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RETENTION OF CONFIGURATION IN THE DESILYLATIVE HYDROXYALKYLATION OF α-SILYL SULFIDES

Patrick G. McDougal* and Brian D. Condon

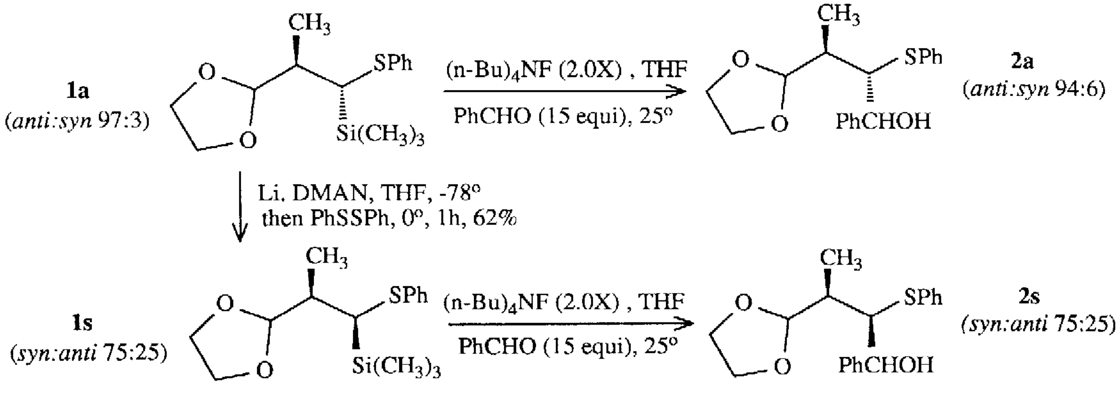
School of Chemistry, Georgia Institute of Technology, Atlanta, GA 30332

Summary: *The C-Si bond α to sulfur is replaced with retention of configuration when an α-silyl sulfide is treated with tetrabutylammonium fluoride in the presence of benzaldehyde.*

Since the advent of the fluoride initiated addition of allyl silanes to carbonyl compounds[1] the use of organosilanes as latent carbanions has attracted a considerable deal of attention.[2] Although majority of the work has concentrated on the transfer of allyl groups from allyl silanes, other groups can be transferred. These transferable groups include sulfur, nitrogen and phosphorus ylides[3a], benzyl[3b], acyl[3c,d], (benzothiazol-2-ylthio)alkyl[3e], azinonylmethyl[3f,g] and most recently phenylthiomethyl[3h]. Despite this activity no study has addressed the issue of stereoselectivity in the C-Si bond replacement of these fluoride initiated reactions.[4] As part of our ongoing studies on the chemistry of α-lithiated sulfides[5] we had synthesized an α silyl sulfide of defined stereochemistry (**1a**) which allowed us to investigate the stereoselectivity of C-Si bond replacement. We would like to report that the fluoride catalyzed desilylative hydroxyalkylation proceeds with retention of configuration.[4]

The preparation of silyl sulfide **1a**, highly enriched as the *anti* diastereomer, was previously reported.[5] From this isomer one could prepare a mixture of silyl sulfides in which the *syn* diastereomer **1s** predominated via the reductive desulfenylation methodology developed by Cohen.[6] With the two isomers in hand we developed a protocol for desilylative hydroxyalkylation which minimized protodesilylation. This involved drying the commercially available trihydrate of tetrabutylammonium fluoride as described in the literature[3,7] and using a large excess of benzaldehyde. Under these conditions the previously described alcohols **2**[8] were produced with between 10-20%

SCHEME 1



protodesilylation. As shown in Scheme I the *anti* isomer **1a** produced the *anti* alcohol **2a** and the mixture enriched in the *syn* isomer **1s** produced a mixture of alcohols **2s** enriched in the *syn* alcohol to the same degree. Consequently the C-Si bond is replaced with retention of configuration. There seems to be a small but noticable leakage of stereochemistry in the case of the *anti* isomer **1a**. We believe this to be due to a more facile protodesilylation of the *anti* isomer relative to the *syn* isomer. Evidence which supports this contention includes the production of more protodesilylated product from **1a** relative to **1s** (18% vs. 10%), an increased amount of stereochemical leakage (never more than 5-7%) with increased amounts of protodesilylation and a small increase in the ratio of **1s** to **1a** when the reaction went to partial completion and the recovered starting silyl material was analyzed by capillary gc. Hence what appears to be a stereochemical leakage is simply an enrichment of the *syn* isomer due to more rapid protodesilylation of **1a**.

The observation of retention of stereochemistry for the desilylative hydroxyalkylation reaction lends more experimental evidence to the notion that these reactions proceed through hypervalent silicon species and not free carbanions.[9] Our system is an especially good test case since we have independently established that the corresponding α-lithiated sulfides are configurationally labile and greatly prefer the α orientation[5]. Consequently the fact that the *syn* isomer **1s** reacts with retention of configuration is most supportive of the hypervalent silicon model for these reactions. No matter what the mechanistic implications of this result the fact that control of C-Si stereochemistry can be translated to control of C-C stereochemistry is significant.

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4. Fluoride initiated protodesilylation of silyloxiranes has been shown to occur with retention of configuration, see Chan, T. H.; Lau, P. W. K.; Li, M. P. *Tetrahedron Lett.* **1976**, 2667.

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7. As previously noted solutions of dry TBAF are unstable toward Hofmann elimination and consequently we prepared fresh TBAF solutions before each reaction, see Sharma, R. K.; Fry, J. L. *J. Org. Chem.* **1983**, *48*, 2112.

8. The crude mixture of the alcohols is converted to the corresponding acetates (acetic anhydride, DMAP, CH_2Cl_2, overall yields from **1a** and **1s** ~60%) and this mixture is analyzed by ^1H NMR. All the stereochemical assignments rest on an x-ray crystal structure of one of the *anti* alcohols (see ref 5). The mixture of stereochemistry at the newly formed stereogenic carbon is close to 1:1 for both **2a** and **2s**.

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