Enantioselective Synthesis of Epoxides: Sharpless Epoxidation of Alkenylsilanols

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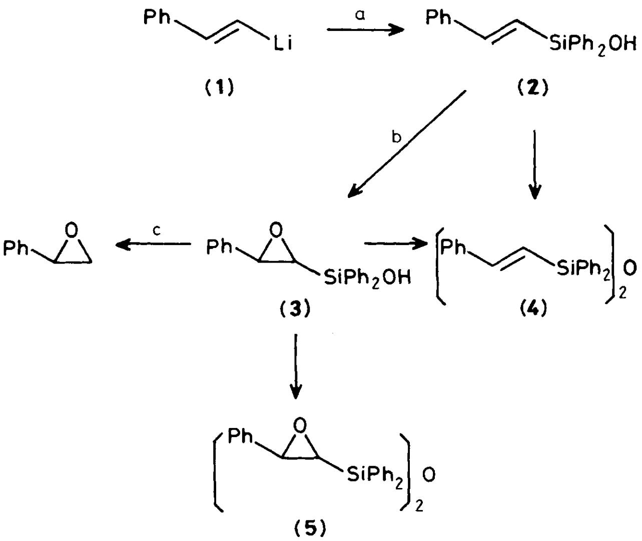
Sharpless epoxidation of the alkenylsilanol (**6**) followed by protodesilylation gave styrene oxide with high enantiomeric excess.

The Sharpless epoxidation[1—3] has been hailed as one of the milestones in organic chemistry. The reaction gives chiral epoxides with predictable stereochemistry and high enantiometric purity. However, the reaction is limited to allylic alcohols. The hydroxy group plays a critical role in assembling the reactants together, thus accelerating the reaction as well as conferring high stereoselectivity. For simple alkenes without the pendant hydroxy group, Sharpless epoxidation is not useful. There is no ready method for preparing simple chiral epoxides (*e.g.* styrene oxide) with high enantioselectivity. We report an approach to this problem.

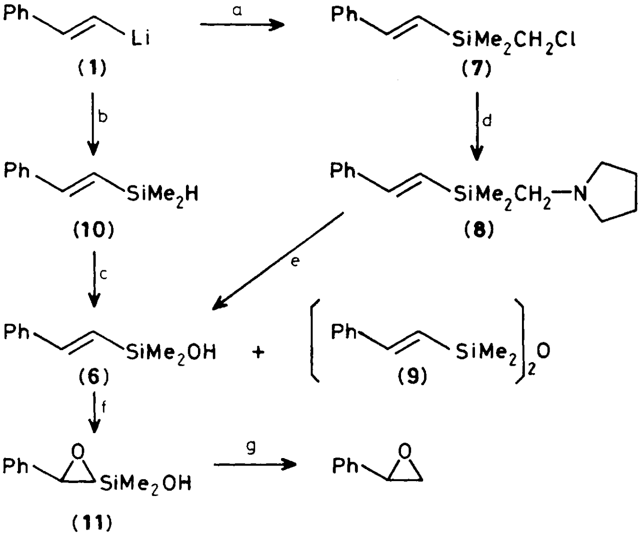
We have previously shown that trimethyl- or triphenyl-silyl epoxides can be protodesilylated in the presence of fluoride ion to give the corresponding epoxides with retention of stereochemistry.[5] It seemed to us that alkenylsilanols, which are structurally similar to allylic alcohols, should be amenable to Sharpless epoxidation. The silyl group could then be excised by fluoride ion to give the simple epoxides. We demonstrated the viability of this approach by the enantioselective synthesis of styrene oxide.

Metal–halogen exchange of *trans*-β-bromostyrene with t-butyl-lithium gave *trans*-β-lithiostyrene (**1**). Reaction of (**1**) with diphenyldichlorosilane followed by aqueous hydrolysis of the product gave the silanol (**2**) in good yield. Epoxidation of (**2**) with *m*-chloroperbenzoic acid gave the corresponding epoxysilanol (**3**). Treatment of (**3**) with tetraethylammonium fluoride hydrate in MeCN gave styrene oxide in excellent yield.

When (**2**) was subjected to Sharpless epoxidation conditions [$\text{Ti(OPr}^i)_4$/(+)-diethyl tartrate (DET)/t-butyl hydroperoxide (TBHP)][1] in CH_2Cl_2 at −40 °C, the reaction was very slow. The reaction was faster at −20 °C, giving (**3**) in 70% yield after 48 h. The epoxide (**3**) was optically active {$[\alpha]_D^{22}$ −4.8° (*c* 0.25, C_6H_6)} The hydroxy group was critical in this reaction as demonstrated by the following experiment. Compound (**2**) dimerised on long standing to give the disiloxane (**4**). When (**4**) was subjected to identical Sharpless epoxidation condi-



Scheme 1. *Reagents and conditions:* (a), Ph_2SiCl_2/Et_2O/−78 °C, then Et_3N/H_2O; (b), $\text{Ti(OPr}^i)_4$/(+)-DET/TBHP/CH_2Cl_2/−20 °C; (c), Et_4NF/MeCN/room temp.



Scheme 2. *Reagents and conditions:* (a), $Me_2Si(Cl)CH_2Cl/Et_2O/$ -25 °C; (b), $Me_2SiHCl/Et_2O/-20$ °C; (c), $AgNO_3 + Ag_2O(1:6)/$ THF/room temp.; (d), pyrrolidine/80 °C; (e), TBHP/VO(acac)$_2$/ acetone; (f), Ti(OPr^i)$_4$/(+)-DET/TBHP/CH_2Cl_2/-20 °C; (g), Et_4NF/ MeCN/room temp.

tions, compound (**5**) was not observed, even after a prolonged reaction time at a higher temperature. Protodesilylation of (**3**) by fluoride ion gave (*S*)-styrene oxide with 7% enantiomeric excess (e.e.) according to optical rotation as well as ^{1}H n.m.r. using tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III), [(+)-Eu(hfc)$_3$]. The use of molecular sieves, as recommended recently by Sharpless,[4] improved slightly the rate of epoxidation and the e.e. of the styrene oxide obtained to 20%. We attributed the low stereoselectivity of the reaction to the steric effect of the diphenylsilyl group. While the Sharpless epoxidation has been successful with allylic primary and secondary alcohols, there is little information on the stereoselectivity for allylic tertiary alcohols. We decided to examine the corresponding dimethylsilanol (**6**).

Compound (**6**) could not be prepared in good yield by the reaction of (**1**) with dimethyldichlorosilane or dimethyldiethoxysilane. On the other hand, reaction of (**1**) with choloromethyldimethylchlorosilane gave compound (**7**) (82% yield). Heating (**7**) in pyrrolidine[6] at 80 °C for 20 h gave the aminosubstituted silane (**8**) in 73% yield. Oxidation[7] of (**8**) with *m*-chloroperbenzoic acid (MCPBA)/$CaCO_3$ in CH_2Cl_2 or TBHP/VO(acac)$_2$ (Hacac = pentanedione) in acetone gave a mixture of the silanol (**6**) and the disiloxane (**9**) which could be separated by flash chromotography (hexane–ethyl acetate, 5 : 1). Compound (**6**) can be more conveniently synthesized by an alternative route. Reaction of (**1**) with dimethylchlorosilane gave the silane (**10**) in 92% yield. Oxidation of (**10**) with silver nitrate/silver oxide (1 : 6) in tetrahydrofuran (THF) at room temperature for 9 h gave (**6**) (71%). Epoxidation of the freshly purified (**6**) under Sharpless conditions[1] with (+)-DET in CH_2Cl_2 at -20 °C for 40 h gave compound (**11**) (50% yield), again purified by flash chromatography. Fluoride ion cleavage of (**11**) gave (*S*)-styrene oxide (90% yield) with high enantiomeric excess [85—95%, depending on different runs, according to optical rotation and ^{1}H n.m.r. with (+)-Eu(hfc)$_3$]. It is interesting that the stereochemistry obtained is in agreement with the stereochemical model proposed by Sharpless for allylic alcohols.[2]

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