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

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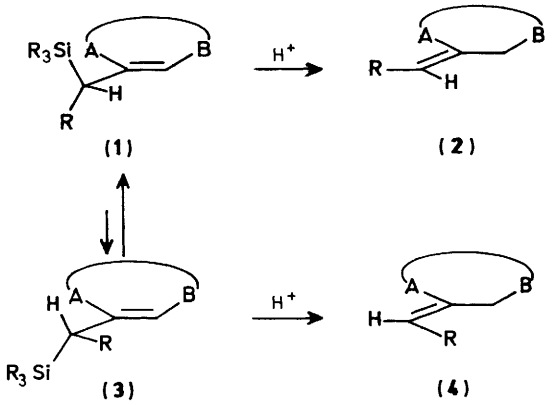
Protodesilylation of the allylsilanes (**5**) and (**6**) is selective for the formation of the geometrical isomers (**7**) and (**8**), respectively, when the group R is isopropyl, but not when it is methyl.

By analogy with our earlier work,[1] and that of others,[2] on the protodesilylation of open-chain allylsilanes, we considered that the reaction (**1**)→(**2**) might show some stereoselection in the geometry of the exocyclic double bond in favour of the isomer (**2**), on the grounds that when the group A is small, the



conformation (**1**), or something close to it, might be more populated than the alternative (**3**) that leads to the isomer (**4**). Open-chain allylsilanes are usually selective in this sense when the group A is a hydrogen atom, giving a *trans* double bond on protodesilylation,[1,2] but clearly a larger group A makes the stereochemical outcome much less predictable. We now report that the geometry of the exocyclic double bond is well controlled when the group R is isopropyl, but selectivity is lower when R is phenyl and very low or absent when R is methyl.

We have kept the group A as small as possible, using an unsubstituted methylene group throughout, and using both five- and six-membered rings ($n = 1$ or 2). In order to differentiate the geometrical isomers of the products (**7**) and (**8**), we incorporated a gem dimethyl group in the ring, and for each substituent and ring size, we carried out pairs of reactions, using each of the allylsilanes (**5**) and (**6**) that might be selective for the geometrical isomers (**7**) and (**8**), respectively. Our best results are summarised in the Table.

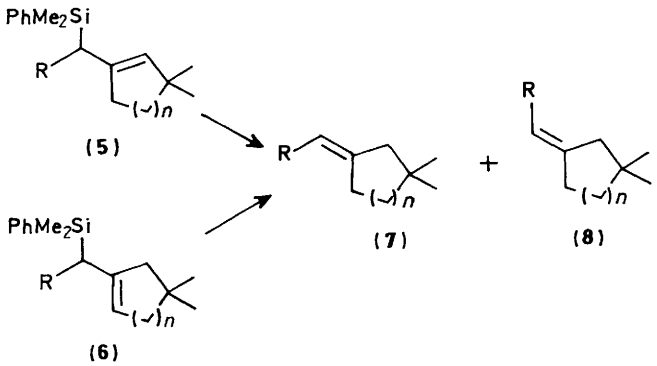
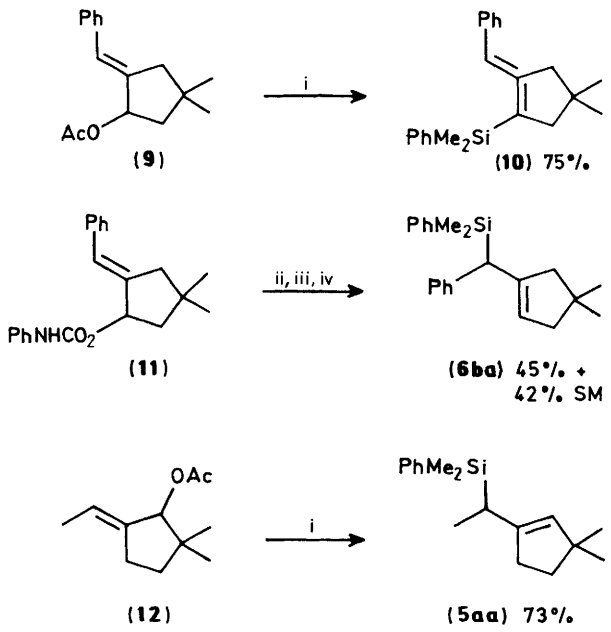


Table. Ratios of the geometrical isomers (**7**):(**8**) from the protodesilylation of the allylsilanes (**5**) and (**6**)

Allylsilane	R	*n*	Conditions	(**7**):(**8**)	Method
(**5aa**)	Me	1	0 °C, 10 min, $CDCl_3$	48:52	N.m.r.
(**6aa**)	Me	1	0 °C, 10 min, $CDCl_3$	45:55	N.m.r.
(**5ab**)	Me	2	0 °C, 10 min, $CDCl_3$	57:43	G.c.
(**6ab**)	Me	2	0 °C, 10 min, $CDCl_3$	38:62	G.c.
(**5ba**)	Ph	1	25 °C, 10 min, $CDCl_3$	57:43	N.m.r. & g.c.
(**6ba**)	Ph	1	−78 °C, 24 h, CD_2Cl_2	17:83	N.m.r. & g.c.
(**5bb**)	Ph	2	25 °C, 10 min, $CDCl_3$	69:31	G.c.
(**6bb**)	Ph	2	25 °C, 10 min, $CDCl_3$	38:62	G.c.
(**5ca**)	Pr^i	1	0 °C, 10 min, $CDCl_3$	90:10	N.m.r.
(**6ca**)	Pr^i	1	0 °C, 10 min, $CDCl_3$	12:88	N.m.r.
(**5cb**)	Pr^i	2	0 °C, 10 min, $CDCl_3$	91:9	G.c.
(**6cb**)	Pr^i	2	0 °C, 10 min, $CDCl_3$	8:92	G.c.

It is clear that when R is isopropyl, the regioisomeric allylsilanes (**5c**) and (**6c**) are highly selective (10:1) for the formation of the products (**7c**) and (**8c**), respectively. There is no consistent trend with respect to ring size, both ring sizes giving very similar results. The low selectivity in the reactions when R is methyl is not surprising in view of several observations[3,4] with open-chain allylsilanes having this group on the chiral centre and a hydrogen atom on the double bond *cis* to the chiral centre. In this situation, the conformation (**3**), with the R group more or less eclipsing the double bond, is not significantly higher in energy than the conformation (**1**), with the hydrogen eclipsing the double bond. When the R group is larger, as with the isopropyl group, there appears to be a clear preference for reaction from conformation (**1**), or something close to it, which mirrors our earlier observation[4] that large groups R on the chiral centre are generally more effective than methyl groups in making allylsilane reactions stereochemically well behaved.

It was impractical, because of the volatility of some of the products, to measure yields in all of these reactions, but they were very clean, as judged by ^1H n.m.r. spectroscopy. As a check, we measured representative yields of 94 and 96% for the reactions of (**6aa**) and (**6ba**), respectively. Protodesilylation at lower temperatures or with different acids rarely gave better stereoselectivity, except for the reaction of (**6ba**), which gave a somewhat worse ratio (26:74) when the reaction was carried out at 25 °C. We assigned the geometry of the double bonds in (**7**) and (**8**) by n.O.e. experiments: all of the isomers (**7**), but none of the isomers (**8**), showed enhancement in the methylene singlet adjacent to the double bond when the sample was irradiated at the resonance frequency of the olefinic hydrogen. As a test that our results reflect kinetic control, we subjected the alkene (**7bb**) to treatment with deuteriated trifluoroacetic acid for 100 min at room temperature, which is at least 10 times longer than the reaction had originally taken at this temperature, and found less than 1% of deuterium incorporation into the alkene. Even after 20 h in refluxing trifluoroacetic acid in deuteriochloroform, the

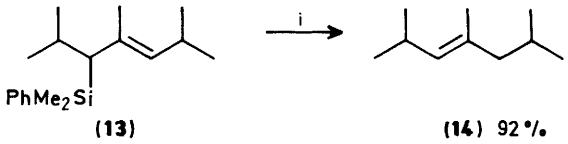


Reagents: i, $(PhMe_2Si)_2CuLi \cdot LiCN$, Ph_3P, THF, pentane; ii, BuLi, THF; iii, CuI, Ph_3P; iv, $PhMe_2SiLi$

interconversion of the isomers (**7bb**) and (**8bb**) was still incomplete.

The allylsilanes (**5**) and (**6**) were made by routes adapted from our allylsilane syntheses using allyl acetates and urethanes.[5] Somewhat surprisingly, the relatively unhindered acetates, like (**9**), were selective for the formation of the unwanted allylsilanes, like (**10**), with an exocyclic double bond. As we have already found in the open-chain series, the corresponding urethane (**11**) was very selective for the formation of the allylsilane with allylic shift, as in the reaction (**11**)→(**6ba**). The sterically hindered allyl acetates, like (**12**), where the acetoxy group is flanked by a gem dimethyl group, were reasonably regioselective for the formation of the allylsilanes (**5**) that have the silyl group on the side chain, which was fortunate, since the corresponding alcohols were too slow to form urethanes. The allylic alcohols were readily available from the corresponding ketones by reduction with sodium borohydride in the presence of cerium(III) chloride.[6]

The principle of our work is not unique to the formation of double bonds exocyclic to rings: it applies equally to open-chain allylsilanes in the construction of mid-chain double bonds, as illustrated by the conversion of the allylsilane (**13**) into the



Reagent: i, TFA, $CDCl_3$

alkene (**14**) (*E*:*Z* 94:6), after 10 min at 0 °C. This is certainly the result of kinetic control, since 8 h under reflux gave the *E* and *Z* alkenes in a ratio of 55:45.

Acknowledgements

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