

The Conversion of Acyl Silanes into Chiral Secondary Alcohols

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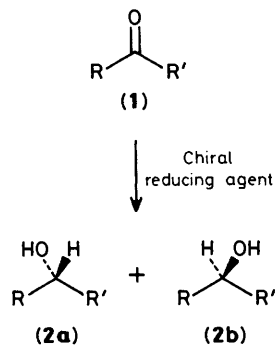
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Chiral secondary carbinols are prepared in high enantiomeric excess by a new process involving the reduction of acyl silanes and utilising a thermal rearrangement of α -acetoxy silanes.

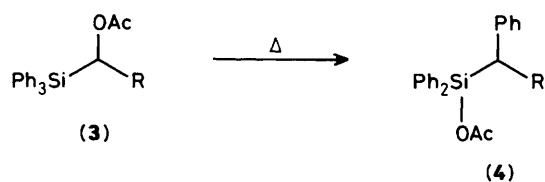
One goal of modern synthetic methodology is the development of a reducing agent which can reduce a prochiral ketone (**1**) to the corresponding alcohol (**2**) (Scheme 1) with high enantioselectivity no matter how small the steric and electronic difference in the two groups R and R'. It is perhaps not surprising that although the enantioselectivity of such reducing agents continues to improve, selective reduction is only possible on compounds in which there is a relatively large difference (either steric or electronic) between the two groups. It is therefore reasonable that the large steric bulk of a trialkyl organosilane might improve the enantioselectivity of such a reduction on an acylsilane ($R' = SiR''_3$, R = alkyl or aryl). While such a reduction would be interesting, its

synthetic importance might be considered minimal as the chemistry of the resultant α -silylcarbinols has not yet been fully developed.

However, Brook and coworkers¹ demonstrated that α -acetoxy silanes (**3**) can, in certain cases, be thermally rearranged to the corresponding silyl acetates with migration of one of the alkyl groups from silicon to carbon (Scheme 2). This rearrangement has been largely unexplored, in terms of mechanistic study, and as a new method for the construction of a carbon-carbon bond. The synthetic utility is extended by the fact that the resultant acetoxy silane is a silafunction compound and is therefore readily convertible to the corresponding alcohol. It occurred to us that a study of the



Scheme 1



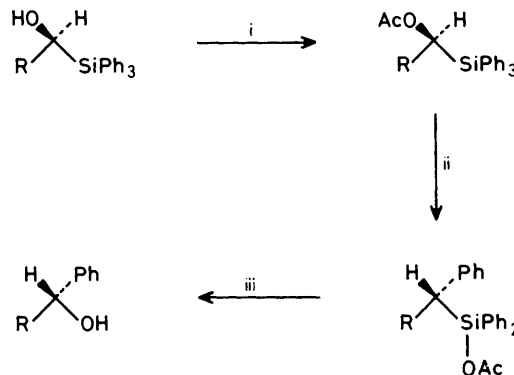
Scheme 2

Table 1. Reduction of acylsilanes using the Itsuno reagent.

Acylsilane	Product (yield)	E. e.
	(56%)	50%
	(71%)	94%
	(87%)	81%

reduction of acylsilanes with known asymmetric reducing agents might provide an unusual opportunity to investigate both the mechanistic and synthetic potential of this process.

We have discovered that the Itsuno reagent² (a 2 : 1 complex of borane and (*S*)-(-)-2-amino-3-methyl-1,1-diphenylbutan-1-ol respectively) reduces acylsilanes with good to excellent enantioselectivity. Not unexpectedly, as the steric bulk of the silyl group increases, so does the specificity of the reduction. Enantiomeric excess was measured by conversion to the Mosher ester and analysis of either the ¹⁹F or ¹H n.m.r. spectra in the presence of Eu(fod)₃ (fod = 1,1,1,2,2,3,3,3-heptafluoro-7,7-dimethyloctane-4,6-dionato) shift reagent.³ Assignment of absolute configuration was made by analogy with Itsuno's results on hindered ketones. As a further confirmation, it was found that the direction of rotation of the tolyl triphenylsilyl carbinol prepared by the Itsuno method was negative, whereas the rotation of resolved (*R*)-phenyl



Scheme 3. Reagents and conditions: i, Ac₂O, pyridine, 4-*N,N*-dimethylaminopyridine, 95% for (5), 96% for (6); ii, heat, quantitative; iii, H₂O₂, KF, KHCO₃, MeOH, 50% for (5) (95% e.e.), 51% for (6) (80% e.e.).

triphenylsilyl carbinol prepared by Mosher⁴ was positive, thus verifying the (*S*) stereochemistry as depicted in Table 1.

Compounds (5) and (6) were converted to the corresponding acetates, pyrolysed (sealed tube at *T* = 250–280 °C), and the resulting silafunctional compounds converted to the corresponding alcohols (Scheme 3). This final transformation is assured to occur with retention of configuration by analogy with the work of Tamao and Kumada⁵ as well as that of Fleming.⁶ The optical purity of these alcohols was once again assessed by the Mosher method (¹H and ¹⁹F n.m.r. spectroscopy) and found to agree with the optical purity of the intermediates (within the limits of error), thus indicating that the overall process is highly stereospecific. The absolute configuration was verified by comparison of the direction of optical rotation of these materials to that of partially chiral samples reported by other authors.⁷ Since the final oxidative cleavage is well established as occurring with retention of configuration, the thermolytic rearrangement must occur with inversion at carbon. This result agrees with that obtained by Larson⁸ in a similar rearrangement of an α-chloroalkylsilane. It should be noted that phenyl tolyl carbinol cannot, at present, be prepared in such high optical purity by direct reduction of the corresponding ketone. This method should thus be an excellent alternative to direct reduction in a number of cases.

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