Diastereoselective Aldol Reactions of β-Silylenolates: A New Regiocontrolled Synthesis of Allylsilanes†

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Allylsilanes are prepared stereospecifically *trans* (**10**) or *cis* (**12**) and with complete regiocontrol by decarboxylative elimination of the β-hydroxy acids (**9**).

Because allylsilanes are very stable with respect to 1,3 allylic transposition, they react with electrophiles reliably with allylic shift.[1] For this reason, we have developed several regiocontrolled syntheses of allylsilanes, including methods for placing the silyl group at the less substituted end[2] and at the more substituted end[3] of the allyl system. More recently, we have developed a method for placing the silyl group at either end of unsymmetrical allyl systems which are secondary at both ends.[4] We now report another method for the synthesis of the latter group of allylsilanes, which, unlike our earlier method,[4] allows us to make allylsilanes with *cis* as well as with *trans* double bonds.

The method is based on our discovery that β-silylenolates (**1**) and (**7**) react with aldehydes in an aldol reaction, in which

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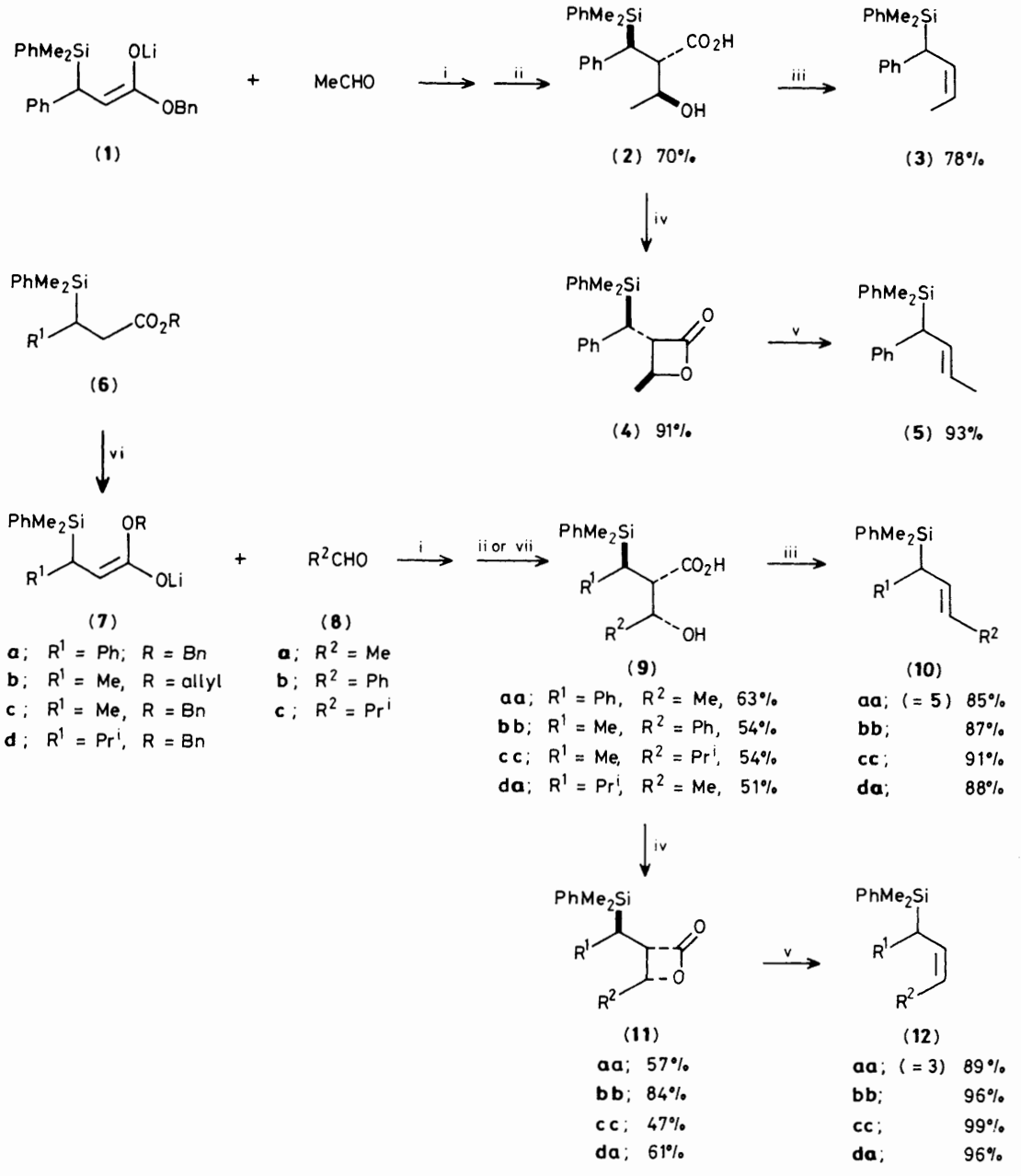

Scheme 1. Bn = benzyl. *Reagents:* i, tetrahydrofuran (THF), −78 °C, 1 h; ii, H_2, Pd; iii, $Me_2NCH(OMe)_2$, $CHCl_3$, reflux, 5 h; iv, $PhSO_2Cl$, pyridine, 0 °C, 12 h; v, collidine, reflux 5 h; vi, Pr^i_2NLi, THF, −78 °C; vii, (R^2 = Ph) $(PhMe_2Si)_2CuLi$.

the relative configuration of all three chiral centres is highly controlled in one step.[5] Thus the (*E*)-enolate (**1**), prepared by conjugate addition of our silyl-cuprate reagent to benzyl cinnamate, reacts with acetaldehyde to give the benzyl ester corresponding to the acid (**2**), into which it is converted by hydrogenolysis. The selectivity is high (90 : 10) with respect to the aldol geometry, with no other isomer detectable by ^1H n.m.r. spectroscopy. The acid (**2**) can be induced to undergo decarboxylative elimination using dimethylformamide dimethyl acetal in refluxing chloroform for 5 h, in an *anti* stereospecific reaction giving the *cis*-allylsilane (**3**) in 78% yield. The same acid can also be induced to undergo a *syn* decarboxylative elimination by refluxing the β-lactone (**4**) in collidine for 5 h, giving the *trans*-allylsilane (**5**) in 85% overall yield. In both cases, the products are free of each other within the limits of detectability (^1H n.m.r.), and they are, of course, free of their regioisomers. The stereospecific decarboxylative elimination reactions are based on the work of Nozaki, Mulzer, and Adam and their co-workers, who developed the methods and showed the stereospecificity of the reactions.[6,7]

We also prepared the corresponding (*Z*)-enolate (**7a**) from the ester (**6a**), using lithium di-isopropylamide, the ester (**6a**) having been made by protonating the enolate (**1**). The (*Z*)-enolate (**7a**) reacted with acetaldehyde (**8a**), with even higher diastereoselectivity (96 : 4), and removal of the ester group by hydrogenolysis gave the hydroxy acid (**9aa**), diastereoisomeric with the hydroxy acid (**2**). The higher diastereoselectivity in this reaction is in line with our earlier observation that (*Z*)-β-silylenolates usually shows higher diastereoselectivity in their aldol reactions than the corresponding

(*E*)-β-silylenolates. For this reason, we have used a range of (*Z*)-enolates (**7**) to demonstrate the scope of the method. Reaction of these enolates with a range of aldehydes (**8**) gave us the hydroxy acids (**9**). The diastereoselectivity with respect to the aldol geometry was regularly high and no other diastereoisomers were detectable (^{1}H n.m.r.). In each case, we converted the β-hydroxy acids separately into the *trans*- and the *cis*-allylsilanes (**10**) and (**12**), the former by treatment with dimethylformamide dimethyl acetal and the latter by pyrolysis of the β-lactone. In two cases the *cis*-allylsilanes were not completely free of their *trans*-isomers: (**12cc**) was contaminated with 16% of (**10cc**), and (**12da**) was contaminated with 11% of (**10da**); otherwise all the allylsilanes were pure (^{1}H n.m.r.).

The sequence also works just as well for the trimethylsilyl group. We repeated the sequence (**6a**) → (**7a**) → (**9aa**) → (**10aa**) and (**12aa**) with a trimethylsilyl group in place of the phenyldimethylsilyl group, and got comparable yields throughout. In the sequence (**7b**) + (**8b**), we could not use hydrogenolysis to remove the benzyl ester group, so we used an allyl ester, and cleaved the ester to give the acid (**9bb**) using our silyl-cuprate reagent (although lithium dimethylcuprate would have worked just as well).[8] It is also noteworthy that in the preparation of the ester (**6b**), we treated allyl crotonate without silyl-cuprate reagent and got, as the main product, the ester (**6b**) and only a little crotonic acid. Evidently the α,β-unsaturated ester function was more reactive towards the silyl-cuprate reagent than the allyl ester function. This is the first time that we have had two functional groups in the same molecule, both of which react with the silyl-cuprate reagent.

Thus we have been able to prepare a range of *cis*- and *trans*-allylsilanes which are unsymmetrical but secondary at each end and completely free of their regioisomers. It has enabled us to confirm our structural assignments to the minor components of our earlier reaction mixtures,[4] when we were treating allylic acetates with the silyl-cuprate reagent, where we could see *cis*-allylsilane products (**12**), but could not separate them from the major, *trans*-allylsilanes (**10**). Furthermore *cis*-allylsilanes react with electrophiles with higher *anti* stereospecificity than *trans*-allylsilanes;[9] a general regiocontrolled synthesis of such molecules is now available for the first time.

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