# Configurational Correlations for Chiral Epoxides by Nuclear Magnetic Resonance Spectroscopy in Optically Active Solvents

By I. Moretti, F. Taddei, and G. Torre*
(*Istituto di Chimica Organica dell'Universita', via Campi* 183,41100 *Modena, Italy*)

and N. Spassky
(*Laboratoire de Chimie Macromoléculaire, Université de Paris* 6,11, *Quai St. Bernard, Paris* 5$^e$, *France*)

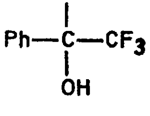
*Summary* The use of optically active 2,2,2-trifluorophenylethanol as an n.m.r. solvent causes enantiomeric spectral dissimilarities for chiral epoxides; the relative field positions of non-equivalent n.m.r. resonances are related to the absolute configuration of the solvated epoxides.

It is well known that enantiomers, although exhibiting identical properties in achiral media, may be readily distinguished by n.m.r. in appropriate optically active solvents.[1] As a consequence of this phenomenon, optical purities and absolute configurations of several series of neutral compounds may now be directly determined by n.m.r. without further chemical transformations.[1]

We have found that the use of optically active 2,2,2-trifluorophenylethanol (I)[2] as an n.m.r. solvent causes enantiomeric spectral dissimilarities for epoxides of type (II).

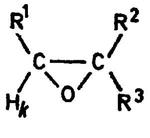
Non-equivalence in the n.m.r. spectra of epoxides in an optically active nematic phase,[3] or by addition of the europium complex of 3-heptafluorobutanoyl-(+)-camphor,[4] have been reported.

By using racemic and optically active epoxides (II) of known absolute configuration in (*R*)-(−)-(I), [$\alpha_D^{25}$ $-39{\cdot}1$ (neat, $l = 1$ cm)] and $CCl_4$, we obtained the results reported in the Table. A doubling of the enantiotopic $H_k$ proton resonances is clearly observed in each case. The relative field position of these resonances is correlated to the absolute configuration of the asymmetric carbon directly linked to the $H_k$ proton, and in (−)-(I) is low for the (*S*) configuration and high for the (*R*) configuration, respectively. The values of the enantiomeric chemical-shift differences are of the order generally reported[1] and allow a direct assessment of the enantiomeric *S*:*R* ratio, as we have experimentally



$$Ph-\overset{H}{\underset{OH}{C}}-CF_3$$

(I)



(II)

determined for a partially resolved sample of *trans*-stilbene oxide (IIh); calculated optical purity 9·6%, observed by relative peak-height measurement of the expanded diastereotopic $H_k$ resonances 10 ± 1%. An examination of the magnitudes of non-equivalence reported in the Table shows that the chemical-shift differences depend on the structure of the epoxides and on the steric and anisotropic character of the substituents directly linked to the oxiran ring, even if the presence of an aromatic group in the epoxides (II) is not a prerequisite for non-equivalence. Thus enantiotopic groups are revealed in the *cis*-[(IIe) and (IIg)] but not in the *trans*-[(IId) and (IIf)] derivatives, and the dependence of $\Delta\delta$ from the substituents follows the order H < Me < $Bu^t$ ⩽ Ph.

TABLE

*Enantiomeric chemical-shift differences and correlation of n.m.r. relative field position with absolute configuration for type* (II) *epoxides*

| | Epoxides | | | $\Delta\delta$, Hz[a] | | | | Known absolute configuration | Field position relative to the reported abs. configuration | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | $R^1$ | $R^2$ | $R^3$ | $H_k$ | $R^1$ | $R^2$ | $R^3$ | | $H_k$ | $R^1$ | $R^2$ | $R^3$ |
| a; | Me | H | H | 0·47 | — | — | — | (−)-(*S*) | low | — | — | — |
| b; | $Bu^t$ | H | H | 1·95 | 0·60 | 1·00 | 1·00 | (+)-(*S*)[b] | low | high | high | high |
| c; | Ph | H | H | 2·36 | n.d. | 0·51 | 0·58 | (−)-(*S*) | low | [c] | low | high |
| d; | Ph | H | Me | 2·08 | n.d. | — | — | (−)-(1*S*, 2*S*) | low | [c] | — | — |
| e; | Ph | Me | H | 1·83 | n.d. | 0·76 | 0·87 | (+)-(1*S*, 2*R*) | low | [c] | high | high |
| f; | Ph | H | $Bu^t$ | 1·43 | n.d. | — | — | — | — | — | — | — |
| g; | Ph | $Bu^t$ | H | 1·35 | n.d. | 0·60 | 1·42 | — | — | — | — | — |
| h; | Ph | H | Ph | 0·98 | n.d. | 0·98 | n.d. | (−)-(*S*,*S*) | low | [c] | low | [c] |

[a] N.m.r. spectra were measured on a JEOL-C60-HL spectrometer at 25° using samples composed of 2 : 1 : *ca.* 3 mol ratios of alcohol epoxide : $CCl_4$ respectively. [b] Personal communication by N. Spassky and M. Sepulchre. [c] Not determined.

Explanations of enantiomeric non-equivalence in chiral solvents have invoked strong and rapid solvent–solute interactions (*i.e.* hydrogen bonding) which afford conformationally mobile 1 : 1 diastereoisomeric solvates and secondary interactions which are essential to the population of the conformations believed responsible for spectral non-equivalence.[1]

At present it seems extremely difficult to rationalise the results observed for our systems with a hypothetical model for specific chiral (I)–(II) interactions. Presumably an association between the basic oxygen atom of the oxiran ring and the acidic alcohol function is responsible for the formation of short-lived diastereoisomeric solvated species whose conformations are dependent on secondary attractive interactions between the oxiran ring of (II) and the electron-rich aromatic group of the chiral solvent (I).†

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† Evidence for the association of the benzene ring with epoxides has been provided by the solvent dependencies of molar Kerr constants[5] and by n.m.r. spectra.[6]

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