TILDEN LECTURE*

Some Uses of Silicon Compounds in Organic Synthesis

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1 Introduction

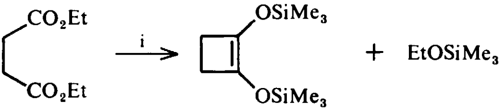
My task in a Tilden lecture is to deal with the progress made in some branch of chemistry. I have, of course, chosen to discuss the contributions made by organosilicon chemistry to the art of organic synthesis. Let us go back to 1968, a date which marks the turning point in the applications of organosilicon chemistry to organic synthesis, a field which has blossomed amazingly in the past few years, and which can be expected now to bear substantial fruit.

To be sure, there were significant contributions before 1968,[1] but, until that date, synthetic organic chemists as a whole were slow to appreciate the potential which the vast amount of known silicon chemistry held for them. Even at that date, silicon chemistry, although second only to carbon chemistry in the number of papers published every year,[2] was the preserve largely of dedicated silicon chemists. In 1968, several key publications alerted us all to this untapped resource, and I want briefly to pay tribute to these formative influences. Pierce's book[3] showed us how easy it was to put silyl groups onto hydroxy-groups and to

$$\mathrm{ROH} \underset{\text{ii}}{\overset{\text{i}}{\rightleftarrows}} \mathrm{ROSiMe_3} \qquad 100\,\%$$

Reagents: i, Me_3SiCI, $(Me_3Si)_2NH$; ii, MeOH

Scheme 1



76 %

Reagent: i, Na, Me_3SiCl

Scheme 2

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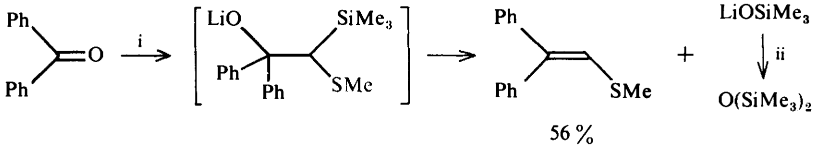
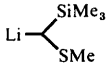
*Delivered in various versions starting on the 15th October, 1980 in the University of Birmingham.

[1] C. Eaborn, 'Organosilicon Chemistry', Butterworths, London, 1960; J. F. Klebe, *Adv. Org. Chem.*, 1972, **8**, 97.

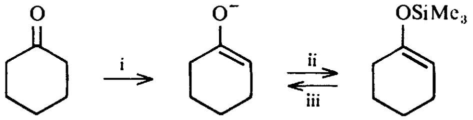
[2] I. Haiduc, *J. Chem. Documentation*, 1972, **12**, 175.

[3] A. E. Pierce, 'Silylation of Organic Compounds', Pierce Chemical Company, Rockford, Illinois, 1968.



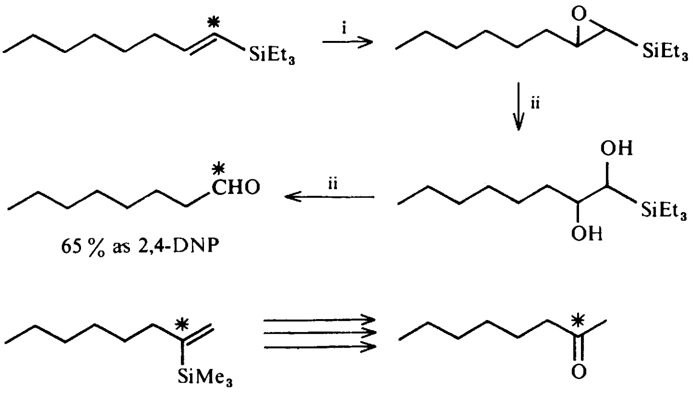
Reagents: i,  $\mathrm{Li{-}CH(SiMe_3)(SMe)}$; ii, H_2O

Scheme 3



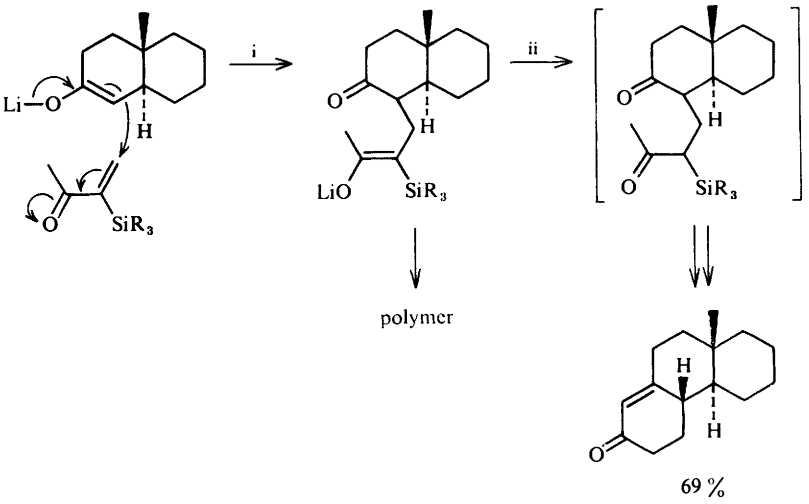
Reagents: i, base; ii, Me_3SiCl; iii, MeLi

Scheme 4



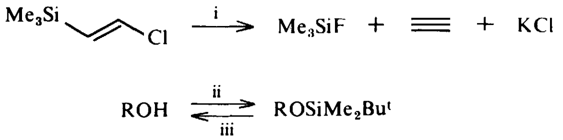
Reagents: i, MCPBA, r.t., CH_2Cl_2, 12h; ii, H_3O^+

Scheme 5



Reagents: i, −78 °C—r.t., 30 min; ii, NaOMe, MeOH, reflux 3h

Scheme 6



Reagents: i, KF, DMSO; ii, Bu^{t}Me$_2$SiCl, imidazole, DMF, 35 °C, 10h; ii, Bu$_4$N$^+$F$^-$, THF, 25 °C, 40 min

Scheme 7

take them off again (Scheme 1), one area which was perhaps already appreciated; Bloomfield published[4] his discovery that Rühlmann's reaction[5] was applicable to the acyloin condensation of succinate esters (Scheme 2); Peterson published[6] his work (Scheme 3) on a silicon-equivalent of the Wittig reaction, a reaction which now bears his name; and Stork and Hudrlik described[7] some key features of the preparation and reactions of silyl enol ethers (Scheme 4). In this last paper, one of the most prominent and influential synthetic chemists set his imprimatur on the subject, and we all took notice. Carbon-bound silicon chemistry also received Professor Stork's imprimatur with the publication[8] three years later of the

[4] J. J. Bloomfield, *Tetrahedron Lett.*, 1968, 587

[5] K. Rühlmann, *Synthesis*, 1971, 236.

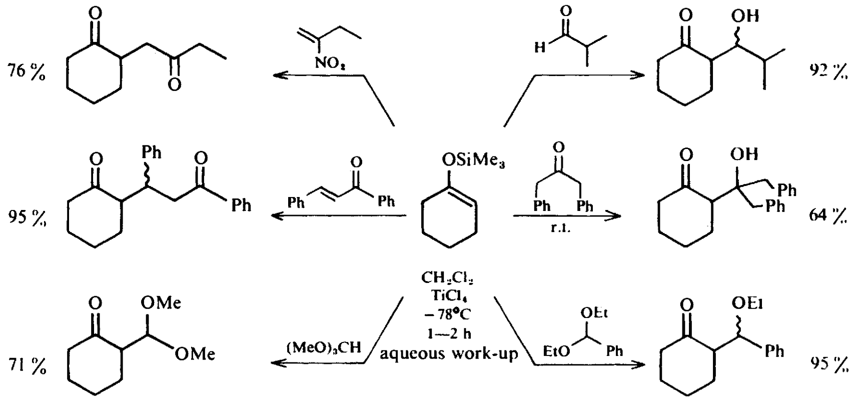
[6] D. J. Peterson, *J. Org. Chem.*, 1968, **33**, 780.

[7] G. Stork and P. F. Hudrlik, *J. Am. Chem. Soc.*, 1968, **90**, 4462, 4464; see also H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, 1969, **34**, 2324.

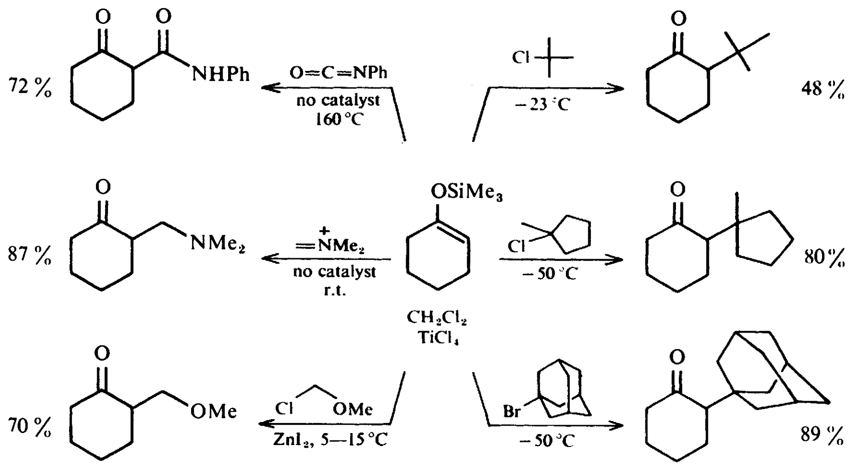
[8] G. Stork and E. Colvin, *J. Am. Chem. Soc.*, 1971, **93**, 2080; G. Stork and M. E. Jung, *ibid.*, 1974, **96**, 3682; P. F. Hudrlik, J. P. Arcoleo, R. H. Schwartz, R. N. Misra, and R. J. Rona, *Tetrahedron Lett.*, 1977, 591.

Stork–Colvin reaction (Scheme 5) and then, two years later,[9] of the Stork–Ganem modification (Scheme 6) of Robinson annelation. Furthermore, in 1972, both Cunico and Dexheimer[10] and another of the most prominent synthetic chemists, E. J. Corey,[11] independently introduced the use of fluoride ion as a powerful and specific method for removing silyl groups (Scheme 7).

Thus the stage was set for what has proved to be a rapidly growing and



Scheme 8



Scheme 9

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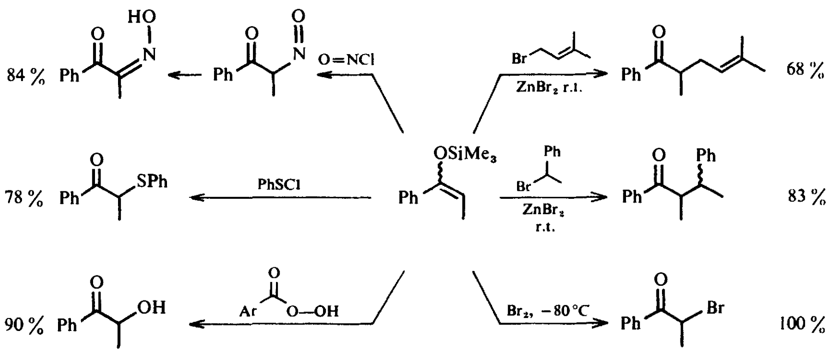
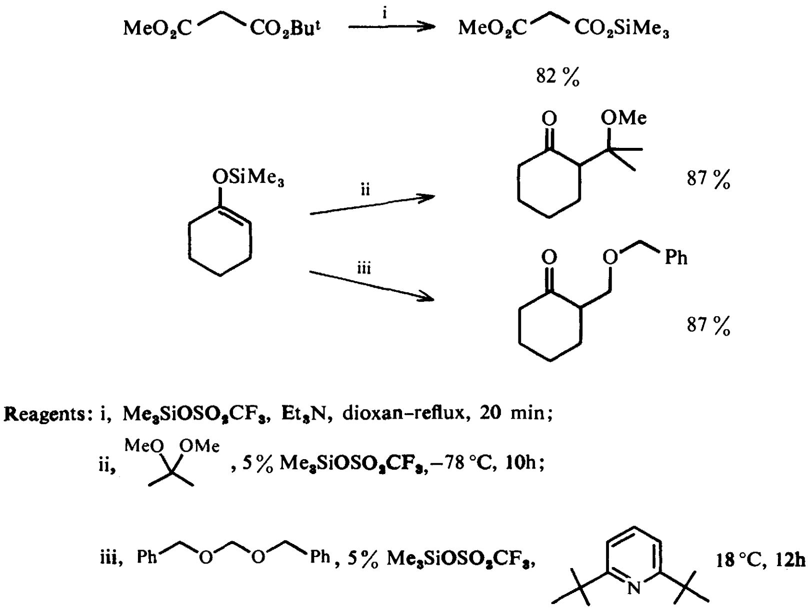
[9] G. Stork and B. Ganem, *J. Am. Chem. Soc.*, 1973, **95**, 6152; R. K. Boeckman, *ibid.*, 1974, **96**, 6179; G. Stork and J. Singh, *ibid.*, 1974, **96**, 6181.

[10] R. F. Cunico and E. M. Dexheimer, *J. Am. Chem. Soc.*, 1972, **94**, 2868.

[11] E. J. Corey and B. B. Snider, *J. Am. Chem. Soc.*, 1972, **94**, 2549; E. J. Corey and A. Venkateswarlu, *ibid.*, 1972, **94**, 6190.



Scheme 10



Reagents: i, $Me_3SiOSO_2CF_3$, Et_3N, dioxan-reflux, 20 min;
ii, MeO OMe, 5% $Me_3SiOSO_2CF_3$, −78 °C, 10h;
iii, Ph O O Ph, 5% $Me_3SiOSO_2CF_3$, N, 18 °C, 12h

Scheme 11

successful line of research entered into by many groups around the world.[12] In this lecture, I shall try to bring out some of the major features of organosilicon chemistry, and illustrate them largely with examples from our own work.

2 Silicon–Oxygen Chemistry

One line of work in which we and others have been engaged is based on the

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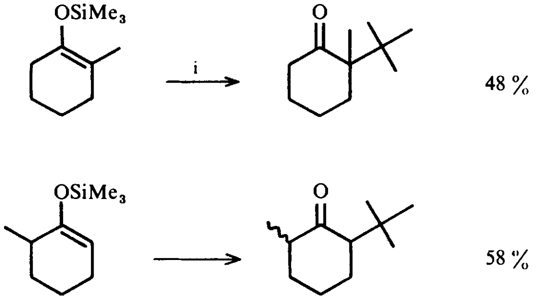
[12] P. F. Hudrlik, *J. Organomet. Chem. Library*, 1976, **1**, 127; E. W. Colvin, *Chem. Soc. Rev.*, 1978, **7**, 15; I. Fleming in 'Comprehensive Organic Chemistry', ed. D. H. R. Barton and W. D. Ollis, Pergamon, Oxford, 1979, Vol. III, p. 541; T. H. Chan and I. Fleming, *Synthesis*, 1979, 761; I. Fleming, *Chimia*, 1980, **34**, 265 and P. Magnus, *Aldrichimica Acta*, 1980, **13**, 43.

chemistry of compounds having a silicon–oxygen bond. Thus silyl groups, especially the t-butyldimethylsilyl group,[11] are extensively used to protect hydroxy-groups (Scheme 7). Similarly, silyl enol ethers act as the most easily made derivatives of enols; they can be used either, as Stork and Hudrlik have shown, as the precursors of enolates (Scheme 4), or, in their own right, as Mukaiyama and his co-workers and others have shown, as versatile carbon nucleophiles (Schemes 8,[13] 9,[14] and 10[15]), duplicating and extending much of enolate chemistry. In all this work on oxygen–silicon compounds, the silyl group functions as a substitute for the proton of an alcohol or enol. Like a proton, a silyl group is easy to put on and take off, yet the silicon–oxygen bond is slower to break than the corresponding hydrogen–oxygen bond. In silicon–oxygen chemistry, therefore, the silyl group is like a rather feeble proton. An intriguing aspect of this idea is that trimethylsilyl triflate is a Lewis acid (Scheme 11)[16] which is compatible with the presence of amine bases.



Reagents: i, Bu^tCl, CH_2Cl_2, $TiCl_4$

Scheme 12

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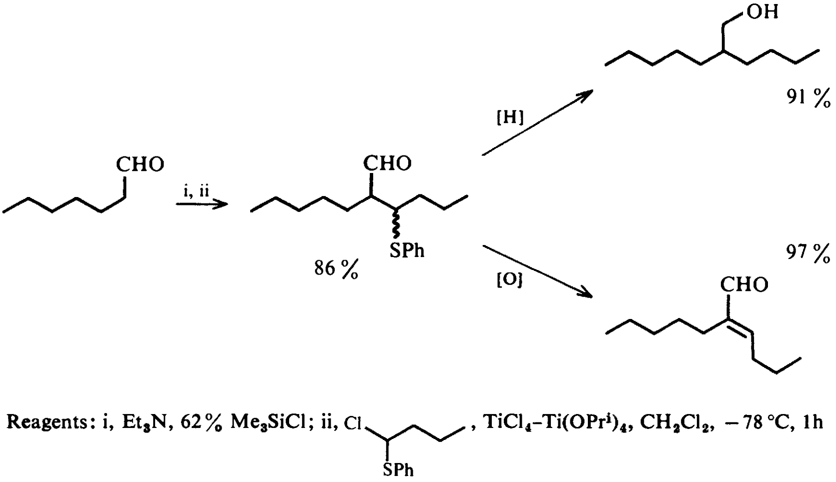
[13] Clockwise from top-left: T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, 1974, **96**, 7503; T. Mukaiyama and M. Hayashi, *Chem. Lett.*, 1974, 15; K. Narasaka, K. Soai, Y. Aikawa, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 1976, **49**, 779; M. Miyashita, T. Yanami, and A. Yoshikoshi, *J. Am. Chem. Soc.*, 1976, **98**, 4769.

[14] Clockwise from top-right: ref. 17 and M. T. Reetz and W. F. Maier, *Angew. Chem. Int. Ed. Engl.*, 1978, **17**, 48, M. T. Reetz, W. F. Maier, H. Heimbach, A. Giannis, and G. Anastassious, *Chem. Ber.*, 1980, **113**, 3734 and M. T. Reetz, W. F. Maier, I. Chatziisifidis, A. Giannis, H. Heimbach, and U. Löwe, *ibid.*, 1980, **113**, 3741, and T. Sasaki, A. Usuki, and M. Ohno, *Tetrahedron Lett.*, 1978, 4925; T. Shono, I. Nishigushi, T. Komamura, and M. Sasaki, *J. Am. Chem. Soc.*, 1979, **101**, 984; S. Danishefsky, T. Kitahara, R. McKee, and P. F Schuda, *ibid.*, 1976, **98**, 6715; S.-I. Inaba, I. Ojima, K. Yoshida, and M. Nagai, *J. Organomet. Chem.*, 1979, **164**, 123.

[15] Clockwise from top-right: I. Paterson, *Tetrahedron Lett.*, 1979, 1519 and M. T. Reetz, S. Huttenhain, P. Walz, and U. Löwe, *ibid.*, 4971; R. H. Reuss and A. Hassner, *J. Org. Chem.*, 1974, **39**, 1785; G. M. Rubottom, J. M. Gruber, R. K. Boeckman, M. Ramaiah, and J. B. Redwind, *Tetrahedron Lett.*, 1978, 4603 and L. Blanco, P. Amice, and J. M. Conia, *Synthesis*, 1976, 194; S. Murai, Y. Yuroki, K. Hasegawa, and S. Tsutsumi, *J. Chem. Soc., Chem. Commun.*, 1972, 946; J. K. Rasmussen and A. Hassner, *J. Org. Chem.*, 1974, **39**, 2558.

[16] J. Borgulya and K. Bernauer, *Synthesis*, 1980, 545; S. Murata, M. Suzuki, and R. Noyori, *J. Am. Chem. Soc.*, 1980, **102**, 3248 and *Tetrahedron Lett.*, 1980, 2527.

A. Phenylthioalkylation of Silyl Enol Ethers.—Our first contribution in this area was made by Ian Paterson as an extension of his work[17] with Professor T. H. Chan on the t-alkylation of silyl enol ethers (Scheme 12). He invented the Lewis acid-catalysed phenylthioalkylation of silyl enol ethers,[18] and showed that it was a high-yielding and regiospecific method for the introduction of primary alkyl or alkylidene groups α to the carbonyl group of aldehydes, ketones, and esters (Schemes 13, 14, and 15). Then he and Jon Goldhill showed[19] that phenylthioalkylation could often be used to introduce primary alkyl or alkylidene groups in the γ-position of silyl dienol ethers (Scheme 16). Although the extent of γ- relative to α-attack was not always complete (Scheme 17), this reaction was strikingly different from the corresponding reaction of alkyl halides on lithium dienolates, where the attack is almost always at the α-position (*e.g.* Scheme 18).[20] More recently, Tom Lee has continued this work; he has found that phenylthiomethyl chloride is the least γ-selective of a range of carbon electrophiles (Scheme 19), and that triphenylsilyl dienol ethers are significantly more γ-selective than the corresponding trimethylsilyl ethers (Scheme 20),[21] giving a high proportion (84:16) of γ-attack even with the least γ-selective carbon electrophile.



Reagents: i, Et_3N, 62% Me_3SiCl; ii, (structure), $TiCl_4$-$Ti(OPr^i)_4$, CH_2Cl_2, −78 °C, 1h

Scheme 13

3 Silicon–Carbon Chemistry

In much of the chemistry of compounds having a silicon–carbon bond, the silyl group again functions as a substitute for a proton. This time, however, the

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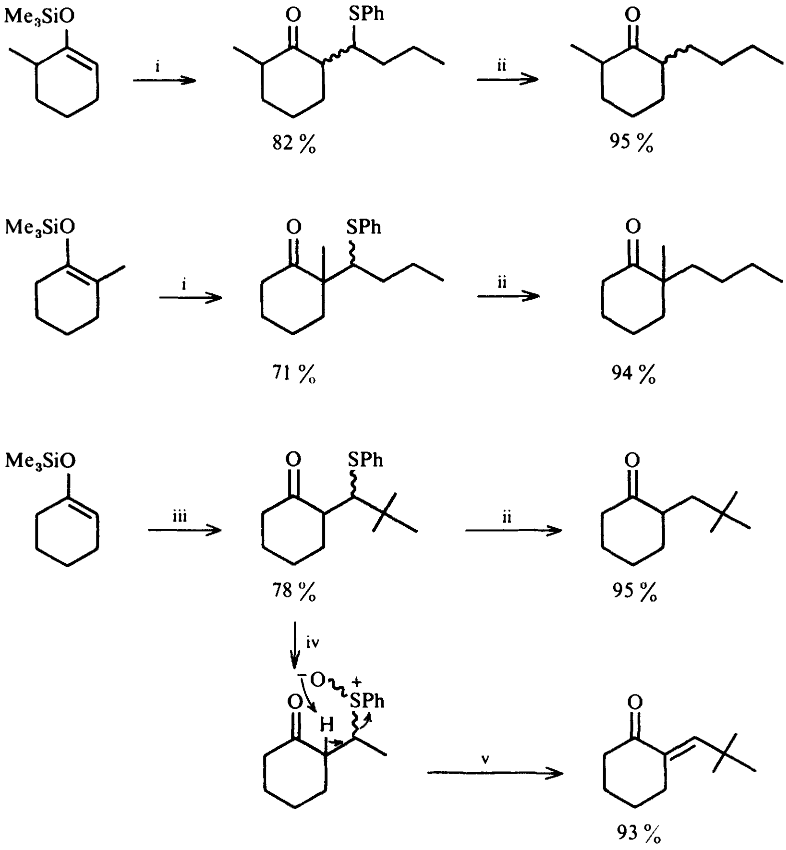
[17] T. H. Chan, I. Paterson, and J. Pinsonnault, *Tetrahedron Lett.*, 1977, 4183.

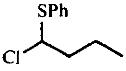
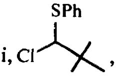
[18] I. Paterson and I. Fleming, *Tetrahedron Lett.*, 1979, 993, 995, 2179.

[19] I. Fleming, J. Goldhill, and I. Paterson, *Tetrahedron Lett.*, 1979, 3205, 3209.

[20] N. W. Atwater, *J. Am. Chem. Soc.*, 1960, **82**, 2847; C. N. Lam, J. M. Mellor, P. Picard, M. F. Rawlins, and J. H. A. Stibbard, *Tetrahedron Lett.*, 1978, 4103.

[21] I. Fleming and T. V. Lee, *Tetrahedron Lett.*, 1981, 705.



Reagents: i, , $ZnBr_2$(0.02 eq.), CH_2Cl_2, r.t., 1h; ii, Ni; iii, , $ZnBr_2$;
iv, $NaIO_4$, MeOH, r.t., 42h; v, CCl_4, 60 °C, 60h

Scheme 14

silicon–carbon bond usually breaks more easily than the corresponding hydrogen–carbon bond (Scheme 21). Thus, Chan and his co-workers[22] have used the β-elimination of haloalkylsilanes to give allenes and allene oxides (Scheme 22), and Hudrlik and his co-workers have shown[23] that the β-eliminations are stereospecific (Scheme 23).

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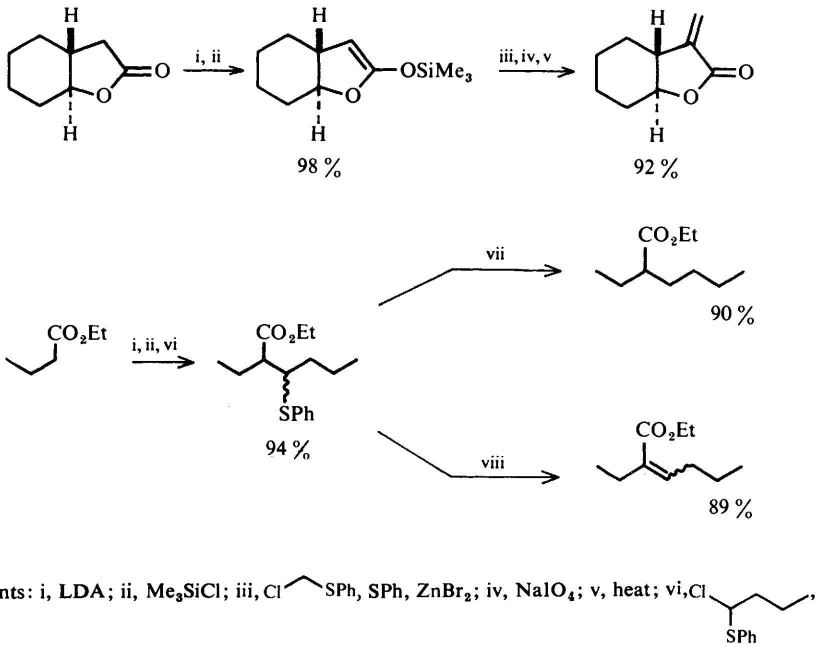
[22] T. H. Chan and W. Mychajlowskij, *Tetrahedron Lett.*, 1974, 171; T. H. Chan, M. P. Li, W. Mychajlowskij, and D. N. Harpp, *ibid.*, 1974, 3511.

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



Reagents: i, LDA; ii, Me_3SiCl; iii, Cl SPh, SPh, $ZnBr_2$; iv, $NaIO_4$; v, heat; vi, Cl SPh, $ZnBr_2$; vii, [H]; viii, [O]

Scheme 15

However, all the applications of this idea stem from another of the publications of that key year, 1968. I have left it until last, because it is so important. In that year, Eaborn and Bott published a long review[24] of the chemistry of compounds containing the silicon–carbon bond, and from this review come many of the insights which have helped to fuel the rapid progress of recent years. Eaborn and Bott made three generalizations of great predictive value. (i) As mentioned above, a silyl group is usually displaced from carbon more easily than a proton is displaced from the corresponding carbon (Scheme 21). (One must now add that it is likely to be true only when the nucleophile is an oxygen or halogen nucleophile, when the carbon is not digonal, and when there are no steric restraints to inhibit the participation of the silyl group.) On carbon, therefore, a silyl group, far from being like a rather feeble proton, as it is on oxygen, is better thought of as a sort of super-proton. (ii) A silicon–carbon bond stabilizes a β-carbocation more than a hydrogen–carbon or carbon–carbon bond does (Scheme 24). This is another example of the silyl group as a super-proton: the stabilization stems from the electropositive (*i.e.* metallic) character of silicon, which leads the orbitals of the silicon–carbon bond to be favourably polarized

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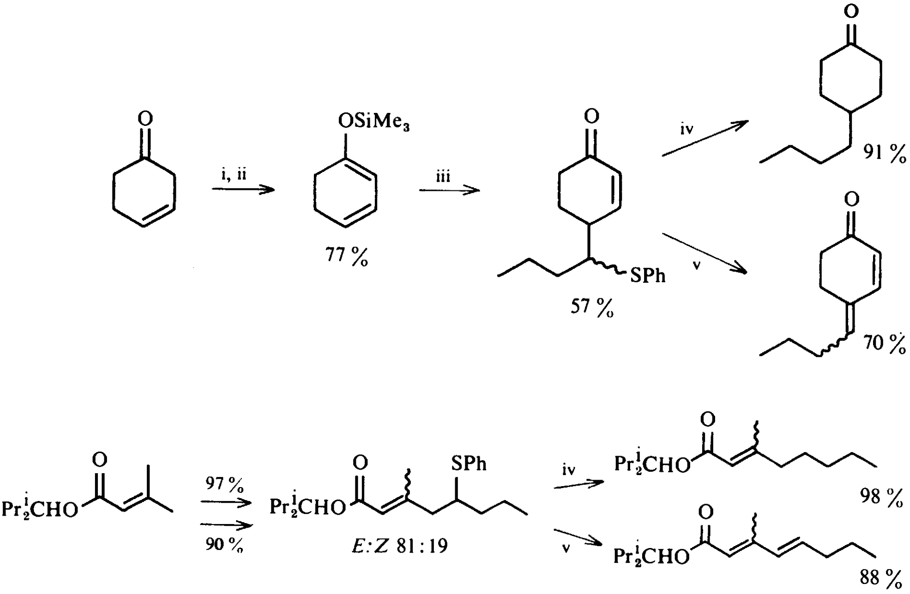
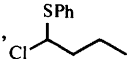
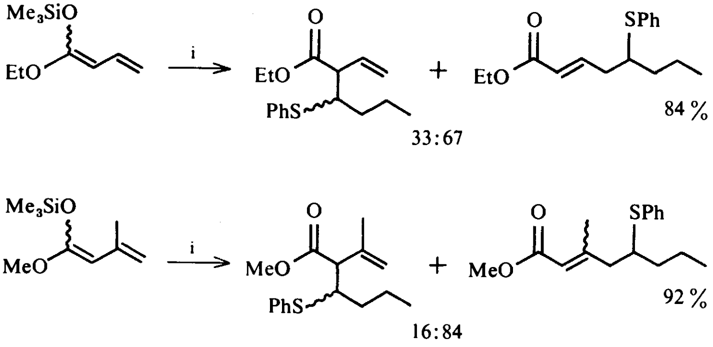
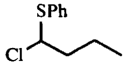
[24] C. Eaborn and R. W. Bott in 'Organometallic Compounds of the Group IV Elements', Vol. 1, Part 1, ed. A. G. MacDiarmid, Dekker, New York, 1968.



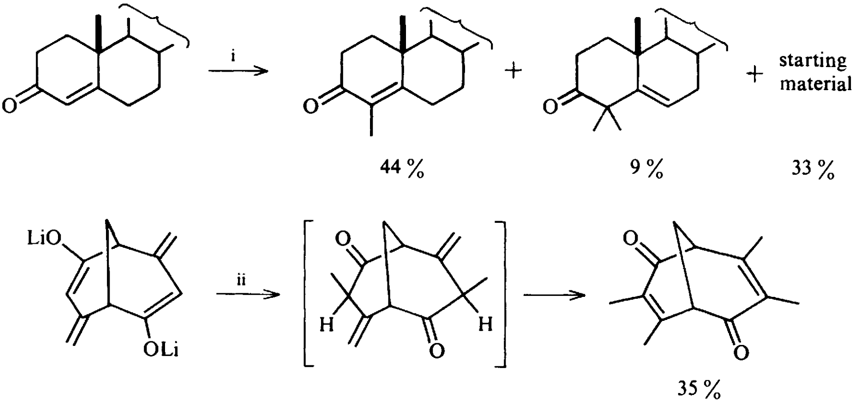
Reagents: i, LDA; ii, Me$_3$SiCl; iii, , ZnBr$_2$(0.02 eq.); iv, [H]; v, [O]

Scheme 16



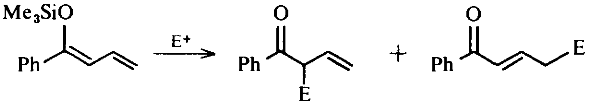
Reagents: i, , ZnBr$_2$

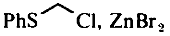
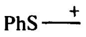
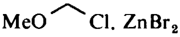
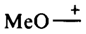
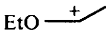
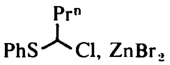
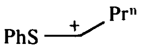
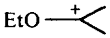
Scheme 17



Reagents: i, KOBu^t, Bu^{t}OH, MeI; ii, MeI

Scheme 18



	E$^+$	α:γ	*yield*/%
		55:45	65
		47:53	53
(EtO)$_2$CHMe, ZnBr$_2$		40:60	78
		34:66	85
(EtO)$_2$CMe$_2$, TiCl$_4$		(0:100)	78
(MeO)$_3$CH, TiCl$_4$		(0:100)	52

Scheme 19

and energetically well-matched for effective overlap with the empty *p*-orbital. (iii) In spite of these useful properties, and the high reactivity that comes from them when the silyl group is close to suitable functionality, a silyl group remote from functionality can be relied upon to survive most of the reaction conditions used in modern organic synthesis. Only strongly nucleophilic (Scheme 25)[25] and

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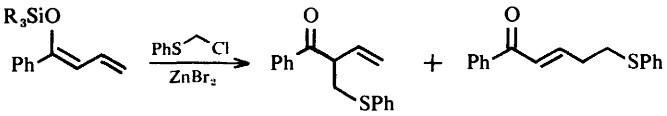
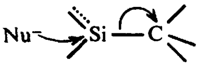
[25] C. C. Price and J. R. Sowa, *J. Org. Chem.*, 1967, **32**, 4126.



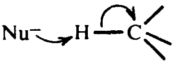
R_3	$\alpha:\gamma$	*yield*/%
Me, Me, Me	55:45	65
Et, Et, Et	62:38	75
Me, Me, Bu^t	77:23	62
Me, Me, Ph	39:61	91
Me, Ph, Ph	32:68	74
Ph, Ph, Ph	14:86	93

Scheme 20

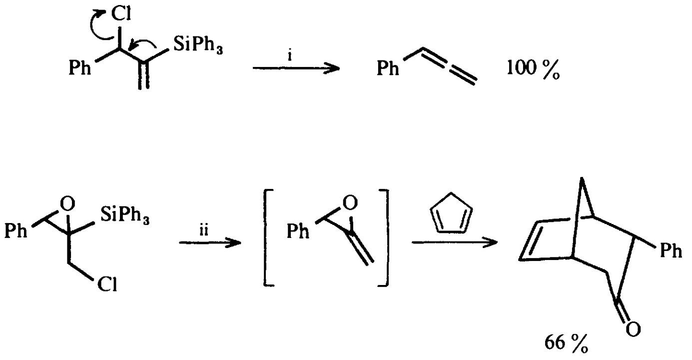
For oxygen and halogen nucleophiles,



is usually faster than the corresponding reaction:



Scheme 21



Reagents: i, KF, DMSO, r.t., 10h; ii, KF, MeCN, r.t., 53h

Scheme 22

strongly electrophilic conditions (Scheme 26)[26] are unsafe, and these can usually be avoided.

It is this last property which is essentially unique to silicon. Whereas other 'weak metals', like boron, aluminium, tin, selenium, phosphorus, and arsenic, might be substitutes for, and even superior to silicon in some reactions, only a

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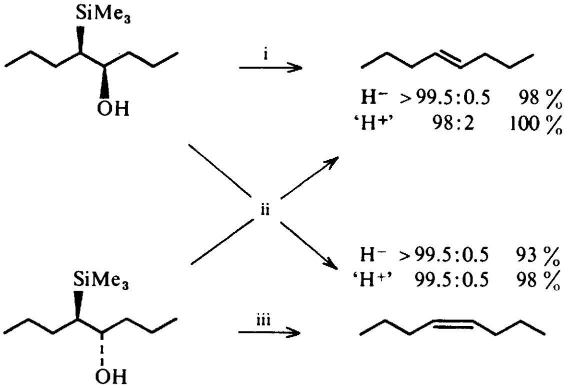
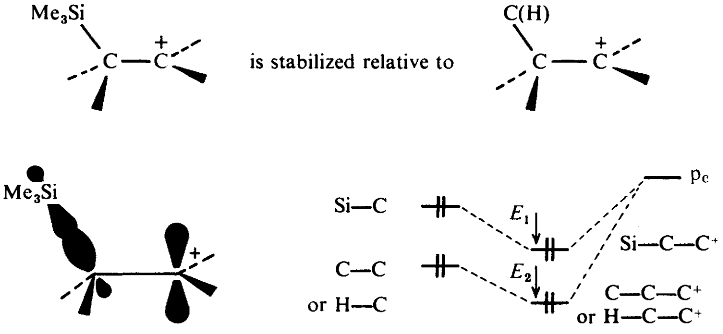
[26] C. Eaborn, *J. Chem. Soc.*, 1949, 2755; L. H. Sommer, R. P. Pioch, N. S. Marans, G. M. Goldberg, J. Rockett, and J. Kerlin, *J. Am. Chem. Soc.*, 1953, **75**, 2932.



Reagents: i, KH, THF, r.t., 1h; ii, BF_3:OEt_2, CH_2Cl_2, 0 °C, 1h

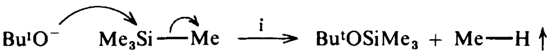
Scheme 23



the coefficients

the energy match

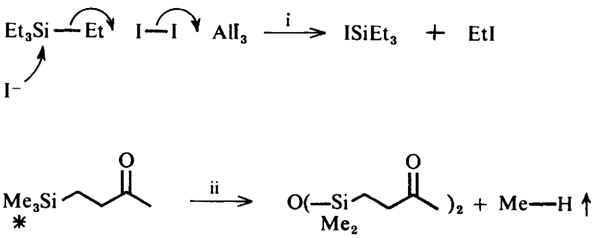
Scheme 24



$$\mathrm{Bu^tO^-}\quad \mathrm{Me_3Si{-}Me} \xrightarrow{i} \mathrm{Bu^tOSiMe_3} + \mathrm{Me{-}H}\uparrow$$

Reagent: i, DMSO, 25 °C, secs

Scheme 25



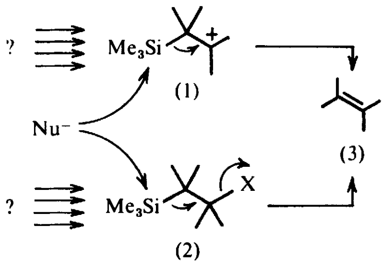
$$\mathrm{Et_3Si{-}Et}\quad \mathrm{I{-}I}\quad \mathrm{AlI_3} \xrightarrow{i} \mathrm{ISiEt_3} + \mathrm{EtI}$$

Reagents: i, 153 °C, 1.5h; ii, H_2SO_4, 10 °C, 1.5h

Scheme 26

silyl group possesses the stability which enables one to carry it with confidence through many different kinds of reaction, before performing the key step which actually uses the silyl group. This unique capability of silicon has been the basis of much of our own work.

We have been intent on demonstrating how the three generalizations above can be put together to give us control of otherwise quite well-known organic reactions. In essence, all our efforts, like those of several other groups, have been based on the proposition that a carbonium ion (1) or an alkyl halide (2) can be relied upon to lose the silyl group, rather than to do anything else, and so lead to a single olefin (3) in which the double bond is placed at a specific site (Scheme 27).



Scheme 27

Perhaps the most dramatic, simple example of this idea came when Andrew Pearce showed[27] that the acetal (4) reacted with Lewis acid to give a single product (5), whereas the corresponding compound without the silyl group was known[28] to give a mixture of products (Scheme 28). This result has recently, and most gratifyingly, been extended by Professor Johnson[29] to a polyolefin cyclization (Scheme 29).

The idea summarized in Scheme 27 is therefore a powerful one. It is a single idea with a wide variety of applications: all that changes is the route by which one arrives at the structure (1) or (2).

A. Vinylsilanes.—Combining the first two generalizations above led us to predict that a vinylsilane, other things being equal, would undergo electrophilic substitution at the carbon atom carrying the silyl group (Scheme 30). Andrew Pearce showed[30] that this extension of an idea, already proved for arylsilanes,[31] worked for vinylsilanes (Scheme 31). The idea has been shown to be fairly general[32] and

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[27] I. Fleming, A. Pearce, and R. L. Snowden, *J. Chem. Soc., Chem. Commun.*, 1976, 182; I. Fleming and A. Pearce, *J. Chem. Soc., Perkin Trans. 1*, 1981, 251.

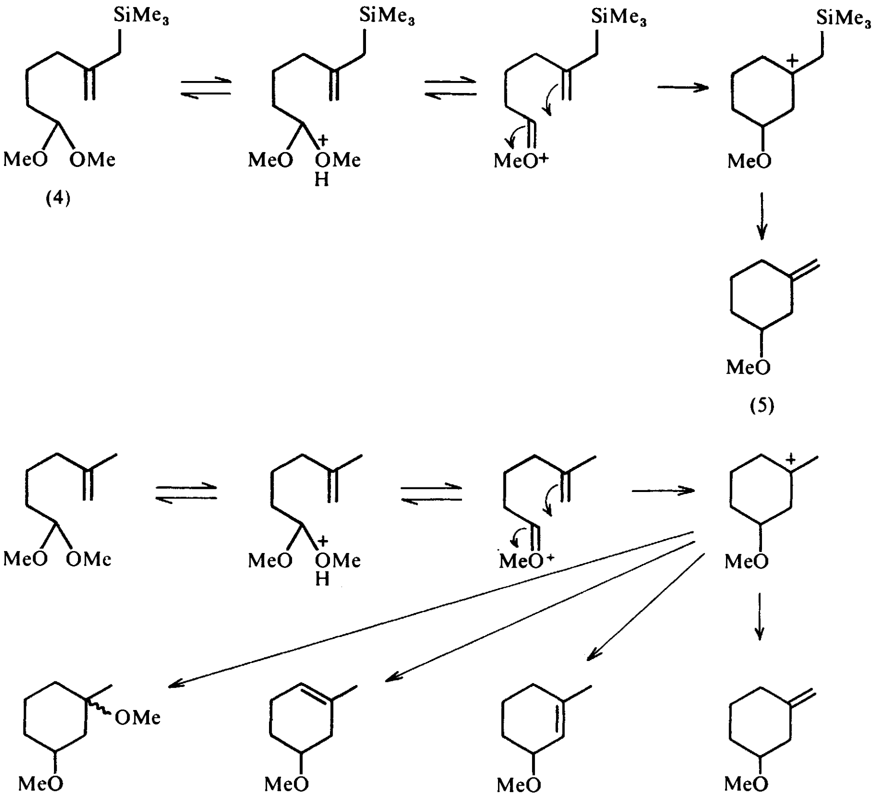
[28] A. van der Gen, K. Wiedhaup, J. J. Swoboda, H. C. Dunathan, and W. S. Johnson, *J. Am. Chem. Soc.*, 1973, **95**, 2656.

[29] L. R. Hughes, R. Schmid, and W. S. Johnson, *Bioorg. Chem.*, 1979, **8**, 513.

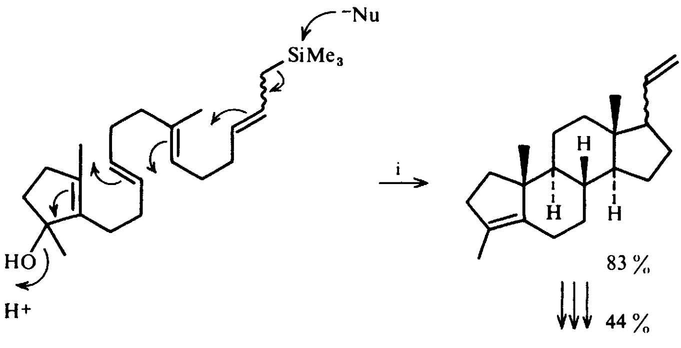
[30] I. Fleming and A. Pearce, *J. Chem. Soc., Chem. Commun.*, 1975, 633; *J. Chem. Soc., Perkin Trans. 1*, 1980, 2485.

[31] D. Häbich and F. Effenberger, *Synthesis*, 1979, 841.

[32] T. H. Chan and I. Fleming, *Synthesis*, 1979, 761.



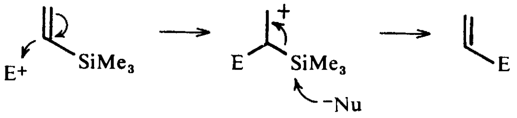
Scheme 28



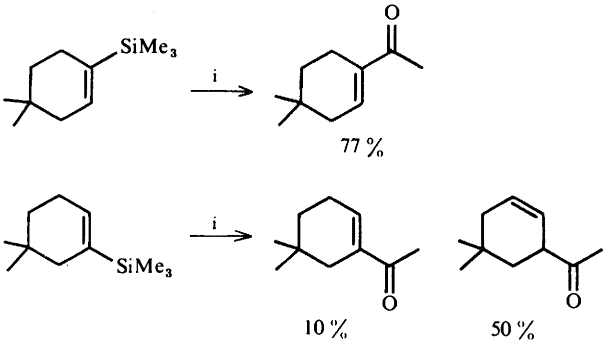
Reagent: i, TFA, CH_2Cl_2, −35 °C

Scheme 29

vinyl silanes

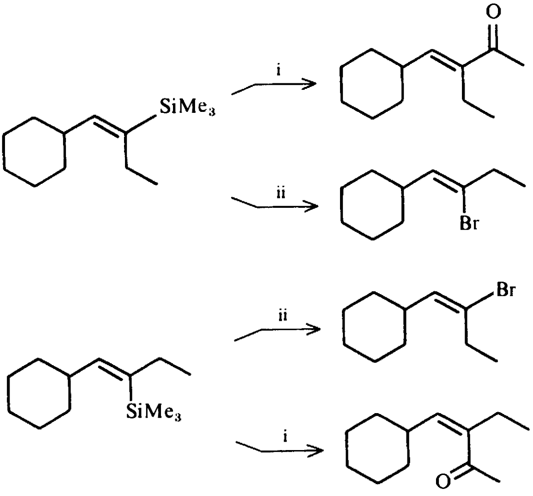


Scheme 30



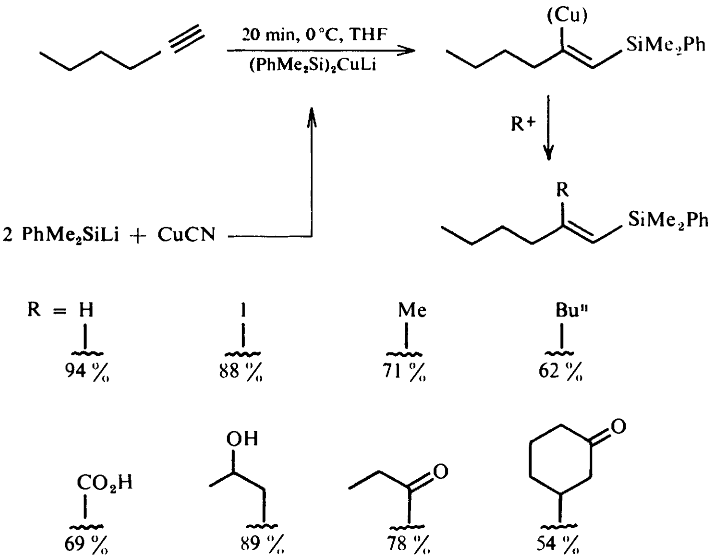
Reagents: i, AcCl, $AlCl_3$, CH_2Cl_2, 0 °C, 15 min

Scheme 31



Reagents: i, AcCl, $AlCl_3$; ii, Br_2, CH_2Cl_2

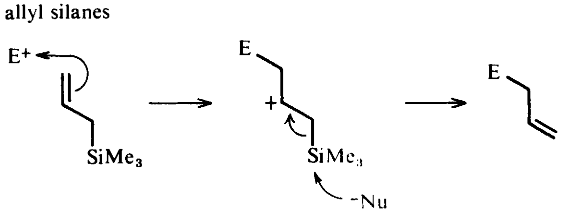
Scheme 32



Scheme 33

the reaction is also highly stereospecific[32,33] (Scheme 32). Our only other contribution[34] to vinylsilane chemistry has been Felix Roessler's new synthesis of vinylsilanes from acetylenes (Scheme 33).

B. Allylsilanes.—The same generalizations suggested that allylsilanes would react with electrophiles with allylic rearrangement (Scheme 34),[35] as many allylmetal compounds are known to react.[36] This had already been shown to be the



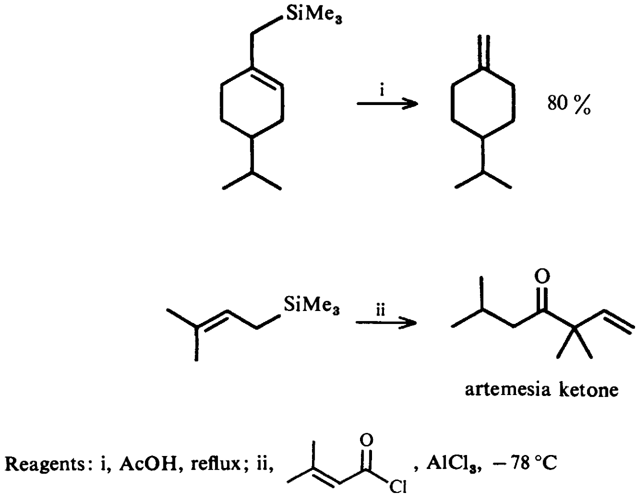
Scheme 34

[33] T. H. Chan, P. W. K. Lau, and W. Mychajlowskij, *Tetrahedron Lett.*, 1977, 3317.

[34] I. Fleming and F. Roessler, *J. Chem. Soc., Chem. Commun.*, 1980, 276; I. Fleming, T. W. Newton, and F. Roessler, *J. Chem. Soc., Perkin Trans. 1*, 1981, in press.

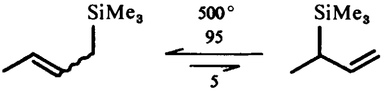
[35] L. H. Sommer, L. J. Tyler, and F. C. Whitmore, *J. Am. Chem. Soc.*, 1948, **70**, 2872.

[36] W. G. Young and J. D. Roberts, *J. Am. Chem. Soc.*, 1946, **68**, 1472; K. W. Wilson, J. D. Roberts, and W. G. Young, *ibid.*, 1950, **72**, 215.



Reagents: i, AcOH, reflux; ii, , AlCl$_3$, −78 °C

Scheme 35



Scheme 36

case by Frainnet[37] and by Calas and Dunoguès and their co-workers[38] (Scheme 35). The unique property of silicon in this context was its comparative immunity from [1,3]-sigmatropic rearrangement (Scheme 36), which takes place only at high temperatures,[39] in contrast to the great ease of such processes with all other metals. Once an allylsilane has been prepared, it can almost always be relied upon not to rearrange in this sense, and hence to behave itself in the manner of Scheme 34. The key to any use of allylsilanes in synthesis is, therefore, to have a method for making them regioselectively. In some very unsymmetrical cases (Scheme 37)[38] this is easy. In others it is an inherent result of the synthetic design (Scheme 38).[40] Our work has been on: (i) Ian Paterson's use of allylsilanes derived from a Wittig reaction (Scheme 39)[41] and Decio Marchi's multi-step substitute for the Wittig reaction (Scheme 40),[42] useful for those ketones, like

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[37] E. Frainnet and R. Calas, *C.R. Hebd. Seances Acad. Sci.*, 1955, **240**, 203; E. Frainnet, R. Collongues, and J. Thery, *Bull. Soc. Chim. Fr.*, 1959, 1441.

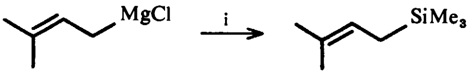
[38] J. P. Pillot, J. Dunoguès, and R. Calas, *Tetrahedron Lett.*, 1976, 1871; and for a review, see R. Calas, *J. Organomet. Chem.*, 1980, **200**, 11.

[39] J. E. Nordlander, W. G. Young, and J. D. Roberts, *J. Am. Chem. Soc.*, 1961, **83**, 494; J. Slutsky and H. Kwart, *ibid.*, 1973, **95**, 8678.

[40] D. J. Coughlin and R. G. Salomon, *J. Org. Chem.*, 1979, **44**, 3784.

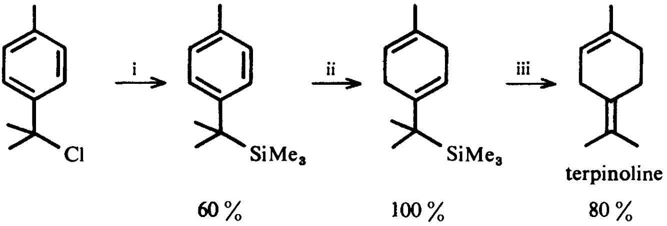
[41] I. Fleming and I. Paterson, *Synthesis*, 1979, 446.

[42] D. Marchi, *Synthesis*, in press.



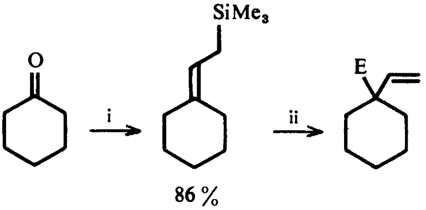
Reagent: i, Me_3SiCl

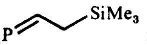
Scheme 37



Reagents: i, Mg, Me_3SiCl, THF, reflux, 2h; ii, Li, NH_3, EtOH; iii, HCl, H_2O, MeOH, THF, r.t., 24h

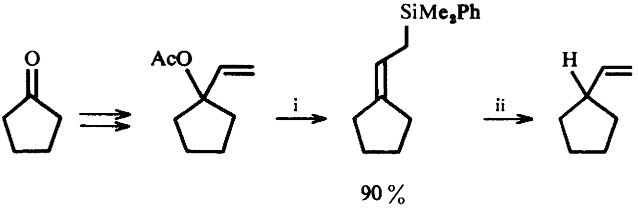
Scheme 38



Reagents: i, 

; ii, E^+

Scheme 39



Reagents: i, $(PhMe_2Si)_2CuLi$; ii, BF_3AcOH

Scheme 40

cyclopentanone, particularly susceptible to enolization; (ii) the Diels–Alder reactions of 1-silylbutadienes, where Martin Carter found useful reactivity (Scheme 41),[43] and Alan Percival found high regioselectivity only when other

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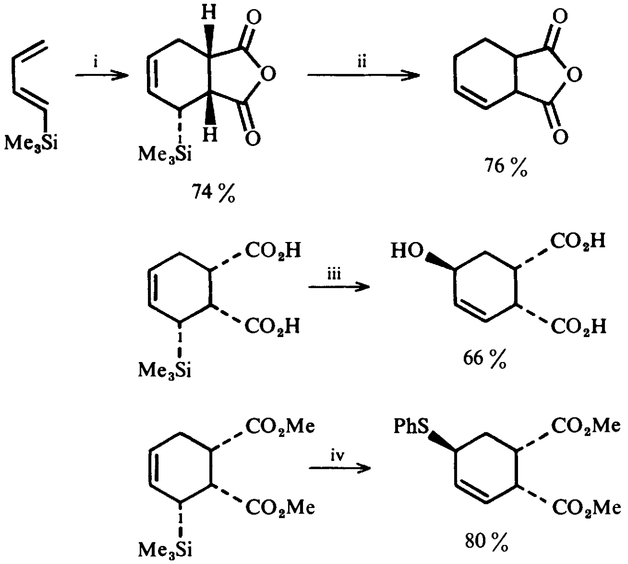
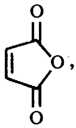
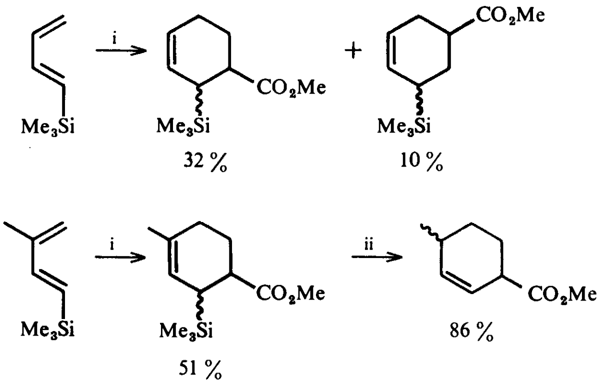
[43] M. J. Carter and I. Fleming, *J. Chem. Soc., Chem. Commun.*, 1976, 679 and ref. 45.

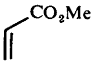


Reagents: i, , 100 °C, 2h; ii, TsOH, C_6H_6, reflux, 2h; iii, AcO_2H, Et_2O, r.t., 24h;

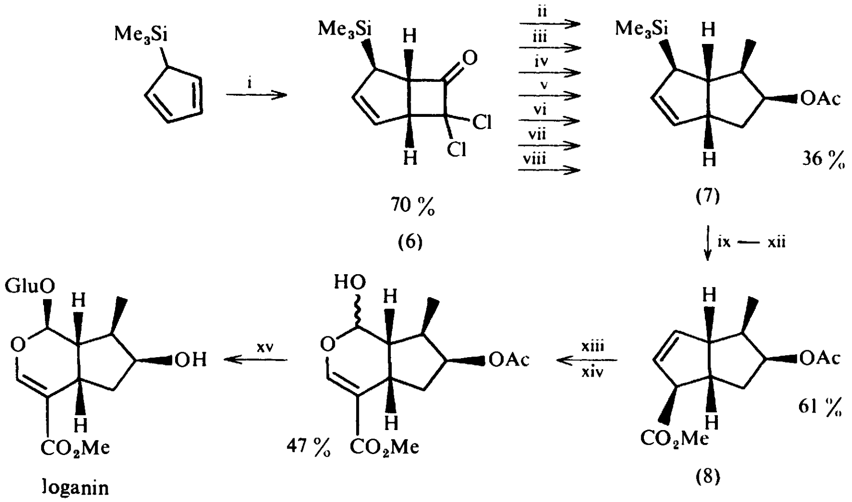
iv, $PhS^+BF_4^-$, $MeNO_2$

Scheme 41



Reagents: i, , 150 °C, 24h; ii, TsOH, C_6H_6, reflux, 3h

Scheme 42



Reagents: i, $CHCl_2COCl$, Et_3N, C_6H_{14}, 0 °C, 5h; ii, Zn, AcOH, H_2O, r.t., 24h; iii, $MeCH{:}N_2$, MeOH, EtOH, 0 °C, 5h; iv, Zn, AcOH, H_2O, r.t., 60h; v, NaOMe, MeOH, r.t., 7h; vi, $NaBH_4$, MeOH, 0 °C, 2h; vii, MsCl, Py, r.t., 18h; viii, $Et_4N^+OAc^-$, Me_2CO, reflux, 2.5h; ix, $O{:}C{:}NSO_2Cl$, CCl_4, r.t., 2.5h; x, $NaNO_2$, AcOH, Me_2CO, Ac_2O, 0 °C, 16h; xi, NaOAc, H_2O, r.t., 3h; xii, CH_2N_2, Et_2O, r.t., 0.5h; xiii, O_3, CH_2Cl_2, −65 °C, 2h; xiv, Me_2S, CH_2Cl_2, r.t., 1h; xv, Büchi, 1970

Scheme 43

substituents were present on the diene (Scheme 42);[44] and (iii) keten cycloadditions to 5-trimethylsilylcyclopentadiene and the subsequent reactions of the adduct (6).[45] This last example gave Boon-Wai Au-Yeung the opportunity to synthesize loganin (Scheme 43).[46] He was easily able to preserve the allylsilane group through seven steps (6) → (7) before the key step (7) → (8), which took advantage of the allylsilane group itself. He was able, therefore, to demonstrate in the most vivid way the unique value of the silyl group as a very special sort of metal.

C. Silicon β to Carbonyl Groups.—The comparative stability of silicon–carbon bonds is also the basis of another major part of our work. A silyl group β to a carbonyl group (10) is stable to most of the conditions used in the enolate chemistry of the carbonyl group. Indeed, when a silicon–carbon bond in (9) is forced to break, it is one of the methyl–carbon bonds which is attacked (Scheme 26),[26] and not the β-carbon–silicon bond. Thus a substantial amount of building could go on, in the sense (9) → (10), without disturbing the silyl group. However, one reaction does bring the silyl group into play, namely bromination (10) → (11),

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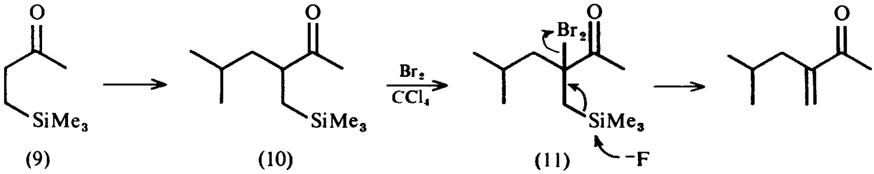
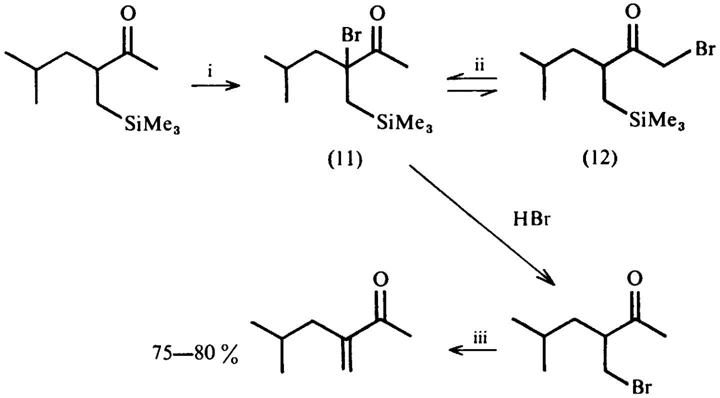
[44] I. Fleming and A. Percival, *J. Chem. Soc., Chem. Commun.*, 1976, 681 and 1978, 178, and ref. 45; M. E. Jung and B. Gaede, *Tetrahedron*, 1979, **35**, 621.

[45] M. J. Carter, I. Fleming, and A. Percival, *J. Chem. Soc., Perkin Trans. 1*, 1981, in press.

[46] B. W. Au-Yeung and I. Fleming, *J. Chem. Soc., Chem. Commun.*, 1977, 79, 81; *Tetrahedron*, in press.

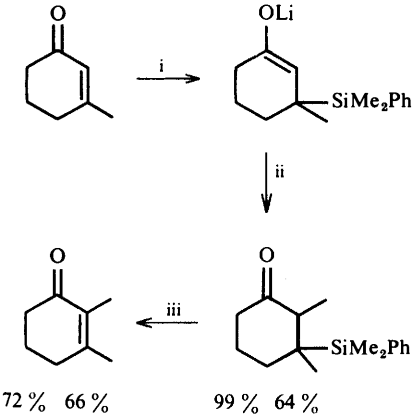


Scheme 44



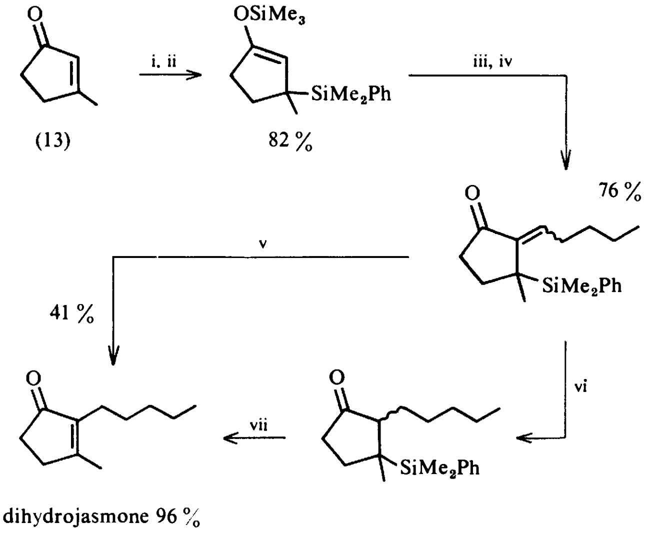
Reagents: i, Br_2, CCl_4; ii, HBr; iii, $NaHCO_3$

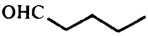
Scheme 45



Reagents: i, $(PhMe_2Si)_2CuLi$; ii, MeI; iii, $CuBr_2$

Scheme 46



Reagents: i, $(PhMe_2Si)_2CuLi$; ii, Me_3SiCl; iii,  , $TiCl_4$; iv, TsOH; v, BF_3, AcOH, CCl_4, reflux, 1h; vi, H_2, Pd–C, r.t., 2h; vii, $Ph\overset{+}{N}Me_3\,\overset{-}{Br_3}$, THF, 0 °C, 2 min

Scheme 47

which will set up the conditions (11; arrows) for desilylbromination, and the formation of a double bond at a site determined by where the silyl group was originally placed (Scheme 44). This idea was shown to be sound by Jon Goldhill,[47] who also proved (Scheme 45) that the initial site of bromination need not matter: equilibration (11) $\rightleftharpoons$ (12) could be used to set up the necessary conditions for desilylbromination (11; arrows), and the final double bond could be put back into the position determined by where the silyl group had originally been placed. David Ager showed[48] that the β-silyl group could be introduced by conjugate addition of a silyl-cuprate reagent, and subsequently removed by desilylbromination (Scheme 46). Shailesh Patel has recently used this reaction to synthesize dihydrojasmone (Scheme 47)[48] from the readily available but rarely used precursor (13). Alan Percival[44] used the silyl enol ether (14) as a substitute for the Danishefsky diene (Scheme 48), with the potential advantage in some situations that development of the C=C double bond in the final product (15) could be delayed while other synthetic steps are carried out. Recently, David Perry has used the β-silylenone (16), the precursor of Percival's diene, in another

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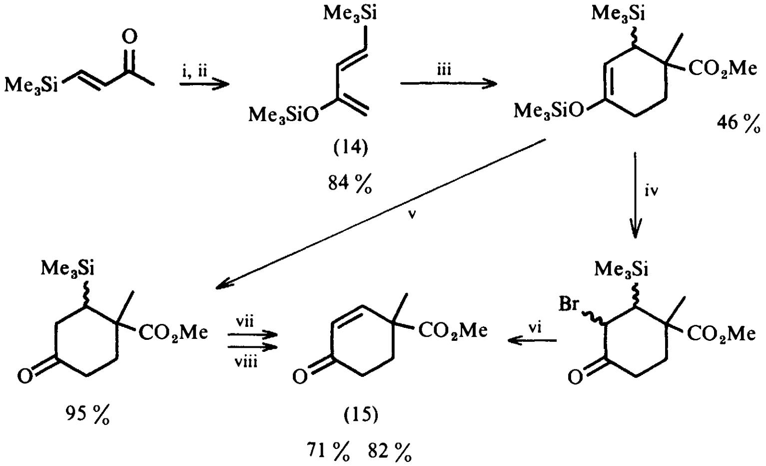
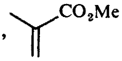
[47] I. Fleming and J. Goldhill, *J. Chem. Soc., Chem. Commun.*, 1978, 176; *J. Chem. Soc., Perkin Trans.*, 1980, 1493.

[48] D. J. Ager and I. Fleming, *J. Chem. Soc., Chem. Commun.*, 1978, 176; D. J. Ager, I. Fleming, and S. K. Patel, *J. Chem. Soc., Perkin Trans. 1*, 1981, in press.



Reagents: i, LDA; ii, Me_3SiCl; iii, , 130 °C, 64h; iv, NBS, THF, r.t., 15 min; v, H_2O, HCl, THF, r.t., 0.5h; vi, DMSO, r.t., 5 min; vii, Br_2; viii, DMSO

Scheme 48

sense (Scheme 49).[49] Conjugate addition to the enone, phenylthioalkylation (17) → (18) of the intermediate silyl enol ether, reduction, and desilylbromination gave, overall, the enone (19). The starting enone is therefore a synthon of the general type (20).

D. Silicon-controlled Carbonium Ion Rearrangements.—Since suitably placed silyl groups control the formation of a double bond from carbocations (1), it seemed possible that the homologous arrangement (21) might lead to cyclopropanes (22) (Scheme 50). Alternatively, rearrangement (21) → (23) might be encouraged, because the silyl group would stabilize the intermediate (23), and the outcome would be controlled by the loss of the silyl group (23) → (24). Both pathways have been observed by others (Scheme 51).[50] Our early work, carried out by Roger Snowden, Andrew Pearce, and Ian Paterson in collaboration with my colleague Stuart Warren, was concerned first with the controlled migration of the diphenylphosphinoyl group (Scheme 52),[51] where the position of the double bond in the product (25) was determined by the placing of the silyl group and a rearrangement (26) → (27) was forced on an otherwise reluctant system by the

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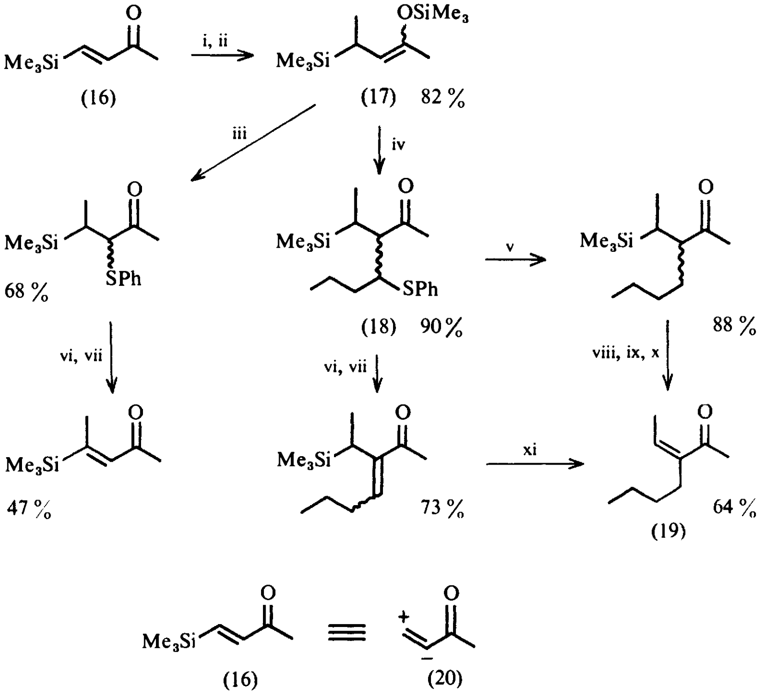
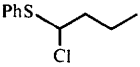
[49] D. A. Perry, unpublished results.

[50] L. H. Sommer, R. E. Van Strien, and F. C. Whitmore, *J. Am. Chem. Soc.*, 1949, **71**, 3056; H. Sakurai, T. Imai, and A. Hosomi, *Tetrahedron Lett.*, 1977, 4045.

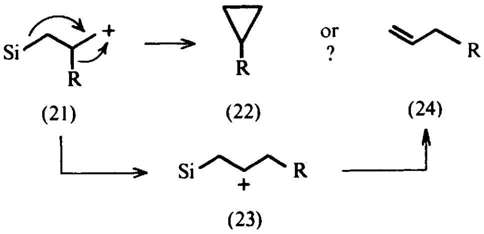
[51] A. H. Davidson, I. Fleming, J. I. Grayson, R. L. Snowden, and S. Warren, *J. Chem. Soc., Perkin Trans. 1*, 1977, 550.



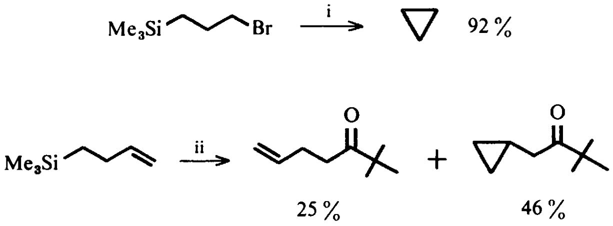
Reagents: i, Me$_2$CuLi; ii, Me$_3$SiCl; iii, PhSCl; iv, 

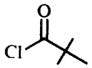
, ZnBr$_2$; v, Ni; vi, MCPBA; vii, CCl$_4$, reflux; viii, $\text{Ph}\overset{+}{\text{N}}\text{Me}_3\ \overset{-}{\text{Br}_3}$; ix, HBr, CCl$_4$, 65 °C; x, DBU; xi, BF$_3$AcOH. only *E* – isomer reacts after 72h, r.t.

Scheme 49

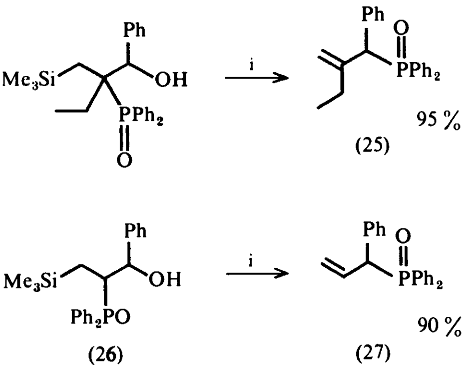


Scheme 50



Reagents: i, AlCl$_3$, r.t.;  , TiCl$_4$, -78 °C, CH$_2$Cl$_2$, 3h

Scheme 51



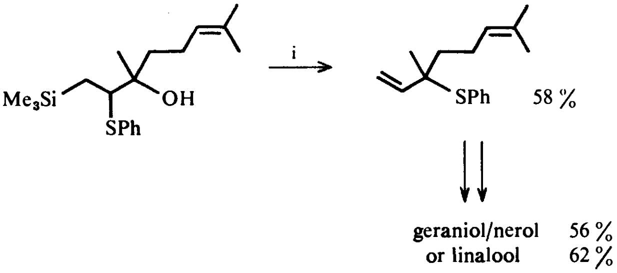
(25)

(26)

(27)

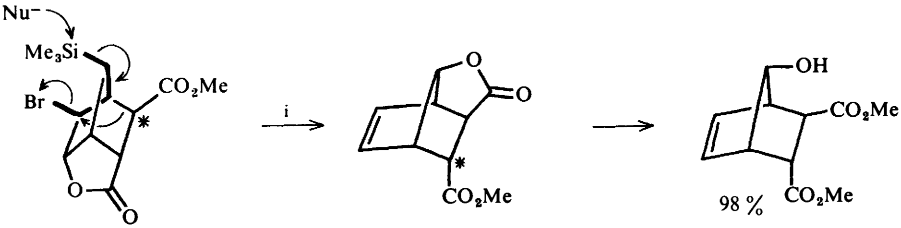
Reagents: i, TFA, r.t., 1.5h

Scheme 52



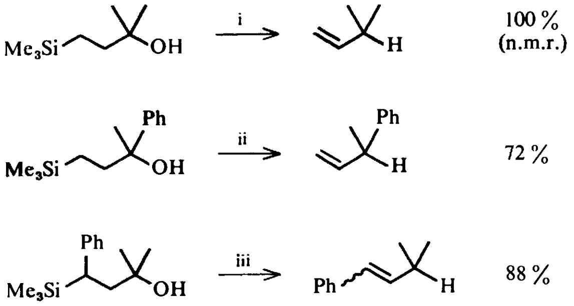
Reagents: i, SOCl$_2$, Et$_3$N, LiCl, HMPA, r.t., 20 min

Scheme 53



Reagents: i, Ag$^+$, MeOH

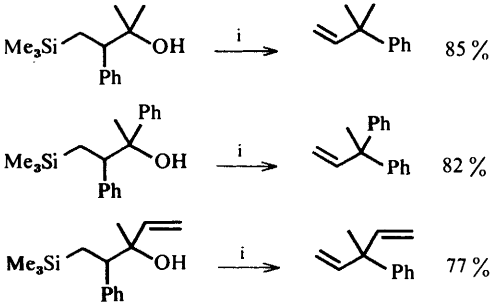
Scheme 54



(28)

Reagents: i, BF_3, AcOH, CCl_4, r.t.. 15 s; ii, BF_3, AcOH, 70 °C, 1 min; iii, BF_3, AcOH, CH_2Cl_2, 0 °C, 5 min

Scheme 55



Reagents: i, BF_3, AcOH, CH_2Cl_2, 0 °C, 5 min

Scheme 56

presence of a silyl group, and secondly with driving the rearrangement, effectively uphill, of a phenylthio group (Scheme 53).[52] Later, Jo Michael showed[53] that a rearrangement of a carbon migrating group could be encouraged in the norbornyl series (Scheme 54). Recently, Shailesh Patel[54] has investigated open-chain systems

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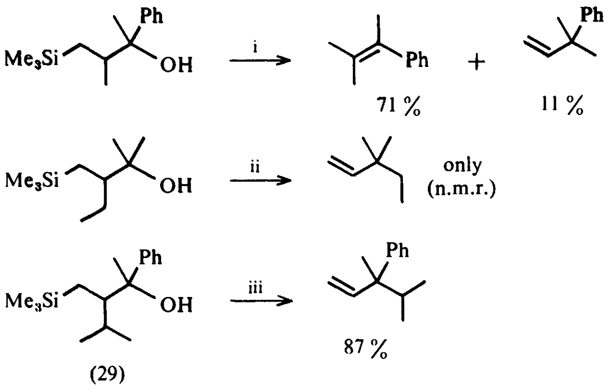
[52] P. Brownbridge, I. Fleming, A. Pearce, and S. Warren, *J. Chem. Soc., Chem. Commun.*, 1976, 751; I. Fleming, I. Paterson, and A. Pearce, *J. Chem. Soc., Perkin Trans. 1*, 1981, 256.

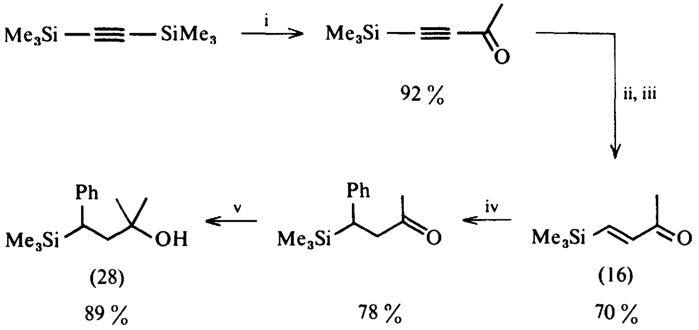
[53] I. Fleming and J. P. Michael, *J. Chem. Soc., Chem. Commun.*, 1978, 245; *J. Chem. Soc., Perkin Trans. 1*, 1981, 1549.

[54] S. K. Patel, unpublished results.



Reagents: i, BF_3, AcOH, CH_2Cl_2, 0 °C, 1 min; ii, BF_3, AcOH, CCl_4, r.t., 15 s; iii, BF_3, AcOH, CH_2Cl_2, 0 °C, 1 min

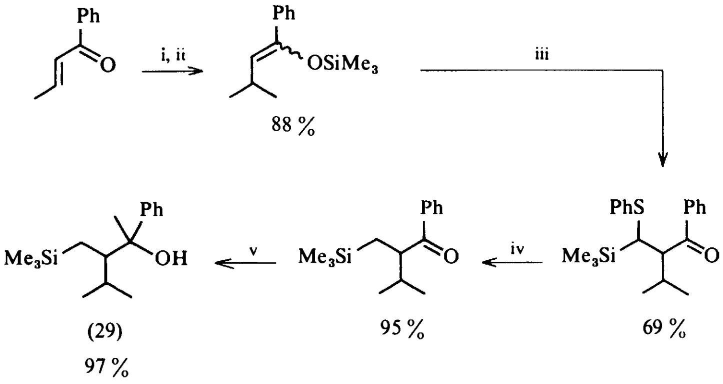
Scheme 57

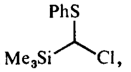


Reagents: i, MeCOCl, $AlCl_3$, CS_2; ii, $LiAlH_4$; iii, $(PyH)^+_2Cr_2O_7^{2-}$; iv, Ph_2CuLi; v, MeLi

Scheme 58

with tertiary migration termini. In every case he gets rearrangement and no cyclopropanes. He has examples of hydrogen shift (Scheme 55), phenyl shift (Scheme 56), and alkyl shift (Scheme 57), all under mild conditions and in high yield. This level of control in carbonium ion rearrangements is remarkable. The γ-silyl alcohols used in this work were easily prepared by a variety of routes, including one which takes advantage again of the versatile chemistry of the β-silylenone (16) (Scheme 58) and another which uses phenylthioalkylation to introduce the silyl group (Scheme 59). These routes show the capacity of a silyl group to be carried through several steps before it is cleanly dispensed with in the rearrangement step, a reaction tamed by the presence of the silyl group.



Reagents: i, Me_2CuLi; ii, $CiSiMe_3$; iii,  $ZnBr_2$; iv, Raney Ni; v, MeLi

Scheme 59

4 Conclusion

Silicon is no longer an exotic element in synthesis. Its organic chemistry is easily understood, first because of the close relationship of silicon to carbon, the element we know most about, and secondly because oversimplified but vivid concepts, such as those that I have presented in this lecture—that a silyl group is a sort of feeble or super proton, depending upon whether it is bonded to oxygen or carbon—help us to appreciate its special, weakly metallic properties. It is getting easier now for us all to work out new ways in which silicon can be used to solve the endless problems we meet in organic synthesis. I hope that I have helped, both by explication and example, to spread the good news.

I warmly thank all my co-workers, both those identified by name in the text above and those others, Chris Floyd, Kathy Flynn, Federico Gianni, Jenny Langley, Patrick Lau, Trevor Newton, Ian Wallace, and Richard Williams, who have done invaluable work, for which there was no room here.