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C-CENTRED OPTICALLY ACTIVE ORGANOSILANES,1. SYNTHESIS OF NEW SILYLATED CHIRAL AUXILIARIES.

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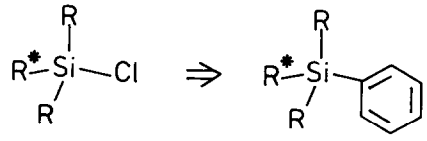
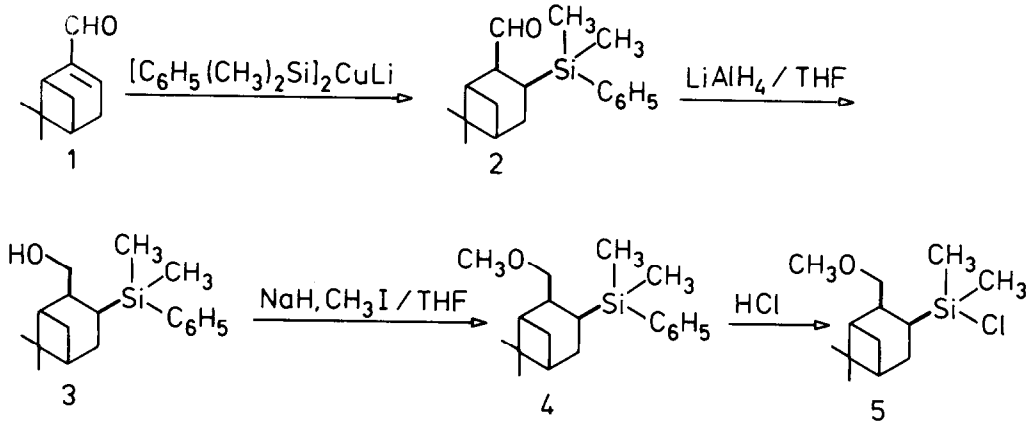
Summary. Different silylating reagents with an optically active ligand bonded to the silicon centre have been synthesized starting from (1R)(-)myrtenal.The key step of the synthesis is the stereocontrolled 1,4 addition of phenyldimethylsilyl-cuprate to thea,βunsaturated aldehyde.

In recent years the study of highly enantioselective reactions has become one of the fields of major interest in organic chemistry[1].
A large number of chiral auxiliaries has been developed for this purpose, commonly employing natural products[2], but a great deal of work has been done also with organometallics. In this field compounds with pure optically active ligands bonded to metal centres such as Sn[3a], B[3b], Al[3c], Li[3d] or to transition-metals[3e] have been employed and also the use of a chiral metal turned out to be a successful choice[4].
Attempts to induce asymmetry by chiral silicon groups have been performed by Paquette [5a] and Larson[5b], who tested some Si-centred optically active organosilanes . Their results however were not fully satisfactory for the low chemical and enantiomeric yields. Successful enantiomeric induction was accomplished instead "via" chiral allylsilanes[6], with the asymmetric centre previously generated on the allyl mojety which underwent the coupling.
Looking for an extension of such enantioselective silicon chemistry, we became interested in the synthesis of easily available C-centred optically active organosilanes which could be used to induce asymmetry through the typical silanes reactions.
Since the most common starting material in organosilicon chemistry is trimethylchlorosilane, we needed to synthesize a C-centred chiral chlorosilane. Furthermore a retrosynthetic analysis envisaged a chiral phenylsilane as suitable precursor, for the possibility to transform a silicon-phenyl bond into a silicon-chlorine bond in the presence of HCl[7].



Using the reaction recently developed by Fleming[8] based on the conjugate addition of phenyldimethylsilyl-cuprate to α,β unsaturated aldehydes, we prepared the chiral phenylsilane **4** and the corresponding chloroderivative **5** as reported in Scheme I.



Scheme I

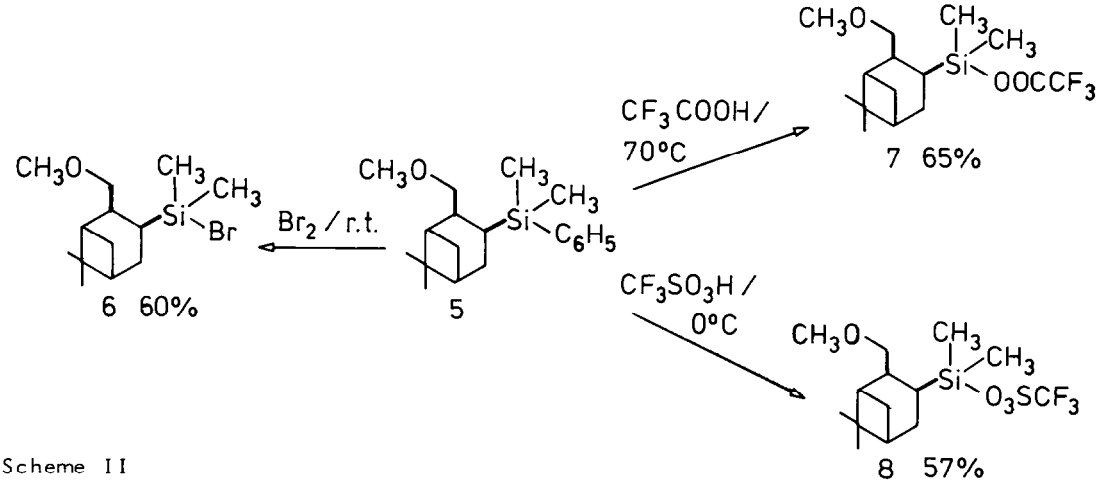
Phenyldimethylsilyl-cuprate, prepared from phenyldimethylsilyllithium and CuCN in THF[9], reacted with (1R)(-)myrtenal[10] **1** giving the silylated aldehyde **2** in 70% yield after fractional distillation under vacuum. The phenyldimethylsilyl group was "cis" to the carbonyl function as revealed by ^{1}H NMR analysis (200 mHz), which showed also no traces of the other isomer.

In order to prevent side-reactions of the CHO group during the following phenyl-chlorine exchange with HCl, compound **2** was submitted to reduction with $LiAlH_4$ in THF (12 h at room temperature), followed by methylation of the OH group (MeI/NaH, 3h in boiling THF)[11] to give product **4** in a 60% overall yield[12].

The phenyl-chlorine exchange was then performed by bubbling dry HCl through a $CHCl_3$ solution of **4** for 24-30 h. Product **5** was isolated by fractional distillation in 78% yield and its isomeric purity checked by ^{1}H NMR and glc analyses [13].

From phenylsilane **4** the other silylating agents **6**, **7** and **8** were prepared as reported in scheme II. These reactions were performed by adding to neat **5**, bromine, trifluoroacetic acid, or trifluoromethansulphonic acid respectively, at the temperature reported in the scheme, and distilling under vacuum products **6**, **7** and **8** directly from the reaction flask[14].

The trifluoroacetate **7** was a stable liquid which could be stored for a long time, whereas the bromoderivative **6** and the triflate **8** were thermally unstable and had to be used quickly after preparation.



Scheme II

The availability of these new C-centred optically active silylating reagents opens a general route for the synthesis of a wide range of organosilanes with the silicon carrying the chiral information, as for example allylsilanes, vinylsilanes or silyl enol ethers; their preparation and use to perform asymmetric induction and/or separation of diastereoisomers is currently being investigated.

References and notes.

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10) l(R)(-)Myrtenal can be considered a relatively cheap and easily available starting material. Purchase from Aldrich costs 3.8 DM per g. (Aldrich Catalogue for Fine Chemicals 1986-87).

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12) **4** b.p. 151-155°C at 0.07 mmHg .
^{1}H NMR (CCl_4/TMS) 0.36 (s, 6H,$(CH_3)_2Si$) 0.63 (d, 1H, J=9Hz, CHSi), 1.09 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 2.0 (m, 3H, CH_2), 2.2 (m, 4H, CH_2 and CH), 2.49 (d+d, 1H, J_a=7.5Hz, J_b=3.5Hz,CHO), 3.16 (s, 3H, OCH_3), 3.39 (d+d, 1H, J_a=7.5Hz, J_b=11Hz,CHO), 7.5 (m, 3H, Arom.), 7.6 (m, 2H, Arom.).
^{13}C NMR ($CDCl_3$/TMS) -4.94, 16.61, 22.65, 27.75, 28.23, 31.44, 38.90, 41.23, 42.17, 58.30, 76.72, 127.54, 128.79, 133.95, 138.34 .
Mass spectrum (m/e) 287 (M^+-15), 271 (M^+-31), 135 (base).
$[\alpha]_{589}^{25}$= +25.0 (c = 6.01 in benzene). Absolute configuration of **4** is same as that of myrtenal. The relative configuration of the two new centres is unknown.

13) **5** b.p. 123-127°C at 0.07 mmHg .
^{1}H NMR (CCl_4/TMS) 0.29 (d, 1H, J=6Hz, CHSi), 0.66 (s, 6H, $(CH_3)_2Si$), 1.0 (m, 1H, CH), 1.1 (m, 1H, CH), 1.28 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 2.3 (m, 5H, CH_2+CH), 3.18 (d, 1H, J=12Hz, CHO), 3.41 (s, 3H, OCH_3), 3.66 (d, 1H, J=11Hz, CHO).
Mass spectrum (m/e) 260 (M^+), 229 (M^+-31), 93 (base).
The hydrolytic unstability prevented us from reporting the[α] value that could not be reproducible due to the possible presence of chiral impurities.

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