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# Some Byproducts in the $S_E2'$ Reactions of an Allenylsilane with Aldehydes

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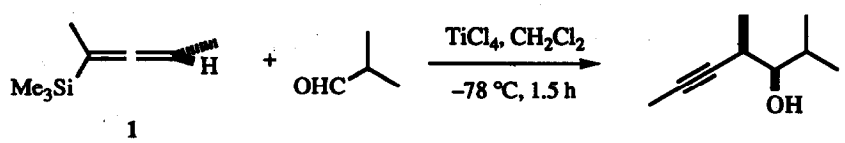
***Abstract*** **The reaction between the allenylsilane 1 and isobutyraldehyde 2 gives a minor byproduct 7, and the reaction between the allenylsilane 1 and the aldehyde 14 gives a succession of products 16, 18, and 19 arising from the phenyl group attacking the aldehyde intramolecularly faster than the allenylsilane can attack it.**

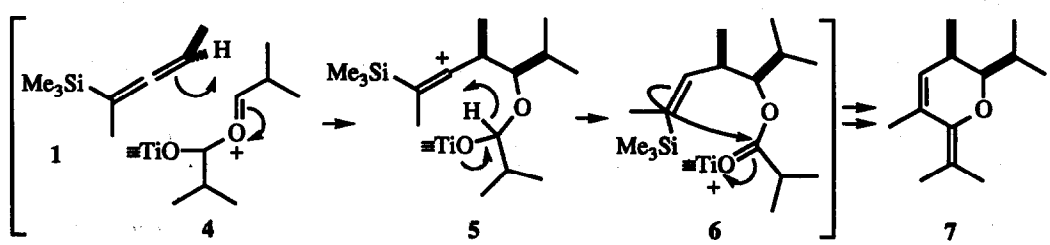
In the preceding paper,[1] we established that the reaction of the homochiral allenylsilane **1** and isobutyraldehyde **2** takes place with a high level of diastereo- and enantiocontrol to give very largely a single product **3**. We had chosen to study this reaction with care because it was a highly simplified model for a key step, **1** + **8** →




**1** **2** **3** 89%

**9**, that we planned to use in our synthesis of ebelactone-a.[2] In this paper we report some more observations on this type of reaction, and reveal that our well-laid plans will not work exactly as we had hoped to use them, because an alternative reaction takes place instead.

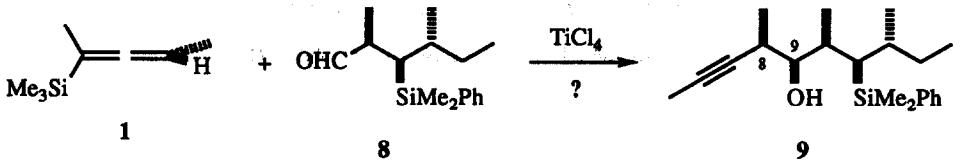
In the first place, even though the reaction **1** + **2** → **3** is high yielding and stereochemically very well behaved, there is a byproduct, usually detectable in up to 20% yield. This was an unstable compound, to which we assign the structure **7**, based on its $^1H$ and $^{13}C$ NMR spectra.[3] We suggest that it is formed by the pathway illustrated. The attack of the allenylsilane **1** sometimes takes place on the "dimer" **4** of the aldehyde to give the cation **5**, which suffers intramolecular hydride transfer, with the hydrogen atom attacking *anti* to the silyl group,




to give the vinylsilane **6**. The vinylsilane can then be attacked intramolecularly by the ester group, inducing an electrophilic substitution reaction **6** → **7** on the vinylsilane, with the usual retention of configuration, together with a dehydration step.[4] We have not been able to synthesise this product regularly nor in high yield. Nor have we been able to see any pattern in our results that might have allowed us to increase the yield, although one might expect that excess of aldehyde would increase the proportion of this product, since its formation is presumably second-order in aldehyde, while the regular reaction is presumably first-order.[5] The only consequence of our

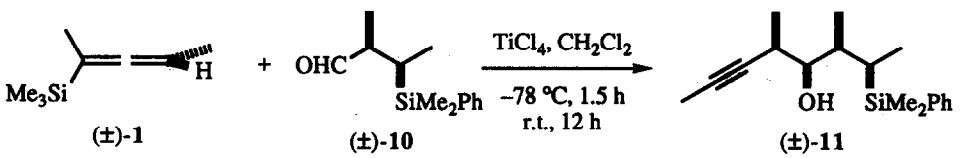
using an excess of aldehyde, and treating it with titanium tetrachloride before adding the allenylsilane, was the formation of the well known trimer of the aldehyde.[6] However, if we used the trimer in place of the aldehyde, the alcohol **3** was produced as usual, but there was no formation of the byproduct **7**.

While interesting, this reaction is hardly a serious obstacle to our plan, in which we expected to prepare both the allenylsilane **1** and the aldehyde **8** enantiomerically pure, and to combine them in a reaction that we confidently expected would give largely the alcohol **9**. At worst a side reaction of the kind discussed above




**1** **8** **9**

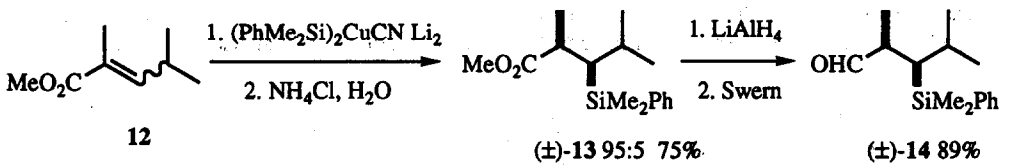
would only reduce the yield somewhat. The silyl group in the aldehyde **8**, is a masked hydroxy group,[7] and cannot participate in chelation. In consequence, the stereochemistry at the centre C-9 (ebelactone numbering) should be controlled simultaneously by Cram's rule and by the preference the allenylsilane-aldehyde reaction has for creating the *syn* relationship between the substituents on C-8 and C-9. In other words, the two components are matched, and we can expect a high degree of chiral recognition between the two partners. We have already




(±)-**1** (±)-**10** (±)-**11**

reported in a published lecture, that this expectation is met, at least in a simple model—the *racemic* allenylsilane **1** and the *racemic* aldehyde **10** combine to give largely one diastereoisomer[8] of the racemic alcohol **11**.[2]

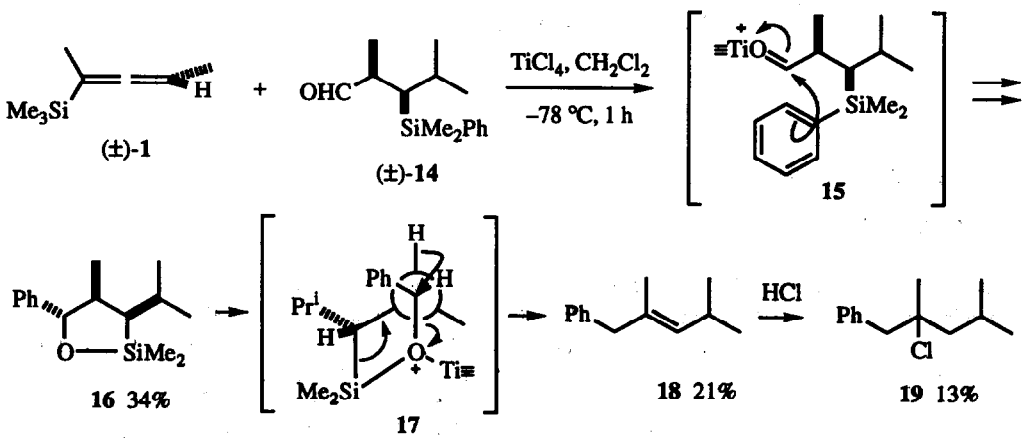
With this model reaction satisfyingly in hand, we turned to the next most complicated model—the combination of the racemic allenylsilane **1** and the racemic aldehyde **14**. The only change was to replace a methyl group in the aldehyde **10** with an isopropyl group, which was now a closer model for the secondary butyl group of the aldehyde **8**. We prepared the aldehyde **14** from the known ester **13**.[9] In the event, the reaction of the



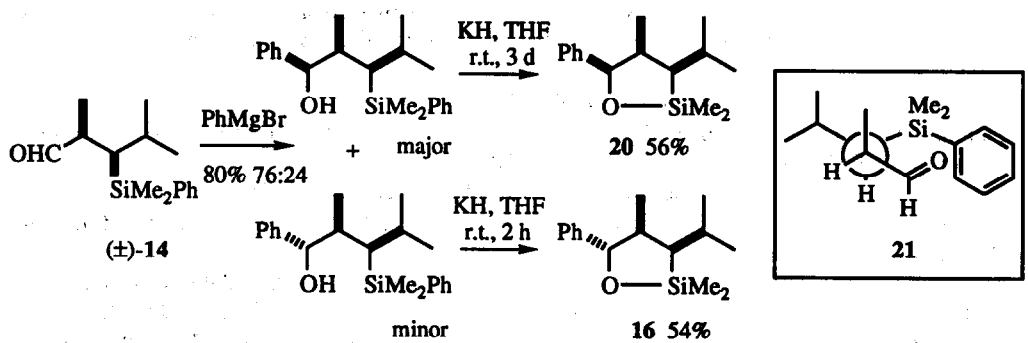

**12** (±)-**13** 95:5 75% (±)-**14** 89%

allenylsilane **1** with the aldehyde **14** gave no trace of any product analogous to the alcohol **11**. Instead it gave three identifiable products: the silyl ether **16**,[10] the alkene **18**,[11] and the tertiary chloride **19**,[12] with none of them derived from the allenylsilane. These were produced in not easily reproducible amounts, and the yields quoted are simply those of one not untypical run. We believe that these are formed in succession: the aldehyde group attacks the phenyl ring of the phenyldimethylsilyl group **15** (arrows), which suffers an electrophilic substitution reaction. We have seen this type of reaction before with a ketone, but on that occasion there was no external nucleophile to compete.[7] The benzylic oxygen function can then leave to give a cation that suffers a 1,2-hydride shift, assisted by the silyl group **17** (arrows). The cation then loses the silyl group to give the *E* alkene **18**, and addition of hydrochloric acid to this alkene gives the chloride **19**. In our work on silicon-controlled

cationic rearrangements,[13] we found that hydride normally migrates in competition with a methyl group, as here, but in the present case, this may be helped by the stereochemistry that we believe these intermediates possess. If there is any element of concertedness, the silyl ether can easily adopt a conformation **17** with the migrating hydride *anti* to the leaving group and the silyl group *anti* to the hydride.




When we added phenylmagnesium bromide to the aldehyde **14**, we obtained two alcohols. We displaced the phenyl group intramolecularly from each of these alcohols, and obtained a new silyl ether **20** from the major product and the silyl ether **16** from the minor. If the Grignard attack on the aldehyde follows Cram's rule, it will give the stereochemistry of **20**, from which we deduce that the stereochemistry of our intermediate **16** is the

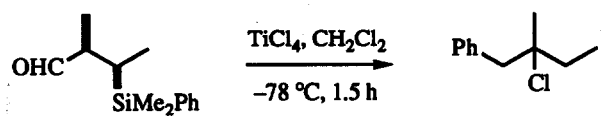



opposite. This is reasonable, in conformation **21**, set up for the intramolecular phenyl transfer, the carbonyl group is oriented so as to eclipse or partly eclipse the medium-sized group, as in the usual Felkin-Anh transition structure,[14] the phenyl group will be delivered on the side of the large group, perforce since it is intramolecular.

We tried several variants in an attempt to avoid the intramolecular reaction with the aldehyde **14**, but to no avail. It is obvious that we must change our plans, and convert the silyl group into a hydroxy before the reaction with the allenylsilane, and avoid chelation some other way. The presence of the phenyl group, or something like it, is necessary for the silyl-to-hydroxy conversion. It is unfortunate that it interferes in this way to make the phenyldimethylsilyl group less inoffensive than we had hoped.

We repeated the reaction with our earlier model **10**, and got closely similar results to those reported before. If we left the allenylsilane out of the mixture, however, the aldehyde **10** also underwent the same type of reaction

that we saw above, giving the chloride **22**. We had evidently been lucky in our earlier work to have got the reaction that we wanted, **1** + **10** → **11**, to work at all.




(±)-**10** **22**

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1 Buckle, M. J. C.; Fleming, I. *Tetrahedron Lett.* **1993**, *34*, preceding paper.

2 Fleming, I. *Pure Appl. Chem.* **1990**, *62*, 1879-1886, reporting work by Anne C. Ware.

3 **7**: $\delta_H$(400 MHz; $CDCl_3$) 5.64 (1 H, br s, CHMeC*H*=CMe), 3.76 (1 H, dd, *J* 7.2 and 10.4, Pr$^i$C*H*O), 2.84 (1 H, br quintet, *J* 6.8, MeC*H*CH=CMe), 1.98 (1 H, dseptet, *J* 10.4 and 6.5, $Me_2CH$), 1.79 (3 H, d, *J* 0.5, CH=C*Me*), 1.74 (3 H, br s, *Me*$_A$Me$_B$C=C), 1.70 (3 H, br s, Me$_A$*Me*$_B$C=C), 1.06 (3 H, d, *J* 6.5, Pr$^i$CHCH*Me*), 0.91 (3 H, d, *J* 6.6, CH*Me*$_A$Me$_B$) and 0.89 (3 H, d, *J* 6.7, CHMe$_A$*Me*$_B$); $\delta_C$(100 MHz; $CDCl_3$) 150.1, 129.8, 117.3, 115.4, 89.7, 40.5, 27.7, 27.0, 20.2, 19.5, 19.4, 12.8 and 12.4. We have no evidence on the relative stereochemistry of **7**. The coupling constants are not definitive, nor are they in agreement with estimates made from Macromodel 3.5a. We assume that the same constraints that led to the *syn* relationship in the major product **3** are still in effect when the allenylsilane attacks the "dimer" **4** as when it attacks the Lewis acid-complexed monomer.

4 Fleming, I.; Dunoguès, J.; Smithers, R. *Org. React. (N.Y.)* **1989**, *37*, 57-575.

5 Although it is tempting to consider the possibility that the 2:1 complex of aldehyde and $TiCl_4$, easily detected by NMR spectroscopy (Denmark, S. E.; Almstead, N. G. *Tetrahedron* **1992**, *48*, 5565-5578), might be the "dimer" **4**.

6 Astle, M. J.; Pinns, M. L. *J. Org. Chem.* **1959**, *24*, 56-60.

7 Fleming, I.; Henning, R.; Plaut, H. *J. Chem. Soc., Chem. Commun.* **1984**, 29-31; Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28*, 4229-4232.

8 Three diastereoisomers were detected in a ratio of 73:18:9 in a total yield of 50%.

9 Crump, R. A. N. C.; Fleming, I.; Hill, J. H. M.; Parker, D.; Reddy, N. L.; Waterson, D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3277.

10 **16**: $\delta_H$(250 MHz; $CDCl_3$) 7.36-7.18 (5 H, m, Ph), 5.00 (1 H, s, PhC*H*), 2.43 (1 H, quintet, *J* 7.0, C*H*MeCHO), 1.78 (1 H, d septet, *J* 11.4 and 6.5, C*H*Me$_2$), 1.21 (3 H, d, *J* 7.2, CH*Me*CHO), 0.85 (6 H, t, *J* 6.8, CH*Me*$_2$), 0.76 (1 H, dd, *J* 6.6 and 11.3, CHSi), 0.33 (3 H, s, Si*Me*$_A$Me$_B$) and 0.32 (3 H, s, SiMe$_A$*Me*$_B$).

11 **18**: $\delta_H$(250 MHz; $CDCl_3$) 7.31-7.24 (5 H, m, Ph), 5.10 (1 H, dq, *J* 9.1 and 1.3, CMe=C*H*), 3.24 (2 H, br s, PhC*H*$_2$), 2.51 (1 H, dseptet, *J* 9.1 and 6.6, $Me_2CH$), 1.52 (3 H, d, *J* 1.4, CH=C*Me*) and 0.96 (6 H, d, *J* 6.6, *Me*$_2$CH).

12 **19**: $\delta_H$(250 MHz; $CDCl_3$) 7.30-7.20 (5 H, m, Ph), 3.12 (1 H, d, *J* 13.7, PhC*H*$_A$H$_B$), 3.00 (1 H, d, *J* 13.7, PhCH$_A$*H*$_B$), 2.01-1.92 (1 H, m, C*H*Me$_2$), 1.76 (1 H, dd, *J* 5.0 and 14.6, Me$_2$CHC*H*$_A$H$_B$), 1.66 (1 H, dd, *J* 5.4 and 14.6, Me$_2$CHCH$_A$*H*$_B$), 1.48 (3 H, s, *Me*CCl), 1.01 (3 H, d, *J* 6.4, CH*Me*$_A$Me$_B$) and 0.99 (3 H, d, *J* 6.4, CHMe$_A$*Me*$_B$).

13 Fleming, I.; Patel, S. K.; Urch, C. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 115-124.

14 Chérest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199-2204; Anh, N. T.; Eisenstein, O. *Nouv. J. Chem.* **1977**, *1*, 61-70.


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