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Synthesis of Optically Active α,β-Epoxysilanes and Silylaminoalcohols

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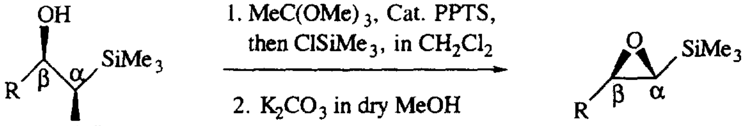
Abstract: A number of optically active α,β-epoxysilanes and silylaminoalcohols have been prepared from the corresponding chiral diols in high enantiomeric excess.

Epoxides are widely recognized as extremely versatile synthetic intermediates[1] and enantiomerically pure epoxides have found widespread use as chiral building blocks[2]. Recently a number of asymmetric catalytic methods have appeared for the synthesis of chiral epoxides[3]. The presence of a trimethylsilyl group on one of the carbons of the epoxide plays a key role in directing the ring opening reactions of epoxides[4], providing a regio and stereo controlled route to a number of β-substituted alcohols. Chiral α,β-epoxysilanes have also been used to prepare chiral α-hydroxyaldehydes[5]. To date most asymmetric syntheses of silylated epoxides have been based on the Sharpless asymmetric epoxidation of silyl substituted allylalcohols[6,7].This has been developed by Chan to include alkenylsilanols[8,9]. This letter describes an extension of our work on the preparation of optically active vicinal silyldiols[10]. We have prepared a range of synthetically valuable α,β-epoxysilanes in up to 65% yield with up to 95% ee, as shown in Scheme 1.We also report one type of selective ring opening leading to optically active silyl substituted aminoalcohols.



(1)

(2)

a. *trans*, R = butyl
b. *trans*, R = pentyl
c. *trans*, R = hexyl
d. *cis*, R = pentyl
e. *cis*, R = hexyl
f. *trans*, R = phenyl

Scheme 1: Synthesis of chiral α,β-epoxysilanes

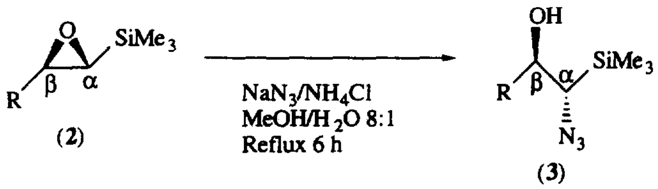
The general route[11,12] to the α, β-epoxysilanes involves initial cyclisation of the vicinal silyldiols with an orthoester in the presence of pyridinium p-toluenesulphonate (PPTS) giving the corresponding cyclic orthoester. This undergoes a ring opening reaction with chlorotrimethylsilane to give a halohydrin derivative. Finally cyclisation of this in the presence of sodium carbonate gives the α, β-epoxysilane. The absolute configurations of the diols are tentatively predicted using the Sharpless mnemonic. This has been confirmed for asymmetric dihydroxylation of trimethylsilyl substituted alkenes by degradation studies and comparison with authentic samples[10]. Other configurations are based on known stereochemical transformations. The isolated yields and enantioselectivites of the α,β-epoxysilanes prepared are reported in Table 1. Unfortunately it was not possible to convert the trimethylsilyl-β,γ-diols into the corresponding epoxides because of the competing Peterson elimination.

Table 1: Yields and purities of optically active α, β-epoxysilanes and Silylaminoalcohols.

Silyldiols		α,β-epoxysilanes				Silylazidoalcohols		Silylaminoalcohols			
No	config	No.	ee%	yield %	config.	No.	yield%	No.	ee%	yield %	config.
1a*	1R,2R	2a*	95	62	1R,2R	3a	81	4a	95	87	1S,2R
	1S,2S		95	63	1S,2S		82		95	85	1R,2S
1b	1R,2R	2b	95	65	1R,2R	3b	84	4b	95	89	1S,2R
	1S,2S		95	64	1S,2S		83		95	87	1R,2S
1c	1R,2R	2c	95	63	1R,2R	3c	87	4c	95	86	1S,2R
	1S,2S		95	65	1S,2S		84		95	90	1R,2S
1d	1R,2R	2d	61	60	1R,2S	3d	85	4d	61	85	1S,2S
	1S,2S		61	62	1S,2R		82		61	89	1R,2R
1e	1R,2S	2e	61	61	1R,2S	3e		4e	-	-	-
	1S,2R		61	62	1S,2R				-	-	-

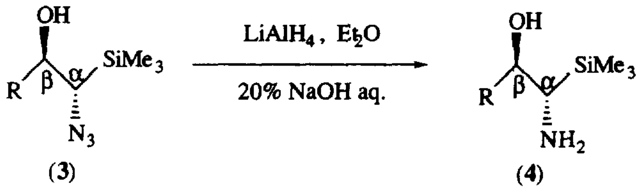
*The enantiomeric excess was determined by glc using a Chiraldex G-PN 20m x 0.25 mm chiral column. In all other cases the enantiomeric excess was determined by ^{13}C NMR in the presence of $[Eu(hfc)_3]$

Like all simple epoxides, α,β-epoxysilanes undergo ring opening with a variety of reagents. However, the silicon exerts a powerful directing effect such that these ring openings usually proceed via nucleophilic attack at the carbon bearing the silicon[4]. Thus we have been able to ring open regioselectively optically active epoxides with azide ion, as shown in Scheme 2[13].



Scheme 2: Formation of silylazidoalcohols

The regiochemistry of the ring opening can be determined from the heteronuclei and homonuclei COSY 2D NMR spectra which clearly show a correlation between the protons on the hydroxy bearing carbon and the proton of the hydroxy group. The hydroxy bearing-carbon and azido-bearing carbon can also be located by comparison between H^1-H^1 COSY 2D NMR spectra and C^1-H^1 COSY 2D NMR spectra. In all the azide ring openings attempted, no evidence of β attack was observed.



Scheme 3: Reduction of silylazidoalcohols

Reduction of the silylazidoalcohols with lithium aluminium hydride led cleanly to the corresponding chiral aminoalcohols, as shown in Scheme 3[14]. The isolated yields and enantiomeric excesses of the aminoalcohols prepared are listed in Table 1. Interestingly when R was a phenyl group, **1f**, no halohydrin was formed and so no α, β-epoxysilane could be obtained. In this case *trans* β–trimethylsilylstyrene was recovered in almost quantitative yield, possibly via an Eastwood reaction[15].

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12. General procedure for the preparation of α, β-epoxysilane: Chlorotrimethylsilane (6 mmol, 0.76 ml) was added to a solution of the trimethylsilyldiol[5] (5 mmol), trimethyl orthoacetate (5.95 mmol, 0.76 ml) and PPTS (0.05mmol, 12.5 mg) in dichloromethane (15 ml) at 0°C under nitrogen. The solution was stirred for 60 min., then evaporated to obtain the crude trimethylsilylacetoxy halide. The crude product was dissolved in a solution of K_2CO_3 (12.5 mmol, 1.73 g) in dry methanol (10 ml). The suspension was stirred vigorously for 100 min., then filtered and the residue washed with CH_2Cl_2. The filtrate was evaporated using a rotary evaporator at room temperature under vacuum (water aspirator) and the residue purified by flash chromatography on silica gel (Hexane : EtOAc : Et_2O = 75 : 20 : 5). The purity of the α, β-epoxysilane was checked using a glc with a BP-5 column (70-170°C).
13. General procedure for the preparation of silylazidoalcohols: To a 100 ml round-bottomed flask equipped with a condenser and a magnetic stirrer bar was added the trimethylsilyl epoxide (3 mmol), ammonium chloride, (6 mmol, 321 mg), sodium azide (15 mmol, 975 mg), methanol (16 ml) and water(2 ml). The mixture was refluxed for 6 h and then cooled to room temperature. The methanol was removed under vacuum and the residue was extracted three times with ether (15ml). The extracts were dried over $MgSO_4$ and concentrated using a rotary evaporator to obtain the crude silylazidoalcohol. The crude product was purified by flash chromatography on silica gel [petroleum ether.(45-60°C) : EtOAc : Et_2O = 75 : 20 ; 5].
14. General procedure for the preparation of silylaminoalcohol: To a round-bottomed flask equipped with reflux condenser, nitrogen inlet bubbler and a magnetic stirrer bar was added the silylazidoalcohol (2 mmol) in dry diethyl ether (15 ml). To this was added lithium aluminium hydride (4 mmol, 152 mg), carefully and slowly. The reaction mixture was stirred at room temperature for 2 hours, and then 5 ml of 20% sodium hydroxide was added gradually. The mixture was separated and the aqueous phase was extracted with ether (15 X 3 ml). The ethereal extracts were dried over $MgSO_4$ and concentrated to give the silylaminoalcohol.
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