OPTICALLY ACTIVE PERFLUORO-2-PROPOXYPROPIONIC ACID

Hajimu KAWA and Nobuo ISHIKAWA*

Department of Chemical Technology, Tokyo Institute of Technology

Ookayama, Meguro-ku, Tokyo 152

The diastereomeric amides prepared from (\pm) -perfluoro-2-propoxypropionyl fluoride and (-)-l-phenylethylamine were separated chromatographically, and subsequent hydrolysis of each amide gave (+) and (-)-perfluoro-2-propoxypropionic acids, the first example of optically active and enantiomeric perfluorocarboxylic acids.

Partially fluorinated optically active compounds such as α -trifluoromethyl benzyl alcohol¹⁾ and α -methoxy- α -trifluoromethylphenylacetic acid²⁾ are known to be a useful compound for spectroscopic studies and they are used for the determination of optical purity of absolute configuration of several asymmetric compounds.³⁻⁵⁾ While some derivatives of perfluorocarboxylic acids are demonstrated to be a volatile and sensitive reagent for chromatographic analysis,^{6,7)} none of perfluorinated optically active compounds have been reported so far. This prompted us to prepare an optically active perfluorocarboxylic acid or its derivative which is expected to be able to protect amines and alcohols easily.

Perfluoro-2-propoxypropionic acid (3) was considered to be suitable for our purpose, since this perfluorocarboxylic acid containing a chiral center was easily prepared from hexafluoro-1,2-epoxy-propane and was thought to afford its derivatives having adequate molecular weights for chromatographic analysis.

Perfluoro-2-propoxypropionyl fluoride (2), which was prepared by the anionic dimerization of perfluoro-1,2-epoxypropane (1) using tetramethylurea in diglyme, 8) was allowed to react with (-)-1-phenylethylamine, $\left[\alpha\right]^{20}$ -40.00 (neat), and an oily mixture of the diastereomeric amides (4a + 4b)

was obtained quantitatively.

The diastereomers, 4a and 4b, were readily separated from each other by means of chromatography on silica gel using a hexane-benzene mixture (3 : 1) as a solvent and eluent. The first fraction contained (-)(-)-isomer (4b), m.p. 55.5 - 56.5 °C; $[\alpha]_D^{20}$ -82.0° (C 1.00, C_6H_6) while the second fraction gave (+)(-)-isomer (4a), m.p. 83 - 83.5 °C (from pentane); $[\alpha]_D^{20}$ -88.0° (C 1.00, C_6H_6).

The ir spectra of each isomer showed similar characteristic bands due to the NH and C=0 groups at 3300 and 1700 cm⁻¹, respectively. In the 1 H nmr spectra (in CCl₄), each isomer gave again a similar pattern, each consists of four signals at δ 1.53 (Me), 5.12 (CH), 6.72 (NH) and 7.27 (Ph). In the 19 F nmr, however, a difference (9 Hz) in chemical shifts due to the terminal CF₃ of perfluoro-propoxyl group was observed for the isomers. They were also characterized from the different g.l.c. retention times of 4a (11 min) and 4b (12 min). Thus, the purity of each isomer could be clearly determined by both 19 F nmr spectra and gas chromatography.

The hydrolysis of these amides was carried out by prolonged refluxing of their aqueous ethanol solution containing 10% sodium hydroxide. The enantiomers of perfluoro-2-propoxypropionic acid thus obtained, the first example of optically active organic perfluoro compounds, were characterized as shown in Table 1.

Table 1 Properties of 3a and 3b

	3a €	<u>3</u> b		
Prepd. from	<u>4</u> a	4b <i>≈</i>		
Yield (%)	69	72		
B.p. (^O C/mmHg)	93 - 94 /	/ 90		
$\left[\alpha\right]_{D}^{20}$ (CHC1 ₃)	+16.5 (C 0.82)	-16.5 (C 0.85)		
IR (film) (cm ⁻¹)	3200 (OH), 1780 (C=O)			
¹ H NMR (CDC1 ₃)	δ 10.3	3		
¹⁹ F NMR* (neat)	2.7(1F), 5.43(3F),	6.3(3F), 10.0(1F), 53.0(2F), 54.8(1F)		

^{*} δ ppm upfield from ext. CF_3CO_2H .

The optically active perfluorocarboxylic acid is a useful reagent for analysis of enantiomers. For example, the (+)- and (-)- α -phenethyl alcohol esters prepared from the alcohols and 3b fluoride reflected in their differences in the nmr chemical shifts due to $C\underline{H}_3$, and $C\underline{F}_3$ $\overline{C}F$ and $C\underline{F}_3$ CF_2 CF_2 as follows.

(b)
$$CF_3$$
 (c) CF_3 (a) CF_3 CF_2 CF_2 CF_3 CF_4 CF_5 CF_6 CF_6 CF_6 CF_7 CF

	Chemical shifts (δ) for $5 \over \infty$		
Phenethyl alcohol	¹ H (a)	¹⁹ F (b)**	¹⁹ F (c)**
(+)	1.67	5.43	6.10
(-)	1.69	5.53	6.17

** $^{\delta}$ ppm from external CF $_3$ CO $_2$ H.

Utilizing the above data, the optical purity of an enantiomeric mixture of phenethyl alcohols could be determined based on their signal intensities of both $^1\mathrm{H}$ and $^{19}\mathrm{F}$ nmr.

Since the perfluorocarboxylic acid $\frac{3}{2}$ contains no hydrogen atom, it is also expected to be a useful solvent for 1 H nmr analysis of chiral molecules. Further, since the $\overset{*}{C}$ -F bond at the chiral center is very stable, no inversion was observed during reactions of $\frac{3}{2}$ even under vigorous conditions. Extensive work on the utilization of this unique perfluoro compounds is now under way.

References and Note

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9) G.1.c. analysis was carried out on a Shimazu GC-3BT apparatus equipped with a TCD. The $4\phi \times 3$ steel column was packed with 15% Thermol-3 on Shimalite. Helium gas was flowed at the rate of 23 ml/min, while the column was kept at 150 $^{\rm O}$ C.

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