## ALLYLSILANES IN ORGANIC SYNTHESIS; STEREOSELECTIVE PREPARATION AND REACTIONS OF FUNCTIONALISED $\beta_{,\gamma}$ -EPOXYSILANES

Patrick J. Murphy, Andrew T. Russell and Garry Procter.\*

Department of Chemistry and Applied Chemistry, University of Salford, Salford M5 4WT, U.K.

Summary. Epoxidation of ester-allylsilanes such as (1) after alkylation adjacent to the carbonyl group produces the corresponding epoxides with high diastereoselectivity.

The epoxidation of chiral functionalised allylsilanes can be a useful method of stereochemical control in the synthesis of organic compounds.<sup>1</sup> We are particularly interested in the epoxidation of ester-allylsilanes of type (1). In our previous papers we described reactions of this type of system which produced  $\gamma$ -lactones and indicated some of their synthetic potential by a stereoselective synthesis of the carpenter bee pheromone.<sup>2</sup> We have investigated the epoxidation of some further members of this type of ester-allylsilane, and we have discovered that it is possible to achieve very high levels of diastereoselectivity in the epoxidation reaction. These preliminary results are presented in this Letter along with some further chemistry of the epoxide (2).



In our earlier work we proposed that the epoxide (2) was an intermediate *en route* to the  $\gamma$ -lactone (3), the major product which was isolated from the reaction of the allylsilane (1) with *meta*-chloroperoxybenzoic acid (*m*-CPBA).<sup>2b</sup> In further work on this reaction we have found that it is possible to isolate epoxide (2) along with the minor diastereoisomeric epoxide (4) and to separate them by flash column chromatography. With pure epoxide (2) in hand we were interested to investigate its chemistry a little and were pleased to find that it was indeed possible to cyclise it to the  $\gamma$ -lactone (3) albeit in low yield. We have found the direct reaction of (1) to produce  $\gamma$ -lactones to be erratic and unpredictable, often the major products are simply the epoxides (2) and (4). If good yields of the  $\gamma$ -lactone (3) are required then it is better to use the carboxylic acid derived by hydrolysis of (1), cyclisation of which is very reliable and can be made to produce the lactone with high diastereoselectivity.<sup>3</sup>



We were also able to alkylate the epoxide (2) as shown, but this alkylation was much more difficult than alkylation of the allylsilane itself and the diastereoselectivity of the alkylation was lower than expected.<sup>4</sup>

As part of our further work on the epoxidation of chiral functionalised allylsilanes, and projected total syntheses using this methodology, we have examined a number of other allylsilanes as substrates for epoxidation. In all of our previous work with ester- and amide-allylsilanes the diastereoselectivity of the epoxidation was in the range 3:1 to 5:1, a level of selectivity which can be synthetically useful given that the yield is good and that the major product is easily separated.<sup>2</sup> Nevertheless it would be of clear benefit to increase the diastereoselectivity. Some of the results of our work in this area are shown in the Table, and have proved to be most interesting. An inspection of the Table reveals that the diastereoselectivity of the epoxidation appears to increase greatly when the group adjacent to the silicon-bearing carbon is branched (entries 1-4 compared with entries 5-9). For entries 5-9 we can detect none of the diastereoisomeric epoxides in the crude product by 300 MHz <sup>1</sup>H nmr spectrometry.

The significant increase in diastereoselectivity observed in entries 5-9 is unlikely to be due to an effect of the silicon group, as compounds with SiMe<sub>2</sub>Ph, SiPh<sub>3</sub>, and SiMe<sub>3</sub> (not shown) groups all show this increase. It is also improbable that the effect is due to the relative stereochemistry of the methyl and silicon groups (e.g. if they happen to be a "matched pair"<sup>5</sup>) since in one case where the other diastereoisomer was available to us (entry 9) the same high diastereoselectivity was observed. A similar effect has been reported by Fleming *et al.*<sup>6</sup> who found that a branched substituent (isopropyl) adjacent to the carbon carrying the silicon group led to a highly diastereoselective epoxidation (and methylenation) (both > 95:5) compared with reaction of the allylsilanes in which this adjacent group was methyl (~ 60:40) or phenyl (~ 90:10).

The origin of this effect is far from clear, although we do suspect that the branched nature of the substituent is important. Molecular mechanics calculations for some of our examples (MacroModel 2.0)<sup>7</sup> suggest that alkylation does increase the difference in the relative energies of the ground state conformations A and B (Figure 1) (A is more stable than B), but that this difference alone is not enough to account for the observed diastereoselectivity). Presumably the difference in energies of the *transition states* arising from A and B is



<sup>a</sup>The epoxidation was carried out in  $CH_2Cl_2$  using m-CPBA (1.5 equiv.) in the deep freeze (~ -20°) <sup>b</sup>Measured on the crude product by 300 MHz <sup>1</sup>H nmr spectrometry;

<sup>S</sup>No attempt was made to optimise the isolated yields. In all cases the crude yields of clean products were >90%, but for SiMe<sub>3</sub> and SiMe<sub>2</sub>Ph epoxides some decomposition was observed on silica gel chromatography. For most synthetic purposes the crude epoxide is suitable and overall yields are good.

greater than the difference in ground state energies. A possible representation of this is provided below in which the C-Si bond has been lined up with the *p*-orbitals of the  $\pi$ -bond for maximum stabilisation.<sup>8</sup> In this situation a branched R group might well exhibit a pronounced steric effect.



Irrespective of the detailed the reason(s) for this effect, the observations presented here make the application of the chemistry for organic synthesis both appealing and practical, and we are currently investigating the uses of this methodology for the synthesis of natural products and their analogues.

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## References

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- 7. We thank Prof. W.C. Still for this programme.
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- 9. Treatment of the epoxide (a) with aq HF/MeCN gave the elimination product (b) with no detectable double bond conjugation.



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