, *Synthesis*, 1973, 537.
[117] B. M. Trost and R. A. Kunz, *J. Org. Chem.*, 1974, **39**, 2648.
[118] A. Horeau, *Tetrahedron Letters*, 1971, 3227.
[119] T. Okada and R. Okawara, *Tetrahedron Letters*, 1971, 2801.
[120] Y. Yamamoto, D. S. Tarbell, J. R. Fehlner, and B. M. Pope, *J. Org. Chem.*, 1973, **38**, 2521.
[121] R. Eastmond, T. R. Johnson, and D. R. M. Walton, *Tetrahedron*, 1972, **28**, 4601.

polyalkynes,[122a] allene-diynes,[122b] and aryl-alkynes[122c] (Scheme 40); terminal substitution also allows selective oxidative transformation into carboxylic acids[123] or methyl ketones.[124] In general, protection is effected by the reaction of the alkyne anion or its equivalent with a trialkylsilyl chloride; after reaction, the terminal alkyne is liberated by hydroxide ion,[125] by methanolysis, by silver(I) ion[126] followed by cyanide ion,[127] or by fluoride ion.[128]



Reagents: i, CuCl; ii, CuBr; iii, $R^4{}_2BH$; iv, $NaOH-H_2O_2$; v, H^+-Hg^{2+}

Scheme 40

Selective reduction[126] of non-terminal triple bonds in polyalkynes is possible if the terminal alkyne is first protected by silylation, as illustrated in the semi-hydrogenation of (42) to give a terminal *Z*-enyne unit in an approach[129] to histrionicotoxin (Scheme 41). The Wittig salt (43), as its ylide, converts[128] aldehydes into *E*-enyne units.

The acidic hydrogen of propyne is masked by silylation, allowing preparation of the alkyl-lithium compound (44), a species used in routes to homologous

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[122] (*a*) B. N. Ghose and D. R. M. Walton, *Synthesis*, 1974, 890; (*b*) P. D. Landor, S. R. Landor, and J. P. Leighton, *Tetrahedron Letters*, 1973, 1019; (*c*) R. Iliver and D. R. M. Walton, *ibid.*, 1972, 5209.

[123] G. Zweifel and S. J. Backlund, *J. Amer. Chem. Soc.*, 1977, **99**, 3184; see also R. Köster and L. A. Hagelee, *Synthesis*, 1976, 118.

[124] D. A. McCrae and L. Dolby, *J. Org. Chem.*, 1977, **42**, 1607.

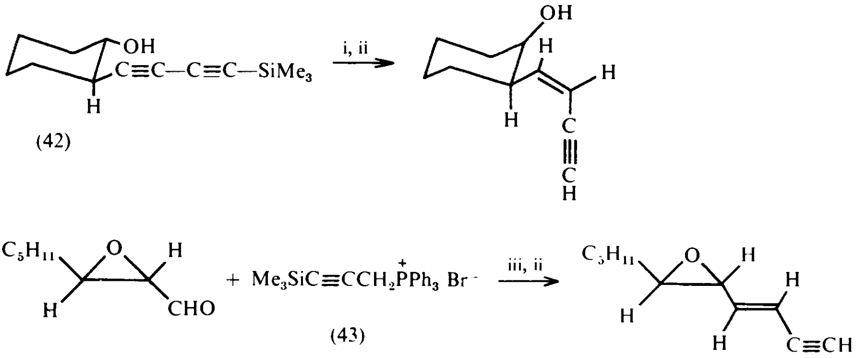
[125] C. Eaborn and D. R. M. Walton, *J. Organometallic Chem.*, 1966, **4**, 217.

[126] H. M. Schmidt and J. F. Arens, *Rec. Trav. chim.*, 1967, **86**, 1138.

[127] E. J. Corey and H. A. Kirst, *Tetrahedron Letters*, 1968, 5041.

[128] E. J. Corey and R. A. Ruden, *Tetrahedron Letters*, 1973, 1495; E. J. Corey, G. W. Fleet, and M. Kato, *ibid.*, 1974, 3963; see also E. Nakamura and I. Kuwajima, *Angew. Chem. Internat. Edn.*, 1976, **15**, 498.

[129] A. B. Holmes, R. A. Raphael, and N. K. Wellard, *Tetrahedron Letters*, 1976, 1539.



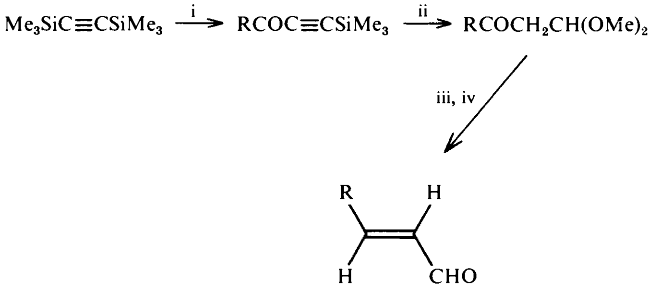
Reagents: i, H_2–Pd/$BaSO_4$–quinoline; ii, F^-; iii, base

Scheme 41

alkyl-alkynes,[127] α-santalol,[130] some triterpenoids,[131] and the classic synthesis of *Cecropia* juvenile hormone.[132] The related organocopper species (45) adds 1,6 to penta-2,4-dienoate esters in a simple route[133] to functionalized 1,5-enynes and 1,4,5-trienes.

$Me_3SiC{\equiv}CCH_2Li$ (44) $\qquad$ $R_3SiC{\equiv}CCH_2Cu$ (45)

Bistrimethylsilylethyne reacts with acid chlorides to give[134] αβ-unsaturated aldehydes (Scheme 42) by two-carbon homologation. It also undergoes a



Reagents: i, RCOCl-$AlCl_3$-CH_2Cl_2; ii, 0.1M-MeO^-; iii, $NaBH_4$; iv, H_3O^+

Scheme 42

cobalt-catalysed reaction with the diyne (46) to give the strained tetrasilylnaphthalene (48), probably *via*[135] the benzocyclobutene (47) (Scheme 43);

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[130] E. J. Corey, H. A. Kirst, and J. A. Katzenellenbogen, *J. Amer. Chem. Soc.*, 1970, **92,** 6314.

[131] R. E. Ireland, M. I. Dawson, and C. A. Lipinski, *Tetrahedron Letters*, 1970, 2247.

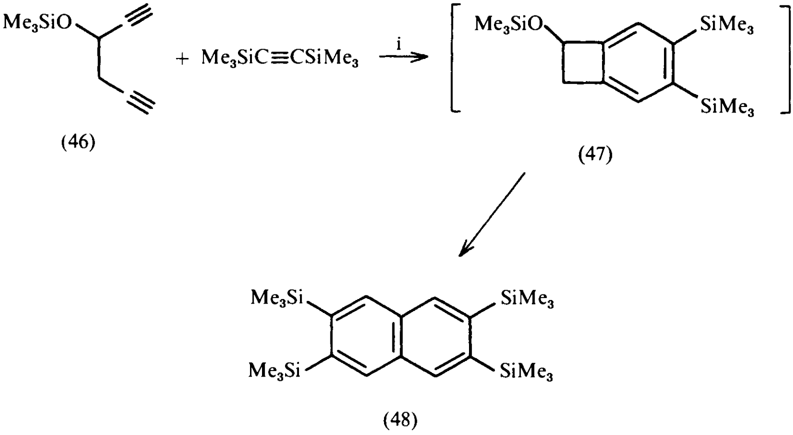
[132] E. J. Corey, J. A. Katzenellenbogen, and G. A. Posner, *J. Amer. Chem. Soc.*, 1967, **89,** 4245.

[133] B. Ganem, *Tetrahedron Letters*, 1974, 4467.

[134] H. Newman, *J. Org. Chem.*, 1973, **38,** 2254.

[135] R. L. Funk and K. P. C. Vollhardt, *J.C.S. Chem. Comm.*, 1976, 833; see also K. P. C. Vollhardt and L. S. Yee, *J. Amer. Chem. Soc.*, 1977, **99,** 2010; R. L. Funk and K. P. C. Vollhardt, *ibid.*, p. 5483.

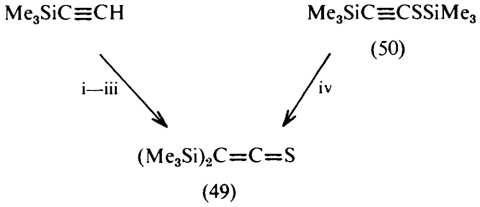
subsequent selective site-specific reaction with electrophiles (see Section 3) offers a potential route to a variety of substituted naphthalenes.



Reagent: i, $[CpCo(CO)_2]$

Scheme 43

Trimethylsilylketen is relatively stable, acting as a potent[136] acylating agent for hindered amines and tertiary alcohols; unlike trimethylsilylbromoketen,[137] it does not undergo cycloaddition reactions. The preparation (Scheme 44) and some reactions of bistrimethylsilylthioketen (49) have been described;[138] interestingly, the isomeric alkyne (50) rearranges thermally to (49).



Reagents: i, Bu^nLi; ii, $\frac{1}{8}S_8$; iii, Me_3SiCl; iv, heat

Scheme 44

7 Silyl Enol Ethers

Until recently, silyl enol ethers[139] were the compounds of major synthetic use of silicon, their utility being in providing regiostable, isolable species which can,

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[136] R. A. Ruden, *J. Org. Chem.*, 1974, **39**, 3607; for bis(trimethylsilyl)keten, see D. F. Sullivan, R. P. Woodbury, and M. W. Rathke, *J. Org. Chem.*, 1977, **42**, 2038.

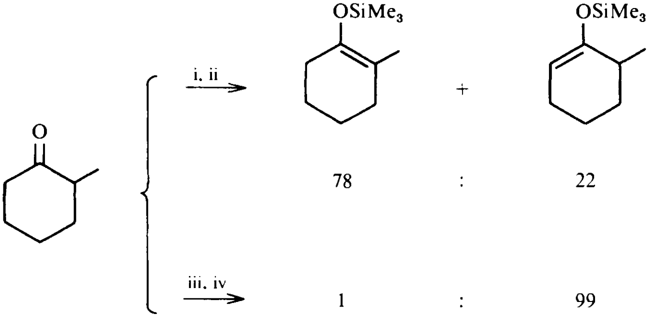
[137] W. T. Brady and R. A. Owens, *Tetrahedron Letters*, 1976, 1553; for (trimethylsilylmethyl)-keten, see W. T. Brady and T. C. Cheng, *J. Org. Chem.*, 1977, **42**, 732.

[138] S. J. Harris and D. R. M. Walton, *J.C.S. Chem. Comm.*, 1976, 1008.

[139] J. K. Rasmussen, *Synthesis*, 1977, 91.

on demand, give regio-pure enolate anions[140] after purification and spectral identification. They were introduced in an effort to avoid the production of an equivalent amount of base that results when metal enolates are formed from enol ethanoates or by reduction of enones with solvated electrons; the presence of such additional base encourages the formation of polyalkylated products.

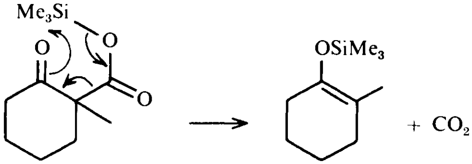
A. Preparation.—Silyl enol ethers are readily prepared[140,141] under conditions of either kinetic or thermodynamic control (Scheme 45).



Reagents: i, Me_3SiCl–Et_3N–DMF–heat; ii, $NaHCO_3$–H_2O; iii, $LiNPr_2{}^i$–DME; iv, Me_3SiCl

Scheme 45

Regiospecific generation can also be achieved by trapping the enolate anion formed from an enone by conjugate reduction[41c] or alkylation,[41b] by retro-Diels–Alder fragmentation,[142a] or by sigmatropic rearrangement[142b] of β-keto-acid silyl esters (Scheme 46).



Scheme 46

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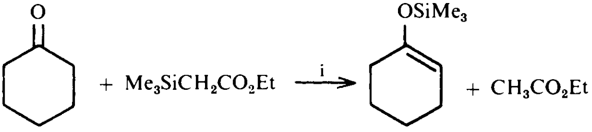
[140] G. Stork and P. F. Hudrlik, *J. Amer. Chem. Soc.*, 1968, **90**, 4462, 4464; G. Stork, *Pure Appl. Chem.*, 1975, **43**, 553; H. O. House, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, 1971, **36**, 2361; H. O. House, 'Modern Synthetic Reactions', 2nd edn., W. A. Benjamin, Menlo Park, California, 1972, pp. 568—569; see also R. E. Donaldson and P. E. Fuchs, *J. Org. Chem.*, 1977, **42**, 2032.

[141] S. Torkelson and C. Ainsworth, *Synthesis*, 1976, 722; *ibid.*, 1977, 431; G. Simchen and W. Kober, *ibid.*, p. 259; H. Sakurai, K. Miyoshi, and Y. Nakadaira, *Tetrahedron Letters*, 1977, 2671; Y. Seki, A. Hidaka, S. Murai, and N. Sonada, *Angew. Chem. Internat. Edn.*, 1977, **16**, 174.

[142] (*a*) J. Haslouin and F. Rouessac, *Bull. Soc. chim. France*, 1976, 1122; (*b*) R. M. Coates, L. O. Sandefur, and R. D. Smillie, *J. Amer. Chem. Soc.*, 1975, **97**, 1619.

An interesting method allows isolation under non-aqueous conditions (Scheme 47), low reaction temperatures favouring kinetic regioselectivity.[143]



Reagent: i, $Bu^n{}_4N^+ F^-$

Scheme 47

B. Applications.—A special feature of silyl enol ethers is their regiostability. The addition of a metal alkyl, usually methyl-lithium,[140] or of a stoicheiometric[144] or catalytic[145] amount of fluoride ion, regenerates the original enolates, which are also regiostable under aprotic conditions, and undergo site-specific alkylation.[140] Silyl enol ethers undergo regiospecific electrophilic substitution with strong electrophiles (Scheme 48), resulting in acylation,[146a] carboxamidation,[146b] sulphenylation,[146a] conversion into enones,[147] sulphonylation,[148] halogenation,[149] hydroxylation,[150] oximation,[151] formation of a Mannich base,[152] and azide-induced ring contraction.[153] Such enol ethers[154] and enol ethanoates[155] react with carbonyl compounds, or their acetals,[156] in the presence of titanium(IV) chloride, to give β-hydroxy- or β-alkoxy-ketones, respectively. Similarly, Lewis-acid-catalysed Michael addition of silyl enol ethers to nitro-alkenes leads directly[157] to synthetically valuable 1,4-diketones. Such diketones are also pro-

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[143] E. Nakamura, T. Murofushi, M. Shimuzu, and I. Kuwajima, *J. Amer. Chem. Soc.*, 1976, **98**, 2346.

[144] I. Kuwajima and E. Nakamura, *J. Amer. Chem. Soc.*, 1975, **97**, 3257.

[145] R. Noyori, K. Yokoyama, J. Sakata, I. Kuwajima, E. Nakamura, and M. Shimuzu, *J. Amer. Chem. Soc.*, 1977, **99**, 1265.

[146] (*a*) S. Murai, Y. Kuroki, K. Hasegawa, and S. Tsutsumi, *J.C.S. Chem. Comm.*, 1972, 946; (*b*) I. Ojima, S. Inaba, and Y. Nagai, *Tetrahedron Letters*, 1973, 4271; *Chem. Letters*, 1974, 1069.

[147] E. Friedrich and W. Lutz, *Angew. Chem. Internat. Edn.*, 1977, **16**, 413.

[148] Y. Kuroki, S. Murai, N. Sonada, and S. Tsutsumi, *Organometallic Chem. Synth.*, 1972, **1**, 465.

[149] R. H. Reuss and A. Hassner, *J. Org. Chem.*, 1974, **39**, 1785; L. Blanco, P. Amice, and J. M. Conia, *Synthesis*, 1976, 194; see also M. Zembayashi, K. Tamao, and M. Kumada, *ibid.*, 1977, 422.

[150] A. G. Brook and D. A. Macrae, *J. Organometallic Chem.*, 1974, **77**, C19; G. M. Rubottom, M. A. Vazquez, and D. R. Pelegrina, *Tetrahedron Letters*, 1974, 4319; G. M. Rubottom, J. M. Gruber, and G. M. Mong, *J. Org. Chem.*, 1976, **41**, 1673; for the related preparation of α-hydroxy-acids, see G. M. Rubottom and R. Marrero, *ibid.*, 1975, **40**, 3783.

[151] J. K. Rasmussen and A. Hassner, *J. Org. Chem.*, 1974, **39**, 2558.

[152] S. Danishefsky, T. Kitahara, R. McKee, and P. F. Schuda, *J. Amer. Chem. Soc.*, 1976, **98**, 6715; see also N. L. Holy and Y. F. Wang, *ibid.*, 1977, **99**, 944; W. Oppolzer, H. Hauth, P. Pfäffli, and R. Wenger, *Helv. Chim. Acta*, 1977, **60**, 1801.

[153] R. A. Wohl, *Helv. Chim. Acta*, 1973, **56**, 1826; *Tetrahedron Letters*, 1973, 3111.

[154] T. Mukaiyama, K. Narasaka, and K. Banno, *Chem. Letters*, 1973, 1011; T. Mukaiyama, K. Banno, and K. Narasaka, *J. Amer. Chem. Soc.*, 1974, **96**, 7503; E. Nakamura and I. Kuwajima, *ibid.*, 1977, **99**, 961.

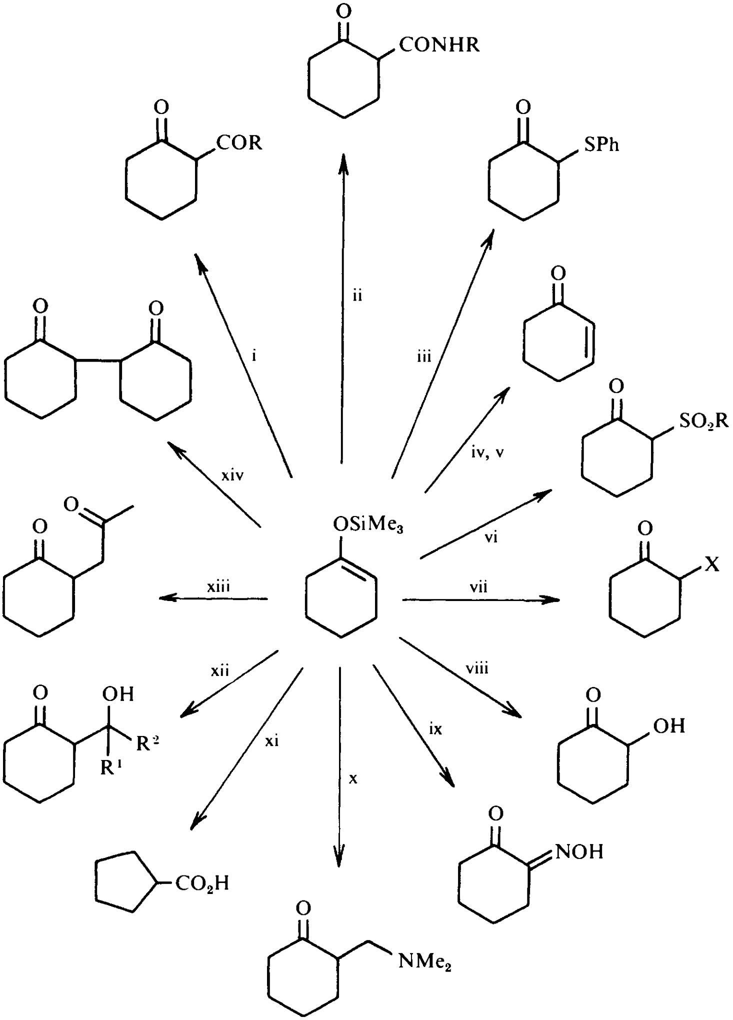
[155] T. Mukaiyama, T. Izawa, and K. Sago, *Chem. Letters*, 1974, 323.

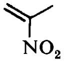
[156] T. Mukaiyama and M. Hayashi, *Chem. Letters*, 1974, 15.

[157] M. Miyashita, T. Yanami, and A. Yoshikoshi, *J. Amer. Chem. Soc.*, 1976, **98**, 4679.

duced by oxidative coupling[158] of enol ethers by silver(I), good yields of cross-coupled products being obtainable.

α-Trimethylsilyl esters react with fluoride ion,[159] giving ester enolates, which



Reagents: i, RCOCl; ii, RNCO–Et$_3$N; iii, PhSCl; iv, $^1O_2$; v, Ph$_3$P; vi, RSO$_2$Cl; vii, X$_2$; viii, *m*-chloroperbenzoic acid; ix, NOCl; x, $CH_2{=}N^+Me_2$ I^-; xi, ArSO$_2$N$_3$; xii, R^{1}COR$_2$– TiCl$_4$; xiii,  and TiCl$_4$; xiv, Ag$_2$O–DMSO

Scheme 48

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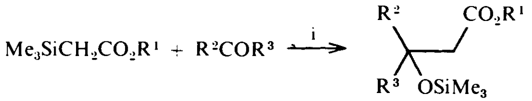
[158] Y. Ito, T. Konoika, and T. Saegusa, *J. Amer. Chem. Soc.*, 1975, **97**, 649; for similar dimeric coupling of esters, see S. Inaba and I. Ojima, *Tetrahedron Letters*, 1977, 2009.

[159] E. Nakamura, M. Shimuza, and I. Kuwajima, *Tetrahedron Letters*, 1976, 1699.

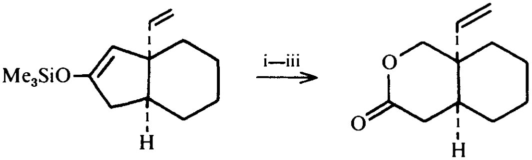
condense with carbonyl compounds to give protected β-hydroxy-esters (Scheme 49).



Reagent: i, $R^4_4 N^+ F^-$

Scheme 49

Silyl enol ethers, as electron-rich alkenes, can be smoothly and selectively ozonized[160] (Scheme 50). They also react readily with Simmons–Smith reagents,[161]



Reagents: i, O_3–MeOH; ii, $NaBH_4$; iii, H_3O^+

Scheme 50

leading initially to cyclopropanol silyl ethers.[162] Conia[163] has described the selective α- or α′-methylation of steroidal αβ-unsaturated ketones (Scheme 51); when *cisoid* or labile enones are involved, an alternative course[164] of ring opening occurs, leading to cyclobutanones and cyclopentanones as shown in Scheme 34.

Simmons–Smith addition to cyclic silyl enol ethers in concentrated solution results in zinc-iodide-induced isomerization[165] of the initially formed cyclopropyl ethers to protected 2-methylenecycloalkanols (Scheme 52).

Allyl esters, as their corresponding silyl keten acetals,[166,167] undergo [3,3]-sigmatropic rearrangement to protected γδ-unsaturated acids (Scheme 53). The use of t-butyldimethylsilyl chloride as the enolate trap is recommended,

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[160] R. D. Clark and C. H. Heathcock, *Tetrahedron Letters*, 1974, 1713, 2027; *J. Org. Chem.*, 1976, **41**, 1396.

[161] J. M. Denis and J. M. Conia, *Tetrahedron Letters*, 1972, 4593; I. Ryu, S. Murai, S. Otani, and N. Sonoda, *Chem. Letters*, 1976, **93**; Y. Ito, S. Fujii, and T. Saegusa, *J. Org. Chem.*, 1976, **41**, 2073.

[162] For a full review, see J. M. Conia, *Pure Appl. Chem.*, 1975, **43**, 317.

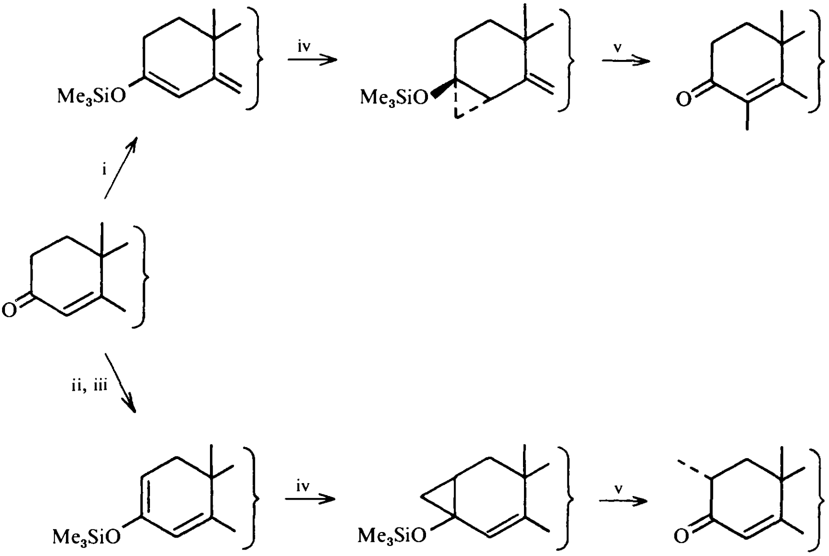
[163] C. Girard and J. M. Conia, *Tetrahedron Letters*, 1974, 3327; for a related route to α-halogeno-αβ-unsaturated carbonyl compounds, see P. Amice, L. Blanco, and J. M. Conia, *Synthesis*, 1976, 196.

[164] J. Salaun, B. Garnier, and J. M. Conia, *Tetrahedron*, 1974, **30**, 1413.

[165] S. Murai, T. Aya, T. Renge, I. Ryu, and N. Sonoda, *J. Org. Chem.*, 1974, **39**, 858; I. Ryu, S. Murai, S. Otani, and N. Sonoda, *Tetrahedron Letters*, 1977, 1995; for conversion into β-bromo-ketones, see S. Murai, Y. Seki, and N. Sonoda, *J.C.S. Chem. Comm.*, 1974, 1032.

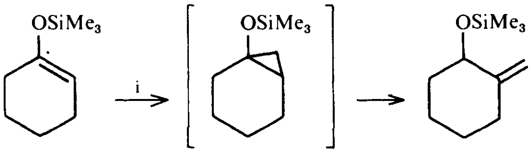
[166] R. E. Ireland, R. H. Mueller, and A. K. Willard, *J. Amer. Chem. Soc.*, 1976, **98**, 2868; *J. Org. Chem.*, 1976, **41**, 986.

[167] J. Boyd, W. Epstein, and G. Fráter, *J.C.S. Chem. Comm.*, 1976, 380.



Reagents: i, Et_3N–Me_3SiCl–DMF; ii, $LiNPr^i_2$; iii, Me_3SiCl; iv, CH_2I_2–Zn–Ag; v, MeOH–H^+

Scheme 51

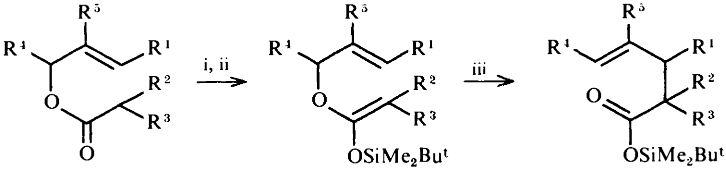


Reagents: i, CH_2I_2–Zn–Cu (concentrated solution)

Scheme 52

permitting stereoselective formation and isolation[166] of the acetals prior to rearrangement; triethylsilyl chloride has also been advocated.[168]

The syntheses and pyrolyses of keten alkyl trimethylsilyl and bistrimethylsilyl



Reagents: i, $LiNPr^i_2$; ii, Bu^tMe_2SiCl, iii, heat

Scheme 53

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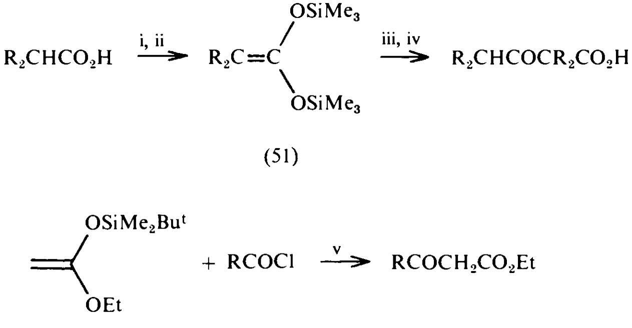
[168] W. C. Still and M. J. Schneider, *J. Amer. Chem. Soc.*, 1977, **99**, 948.

acetals (51) have been described;[169] the latter compounds provide a route to β-keto-acids (Scheme 54); *O*-t-butyldimethylsilyl keten acetals such as (52) are valuable equivalents of ester enolates.[170]



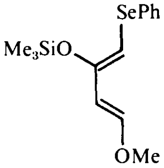
(51)

(52)

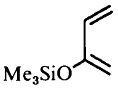
Reagents: i, $LiNPr^i_2$; ii, Me_3SiCl; iii, heat; iv, H_3O^+; v, Et_3N

Scheme 54

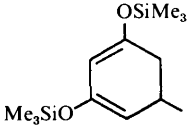
The trimethylsilyloxybuta-1,3-dienes (53),[171] (54),[172] (55),[173] and (56)[174] have been used as 4π components in Diels–Alder cycloadditions, silyl enol ether masking being preferred to the alternative alkyl enol ethers or enol ethanoates.



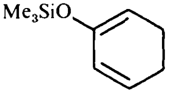
(53)



(54)



(55)



(56)

Metallated allyloxy-silanes (57) behave[175] as β-acyl carbanion equivalents (Scheme 55); metallated allyl alkyl ethers[176] show similar properties. The sym-

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[169] C. Ainsworth, F. Chen, and Y.-N. Kuo, *J. Organometallic Chem.*, 1972, **46**, 59; C. Ainsworth and Y.-N. Kuo, *ibid.*, p. 73.

[170] M. W. Rathke and D. F. Sullivan, *Synthetic Comm.*, 1973, **3**, 67; *Tetrahedron Letters*, 1973, 1297.

[171] S. Danishefsky, C. F. Yan, and P. M. McCurry, *J. Org. Chem.*, 1977, **42**, 1819; see also S. Danishefsky, T. Kitahara, P. F. Schuda, and S. J. Etheredge, *J. Amer. Chem. Soc.*, 1976, **98**, 3028; J. F. W. Keana and P. E. Eckler, *J. Org. Chem.*, 1976, **41**, 2850.

[172] M. E. Jung and C. A. McCombs, *Tetrahedron Letters*, 1976, 2935.

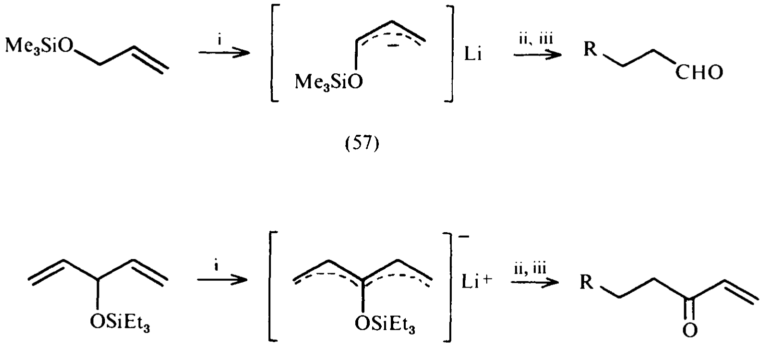
[173] T. Ibuka, Y. Mori, and Y. Inubushi, *Tetrahedron Letters*, 1976, 3169.

[174] G. M. Rubottom and D. S. Krueger, *Tetrahedron Letters*, 1977, 611; G. M. Rubottom and J. M. Gruber, *J. Org. Chem.*, 1977, **42**, 1051.

[175] W. C. Still and T. L. Macdonald, *J. Amer. Chem. Soc.*, 1974, **96**, 5561; with carbonyl compounds as electrophiles, exclusive α-attack is observed: *J. Org. Chem.*, 1976, **41**, 3620.

[176] D. A. Evans, G. C. Andrews, and B. Buckwalter, *J. Amer. Chem. Soc.*, 1974, **96**, 5560.

metrical anion (58) is an equivalent[177] for the hypothetical homoenolate anion of ethyl vinyl ketone, undergoing electrophilic attack at mainly the γ-position.



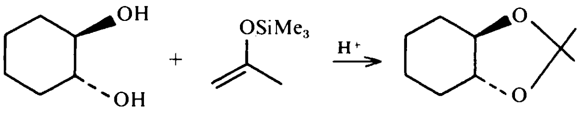
(57)

(58)

Reagents: i, Bu^{s}Li; ii, RX; iii, H_3O^+

Scheme 55

Acetonides, including the hitherto unknown acetonide of *trans*-cyclohexane-1,2-diol, are readily prepared[178] from 2-trimethylsilyloxypropene and 1,2-diols (Scheme 56).



Scheme 56

C. Acyloin Trapping and Reductive Cleavage.—The enolate anion intermediates in the acyloin condensation[179] can be trapped by silylation, preventing[180] the condensation and polymerization which often complicate this route to cyclic α-hydroxy-ketones. The resulting bis-silyl enol ethers are readily hydrolysed or oxidized,[181] allowing the preparation of, *inter alia*, cyclobutanedione[182] (Scheme 57), all attempts to oxidize the readily accessible α-hydroxycyclobutanone having failed.

[177] W. Oppolzer and R. L. Snowden, *Tetrahedron Letters*, 1976, 4187.

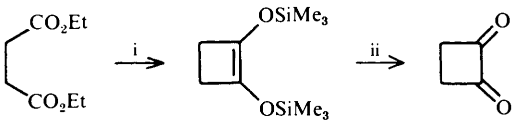
[178] G. L. Larsen and A. Hernandez, *J. Org. Chem.*, 1973, **38**, 3935.

[179] J. J. Bloomfield, D. C. Owsley, C. Ainsworth, and R. E. Robertson, *J. Org. Chem.*, 1975, **40**, 393.

[180] K. Ruhlmann, *Synthesis*, 1971, 263.

[181] T. Kowar and E. LeGoff, *Synthesis*, 1973, 212; J. Strating, S. Reiffers, and H. Wynberg, *ibid.*, 1971, 209; for the alkylation of the derived lithium 1,2-enediolates, see T. Wakamatsu, M. Fukui, and Y. Ban, *ibid.*, 1976, 341; for their conversion into alkynes, see D. P. Bauer and R. S. Macomber, *J. Org. Chem.*, 1976, **41**, 2640.

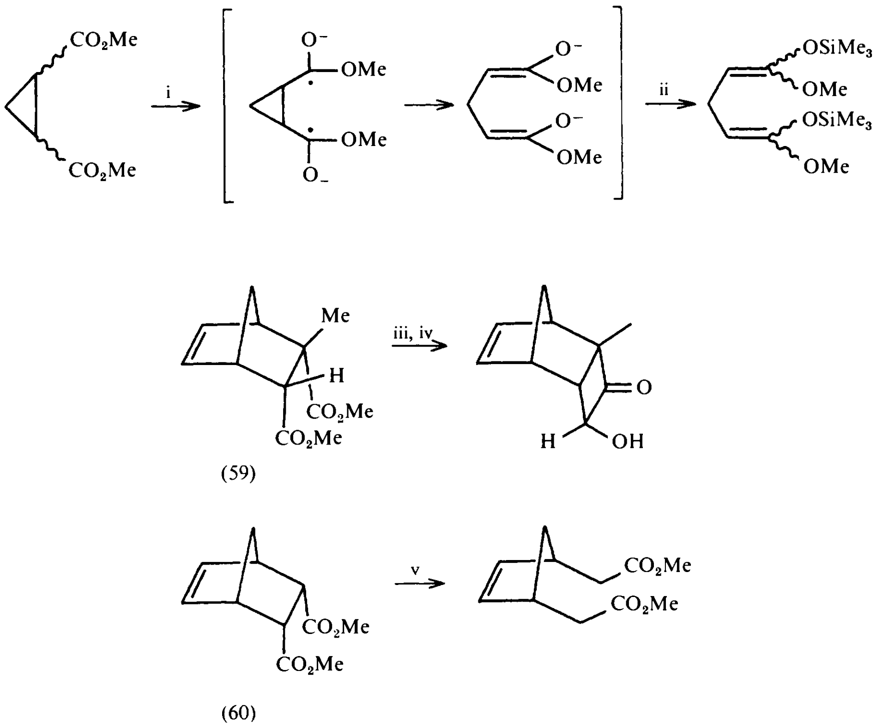
[182] H.-G. Heine, *Chem. Ber.*, 1971, **104**, 2869; J. M. Conia and J. M. Denis, *Tetrahedron Letters*, 1971, 2845; see also H.-G. Heine and D. Wendisch, *Annalen*, 1976, 463.



Reagents: i, Na–PhMe–Me_3SiCl; ii, Br_2

Scheme 57

Under certain conditions, 1,2-diesters undergo reductive cleavage of the connecting σ-bond. An extension to provide a method for the introduction of ethanoic acid fragments has also provided evidence[183] for the mechanism of this reaction, which appears to proceed as shown in Scheme 58. The competitiveness and solvent dependence of these two reductive processes are seen in the acyloin condensation[184] of (59) and the σ-cleavage[183] of (60).



Reagents: i, $2e^-$; ii, Me_3SiCl; iii, Na–PhMe–Me_3SiCl; iv, H_3O^+; v, Na–NH_3

Scheme 58

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[183] P. G. Gassman and X. Creary, *J.C.S. Chem. Comm.*, 1972, 1214.
[184] M. E. Jung, *J.C.S. Chem. Comm.*, 1974, 956.

8 Activation/Protection of Nitrogen

After the halogeno-silanes, amino-silanes are the next most reactive class of organosilane in which silicon is bonded to a more electronegative element; the silicon–nitrogen bond is readily cleaved[4,6] (Scheme 59). This section will explore the fate of the nitrogen moiety.

Scheme 59

N-Trimethylsilyl secondary amines are recommended[185] for easy formation of enamines. Acid halides react readily with amino-silanes, providing a now standard method[4,6] for amide (peptide) bond formation. The silylated amines are normally more reactive than the parent compounds, and the co-produced silyl halide or equivalent plays no further part in the reaction.

It is not normally possible to convert an inactive, ester-protected acid directly and non-hydrolytically into an activated acid derivative under mild conditions.[186] Masamune[187] reasoned (Scheme 60) that, if R^1O^- could be removed by reaction with MY, M^+ being a relatively hard acid (with a strong affinity for oxygen), and Y^- being a relatively soft base, then such a desirable sequence might become feasible. Both phenyl and trichloroethyl esters have an acceptable degree of stability, yet are rapidly converted into acid imidazolides by treatment with *N*-trimethylsilylimidazole.

Nitrile α-anions react with trimethylsilyl chloride to give, as expected, α-silyl-nitriles. If, however, t-butyldimethylsilyl chloride is employed, the anions are trapped in their ketenimine form; this results in an efficient method[188] for the oxidative decyanation of secondary aralkyl- and diaryl-nitriles (Scheme 61).

A wide range of Grignard reagents react with trimethylsilyl isocyanate (61) to give homologous primary amides;[189] the silylated aminocopper compound (62) converts aryl iodides into primary amines[190] in modest yield.

9 Silicon-substituted Bases

Lithium,[191] sodium,[192] and potassium[193] bistrimethylsilylamide (Scheme 62) have all found extensive use as strong, non-nucleophilic bases.

[185] R. Comi, R. W. Franck, M. Reitano, and S. M. Weinreb, *Tetrahedron Letters*, 1973, 3107; but see L. H. Hellberg and A. Juarez, *ibid.*, 1974, 3553.

[186] See, however, A. G. Anderson and D. H. Kono, *Tetrahedron Letters*, 1973, 5121; D. J. Burton and W. F. Koppes, *J.C.S. Chem. Comm.*, 1973, 425.

[187] G. S. Bates, J. Diakur, and S. Masamune, *Tetrahedron Letters*, 1976, 4423.

[188] D. S. Watt, *J. Org. Chem.*, 1974, **39**, 2799; S. J. Selikson and D. S. Watt, *Tetrahedron Letters*, 1974, 3029.

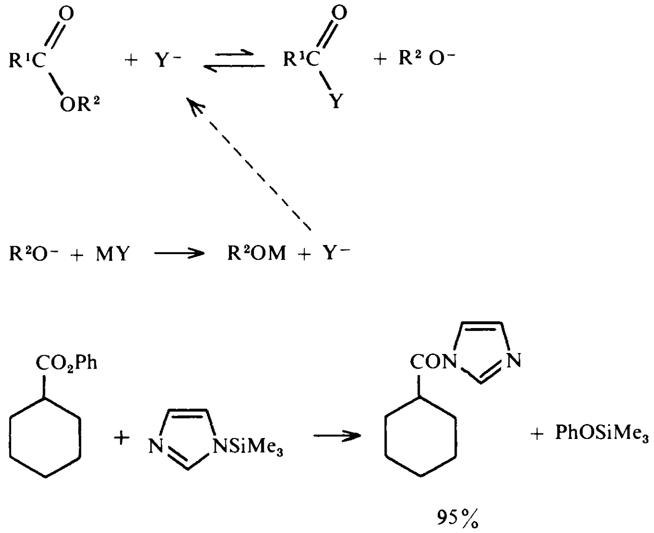
[189] K. A. Parker and E. G. Gibbons, *Tetrahedron Letters*, 1975, 981; see also P. Bourgeois, G. Merault, and R. Calas, *J. Organometallic Chem.*, 1973, **59**, C4.

[190] F. D. King and D. R. M. Walton, *J.C.S. Chem. Comm.*, 1974, 256; *Synthesis*, 1976, 40; see also T. Tsuda, H. Washita, and T. Saegusa, *J.C.S. Chem. Comm.*, 1977, 468.

[191] E. H. Amonoo-Neizer, R. A. Shaw, D. O. Skovlin, and B. C. Smith, *J. Chem. Soc.*, 1965, 2997.

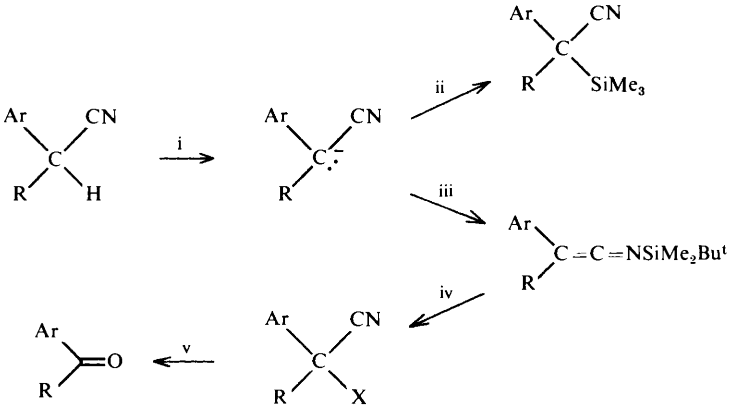
[192] U. Wannagat and H. Niederprüm, *Chem. Ber.*, 1961, **94**, 1540; U. Wannagat, *Pure Appl. Chem.*, 1969, **19**, 329.

[193] C. A. Brown, *Synthesis*, 1974, 427.



Reagent: i, PhO⁻ (catalytic)

Scheme 60



Reagents: i, $LiNPr^i_2$; ii, Me_3SiCl; iii, Bu^tMe_2SiCl; iv, I_2, Br_2, or PhSCl; v, H_3O^+

Scheme 61

Me_3SiNCO (61)

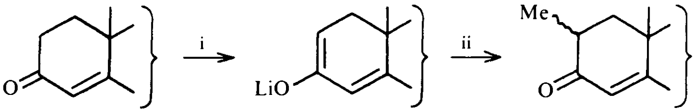
$(Me_3Si)_2NCu$ (62)

$$(Me_3Si)_2NH \xrightarrow{\text{i, ii, or iii}} (Me_3Si)_2NM$$

Reagents: i, Bu^nLi; ii, $NaNH_2$; iii, KNH_2

Scheme 62

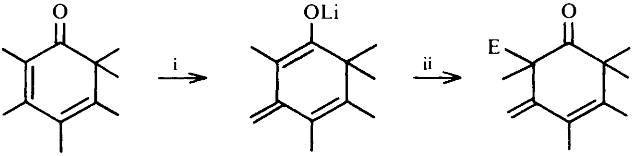
The lithium amide is recommended[194] for the generation of kinetic enolates (Scheme 63); the sodium amide can also be used,[195] but the resulting enolates are, as expected, less regiostable.



Reagents: i, $LiN(SiMe_3)_2$; ii, MeI

Scheme 63

With dienones, the γ- rather than the ϵ-proton is removed,[196] to give cross-conjugated enolate anions (Scheme 64).



Reagents: i, $LiN(SiMe_3)_2$; ii, electrophile

Scheme 64

The lithium amide is also the preferred[197] base in Darzens condensations, allowing the use even of ethanal as electrophile. The sodium amide has been advantageously employed in Dieckmann condensations[198] of $\alpha\omega$-diesters, especially in those cases where additional nucleophilically labile groups are present. It is also recommended[199] for the convenient generation of monobromo- and monochloro-carbenes from the corresponding dihalogenomethanes.

Intramolecular displacement of halide ions from halogeno-acetals provides a synthesis[200] (Scheme 65) of functionalized bicyclic diketones; when the lithium amide is used as a base, the product is 95% *trans*-(63), whereas, remarkably, if the metal ion is potassium, the stereochemistry is completely reversed, giving 95% *cis*-(63).

Cyclizations involving attack by a carbanion on an electrophile usually result in the formation of a five- rather than of a six-membered ring, and rarely a four-membered ring. Stork[201] has reported a process of 'epoxynitrile cyclization',

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[194] M. Tanabe and D. F. Crowe, *J.C.S. Chem. Comm.*, 1973, 564.

[195] D. H. R. Barton, R. H. Hesse, G. Tarzia, and M. M. Pechet, *Chem. Comm.*, 1969, 1497; M. Tanabe and D. F. Crowe, *ibid.*, p. 1498.

[196] H. Hart, G. M. Love, and I. C. Wang, *Tetrahedron Letters*, 1973, 1377.

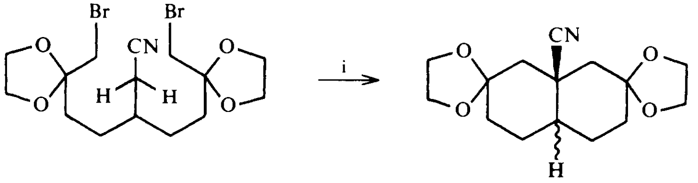
[197] R. F. Borch, *Tetrahedron Letters*, 1972, 3761; but see G. Kyriakakou and J. Seyden-Penne, *ibid.*, 1974, 1737.

[198] R. N. Hurd and D. H. Shah, *J. Org. Chem.*, 1973, **38**, 390.

[199] B. Martel and J. M. Hiriart, *Synthesis*, 1972, 201.

[200] G. Stork, J. O. Gardner, R. K. Boeckman, and K. A. Parker, *J. Amer. Chem. Soc.*, 1973, **95**, 2014; G. Stork and R. K. Boeckman, *ibid.*, p. 2016.

[201] G. Stork, L. D. Cama, and D. R. Coulson, *J. Amer. Chem. Soc.*, 1974, **96**, 5268.

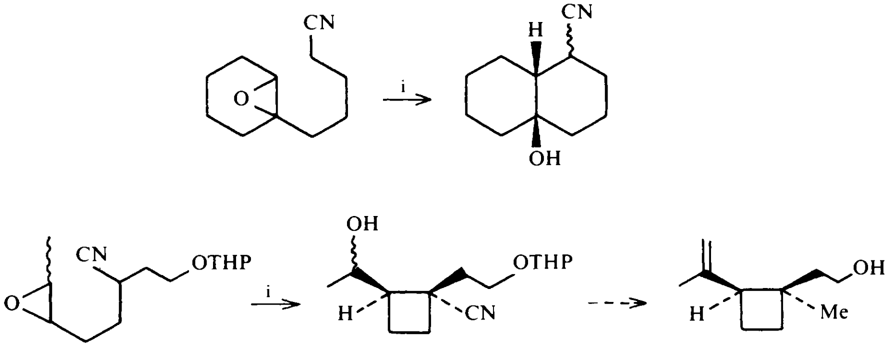


(63)

Reagent: i, $LiN(SiMe_3)_2$ or $KN(SiMe_3)_2$

Scheme 65

in which these tendencies are reversed (Scheme 66); these reversals are ascribed to the geometric constraints imposed by the oxiran ring in each case, making it difficult for the nitrile anion and the oxiran C—O bond to come into line for formation of a five-membered ring. The second reaction shown is highly stereoselective, and has been employed[202] in a synthesis of (±)-grandisol (64).



(64)

Reagent: i, $NaN(SiMe_3)_2$

Scheme 66

Lithium 1,1-bistrimethylsilyl-3-methylbutoxide (65) is an exceptionally hindered strong base;[203] it regiospecifically removes methyl protons from ethanoates[204a] and methyl ketones,[204b] even in the simultaneous presence of aldehydes, which then trap the enolate anions and provide a new range of regiospecific aldol condensations (Scheme 67).

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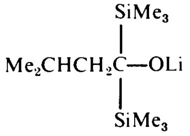
[202] G. Stork and J. F. Cohen, *J. Amer. Chem. Soc.*, 1974, **96**, 5270.

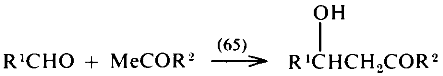
[203] I. Kuwajima. T. Sato, N. Minami, and T. Abe, *Tetrahedron Letters*, 1976, 1591; I. Kuwajima, M. Arai, and T. Sato, *J. Amer. Chem. Soc.*, 1977, **99**, 4181.

[204] (*a*) I. Kuwajima, N. Minami, and T. Sato, *Tetrahedron Letters*, 1976, 2253; see also N. Minami and I. Kuwajima, *ibid.*, 1977, 1423; (*b*) I. Kuwajima, T. Sato, M. Araki and N. Minami, *ibid.*, 1976, 1817.



$Me_2CHCH_2C(SiMe_3)_2{-}OLi$

(65)



$$R^1CHO + MeCOR^2 \xrightarrow{(65)} R^1CH(OH)CH_2COR^2$$

$R^2 = CH_2R$ or OR

Scheme 67

Trimethylsilylpotassium is recommended[205] for the metallation of vinylic, allylic, and benzylic substrates.

10 Silanes as Reducing Agents

The addition of the Si—H linkage to unsaturated substrates is important not only as a method of reduction but also as a major route to complex organosilanes. Such additions can be brought about under catalytic or ionic conditions. A distinctly different method of reduction uses trimethylsilyl chloride–metal systems.

A. Catalytic Reduction.—Silanes will reduce a wide variety of functional groups under catalysis by transition metals. Alkynes undergo *cis*-addition,[206] with the terminal regiospecificity shown (Scheme 68); peroxide initiation yields the *trans*-isomer, and nickel(II) catalyses a double addition.[207]

Whereas the catalysed addition of trialkylsilanes to ketones gives silyl ethers,[208] $\alpha\beta$-unsaturated ketones react by a process of 1,4-addition[209] to give silyl enol ethers (Scheme 69); only conjugated double bonds are affected. Asymmetric hydrosilylation[210] of either class of substrate can be achieved using chiral catalysts.

Carboxylic acid chlorides are reduced[211] to aldehydes (Scheme 70) in an alternative to the Rosenmund reduction; yields are lower if there is α-branching.

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[205] J. Hartmann and M. Schlosser, *Helv. Chim. Acta*, 1976, **59**, 453; M. Schlosser and J. Hartmann, *J. Amer. Chem. Soc.*, 1976, **98**, 4674; M. Stähle, J. Hartmann, and M. Schlosser, *Helv. Chim. Acta*, 1977, **60**, 1730.

[206] R. A. Benkeser, M. L. Burrous, L. E. Nelson, and J. V. Swisher, *J. Amer. Chem. Soc.*, 1961, **83**, 4385.

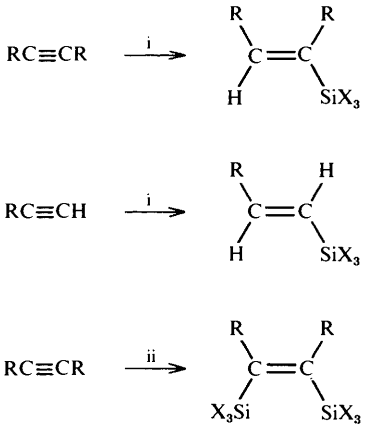
[207] K. Tamao, N. Miyake, Y. Kiso, and M. Kumada, *J. Amer. Chem. Soc.*, 1975, **97**, 5603.

[208] I. Ojima, M. Nihonyanagi, and Y. Nagai, *J.C.S. Chem. Comm.*, 1972, 938.

[209] T. Ojima, T. Kogure, and Y. Nagai, *Tetrahedron Letters*, 1972, 5035.

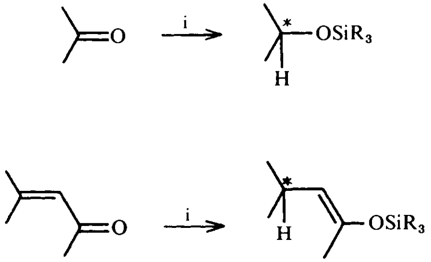
[210] H. B. Kagan, *Pure Appl. Chem.*, 1975, **43**, 401; T. Hayashi, K. Yamamoto, and M. Kumada, *Tetrahedron Letters*, 1975, 3; I. Ojima, T. Kogure, and M. Kumagai, *J. Org. Chem.*, 1977, **42**, 1671.

[211] J. D. Citron, *J. Org. Chem.*, 1969, **34**, 1977; see also S. P. Dent, C. Eaborn, and A. Pidcock, *Chem. Comm.*, 1970, 1703.



Reagents: i, $X_3SiH–H_2PtCl_6$; ii, $X_3SiH–Ni^{II}$

Scheme 68



Reagents: i, $R_3SiH–Rh^*$ catalyst

Scheme 69

$$RCOCl \xrightarrow{i} RCHO$$

Reagents: i, $Et_3SiH–Pd$

Scheme 70

Imines are reduced[212] to amines, again with potential chirality,[213] in what is claimed to be the best method of reduction of such compounds (Scheme 71). Pyridines undergo 1,4-addition to give *N*-silyl species, which can be converted into the parent 1,4-dihydropyridines[214] by controlled hydrolysis.

Commercially available polymethylhydrosiloxane (66), in the presence of an organotin catalyst in a protic solvent, functions[215] as a mild reagent for the

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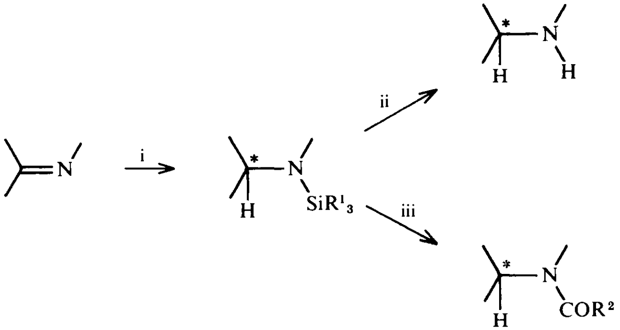
[212] I. Ojima, T. Kogure, and Y. Nagai, *Tetrahedron Letters*, 1973, 2475.

[213] N. Langlois, T.-P. Dang, and H. B. Kagan, *Tetrahedron Letters*, 1973, 4865.

[214] N. C. Cook and J. E. Lyons, *J. Amer. Chem. Soc.*, 1965, **87**, 3283.

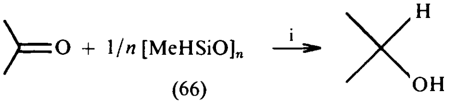
[215] J. Lipowitz and S. A. Bowman, *J. Org. Chem.*, 1973, **38**, 162.



Reagents: i, R^1_3SiH-Rh* catalyst; ii, MeOH; iii, R^2COCl

Scheme 71

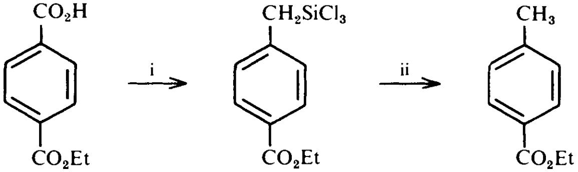
selective reduction of aldehydes and ketones to carbinols (Scheme 72), the catalyst providing a tin hydride as the active reducing agent. In the presence of Pd/C, alkenes and nitro-groups are smoothly reduced. Primary and secondary alcohol chloromethanoates are reduced to the corresponding alkanes by radical-induced reaction[216] with tri-n-propylsilane.



Reagents: i, $(R_3Sn)_2O$-EtOH

Scheme 72

The combination of trichlorosilane and tertiary amines[217] reduces a range of aromatic carbonyl compounds, including acids[218] (Scheme 73), to hydrocarbons: such a system also reduces phosphine oxides to phosphines[219] with retention of configuration; similar deoxygenation can be achieved with trichlorosilane[220] or phenylsilane[221] alone.



Reagents: i, Cl_3SiH-Et_3N; ii, KOH-EtOH

Scheme 73

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[216] N. C. Billingham, R. A. Jackson, and F. Malek, *J.C.S. Chem. Comm.*, 1977, 344; see also M. G. Adlington, M. Orfanopoulos, and J. L. Fry, *Tetrahedron Letters*, 1976, 2955; M. P. Doyle, C. C. McOsker, and C. T. West, *J. Org. Chem.*, 1976, **41**, 1393.

[217] R. A. Benkeser, *Accounts Chem. Res.*, 1971, **4**, 94.

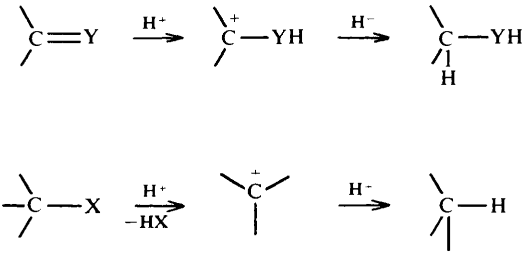
[218] R. A. Benkeser and D. F. Ehler, *J. Org. Chem.*, 1973, **38**, 3660; see also G. S. Li, D. F. Ehler, and R. A. Benkeser, *Org. Synth.*, 1973, **53**, 159.

[219] C. R. Hall and D. J. H. Smith, *Tetrahedron Letters*, 1974, 1693.

[220] Y. Segall, I. Granoth, and A. Kalir, *J.C.S. Chem. Comm.*, 1974, 501.

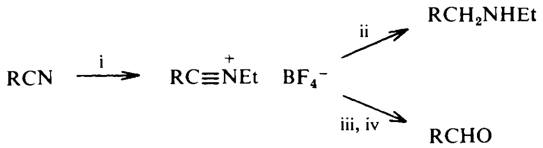
[221] K. L. Marsi, *J. Org. Chem.*, 1974, **39**, 265.

B. Ionic Hydrogenation.—This system (Scheme 74) involves the stepwise addition to the substrate of H^+ and H^-, the most efficient reagent combination[222] being trifluoroethanoic acid–triethylsilane. The procedure has been extensively explored and detailed,[223] and will definitely find increasing use.



Scheme 74

Reduction of nitrilium ions by silane produces aldimines,[224] and thence aldehydes (Scheme 75), complementing the known method for reduction of such ions to amines by using borohydride.



Reagents: i, Et_3O^+ BF_4^-; ii, $NaBH_4$; iii, Et_3SiH; iv, H_3O^+

Scheme 75

C. Chlorosilane–Metal Systems.—This area has been thoroughly investigated by French workers, who have reviewed[225] their progress. The reagent system most commonly used, trimethylsilyl chloride–magnesium–hexamethylphosphoramide, probably involves a silyl Grignard reagent, which, on reaction with a range of $\alpha\beta$-unsaturated ketones[226] and esters,[227] causes reductive dimerization, producing 1,4-dicarbonyl compounds in synthetically useful yields (Scheme 76).

Benzene is converted into cyclohexa-1,4-diene in moderate yield by a reducing system consisting of lithium and trimethylsilyl chloride[228] (Scheme 77).

---

[222] M. P. Doyle, D. J. DeBruyn, S. J. Donnelly, D. A. Kooistra, A. A. Odubela, C. T. West, and S. M. Sonnebelt, *J. Org. Chem.*, 1974, **39**, 2740.

[223] D. N. Kursanov, Z. N. Parnes, and N. M. Loim, *Synthesis*, 1974, 633.

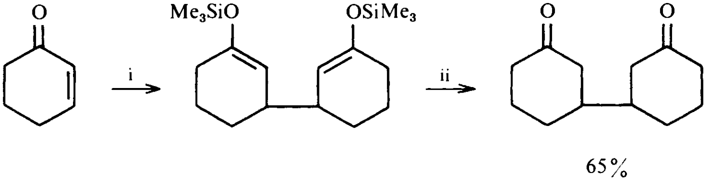
[224] J. L. Fry, *J.C.S. Chem. Comm.*, 1974, 45.

[225] R. Calas and J. Dunoguès, ref. 2, Vol. 2, p. 277.

[226] J. Dunoguès, R. Calas, M. Bolourtchian, C. Biran, and N. Duffaut, *J. Organometallic Chem.*, 1973, **57**, 55.

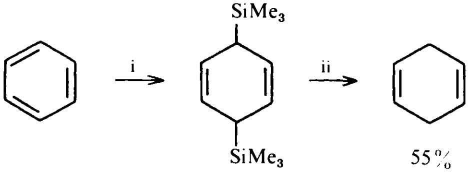
[227] J.-P. Pichard, J. Dunoguès, and R. Calas, *J. Organometallic Chem.*, 1974, **77**, 167.

[228] J. Dunoguès, R. Calas, and N. Ardoin, *J. Organometallic Chem.*, 1972, **43**, 127; see also L. Birkofer and N. Ramadan, *Chem. Ber.*, 1971, **104**, 138.



Reagents: i, Me_3SiCl–Mg–HMPA, $FeCl_3$ or $TiCl_4$ catalyst; ii, MeOH

Scheme 76



Reagents: i, Li–Me_3SiCl–THF; ii, KOH

Scheme 77

11 Trimethylsilyl Cyanide

Trimethylsilyl cyanide is a potent agent for effecting cyanide transfer,[229–232] aldehydes, ketones, and $\alpha\beta$-unsaturated carbonyl systems all reacting smoothly with the reagent in the catalytic presence of Lewis acids[233] or crown-ether-solubilized potassium cyanide (Scheme 78). Its use permits an efficient and reliable synthesis[234a] of β-aminomethyl alcohols, including those from ketones which do not form stable cyanohydrins, and those from conjugated enones,[234b] where clean 1,2-addition is observed. Aryl and heteroaryl aldehydes can be converted[232] into ketones, as shown in Scheme 78.

Cyanosilylation of *p*-benzoquinones not only affords a degree of protection to the quinone system, but also provides a new synthesis[234c] of quinols (Scheme 79).

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[229] D. A. Evans, L. K. Truesdale, and G. L. Carroll, *J.C.S. Chem. Comm.*, 1973, 55.

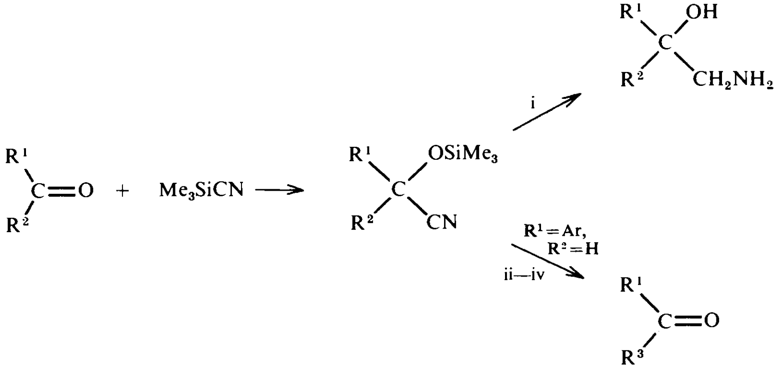
[230] W. Lidy and W. Sundermeyer, *Chem. Ber.*, 1973, **106**, 587.

[231] H. Neef and R. Müller, *J. prakt. Chem.*, 1973, **315**, 367.

[232] K. Deuchert, U. Hertenstein, and S. Hunig, *Synthesis*, 1973, 777.

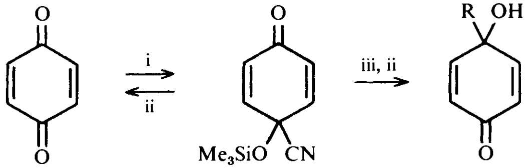
[233] D. A. Evans and L. K. Truesdale, *Tetrahedron Letters*, 1973, 4929; for an alternative preparation of the reagent, see J. W. Zubrick, B. I. Dunbar, and H. D. Durst, *ibid.*, 1975, 71.

[234] (*a*) D. A. Evans, G. L. Carroll, and L. K. Truesdale, *J. Org. Chem.*, 1974, **39**, 914; (*b*) for the alkylation of the anions derived from such unsaturated cyanohydrins, see U. Hertenstein, S. Hünig, and M. Öller, *Synthesis*, 1976, 416; (*c*) D. A. Evans, J. M. Hoffman, and L. K. Truesdale, *J. Amer. Chem. Soc.*, 1973, **95**, 5822; for improved procedure and application, see D. A. Evans and R. Y. Wong, *J. Org. Chem.*, 1977, **42**, 350.



Reagents: i, $LiAlH_4$; ii, $LiNPr^i_2$; iii, R^3X; iv, H_3O^+

Scheme 78



Reagents: i, Me_3SiCN–catalyst; ii, AgF; iii, RMgX or RLi

Scheme 79

The analogous carbonyl-insertion properties of ethyl trimethylsilyldiazoethanoate,[235a] thiosilanes,[235b] and mixed tervalent phosphorus–organosilicon reagents[235c] have been delineated.

12 Trimethylsilyl Azide

Trimethylsilyl azide[236] is preferable to the highly explosive hydrazoic acid for the synthesis of 1,2,3-triazoles[237] (Scheme 80) and related[238] heterocyclic systems, the silyl group in the products being hydrolytically labile. It complements sodium azide in such cycloadditions, working best with electron-rich alkynes; azide ion is more effective with electron-poor substrates. It is also preferable[239] to aryl sulphonyl azides for the preparation of aziridines.

The reagent converts acid chlorides and anhydrides into acid azides prior to Curtius rearrangement to isocyanates;[240] it also converts halogeno-ethanoates

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[235] (*a*) D. A. Evans, L. K. Truesdale, and K. G. Grimm, *J. Org. Chem.*, 1976, **41**, 3335; (*b*) D. A. Evans, L. K. Truesdale, K. G. Grimm, and S. L. Nesbitt, *J. Amer. Chem. Soc.*, 1977, **99**, 5009; (*c*) D. A. Evans, K. M. Hurst, L. K. Truesdale, and J. M. Takacs, *Tetrahedron Letters*, 1977, 2495.

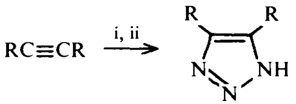
[236] L. Birkofer and P. Wegner, *Org. Synth.*, 1970, **50**, 107; see also S. S. Washburne and W. R. Peterson, *J. Organometallic Chem.*, 1971, **33**, 153.

[237] Y. Tanaka, S. R. Velen, and S. I. Miller, *Tetrahedron*, 1973, **29**, 3271.

[238] E. Ettenhuber and K. Ruhlmann, *Chem. Ber.*, 1968, **101**, 743.

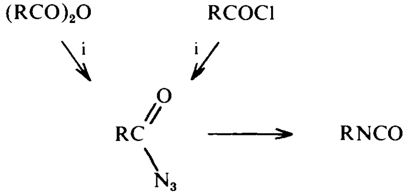
[239] K. Wiesner, Chemical Society Centenary Lecture, Glasgow, 1977 (*Chem. Soc. Rev.*, 1977, **6**, 413).

[240] S. S. Washburne and W. R. Peterson, *Synthetic Comm.*, 1972, **2**, 227; S. S. Washburne, W. R. Peterson, and D. A. Berman, *J. Org. Chem.*, 1972, **37**, 1738; J. H. MacMillan and S. S. Washburne, *ibid.*, 1973, **38**, 2982.



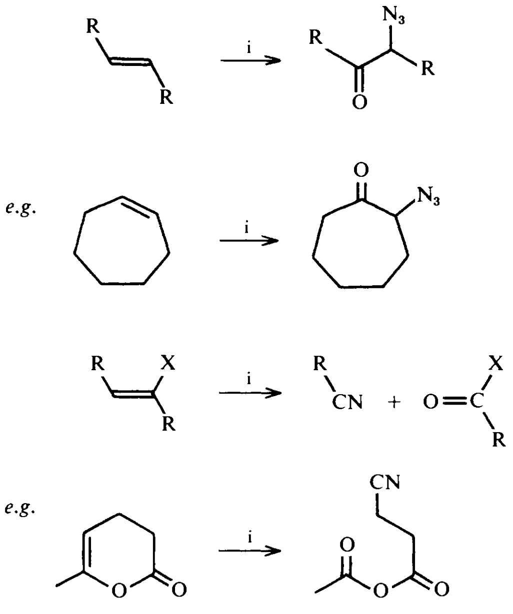
Reagents: i, Me_3SiN_3; ii, H_2O **Scheme 80**

into azido-ethanoates,[241] which are precursors to alkoxycarbonylnitrenes (Scheme 81).



Reagent: i, Me_3SiN_3 **Scheme 81**

Trimethylsilyl azide, in combination with lead(IV) ethanoate or iodobenzene diethanoate, reacts with alkenes to give a variety of products.[242] The latter, milder, reagent combination converts[243] cyclic alkenes into α-azido-ketones; enol ethers and other electron-rich alkenes, on the other hand, undergo regiospecific cleavage (Scheme 82).



Reagents: i, $PhI(OAc)_2$–Me_3SiN_3 **Scheme 82**

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[241] H. R. Kricheldorf, *Synthesis*, 1972, 695.

[242] E. Zbiral, *Synthesis*, 1972, 285.

[243] J. Ehrenfreund and E. Zbiral, *Annalen*, 1973, 290.

13 Miscellaneous

A major area of application of trialkylsilyl groups utilizes their extreme bulk to provide ligands capable of stabilizing metals in low-co-ordinative environments; this area has been extensively reviewed.[244] A recent example[245] can be seen in the first preparation of stable two-co-ordinate phosphorus- and arsenic-centred radicals, (67) and (68). A related use of such bulky substituents has allowed the preparation and conformational study[246] of relatively long-lived carbon radicals such as (69).

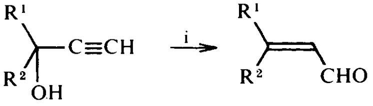
$[(Me_3Si)_2CH]_2\,M^{\bullet}$ $\qquad$ $[(Me_3Si)_2N]_2\,M^{\bullet}$

(67) $M = P$ or As $\qquad$ (68) $M = P$ or As

$(Me_3Si)_2\dot{C}CH(SiMe_3)_2$

(69) $t_{\frac{1}{2}}\ (50\,^{\circ}C) = 120$ h

Tertiary propynyl alcohols rearrange[247] smoothly in the presence of polymeric silyl vanadates to $\alpha\beta$-unsaturated aldehydes (Scheme 83).



Reagent: i, $-(Ph_2SiOV{=}O)_n$, heat

Scheme 83

Trimethylsilyl iodide converts[248] esters into the corresponding labile silyl esters, and thence into the acids, probably by the process shown in Scheme 84. No selectivity is seen with simple esters, although it may be possible to cleave t-butyl and benzyl esters selectively. Trimethylsilyl bromide cleanly dealkylates[249] phosphonic acid dialkyl esters under mild conditions.

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[244] D. H. Harris and M. F. Lappert, ref. 2, Vol. 2, p. 13; D. C. Bradley and M. H. Chisholm, *Accounts Chem. Res.*, 1976, **9**, 273.

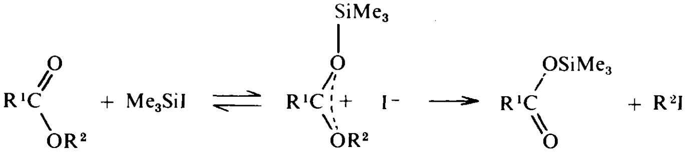
[245] M. J. S. Gynane, A. Hudson, M. F. Lappert, P. P. Power, and H. Goldwhite, *J.C.S. Chem. Comm.*, 1976, 623.

[246] D. Griller and K. U. Ingold, *J. Amer. Chem. Soc.*, 1974, **96**, 6203; *Accounts Chem. Res.*, 1976, **9**, 13.

[247] H. Pauling, D. A. Andrews, and N. C. Hindley, *Helv. Chim. Acta*, 1976, **59**, 1233; G. L. Olson, K. D. Morgan, and G. Saucy, *Synthesis*, 1976, 25; M. B. Erman, I. S. Aul'chenko, L. A. Kheifits, V. G. Dulova, Yu. N. Novikov, and M. E. Vol'pin, *Tetrahedron Letters*, 1976, 2981.

[248] M. E. Jung and M. A. Lyster, *J. Amer. Chem. Soc.*, 1977, **99**, 968; T.-L. Ho and G. A. Olah, *Angew. Chem. Internat. Edn.*, 1976, **15**, 774; *Synthesis*, 1977, 417; for the conversion of alcohols into iodides using this reagent, see M. E. Jung and P. L. Ornstein, *Tetrahedron Letters*, 1977, 2659.

[249] C. E. McKenna, M. T. Higa, N. H. Cheung, and M. C. McKenna, *Tetrahedron Letters*, 1977, 155.



Scheme 84

14 Concluding Remarks

It is to be hoped that this short review has given some indication of the exceptional utility of silicon in synthetic organic chemistry; space does not permit discussion of its applicability elsewhere, which is equally impressive, nor of the more physical aspects of its properties. For more detailed information on the silicon reagents mentioned, the reader is recommended to consult the books by Fieser and Fieser,[250] in addition to the primary references.

The author gratefully acknowledges many stimulating and helpful discussions with Dr. B. J. Hamill. Most of all, however, sincere tribute must be paid to Professor Gilbert Stork, whose inspiration and talents have contributed so much to the current explosive growth in this area.

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[250] M. Fieser and L. F. Fieser, 'Reagents for Organic Synthesis', Vols. 1—5, Wiley-Interscience, New York, 1967—1975.