Pure & Appl. Chem., Vol. 55, No. 11, pp. 1707-1713, 1983.
Printed in Great Britain.

0033-4545/83 $3.00+0.00
Pergamon Press Ltd.

SOME USES OF SILICON COMPOUNDS IN ORGANIC SYNTHESIS

Ian Fleming* and Nicholas K. Terrett

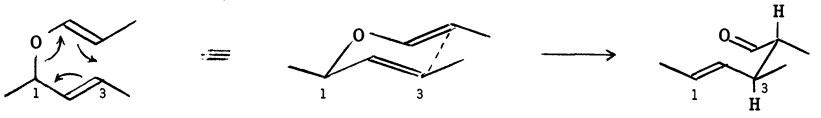
University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England

Abstract—The stereochemistry with which allylsilanes react with electrophiles is reviewed. Stereochemically defined allylsilanes (**14** and **15**) can be prepared by the stereospecific *anti* displacement of tertiary allylic acetates (**9-12**) with the phenyldimethylsilyl-cuprate reagent (**13**). These allylsilanes react with electrophiles with an overall *anti* bias. In protonation (Scheme 13) and especially in acylation (Scheme 15), the *anti* bias is not strong enough completely to overcome the axial and equatorial preferences shown by the electrophiles. In epoxidation, however, the *anti* bias nearly completely overcomes the inherent axial preference of this reaction. The method can be applied in other systems: for example, *endo*-2-propenyl-*exo*-2-norbornanol (**42**) can be easily prepared from norbornanone.

INTRODUCTION

The complete control of stereochemistry is a major goal in organic synthesis. The problem is especially acute when chiral centres are neither adjacent nor in ring systems, and remote chiral control is therefore particularly challenging. One way of achieving this kind of control is to move chiral information one, two, or three places along a chain using a stereospecific reaction. Thus, it has long been established (Ref. 1) that the S_N2' reaction can have overall *syn* selectivity, and can therefore pass chirality three places along a carbon chain. The problem is that the S_N2' reaction is rare (S_N2 reactions in allylic systems are far more common that S_N2') and the *syn* preference is neither strong nor reliable (Ref. 2). However, the Claisen rearrangement can be viewed as a variation of the S_N2' reaction; it is regiochemically and stereochemically reliable (Scheme 1), and it has therefore found much use

SCHEME 1

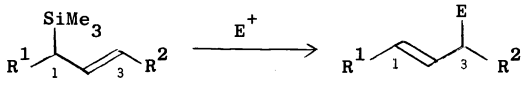


in synthesis precisely to move stereochemical information along a carbon chain (Ref. 3). However, it is limited in the range of substituents and functionality that it can set up, and it would clearly be useful to have other methods as reliable as this. One possible candidate is the S_E2' reaction, except that this has received almost no attention until very recently.

THE STEREOCHEMISTRY OF THE S_E2' REACTION OF ALLYLSILANES

The S_E2' reaction of allylsilanes (Scheme 2) is regiochemically reliable (Ref. 4). What is needed is much more information about its stereochemistry. The problem has been the dearth

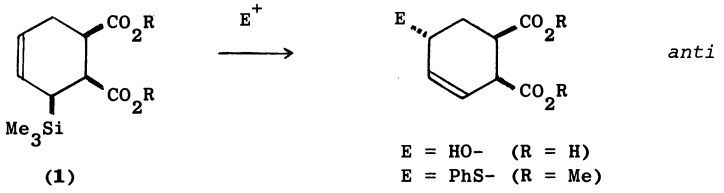
SCHEME 2



of stereochemically defined allylsilanes. Two that were known (**1** and **2**) were from our work, and we did look at the stereochemistry of their reactions. With the first of these (**1**), we observed (Ref. 5) two reactions which were stereoselectively *anti* (Scheme 3), and with the second (**2**) five reactions (Ref. 6) which were stereoselectively *syn* (Scheme 4). We felt at the time that the stereochemical constraints of the ring systems were likely to be the

dominant influence on the stereochemistry, and that these results said nothing about the preferred stereochemistry of the S_E2' reaction. Along with many other people, we guessed, by a rather crude analogy with the S_N2' reaction, that the S_E2' reaction would prefer to be *anti*. However, the only sign that this might indeed be the case came (Ref. 7) from three reactions

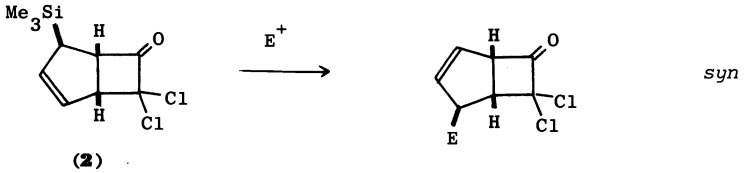
SCHEME 3



(1)

E = HO- (R = H)
E = PhS- (R = Me)

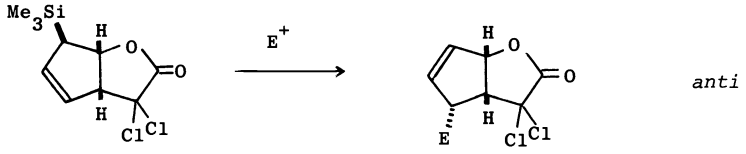
SCHEME 4



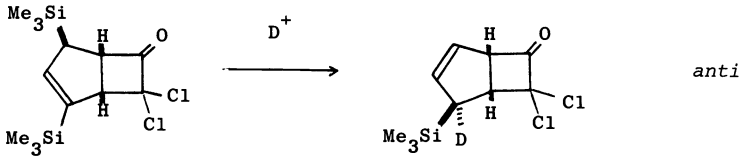
(2)

E = D-, Br-, PhS-, Ac-, and $MeOCH_2$-

SCHEME 5



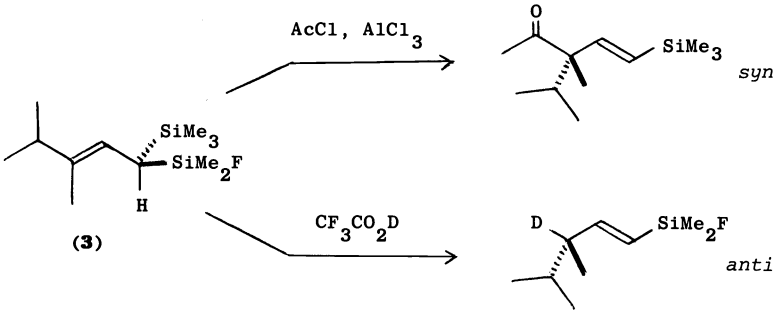
E = HO- and PhS-



(Scheme 5), in which the stereochemical preference of the ring system appeared to have been overridden by some other factor, perhaps the inherent *anti* S_E2' stereochemistry.

The first result (Ref. 8) in an open-chain allylsilane was the acylative desilylation of the optically active allylsilane (**3**)(Scheme 6). This was largely, and unexpectedly, *syn*. However, this result has proved to be an anomaly, for Wetter has now shown (Ref. 9) that the deuterodesilylation of the same allylsilane (Scheme 6) is mainly *anti*, and Eschenmoser (Ref. 10) has supported this with a less heavily substituted allylsilane (**4**)(Scheme 7). Furthermore,

SCHEME 6

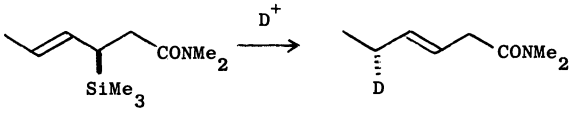


(3)

Kumada has shown (Ref. 11) that the optically active allylsilanes (**5**) react with a wide range of electrophiles with high *anti* selectivity, leading very largely to the *E*-alkenes (**6**) (Scheme 8). This result is consistent with a geometry (**7**), in which the hydrogen atom eclipses the double bond, and the *C*-silyl and *C*-phenyl bonds overlap with the π-system;

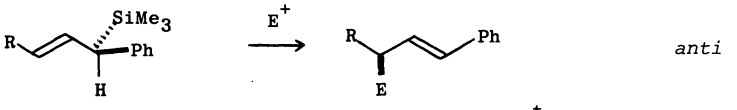
attack *anti* to the silyl group is then preferred for steric or for electronic reasons, or for both combined. Incidentally, Kumada has shown that when the electrophile is an aldehyde, the new chiral centre at the carbon atom derived from the carbonyl group is also stereocontrolled

SCHEME 7



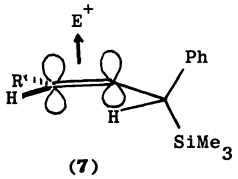
(4)

SCHEME 8



(5) R = Me or Ph

(6) E = D-, Bu^t-, Ac-, $HOCH_2$-, and HOCHR-



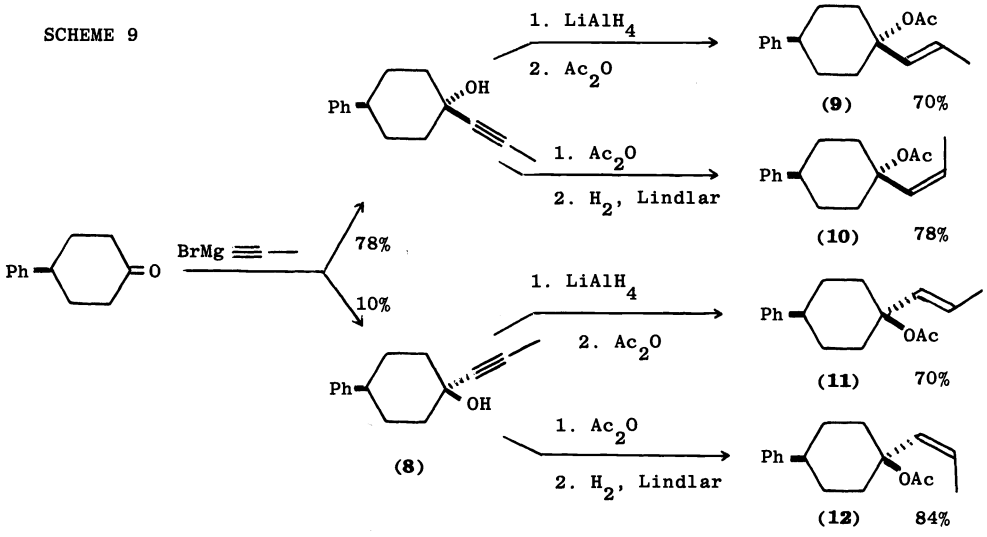
(7)

even when R in **5** is hydrogen. This striking result shows that chiral information can be passed not only three places but also four places along a carbon chain in an S_E2' reaction.

A NEW STEREOSPECIFIC ALLYLSILANE SYNTHESIS

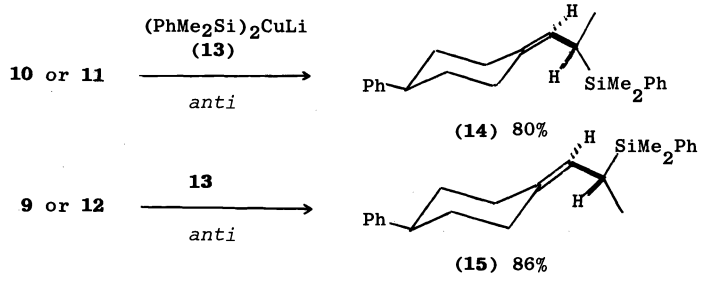
In our own work in this area (Ref. 12), we have continued to look not at enantioselectivity, as in Wetter's, Eschenmoser's and Kumada's work above, but at diastereoselectivity. In other words, we want to continue to set the stereochemistry of the S_E2' reaction against other stereochemical constraints, in order to find out how powerful this method of stereocontrol is. To do this, we need a stereocontrolled allylsilane synthesis, and this we now have. We already knew (Ref. 13) that tertiary allylic acetates reacted with our silyl-cuprate reagent

SCHEME 9

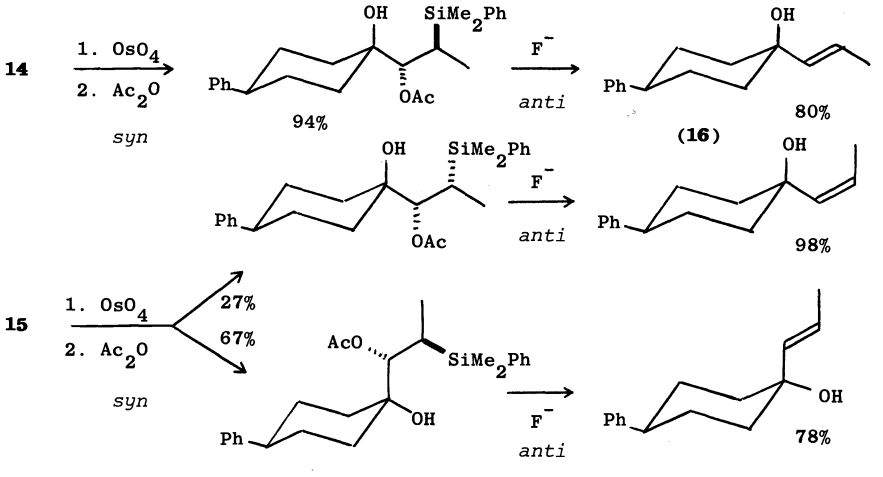


(13) to give allylsilanes. We have now made the stereochemically defined allylic acetates **(9-12)** by the routine methods shown in Scheme 9, and each of these reacts stereospecifically *anti* with the silyl cuprate reagent **(13)**(Scheme 10). As far as we could tell (^{13}C-NMR), there was no cross contamination in any of the four reactions of Scheme 10. The structures of the allylsilanes **(14** and **15)** were proved (Scheme 11) by osmylation, which we assume to be stereospecifically *syn*, acetylation, and desilylative elimination, which we assume to be stereospecifically *anti*. That the displacement of acetate by the silyl group turns out to be *anti* was no surprise, since alkyl-cuprates also react with this stereochemistry (Ref. 14). The allylic alcohols produced in Scheme 11 were, of course, easily recognisable; thus, the alcohol **(16)** was the intermediate we had already handled as the product from the reduction of the propargylic alcohol **(8)** in Scheme 9.

SCHEME 10



SCHEME 11



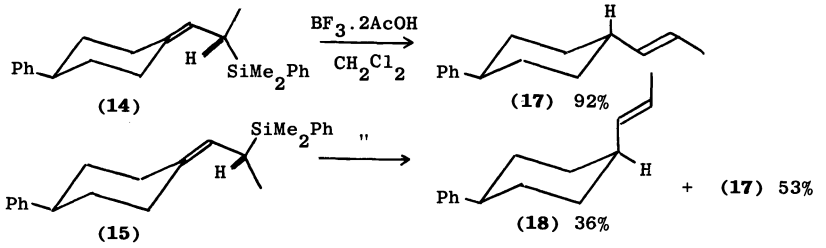
THE STEREOCHEMISTRY OF THE REACTIONS OF THE ALLYLSILANES (14 AND 15)

The two allylsilanes (**14** and **15**) set the *anti* selectivity of the allylsilane portion of the molecule against the axial or equatorial preference of the ring system. What we were interested in finding out was whether the two constraints worked for or against each other, and how their relative importance varied from electrophile to electrophile. So far, we have studied three representative electrophilic reagents: the proton (and deuteron), Lewis acid-acetyl chloride mixtures, and peracid.

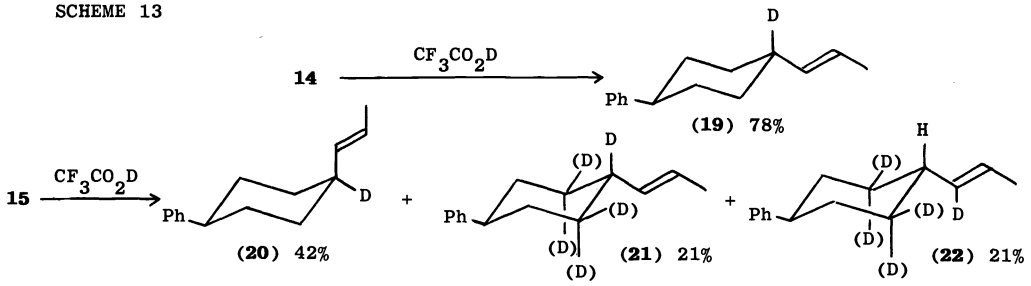
Protonation

Protodesilylation of the allylsilanes (**14** and **15**) gave the products shown in Scheme 12. Axial protonation of the allylsilane (**14**) cleanly gave the product (**17**), which is the result of an

SCHEME 12

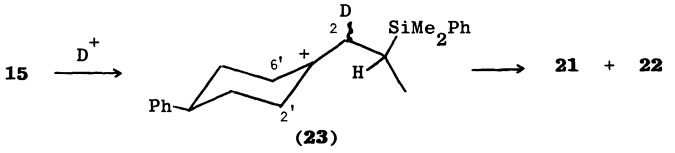


SCHEME 13



anti process. However, the other allylsilane (**15**), which ought to give only the equatorially protonated product (**18**), if a purely *anti* process were to take place, misbehaves. Deuterodesilylation (Scheme 13) reveals more about this reaction. The allylsilane (**14**) is again

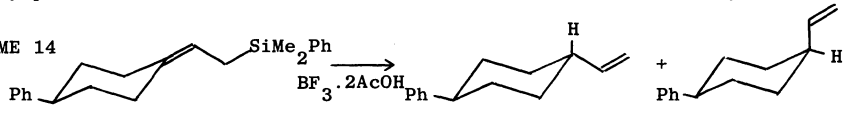
perfectly straightforward, within the limits of ^{2}H-NMR analysis, but the other allylsilane (**15**), while it gives the equatorially deuteronated product (**20**) in a straightforward S_E2' reaction, also gives an equal amount of the axially deuteronated and protonated products (**21** and **22**), each of which is a mixture of mono-, di-, tri-, tetra-, and penta-deuteroalkenes. The explanation is that *anti* and equatorial attack (**15** → **20**) is in competition with attack by the deuteron on the *central* carbon (C-2) of the allyl system, giving an intermediate cation (**23**).



(23)

This cation can reversibly lose protons from C-2' and C-6', and hence gain deuterons at these positions, and it can also undergo deuteride or hydride shift before loss of the silyl group, giving **21** and **22**, respectively. We have observed before (Ref. 15) this pattern of electrophilic attack on C-2, followed by a shift and loss of the silyl group, but not, as it happens, when the allylsilane was exocyclic to a six-membered ring. It seems likely that axial attack is preferred by protons (deuterons) and that therefore the *anti* selectivity in the allyl-

SCHEME 14



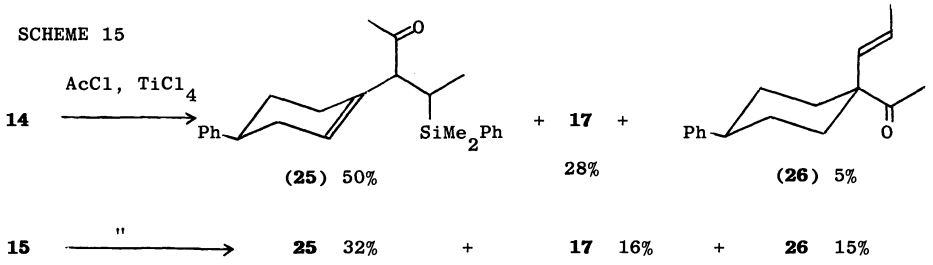
(24) 74% 15%

silane (**14**) is reinforced in the production of the equatorial alkenes (**17** and **19**). With the other allylsilane, the axial preference of the ring system and the *anti* selectivity of the allylsilane are in conflict, and the molecule finds an alternative reaction to the straightforward S_E2' pathway. This analysis is supported by the observation that the allylsilane (**24**), which has only the axial vs. equatorial constraint, is indeed attacked largely from the axial direction (Scheme 14).

Acetylation

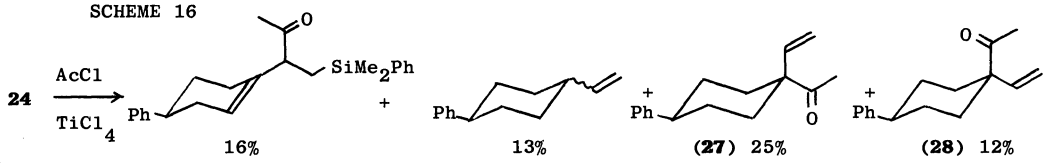
Acetylation is even more complicated (Scheme 15). The major product (50%) with the allylsilane (**14**) was a mixture of three diastereoisomers (**25**), in which the attack is clearly at C-2, and no 1,2-shift and no desilylation has taken place. Protodesilylation with *anti* sel-

SCHEME 15



ectivity (**14** → **17**) is another major pathway (28%), and the only S_E2' product (**26**) was very minor (5%), and the result of a *syn* reaction. The other allylsilane (**15**) gave a little more of this product (15%), presumably because it is now the result of the preferred *anti* pathway. Protodesilylation is somewhat less in evidence (16%), presumably because it is a *syn* reaction, and the major product (**25**)(32%) is remarkable only for being a single, crystalline diastereo-

SCHEME 16



16% 13% **(27)** 25% **(28)** 12%

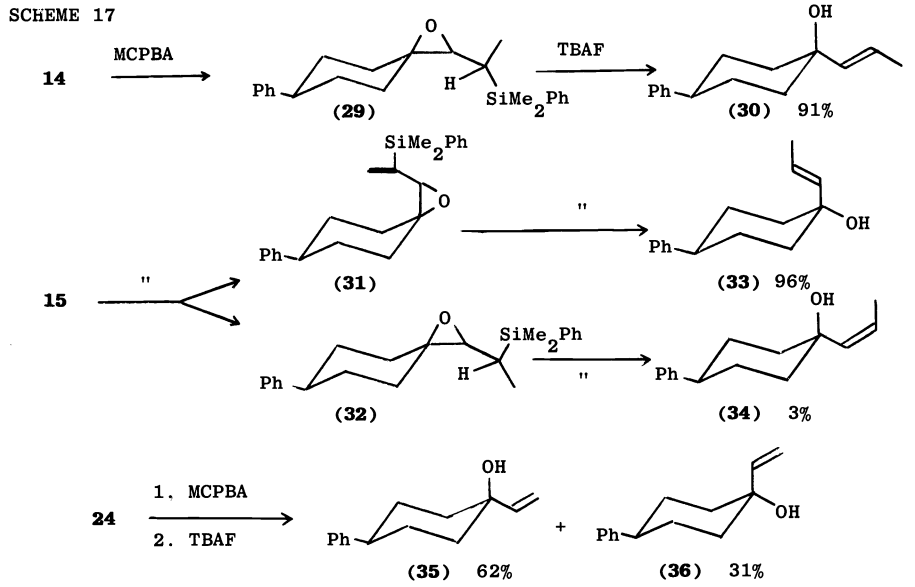
isomer of unknown relative configuration. This pattern implies that acylation prefers to take place from an equatorial direction, and again this is supported by the reaction of the allylsilane (**24**), which gives more equatorial ketone (**27**) than axial (**28**)(Scheme 16).

Epoxidation

In contrast, epoxidation is a very well-behaved reaction (Scheme 17). The allylsilane (**14**) gives only one epoxide (**29**), as far as we could tell, and fluoride-induced opening gave the allylic alcohol (**30**) in an overall yield of 91%, with none of the other alcohols detectable even though we had samples of each of the four possible isomers. The structure of this product (**30**) was readily identified, since it was identical with the alcohol (**16**) which we

had encountered twice before. The other allylsilane (**15**) gave a major and a minor epoxide (**31** and **32**), and fluoride-induced opening gave the alcohols (**33** and **34**), both of which were again readily recognisable. Thus the overall result is pure *anti* selectivity, with perhaps

SCHEME 17



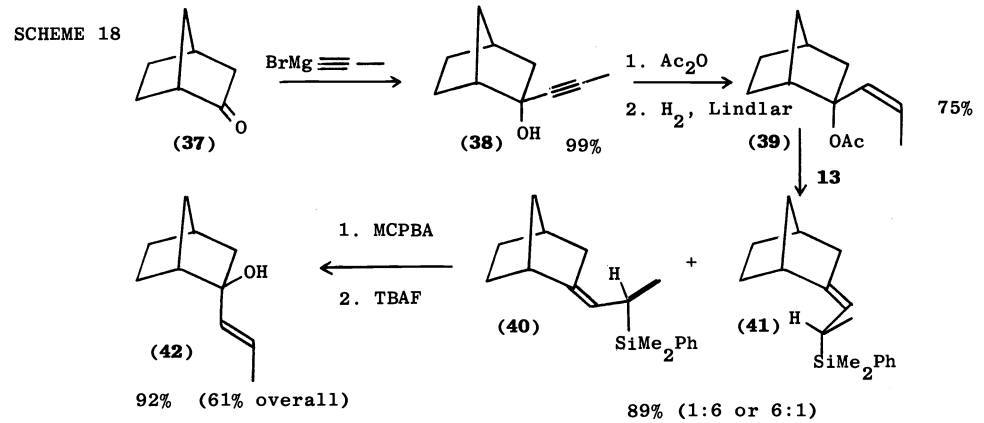
some evidence for a preference for axial attack. This is supported by the reaction of the allylsilane (**24**), which gives a little more axial alcohol (**35**) than equatorial (**36**).

We are tempted to summarise these results by saying that bridging electrophiles may prove to be very well-behaved stereochemically, in the sense that the stereochemistry of the allylsilane can be expected to exert a strong influence. Other electrophiles are less certain to work well, especially when they are large. What is clear is that allylsilanes can be used to control stereochemistry in favourable cases, and we now have a better picture of what limitations there may be. There is some promise that in suitable cases stereochemical control in the synthesis of quaternary centres in open-chain compounds will be possible.

A FIRST GLIMPSE AT AN APPLICATION OF STEREOCHEMICAL CONTROL USING STEREOCHEMICALLY DEFINED ALLYLSILANES

It is well known that norbornanone (**37**) is attacked from the *exo* direction, so that, for example, only the alcohol (**38**) is obtained even with the small propyne-anion nucleophile (Scheme 18). Acetylation and *syn* hydrogenation, followed by the *anti* displacement of the

SCHEME 18



acetate by our silyl-cuprate reagent (**13**) gave a mixture of allylsilanes (**40** and **41**). These differ in their geometry about the double bond, but *both* have now been set up so that the *anti* selectivity of the allylsilane group and the *exo* selectivity of the norbornane system reinforce one another. Epoxidation is clean, and the only product at the end of the sequence is the otherwise inaccessible *exo* alcohol (**42**).

REFERENCES

1. G. Stork and W. N. White, *J. Am. Chem. Soc.*, **75**, 4119 (1953).
2. G. Stork and A. F. Kreft, *J. Am. Chem. Soc.*, **99**, 3850 and 3851 (1977); R. M. Magid and O. S. Fruchey, *ibid.*, 8368; T. Oritani and K. H. Overton,*J. Chem. Soc., Chem. Commun.*, 454 (1978); and ref. 14.
3. See, for examples, R. E. Ireland and J. P. Daub, *J. Org. Chem.*, **46**, 480 (1981); Y. Hirano and C. Djerassi, *ibid.*, **47**, 2420 (1982); M. A. Gilhooly, D. S. Morris, and D. H. Williams, *J. Chem. Soc., Perkin Trans 1.*, 2111 (1982).
4. T. H. Chan and I. Fleming, *Synthesis*, 761 (1979).
5. M. J. Carter and I. Fleming, *J. Chem. Soc., Chem. Commun.*, 679 (1976) and M. J. Carter, I. Fleming, and A. Percival, *J. Chem. Soc., Perkin Trans. 1*, 2415 (1981).
6. B.-W. Au-Yeung and I. Fleming, *J. Chem. Soc., Chem. Commun.*, 79 (1977) and *Tetrahedron*, **37** Supplement 1, 13 (1981).
7. Ref. 6 and I. Fleming and R. V. Williams, *J. Chem. Soc., Perkin Trans. 1*, 684 (1981).
8. H. Wetter, P. Scherer and W. B. Schweizer, *Helv Chim Acta*, **62**, 1985 (1979).
9. H. Wetter and P. Scherer, *Helv. Chim. Acta*, **66**, 118 (1983).
10. V. Matassa, P. R. Jenkins, and A. Eschenmoser, personal communication.
11. T. Hayashi, M. Konishi, H. Ito, and M. Kumada, *J. Am. Chem. Soc.*, **104**, 4962 (1982); T. Hayashi, M. Konishi, and M. Kumada, *ibid.*, 4963; T. Hayashi, H. Ito, and M. Kumada, *Tetrahedron Lett.*, **23**, 4605 (1982); see also, T. Hayashi, M. Konishi, and M. Kumada, *J. Org. Chem.*, **48**, 281 (1983).
12. N. K. Terrett, unpublished results 1981-1983.
13. I. Fleming and D. Marchi, *Synthesis*, 560 (1981).
14. D. M. Magid, *Tetrahedron*, **36**, 1901 (1980).
15. I. Fleming, D. Marchi, and S. K. Patel, *J. Chem. Soc. Perkin Trans. 1*, 2518 (1981).

Print: 55/11-b