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ASYMMETRIC SYNTHESIS VIA CHIRAL SILICON REAGENTS.[1]
CHIRAL α-HYDROXYALKYL ANION EQUIVALENTS FROM VINYLSILANES CONTAINING OPTICALLY ACTIVE AMINO OR ALKOXY GROUPS ON SILICON

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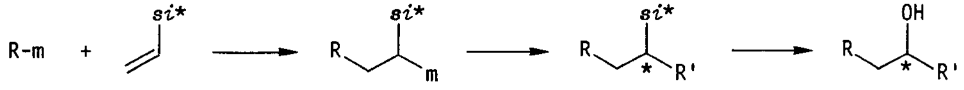
Summary: Chiral vinylsilanes containing optically active functional groups on silicon have been used as precursors for chiral α-hydroxyalkyl anion equivalents via a sequence of addition of *n*-butyllithium, coupling with organic halides, and oxidative cleavage of the silicon-carbon bond, to give optically active alcohols of up to 60% ee.

In spite of a wide spread synthetic applications of organosilicon compounds,[2] little attention has been paid to asymmetric synthesis via chiral organosilicon reagents. The main reason is apparently due to the difficulties in obtaining optically active organosilicon compounds, especially those in which the chiral center is the silicon atom itself.[3] Quite recently myrtanylhydrosilanes, in which chiral centers lie remote from silicon, have been used as asymmetric reducing agents for ketones.[4]

We have been interested in exploring the utility of silafunctional compounds as synthetic reagents. One of the advantages of silafunctional silicon reagents resides in the ready availability of a variety of alkoxy- or amino-silicon compounds. Optically active alcohols or amines promise a short route to chiral silicon compounds.[5] In this report we describe our initial results concerning asymmetric synthesis via chiral silafunctional compounds.

Chiral vinylsilanes, 1 and 2, have been prepared and used as precursors for chiral α-hydroxyalkyl anion equivalents[6] on the basis of our previous results,[1] as shown in eq. 1, where *si** represents a chiral silicon moiety.



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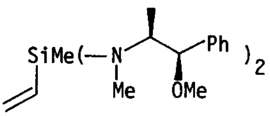

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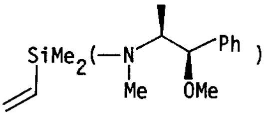

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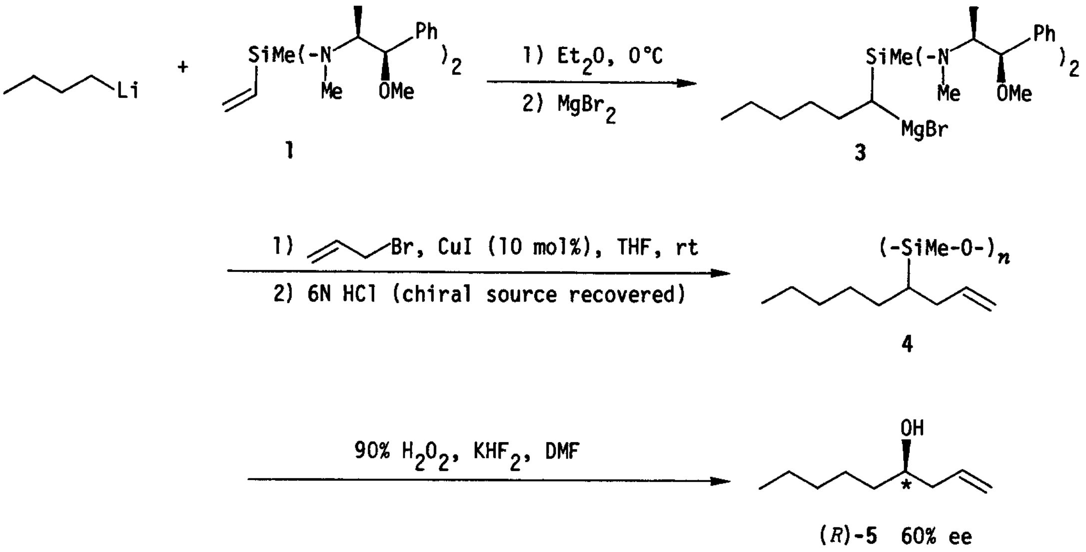
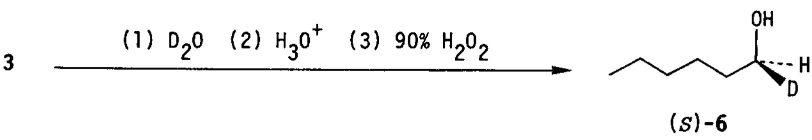


Scheme 1

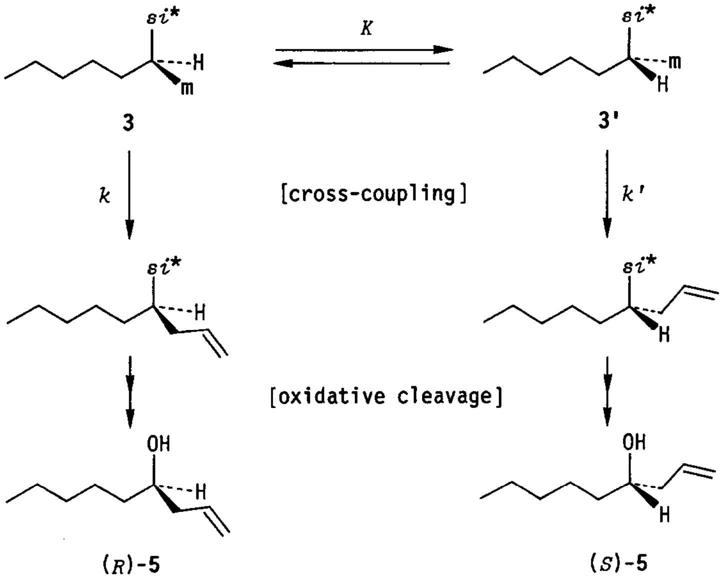
A typical transformation is illustrated in Scheme 1. The chiral vinylsilane 1 was prepared in situ by treatment of vinylmethyldichlorosilane, CH_2=$CHSiMeCl_2$, with an *N*-lithio derivative of (-)-ephedrine methyl ether[7] in ether at -78°C ∿ 0°C. To the resulting mixture was added *n*-BuLi (2 equiv) in hexane at 0°C to form the α-silylalkyllithium reagents, which was converted to the magnesium reagent 3 by treatment with $MgBr_2$. The cross-coupling reaction was carried out by successive addition of THF, allyl bromide (2 equiv), and CuI (10 mol%) at 0°C followed by stirring at room temperature for 6 h. The mixture was decomposed by 6N HCl to give polysiloxanes 4. By this operation the chiral ligand was recovered in about 80% recovery.[8] The resulting siloxanes were oxidized by 90% H_2O_2 in the presence of KHF_2 to form optically active 1-nonen-4-ol (5) with $[\alpha]_D^{20}$ +2.37° (*c* 2.3, $CHCl_3$) in 51% overall yield based on the vinylchlorosilane. The enantiomeric purity of 5 was determined to be 60% by ^1H NMR studies of its acetate using $Eu(dcm)_3$. Hydrogenation (H_2, Pd/C) of (+)-5 gave (*S*)-(+)-4-nonanol[9] with $[\alpha]_D^{20}$ +0.57° (*c* 5.8, hexane), indicating that (+)-5 should have the *R* configuration.

Although the mechanism of this new type of asymmetric reaction seems not to be simple, as shown in Scheme 2, the following results may delineate the crucial step for the asymmetric induction. (1) It has already been established that the oxidative cleavage of the silicon-carbon bond by H_2O_2 proceeds with retention of configuration at carbon.[10] (2) The α-silylalkyl anion species 3 was quenched by D_2O at 0°C and at -78°C, followed by oxidative cleavage to form 1-deuterio-1-hexanol (6) with, respectively, 19% ee and 28% ee of *S* isomer[11] (eq. 2).



(2)

Although (*S*)-6 has the same relative configuration as that of (*R*)-5, the optical purity is much lower than that of the latter. (3) The optical yields were not largely affected by the temperatures at which the coupling reaction was conducted, as shown by the following results: 56% ee at -10°C and 52% ee at +40°C.



Scheme 2

The D_2O-quenching experiment indicates that the anion 3 exists as an equilibrium diastereomeric mixture in unequal amounts at 0°C ∿ -78°C; $K \approx 60/40 \sim 65/35$. Since the optical yield of (*R*)-5 was higher than that of α-deuterio alcohol 6, the coupling should be the crucial step for the asymmetric induction, $k > k'$ in this case, although the temperature dependency was small in the range examined.

In accordance with this mechanism, the optical yields were dependent upon the structure of alkyl halides. For example, allyl chloride and iodide gave (*R*)-5 of 48% ee and 57% ee, respectively, while methallyl chloride, methyl iodide, and *n*-propyl iodide gave 2-methyl-1-nonen-4-ol (18% ee), 2-heptanol (2% ee), and 4-nonanol (4% ee), respectively.

Monoaminosilyl derivative 2 also gave (*R*)-5 of 51% ee in 38% overall yield, indicating that only one chiral ligand is sufficient for the similar asymmetric induction.[12]

Although the optical yields are not necessarily satisfactory at the present time, the results described herein suggest that chiral silafunctional reagents may open a new field in asymmetric synthesis. Desigh of chiral ligands on silicon and further applications of chiral silicon reagents will be the subject of our future publications.

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(7) The methyl ether was prepared in 73% yield, bp 84-85°C/7 mmHg, from (-)-ephedrine by the successive treatment with KH and methyl iodide in THF: $[\alpha]_D^{20}$ -84.4° (*c* 1.0, $CHCl_3$). Cf., A. I. Meyers, G. S. Poindexter, and S. Brich, *J. Org. Chem.*, 43, 892 (1978).

(8) The recovered chiral ligand 1 showed $[\alpha]_D^{20}$ -83.8° (*c* 1.0, $CHCl_3$) and was used for the same transformation to give (*R*)-5 of 50% ee in 55% overall yield.

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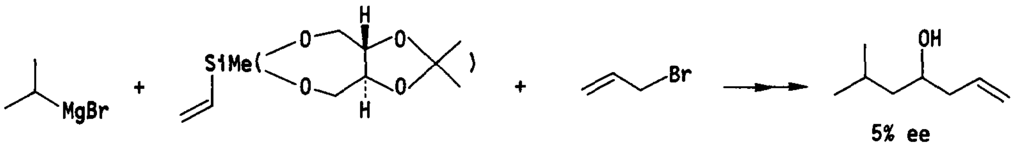
(11) Determined by ^1H NMR using $Eu(hfc)_3$. C. J. Reich, G. R. Sullivan, and H. S. Mosher, *Tetrahedron Lett.*, 1505 (1973).

(12) In the early stages of this study, chiral (alkoxy)vinylsilanes, 7 and 8, were also examined in the similar transformation, but, unfortunately, the optical yields were lower than 10% ee, as shown by the following results.



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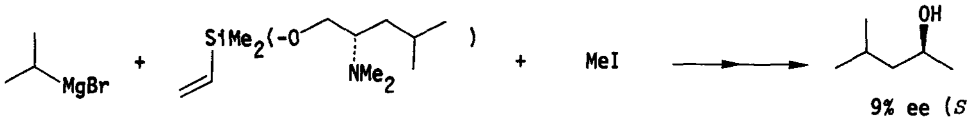

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