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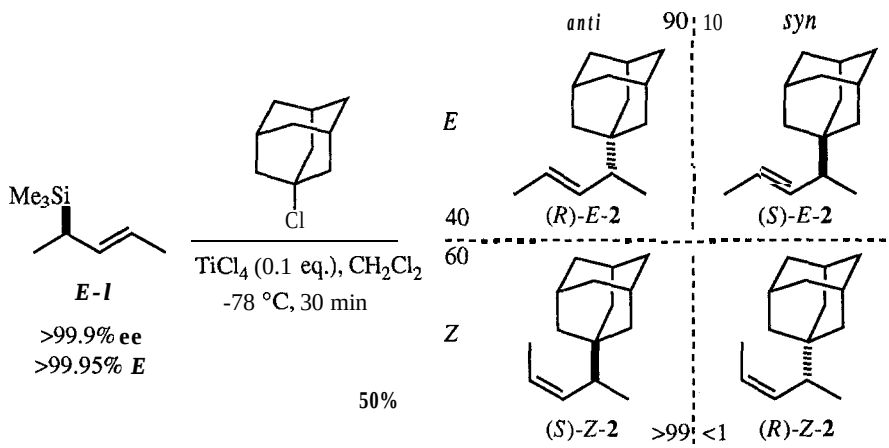
Accurate Determination of the Extent to which an S_E2' Reaction of an Allylsilane is *anti*

Michael J. C. Buckle, Ian Fleming* and Salvador Gil

University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW

Abstract The *E* and *Z* allylsilanes **E-1** and **Z-1** have been prepared essentially 100% geometrically and enantiomerically pure; their S_E2' reactions with adamantyl chloride are highly, but not completely, stereospecific.

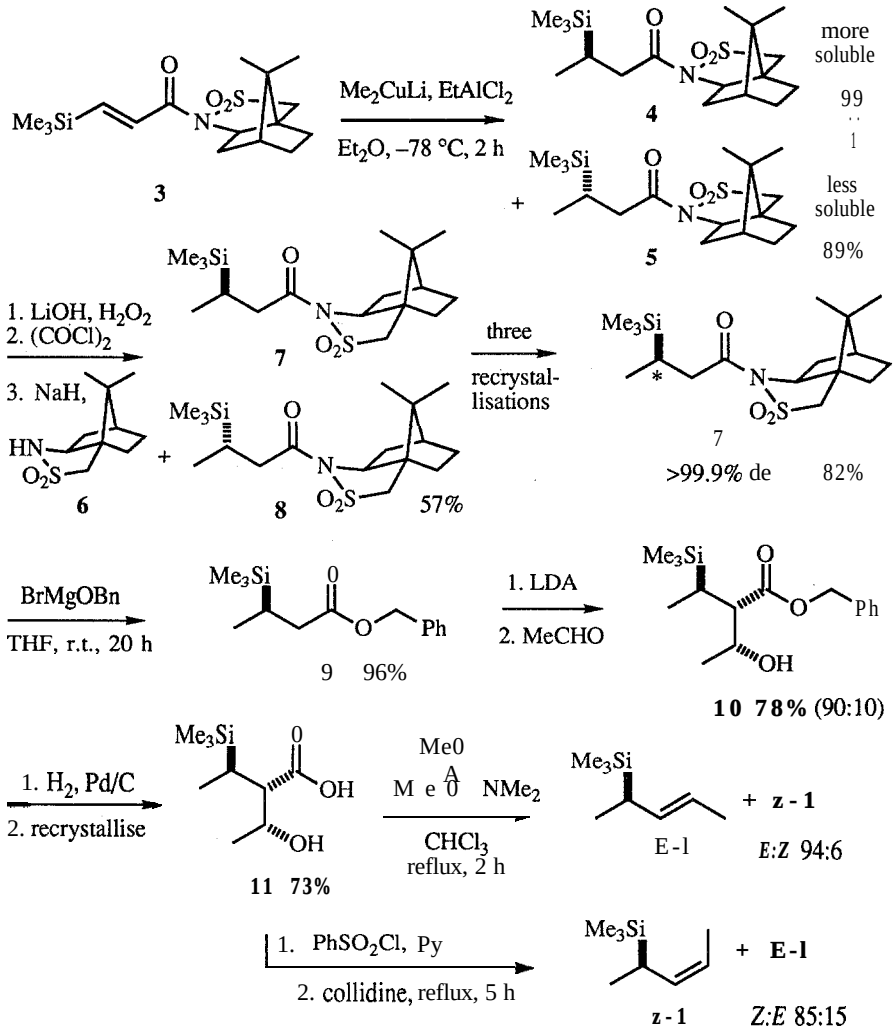
It has been well established, principally by Kumada,[1] Wetter2 and Eschenmoser,[3] that, in the absence of other constraints, the S_E2' reaction of allylsilanes is stereospecifically ***anri.*** The degree of stereospecificity is certainly very high, probably >95%, but it was not possible in any of their work to measure more accurately than that how completely stereospecific the reactions were, largely because the allylsilanes that they used were, necessarily at that time, less than 100% homochiral (optically pure). With new methods available for the synthesis of allylsilanes, we have now examined more accurately than has been possible in the past the degree of stereospecificity of the electrophilic substitution reaction **E-1** → 2, which we offer as a paradigm, using an allylsilane **E-1** that is essentially 100% homochiral.



In order to set up the stereogenic centre we tried several combinations of nucleophile, chiral auxiliary, and double bond geometry. We obtained the highest level of stereochemical purity (99:1) at the silicon-bearing carbon by the conjugate addition of iithium dimethyl-cuprate to the silicon-containing E-substrate 3 based on Oppolzer's sultam derived from (+)-camphor.[4] Unfortunately, the major product 4 was the more soluble, and recrystallisation was not an efficient method for removing even the 1% of diastereoisomer 5 that was present. We resorted therefore to a simple device that was guaranteed to work-we removed the chiral auxiliary and ***replaced it with its enantiomer*** 6 derived from (-)-camphor.5 The major product 7 was now, inevitably, the less soluble diastereoisomer, and one recrystallisation served to remove all but 0.2% of the minor component 8. This procedure is not to be recommended in synthesis, because of the inevitable losses, nor would it be needed. It served us well here, because the overall yield was not our primary concern.

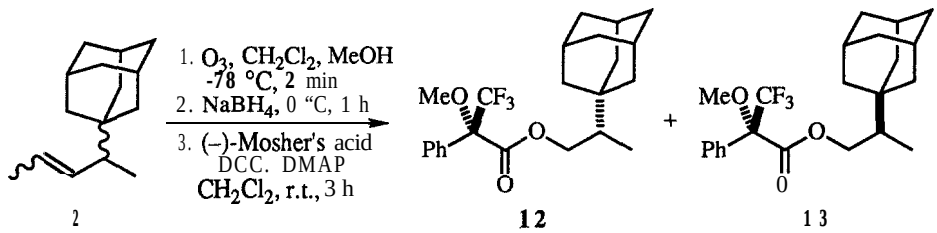
For good measure, we recrystallised the sultam 7 three times, at which point we could not detect, by careful GC analysis, any (<0.05%)[6] of the diastereoisomer 8. We removed the chiral auxiliary with magnesium

benzyloxide, and used the benzyl ester 9 in our allylsiiane synthesis, 9 → 10 → **11** → E-l or Z-l, based on the highly diastereoselective aldol reactions of β-silyl enolates and stereospecific decarboxylative eliminations.[7] Since the *E*-allylsilane E-l and its Z isomer Z-l will give opposite enantiomers on electrophilic substitution, it was necessary to be as thorough in removing each from the other as we had been in setting up the silicon-bearing stereogenic centre in the first place. We achieved this using repeated column chromatography on silica gel heavily impregnated with silver nitrate. After this procedure, the allylsilanes E-l and **Z-l** were both geometrically pure, with <0.05%[6] of the other present in each, as determined by careful GC analysis.



We carried out the reaction E-l → 2 twice, using adamantyl chloride as a representative simple electrophile[8] and a catalytic amount of titanium tetrachloride at -78 °C, with the same result each time. We separated the *E* and Z products 2, which were present in a ratio of 40:60, using the same silver nitrate-impregnated column, obtaining each free of the other (<0.05%[6]), as determined yet again by careful GC analysis. We measured the enantiomeric purity of both alkenes by ozonolysis, followed by reduction with sodium borohydride, and derivatisation with Mosher's acid .[9] We were unable to use GC analysis at this stage,

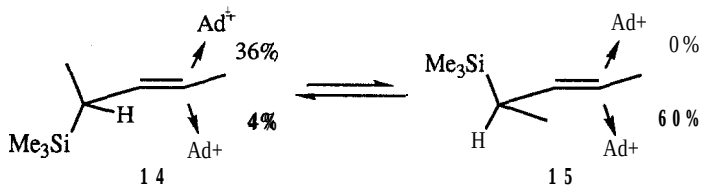
but the ^{19}F-NMR and ^{1}H-NMR spectra allowed us to measure the diastereoisomeric ratio of the final products 12 and 13 to within 1%. We find that the major product ***Z-2***[10] is enantiomerically pure (>99%),[11] but that the minor product ***E-2*** is present as a 90: 10 mixture of enantiomers. Clearly the degree of stereospecificity is, as expected,[1-3] very high, but is also measurably incomplete, in agreement with our observations,[12] and those of Kitching,[13] that, when other stereochemical constraints are present, the extent to which allylsilane S_E2' reactions are ***anti*** is easily eroded.



2 **12** 13

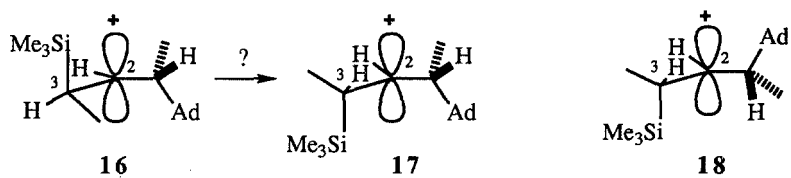
50% 90: 10 from E-2 derived from E-l
60% <1:>99 from Z-2 derived from **E-l**
73% 5:95 from ***E-2*** derived from Z-1

We offer two simplified explanations for why the Z product should be formed with higher enantiomeric purity. Attack on the allylsilane E-l in a conformation close to 15 may take place on the lower surface more selectively than attack takes place on the upper surface of the alternative conformation 14, because the lower



14 **15**

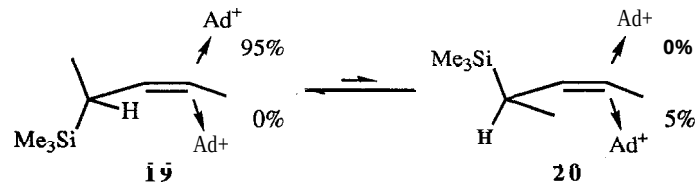
surface of 15 is occupied by a hydrogen atom, whereas the upper surface of 14 is occupied by a methyl group. This argument assumes that ***all*** of the ***E*** product is formed by attack taking place in conformation 14, and that ***all*** of the Z product is formed by attack taking place in conformation 15; in other words, there is no rotation about the C2—C3 bond in the intermediate cations before the silyl group is plucked off by a nucleophile, presumably chloride ion. Alternatively, the intermediate cation 16, produced by attack on the lower surface of the conformation 15, may change its conformation, by rotation about the C2—C3 bond 16 →**17** before the silyl group is lost, to a greater extent than the intermediate 18, produced by attack on the upper surface of conformation 14, changes its conformation, because the lowering of energy is greater in the former case.



16 **17** **18**

We have carried out one rather inconclusive experiment to try to find out which of these explanations is the more plausible. We repeated the S_E2' reaction three times using the Z-allylsilane **Z-l** in place of the ***E***-allylsilane **E-l.** In each of these reactions, we obtained only the E-product, **14** which proved to be a 95:5 mixture of enantiomers.[15] This result is consistent with electrophilic attack taking place only in conformation 19 and not

in conformation 20, with a 95:5 ratio of attack from above to that from below. It is also consistent with 5% of the reaction taking place in the high-energy conformation 20, with the intermediate cation, not implausibly, changing its conformation completely by rotation about the C2—C3 bond before the loss of the silyl group. Because the 95:5 ratio in this experiment and the 90: 10 ratio in the experiments on the E-isomer are so similar,



we are unable to distinguish between these explanations, and must rest on the possibility that a combination of the two is also possible. In summary, we have confirmed that the S_E2' reaction of an allylsilane is highly stereospecific, and have detected that, nevertheless, it is not completely so.

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5. We checked that this sample of camphor sultam was enantiomerically pure following: Oppolzer, W.; Vandewalle, M.; Van der Eycken, J.; Vullioud, *C. Tetrahedron* **1986**, *42*, 4035-4043.
6. This is a conservative estimate of the amount of isomer that we could have detected, on the expanded GC traces, based on comparisons with the amount of various (and unknown) adventitious impurities present to the easily measurable extent of 0.62%.
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10. We assume that the reaction is *anti* stereospecific, not *syn,* there being little doubt that it would not be.
11. This result helpfully confirms that the samole of Mosher's acid was enantiomericallv oure. and that there was no loss of configurational purity during the synthesis and degradation, including, most worryingly, the chromatographic separations, where silver-coordination might have allowed some racemisation.
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14. The *Z* product was just detectable as 0.2% of the mixture, too little to measure its optical purity.
15. The three runs gave ratios of enantiomer of 97:3, 95:5 and 93:7.

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