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Enantioselective Synthesis of γ-Hydroxysilanes, 1,3-Diols and Cyclopropanes by Reaction of a Chiral Epoxide with a Racemic α-Silyl Organolithium Reagent

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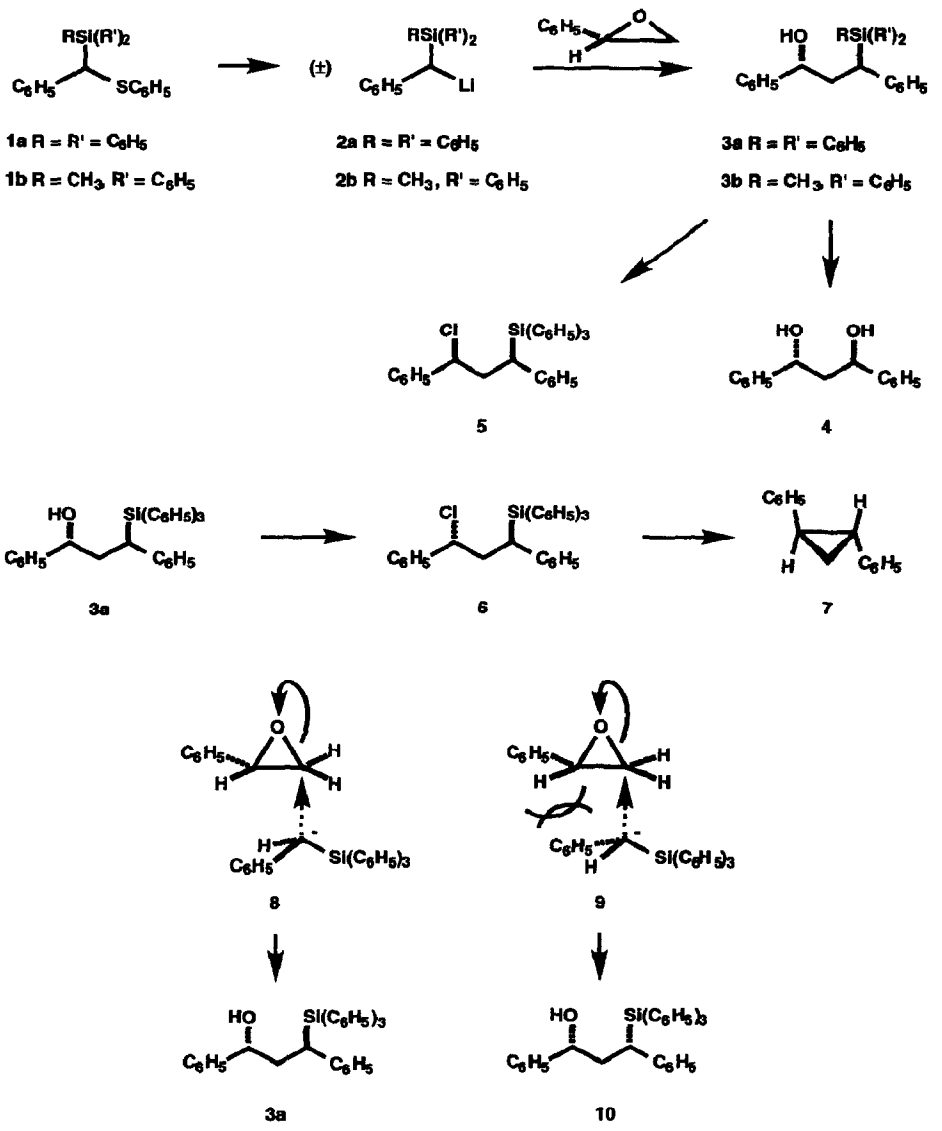
*Summary: The racemic α-silyl organolithium reagents **2a** and **2b** react with (R)-styrene oxide enantioselectively to produce the chiral γ-hydroxysilanes **3a** and **3b**, respectively. The chiral 1,3-diol **4** and cyclopropane **7** are readily obtained in enantiomerically pure form from these γ-hydroxysilanes.*

In this paper we describe the application of α-silyl organolithium reagents to the synthesis of chiral γ-hydroxysilanes, 1,3-diols and cyclopropanes of high enantiomeric purity. The specific substrates used in this study were (*R*)-(–)-styrene oxide and a racemic α-triorganosilylbenzyllithium reagent. Under the proper conditions these reagents react with a surprisingly high degree of 1,3-diastereoselectivity to produce a single γ-hydroxysilane. This diastereoselectivity, which has been shown to be the result of three different factors, demonstrates still another facet of silicon-mediated stereochemical control[1] and an enhanced synthetic versatility of the readily available α-silyl organolithium reagents.[2]

α-Triphenylsilylbenzyl phenyl sulfide (**1a**) was converted to α-triphenylsilylbenzyllithium **2a**[3] by reaction with 4 equiv of lithium dispersion and 0.05 equiv of naphthalene in tetrahydrofuran (THF) at -30 °C for 3 h, and the resulting reagent was treated with 1.1 equiv of (*R*)-(–)-styrene oxide (97.2% ee)[4] at -78 °C initially, with gradual warming to 23 °C over 12 h. After extractive isolation and chromatography on silica gel, the γ-hydroxysilane **3a**, mp 63-66 °C, $[\alpha]_D^{23}$ +63.1° (c=1.15, $CHCl_3$), was obtained in 64% yield and 97% enantiomeric excess (ee) as determined by HPLC analysis using a chiral column.[5] Chromatographic analysis of **3a** revealed only a trace of the diastereomeric γ-hydroxysilane (ratio of **3a** to diastereomer *ca.* 200 : 1). In parallel experiments the α-silylsulfide **1b** was converted via **2b** to the γ-hydroxysilane **3b** in 66% yield and 97% enantiomeric excess.[5] The absolute and relative configuration of **3b**, isolated as a colorless glass, $[\alpha]_D^{23}$ +53.4° (c=1, $CHCl_3$), was determined by oxidative desilylation using Fleming's method.[6] Reaction of **3b** with 2 equiv of mercuric acetate and excess 15% peroxyacetic acid in acetic acid at 23 °C for 12 h followed by treatment of the resulting mixture of **4** and its monoacetate with potassium hydroxide in methanol at 75 °C for 2 h gave after chromatography the chiral 1,3-diol **4**[7] in 77% yield and with >99% ee,[5] mp 146.5-147.5 °C, $[\alpha]_D^{23}$ +52° (c=0.5, $CHCl_3$). Similarly, oxidative desilylation of **3a** also afforded **4**.

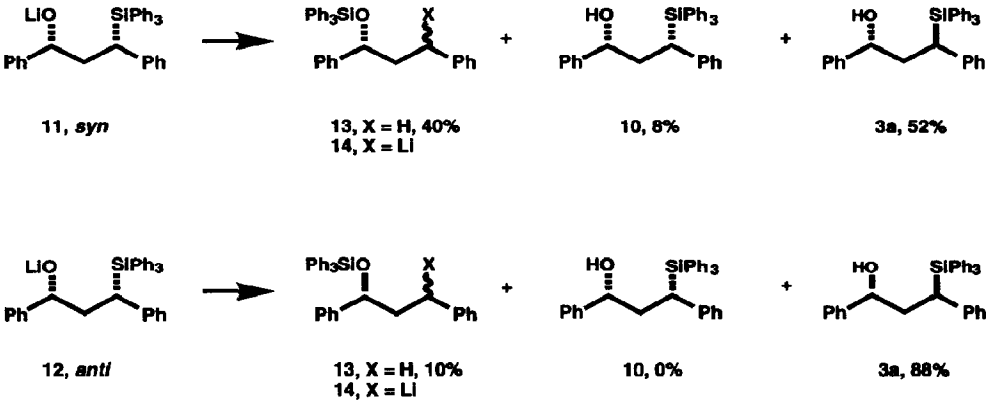
Reaction of **3a** with hexachloroacetone and triphenylphosphine in THF at -78 °C for 30 min (Mitsunobu inversion conditions[8]) afforded 91% yield of a single γ-chlorosilane (**5**), mp 144-147 °C, $[\alpha]_D^{23}$ +46.6° (c=1.1, $CHCl_3$), whereas reaction of **3a** with $SOCl_2$ and pyridine in CH_2Cl_2 at 23 °C for 30 min gave cleanly (in 92%



yield) a different diastereomer **6**, mp 139-142 °C, $[\alpha]_D^{23}$ +125° (c=1.1, $CHCl_3$). Treatment of **6** with excess anhydrous CsF in CH_3CN at 23 °C for 60 h produced in 87% yield *trans*-(*R*,*R*)-(–)-1,2-diphenylcyclopropane, $[\alpha]_D^{23}$ -425° (c=1, $CHCl_3$).[9,10]

Several of the transformations outlined above are noteworthy from a stereochemical and mechanistic point of view. Foremost is the highly selective reaction of (*R*)-(–)-styrene oxide with α-silylcarbanions **2a** and **2b** which we discuss for the case of **2a**. The sterically most favorable transition state geometries for the enantiomers of **2a** in an S_N2 displacement with styrene oxide are depicted in formulas **8** and **9**. Reaction via pathway **8**,

which leads to the observed reaction product **3a**, is clearly favored relative to reaction via **9** (which produces **10**) because of the serious phenyl–phenyl repulsion which is shown in **9**. However, it can be demonstrated experimentally that two other factors also contribute to the high degree of diastereoselectivity observed under the conditions described above for the transformation **2a** → **3a**. When the reaction of (*R*)-(–)-styrene oxide and **2a** is conducted at -78 °C for 2 h and quenched at that temperature, *two* γ-hydroxysilanes are obtained, **3a** (63%) and the *syn* diastereomer **10** (20%). Diastereomers **3a** (*anti*) and **10** (*syn*) were readily separated by silica gel chromatography (ether–hexane) and isolated in pure condition. Each of these diastereomers was converted to the lithium alkoxide (1 equiv of *t*-BuLi at -78 °C in THF for 5 min) which was allowed to undergo reaction at 0 °C for 1 h with the following results:

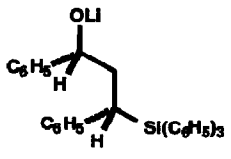


Clearly, equilibration of *syn*- and *anti*-γ-oxidosilanes (**11** and **12**), occurs at 0 °C via C ⇆ O rearrangement of Ph_3Si to form the benzylic anion **14**, and **13** is simply the product of protonation of **14**. Further, the *anti* γ-oxidosilane **12** is both thermodynamically more stable than the *syn* γ-oxidosilane **11**, and kinetically more stable with regard to C → O rearrangement of Ph_3Si to form **14**. The relative stabilities of **11** and **12** may be explained on the basis of the preferred conformers **11'** and **12'**.

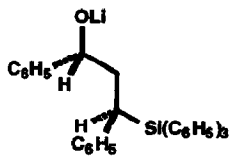
The completely stereospecific replacement of hydroxyl in **3a** by chlorine with retention of configuration to give chlorosilane **6** is of considerable interest since it is suggestive of participation by the γ-silicon substituent. *One* possibility for such participation is shown in the sequence **15** → **16** → **6**.

Finally, the fluoride-induced stereospecific cyclization of the γ-chlorosilane **6** to *trans*-(*R*,*R*)-(–)-1,2-diphenylcyclopropane (**7**) can be explained by a process such as that summarized in formula **17**.[10] In the case of the transformations involving **16** and **17**, electrophilic attack occurs at the backside of carbon relative to the triphenylsilyl group. Excellent precedence for this stereochemistry is found in the studies by Shiner et al. on the kinetics of solvolysis of *cis* and *trans*-3-trimethylsilylcyclohexyl brosylates.[11]

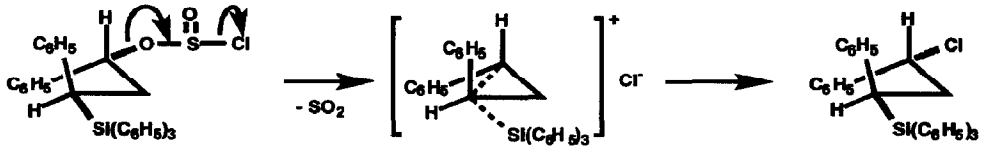
In summary, this research has demonstrated an interesting way to produce carbon stereocenters bearing a triorganosilyl substituent and the application of such compounds to enantioselective synthesis of *inter alia* chiral 1,3-diols and cyclopropanes.[12]



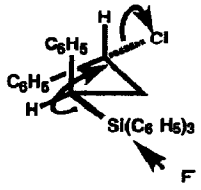
11', *syn*
(less stable)



12', *anti*
(more stable)



15 16 6



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References and Notes

1. For a review see Fleming, I. in *Silicon Compounds, Register and Review, Petrarch Systems*, Bristol, PA 19007, 1987, pp. 21-31.
2. For reviews see (a) Colvin, E. W. *Silicon in Organic Synthesis*, Butterworths, London, 1981; Chapter 4. (b) Weber, W. P. *Silicon Reagents for Organic Synthesis*, Springer Verlag, Berlin, 1983; Chapter 6. (c) Colvin, E. W. in *Chemistry of the Metal–Carbon Bond*, Hartley, F. R., Ed., John Wiley and Sons, Inc., New York, 1987; Vol. 4, Chapter 6.
3. Ager, D. J. *J. Chem. Soc. Perkin Trans. I* **1986**, *186*, 195.
4. Corey, E. J.; Shibata, S.; Bakshi, R. K. *J. Org. Chem.* **1988**, *53*, 2861.
5. HPLC analysis for enantiomeric purity was performed using a Chiral Technologies AD analytical column at 23 °C, 1 ml/min flow rate with 5% isopropyl alcohol in hexane for elution of **3a** and **3b** and 7.5% isopropyl alcohol in hexane for elution of **4**.
6. Fleming, I.; Sanderson, E. J. *Tetrahedron Lett.* **1987**, *28*, 4229. The conversion of **3** → **4** proceeds with overall retention of configuration by Hg(II)-promoted replacement of phenyl by acetoxy at silicon, then silylperoxyacetate formation and rearrangement.
7. (a) For the absolute configuration of **4**, see Yamamoto, K.; Ando, H.; Chikamatsu, H. *J. Chem. Soc. Chem. Commun.* **1987**, 334 and refs cited therein. (b) For the application of chiral organosilicon compounds to the synthesis of chiral 1,3-diols see Chan, T. H.; Nwe, K. T. *J. Org. Chem.* **1992**, *57*, 6107.
8. Magid, R. M; Fruchey, O. S.; Johnson, W. L.; Allen, T. G. *J. Org. Chem.* **1979**, *44*, 359.
9. For absolute configuration of **7**, see Aratani, T.; Nakanisi, Y.; Nozaki, H. *Tetrahedron* **1970**, *26*, 1675.
10. The reaction of chlorosilane **5** with CsF, as expected, leads to *cis*-1,2-diphenylcyclopropane. In addition, some *trans-(S,S)*-(+)-1,2-diphenylcyclopropane, $[\alpha]_D^{23}$ +423° (c=0.4, $CHCl_3$), is formed by what is probably a two-step, carbanion-mediated internal S_N2 pathway.
11. Shiner, V. J.; Ensigner, M. W.; Kriz, G. S. *J. Am. Chem. Soc.* **1986**, *108*, 842.

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