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Nuclear Magnetic Resonance Studies of Sulfur Compounds. III.¹⁾
The Substituent and Solvent Effect on Magnetic Nonequivalence of
the Methylene Protons of Phenyl Phenacyl
and Phenyl Benzyl Sulfoxides²⁾

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The magnetic nonequivalences between the methylene protons of phenyl phenacyl sulfoxides and phenyl benzyl sulfoxides have been measured in a variety of solvents. A clear correlation observed between the electron withdrawal power of substituent and $\nu_A - \nu_B$ is discussed by considering the geometry of these protons with respect to the S-O bond.

It is suggested that reaction field effects, specific solvent-solute interactions, as well as the electronic character of substituents are responsible for the observed change in magnetic nonequivalence. It is also suggested that, by a careful consideration of solvent effects, it is possible to make an assignment of these protons, a method for which has not hitherto been proposed for acyclic systems.

It is well known that methylene protons alpha to a sulfoxide group are magnetically nonequivalent, due to the absence of a plane of symmetry on sulfur atom, to give a quartet signal of the AB-type.⁴⁻⁸⁾ In a previous paper,⁹⁾ we studied correlations between the degree of magnetic nonequivalence of the protons of a methylene group¹⁰⁾ adjacent to a sulfoxide group and the structure of the molecule close to the methylene group, using phenyl phenacyl and phenyl benzyl sulfoxides and related compounds as model substances. These experiments led us to findings that the electronic character of the substituent plays an important role in determining the magnetic nonequivalence of the methylene protons ($\nu_A - \nu_B$) and that there is a linear correlation between $\nu_A - \nu_B$ and the electron withdrawal power of the substituent. The most interesting feature of these experiments, however, was the finding that the chemical shift of each proton depended upon the electron withdrawal power of the substituent to a varying degree.

In order to discover the mechanism whereby the substituent R influences the chemical shifts of two protons to a different degree, we extended this work to an examination of the magnetic nonequivalence of these protons in a variety of solvents. A careful inspection of the

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- 2) This work was presented at The 6th Symposium on Nuclear Magnetic Resonance (Japan) at Kyoto, October 1967.
- 3) Location: Morooka-cho, Kohoku-ku, Yokohama.
- 4) T.D. Coyle and F.G.A. Stone, *J. Am. Chem. Soc.*, **83**, 4138 (1961).
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- 6) K. Griesbaum, A.A. Oswald, and B.E. Hudson, *J. Am. Chem. Soc.*, **85**, 1969 (1963).
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- 8) M. Nishio and T. Ito, *Chem. Pharm. Bull.* (Tokyo), **13**, 1392 (1965).
- 9) M. Nishio, *Chem. Pharm. Bull.* (Tokyo), **15**, 1669 (1967).
- 10) For other correlations between the magnitude of magnetic nonequivalence in benzylic methylene groups and the structure of the molecules, see refs. 11-13.
- 11) G.M. Whitesides, D. Holtz, and J.D. Roberts, *J. Am. Chem. Soc.*, **86**, 2628 (1964).
- 12) G.M. Whitesides, J.J. Grocki, D. Holtz, H. Steinberg, and J.D. Roberts, *J. Am. Chem. Soc.*, **87**, 1058 (1965).
- 13) J.C. Randall, J.J. McLeskey, III, P. Smith, and M. E. Hobbs, *J. Am. Chem. Soc.*, **86**, 3229 (1964).

present data led us to a possibility of assigning these two protons and to an understanding of the marked substituent and solvent dependences observed for the methylene chemical shift difference in these sulfoxides.

Results

a) $\tau \frac{A+B}{2}$

In Table I are summarized the methylene chemical shifts $\tau \frac{A+B}{2}$ of *para*-substituted phenyl phenacyl sulfoxides (Ia-d) phenyl benzyl (IIa-d), phenyl *p*-chlorobenzyl (IIIa-d) and phenyl *p*-nitrobenzyl sulfoxides (IVa-d) in methyl iodide.¹⁴⁾ The solvent shifts induced in deuteriochloroform, acetone, dimethylformamide, benzene, pyridine, acetic acid and trifluoroacetic acid solutions are given; a positive value indicates an upfield shift and a negative value indicates a downfield shift relative to methyl iodide.

Of particular interest among the data listed in Table I is the substituent dependence of solvent shifts ($\Delta_{\text{solvent}}^{\text{MeI}}$) observed in benzene, acetic acid (AcOH) and in trifluoroacetic acid (TFA).

Benzene shift increases with the increasing electron withdrawal power of the substituent R. Hydrogen bond formation of solute C-H¹⁵⁾ groups with π -electrons of benzene should be the major mechanism responsible for this phenomenon. The ability of the C-H group to act as proton donor depends on the electron withdrawal power of the substituent. It is very natural to expect an enhanced upfield shift to the methylene chemical shift (in benzene) from the substitution of a more electron withdrawing group, since a C-H... π interaction increases with an increase of the acidity of C-H group. Increased upfield shift is also observed upon changing the substituent R' from H to a NO₂ group. This phenomenon is consistent with the finding formerly reported by Nakagawa, *et al.*¹⁷⁻¹⁹⁾ that methyl protons of *p*-nitrotoluene resonate at a lower magnetic field in CCl₄ and at a higher field in benzene than any other methyl protons of *para*-substituted toluene series. To obtain evidence supporting the responsibility of a C-H... π interaction mechanism, we examined nuclear magnetic resonance (NMR) spectra of (Ia-d) in mesitylene, which is known to be a strong proton acceptor. Greater solvent shifts were in fact observed in this solvent than in benzene as is shown in Table I.

The direct C-H... π interaction is not the single factor, however, since solvent shift of about a same order ($\Delta_{\text{benzene}}^{\text{CDCl}_3} = +0.41 - +0.44$ ppm) was observed for chemical shift of methyl

- 14) A carbon tetrachloride solution is thought to be most suitable as a reference because of its nonpolar property as well as the absence of specific interactions with a sulfoxide molecule. Unfortunately, however, several compounds were not sufficiently soluble in CCl₄ to give nuclear magnetic spectra. We therefore took a methyl iodide solution as a reference, since interaction of MeI with a solute molecule is negligible.
- 15) For a survey of C-H groups as proton donors in hydrogen bonding, see ref. 16.
- 16) A. Allerhand and P. von Raugè Schleyer, *J. Am. Chem. Soc.*, **85**, 1715 (1963).
- 17) N. Nakagawa, *Nippon Kagaku Zasshi*, **82**, 141 (1961).
- 18) N. Nakagawa and S. Fujiwara, *Bull. Chem. Soc. Japan*, **34**, 143 (1961).
- 19) N. Nakagawa, "N.M.R. supekutoru no Kaishaku (in Japanese)," Kyoritsu Shuppan Inc., Tokyo, 1966, p. 76.

TABLE I. Chemical Shifts $\left(\tau \frac{A+B}{2}\right)$ and Solvent Shifts^{a)} [$\Delta = \tau(\text{Solvent}) - \tau(\text{MeI})$] of Phenyl Sulfoxides $R-C_6H_4SOCH_2-X$

Solvent	R		Me (a)	H (b)	Cl (Br) (c)	NO ₂ (d)
MeI	COC ₆ H ₅	I	5.64	5.61	5.57	5.47
	C ₆ H ₅	II	6.06	6.04	6.00	5.89
	C ₆ H ₄ Cl	III	6.06	6.03	6.01	5.91
	C ₆ H ₄ NO ₂	IV	5.92	5.88	5.87	5.76
CDCl ₃		I	-0.04	-0.02	+0.01	+0.03
		II	-0.07	-0.07	-0.02	+0.01
		III	-0.03	0.00	+0.03	+0.03
		IV	+0.01	+0.04	+0.05	+0.07
Acetone		I	-0.16	-0.18	-0.19	-0.22
		II	-0.07	-0.11	-0.10	-0.12
		III	-0.12	-0.12	-0.14	-0.18
		IV	-0.17	-0.16	-0.19	-0.21
DMF		I	-0.34	-0.35	-0.36	-0.40
		II	-0.18	-0.19	-0.20	-0.21
		IV	-0.28	-0.27	-0.31	-0.33
C ₆ H ₆		I	+0.41	+0.50	+0.64	+0.82
		II	+0.31 ^{b)}	+0.38	+0.53	+0.73
		III	+0.51	+0.60	+0.71	+0.90
		IV	+0.75	+0.85	+0.95	+1.13
C ₅ H ₅ N		I	-0.49	-0.46	-0.49	-0.54
		II	-0.19 ^{c)}	-0.17	-0.13	-0.16
		III	-0.14	-0.12	-0.12	-0.14
		IV	-0.17	-0.14	-0.16	-0.17
Me ₃ C ₆ H ₃		I	+0.47	+0.66	+0.74	
TFA		I	-0.69	-0.63	-0.57	-0.48
		II	-0.57 ^{d)}	-0.55	-0.46	-0.36
		III	-0.55	-0.49	-0.45	-0.34
		IV	-0.49	-0.46	-0.40	-0.28
AcOH		I	-0.43	-0.41	-0.38	-0.33
		II	-0.31	-0.30	-0.26	-0.19
		III	-0.29	-0.27	-0.25	-0.22
		IV	-0.28	-0.26	-0.25	-0.21

a) A positive value indicates an upfield shift and a negative value indicates a downfield shift relative to methyl iodide.

b) $\Delta_{\text{benzene}}^{\text{CDCl}_3} = +0.41, +0.44$ and $+0.43$ ppm for methyl protons of IIa, IIIa and IV respectively

c) $\Delta_{\text{pyridine}}^{\text{CDCl}_3} = +0.19, +0.23$ and $+0.16$ ppm for methyl protons of IIa, IIIa and IVa respectively

d) $\Delta_{\text{TFA}}^{\text{CDCl}_3} = -0.06, -0.04$ and -0.04 ppm for methyl protons of IIa, IIIa and IVa respectively

protons on the phenyl ring (Table I, footnote b). Interaction between the phenyl groups of these molecules with solvent benzene molecules should be also taken into account.

The other aromatic solvents studied did not show such a remarkable solvent shift as was observed for benzene and mesitylene. This is probably due to the presence of a functional group on these solvent molecules, which reduces the ability of an aromatic molecule to form a collision complex with sulfoxide. By means of a functional group, these solvents are able to form a specific complex with the active methylene of the sulfoxide molecules, and this also disturbs the interaction of an aromatic molecule with a proton donor.

In pyridine solutions of *p*-methylphenyl benzyl sulfoxides (IIa), (IIIa) and (IVa), downfield solvent shifts ($\Delta_{\text{pyridine}}^{\text{MeI}} -0.14$ — -0.19 ppm) were in fact observed for methylene peaks. In contrast, upfield shifts ($\Delta_{\text{pyridine}}^{\text{CDCl}_3} = +0.19$ — $+0.23$ ppm) were observed for methyl protons in the same compounds (Table I, footnote c)

Another interesting feature shown in Table I is the substituent dependence of solvent shifts observed in acidic solvents. TFA-shift ($\Delta_{\text{TFA}}^{\text{MeI}}$) decreases as the electron withdrawal power of the substituent R increases. Kawazoe, *et al.*²⁰⁾ reported that the protons adjacent to amino, amide, ether or carbonyl groups show considerable downfield shift in TFA according to the basicities of the functional group.

TFA shifts of methylene protons adjacent to sulfoxide group are much larger than those observed for alpha-methylenes of some carbonyl compounds.²¹⁾ The greater TFA-shifts observed for methylene protons alpha to the sulfoxide group indicate that hydrogen accepting ability of sulfoxide is larger than that of the carbonyl group. The dependence of solvent shifts ($\Delta_{\text{AcOH}}^{\text{MeI}}$ and $\Delta_{\text{TFA}}^{\text{MeI}}$) can be explained by a consideration of the basicity change of the sulfoxide oxygen, which decreases as the electron withdrawal power of the substituent increases.

It is well known that sulfoxides form co-ordination compounds with metal derivatives and it has been suggested that the oxygen and not the sulfur was responsible for complex formation with respect to a number of complexes, and only for a few complexes was sulfur-donation assumed.²²⁻²⁴⁾ It is also reported that sulfoxides form a strong hydrogen bond with CHCl_3 and MeOD by means of S-O oxygen atom.²⁵⁾ From evidences cited above, which are based

TABLE II. Chemical Shifts and Solvent Shifts [$\Delta = \tau(\text{Solvent}) - \tau(\text{MeI})$] of Methylene Protons of Phenyl Benzyl Sulfides (II', III' and IV') and Phenyl Benzyl Sulfones (II'', III'' and IV'') $\text{R}-\text{C}_6\text{H}_4-\text{X}-\text{CH}_2\text{C}_6\text{H}_4-\text{R}'$

Solvent	Compound	X	R'/R	Me (a)	H (b)	Cl (c)	NO ₂ (d)
MeI	II'	S	H	5.97 ^{a)}	5.90	5.91	5.71
	III'		Cl	5.99	5.98	5.93	5.72
	IV'		NO ₂	5.88	5.82	5.82	5.59
	II''	SO ₂	H	5.74	5.71	5.69	5.60
	III''		Cl	5.76	5.73	5.71	5.61
	IV''		NO ₂	5.59	5.55	5.54	5.43
TFA	II'	S	H	-0.06 ^{b)}	-0.02	-0.01	0.00
	III'		Cl	-0.04	-0.02	+0.01 ^{c)}	+0.03
	IV'		NO ₂	-0.01	+0.02	+0.04	+0.02
	II''	SO ₂	H	-0.27	-0.26	-0.24	-0.21
	III''		Cl	-0.28	-0.27	-0.24	-0.21
	IV''		NO ₂	-0.29	-0.26	-0.25	-0.22
AcOH	II'	S	H	-0.01	0.00	0.00	+0.01
	III'		Cl	0.00	+0.01	+0.01	0.00
	IV'		NO ₂	0.00	0.00	0.00	+0.01
	II''	SO ₂	H	-0.12	-0.11	-0.10	-0.09
	III''		Cl	-0.14	-0.13	-0.13	-0.11
	IV''		NO ₂	-0.13	-0.12	-0.12	-0.09

a) These values are recorded in τ -scale from internal TMS ($\tau=10.0$).

b) A negative value indicates a downfield shift relative to a MeI solution.

c) A positive value indicates an upfield shift relative to a MeI solution.

21) They reported TFA-shifts ($\Delta_{\text{TFA}}^{\text{CCl}_4}$) of -0.27—-0.29 ppm for these protons.

22) R.G. Laughlin, *J. Org. Chem.*, **25**, 864 (1960).

23) F.A. Cotton and R. Francis, *J. Am. Chem. Soc.*, **82**, 2986 (1960).

24) M.F. Lappert and J.K. Smith, *J. Chem. Soc.*, 1961, 3224.

25) M. Tamres and S. Searles, Jr., *J. Am. Chem. Soc.*, **81**, 2100 (1959).

mainly on infrared analysis, it is probably safe to assume that oxygen-donation predominates in sulfoxide-acid complexes.

In order to confirm the structure of sulfoxide-acid complexes, we measured methylene NMR spectra of some sulfides and sulfones and compared their solvent shifts with those observed for corresponding sulfoxides. In Table II are listed methylene chemical shifts of phenyl benzyl (II' and II''), phenyl *p*-chlorobenzyl (III' and III'') and phenyl *p*-nitrobenzyl sulfides (IV') and sulfones (IV'') recorded in MeI solutions and solvent shifts induced in TFA and AcOH relative to MeI solution.

As is shown in Table II, methylene protons alpha to a sulfide group do not show an appreciable TFA-shift ($\Delta_{\text{TFA}}^{\text{MeI}} = -0.06$ — $+0.04$ ppm). In contrast, those of sulfone derivatives show a significant TFA-shift (-0.21 — -0.29 ppm). TFA-shifts of sulfonyl methylene protons, however, are appreciably smaller than those observed for sulfoxide methylenes (-0.28 — 0.57 ppm). Essentially the same result, although the magnitude of solvent shift is smaller than that observed in TFA, was obtained also in AcOH solutions, where $\Delta_{\text{AcOH}}^{\text{MeI}}$ are -0.01 — $+0.01$ ppm for $-\text{SCH}_2-$, -0.19 — -0.31 ppm for $-\text{SOCH}_2-$ and -0.09 — -0.14 ppm for $-\text{SO}_2\text{CH}_2-$. Above results clearly demonstrate that the donor resides on oxygen atom in sulfoxides. If it were on sulfur, sulfoxides should be less basic than sulfides. The relative basicity in this series toward acidic solvent molecules is in the following order:

This is consistent with the finding of Laughlin²²⁾ that dimethyl sulfoxide is considerably more basic toward BF_3 than either sulfide or sulfone.

b) $\nu_A - \nu_B$

Magnetic nonequivalences ($\nu_A - \nu_B$) of methylene protons in Ia-d, IIa-d, IIIa-d and IVa-d are listed in Table III. As is shown in Table III, $\nu_A - \nu_B$ is quite solvent sensitive. $|\nu_A - \nu_B|$ for phenyl phenacyl sulfoxides (Ia-d) is smaller in solvents of high dielectric constants (ϵ) than in solvents of low dielectric constant. In contrast, $|\nu_A - \nu_B|$ for phenyl benzyl (IIa-d), phenyl *p*-chlorobenzyl (IIIa-d) and phenyl *p*-nitrobenzyl sulfoxides (IVa-d) is larger in high dielectric constant solvents than in solvents of low dielectric constant.

Figures 1a and 1b illustrate the plots of $\nu_A - \nu_B$ versus solvent dielectric constant observed for *p*-methylated phenacyl sulfoxide (Ia) and *p*-nitrophenyl benzyl sulfoxide (IIId) (For the meaning of signs given to $\nu_A - \nu_B$ in Fig. 1a and 1b, see discussion below). Although it seems that there is an approximately linear relationship between $\nu_A - \nu_B$ and ϵ , several solvents are exceptions. Hydrogen-bonding solvents, such as trifluoroacetic acid are clearly exceptions, in which $\nu_A - \nu_B$ is considerably smaller than would be expected from a consideration of dielectric constants. These evidences suggest that the electric field effect and hydrogen bonding are responsible for determining the magnitude of magnetic nonequivalence and this will be discussed in a separate section.

Another interesting feature seen in Table III is that the magnetic nonequivalence of these protons depends on the electronic character of the substituents. $|\nu_A - \nu_B|$ increases with the increasing electron withdrawal power of the substituent R in some cases and decreases in the others. Exceptions were observed for the series of phenyl *p*-chlorobenzyl sulfoxides (IIIa-d) in AcOH and for the series of phenyl *p*-nitrobenzyl sulfoxides (IVa-d) in TFA, in which $|\nu_A - \nu_B|$ decreases at first and then increases with increasing electron withdrawal power of the substituent R.

By plotting the chemical shifts of each proton against $\nu_A + \nu_B / 2$ (considered as a parameter of the electron withdrawal power of the substituent²⁶⁾), two linear slopes were obtained. For example, slopes obtained for IIa-d ($\text{R}' = \text{H}$), IIIa-d ($\text{R}' = \text{Cl}$) and IVa-d ($\text{R}' = \text{NO}_2$) in deuterochloroform are shown in figure 2.

26) B.P. Dailey and J.N. Shoolery, *J. Am. Chem. Soc.*, **77**, 3977 (1955).

TABLE III. Magnetic Nonequivalence of Methylene Protons^{a)} of Phenyl Sulfoxides $\text{RC}_6\text{H}_4\text{SOCH}_2\text{-X}$

Solvent	ϵ	R	Me (a)	H (b)	Cl(Br) (c)	NO_2 (d)
MeI	7.00	COC_6H_5 I	-21.3 ^{b,c)}	-18.9	-16.0	-7.7
		C_6H_5 II	< 3	< 3	< 3	< 3
		$\text{C}_6\text{H}_4\text{Cl}$ III	9.0	12.5	14.3	20.2
		$\text{C}_6\text{H}_4\text{NO}_2$ IV	21.8	24.0	24.5	28.8
CDCl_3	5.05	I	-28.8	-26.4	-24.2	-16.3
		II	-10.6	-9.2	-10.8	-3.6
		III	< 3	< 3	< 3	8.2
		IV	18.4	20.8	19.6	25.3
Acetone	21.4	I	-6.2	< 3	< 3	< 3
		II	8.1	10.5	10.5	17.8
		III	17.3	17.5	18.5	22.8
		IV	21.6	24.4	23.4	26.6
DMF	36.7	I	< 3	< 3	< 3	11.5
		II	17.6	19.2	19.4	25.0
		IV	25.2	26.6	27.4	30.2
		I	-27.3	-29.3	-25.8	-15.6
C_6H_6	2.28	II	< 3	< 3	< 3	5.0
		III	5.0	10.6	12.0	17.2
		IV	18.4	21.9	23.0	25.9
		I	-19.1	-14.3	-13.2	< 3
$\text{C}_5\text{H}_5\text{N}$	12.5	II	< 3	5.0	5.0	12.0
		III	12.4	15.2	16.0	24.0
		IV	22.2	23.4	23.6	28.2
		I	-40.2	-35.9	-34.0	-25.6
TFA	39.5	II	-29.4	-29.2	-31.6	-23.0
		III	-25.6	-23.6	-22.8	-11.0
		IV	-13.6	-9.3	< 3	+11.0
		I	-36.2	-35.0	-32.1	-25.4
AcOH	6.3	II	-17.3	-13.1	-12.0	-10.6
		III	-5.0	< 3	< 3	+8.2
		IV	< 3	+10.5	+11.1	+18.8

a) $\nu_A - \nu_B$ given in c/s at 100 Mc/sb) J_{AB} for I; 14.0–15.5 c/s, for II, III and IV; 12.0–13.5 c/s

c) For the meaning of signs, refer to the explanation given in the discussion.

This figure well demonstrates that one proton is more dependent on the change of the substituent and the other less dependent. The proton which resonates originally in a higher magnetic field suffers a more pronounced downfield shift with increasing electron withdrawal power of the substituent than does the other proton. After the "crossing", the dependent proton resonates in a lower magnetic field than the less dependent proton. Essentially similar results were obtained in other cases except in acidic solvents.

Thus, if we define the "more dependent proton" as H_A and the "less dependent proton" as H_B , it is possible to give signs to the values of $\nu_A - \nu_B$. In Table III and figures 1a, 1b are given the sign to $\nu_A - \nu_B$ thus defined. H_A resonates at a higher magnetic field when $\nu_A - \nu_B < 0$ and at a lower field when $\nu_A - \nu_B > 0$.

In order to be certain of the relative assignments of these signals thus determined, we examined the solvent shifts of proton signals induced from a portionwise addition of an acidic solvent to reference solutions of several compounds. In figures 3a and 3b are illustrated the solvent shifts induced from a gradual addition of TFA in methyl iodide solutions of Ic and IIIb.

The lower peaks of the AB-quartet (H_B) in a MeI solution of Ic is more sensitive to an increase of TFA-concentration and $|\nu_A - \nu_B|$ increases with an increase of additional TFA

Fig. 1a. A Plot of Solvent Dielectric Constant (ϵ) versus $\nu_A - \nu_B$ of *p*-Methylphenyl Phenacyl Sulfoxide (I)_a, Numbers refer to the Solvents Listed Below

1. CCl_4 , 2. C_6H_6 , 3. ether 4. CDCl_3 , 5. AcOH , 6. MeI , 7. CH_2Cl_2 , 8. $\text{C}_6\text{H}_5\text{N}$, 9. Ac_2O , 10. acetone, 11. $\text{C}_6\text{H}_5\text{CN}$, 12. $\text{C}_6\text{H}_5\text{NO}_2$, 13. DMF, 14. MeCN, 15. TFA, 16. DMSO, 17. HCOOH

Fig. 1b. A Plot of Solvent Dielectric Constant (ϵ) versus $\nu_A - \nu_B$ of *p*-Nitrophenyl Benzyl Sulfoxide (II)_d, Numbers refer to the Solvents Listed in Fig. 1a

Fig. 2. Plots of Chemical Shifts (ν_A and ν_B) versus $\nu_A + \nu_B/2$ of Substituted Phenyl Benzyl Sulfoxides $\text{R-C}_6\text{H}_4\text{SO-CH}_2\text{C}_6\text{H}_4\text{-R'}$ (II, III and IV) in CDCl_3

(Fig. 3a). For IIIc, in contrast, it is the upper peaks of the quartet (H_B) which suffer a more enhanced addition shift (Fig. 3b). In this case, the original AB-quartet in a MeI solution gradually coalesces to a singlet and then separates again to give finally another AB-quartet by a portionwise addition of TFA. These facts support the relative assignments which have been tentatively given in Table III. The relative signs given to $\nu_A - \nu_B$ in other solutions were also confirmed to be correct from a similar method.

Thus, it is concluded that, according to the definition mentioned above, $\nu_A - \nu_B$ is smaller in low dielectric constant solvents than in solvents of higher dielectric constant, and increases with increasing electron withdrawal power of the substituent R. In other words, chemical shifts of these proton suffer a downfield movement with increasing electron withdrawal power of the substituent and with increasing solvent dielectric constant, in which the degree of dependence is always greater for H_A than for H_B . This evidence suggests that we may be able to determine each proton assignment which, in an aliphatic noncyclic system, has not generally been possible.

Fig. 3a. Schematic Illustrations of the Effect of Additive Trifluoroacetic Acid on the Methylene Chemical Shifts for a Methyl Iodide Solution of *p*-Bromophenyl Phenacyl Sulfoxide (Ic)

Fig. 3b. Schematic Illustrations of the Effect of Additive Trifluoroacetic Acid on the Methylene Chemical Shifts for a Methyl Iodide Solution of Phenyl *p*-Chlorobenzyl Sulfoxide (IIIb)

Discussion

For detailed discussion of the substituent and solvent dependence of $\nu_A - \nu_B$ in the molecules studied here, it is very important to consider dipolar association of sulfoxides, populations of rotational isomers, and specific solvent solute interactions.

Watson, *et al.*²⁷⁾ reported on the NMR spectra of 2-thiaindane 2-oxide in CDCl_3 at various temperatures. It is pointed out that, on lowering the temperature, $\nu_A - \nu_B$ decreases and finally coalesces into a singlet at -37° . This phenomenon was attributed to the presence of monomer-dimer equilibrium, the dimer predominating at lower temperatures. Ōki, *et al.*⁷⁾ examined the same compound in C_6D_6 , DMSO-d_6 and D_2O and reported that this phenomenon does not always occur with other solvents. They noted that the solvent solute interactions, such as hydrogen bond formation, are also to be taken into account. We examined the effect of concentration changes on the NMR spectra of these compounds and found that $\nu_A - \nu_B$ and $\tau \frac{A+B}{2}$ do not show an observable change on dilution (from 20 to 1%). Thus it is safe to assume that a dipolar association of sulfoxides is not responsible for the observed changes in $\nu_A - \nu_B$ of these protons of sulfoxides studied in this work.

It was also reported by Ōki, *et al.*⁷⁾ that $\nu_A - \nu_B$ of *t*-butyl neopentyl sulfoxide hardly changes with temperature from $+60^\circ$ down to -40° (from 19.8 c/s to 17.9 c/s at 60 Mc/s). This fact indicates that the conformation of this molecule is fixed, having two bulky groups in a *trans* relation. In Tables IV and V are listed the variation of $\nu_A - \nu_B$ of some compounds with temperature from 118° down to -41° .

$\nu_A - \nu_B$ increases on lowering the temperature, and decreases at elevated temperatures, but does not show such a marked effect as was observed for 2-thiaindane 2-oxide in CDCl_3 and in C_6D_6 . It seems that there are some changes in the population of rotational isomers, how-

27) R.F. Watson and J.F. Eastham, *J. Am. Chem. Soc.*, **87**, 644 (1965).

TABLE IV. Temperature Dependence of $\nu_A - \nu_B$ (c/s at 100Mc/s) of $RC_6H_4SOCH_2C_6H_4NO_2$ [IV_{a-d}] and in $CDCl_3$

Temp.(°C)/R	Me	H	Cl	NO ₂
-41	24.6	29.0	30.0	35.4
+24	18.4	20.8	19.6	25.3
+65	14.0	16.2	16.9	20.2

 TABLE V. Temperature Dependence of $\nu_A - \nu_B$ (c/s at 100 Mc/s) $RC_6H_4SOCH_2C_6H_5$ [II_{a-d}] in $DMSO-d_6$

Temp.(°C)/R	Me	H	Cl	NO ₂
+24	15.6	17.8	19.5	25.8
49	14.3	15.0	16.6	23.0
82	11.2	12.2	13.2	19.9
101	9.6	11.5	13.4	18.7
118	8.3	10.9	11.5	16.6

ever, it is probably safe to assume that the conformer having two phenyl groups in a *trans* relation predominates at room temperature (see V and VI).

Assuming that the conformation is rather fixed, or that the change in the populations of rotational isomers is not the major factor determining the magnetic nonequivalence in a solvent, we are now led to the possibility of assigning two protons by a careful consideration of substituent and solvent effect on $\nu_A - \nu_B$.

Consideration of the Substituent Effect

There are at least three mechanisms by which the change of the substituent R may influence the chemical shift of each proton to a different degree.

i) One explanation is that the anisotropy of the magnetic susceptibility of S-O bond,^{7,28)} is affected by the change of the electron withdrawal power of the substituent. Thus the change of the magnetic anisotropic shielding effect of this bond may cause a more pronounced effect on the proton *gauche* which is in the proximity of the S-O bond.

ii) To explain an unusually large chemical shift difference between C_4-H_{ax} and C_4-H_{eq} of quinolizidine (VII), Hamlow, *et al.*²⁹⁾ proposed a mechanism in which a charge transfer hyper-

28) J.G. Pritchard and P.C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 2105 (1961).

29) H.P. Hamlow, S. Okuda, and N. Nakagawa, *Tetrahedron Letters*, **1964**, 2553.

conjugation of the lone pair in a σ^*C-H orbital is considered. The same arguments, applied to the sulfoxide molecules, lead us to another explanation in terms of the difference in the bonding character between $C-H_{gauche}$ and $C-H_{trans}$ bond (See X). It is possible that the substituent R affects these protons to a different degree, since such a charge transfer hyperconjugation can be expected only in the direction *trans* to the unshared pair on sulfur atom (*gauche* to the S-O bond).

iii) Another mechanism, which may be also responsible for the observable difference in the change of chemical shift for these two protons, requires that the change of electron withdrawal power of the substituent affects the resonance of the A-phenyl group with the S-O group,³⁰⁾ which is generally accepted to have a partial double bond character, and thus influences the rigidity of the C-S bond between the carbon atom of the A-phenyl group and the sulfur. The change of conformational preference of the phenyl group might also be responsible for the observed difference in the dependence of chemical shift (see V and VI).

The data presently available do not permit a final interpretation of the mechanism nor an estimation of the contributions of the three possible mechanisms discussed above. To approach this problem, and to throw light to the absolute assignment of these protons, efforts are now being made by examining NMR spectra of 3,3-disubstituted thiochromanone 1-monooxides (VIII) and 3-benzal thiochromanone 1-monooxides (IX).

Rauk, *et al.*³¹⁾ and Bullock, *et al.*³²⁾ reported that there was a difference in the rates of deuterium exchange of the two methylene protons of methyl benzyl sulfoxide and phenylsulfoxyacetic acid. Since the assignment of individual protons can be made for compounds studied in the present work, it is possible, by examining the difference in the rates of exchange of the protons, to know which of the methylene protons is preferentially exchanged and to know the steric course of this reaction. In view of this, current efforts are being made by experiments on the rate of deuterium exchange and will be published elsewhere.

Consideration of the Effect of S-O Electric Field

As was shown in figures 1a and 1b, $\nu_A - \nu_B$ bears an approximate linear relationship to the solvent dielectric constant (ϵ). This suggests that the polar effect³⁵⁾ is responsible for the variation of $\nu_A - \nu_B$ induced by solvent change. Those compounds studied in the present work have a polar S-O group in the molecule, and it is quite possible that two methylene protons are influenced unequally by the change of solvent, since the geometry of these protons with respect to the polar S-O bond is different. It has been well established that the S-O bond in sulfoxides has an electric moment corresponding to a charge separation on the atoms of about one third of an electron in the sense $S^{\delta+}-O^{\delta-}$. For a qualitative estimation of the effect of the reaction field, we assumed that the direction of the point dipole of these molecules is mainly determined by S-O bond moment³⁶⁾ when these molecules contain no other functional group having a large group moment (see X).

From the equation of Buckingham, Schaefer and Schneider³⁷⁾:

30) G. Leandri, A. Mangini, and R. Passerini, *J. Chem. Soc.*, **1957**, 1386.

31) A. Rauk, E. Buncel, R.Y. Moir, and S. Wolfe, *J. Am. Chem. Soc.*, **87**, 5498 (1965).

32) E. Bullock, J.M.W. Scott, and P.D. Golding, *Chem. Comm.*, **1967**, 168, see also refs. 33 and 34.

33) S. Wolfe and A. Rauk, *Chem. Comm.*, **1966**, 778.

34) S. Wolfe, A. Rauk, and I.G. Csizmadia, *J. Am. Chem. Soc.*, **89**, 5710 (1967).

35) A.D. Buckingham, *Can. J. Chem.*, **38**, 300 (1960).

36) Pritchard and Lauterbur estimated the bond moment of the S-O group as 2.8D., see ref. 28 and references therein.

37) A.D. Buckingham, T. Schaefer, and W.G. Schneider, *J. Chem. Phys.*, **32**, 1227 (1960).

$$\Delta\sigma_E = -2 \times 10^{-12} \left(\frac{\epsilon - 1}{2\epsilon + 2.5} \right) \frac{\mu \cos \phi}{\alpha} - 10^{-18} \left(\frac{\epsilon - 1}{2\epsilon + 2.5} \right)^2 \frac{\mu^2}{\alpha^2}$$

where ϕ is the angle between point dipole μ and the C-H bond, it is expected that an increase of ϵ results in a downfield shift of H_{trans} , which lies in the plane of dipole of the molecule ($\cos\phi=1$). It is also expected that an increase of ϵ results in an upfield shift for the proton which lies in a *gauche* relation with respect to the S-O bond ($\cos\phi=-1/2$).

In figure 4, methylene NMR spectra of *p*-methylphenyl phenacyl (Ia), *p*-methylphenyl benzyl (IIa), *p*-methylphenyl *p*-chlorobenzyl (IIIa) and *p*-methylphenyl *p*-nitrobenzyl sulfoxide (IVa) in deuterochloroform ($\epsilon=5.05$) and in acetone ($\epsilon=21.4$) are illustrated.

Fig. 4

On passing from a CDCl₃ to a acetone solution, H_A shows more significant downfield shift in all cases than H_B does. H_B of *p*-methylphenyl benzyl sulfoxide (IIa) shows an upfield shift with an increase of ϵ (Fig. 4b). Those of *p*-methylphenyl phenacyl sulfoxide (Ia) and *p*-methylphenyl *p*-chlorobenzyl sulfoxide (IIIa) do not show a significant shift (Fig. 4a and 4c). In the cases where the molecules have a nitro group ($R'=\text{NO}_2$), (IVa-d), downfield shifts of about the same order are observed for H_A and H_B.³⁸⁾ Above facts suggest that, although other factors such as specific solvent solute interactions and conformational preference⁴⁰⁾ are also responsible for determining the magnetic nonequivalence, the contribution from the electric field is an important factor in determining the observed variation of $\nu_A - \nu_B$ induced by a solvent change. As far as above data are concerned, H_A can be assigned tentatively to the proton *trans* with respect to the S-O bond.

Consideration of the Hydrogen-bond Shifts

In Table VI are listed the solvent shifts induced in TFA and in AcOH solutions relative to MeI or CDCl₃ observed independently for H_A and H_B.

The most interesting feature shown in Table VI is the fact that the hydrogen-bond shift observed for H_B is remarkably greater than that observed for H_A. Assuming that specific complex formation takes place about the S-O oxygen atom, considerable difference of solvent

38) This may be explained by considering that the presence of a nitro group (on the B-phenyl ring) with such a large group moment (4.21 D)³⁹⁾ causes a change in the direction of the molecular dipole.

39) E.S. Gould, "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, 1962, p. 62.

40) Roberts, *et al.*¹²⁾ suggested that the variation in $\nu_A - \nu_B$ with solvent may reflect changes in the conformation of the benzylic phenyl ring with respect to the methylene group. see also ref 41).

41) E.I. Snyder, *J. Am. Chem. Soc.*, **85**, 2624 (1963).

TABLE VI. Solvent Shifts for Proton Resonance^{a)} ($\Delta_{\text{solvent}}^{\text{reference}}$) of Phenyl Sulfoxides $R-C_6H_4SOCH_AH_B-X$ in TFA and AcOH

$\Delta_{\text{solvent}}^{\text{reference}}$	R		Me(a)		H(b)		Cl(Br)(c)		NO ₂ (d)	
			H _A	H _B	H _A	H _B	H _A	H _B	H _A	H _B
$\Delta_{\text{TFA}}^{\text{MeI}}$	COC ₆ H ₅	I	-0.60 ^{b)}	-0.78	-0.54	-0.71	-0.48	-0.66	-0.38	-0.57
$\Delta_{\text{TFA}}^{\text{COCl}_3}$ c)	C ₆ H ₅	II	-0.40	-0.60	-0.38	-0.59	-0.33	-0.55	-0.26	-0.47
$\Delta_{\text{TFA}}^{\text{MeI}}$	C ₆ H ₄ Cl	III	-0.37	-0.73	-0.31	-0.67	-0.28	-0.62	-0.21	-0.48
$\Delta_{\text{TFA}}^{\text{MeI}}$	C ₆ H ₄ NO ₂	IV	-0.31	-0.67	-0.29	-0.63	-0.28	-0.53	-0.20	-0.37
$\Delta_{\text{AcOH}}^{\text{MeI}}$		I	-0.36	-0.50	-0.33	-0.49	-0.30	-0.46	-0.24	-0.42
$\Delta_{\text{AcOH}}^{\text{COCl}_3}$		II	-0.20	-0.28	-0.21	-0.26	-0.23	-0.25	-0.16	-0.23
$\Delta_{\text{AcOH}}^{\text{MeI}}$		III	-0.22	-0.37	-0.21	-0.33	-0.19	-0.31	-0.18	-0.26
$\Delta_{\text{AcOH}}^{\text{MeI}}$		IV	-0.17	-0.39	-0.19	-0.33	-0.19	-0.33	-0.17	-0.25

a) These values are recorded in ppm.

b) A negative value indicates a downfield shift relative to the reference solvent.

c) Methylene protons of IIa-d gave rise to single peaks in MeI. To eliminate errors in calculating the solvent shift, we took a CDCl₃ solution as a reference for IIa-d. Chloroform is not an ideal solvent for a reference, but specific interaction of this solvent with a solute molecule is considered to be not so large.

shift between H_A and H_B can be interpreted in terms of the geometry of these protons with respect to the S-O bond. But it is not certain whether H_{trans} or H_{gauche} exhibits the more pronounced shift of complex formation (see XI).

There are at least four possible mechanisms which might produce such a clear stereospecific H-bond shift. They are; i) electric field effect, ii) magnetic anisotropy of solvent, iii) change of magnetic susceptibility of the S-O bond induced from H-bond formation and iv) change of electronic characters of C-H_{trans} and C-H_{gauche} bonds induced from H-bond formation. In order to answer this problem, and to make an absolute assignment of these signals, efforts are now being made by examining solvent effects on NMR spectra of some thiochromanone-oxide derivatives (VIII and IX), in which the configuration of the S-O bond is fixed and the stereochemistry of methylene protons can be unambiguously determined, and this will be presented in a subsequent paper.

Experimental

The preparations of compounds mentioned in this study were reported previously.^{8,9)}

Unless otherwise noted, spectra were taken at 100 Mc/s on a JEOL JNM-4H-100 spectrometer at 24° using 2% or, when samples are sparingly soluble, saturated solutions. Chemical shifts were reported in τ -scale from internal tetramethylsilane. The calibration was made with an electronic frequency counter and the accuracy of the measurements is within 0.01 ppm. For studies at elevated and low temperatures, the JEOL JES-VT-2 assembly was used.

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