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APPLICATION OF OPTICALLY ACTIVE ORGANOSILANE TO THE DETERMINATION OF OPTICAL PURITIES OF AMINES, ALCOHOLS, AND CARBOXYLIC ACIDS

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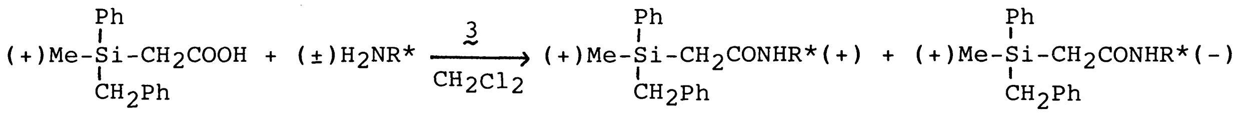
Application of optically active carbonfunctional organosilanes for the determination agent of optical purities of chiral amines, alcohols, and carboxylic acids by using NMR spectrometer were investigated.

A new optically active organosilicon compound; benzylmethylphenylsilylacetic acid(1),$^{1)}$ which was prepared from chloromethyl(dichloro)methylsilane in 50% yield, was obtained by the fractional crystallization using (+)- or (-)-1-phenylethylamine(2) as a resolving agent. Although it was indicated that the trisubstituted silylacetic acids were relatively unstable,$^{2)}$ this acid(1) can react with the chiral amines such as 2, 3-methyl-2-phenylbutylamine, and 2-(4-chlorophenyl)-3-methylbutylamine, or the alcohols such as 1-phenylethanol and 1-phenylpropanol, in the presence of 2-chloro-1-methylpyridinium iodide(3)$^{3)}$ to give the corresponding diastereoisomeric amides and esters, respectively.



$$(+)\mathrm{Me}\text{-}\underset{\mathrm{CH_2Ph}}{\overset{\mathrm{Ph}}{\mathrm{Si}}}\text{-}\mathrm{CH_2COOH} + (\pm)\mathrm{H_2NR^*} \xrightarrow[\mathrm{CH_2Cl_2}]{3} (+)\mathrm{Me}\text{-}\underset{\mathrm{CH_2Ph}}{\overset{\mathrm{Ph}}{\mathrm{Si}}}\text{-}\mathrm{CH_2CONHR^*}(+) + (+)\mathrm{Me}\text{-}\underset{\mathrm{CH_2Ph}}{\overset{\mathrm{Ph}}{\mathrm{Si}}}\text{-}\mathrm{CH_2CONHR^*}(-)$$

The NMR spectrum of N-(1-phenyl)ethyl-benzylmethylphenylsilylacetamide(4) prepared from (+)-1 and (±)-2, shows two singlets at 0.30 and 0.34 ppm(Si-Me), however that of the amide prepared from (+)-1 and (+)-2 shows only one singlet at 0.30 ppm. These results indicate that optically active 1 can be used for the determination of the optical purities of chiral amines.

And the measurments of the NMR spectra of the amides and esters prepared from (+)- or (-)-1 and racemic and optically active amines or alcohols were carried out.$^{4)}$(Table 1) From these observations it was noted that optically active 1 could be used successfully for the determination of the optical purities of chiral amines and alcohols.

Furthermore, it was found that the optically active benzylmethyl-o-tolylsilylmethylamine(5)$^{5)}$ could also be used for the determination of the optical purities of chiral carboxylic acids.(Table 1)

In a typical proceduer, a solution of (+)-1(51 mg, 0.19 mmol), (±)-2(22 mg, 0.19 mmol), and $(n\text{-Bu})_3N$(82 mg, 0.44 mmol) in CH_2Cl_2(0.5 ml) was added to a mixture of 3(56 mg, 0.22 mmol) in CH_2Cl_2(0.5 ml) at room temperature under nitogen atmosphere. The reaction mixture was stirred for 1 h under refluxing. After evaporation of the solvent, the amide 4(57 mg, 0.15 mmol) was isolated by TLC in 80% yield.

The advantages of these optically active silanes for using the determination of optical purities of chiral amines, alcohols, and carboxylic acids are: a) any other signal rarely appears in the Si-Me region in the ^{1}H NMR spectra of ordinary organic compounds; b) the shape of the Si-Me signal is always observed as a sharp singlet; c) the differences of the reaction rates of these silanes with the corresponding chiral compounds having the same and different sign of rotation with optically active **1**, are negligible.

Table 1. Chemical Shifts of Amide and Ester Derivatives of **1** and **5**

Silane	Chiral amine, alcohol, and carboxylic acid	Chemical shift of Si-Me(PPM) Racemic	(+)-(+) or (-)-(-)	(+)-(-) or (-)-(+)
1	1-Phenylethylamine	0.30, 0.34	0.30	0.34
1	3-Methyl-2-phenylbutylamine	0.21, 0.24	0.24	0.21
1	2-(4-Chlorophenyl)-3-methylbutylamine	0.21, 0.25	0.25	0.22
1	2-Phenylpropylamine	0.27, 0.29	—	—
1	2-Amino-3-phenylpropanol	0.28, 0.32	—	—
1	1-Phenylethanol	0.29, 0.31	—	—
1	1-Phenylpropanol	0.26, 0.29	—	—
5	2-(4-Fluorophenyl)-3-methylbutanoic acid	0.17, 0.24	0.25	0.17
5	2-Hydroxy-2-phenylethanoic acid	0.22, 0.23	0.23	0.21
5	2-(4-Methylphenyl)-3-methylbutanoic acid	0.19, 0.23	0.23	0.19
5	N-Benzoly-trans-2-aminocyclohexane-carboxylic acid	0.30, 0.33	0.33	0.30

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References

1) NMR(δ)(CCl_4) 0.38(s, 3H, Si-CH_3), 2.12(s, 2H, CH_2CO), 2.43(s, 2H, CH_2Ph), 6.7-7.6(m, 10H, Ph), 8.42(broad s, 1H, COOH). $[\alpha]_D$ + and/or -6.5°(c 2, $CHCl_3$). Mp 36-38 °C(racemic), 69-70.5 °C(optically active). Found: C, 70.83; H, 6.93%. Calcd for $C_{16}H_{18}O_2Si$: C, 71.07; H, 6.71%.

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4) The NMR spectra were determined at 90 MHz with JEOL FX90Q spectrometer in $CDCl_3$ using TMS as the internal standard.

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