THE USEFULNESS OF OPTICALLY ACTIVE PERFLUORINATED COMPOUNDS

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SUMMARY

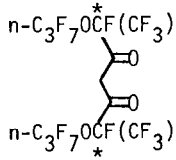
The usefulness of optically active (+),(-)-perfluoropropoxy- and perfluoroisopropoxypropionic acids as derivatives for the analysis of chiral amines and alcohols is mentioned. Lanthanide chelates of (+),(-)-di(perfluoropropoxypropionyl)methane behaved as a useful shift reagent for the pmr analysis of optically active compounds.

INTRODUCTION

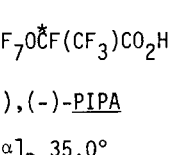
Perfluorocarbon compounds are completely artificially made, so that these compounds have never been related to natural products. However, the general properties of perfluorocarbon compounds such as their high thermal and chemical stability, the low interaction between molecules, and the strong electronegativity of perfluoroalkyl or perfluoroaryl groups, seem to make them useful derivatives for natural products.

As the first example of optically active perfluorinated compounds carrying a functional group, we prepared (+),(-)-perfluoropropoxypropionic acid (PPPA) and (+),(-)-perfluoroisopropoxypropionic acid (PIPA) and a nearly perfluorinated (+),(-)-di(perfluoropropoxypropionyl)methane (DPPM) [1-3]. These compounds were found to be very effective derivatives for chiral amines or alcohols for analysis.

The enantiomeric precursor of PPPA is the dimer of hexafluoropropene oxide (HFPO), a useful monomer for perfluorinated polyether, while that of PIPA is the adduct of HFPO and hexafluoroacetone (HFA). The optical resolution of these mixtures was achieved by the conventional method, i.e., repeated recrystallization of diastereomeric mixtures of the salts of (±)-PPPA or (±)-PIPA with cinchonidine from organic solvents.



n-$C_3F_7O\overset{*}{C}F(CF_3)CO_2H$ (+),(-)-PPPA $[\alpha]_D$ 27.4°



i-$C_3F_7O\overset{*}{C}F(CF_3)CO_2H$ (+),(-)-PIPA $[\alpha]_D$ 35.0°

n-$C_3F_7O\overset{*}{C}F(CF_3)$ ⟩C=O ⟩C=O n-$C_3F_7O\overset{*}{C}F(CF_3)$ DPPM

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RESULTS AND DISCUSSION

The thermal, chemical and optical stability of both (+),(-)-PPPA and (+),(-)-PIPA is extremely high, and these properties make them useful to protect nucleophilic compounds, in particular those carrying a chiral center. The acid chlorides of (+),(-)-PPPA and PIPA, especially the former, are very reactive with alcohols or amines, and corresponding perfluoroacyl compounds were quantitatively formed at room temperature. The resultant esters or amides are quite resistant to hydrolysis and to heat, and they have considerable volatility. These properties make these derivatives suitable for a variety of analytical procedures. For example, for the determination of optical purities of α-amino acids, the methyl ester of the enantiomeric mixture was acylated by (+)-PPPA, and the resultant diastereomeric mixture, (+)-PPPA/(+)-amino acid and (+)-PPPA/(-)-amino acid, was subjected to ^{19}F nmr analysis. In most cases the signal due to the trifluoromethyl group attached to the chiral carbon atom was split into a doublet, and the signal intensities for each peak revealed the optical purity of the amino acid. Examples are shown in Table 1.

TABLE 1

Determination of optical purities of several α-amino acids derivative

$CF_3CF_2CF_2O\text{-}\overset{*}{C}F(CF_3)\text{-}CO\text{-}NH\text{-}\overset{*}{C}H(R)\text{-}CO_2Me$

Amino acid	R	Optical purity (%)		Δδ (Hz)
		Calcd.	Obsd.	
PheGly	C_6H_5	33.3	32.6	10.9
Ala	CH_3	47.8	44.2	12.2
Val	$(CH_3)_2CH$	20.0	21.2	12.3
Leu	$(CH_3)_2CHCH_2$	50.0	48.0	21.2
Ile	$CH_3CH_2CH(CH_3)$	47.8	45.0	14.9
Phe	$C_6H_5CH_2$	50.0	49.0	13.0
Met	$CH_3SCH_2CH_2$	70.4	68.5	15.4
Glu	$CH_3OCOCH_2CH_2$	48.6	49.8	15.2

Glc analysis for optical purities of α-amino acids can be achieved under mild conditions by using optically active perfluorinated carboxyl chlorides. For example, a mixture of six optically impure amino acids was acylated with (+)-PIPA chloride, and the resultant mixture of amides

was subjected to glc analysis. The result (Fig. 1) shows that the enantiomers of all amino acids examined, except for methionin, were clearly distinguished from each other at relatively low temperature and within a short period.

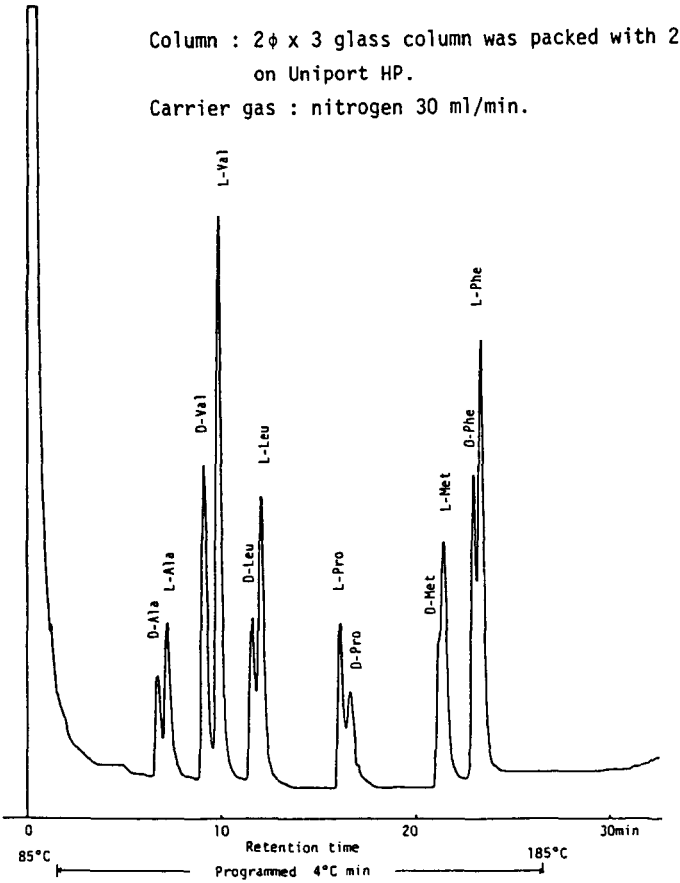

Fig. 1. Gas chromatogram of N-(-)-perfluoro-2-isopropoxypropionyl amino acid methyl esters

We have also prepared lanthanide chelates of an optically active β-di ketone (DPPM), which is obtained from (+)-PPPA. The Eu and Pr chelates of DPPM were found to be very effective and useful nmr shift reagents for the direct determination of the enantiomeric composition of chiral compounds. The nearly perfluorinated β-diketone lanthanide chelate (only one hydrogen atom remains at the methine group) is a strong Lewis acid, which has strong interaction with nucleophilic atoms of substrates. Practically no signals due to hydrogen atoms are present in the spectra, so that it behaves as

a 'ghost agent' in ^{1}H nmr spectra. Further, the compounds DPPM(Ln) are soluble in non-polar organic solvents and, in particular, miscible with fluorinated solvents such as F-113. This is another advantage of this reagent, as it makes the microvolume addition of DPPM(Ln)/F-113 solution easy, which is useful in nmr analysis. For example, the ^{1}H nmr spectra of a partially resolved 1-phenylethylamine (o.p. 28.8%) in CCl_4 with the addition of (+)-DPPM(Eu) revealed the induced downfield shifts which separated the α-methyl resonance into two peaks. Thus, signals for each enantiomer of the phenylethylamine were clearly distinguished from each other, and their relative signal intensities could be integrated. The optical purity thus determined for this sample was 30.3% in satisfactory agreement with that determined by polarimetry (Fig. 2). Even a small amount of DPPM chelate (r/s 0.11) was sufficient to achieve a satisfactory ΔΔδ value (magnitude of enantiomeric shift difference) of 0.20 ppm.

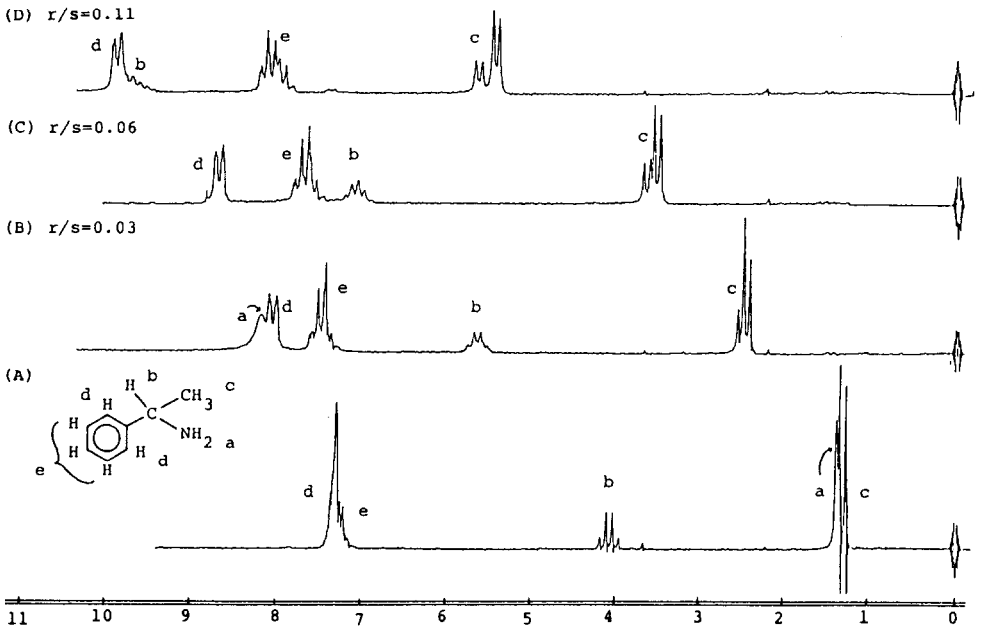

Fig. 2. ^{1}H NMR spectra for (-)rich-1-phenylethylamine in CCl_4 in the absence (A) and presence (B)~(D) of (+)-DPPM(Eu) at three different (+)-DPPM(Eu)/substrate molar ratios (r/s).

REFERENCES

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