Tetrahedron Letters,Vol.28,No.47,pp 5921-5924,1987
Printed in Great Britain

0040-4039/87 $3.00 + .00
Pergamon Journals Ltd.

THE STEREOCHEMISTRY OF AN S_E2'' REACTION OF A CHIRAL DIENYLMETHYLSILANE[1]

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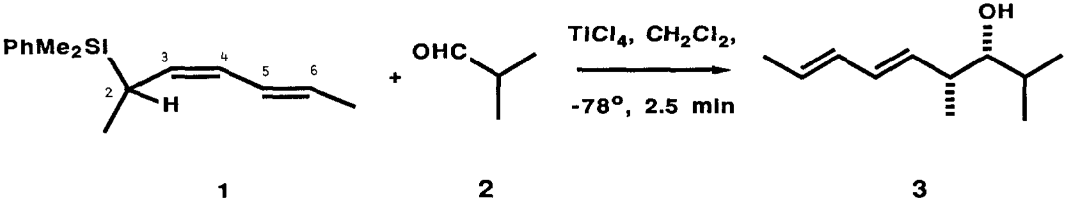
Summary—The optically active heptadienylsilane (**1**) reacts with isobutyraldehyde in a stereospecifically anti reaction to give predominantly (90:10) the enantiomer (**3**).

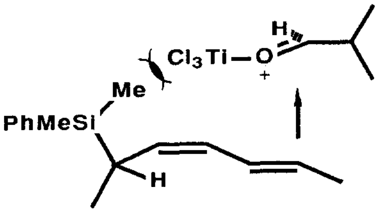
Open-chain allylsilanes react with electrophiles in an S_E2' reaction, and the reaction is usually anti stereospecific.[2,3] We now report that a vinylogous version of this reaction, an S_E2'' reaction (**1** + **2** → **3**), is also stereospecifically anti, giving **3** as the major product. The selectivity for attack on the lower surface of **1**, anti to the silyl group, is 90:10, which is remarkably high, given that the newly created chiral centres in **3** are five and six atoms removed from the stereogenic centre in **1**.



In order to optimise the chance of getting a high degree of stereocontrol, we chose as our dienylmethylsilane the (Z,E)-heptadienylsilane (**1**). It was already known that (Z)-allylsilanes are more selective for anti attack on the double bond than the corresponding (E)-allylsilanes,[3] because the conformation is more or less fixed in the (Z)-isomer as that shown in the drawing (**1**), in which the hydrogen is forced to be the substituent on the stereogenic centre, C-2, eclipsing the double bond. This factor ought to carry over to the vinylogous version of the reaction, and determined our choice of double bond geometry between C-3 and C-4. For the double bond between C-5 and C-6, we chose the E geometry, because (E)-allylsilanes react with aldehydes to give very largely the syn arrangement of methyl and hydroxy substituents on the backbone, whereas the corresponding (Z)-allysilanes give quite substantial amounts of the product with the methyl group and the hydroxy groups anti.[4] We chose isobutyraldehyde (**2**) as the electrophile, both because aldehydes have already been successfully combined with achiral dienylmethylsilanes, and because a large alkyl group on the aldehyde increases the proportion of the product having the methyl and hydroxy groups syn to each other.[5]

In the event, these precautions paid off, because the silane (**1**), prepared with an e.e. of 80%, reacted with isobutyraldehyde (**2**) in the presence of titanium tetrachloride to give the dienealcohol (**3**) with an e.e. of 64%. The yield was 40%, of which 79% was the mixture of **3** and its enantiomer and 21% was a mixture of four other products, probably the anti isomers of **3** and isomers having Z double bonds. The formation very largely of the (E,E)-diene (**3**) defines the conformation at the time of reaction as that shown in **1**; it is very unlikely that the heptadienylsilane reacts in a substantially different conformation, and then changes conformation further along the reaction coordinate in such a way as to give the (E,E)-diene. Furthermore, the coupling constants both between the hydrogens on C-2 and C-3 and between the hydrogens on C-4 and C-5 are 11 Hz, indicating that the ground state conformation of **1** must be close to that illustrated.

We are not yet in a position to identify whether the stereospecificity is determined by steric or electronic influences: it may be that the S_E2'' reaction is stereospecifically anti for electronic reasons, but in this particular example it is possible that the aldehyde, attached to the Lewis acid, is large enough for the combined electrophilic species to experience steric repulsion on the syn face of the diene, as illustrated in **4**.[6] It is unlikely that the various angles of approach would make the steric repulsion quite as bad as **4** implies, but there is nevertheless a possibility that the size of this particular electrophile allows it to reach the silyl substituent. A definitive answer to this intriguing question must wait until we have found a less ambiguous electrophile.



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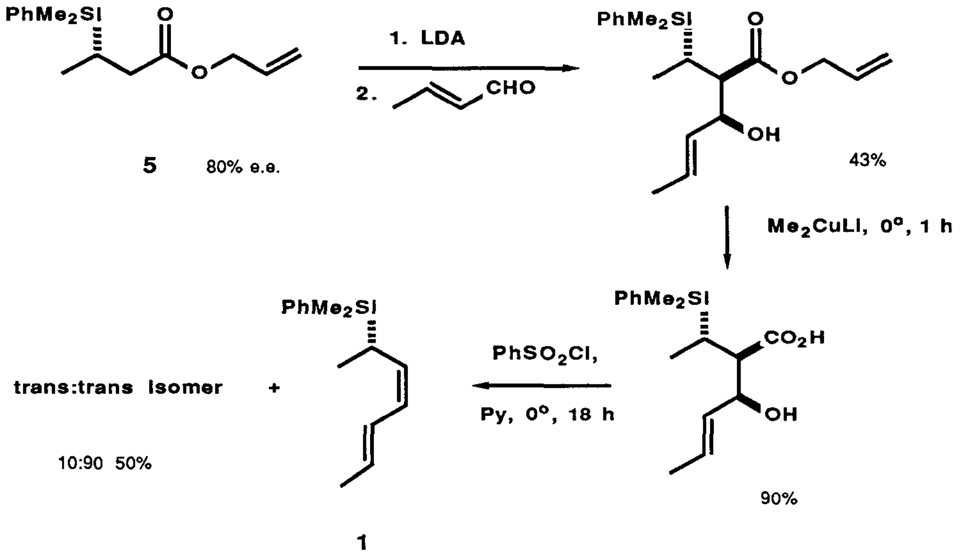
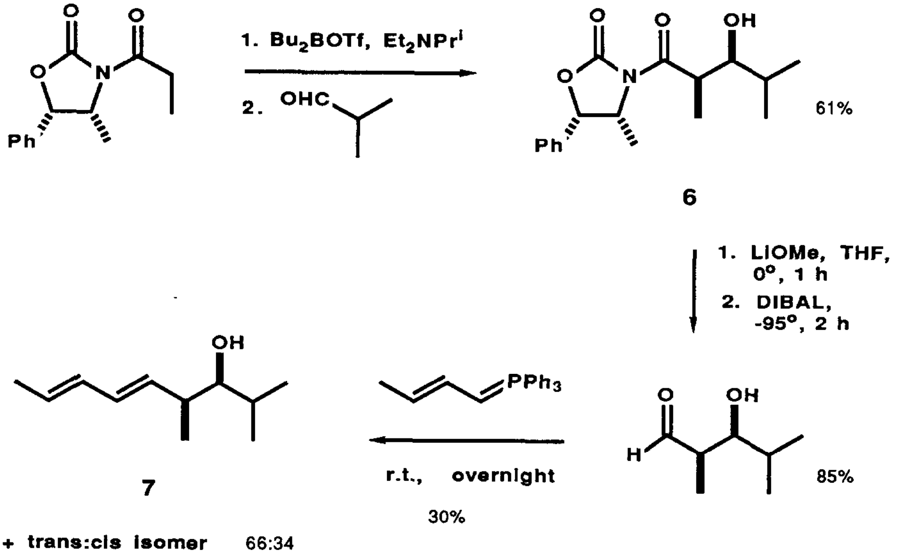
We prepared the silane (**1**) from the optically active allyl ester (**5**)[7] having an e.e. of 80%, following the sequence in Scheme 1, which is one of the methods we have already developed for synthesising allylsilanes.[8] We removed the small amount (10% of the mixture) of the (E,E)-diene by carrying out a Diels-Alder reaction,[9] in which only the (E,E)-diene participated. We proved the degree of stereospecificity in the reaction by making the Mosher's esters[10] of the product mixture, and examining them by ^{19}F NMR spectroscopy: six lines were present in ratios of 14:64:9:6:2:5 (reading from low to high field), of which the second and first are from **3** and its enantiomer, respectively; these are therefore present in a ratio of 82:18. We knew that these two lines were produced by the enantiomers of the major product, because they were much the most intense, and equal in intensity, when the reaction was carried out with racemic diene (**1**).[11] We identified which enantiomer was which by synthesising an authentic sample of the diene (**7**), the enantiomer of the diene (**3**), using the sequence shown in Scheme 2. Evans and his coworkers reported that the aldol reaction in Scheme 2 is very diastereoselective (>99:1) and very enantioselective (>500:1) in favour of the syn isomer (**6**).[12] The Wittig reaction, somewhat surprisingly, gave more (66:34) of the (E,E)-diene than of the (E,Z)-diene.[13] The major product (**7**) from this sequence gave a Mosher's ester with a line in the ^{19}F NMR spectrum coincident in chemical shift with the first

Scheme 1



Scheme 2



line of the spectrum of the Mosher's esters prepared from the reaction mixture. A just visible line coincided with the line from the major product (**3**), and a new line, not present in the spectrum of the Mosher's esters of the products of the reaction, was presumably produced by the isomer of **7** having a *cis* double bond between C-4 and C-5. Finally, we confirmed that the geometry of the diene (**3**) is *E*,*E* by double resonance experiments, which revealed that the olefinic coupling constants were 14.3 and 14.05 Hz.

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6 We ruled out the possibility that the phenyl group on the phenyldimethylsilyl substituent was a major steric influence, by repeating the sequence with a trimethylsilyl group in place of the phenyldimethylsilyl group. The heptadienyltrimethylsilane that we prepared was enantiomeric with **1**, had an e.e. of 64%, and gave the enantiomer of **3** with an e.e. of 46%. The selectivity for attack on the surface of the diene *anti* to the trimethylsilyl group was therefore 86:14, insignificantly different from the result (90:10) with **1**.

7 We prepared the ester (**5**) by conjugate addition of our silyl-cuprate reagent to the crotonoyl derivative of Koga's glutamic acid-derived chiral auxiliary, followed by removal of the chiral auxiliary.[14] The e.e. was measured using proton NMR spectroscopy immediately after the conjugate addition, when the chiral auxiliary was still attached. We assume that the chiral auxiliary is 100% optically pure and that no loss of chirality took place from this stage on. If either of these assumptions is wrong, the degree of transfer of chiral information is even higher.

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(Received in UK 14 September 1987)