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212. Motohiro Nishio[*1] : Nuclear Magnetic Resonance Studies of Sulfur Compounds. II.[*2] The Substituent Effect on Geminal Coupling Constants and on Magnetic Nonequivalence of the Methylene Protons of Sulfoxides.[*3]

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Nuclear magnetic resonance spectra were obtained for a number of sulfoxides, whose methylene protons are magnetically nonequivalent. The coupling constants between these protons depend on the electronic properties of the substituent adjacent to the coupling protons. The substituent effect on magnetic nonequivalence was also studied and it is demonstrated that the electronic properties of the substituent constitute an important factor responsible for the magnitude of magnetic nonequivalence.

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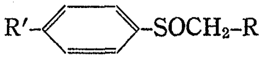
It was shown in a previous paper[*2] that the methylene protons of sulfoxides of the type X-$SOCH_2$-Y give AB-type nuclear magnetic resonance (NMR) spectra when Y contains no other nuclei to interact with the methylene protons. Since an AB-type spectrum can be analysed unambiguously, this type of molecule is suitable for the investigation of effects caused by X and Y. The purpose of the work reported herein was to study the effects of substituent on geminal coupling constants and on the magnitude of the magnetic nonequivalence of methylene protons in sulfoxides.

The compounds chosen were *p*-substituted phenyl sulfoxides of the type A.



[A]

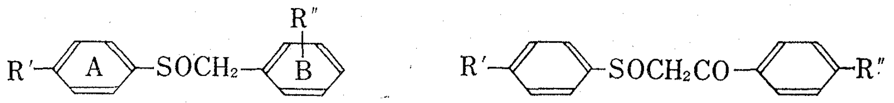
Fig. 1.

In this molecule, R is phenyl (I), *p*-chlorophenyl (II), *p*-nitrophenyl (III), *o*-chlorophenyl (IV), benzoyl (V), *p*-bromobenzoyl (VI), acetyl (VII) or substituted and non-substituted carbo-anilide (VIII, R $=CONHC_6H_4-R''$) groups; and R′, CH_3, H, Cl and NO_2, in the increasing order of electron withdrawing power.

The chemical shifts and geminal coupling constants for methylene protons of these compounds are summarized in Tables I, II and III.

The effect of the substituent R

a) J_{AB}



I : R″=H
II : R″=*p*-Cl
III : R″=*p*-NO_2
IV : R″=*o*-Cl

V : R″=H
VI : R″=Br

R′=CH_3,H,Cl,NO_2

Fig. 2.

[*1] Morooka-cho, Kohoku-ku, Yokohama (西尾元宏).

[*2] Part I: M. Nishio, T. Ito: This Bulletin, **13**, 1392 (1965).

[*3] This work was presented at "The 4th Symposium on Nuclear Magnetic Resonance (Japan)" in Tokyo, November (1964).

Table I. Coupling Constants and Chemical Shifts of Methylene Protons in *p*-R′-$C_6H_4SOCH_2$-R

	R	R′ / Solvent		CH_3 (a)	H (b)	Cl (c)	NO_2 (d)
I	C_6H_5	$CDCl_3$	J_{AB}(c.p.s.)	12.7	—	12.7	—
			$(\tau \frac{A+D}{2})$	(5.98)	(5.97)	(5.96)	(5.88)
		C_5H_5N		—	—	—	12.9
				(5.83)	(5.82)	(5.81)	(5.69)
		Me_2CO			12.9		
					(5.93)		
II	C_6H_4Cl-*p*	$CDCl_3$		—	—	—	
				(6.04)	(6.01)	(6.01)	
		C_5H_5N		12.9	12.9	13.0	13.0
				(5.85)	(5.86)	(5.82)	(5.69)
		Me_2CO				12.9	
						(5.85)	
III	$C_6H_4NO_2$-*p*	$CDCl_3$		12.8	12.8	12.9	13.0
				(5.91)	(5.89)	(5.89)	(5.80)
		C_5H_5N		12.6	12.8	13.0	13.0
				(5.69)	(5.68)	(5.59)	(5.51)
		Me_2CO		13.1	13.4	13.2	13.4
				(5.61)	(5.58)	(5.53)	(5.40)
IV	C_6H_4Cl-*o*	$CDCl_3$				13.0	—
						(5.73)	(5.70)
		C_5H_5N				—	—
						(5.63)	(5.53)
		Me_2CO				—	—
						(5.60)	(5.48)
V	COC_6H_5	$CDCl_3$		14.1	14.1	14.3	14.7
				(5.59)	(5.57)	(5.56)	(5.46)
		C_5H_5N			14.0	14.8	—
					(5.07)	(5.10)	(4.91)
		CCl_4		13.7	13.9	14.3	
				(5.67)	(5.64)	(5.62)	
VI	COC_6H_4Br-*p*	$CDCl_3$		14.4	14.4	14.8	
				(5.59)	(5.57)	(5.57)	
		C_5H_5N		14.2	14.7	—	
				(5.16)	(5.14)	(5.09)	
VII	$COCH_3$	$CDCl_3$				—	—
						(6.11)	(6.06)

The sign "–" indicates that the chemical shift difference between two protons is too small (assumed to be less then 3 c.p.s.) for the coupling constant to be obtained.

Table II. Chemical Shifts and Coupling Constants of Methylene Protons in $C_6H_5SOCH_2CONHC_6H_4$-R″(VIII) (in $CDCl_3$) (R=$CONHC_6H_4$-R″)

R″	Chemical shift $(\tau \frac{A+B}{2})$	Coupling constant J_{AB} (c.p.s.)	$\nu_A-\nu_B$ (c.p.s.)
H	6.22	14.1	13.6
o-CH_3	6.31	14.2	18.6
m-CH_3	6.30	13.8	13.9
p-CH_3	6.33	13.9	15.2
p-OCH_3	6.32	13.8	11.4
o-Cl	6.29	14.1	21.1
m-Cl	6.30	14.1	17.9
p-Cl	6.30	13.8	13.5
o-Br	6.28	14.2	19.5
m-Br		insoluble	
p-Br	6.31	14.1	16.8
o,m,p-NO_2		insoluble	

Table III. Magnetic Nonequivalence of Methylene Protons in p-R'$C_6H_4SOCH_2$-R (c.p.s.)

R	R' / Solvent	CH_3 (a)	H (b)	Cl (c)	NO_2 (d)
C_6H_5 I	$CDCl_3$	6.3	<3	5.7	<3
	C_5H_5N	<3	<3	<3	7.0
	Me_2CO		5.4		
p-ClC_6H_4 II	$CDCl_3$	<3	<3	<3	
	C_5H_5N	7.9	8.9	9.8	12.6
	Me_2CO			10.8	
p-$NO_2C_6H_4$ III	$CDCl_3$	9.4	12.0	11.2	15.2
	C_5H_5N	12.8	14.4	14.7	16.0
	Me_2CO	13.5	14.7	14.6	16.6
o-ClC_6H_4 IV	$CDCl_3$			5.2	<3
COC_6H_5 V	CCl_4	16.2	15.3	13.6	insoluble
	$CDCl_3$	16.7	14.7	13.9	8.3
	C_5H_5N	10.8	9.1	7.9	<3
COC_6H_4Br-p VI	$CDCl_3$	12.1	12.1	9.9	
	C_5H_5N	7.2	4.9	<3	

Since the substituents R are in the nearer position to the methylene group than R', one would expect that the effect of R is more important. In fact, a difference in the magnitude of the coupling constant is observed between I~IV (12.6~13.4 c.p.s.) and V, VI (14.0~14.8 c.p.s.). The only structural difference common to all members of these two series of compounds is the presence of an adjacent carbonyl group in the latter series. Geminal coupling constants in the former series (I~IV), where the methylene group is directly bonded to a phenyl group, are smaller than in the latter series (V and VI), in which the methylene is bonded to a carbonyl group conjugated with a phenyl group. Coupling constants of amide derivatives (VIII) were found to be between these values (13.8~14.2 c.p.s.). The coupling constants of the geminal protons are given in Table IV.

Table IV.

		Solvent	J_{AB} (c.p.s.)	Number of compounds examined	References
I~IV	$ArSOCH_2Ar$	$CDCl_3$	12.7~13.0	7	a)
		C_5H_5N	12.6~13.0	9	a)
		Me_2CO	12.9~13.4	6	a)
V~VI	$ArSOCH_2COAr$	$CDCl_3$	14.1~14.8	7	a)
		C_5H_5N	14.0~14.8	4	a)
VIII	$ArSOCH_2CONHAr$	$CDCl_3$	13.8~14.2	10	a)
IX	$C_6H_5SOOCH_2C_6H_5$	CCl_4	11.4	1	1)
X	$(RC_6H_4CH_2O)_2SO$				
	R=p-Cl, $-OCH_3$, $-CH_3$, H	CCl_4	11.2~12.0	4	1)
	R=p-NO_2	$CHCl_3$	12.8	1	1)

a) This work

Compared with the values obtained for sulfoxides I~IV (12.6~13.4 c.p.s.), those of the sulfites[1] (IX and X; 11.2~12.0 c.p.s.) are appreciably smaller.

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1) M. Ōki, H. Iwamura: Bull. Chem. Soc. Japan, **35**, 1428 (1962).

IX X

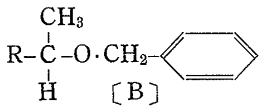
Fig. 3.

This may be explained qualitatively by considering the contribution of π-electron on sulfur atom for sulfoxides. It has been well established that a S-O bond has some π-character.[2,3] Therefore, it is expected that π-electrons of this group contribute to the magnitude of coupling constant to some extent. Barfield and Grant[4] estimated the π-electron contribution for a coupling constant of methylene group adjacent to a π-bond to be -1.5 c.p.s. In sulfites, however, contribution by the sulfur π-electrons is structurally impossible because of the extra oxygen atom.

In Table II, chemical shifts and coupling constants of anilides $C_6H_5SOCH_2CONH$-C_6H_4-R'' (VIII) are summarized. Efforts have been made to correlate J_{AB} with the Hammett's sigma-parameters. Although there seems to be a relationship between them, it was not possible to demonstrate a clear dependence because the differences are very small among these derivatives.

b) $\nu_A - \nu_B$

An interesting feature seen in Table III is that the magnitude of magnetic nonequivalence is markedly dependent on the substituent R. For example, phenyl benzyl (I), phenyl *p*-chlorobenzyl (II), phenyl *o*-chlorobenzyl sulfoxides (IV) exhibited very small chemical shift differences between two protons in $CDCl_3$. On the other hand, phenyl *p*-nitrobenzyl sulfoxides (III), which contain a *p*-nitro group on B-phenyl ring (see Fig. 2), exhibited large chemical shift differences (9.4~15.2 c.p.s.) in the same solvent. In contrast, the compounds which contain a *p*-nitro group on the A-phenyl ring (Id and IVd) give a singlet which may be due to the small chemical shift difference between the methylene protons (assumed to be less than 3 c.p.s.). Phenyl phenacyl (V) and phenyl *p*-bromophenacyl sulfoxides (VI) exhibited a large chemical shift difference in the same solvent (8.3~16.7 c.p.s.). It should be noted that the *p*-chloro (IVc) and *p*-nitrophenyl *o*-chlorobenzyl sulfoxides (IVd), which possess a bulky chlorine atom in the *o*-position of the B-phenyl ring, give rise to signals with small chemical shift differences, as in the case of compounds I, which possess no substituent on the *o*-position of the B-ring. Whitesides, *et al.*[5] studied the effect of structure on the magnitude of the magnetic nonequivalence of the methylene protons in benzyl ethers of the structure B, and observed a correlation between methylene protons and the size of R where R is an alkyl group. In the present case of sulfoxides, however, the electronic properties of the substituent are more important in determining the magnitude of magnetic nonequivalence.



[B]

Fig. 4.

The effect of substituent R′

a) J_{AB}

The results are summarized in Table I. No appreciable relationship was found between the substituent R′ and geminal coupling constants.

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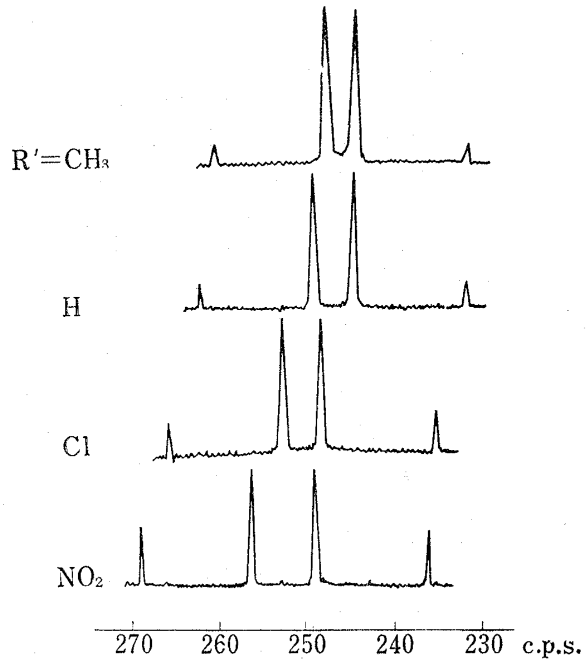
[2] N. Kharasch: "Organic Sulfur Compounds," Vol. I, p. 35 (1961), Pergamon press.
[3] G. Leandri, A. Mangini, R. Passerini: J. Chem. Soc., **1957**, 1386.
[4] M. Barfield, D.M. Grant: J. Am. Chem. Soc., **85**, 1899 (1963).
[5] G.M. Whitesides, D. Holtz, J.D. Roberts: J. Am. Chem. Soc., **86**, 2628 (1964).

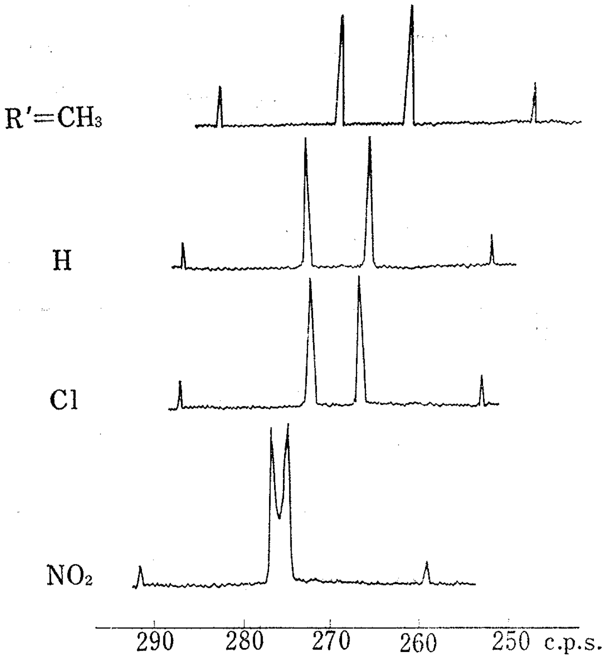
b) $\nu_A-\nu_B$

In substituted phenyl benzyl (I) and phenyl *o*-chlorobenzyl sulfoxides (Ⅳ), no relationship was found between $\nu_A-\nu_B$ and the substituent R′. In these compounds, it seems that it is the interaction of solute and solvent molecules which plays an important rôle in determining the magnitude of the magnetic nonequivalence.

On the other hand, an interesting relationship between $\nu_A-\nu_B$ and substituent R′ is observed for Ⅱ (in pyridine), Ⅲ (in $CDCl_3$, pyridine and Me_2CO), V (in CCl_4, $CDCl_3$ and pyridine) and Ⅵ (in $CDCl_3$ and pyridine). It is noteworthy that $\nu_A-\nu_B$ of Ⅱ and Ⅲ increases with the increasing electronegativity of the substituent R′. In contrast, in V and Ⅵ, $\nu_A-\nu_B$ decreases as the electron withdrawing power of R′ increases. In Fig.



p-R′$C_6H_4SOCH_2C_6H_4$-NO_2-*p* (Ⅲ) in $CDCl_3$
Fig. 5a.

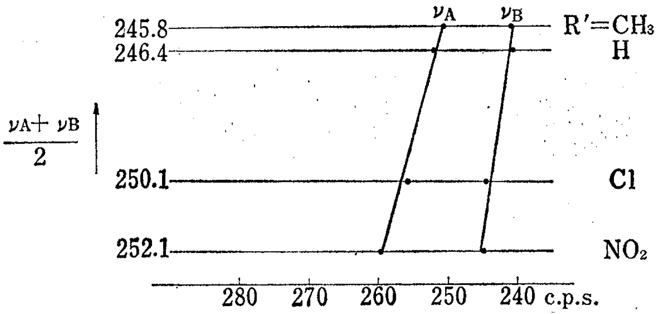


p-R′$C_6H_4SOCH_2COC_6H_5$ (V) in $CDCl_3$
Fig. 5b.

Table V.

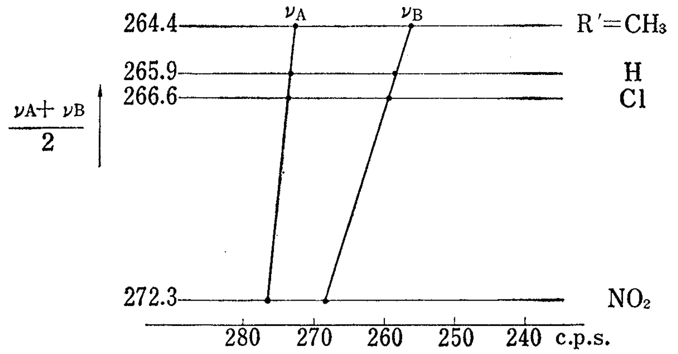
R′	$\nu_A+\nu_{B/2}$	ν_A	ν_B	$\nu_A-\nu_B$	$\nu_A+\nu_{B/2}$	ν_A	ν_B	$\nu_A-\nu_B$(c.p.s)
		Ⅲ in $CDCl_3$				Ⅱ in C_5H_5N		
CH_3	245.8	250.5	241.1	9.4	249.1	253.1	245.1	7.9
H	246.4	252.4	240.4	12.0	248.5	253.0	244.0	8.9
Cl	250.1	255.7	244.5	11.2	250.5	255.4	245.6	9.8
NO_2	252.1	259.7	244.5	15.2	258.3	264.6	252.0	12.6
		Ⅲ in Me_2CO				V in $CDCl_3$		
CH_3	263.0	269.8	256.2	13.5	264.6	272.8	256.0	16.7
H	265.0	272.4	257.6	14.7	265.9	273.3	258.5	14.7
Cl	268.0	275.3	260.7	14.6	266.6	273.6	259.6	13.9
NO_2	276.0	284.3	267.7	16.6	272.3	276.5	268.1	8.3
		Ⅲ in C_5H_5N				V in CCl_4		
CH_3	258.5	264.9	252.1	12.8	259.9	268.0	251.7	16.2
H	259.4	266.6	252.2	14.4	261.8	269.5	254.1	15.3
Cl	264.6	272.0	257.2	14.7	262.5	269.3	225.7	13.6
NO_2	269.7	277.7	261.7	16.0		insoluble		

5a and 5b are shown a part of their NMR spectra. An independend inspection of chemical shifts ν_A and ν_B summarized in Table V may give a solution to this apparent paradox. In the case of compounds Ⅱ and Ⅲ, the chemical shift of the proton which gives rise to a peak in a lower field (ν_A) is more sensitive to the substituent. On the contrary, for V and Ⅵ, the proton in a higher field (ν_B) is more sensitive to the substituent R′. By plotting the chemical shift of each proton independently as a function of the mean value of chemical shift, linear relationships are shown to exist between ν_A, ν_B and $\nu_A + \nu_B/2$. A comparison of the two slopes is illustrated in Fig. 6a (Ⅲ in $CDCl_3$). These linearities suggest that there is a relationship between the chemical shift (ν_A and ν_B) and the electronegativity of the substituent R′, since it is well known that the electronegativity of a substituent is proportional to the chemical shift of methyl or methylene protons adjacent to the substituent.[6] In this case it is shown that the lower proton is more sensitive to the electronegativity of substituent R′. Two different slopes demonstrate that the electronegativity of substituent E_R' does contribute in a different degree to each proton. Two linear slopes were obtained also for V (in $CDCl_3$). In this case, however, it is the higher proton which is more sensitive to the electronegativity of substituent R′ (Fig. 6b).



p-$R'C_6H_4SOCH_2C_6H_4NO_2$-p (Ⅲ) in $CDCl_3$

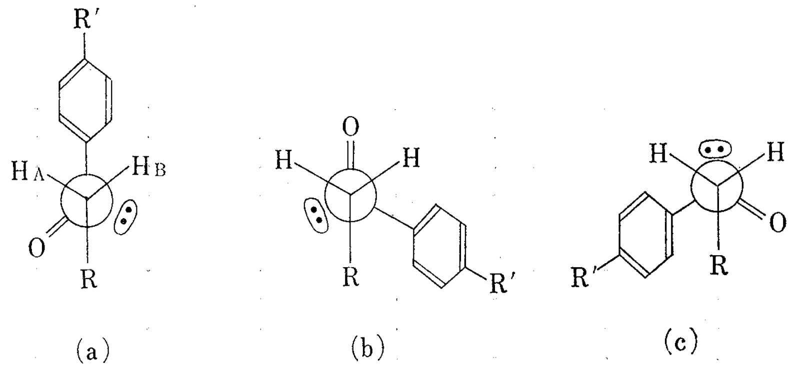
Fig. 6a.



p-$R'C_6H_4SOCH_2COC_6H_5$ (V) in $CDCl_3$

Fig. 6b.

Since the nonequivalence of the methylene protons in an asymmetric acyclic compound is considered to be mainly due to conformational preference,[5] the conformations (a), (b) and (c) are unequally populated under the conditions of this experiment, and it is very likely that a conformation which possesses two bulky groups in a *trans* relation



(a) (b) (c)

Fig. 7.

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[6] B.P. Dailey, J.N. Shoolery: J. Am. Chem. Soc., **77**, 3977 (1955).

[7] M. Ōki, H. Iwamura, K. Sakaguchi: Preliminary reports of International Symposium on NMR, Tokyo, (1965), N-3-8; from a NMR study of t-butyl neopentyl sulfoxide in $CDCl_3$ at various temperatures, they concluded that this compound is fixed to a conformation having two bulky groups in a *trans* relation.

such as (a) exists in predominance[7] (see Fig. 7; R=C_6H_4Cl-*p*, $C_6H_4NO_2$-*p*, COC_6H_5 or COC_6H_4Br-*p*). The data presently available do not permit an interpretation of the mechanism by which the substituent R′ influences the chemical shifts of two protons in a different degree. Assuming that the conformation having two bulky groups is a *trans* relation, however, a speculation based on an anisotropic deshielding effect of the A-phenyl ring on these protons leads us to some such explanation as a preferred conformation having a twisted structure.

Another speculation, which seems to be more likely, is that the proton which is more sensitive to the change of electronegativity of substituent R′ is that which exists in the *trans* position to the unshared pair on sulfur[8] (H_A; see Fig. 7). As discussed by Hamlow, *et al.*, a partial participation of the lone pair in a σ^* C–H_A orbital is possible[9] and such a participation allows some overlap between σ^* and lone pair obritals to generate some double bond character between C and S. Since such an interaction can be expected only in the direction of H_A (*trans* to the lone pair on sulfur atom), it is possible that the substituent R′ affects these protons to a different degree. In view of this, efforts are now being made to answer this problem, especially by experiments on deuterium-exchange and on solvent effect, and the results will be published in a subsequent paper.

TABLE VI. *p*-$R'C_6H_4SOCH_2$-R

R′	R	m.p. (°C)	Analyses (%)						ν_{S-O} (cm^{-1})
			Calcd.			Found			
			C	H	S	C	H	S	
CH_3	C_6H_5	140	73.0	6.09	13.9	73.05	6.28	14.13	1034
H	C_6H_5	127							1033
Cl	C_6H_5	134	62.3	4.39		62.61	4.28		1034
NO_2	C_6H_5	159～166	59.8	4.22	12.25	60.07	4.17	12.60	1032
CH_3	*p*-ClC_6H_4	160	63.5	4.92		63.07	4.90		1032
H	*p*-ClC_6H_4	171	62.3	4.39		61.55	4.43		1030
Cl	*p*-ClC_6H_4	126	54.8	3.51		54.69	3.67		1039
NO_2	*p*-ClC_6H_4	139	52.8	3.39		53.11	3.49		1047
CH_3	*p*-$NO_2C_6H_4$	164	61.1	4.73	11.6	60.79	4.89	11.65	1040
H	*p*-$NO_2C_6H_4$	161	59.8	4.22	12.25	59.30	4.73	12.50	1020
Cl	*p*-$NO_2C_6H_4$	154	52.8	3.39		53.02	3.33		1040
NO_2	*p*-$NO_2C_6H_4$	176	51.0	3.26	10.8	51.08	3.07	10.87	1044
Cl	*o*-ClC_6H_4	83	54.8	3.51		54.07	3.78		1033
NO_2	*o*-ClC_6H_4	137	52.8	3.39		53.54	3.36		1042
CH_3	COC_6H_5	109	69.8	5.43	12.4	68.75	5.01	12.57	1036
H	COC_6H_5	81							1052
Cl	COC_6H_5	85	60.3	3.96		60.26	4.34		1022
NO_2	COC_6H_5	126	60.2	3.97	11.5	57.39	4.07	11.50	1030
CH_3	COC_6H_4Br-*p*	139 (decomp.)	53.4	3.86		53.61	3.81		1035
H	COC_6H_4Br-*p*	134 (decomp.)	52.1	3.41		52.23	3.43		1047
Cl	COC_6H_4Br-*p*	139 (decomp.)	47.0	2.80		46.74	2.51		1046
Cl	$COCH_3$	108	49.9	4.17		49.48	4.30		1026
NO_2	$COCH_3$	129	49.8	4.15	14.75	48.24	4.07	13.98	

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8) cf. J. Am. Chem. Soc., **87**, 5498 (1965), A. Rauk, E. Buncel, R. Moir, S. Wolfe; they observed a difference in the rates of deuterium exchange of the two methylene protons of benzyl methyl sulfoxide and speculated that, for a proton to be exchanged, it must be *trans* to the unshared pair on sulfur.

9) H. Hamlow, S. Okuda, N. Nakagawa : Tetrahedron Letters, 2553 (1964). cf. F. Bohlmann, D. Schumann, H. Schulz : Tetrahedron Letters, 173 (1965) and F. Bohlmann : Ber. **91**, 2157 (1958).

Experimental

The proton magnetic resonance spectra were obtained with a Varian Associates A-60 high-resolution NMR spectrometer. Samples were run as 5% or saturated solution with tetramethylsilane as an internal reference at the operating temperature (35°) of the instrument. Chemical shifts are reported in τ-values and are accurate to ± 1 c.p.s. and coupling constants are accurate to ± 0.3 c.p.s. The infrared spectra were obtained with Nippon Bunko DS-401 type spectrometer in solid state (nujol suspension).

Materials——Sulfoxides are easily distinguished from sulfides or sulfones by examining the infrared spectra in S-O stretching region. As summarized in Tables Ⅵ and Ⅶ, all sulfoxides exhibited strong S-O stretching absorption between 1012~1052 cm^{-1}. Sulfoxides examined in this experiment were prepared by general procedures illustrated below, and the properties of these compounds are listed in Tables Ⅵ and Ⅶ. Melting points are uncorrected.

General Procedures——Sulfides, except those corresponding to Ⅷ, were prepared by condensation of thiophenol derivatives $R'C_6H_4SH$ with substituted or nonsubstituted benzyl halide $R''C_6H_4CH_2X$, ω-bromoacetophenone $R''C_6H_4COCH_2Br$ or chloroacetone in EtOH in the presence of equimolecular amount of KOH.

Oxidation of Sulfides to Sulfoxides——To a solution of 0.01 mole of sulfide in 10 ml. of AcOH, 1.2 g. (0.01 mole) of 30% aqueous H_2O_2 was added dropwise with stirring at room temperature. After the initial reaction was over, the mixture was kept at room temperature for 3 hr. On dilution with H_2O, a sulfoxide separated. After standing in refregerator for a while, the precipitate was filtered, washed with H_2O and dried. Recrystallization from EtOH, MeOH or from AcOH gave pure crystals.

Derivatives of Benzenesulfinylacetic Acid Anilide (VIII)——Phenylthioacetic acid chloride, obtained by chlorination of phenylthioacetic acid with thionylchloride, was treated with aniline or substituted aniline in benzene solution to give corresponding anilides $C_6H_5SCH_2CONHAr$. Oxidation of these compounds with 30% aqueous H_2O_2 in AcOH at room temperature gave the corresponding sulfoxides.

TABLE Ⅷ. $C_6H_5SOCH_2CONHC_6H_4$-R'' (Ⅷ)

R''	m.p. (°C)	Analyses (%)						ν_{S-O} [a] (cm^{-1})
		Calcd.			Found			
		C	H	S	C	H	S	
H	148	64.9	5.02	12.7	64.63	4.97	11.47	1013
o-CH_3	134	66.0	5.50	11.7	65.09	5.43	11.82	1040
m-CH_3	142				65.87	6.01	11.50	1027
p-CH_3	122				66.25	5.25	11.91	1014
p-OCH_3	130	62.3	5.19	11.1	61.62	5.46	11.22	1013, 1022 1029, 1038
o-Cl	123	57.3	4.09		57.14	3.91		1040
m-Cl	159				57.54	4.60		1030
p-Cl	168				58.07	4.54		1012
o-Br	129	49.7	3.56		49.24	4.19		1049
m-Br	161				50.01	3.75		1032
p-Br	177				49.83	4.12		1020
o-NO_2	155	55.3	3.95	10.5	55.19	4.20	10.55	1035
m-NO_2	171				54.95	4.21	10.60	1032
p-NO_2	223 (decomp.)				55.66	4.20	10.70	1020, 1030

a) An interesting relationship between ν_{S-O} and the position of the subtituent was observed. The S-O stretching vibration frequency decreased in the order: ortho>meta>para for all substituents except the nitro group.

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