

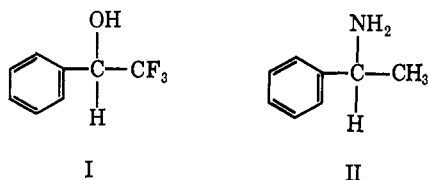
The Nonequivalence of Physical Properties of Enantiomers in Optically Active Solvents. Differences in Nuclear Magnetic Resonance Spectra. I

Sir:

We consider it manifest that enantiomers must be in different average environments when in an optically active solvent. In asymmetrical environments, enantiomers need not possess identical properties toward symmetrical agents. Such differences in behavior toward symmetrical agents may be detected by those physical measurements which are sensitive environmental probes. Nmr spectroscopy falls into this category and we have used this technique to demonstrate spectral differences between enantiomers. A recent postulation¹ of this effect prompts us to give a preliminary account of our findings.

A priori, it was thought that strong solute-solvent interactions, such as hydrogen bonding, dipolar attraction, and charge-transfer interaction, would lead to the greatest difference in average spatial environment of the enantiomers. Moreover, it seemed likely that, for the purpose of nmr measurements, the presence of a group of high diamagnetic anisotropy near the solvent asymmetric center would maximize the probability that a difference in average spatial environment would lead to a difference in average magnetic environment, thus enabling one to distinguish between enantiomers. Incorporation of fluorine into the solute offers a twofold advantage. Not only do the chemical shifts of fluorine resonances occur over a wider range than do those of hydrogen (and hence are expected to be more sensitive environmental probes), but the spectra are uncluttered by solvent proton resonances. These criteria were used in selecting solute-solvent pairs for study.

In carbon tetrachloride, the fluorine resonance of racemic 2,2,2-trifluoro-1-phenylethanol (I) [bp 93° (15 mm), n_D^{25} 1.4593, reported² bp 87° (13 mm) n_D^{25}



1.4590] appears as a doublet ($|J|_{\text{HF}} = 6.7$ cps) centered at +4445 cps from internal fluorotrichloromethane.³ No fine structure is evident. In pyridine, the resonance appears as a doublet of triplets ($|J|_{\text{HF}} = 7.3$ cps $|J|_{\text{H'F}} = 0.7$ cps) centered at +4387 cps from internal fluorotrichloromethane. The fine structure must result from long-range coupling of the fluorines with protons on the aromatic ring.⁴ However, in optically active α -

(1) M. Raban and K. Mislow, *Tetrahedron Letters*, No. 48, 4249 (1965).

(2) R. Stewart and R. Van der Linden, *Can. J. Chem.*, **38**, 399 (1960).

(3) All nmr spectra were determined by means of a Varian A-56/60A spectrometer using ca. 25% solutions.

(4) The appearance of long-range coupling in basic solvents and its absence in neutral solvents such as carbon tetrachloride and 2-octanol suggests that the enhanced acidity of the trifluoromethylcarbinol ($pK = 11.8$)² [see also B. L. Dyatkin, E. P. Machalina, and I. L. Knunyan, *Tetrahedron*, **21**, 2991 (1965)] causes the oxygen to have considerable negative character when solvated by polar basic solvents. Both the consequent change in electronic structure of intervening bonds and possible changes in conformer populations (arising from the increased size of the solvated oxygen atom) could lead to enhanced long-range coupling.

phenethylamine (II) ($[\alpha]_D^{25} -37.0^\circ$ (neat), reported⁵ $[\alpha]_D^{25} -40.3^\circ$) the fluorine resonances appear as two sets of doublets, each of $|J|_{\text{HF}} = 7.2$ cps and centered at +4374 and +4376 cps from internal fluorotrichloromethane. The two sets were of equal intensity as expected for a racemate. Additionally, each of the four lines is further split into a triplet ($|J|_{\text{H'F}} = 0.7$ cps) by long-range coupling in the basic solvent. The fluoroalcohol can be recovered unchanged.

When racemic α -phenethylamine is used as solvent, only a doublet ($|J|_{\text{HF}} = 7.2$ cps) of triplets ($|J|_{\text{H'F}} = 0.7$ cps) is observed. The smaller splitting again appears to be long-range coupling with (presumably) the *ortho* aromatic protons. The coalescence of the spectra of the enantiomers suggests that, in this case, the exchange of (+) and (-) solvent partners by solvated fluoroalcohol is sufficiently fast so that all fluoroalcohol molecules have the same average magnetic environment.⁶

A sample of partially resolved⁷ ($[\alpha]_D^{25} +2.19^\circ$ (neat)) fluoroalcohol in *l*- α -phenethylamine again showed two sets of doublets plus triplet fine structure, but now the highest field set was discernibly more intense than the low-field set. When *d*- α -phenethylamine was used as solvent, the low-field set became the most intense. From measurements of the relative intensities of the two sets, it appears that this fluoroalcohol sample is a 47:53 \pm 0.6 mixture of enantiomers. The specific rotation of the dextrorotatory enantiomer is accordingly calculated to be 36.5 \pm 7.5°.⁸

To our knowledge, this is the first reported example of the determination of optical purity by nmr using an asymmetric solvent to render the spectra of the enantiomers nonequivalent.

(5) W. Theilaker and H. G. Winkler, *Chem. Ber.*, **87**, 691 (1954).

(6) Should this exchange be slowed, a more complex spectrum might arise. In the simplest case, racemic solvent, (\pm), and racemic solute, DL, could form four 1:1 solvates: (+)-D, (-)-L, (+)-L, and (-)-D. The first and second solvates are enantiomeric as are the third and fourth. Each set could have different spectra however, for the sets are diastereomeric. Being diastereomeric, their stabilities may differ and the populations of the two sets may be unequal. Interactions more complex than 1:1 could give rise to additional spectrally nonequivalent species ((+) (+)-D, (+) (+)-L, (+) (-)-D, etc.). Temperature studies and labeling experiments are being carried out to elucidate this point further.

(7) This sample was produced by reduction of the trifluoroacetophenone with a complex of lithium aluminum hydride-*l*- α -phenethylamine in tetrahydrofuran.

(8) Professor Harry Mosher has informed us that the maximum possible rotation of this enantiomer is 41.2°.

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The Reductive Amination of Polynuclear Aromatic Hydrocarbons. A Side Reaction of the Birch Reduction

Sir:

We wish to report the discovery of conditions which allow reductive amination of polynuclear aromatic hydrocarbons to tertiary or secondary amines under Birch reduction conditions as shown for the preparation of N-(1,2,3,4-tetrahydro-2-naphthyl)perhydroazepine (I) from naphthalene using hexamethylenimine and sodium. Birch reduction has been widely applied to aromatic hydrocarbons, using as reducing systems alkali