

CHIRALITY TRANSFER FROM SILICON TO CARBON: USE OF OPTICALLY PURE CYCLIC SILANES WITH A BINAPHTHALENE CHIRAL UNIT

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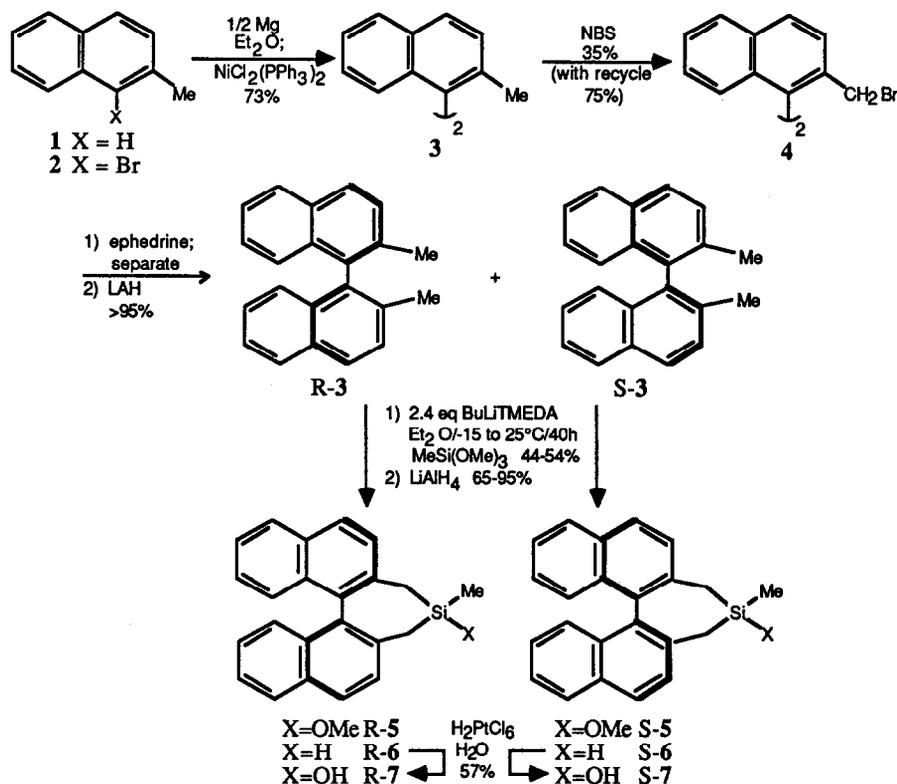
Abstract: The optically pure binaphthyl cyclic silanes R-6 and S-6 have been prepared and used in reductions and aldol condensations to achieve some of the highest ee's yet reported for chirality transfer with organosilanes.

A major goal in synthetic organic chemistry today is the easy and efficient production of optically active materials from prochiral precursors by asymmetric induction.² Great advances have been made recently in this area in a wide variety of reaction types: epoxidation,^{3a} oxidation,^{3b-e} reduction,^{3e-h} 1,4-addition,^{3e} alkylation,^{3ijk} aldol condensation,^{3il} and cycloaddition.^{3m-p} These procedures provide excellent methods for chirality transfer from a chiral substrate or auxiliary to a prochiral molecule to give high diastereomeric or enantiomeric excess, with return of the chiral auxiliary for recycling in most cases. However, even with all the recent advances, further developments are still needed. In particular it would be extremely valuable if the hundreds of synthetically useful reactions of organosilanes could be carried out with chirality transfer. We report now one of the highest enantioselections reported to date for chirality transfer from an optically active organosilane to a prochiral molecule.

The last twenty years or so have witnessed an exponential growth in the use of organosilicon compounds in synthesis. And yet the attempts to use chiral organosilanes to effect chirality transfer are quite few and have been generally unsuccessful. Nearly all of them have used the chiral methyl 1-naphthyl phenyl silane substitution first developed by Sommer. Paquette reported very low ee's (3.9-5.5%) in the reaction of chiral allyl silanes with acetals^{4a} while Fry also observed low ee's (6.6-12.7%) in hydride reductions of alkyl aryl ketones.^{4b} Even when the chiral silyl unit remains as part of the final molecule, the diastereoselection is often quite low.^{5,6} We believe that the very low ee's seen in these systems may be due to the nature of the Sommer chiral silyl system where the enantioselectivity depends on the difference between a 1-naphthyl and a phenyl group, a difference which would be expected to be quite small.⁷ For this reason we began a study of the use of more chirally biased systems and chose as our first system one containing a binaphthyl unit, which would have C-centered rather than Si-centered asymmetry.

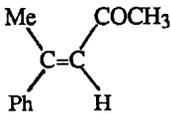
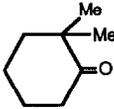
The optically pure binaphthyl cyclic silanes R-6 and S-6 were prepared from 2-methylnaphthalene **1** as follows. Nickel-catalyzed coupling of 1-bromo-2-methylnaphthalene **2** (prepared in high yield by bromination of **1**) via its Grignard reagent produced the racemic dimethylbinaphthalene **3** in 73% yield. Free radical bromination of **3** produced the bis(bromomethyl)binaphthalene **4** in a yield of 35% after two recrystallizations. The rest of the material was recycled in 4 steps [rebromination to give the bis(dibromomethyl)binaphthalene, hydrolysis to the dialdehyde, reduction to the diol, and final conversion to the dibromide **4**]. In this way, the overall yield of **4** from **3** was raised to 75%. Formation of the diastereomeric salts with ephedrine and separation of the diastereomers proceeded quite well by the literature procedure.⁸ Reduction of the separated salts with LAH produced the desired optically pure enantiomers of the dimethylbinaphthyl R-3 and S-3 in >95% yield. Finally formation of the dianion of the separate enantiomers of **3** with

2.4 eq of butyllithium/TMEDA in ether⁹ followed by addition of methyltrimethoxysilane afforded the enantiomeric cyclic methoxysilanes R-5 and S-5 in 44-54% yield, based on recovered starting materials.¹⁰ Reduction of the silicon-oxygen bond of 5 was easily accomplished with LiAlH₄ in 65-95% yield to produce the desired silanes R-6 and S-6. In order to determine the optical purity of the cyclic silane enantiomers, each enantiomer of 6 was converted into the corresponding silanol, R-7 and S-7, with aqueous chloroplatinic acid in good yield. High-field (200 MHz) proton NMR of an approximately 1:1 mixture of R-7 (or S-7) with the optically active europium shift reagent [Eu(hfc)₃] indicated that each enantiomer was essentially completely pure, containing less than 2% (lower detection limit) of the opposite enantiomer. It should be pointed out that all of these chiral silanes have C-centered rather than Si-centered asymmetry and thus the asymmetry is independent of the stereochemistry at the silicon atom.



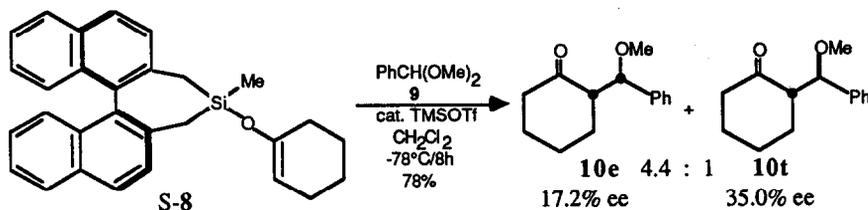
With the optically pure silanes in hand, we investigated their ability to effect chirality transfer in various organic reactions. The results of the reduction of enones and ketones are shown in Table 1. The optical purity of the products (and thus the enantioselectivity) was determined by ¹H NMR of their complexes with the optically active europium shift reagent [Eu(hfc)₃]. The ee's obtained ranged from a low of 6.2% to a high of 25.6%, with the majority being between 14% and 26%. This is an increase of at least a factor of two over the ee's obtained by both Paquette and Fry, and therefore represents one of the best chirality transfers achieved to date. Although this enantioselectivity is still too low to be of great practical use, they are really quite high considering that the silicon atom may not be very near the forming C-H bond in the transition state for these reductions. However, the highest ee we have obtained is in a transition metal-catalyzed aldol reaction. The cyclohexyl silyl enol ether S-8 reacted with dimethoxytoluene 9 in a Mukaiyama/Noyori

Table 1: Chirality Transfer with Binaphthyl Silane S-6

Compound	Catalyst	Conditions	Yield	% ee	Chirality
	(Ph ₃ P) ₃ RhCl	PhCH ₃ /110°C/8h	64%	14.4	(-) (R)
	"	PhH/50°C/24h	68%	25.6	(-) (R)
	TiCl ₄	CH ₂ Cl ₂ /0-25°C/63h	26%	6.2	(-) (R)
<u>MeCOR</u>					
R=Ph	(Ph ₃ P) ₃ RhCl	PhH/80°C/14h	70%	11.9	(+) (R)
R=(CH ₂) ₅ CH ₃	TiCl ₄	CH ₂ Cl ₂ /-78°C/4h	75%	15.3	(+) (S)
R=C(CH ₃) ₃	TiCl ₄	CH ₂ Cl ₂ /-78°C/4h	55% ¹	21.4 ²	
R=(CH ₂) ₂ COOEt	TiCl ₄	CH ₂ Cl ₂ /-11°C/69h	71% ³	16.8	(-) (S)
R=C(CH ₃) ₂ COOEt	TiCl ₄	CH ₂ Cl ₂ /-30 to -11°C/72h	97%	22.8	(+) (S)
	TiCl ₄	CH ₂ Cl ₂ /-78°C/4h	82%	16.4 ²	

1) Isolated as the benzoate. 2) The chirality of the alcohol product was not determined. 3) Isolated as the lactone.

aldol process¹¹ to give, in 78% yield, a 4.4:1 mixture of the separable erythro and threo isomers **10e**t. The enantioselectivity was 17.2% for **11e** and 35.0% for **10t**. Thus in a reaction where the silicon atom is presumably closer to the forming C-C bond in the transition state, we are able to achieve the highest enantioselection yet seen for chirality transfer from silicon to prochiral carbon.



It should be pointed out that the chiral auxiliary is easily recyclable. The silyl products from the above reactions (the silanol and disiloxane from the reductions and the methoxysilane from the aldol) are easily separated chromatographically from the products, due to their very non-polar nature. The methoxysilane **5** is reduced to **6** in high yield with LiAlH₄, as described earlier. Refluxing a mixture of the silanol or disiloxane in benzene with aluminum and iodine for 4h followed by reduction at 0°C with DIBAL afforded **6** in excellent yield.

Thus we have developed a new class of chiral silanes in which the asymmetry is independent of the stereochemistry at the silicon atom and have shown that they allow one to achieve the highest levels of enantioselection yet obtained in any chirality transfer process for organosilanes. Work to develop even better chiral silanes with larger chiral barriers nearer to the silicon atom is currently underway.

Acknowledgement: We thank the National Institutes of Health (GM-34670) for financial support and Dr. Martin Grissom and Mr. Rich Budhu for their assistance.

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(Received in USA 7 July 1988)