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Accurate Determination of the Extent to which the S_E2' Reactions of an Allenylsilane are Stereospecifically *anti*

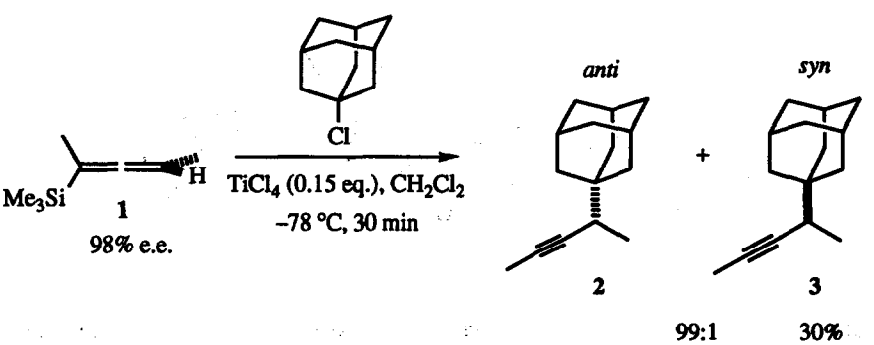
Michael J. C. Buckle and Ian Fleming*

University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW

Abstract **The allenylsilane 1 has been prepared in high enantiomeric purity (98% e.e.); its S_E2' reactions with adamantyl chloride and isobutyraldehyde are stereospecifically *anti* to a very high degree (>99:1).**

Last year we described the synthesis of the enantiomerically and geometrically very pure (>99.5:0.5) allylsilane, *E*-4-trimethylsilylpent-2-ene.[1] We also described its S_E2' reaction with the adamantyl cation, which produced both an *E* and a *Z* product, the latter enantiomerically as pure (>99:1) as the starting material, but the former showing some erosion of the stereospecificity (to 90:10). This loss of stereospecificity could be interpreted as a measure of the extent to which the electrophile attacking the π-bond discriminated between the two substituents, trimethylsilyl and methyl, on the stereogenic centre. Alternatively, it could represent a measure of the extent to which the intermediate cation loses its configurational purity before the silyl group is lost.[2] A similar reaction on the corresponding *Z*-allylsilane gave only the *E*-product, which also showed some, but less, erosion of the stereospecificity (95:5). This result did not help us to decide which of the two reasons for the small loss of stereospecificity might be the more important.

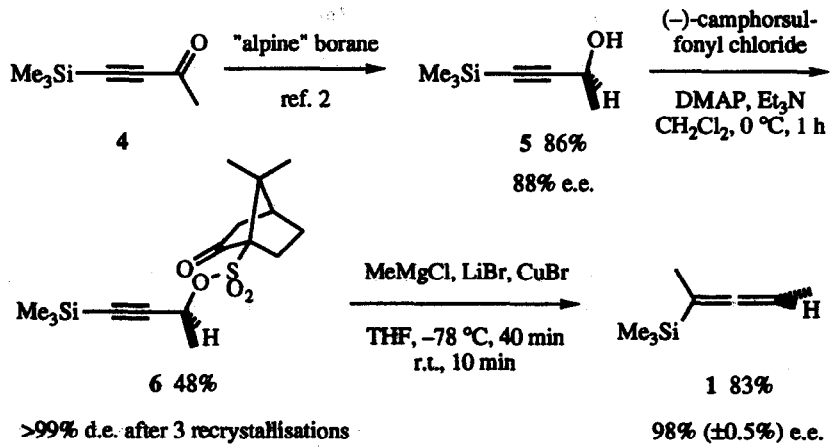
We now report that the corresponding allenylsilane **1**, prepared in a state of high, although not quite complete, enantiomeric purity (98% e.e.), reacts with the adamantyl cation to give the acetylenic products **2** and **3** in a ratio of 99:1, identical within experimental error with the ratio of enantiomers present in the starting material. The reaction is, as far as we can measure, completely stereospecific. It seems likely that the small losses



in stereospecificity in the earlier work with the corresponding allylsilane largely represent incomplete preservation of the stereochemical integrity in the intermediate cations. With the two surfaces of the allene **1** rigidly differentiated by the silyl and methyl groups, and with no ambiguity about the conformation at the time of attack, the upper surface must be at least one hundred times more nucleophilic towards the adamantyl cation than the lower, even with the most conservative estimates of the errors in our measurements.

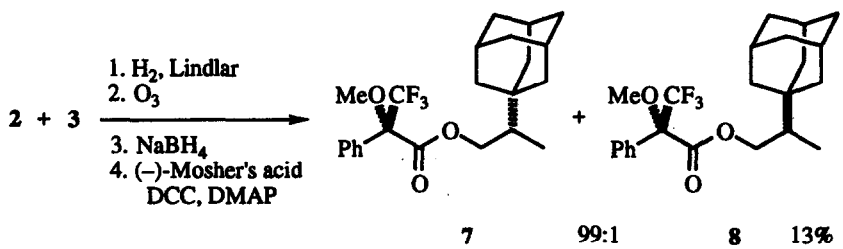
We prepared the allenylsilane **1** from the ketone **4** using Brown's[3] and Midland's[4] method to prepare the propargyl alcohol **5**, followed by a two-step sequence based on our earlier synthesis of the corresponding

racemic allenylsilane.[5] We have improved the procedure in two ways, first increasing the enantiomeric purity of the propargyl intermediate by recrystallising the camphorsulfonate **6** until it was present in essentially 100% d.e., and second by treating this derivative with the methyl Grignard reagent and copper bromide in place of lithium dimethylcuprate. The latter reagent is known to racemise allenes,[6] and did indeed give us allene with considerable, and variable, loss of enantiomeric purity. The enantiomeric purity of the allene **1** was measured for us by Professor König[7] using gas chromatography with a homochiral column giving far more than just base-line



resolution. Three different samples were prepared, with 97.4%, 98.0% and 98.5% e.e. There must have been some very minor losses of stereospecificity in the last step **6** → **1**, since we would certainly have detected the presence of 1% of the diastereoisomer of the camphorsulfonate **6**.

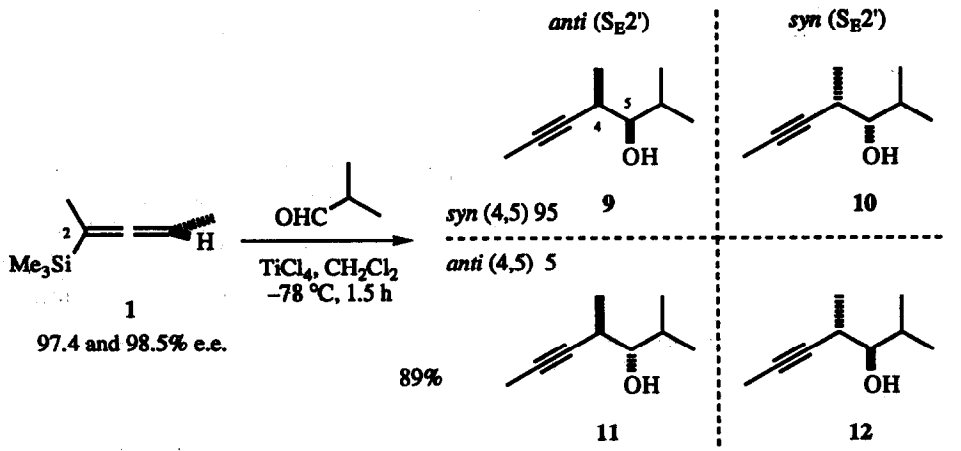
We measured the proportion of the products **2** and **3** from the reaction with adamantyl chloride by hydrogenation of the mixture of acetylenic products to the mixture of the corresponding *Z*-alkenes, the proportion of which we determined as described in our earlier paper,[1] using the ^{19}F and ^{1}H NMR spectra of the Mosher's esters[8] **7** and **8**. We estimate from our NMR measurements, which agree with each other, that the amount of the minor diastereoisomer present is 1%, and certainly less than 2%.



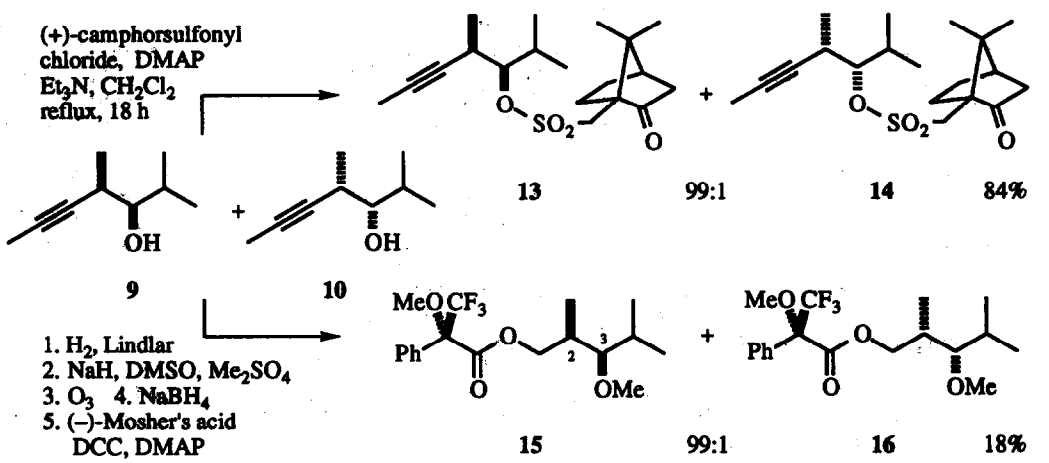
Although we have proved that the reactions in this and in our earlier paper are highly stereospecific, in neither have we proved that the reactions are *anti*. This has simply been assumed by analogy with much work on the S_E2' reactions of allylsilanes,[9,10] and is hardly in doubt. The alcohol **5** is of known absolute configuration, and the reaction **6** → **1** is well established to be stereospecifically *anti*.[11] It follows that the structures drawn here reinforce our assumptions, since the major product of an *anti* attack on the allene **1** should be the acetylene **2**, and this will give the Mosher's ester **7**. The spectra of the compounds assigned this structure in the present work and in the earlier work match. However, the *anti* stereospecificity of allenylsilane reactions has been proved in only one reaction,[10] a diastereoselective protodesilylation, which appeared to be not quite completely *anti* stereo-

specific. We decided therefore to prove that the allenylsilane **1** was indeed reacting in the *anti* sense, by treating it with an electrophile that would give a product of known absolute configuration.

We treated the allenylsilane **1** with isobutyraldehyde in the presence of titanium tetrachloride and got a good yield of the homopropargyl alcohols **9-12** in three runs. We have a further interest in this reaction, since it is a model for a key step in our synthesis of ebelactone-a, for which we shall want the diasteroisomer modelled by **9**.[12] The diastereoisomers, *syn* and *anti* with respect to the relative configuration between C-4 and C-5, were



present in a ratio **9** + **10** : **11** + **12** of 95:5, noticeably higher than that (80:20) for the known reaction of the corresponding allenylsilane lacking a methyl group on C-2 with cyclohexanecarboxaldehyde.[13] As a result, there was not enough of the *anti* alcohols **11** and **12** with which to measure accurately the enantiomeric excess, but the *syn* pair **9** and **10**, separated from the *anti* isomers by chromatography, gave the camphorsulfonates **13** and **14**,



with which we could measure the ratio of 99:1 by ^{1}H NMR spectroscopy, essentially the same for all three runs.[14] Again, the products and the starting material had the same degree of enantiomeric purity, indicating that the transfer of chirality was very close to 100%. We also converted the same mixture of alcohols into the Mosher's acid derivatives **15** and **16**, which were also present in a ratio of 99:1. All of the possible

stereoisomers of the Mosher's esters were already known to us, with assigned absolute configurations at C-2 and C-3,[15] confirming that the S_E2' reactions of allenylsilanes are indeed stereospecifically *anti*, and to a very high degree. This work also confirmed that the major product **9** was the isomer with the *syn* relationship between C-4 and C-5.

We thank Professor König (Hamburg) for his generous help in measuring the enantiomeric purity of our allenylsilane, Jérôme Bazin for preliminary work on the synthesis of the homochiral allenylsilane, Professor Rick Danheiser for steering us towards the successful recipe for that synthesis, Ken Takaki, Anne Ware and Sarah Archibald for exploratory work on the reaction with isobutyraldehyde, and the SERC for a maintenance award (MJCB).

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2 The difference in energy between the two conformations of a secondary cation stabilised by a β SiH_3 group in which the C-Si bond and the empty p-orbital are either parallel or orthogonal has been calculated to be 85-93 kJ mol^{-1} in the gas phase.[16] This is a possible measure of the barrier to rotation, if we assume that these conformations are minima and maxima. We can expect this barrier to be less in solution.[17] If the barrier were 52 kJ mol^{-1}, the cation would, using the usual Arrhenius parameters, have a half-life with respect to rotation of 1 s at –78 °C. Rotation in the intermediate cation has been suggested as an explanation for the large loss in the *anti* selectivity of an S_E2' reaction of a homochiral propargylsilane.[18]

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