Protodesilylation of Allylsilanes for the Control of Double Bond Geometry Exocyclic to a Ring

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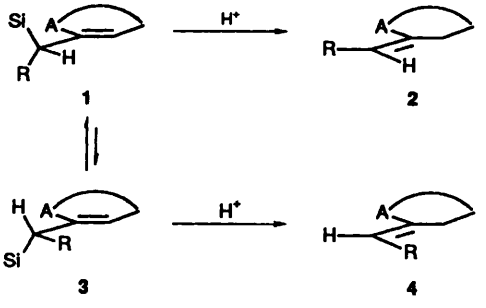
Protodesilylation of the allylsilanes **5** and **6** is selective for the formation of the exocyclic double bond isomers **7** and **8**, respectively, when the group R is isopropyl, but not when it is methyl.

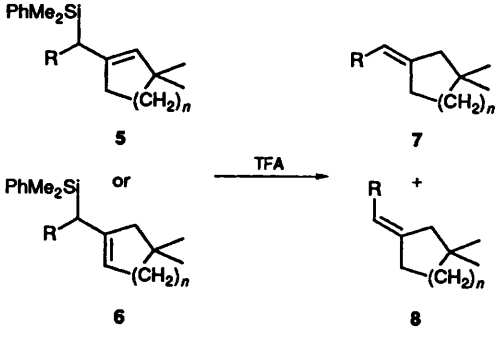
In the immediately preceding papers we have identified some of the factors that determine which side of a double bond will be attacked by an electrophile when the neighbouring atom carries a silyl group, a carbon group and a hydrogen atom. In the work described in this paper, we transfer our attention from the stereochemistry of attack on the double bond to the stereochemistry of the double bond produced in an electrophilic substitution reaction of the type **1**→**2**, choosing for simplicity an electrophile, the proton, that will not create stereochemistry at the atom it attacks. By analogy with the work described in the preceding papers,[1,2] and with other work both of ours and of others, referred to in our earlier papers, we can expect that the double bond geometry in the electrophilic substitution reaction **1**→**2** would show stereoselectivity in favour of the formation of the isomer with the double-bond geometry of **2** rather than **4**, because the starting material will adopt the conformation **1**, or something close to it, rather than the conformation **3**. However, we can only expect this to be true, given that the substituent on the double bond *cis* to the stereogenic centre is only a hydrogen atom, if the group R is larger than a methyl group. Our earlier work[2] and that of others[3] has established that, if R is a methyl group, the conformation close to **3** is likely to be significantly populated, and a double bond with the geometry of **4** will be produced to a substantial, but not necessarily predictable extent. As we have shown in the two papers immediately preceding this one, a larger R group than methyl seems to cause the conformation **3** to be less populated, and this should lead to a greater proportion of the reaction taking the pathway **1**→**2** rather than **3**→**4**. Also, we can expect control of double-bond geometry only when the substituent A is reasonably small. In most electrophilic substitution reactions of allylsilanes[4] where the geometry of the double bond in the product has been studied, this substituent is hydrogen, and the double bond is



mainly *trans*. As we have already found in protonation and alkylation reactions of enolates having larger groups in this position than a hydrogen atom or a methyl group, it appears that the conformation corresponding to **1** is no longer the most populated, and control of stereochemistry is at best uncertain and quite frequently lost.[1] Accordingly, for the present work, we restricted ourselves to having A as a methylene group, to keep it as small as possible. We also chose to study the formation of double bonds exocyclic to five- and six-membered rings, because this seemed to be an area where the knowledge we might gain could be put to use in synthesis. We reported our results in a preliminary communication,[5] and report them in full here.

Results and Discussion

As representative carbon groups R on the stereogenic centre in the twelve allylsilanes that we used, **5** and **6**, we chose methyl, phenyl and isopropyl. In order to differentiate the geometrical isomers of the products, **7** and **8**, we incorporated a gem dimethyl group in the ring for each substituent and for both ring sizes. In each case we carried out pairs of reactions, protodesilylating both the allylsilane **5** and its isomer **6**, to ensure that we would be detecting stereospecificity, even though the difference in energy of the two products in each pair would probably be negligible. If the protodesilylation takes place in conformation **1**, then the allylsilanes **5** will give the alkenes **7**, and the allylsilanes **6** will give the geometrically isomeric alkenes **8**.



We expected that a methyl group as the substituent R would not be large enough to allow control of the exocyclic double bond geometry, but that both the phenyl group and the isopropyl group might. Our results are presented in Table 1, where the pairs of experiments are the alternating odd- and even-numbered entries. It is clear that our expectations were met when R is a methyl group—the selectivity is negligible (entries 1–4). The selectivity is a little better, and in the expected sense, when R is a phenyl group (entries 5–8), but, somewhat to our surprise, it is not reliably at a level that can be considered synthetically interesting. Only with an isopropyl group on the stereogenic centre (entries 9–12) was the selectivity both substantial and reliable—with close to 90% of the reaction taking place in the sense **1**→**2** in all four permutations.

It was impractical, because of the volatility of some of the products, to measure yields in all of these reactions. The protodesilylation of allylsilanes is nearly always high-yielding, and ours are almost certainly no exception—the ^{1}H NMR

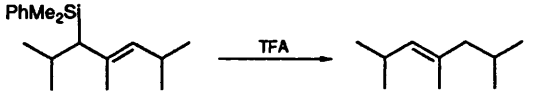
Table 1 Ratios of the geometrical isomers **7**:**8** from the protodesilylation of the allylsilanes **5** and **6**, using trifluoroacetic acid in deuteriochloroform at 0 °C for 10 min

Entry	Allylsilane	R	*n*	7:8	Method
1	**5aa**	Me	1	48:52	^{1}H NMR
2	**6aa**	Me	1	45:55	^{1}H NMR
3	**5ab**	Me	2	57:43	GC
4	**6ab**	Me	2	38:62	GC
5	**5ba**	Ph	1	57:43[a]	^{1}H NMR and GC
6	**6ba**	Ph	1	26:74[a]	^{1}H NMR and GC
7	**5bb**	Ph	2	69:31[a]	GC
8	**6bb**	Ph	2	38:62[a]	GC
9	**5ca**	Pr^i	1	90:10	^{1}H NMR
10	**6ca**	Pr^i	1	12:88	^{1}H NMR
11	**5cb**	Pr^i	2	91:9	GC
12	**6cb**	Pr^i	2	8:92	GC

[a] Reaction carried out at 25 °C.

spectra of our products were all very clean, and we also measured representative yields of 94 and 96% for the reactions of **6aa** and **6ba**, respectively, as measured using a non-volatile internal standard and integration of appropriate signals in the ^{1}H NMR spectra. There was no visible trend with respect to ring size, both giving very similar ratios. Protodesilylation at lower temperatures or with different acids had little effect. The only change worth mentioning was that the allylsilane **6ba** underwent protodesilylation at −78 °C in dichloromethane to give a ratio of 17:83, slightly better than the 26:74 recorded in Table 1 for the reaction at 25 °C. We assigned stereochemistry to the products by NOE experiments: each of the alkenes **7**, but none of the isomers **8**, showed enhancements in the singlet from the methylene group between the double bond and the gem dimethyl group when the sample was irradiated at the resonance frequency of the olefinic hydrogen. As a test that our results reflected complete kinetic control, we treated the 69:31 mixture of alkenes **7bb** and **8bb** with deuteriated trifluoroacetic acid for 100 min at room temperature, which is at least 10 times longer than the protodesilylation of the allylsilane **5bb** had originally taken. We found less than 1% of deuterium incorporation into the alkenes, which were unchanged in structure and still present in the same proportion. Even after 20 h with trifluoroacetic acid in refluxing chloroform, the ratio of the isomers **7bb** and **8bb** had fallen only slightly as two new alkenes, presumably the endocyclic isomers, not detectable in the protodesilylation reactions, began to appear.

Although restricted by the need to have a large group R on the stereogenic centre, the method for controlling the geometry of a double bond described in this paper is not restricted to exocyclic double bonds—the principle should work for trisubstituted double bonds in general. To confirm this, we carried out the protodesilylation of the allylsilane **9** and obtained in 92% yield



9 **10** 92% *E*:*Z* 94:6

largely the *E* alkene **10**, with an *E*:*Z* ratio of 94:6. This is certainly the result of kinetic control, since 8 h at reflux gave the *E* and *Z* alkenes in a ratio of 55:45. This reaction was important to us as a model reaction for one of the steps in our work on the synthesis of ebelactone-a.[6] We have also used the protodesilylation of an allylsilane to control the double bond geometry exocyclic to a 5-membered ring in our synthesis of a carbacyclin precursor.[7]

The synthesis of all the allylsilanes used in this work is described in the next paper in this series.[8]

Experimental

Protodesilylation of the Allylsilanes.—Typically, trifluoroacetic acid (0.1 mmol) was added to the allylsilane (0.01 mmol) in $CDCl_3$ at 0 °C and stirred for 10 min. The reaction was quenched with aqueous sodium hydrogen carbonate and extracted with deuteriochloroform. The organic layer was dried ($MgSO_4$) to give a mixture of the two exocyclic alkenes as a solution in deuteriochloroform, in better than 90% yield as judged by ^{1}H NMR spectroscopy, using 9,10-dihydroanthracene as an internal standard in the two cases quoted in the text. The following alkene mixtures were made by this method:

1-*Ethylidene*-3,3-*dimethylcyclopentane*. As a 48:52 mixture of *E* and *Z* isomers from **5aa** and as a 45:55 mixture from **6aa**; $\nu_{max}(CDCl_3)/cm^{-1}$ 1650 (C=C); $\delta(CDCl_3)$ *E* isomer **7aa**: 5.29–5.22 (1 H, m, HC=C), 2.26 (2 H, t, *J* 7, CH_2CHC=C), 2.04 (2 H, s, CH_2C=C), 1.56 (3 H, d, *J* 7, MeC=C), 1.47 (2 H, t, *J* 7, CH_2CH_2C=C) and 0.95 (6 H, s, Me_2); *Z* isomer **8aa**: 5.29–5.22 (1 H, m, HC=C), 2.33 (2 H, t, *J* 7, CH_2CH_2C=C), 2.00 (2 H, s, CH_2C=C), 1.55 (3 H, d, *J* 7, MeC=C), 1.43 (2 H, t, *J* 7, CH_2CH_2C=C) and 0.99 (6 H, s, Me_2); *m*/*z* 124 (100%, M^+) (Found: M^+, 124.1255. C_9H_{16} requires *M*, 124.1252).

1-*Benzylidene*-3,3-*dimethylcyclopentane*. As a 57:43 mixture of *E* and *Z* isomers from **5ba** and as a 26:74 mixture from **6ba**; R_f (hexane) 0.35; ν_{max}(film)/cm^{-1} 1640 (C=C), 1600 and 1500 (Ph); $\delta(CDCl_3)$ *E* isomer **7ba**: 7.40–7.11 (5 H, m, Ph), 6.30 (1 H, m, HC=C), 2.63 (2 H, t, *J* 7, CH_2CH_2C=C), 2.29 (2 H, s, CH_2C=C), 1.59 (2 H, t, *J* 7, CH_2CH_2C=C) and 1.02 (6 H, s, Me_2); *Z* isomer **8ba**: 7.40–7.11 (5 H, m, Ph), 6.32 (1 H, m, HC=C), 2.60 (2 H, t, *J* 7, CH_2CH_2C=C), 2.37 (2 H, s, CH_2C=C), 1.49 (2 H, t, *J* 7, CH_2CH_2C=C) and 1.03 (6 H, s, Me_2); *m*/*z* 186 (10%, M^+) and 135 (100%) (Found: M^+, 186.1397. $C_{14}H_{18}$ requires *M*, 186.1408).

1-(2-*Methylpropylidene*)-3,3-*dimethylcyclopentane*. As a 90:10 mixture of *E* and *Z* isomers from **5ca** and as a 12:88 mixture from **6ca**; no C=C peak detected in the IR region; $\delta(CDCl_3)$ *E* isomer **7ca**: 5.04 (1 H, m, HC=C), 2.45–2.22 (1 H, m, Me_2CH), 2.26 (2 H, t, *J* 7, CH_2CH_2C=C), 1.99 (2 H, s, CH_2C=C), 1.44 (2 H, t, *J* 7, CH_2CH_2C=C), 0.95 (6 H, s, Me_2), 0.91 (6 H, d, *J* 7, Me_2CH); *Z* isomer **8ca**: 5.03 (1 H, m, HC=C), 2.38–2.19 (1 H, m, Me_2CH), 2.29 (2 H, t, *J* 7, CH_2CH_2C=C), 1.99 (2 H, s, CH_2C=C), 1.39 (2 H, t, *J* 7, CH_2CH_2C=C), 0.98 (6 H, s, Me_2), 0.91 (6 H, d, *J* 7, Me_2CH); *m*/*z* 152 (77%, M^+) and 137 (100%, M − Me) (Found: M^+, 152.1560. $C_{11}H_{20}$ requires *M*, 152.1565).

1-*Ethylidene*-3,3-*dimethylcyclohexane*.[9] As a 57:43 mixture of *E* and *Z* isomers from **5ab** and as a 38:62 mixture from **6ab**; C=C peak not detected by IR spectroscopy; $\delta(CDCl_3)$ *E* isomer **7ab**: 5.09 (1 H, q, *J* 8, HC=C), 2.07 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 1.80 (2 H, s, CH_2C=C), 1.57 (3 H, d, *J* 8, MeC=C), 1.48 (2 H, quintet, *J* 6, $CH_2CH_2CH_2C$=C), 1.33 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 0.83 (6 H, s, Me_2); *Z* isomer **8ab**: 5.26 (1 H, q, *J* 8, HC=C), 1.98 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 1.89 (2 H, s, CH_2C=C), 1.55 (3 H, d, *J* 8, MeC=C), 1.48 (2 H, quintet, *J* 6, $CH_2CH_2CH_2C$=C), 1.33 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 0.87 (6 H, s, Me_2); *m*/*z* 138 (34%, M^+) and 110 (100%) (Found: M^+, 138.1399. $C_{10}H_{18}$ requires *M*, 138.1408).

1-*Benzylidene*-3,3-*dimethylcyclohexane*. As a 69:31 mixture of *E* and *Z* isomers from **5bb** and as a 38:62 mixture from **6bb**; R_f (hexane) 0.29; $\nu_{max}(CDCl_3)/cm^{-1}$ 1640 (C=C), 1600, 1580 and 1500 (Ph); $\delta(CDCl_3)$ *E* isomer **7bb**: 7.38–7.19 (5 H, m, Ph), 6.17 (1 H, s, HC=C), 2.30 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 2.01 (2 H, s, CH_2C=C), 1.62–1.49 (2 H, m, $CH_2CH_2CH_2C$–C), 1.38 (2 H, t, *J* 7, $CH_2CH_2CH_2C$=C) and 0.92 (6 H, s, Me_2); *Z* isomer **8bb**: 7.40–7.16 (5 H, m, Ph), 6.32 (1 H, s, HC=C), 2.18 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 2.11 (2 H, s, CH_2C=C), 1.65–1.49 (2 H, m, $CH_2CH_2CH_2C$=C), 1.38 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C) and 0.86 (6 H, s, Me_2); *m*/*z* 200 (75%, M^+) and 123 (100%) (Found: M^+, 200.1560. $C_{15}H_{20}$ requires *M*, 200.1565).

1-(2-*Methylpropylidene*)-3,3-*dimethylcyclohexane*. As a 91:9 mixture of *E* and *Z* isomers from **5cb** and as an 8:92 mixture from **6cb**; $\nu_{max}(CDCl_3)/cm^{-1}$ 1650 (C=C); $\delta(CDCl_3)$ *E* isomer **7cb**: 4.87 (1 H, d, *J* 9, HC=C), 2.55 (1 H, d septet, *J* 9 and 7, Me_2CH), 2.04 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 1.78 (2 H, s, CH_2C=C), 1.48 (2 H, quintet, *J* 6, $CH_2CH_2CH_2C$=C), 1.31 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 0.92 (6 H, d, *J* 7, Me_2CH) and 0.84 (6 H, s, Me_2); *Z* isomer **8cb**: 4.96 (1 H, d, *J* 9, HC=C), 2.54 (1 H, d, septet, *J* 9 and 7, Me_2CH), 1.96 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 1.90 (2 H, s, CH_2C=C), 1.50 (2 H, quintet, *J* 6, $CH_2CH_2CH_2C$=C), 1.33 (2 H, t, *J* 6, $CH_2CH_2CH_2C$=C), 0.90 (6 H, d, *J* 7, Me_2CH) and 0.87 (6 H, s, Me_2); *m/z* 166 (45%, M^+) and 123 (100%, $M - Pr^i$) (Found: M^+, 166.1712. $C_{12}H_{22}$ requires *M*, 166.1722).

2,4,6-*Trimethylhept*-3-*ene*. As a 94:6 mixture of *E* and *Z* isomers from **9**; $\nu_{max}(CDCl_3)/cm^{-1}$ 1640 (C=C); $\delta(CDCl_3)$ *E* isomer **10**: 4.91 (1 H, dq, *J* 9 and 1, HC=C), 2.48 (1 H, d septet, *J* 9 and 7, Me_2CHC=C), 1.81–1.70 (1 H, m, Me_2CH), 1.78 (2 H, d, *J* 7, CH_2C=C), 1.55 (3 H, d, *J* 1, MeC=C), 0.92 (6 H, *J* 7, Me_2CH) and 0.82 (6 H, d, *J* 7, Me_2CH); *Z* isomer: 4.97 (1 H, dq, *J* 9 and 1, HC=C), 2.50 (1 H, d septet, *J* 9 and 7, Me_2CHC=C), 1.89 (2 H, d, *J* 7, CH_2C=C), 1.80–1.64 (1 H, m, Me_2CH), 1.61 (3 H, d, *J* 1, MeC=C), 0.89 (6 H, d, *J* 7, Me_2CH) and 0.85 (6 H, d, *J* 7, Me_2CH); *m/z* 140 (12%, M^+) and 84 (100%, $M - CH_2CMe_2$) (Found: M^+, 140.1564. $C_{10}H_{20}$ requires *M*, 140.1564).

Isomerisation of Alkenes.—Trifluoroacetic acid or deuteriotrifluoroacetic acid (0.01 mmol) was added to the alkene (0.002 mmol) in deuteriochloroform, and the mixture refluxed for various lengths of time. The product was analysed by GC (on a Carlo Erba 4130 instrument using a 5% polyphenylmethylsiloxane column) and ^1H NMR spectroscopy without purification.

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