

## Configurational Assignment of Diastereomeric Sulphoxides by Nuclear Magnetic Resonance Substituent and Solvent Effects

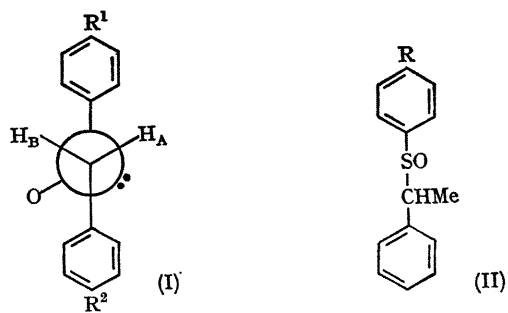
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WE have reported that an absolute assignment of methylene signals of benzyl phenyl sulphoxides (I) can be made from a study of the effects of substituents and solvents on n.m.r. chemical shifts.<sup>1,2</sup> The proton *gauche* to the lone pair on sulphur ( $H_A$ ) is more sensitive to a substituent change,<sup>†</sup> and the proton *trans* to the lone pair ( $H_B$ ) is more sensitive to addition of trifluoroacetic acid (TFA).<sup>‡</sup> We now report an application of this method to a structural assignment of diastereoisomeric  $\alpha$ -methylbenzyl phenyl sulphoxides (II).

Racemic sulphides were oxidized at room temperature with peracetic acid. N.m.r. analysis of the resulting sulphoxides allowed quantitative assessment of the ratios of diastereoisomers, since the appropriate signals are well

separated from each other (Figure). The ratios depend on



<sup>†</sup>  $\rho(H_A)$  13.9 c./sec./ $\sigma_p$ ,  $\rho(H_B)$  6.3 c./sec./ $\sigma_p$  in  $\text{CDCl}_3$ .

<sup>‡</sup>  $\Delta(H_A)$  -0.26 to -0.40,  $\Delta(H_B)$  -0.47 to -0.60 p.p.m. [ $\Delta = \tau(\text{TFA}) - \tau(\text{CDCl}_3)$ ].

TABLE

Solvent R =	(II)-major				$\Delta(R)^c$	(II)-minor				$\Delta(R)$
	Me	H	Cl	$\text{NO}_2$		Me	H	Cl	$\text{NO}_2$	
$\text{CCl}_4$	$\tau$ 6.38	6.34	6.34	6.29	-0.09	6.12	6.09	6.05	5.95	-0.17
$\Delta(\text{TFA})^a$	-0.84	-0.76	-0.70	-0.61		-0.64	-0.59	-0.51	-0.50	
$\Delta(\text{benzene})^b$	+0.09	+0.14	+0.22	+0.37		+0.21	+0.25	+0.35	+0.57	

<sup>a</sup>  $\tau(\text{TFA}) - \tau(\text{CCl}_4)$ , <sup>b</sup>  $\tau(\text{benzene}) - \tau(\text{CCl}_4)$ , <sup>c</sup>  $\tau(\text{NO}_2) - \tau(\text{Me})$ .

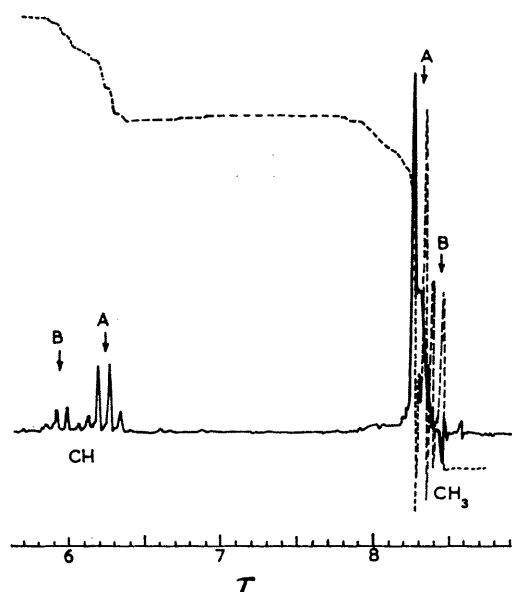
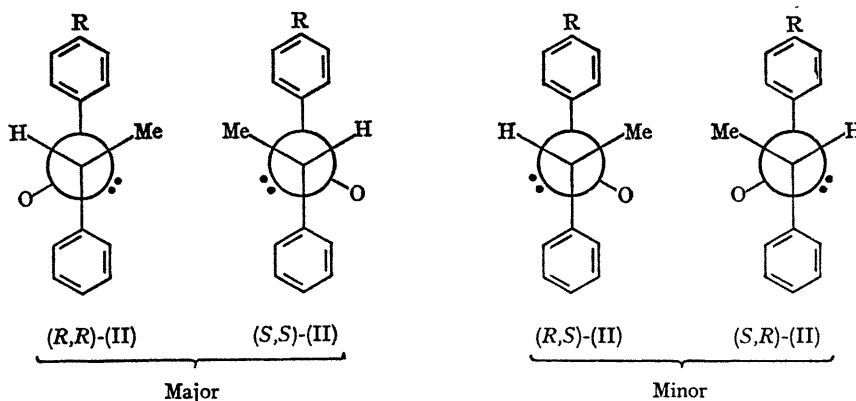


FIGURE. Nuclear magnetic resonance spectrum of diastereomeric mixture of methylbenzyl *p*-chlorophenyl sulphoxides (II) in deuteriochloroform; A, (*R,R*)- and (*S,S*)-(II); B, (*R,S*)- and (*S,R*)-(II).

the substituent R; however, it was always the higher-melting isomer that predominated in the reaction mixture.

The Table shows methine chemical shifts of these compounds in carbon tetrachloride and solvent shifts induced in TFA and benzene. The substituent shift when the substituent R is changed from methyl to nitro is  $-0.09$  p.p.m. for (II)-major (see formulae) and  $-0.17$  p.p.m. for (II)-minor (in  $\text{CCl}_4$ ). The solvent shifts induced in TFA are greater for the former than for the latter. These facts show that (II)-major has its methine proton *gauche* to the sulphoxide oxygen and (II)-minor has its methine proton *trans* to the oxygen atom in its most stable conformer.

The Table also shows that solvent shifts induced in benzene are greater for (*R,S*)- and (*S,R*)-diastereoisomers than for (*R,R*)- and (*S,S*)-sulphoxides. It is known that benzene molecules are transiently oriented by local or molecular solute dipoles, so that the benzene molecules avoids the negative end<sup>¶</sup> in a collision complex.<sup>3</sup> This explains the larger shielding of the methine proton or (*R,S*)- or (*S,R*)-(II) by benzene in terms of the anisotropy of the aromatic solvent molecules<sup>\*\*</sup> and provides strong support for the configuration assignment.

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<sup>¶</sup> The S-O bond in sulphoxides has an electric moment corresponding to a charge separation in the sense  $\text{S}^+-\text{O}^-$ .

<sup>\*\*</sup> A gradual increase in  $\Delta(\text{benzene})$  and decrease in  $\Delta(\text{TFA})$  is explicable in terms of the decreased basicity of sulphoxide oxygen with increasing electron-withdrawal by the substituent R.

<sup>1</sup> M. Nishio, *Chem. and Pharm. Bull. (Japan)*, in the press.

<sup>2</sup> M. Nishio, *Chem. Comm.*, 1968, 562.

<sup>3</sup> N. S. Bhacca and D. H. Williams, "Applications of N.M.R. Spectroscopy in Organic Chemistry," Holden-Day Inc., San Francisco, 1964, ch. 2; P. Laszlo, *Progr. N.M.R. Spectroscopy*, 1966, 3, 348.