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Nuclear Magnetic Resonance Studies of Sulfur Compounds. IV[1]. The Substituent and the Solvent Effects on Methylene Resonances of 6-Substituted 3-Benzalthiochromanone 1-Oxides and 3,3-Dibromothiochromanone 1-Oxides

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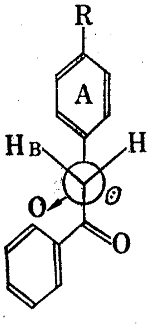
The methylene proton resonances of 3-benzalthiochromanone 1-oxides (III) and 3,3-dibromothiochromanone 1-oxides (IV) were determined in deuterochloroform and in trifluoroacetic acid.

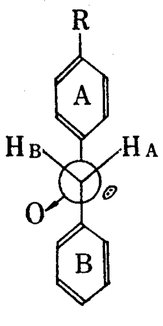
From a consideration of the solvent shift induced from a hydrogen-bond formation, it is concluded that the sulfoxide functions in these compounds prefer the axial configuration. Assignments of methylene signals were made by an examination of long-range coupling and by examining the difference in TFA-induced shifts of these proton resonances.

Assignments of individual methylene AB-signals of phenyl phenacyl (I) and phenyl benzyl sulfoxides (II) were also made, based on the above evidences, and it is concluded that the proton which is more sensitive to a substituent change is in the position *trans* with respect to the S–O group and *gauche* to the unshared electron pair on sulfur atom. It is also suggested that the conformational preference of the phenyl group which is bonded to the sulfoxide group is responsible for the discrepancy observed in the substituent effect of the methylene chemical shifts in phenyl sulfoxides I and II.

In a previous paper,[1] we studied the substituent and the solvent effects on magnetic nonequivalence of methylene protons (ν_A–ν_B) of phenyl phenacyl (I) and phenyl benzyl sulfoxides (II).



I



II

These experiments led us to a conclusion that the relative assignment of individual methylene signals is possible by examining the difference in the substituent dependence of ν_A and ν_B. Another interesting finding reported in the previous study was that the proton which is more sensitive to the substituent (R) change (H_A) was less sensitive to the addition of trifluoroacetic acid than the proton which is less sensitive to the substituent change (H_B). Since such a discrepancy in TFA-induced shifts is considered to be a consequence of the differing geometrical positions of these protons with respect to the hydrogen bonding center (S–O oxygen atom[3]), it is possible to make an absolute assigment of these signals from an examination of H-bond shifts of methylene resonances of some fused ring systems for which the configuration of S–O bond is fixed and individual methylene peaks can be unambiguously assigned.

The purpose of the present study was to determine the absolute assignment of methylene AB-signals of I and II by an examination of nuclear magnetic resonance (NMR) spectra of

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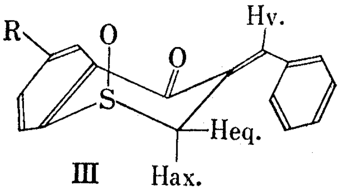
[1] Part III: M. Nishio, *Chem. Pharm. Bull.* (Tokyo), 17, 262 (1969).

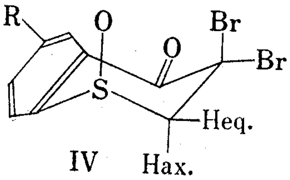
[2] Location: *Morooka-cho, Kohoku-ku, Yokohama.*

[3] It has been restablished that the donor resides on the oxygen atom of the S–O group in a sulfoxide–TFA complex.[1]

6-substituted 3-benzalthiochromanone 1-oxides (III) and 3,3-dibromothiochromanone 1-oxides (IV) and their solvent shif tsinduced from a H–bond formation.



III



IV

Results and Discussion

IIIa–c and IVa–c (R=Me, H and Cl) were prepared by oxidation of corresponding sulfides with peracetic acid (Chart 1).

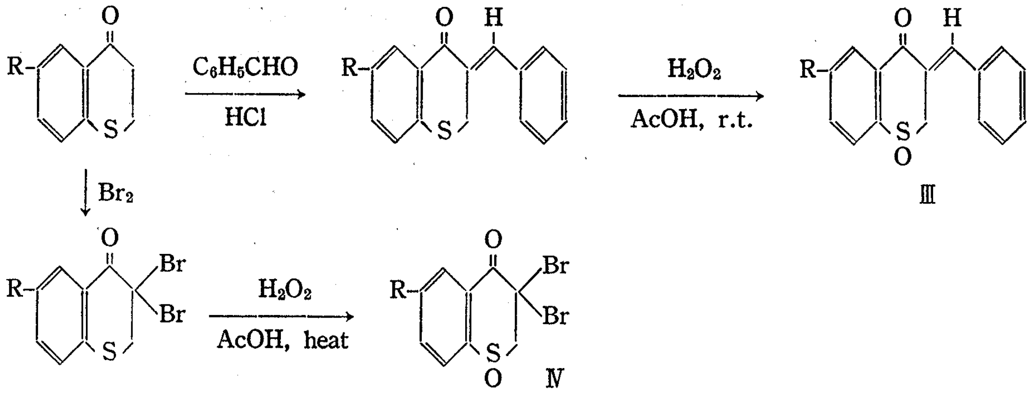


Chart 1

The properties of these compounds are listed in Table III. Attempts to separate each isomer (S–O axial and equatorial) were unsuccessful. In the infrared spectra, these compounds exhibited strong absorption bands characteristic to the S–O stretching viblation (III; 1036—1040 cm^{-1} in $CHCl_3$, 1040—1041 cm^{-1} in Nujol, IV; 1040—1044 cm^{-1} in $CHCl_3$, 1028—1029 cm^{-1} in Nujol). De la Mare and his co-workers[4] reported that, in a 1,4-dithiane 1,4-dioxide ring in the chair conformation, the equatorial S–O bond is associated with infrared stretching frequency higher (1032 or 1047 cm^{-1} in Nujol) than that of the axial bond (1020 cm^{-1}). In the present case of thiochromanone derivatives, however, it was difficult to know the configuration of the S–O bond by an infrared analysis alone, because of the lack of the corresponding data on the other isomers.

TABLE I

	R	solv.	$\tau\frac{A+E}{2}$	$\tau_{ax.}$	$\tau_{eq.}$	τ_{AE}[a]	τ_v	J_{AE}	J_{AV}
IIIa	Me	$CDCl_3$	5.56	5.70	5.42	+0.28	1.83	12.5	1.5
IIIb	H	$CDCl_3$	5.51	5.69	5.32	+0.37	1.80	12.5	1.5
IIIc	Cl	$CDCl_3$	5.51	5.70	5.32	+0.38	1.80	12.5	1.5
IIIa	Me	TFA	−0.41	−0.22	−0.60	+0.66	−0.36	14.5	1.3
IIIb	H	TFA	−0.46	−0.31	−0.50	+0.56	−0.35	14.5	1.3
IIIc	Cl	TFA	−0.39	−0.31	−0.47	+0.54	−0.35	14.5	1.3

a) $\tau_{ax.}-\tau_{eq.}$

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4) P.B.D. de la Mare, D.J. Millen, J.G. Tillett and D. Watson, *J. Chem. Soc.*, **1963**, 1619.

TABLE II

	R	Solv.	$\tau\frac{A+E}{2}$	$\tau_{ax.}$	$\tau_{eq.}$	τ_{AE}[a)]	J_{AE}
IVa	Me	$CDCl_3$	5.53	5.22	5.84	−0.62	13.0
IVb	H	$CDCl_3$	5.49	5.20	5.78	−0.58	13.0
IVc	Cl	$CDCl_3$	5.50	5.20	5.80	−0.60	13.0
IVa	Me	TFA	−0.42	−0.31	−0.53	−0.40	13.5
IVb	H	TFA	−0.41	−0.31	−0.48	−0.41	13.5
IVc	Cl	TFA	−0.39	−0.30	−0.47	−0.43	13.5

a) $\tau_{ax.}-\tau_{eq.}$

In Tables I and II are summarized chemical shifts and coupling constants in the NMR spectra of IIIa—c and IVa—c, as determined in deuterochloroform ($CDCl_3$) solution. The solvent shifts induced in trifluoroacetic acid (TFA) are also given; a negative value indicates a downfield shift relative to $CDCl_3$.

The NMR spectrum (in $CDCl_3$) of 6-chloro-3-benzalthiochromanone 1-oxide (IIIc)′ is shown in Fig. 1, along with the methylene part NMR spectrum of the same compound measured in TFA.

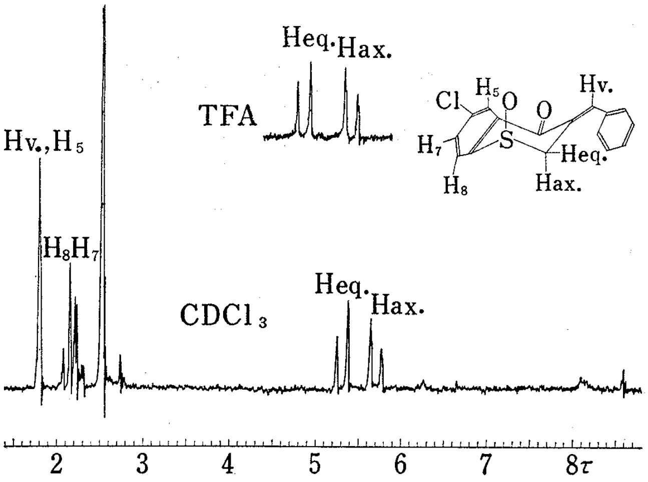

Fig. 1

The vinylic proton (H_v) gives rise to a singlet at 1.82τ ($CDCl_3$) indicating that H_v is *cis* with respect to the carbonyl group. The upper part of the methylene AB–quartet $\left(\tau\frac{A+E}{2}=5.51, J_{AE}=12.5\ \text{cps}\right)$ shows a splitting ($J=1.5$ cps) to indicate a long–range coupling of this proton with the vinylic proton. This signal is assigned to the axial proton (H_{ax}, see III), since an allylic long–range coupling is expected only for the proton perpendicular to the plane of the unsaturated bond.[5)] Figure 1 shows also that the upper part of the AB–signal in TFA$\left(\tau\frac{A+E}{2}=5.12, J_{AE}=14.5\ \text{cps}, J_{AV}=1.3\ \text{cps}\right)$ is appropriate to H_{ax}.

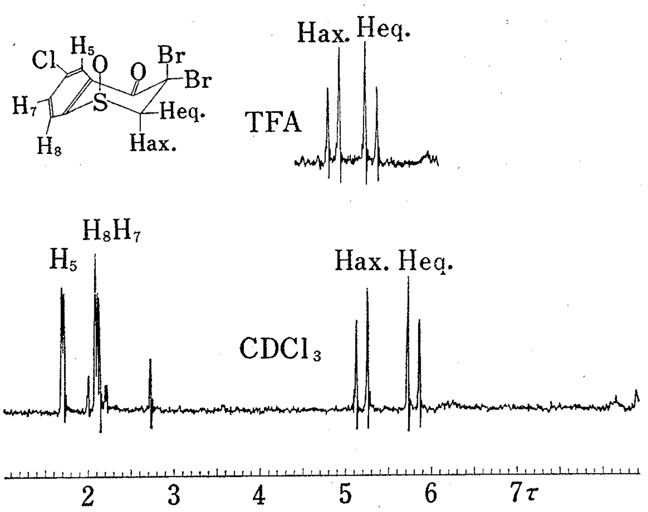

Fig. 2

Table I shows that solvent shifts induced in TFA ($\Delta^{\mathrm{CDCl_3}}_{\mathrm{TFA}}$) observed for $H_{ax.}$ are considerably smaller (−0.22——0.31 ppm; about the same order with those observed for H_v: −0.35——0.37 ppm) than those observed for $H_{eq.}$ (−0.47——0.60 ppm). Such a large

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5) S. Sternhell, *Rev. Pure and Appl. Chem.*, **14**, 15 (1964).

discrepancy in TFA–induced shifts cannot be interpreted without considering the difference in the geometrical positions of these protons with respect to the hydrogen accepting center (S–O oxygen atom³⁾). This fact demonstrates also that the S–O group has an axial configuration,⁶⁾ since such a large discrepancy could not be expected if S–O bond were equatorial and bisected the $H_{ax.}$–C_2–$H_{eq.}$ angle. From above evidences, it is concluded that TFA–shift is more important for the proton *gauche* to the S–O bond than for the *trans* proton.

Going back to the problem mentioned in the top of this paper, now we can make the absolute assignment of each methylene signal of I and II. The signal for which more pronounced TFA–shift was observed¹⁾ (H_B; this proton is less sensitive to the substituent change) is appropriate to the proton *gauche* and H_A (for which TFA–shift was less important) to the proton *trans* with respect to the S–O bond. This conclusion agrees with the assignment which has been tentatively given to these protons by a consideration of S–O electric field.¹⁾

The NMR spectrum (in $CDCl_3$) of 6-chloro-3,3-dibromothiochromanone 1-oxide (IV)c is shown in Fig. 2, along with the methylene part NMR spectum of the same compound measured in TFA.

In this case, it is the upper part of the methylene AB–quartet which suffers more pronounced TFA–shift ($\Delta_{TFA}^{CDCl_3}$=−0.47——0.53 ppm for the upper part, −0.30——0.31 ppm for the lower part, see Table II). From this, we conclude that the upper part of the methylene AB–signals is appropriate to the proton equatorial ($H_{eq.}$) and that the S–O groups in IVa–c prefer the axial configuration.

Consideration of the Substituent Effect

In the preceeding paper,¹⁾ we discussed a clear discrepancy in the substituent dependences of two methylene signals⁸⁾ of I and II. In order to explain why the substituent R influences the chemical shifts of two protons to a different degree, we proposed three possible mechanisms in terms of; (1) the anisotropy of the magnetic susceptibility of the S–O bond, (2) the charge transfer hyperconjugation of the lone pair in a σ^* C–H bond and (3) the conformational preference of the A-phenyl group (see I and II).

According to the forementioned assignment, H_A (more dependent proton) is appropriate to the proton *gauche* with respect to the unshared electron pair on sulfur atom. From this, we can rule out the mechanism (2), since this mechanism requires that H_B (*trans* to the unshared pair) should be more dependent on a substituent change.

As is shown in Tables I and II, in the present case of fixed ring compounds, no appreciable difference in the substituent dependences of chemical shifts is found between $H_{ax.}$ and $H_{eq.}$ $\tau_{ax.}$ and $\tau_{eq.}$ should be influenced to a different degree by a substituent change, if the contribution from the mechanism (1) were important.

We therefore conclude that the conformational preference of the A–phenyl group (mechanism 3) is most important in determining the magnitude of the magnetic nonequivalence⁹⁾ of the methylene protons in phenyl sulfoxides I and II. This conclusion is compatible with the present data that τ_{AB} does not depend significantly on the substituent R, since, for the sulfoxides of fixed ring system such as III and IV, the conformation of the phenyl group is fixed and cannot be influenced by a substituent change.

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6) This is consistent with the evidences that S–O groups in *trans*-1,4-dithiane 1,4-dioxide⁷ᵃ⁾, in 4-substituted thiane oxides,⁷ᵇ,ᶜ⁾ in 1,3,5-trithiane 1-oxide⁷ᵈ⁾ and in thiane 1-oxide-3,3,5,5-$d_6$⁷ᵉ⁾ prefer the axial configuration.

7) *a*) C.-Y. Chen and R.J.W. LeFèvre, *Australian J. Chem.*, **16**, 917 (1963); *b*) C. R. Johnson and D. McCants, Jr., *J. Am. Chem. Soc.*, **86**, 2935 (1964); *c*) J.C. Martin and J.J. Uebel, *ibid.*, **86**, 2936 (1964); *d*) M. Ōki, H. Iwamura and K. Sakaguchi, Preliminaly Report of International Symposium on NMR (Tokyo), N-3-8 (1965); *e*) J.B. Lambert and R.G. Keske, *J. Org. Chem.*, **31**, 3429 (1966).

8) There is a linear correlation between the magnitude of magnetic nonequivalence (ν_A–ν_B) and the electron withdrawal power of the substituent R.

9) By a substituent change; variation in ν_A–ν_B with solvent represents quite a different problem; see ref. 1.

Experimental

The proton magnetic resonance spectra were obtained with a JEOL JNM-4H-100 (100 Mc) high-resolution NMR spectrometer at 24° using 2% solutions. Chemical shifts were reported in τ-scale from internal tetramethylsilane and coupling constants were reported in cps. The calibration was made with an electronic frequency counter and the accuracy of the measurements is within ±0.01 ppm for chemical shifts and ±0.1 cps for coupling constants. Infrared spectra were recorded with a Nippon Bunko DS 401 spectrometer in solid state (Nujol) and in chloroform (5%).

Materials——Sulfoxides examined in this experiment were prepared by general procedures illustrated below, and the properties of these compounds are listed in Table III.

TABLE III

			Analysis (%)							
			Calcd.			Found			ν_{S-O} (cm^{-1})	
	R	mp° (C)	C	H	S	C	H	S	$CHCl_3$	Nujol
IIIa	Me	154	72.4	4.97	11.4	72.61	5.22	11.57	1036	1041
IIIb	H	99	71.6	4.48	11.9	70.29	4.98	12.38	1039	1041
IIIc	Cl	175	63.4	3.64		63.57	3.93		1040	1041
IVa	Me	163 (166)[10]							1040	1028
IVb	H	156.5	32.0	1.77		32.20	1.99		1041	1029
IVc	Cl	179.5	29.8	1.34		29.19	1.63		1044	1028

3-Benzalthiochromanone 1-Oxides (IIIa—c)——3-Benzalthiochromanones, obtained by condensation of benzaldehyde with thiochromanones in HCl-saturated C_6H_6, were suspended in AcOH. 1.2 mole of aqueous 30% H_2O_2 was added and stirred at room temperature for 3—5 hr. Starting material slowly disappeared and a clear solution was obtained. On dilution with H_2O, a sulfoxide separated. The precipitate was filtered, washed with H_2O and dried. Recrystallization from EtOH gave pure crystals.

3,3-Dibromothiochromanone 1-Oxides (IVa—c)——3.3-Dibromothiochromanones[10] were dissolved in AcOH, 2 moles of aqueous 30% H_2O_2 was added and refluxed for 5 min. On dilution with H_2O, a sulfoxide separated. The precipitate was filtered, washed with H_2O and recrystallized from EtOH.

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[10] F. Arndt, *Chem. Ber.*, **58**, 1612 (1925).