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133. **Yoshio Sasaki, Miyoko Suzuki, Akiko Shimazu** (née **Hoshi**), **and Atsuko Misaki**: Studies on the Proton Magnetic Resonance Spectra in Aromatic Systems. Ⅱ.[*1] Discussions on the Polysubstituted Benzene Derivatives.

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The reliability and limitation on the simple sum rule of the shielding parameters in polysubstituted benzene series have been discussed and the ring proton chemical shifts for several systems have been estimated from the above parameters.

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In the first paper of this series[1] the reliabilities on the simple sum rule of the shielding parameters[2~4] with respect to ring proton chemical shifts in para-substituted benzene, 1-substituted-3,4-dimethoxy- and 1-substituted-3,4-methylenedioxy benzene series, had been investigated. This work was undertaken to estimate the applicability, limitation and practical utility of the above treatment in substituted anisole, methylenedioxy benzene, guaiacol and veratrol series, etc.

Experimental

Materials and Measurements of Spectra

All materials are prepared by the authorized procedures. The details of measurement are the same as described in the preceding papers.[1]

1. The observed shifts in Table Ⅱ, Ⅲ, Ⅳ are measured in p.p.m. scale *vs.* C_6H_6 (7.37 p.p.m.) in CH_2Cl_2 (TMS int. ref.).
2. The calculated shifts in Table Ⅰ, Ⅱ, Ⅲ, Ⅳ, Ⅴ, Ⅵ are estimated by* J. S. Martin & B.P. Dailey's,[2] H. Spiesecke & W.G. Schneider's,[3] P. Diehl's[4] parameters respectively.
3. The calculated shifts in Table Ⅵ are expressed in τ scale *vs.* C_6H_6(2.73 τ) in $CDCl_3$(TMS int. ref.).
4. The positive sign indicates "more shielded protons" than that of C_6H_6 and the negative sign indicates "less shielded ones."

[*1] Part Ⅰ: This Bulletin, **15**, 599 (1967).

[*2] Toneyama, Toyonaka, Osaka (佐々木喜男, 鈴木美代子, 島津(星)昌子, 三崎敦子).

1) Y. Sasaki, M. Suzuki, T. Hibino, K. Karai: This Bulletin, **15**, 599 (1967).
2) J.S. Martin, B.P. Dailey: J. Chem. Phys., **39**, 1722 (1963).
3) H. Spiesecke, W.G. Schneider: *Ibid.*, **35**, 731 (1961).
4) P. Diehl: Helv. Chim. Acta, **44**, 829 (1961).

Results and Discussion

Para-substituted Anisole Series

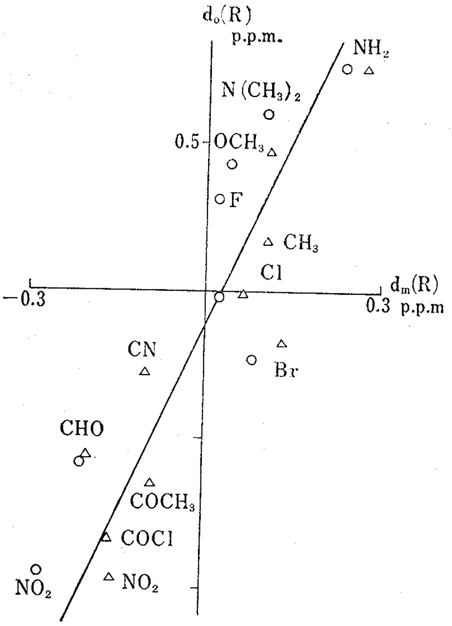

Fig. 1.*4

Formerly, J. S. Martin & B. P. Dailey⁵⁾ analysed the ring proton magnetic resonance spectra of numerous para-substituted anisole derivatives as an A_2B_2 system, and tried to discuss the simple sum rule of the shielding parameter in disubstituted benzene series.

In the para-substituted anisole series the ring proton chemical shifts are shown as follows:

$$\delta_{\mathrm{HA}} = d_o{}^{*3}\text{-}OCH_3 + d_m\text{-}R$$

$$\delta_{\mathrm{HB}} = d_m\text{-}OCH_3 + d_o\text{-}R$$

As is illustrated in Table I, the observed shifts are compared with those of the calculated shifts from 3 parameters,²⁾⁻⁴⁾ and the same conclusions confirmed in the preceding papers¹⁾ have been verified. And, moreover, among above data, a definite $\delta_{\mathrm{HA}}/\delta_{\mathrm{HB}}$ correlation, which is accepted from d_m-R/d_o-R ratio, is also approved.

TABLE I.

Substituents	Observed²⁾		Calculated (p.p.m.)²⁾		Calculated (p.p.m.)³⁾		Calculated (p.p.m.)⁴⁾	
	H_A	H_B	H_A	H_B	H_A	H_B	H_A	H_B
NH$_2$	+0.643	+0.790	+0.748	+0.876	+0.63	+0.80	+0.64	+0.78
OCH$_3$	+0.533		+0.585		+0.47		+0.52	
Cl	+0.525	+0.108	+0.542	+0.108	+0.46	+0.02	+0.48	+0.05
Br	+0.567	+0.043	+0.611	−0.051	+0.51	−0.18	+0.53	−0.12
I	+0.663	−0.240	+0.742	−0.255	+0.68	−0.36	+0.64	−0.31
NO$_2$	+0.380	−0.887	+0.322	−0.847	+0.22	−0.91	+0.21	−0.88
CHO	+0.335	−0.485	+0.282	−0.432	+0.22	−0.54		
CN	+0.412	−0.160	+0.377	−0.162			+0.29	−0.25
COCH$_3$	+0.417	−0.610	+0.386	−0.532				
COCl	+0.373	−0.812	+0.321	−0.722				
CH$_3$	+0.552	+0.283	+0.584	+0.291			+0.55	+0.27

2) solvent C_6H_{12}

Substituted Methylenedioxy Benzene, Guaiacol and Veratrol Series

The observed and calculated ring proton shifts in these series are summarised in Table II, III and IV respectively.

In these data, whenever steric interaction of substituents is effective, the difference between the observed and calculated shift —— more than 0.1 p.p.m. —— is

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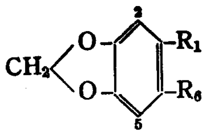
*3 *d*: shielding parameters, *o*: ortho, *m*: meta, *p*: para.

*4 ○: H. Spiesecke, W.G. Schneider,³⁾ △: J.S. Martin, B.P. Dailey.²⁾

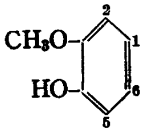
5) J.S. Martin, B.P. Dailey: J. Chem. Phys., **37**, 2594 (1962).

Table II.



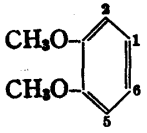
Substituents		Observed (p.p.m.)		Calculated (p.p.m.)2)		Calculated (p.p.m.)3)		Calculated (p.p.m.)4)	
R_1	R_2	2-H(?)	5-H(?)	2-H	5-H	2-H	5-H	2-H	5-H
NO_2	NO_2	0		−0.53		−0.69		−0.67	
CH_3	Cl	+0.70	+0.35	+0.83	+0.69			+0.75	+0.60
CHO	NO_2	+0.15	−0.09	−0.11	−0.57	−0.32	−0.69		
CHO	Br	+0.07	+0.31	+0.18	+0.23	−0.03	+0.04		
CHO	Cl	+0.08	+0.48	+0.11	+0.39	−0.09	+0.24		
CHO	NH_2	+0.55	+1.21	+0.32	+1.16	+0.09	+1.02		

Table III.



Substituents				Observed (p.p.m.)				Calculated (p.p.m.)4)			
R_1	R_2	R_5	R_6	1-H	2-H	5-H	6-H	1-H	2-H	5-H	6-H
Br			CHO		+0.20	−0.10					
$COCH_3$			CH_3		+0.06	+0.57					
CH_3		Br			+0.70		+0.44		+0.81		+0.44
CHO		Br			−0.03		−0.32				
		Br	CHO	−0.23	+0.37						
		Br	CH_3	+0.65	+0.65				+0.77		

Table IV.



Substituents			Observed (p.p.m.)				Calculated (p.p.m.)2)				Calculated (p.p.m.)3)				Calculated (p.p.m.)4)			
R_1	R_5	R_6	1-H	2-H	5-H	6-H	1-H	2-H	5-H	6-H	1-H	2-H	5-H	6-H	1-H	2-H	5-H	6-H
CO_2CH_3	OCH_3			+0.03		+0.03										+0.11		+0.11
CH_3		$COCH_3$		+0.62	+0.06			+0.68	−0.05									
CHO	Br			+0.03		−0.26		+0.12		−0.18		−0.08		−0.40				
	OCH_3		+0.37	+0.78		+0.78	+0.63	+1.00		+1.00	+0.45	+0.84		+0.84	+0.53	+0.85		+0.85

Table V.

1. P. Diehl's[4] parameter, Helv. Chim. Acta, 44, 829 (1961).

	Ortho (p.p.m.)	Meta (p.p.m.)	Para (p.p.m.)
OCH_3	+0.42	+0.10	+0.33
CH_3	+0.17	+0.13	+0.17
Br	−0.22	+0.11	+0.06
OH	+0.50	+0.16	

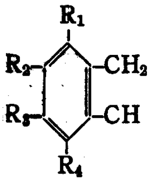
2. J. Martin, B.P. Dailey's[3] parameter, J. Chem. Phys., 39, 1722 (1963).

	Ortho (p.p.m.)	Meta (p.p.m.)	Para (p.p.m.)
OCH_3	+0.477	+0.108	+0.41
CH_3	+0.183	+0.107	+0.16
Br	−0.16	+0.13	+0.07
OH			

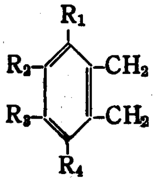
3.

	$C_6H_5 \cdot CH_2$ (p.p.m.)	$C_6H_5 \cdot CH$ (p.p.m.)	$C_6H_5 \cdot C$ (p.p.m.)
Ortho	+0.113(0.122)	+0.057(0.061)	0
Meta	+0.087(0.071)	+0.043(0.036)	0
Para	+0.113(0.107)	+0.057(0.053)	0

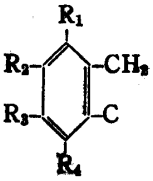
Table VI.[a]



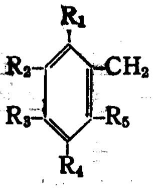
R_1	R_2	R_3	R_4
H 3.47(3.54)	OCH_3	OCH_3	Br
H 3.41(3.47)	OCH_3	OCH_3	H 3.39(3.45)
H 3.74(3.88)	OCH_3	OCH_3	OCH_3
H 3.47	OCH_3	OH	H 3.47
H 3.49	OH	OCH_3	H 3.45
H 3.05	H 3.37	OH	H 3.37
H 2.99(3.00)	H 3.29(3.33)	OCH_3	H 3.29(3.34)
H 3.31(3.37)	OCH_3	H 3.31(3.35)	H 2.97(2.97)



R_1	R_2	R_3	R_4
$-O \cdot CH_2 \cdot O-$		H 3.45(3.49)	H 3.36(3.44)
OCH_3	OCH_3	H 3.45(3.49)	H 3.36(3.44)
H 3.45(3.51)	$-O \cdot CH_2 \cdot O-$		H 3.45(3.51)
H 3.78(3.92)	$-O \cdot CH_2 \cdot O-$		OCH_3



R_1	R_2	R_3	R_4
H 3.27(3.37)	3.34(3.39)	CH_3O	CO_3O
H 3.27(3.37)	3.34(3.39)	$-O \cdot CH_2 \cdot O-$	
	H 3.40	CH_3O	OH



R_1	R_2	R_3	R_4	R_5
H 3.00	H 3.32	OH	H 3.32	H 3.00
H 2.94(2.96)	H 3.24(3.28)	OCH_3	H 3.24(3.28)	H 2.94(2.96)
H 3.36(3.44)	OCH_3	OCH_3	H 3.34(3.39)	H 3.27(3.37)
H 3.42	OCH_3	OH	H 3.42	H 3.33

[a] The number and these in parenthesis indicates the shift calculated by 1,2 and 3 parameters respectively.

observed and in this case the simple sum rule of substituent's shielding parameter is unavailable.

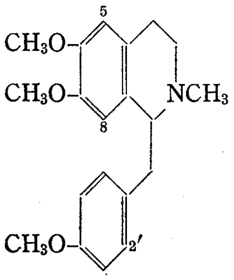
In the next place, using the parameters described in Table V, the ring proton chemical shifts in several aromatic systems have been estimated as follows (cf. Table VI).

These calculated shifts in Tables VI generally agree well with several experimental date,[6~9] and afford more successful results in estimating the ring proton chemical shifts in numerous organic molecules.

Accordingly, it is concluded that, in interpreting the spectra of complex organic molecule with aromatic fragment, the difference between the observed and calculated ring proton shift is dependent on the molecular environment, and therefore we can estimate quantitatively the effect of environmental factors —— for example, the magnetic anisotropy effect of the substituent, the steric or mutual interaction of the molecular fragment, etc.

Therefore, in this way, we are able to establish an effective stereochemical interpretation in complex organic molecule, as is illustrated in the following example.

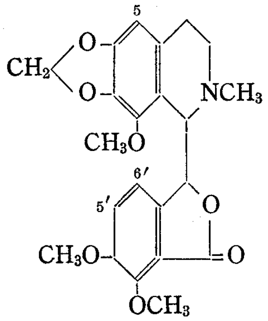
Example 1 1-(4'-Methoxybenzyl)-2-methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline[6)]



	cal (τ)	obs. (τ)
δ_{H_5}	3.45(3.47)	3.45
δ_{H_8}	3.39(3.45)	3.97 +0.5 p.p.m.
$\delta_{H_2'}$	2.94(2.96)	3.00

An upfield shift (by+0.5 p.p.m.) in δ_{H_8} is attributed to the diamagnetic anisotropy of the benzyl moiety in the molecule, therefore the preferred conformation proposed by M. Tomita, *et al.*[6)] is reasonable.

Example 2 Narcotine



	cal (τ)	obs. (τ)
δ_{H_5}	3.74(3.88)	3.70
$\delta_{H_5'}$	3.09	3.03
$\delta_{H_6'}$	3.12	3.93 +0.8 p.p.m.

$J_{\text{-O-CH-CH-N}} \simeq 4.3$ c.p.s.
$\angle_{\text{-O-CH-CH-N}} \simeq 50°$

An upfield shift (by+0.8 p.p.m.) in δ_{H_6} is attributed to the diamagnetic anisotropy of the benzene moiety in the tetrahydroisoquinoline part, and this is also compatible with $J_{\text{-O-CH-CH-N}}$ value.

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6) M. Tomita, *et al.*: This Bulletin, **13**, 921 (1965).
7) M. Tomita, H. Furukawa: Yakugaku Zasshi, **86**, 373 (1966).
8) S. Okuda, *et al.*: This Bulletin, **12**, 104 (1964).
9) M. Tomita, *et al.*: *Ibid.*, **13**, 538, 695, 704 (1965).