Asymmetric Induction by Chiral Silicon. Synthesis and Electrophilic Reactivity towards Dienes and Carbanions of *R*-(−)-Methyl-α-naphthyl-phenylsilyl Phenyl Thioketone

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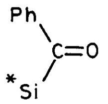
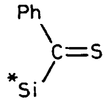
The title compound was prepared by acid catalysed reaction of the corresponding ketone with hydrogen sulphide, and its ability to transfer chirality to the carbon α to silicon in reactions with buta-1,3-diene and methyl-lithium was tested; good levels of asymmetric induction were observed.

Only a few examples of the use of silicon in asymmetric synthesis are known[1] and the asymmetric inductions reported are rather discouraging. This could be due to a low selectivity of the chosen reactions or to a poor effectiveness of silicon as a chiral auxiliary. In order to gain better insight into the use of silicon in asymmetric synthesis, we prepared a chiral silyl thione and tested its ability to transfer chirality from silicon to carbon in electrophilic reactions of carbanions and dienes. It is well known[2] that silyl thiones have a special reactivity in addition reactions with 1,3-dipoles and dienes.



(1)



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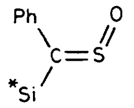

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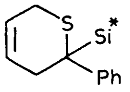

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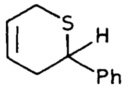
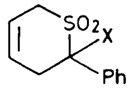
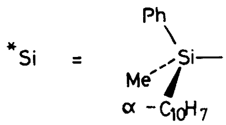
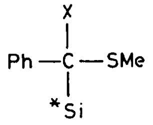


(6)



(7)
a, X = H
b; X = D





(4)
a; X = Li
b; X = H

Ketone (**1**),[3] m.p. 82—84 °C, $[\alpha]_D^{20}$ +6.0° (*c* 10, C_6H_6), was converted into the thione (**2**) (95% yield) with hydrogen sulphide and hydrogen chloride, according to a procedure already described;[2a] purification by column chromatography on Florisil under nitrogen gave the pure thione as a blue-green viscous oil {$[\alpha]_D^{20}$ −132.2° (*c* 0.18, C_6H_6); $\nu_{max.}$ (CCl_4) 1215 cm^{-1} (C=S); δ_H ($CDCl_3$) 1.03 (3H, s), 6.8—8 (17H, m, ArH); $\lambda_{max.}$ (cyclohexane) 692 nm (ε 30); Δε +3 at 685 nm}. Absolute configuration of thione (**2**) and its optical purity were established through its reconversion into the starting ketone (**1**), of known absolute configuration,[3] with reactions of known mechanism:[4] thione (**2**) was oxidised with 1 mol. equiv. of *m*-chloroperbenzoic acid (MCPBA) to the sulphine (**3**) {m.p. 116—118 °C from diethyl ether, $[\alpha]_D^{20}$ +17° (*c* 3.27, C_6H_6); $\nu_{max.}$ (CS_2) 1130 cm^{-1} (CSO); δ_H ($CDCl_3$) 0.97 (3H, s), 7.3—8.2 (17 H, m)}. The geometry of (**3**) is assumed to be *E* by analogy with other silylsulphines.[2a] Sulphine (**3**), with a second molar equivalent of MCPBA, gave ketone (**1**) {m.p. 80—82 °C, $[\alpha]_D^{20}$ +5.7° (*c* 10, C_6H_6)}; this value, within the experimental errors, can be considered coincident with that of the starting ketone, corresponding to an optical purity of 100%.

Thione (**2**) shows a good reactivity towards organolithium derivatives giving only the products of thiophilic addition.

Reaction of methyl-lithium with (**2**) in tetrahydrofuran (THF) at −78 °C followed by quenching with methanol at the same temperature, gave in 60% yield, the two diastereoisomeric α-silylated sulphides (**4b**) in a ratio 70:30, corresponding to a diastereomeric excess (d.e.) of 40%. The two diastereoisomers were not separated, but their ratio was determined by ^{1}H n.m.r. analysis of the mixture at 60 MHz by integrating the signals of SiMe groups (at δ 0.57 and 0.70) SMe (at δ 1.87 and 1.93), and H (at δ 3.95 and 3.98) in the two diastereoisomers.

The crude mixture has $[\alpha]_D^{20}$ −34° (*c* 2.6, cyclohexane) and *m/z* 384 (M^+).

The asymmetry induced by chiral silicon to the vicinal carbon is probably due to the initial formation of the two diastereomeric lithiated sulphides (**4a**).

Similar good diastereoselectivity was found in the cycloaddition of (**2**) with buta-1,3-diene. The two diastereomeric thiopyrans (**5**) (the absolute configuration of the two products was not attributed) were obtained in 87% yield as a 75:25 mixture, corresponding to 50% d.e., when a solution of (**2**) in CH_2Cl_2 was allowed to react with an excess of buta-1,3-diene at −75 °C for 24 h. Higher reaction temperatures gave poorer d.e., and lower temperatures made the reaction too slow. The ratio of the two diastereoisomers of (**5**) was established by ^{1}H n.m.r. analysis of the mixture at 300 MHz by integrating the signals of the Si-methyl groups at δ 0.86 and 0.89. The mixture (**5**) was a low melting solid which gave correct mass and n.m.r. spectra.

After protodesilylation with tetrabutylammonium fluoride (TBAF) in THF/H_2O, the mixture (**5**) gave 2-phenyl-3,6-dihydro-2*H*-thiopyran (**6**) {m.p. 44—45 °C, $[\alpha]_D^{20}$ +12.9° (*c* 2.63, n-hexane); δ_H($CDCl_3$) 2.4—3.8 (4H, m), 4.0 (1H, t, *J* 7 Hz), 5.8—6.1 (2H, m), and 7.4 (5H, s); *m/z* 176 (M^+)}.

The enantiomeric excess (e.e.) of (**6**) was found to be 51 ± 8%. This value was obtained with the isotope dilution technique[5] applied to the corresponding sulphone† (**7a**) prepared from (**6**) by peroxyacid oxidation, a reaction which is well known[6] not to interfere with the α-benzylic chiral carbon. Deuterium was used as an isotopic label and its dilution was measured by mass spectrometry. The labelled racemic sulphone (**7b**) was obtained through deuterodesilylation of (±)-2-phenyl-2-trimethylsilyl-3,6-dihydro-2*H*-thiopyran[2b] in $TBAF/D_2O$, followed by peroxyacid oxidation of the [2-^{2}H]thiopyran obtained.

Two crystallizations of the mixture of (**7a**) and (**7b**) from absolute ethanol gave a labelled racemate whose deuterium content was introduced into the appropriate formula,[5] giving an e.e. of 51 ± 8%.

From these data it appears that the e.e. of (**6**) is practically the same, within the experimental errors, as the d.e. of (**5**), leading to the conclusion that the protodesilylation of (**5**) is a stereospecific process which occurs without loss of the induced chirality to the carbon α to silicon.‡

As far as the fate of silicon is concerned, in the desilylation of (**6**) with fluoride ion, after the usual work up, we always isolated racemic methyl-α-naphthyl-phenylsilanol and the corresponding disiloxane.[8]

Racemic silanol, very likely derived from the hydrolysis of fluorosilane, was initially formed and was racemized by fluoride ion. To support this hypothesis, we treated a THF solution of (−)-methyl-α-naphthyl-phenylfluorosilane[8a] with 1 mol. equiv. of TBAF in THF in the polarimetric cell, and observed an instantaneous racemization.§ We then performed a blank experiment by treating the (−)-fluorosilane under the same conditions used in the desilylation of (**5**), and obtained racemic silanol and disiloxane, which can be easily reconverted into the chiral auxiliary.[8]

The values reported here for the transfer of chirality from silicon to the α-carbon, even though not spectacular if compared with those obtained with other chiral auxiliaries, represent a noteworthy achievement in this field, encouraging the use of chiral silylthiones in asymmetric synthesis. The easy

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† This technique was not applied directly to (**6**) owing to its low melting point which hinders a good crystallization.

‡ Complete stereoselectivity was found in other protodesilylation reactions at an sp^3 carbon (ref. 7).

§ The hypothesis of racemization at the fluorosilane stage is in agreement with the results of Fry (ref. 1d) and Cremer (ref. 9).

removability of silicon without loss of the chirality induced to the α-carbon and the possibility of recovering the auxiliary, although in racemic form, represent other advantageous features of the above reported reactions.

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