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Determination of the extent to which an S_E2' reaction of a propargylsilane is *anti*

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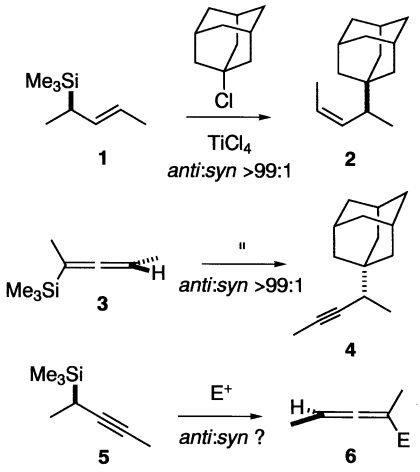
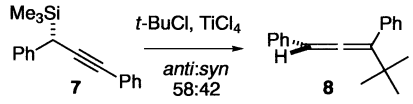
Abstract—The propargylsilane, 1,3-bistrimethylsilylbut-1-yne, **11** reacts with aldehydes in the presence of titanium tetrachloride in *anti* S_E2' reactions, but with a low level of stereospecificity, 75:25 with 2,4-dinitrobenzaldehyde and close to 50:50 with isobutyraldehyde.

We reported some time ago in this journal accurate measurements of the extent to which allylsilanes and allenylsilanes react with cationic electrophiles stereospecifically in the *anti* sense **1**→**2** and **3**→**4**.[1,2] This paper reports our belated work on the third of the series, the degree of stereospecificity in the corresponding reactions of propargylsilanes **5**→**6**.



Stereospecificity in the *anti* sense had been established for allylsilanes in work largely by Hayashi and Kumada,[3] but also by others.[4] In our work, we measured the degree of stereospecificity more accurately than had been possible hitherto. We used the allylsilane **1**, and later the allenylsilane **3**, of notably high enantiomeric purity in both cases, and measured the enantiomeric purity of the products by attaching chiral auxiliaries to their oxidation products. In the reactions of the allylsilane **1**, the degree of stereospecificity was high but not quite complete, being at worst 90:10, but for the major product **2** >99:1. The small losses of stereospecificity in the formation of the *E*-product could be explained by rotations in the intermediate cations, since the same losses were not seen in the corresponding reactions of the allenylsilane **3**, for which the enantiomeric purity of the major product **4** was, as accurately as we could measure it, the same as that of the starting material.



This left propargylsilanes to be investigated, an especially interesting case, because Hayashi and Kumada had already found that, although the one reaction they looked at, **7**→**8**, was stereospecifically *anti*, the degree of stereospecificity appeared to be low.[5] They found that the propargylsilane **7**, prepared as a mixture of enantiomers in a ratio of 59:41 (18% ee), reacted with the *tert*-butyl cation to give the allene **8** in 23% yield as a mixture of enantiomers in a ratio estimated on the basis of semi-empirical rules[6] to be 51.5:48.5 (3% ee). This indicated that the reaction had been stereospecific in Zimmerman's sense,[7] but the ratio of *anti*:*syn* attack was only about 58:42. Although there was no reason to doubt their conclusions, the proof of the absolute configuration of the product, and, less reliably, the measurements of the ratios of enantiomers were all based upon rules, and estimates, rather than upon more direct physical measurements. To complete the series,

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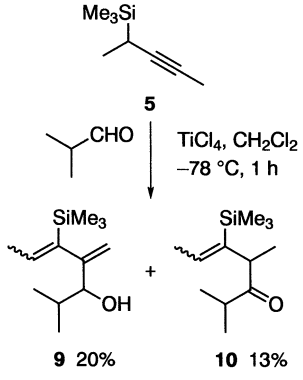
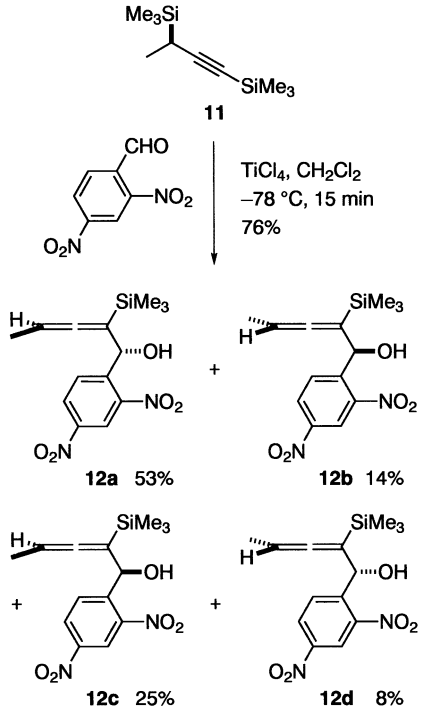
we now report our work on propargylsilanes, in which we have attempted to use the same degree of thoroughness as we deployed in our work on allylsilanes and allenylsilanes.

In preparation for this work, we developed some years ago a synthesis of the propargylsilane **5** with a high level of enantiomeric purity, and have reported it in full.[8] Since then we have had much difficulty finding a suitable reaction. The products must be allenes, and they must have a substituent to which a chiral auxiliary can be attached, in order to measure the enantiomeric purity without having to rely upon the rotation of polarised light. In this series, adamantyl chloride would not work, because oxidation of any allene products would lose the chiral information, but in any case the propargylsilane **5** did not give an allene product when it was treated with adamantyl chloride and titanium tetrachloride.[9] Although there are reports in the literature in which propargylsilanes react with aldehydes in the presence of a Lewis acid to give allenyl carbinols,[10] they are mostly reactions of achiral propargylsilanes in which the silyl group is attached to an unsubstituted methylene group. We found that these same reactions using the propargylsilane **5** gave the dienes **9** (*E*:*Z* 66:34 or 34:66) and the ketones **10** (*E*:*Z* 50:50), resulting from migration of the silyl group in the intermediate cation, followed by proton loss instead of the loss of the silyl group. There is ample precedent for silyl migration,[11] and the presence of the silyl group on a secondary centre in the propargylsilane **5** only made it easier.

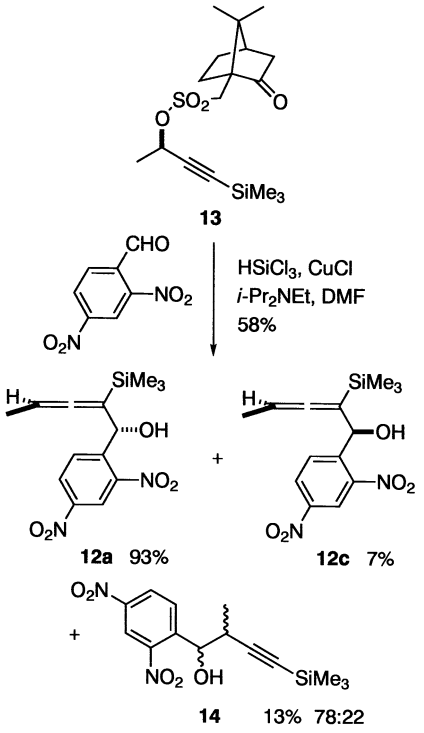


Using different electrophiles[12] and different propargylsilanes,[13] we uncovered several other unproductive pathways, with and without the silyl migration, including the formation of dihydrofurans,[11] but none giving an allene functionalised in a way that would allow us to measure both the stereochemical sense of the reaction and the enantiomeric purity of the product with reliable accuracy. We had been using the propargylsilane **5**, in order to match as closely as possible our work with the allylsilane **1** and the allenylsilane **3**. We have been forced to abandon the close analogy, and have used instead the propargylsilane **11**, in which the acetylenic terminus carries another silyl group. We reasoned that the second silyl group would stabilise, and hinder, the intermediate cation enough to prevent silyl migration, and allow the formation of an allene product. Happily, the propargylsilane **11** rich in the *R* enantiomer (>99.8:0.2), prepared in the same way as in the earlier work,[8] gave the allenyl carbinols **12a–d** with 2,4-dinitrobenzaldehyde in good yield in the presence of titanium tetrachloride.



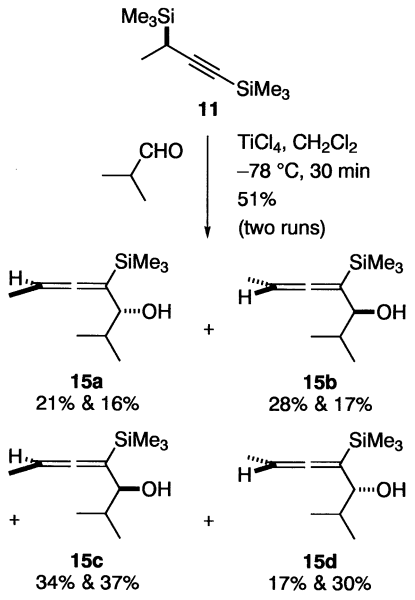
We measured the relative amounts of these compounds by attaching Mosher's *R*-acid to them, and integrating the well resolved ^{19}F NMR singlets, which appeared at δ −70.81, −70.88, −71.03 and −70.96, respectively. We identified the pairs of enantiomers **a**+**b** and **c**+**d** by carrying out the same reaction with racemic propargylsilane, which led the two signals at δ −70.81 and −70.88 and the two signals at δ −71.03 and −70.96 to be of equal intensity, with the first pair twice as intense as the second. We assigned relative stereochemistry using the ^{1}H NMR method of Kakisawa and his co-workers,[14] in which the Mosher's derivatives with the *R*- and the *S*-acid are compared. Finally, we assigned the absolute stereochemistry by synthesising the allenyl carbinols **12a** and **12c** by a small variation of the method of Marshall and Adams.[15] The propargyl sulfonate **13**, prepared from (+)-camphorsulfonyl chloride and the *R*-alcohol, and recrystallised to give a >99:1 ratio of diastereoisomers, reacted with trichlorosilane and 2,4-dinitrobenzaldehyde to give a mixture of the alcohols **12a** and **12c** (58%), $[\alpha]_D$ −203, together with a little of the corresponding homopropargylic alcohols **14** (13%). The Mosher's derivatives of the allenyl carbinols showed that the diastereoisomers **12a** and **12c** were present in a ratio of 93:7, similar to the diastereoisomer ratios found by Marshall with other aldehydes. The absolute configuration for **12a** and **12c** is based on the stereochemistry Marshall has proved for reactions like **13**→**12a**+**12c**, and like his they fit the Lowe–Brewster rules. Our proof of the relative and absolute stereochemistry is not quite as complete as we would like,[16] but, coupled with Marshall's extensive work with several interrelated conversions, it fits an internally consis-

tent pattern that is compelling. Evidently, the S_E2' reaction **11**→**12** takes place predominantly in the *anti* sense, but the *anti*:*syn* ratio is only 75:25.



In addition, we carried out the same series of reactions with isobutyraldehyde, which we had also used in our work with the allenylsilane **3**. The products **15a–d** were formed, and their structures assigned in the same way as for the reaction with 2,4-dinitrobenzaldehyde. The Mosher's derivatives from the *R*-acid showed four singlets in the ^{19}F NMR spectrum at δ −71.42, −71.68, −71.86 and −71.75, respectively. From the racemic propargylsilane, the product mixture showed the two signals at δ −71.42 and −71.68 and the two signals at δ −71.86 and −71.75 of equal intensity within the pair, with the first pair twice as intense as the second. Comparison of the ^1H NMR spectra of the derivatives of the alcohol **15a** with Mosher's *R*-acid and *S*-acid identified that this diastereoisomer was *R* at the carbinol carbon. Finally, the synthesis using Marshall's method gave only the pair **15a** and **15c** in low yield (9%), but the Mosher's derivatives showed that they were present in a ratio of 98:2. The results of two runs were not completely consistent, the major pair of diastereoisomers indicated that the reaction had been selectively *anti* (*anti*:*syn* 66:34 and 54:46), while the minor indicated that it had been selectively *syn* (*anti*:*syn* 43:57 and 48:52). Combined, and averaged over the two runs, this S_E2' reaction appeared to be *anti*:*syn* in a ratio of 53:47, which within experimental error is as close to 50:50 as makes no matter.

In conclusion, we have found that the S_E2' reaction of the propargylsilane **11** with 2,4-dinitrobenzaldehyde is stereospecifically *anti* to a lower degree (75:25 for the major diastereoisomer) than for the corresponding reactions of allyl- and allenylsilanes. Furthermore, the selectivity depends upon the electrophile, being negligible with isobutyraldehyde.[17] Our *anti*:*syn* ratios fall one on each side of Hayashi and Kumada's, confirming their tentative conclusion that the reaction suffers considerable erosion of its stereospecificity. We are inclined to agree with their tentative explanation: that the intermediate cation is able to undergo rotation about the σ-bond before the loss of the silyl group. In our series, with a second silyl group stabilising the intermediate cation, we may have unwittingly exacerbated this problem. There is also the possibility that the direction of attack on a triple bond, with nearly cylindrical symmetry in the π-orbitals, is less constrained than it is on a double bond, where attack is only profitable if it is more or less directly above or below the plane of the π-bond.



Acknowledgements

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9. The products isolated were conjugated dienes, $C_{25}H_{36}$, which corresponds to *two* adamantyl units for each C_5 unit derived from the propargylsilane. They were probably the result of electrophilic attack by a second adamantyl cation on the first-formed allene, but we were unable to stop the reaction at the earlier stage.
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11. Adamantyl cations, aldehydes and their acetals.
12. Phenyldimethylsilyl in place of trimethylsilyl, and/or a terminal acetylene in place of the methyl-substituted **5**.
13. Pornet, J.; Miginiac, L.; Jaworski, K.; Randrianoelina, B. *Organometallics* **1985**, *4*, 333–338.
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16. Neither we nor he has been able to prepare a crystalline derivative. Our choice of 2,4-dinitrobenzaldehyde was made in the forlorn hope that one of the products might crystallise.
17. We have too little information to explain why isobutyraldehyde should be less selective than 2,4-dinitrobenzaldehyde. The reactive species will be the aldehyde coordinated to the Lewis acid. 2,4-Dinitrobenzaldehyde may be more reactive than isobutyraldehyde, but its coordinated form will probably be present in lower concentration. As a result it is only possible to guess whether its greater selectivity is a violation of the reactivity–selectivity principle. Since we do not know whether the erosion of stereospecificity is caused by rotation in the intermediate cation or by the initial attack not being *anti* to the silyl group, we can only speculate. One possibility is that the intermediate cation in the isobutyraldehyde reaction might be a little more stable than that in the 2,4-dinitrobenzaldehyde reaction, and might therefore have lived long enough to lose its stereochemical information.