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Studies on the Proton Magnetic Resonance Spectra in Aromatic Systems. IV.[1] Discussions on the 1-Substituted-3,4-dimethoxybenzene Series

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The ^{1}H magnetic resonance spectra in 1-substituted-3,4-dimethoxybenzene series were examined in the following items.

i) simple sum rule in the chemical shift estimation.
ii) simple sum rule in the π-electron charge density estimation.
iii) revised ring ^{1}H chemical shift and π-electron charge density correlation.
iv) OCH_3 chemical shift and σ_π value of substituent R.
v) coupling constant and electronegativity of substituent group.

In the first paper of this series,[3] the apparent correlations had been acknowledged between ring ^{1}H chemical shift and substituent's shielding parameter, coupling constant and electronegativity of an atom attached to ring carbon, side chain ^{1}H shift and Hammett constant in 1-substituted-3,4-methylenedioxy- and 1-substituted-3,4-dimethoxybenzene series.

The present study was to investigate the correlation between ring ^{1}H chemical shift *vs.* ρ calcd.[4] value, side chain ^{1}H chemical shift and σ_π, coupling constant and electronegativity of substituent group, and simple sum rule of ρ calcd. value in 1-substituted-3,4-dimethoxybenzene series measured in cyclohexane solution. Moreover, ρnmr has been estimated from the revised shielding parameter[5] and compared with ρ calcd. from simplified LCAO MO method.

Experimental

All materials and the details of measurement are the same as shown in the previous papers.[3] Spectra are obtained in dil. cyclohexane solution (*ca.* 0.3 M), except 1-NH_2(0.2 M, CH_2Cl_2) and 1-NO_2(0.3 M, CCl_4) derivatives. The ring ^{1}H chemical shifts are calibrated relative to C_6H_6, and positive sign indicates higher shielding than C_6H_6, negative sign indicates lower shielding (*cf.* Table I). The side chain ^{1}H shifts are measured from TMS reference. The ρ calcd. value calculation has been carried out on a NEAC 2203 computer at Osaka University Computer Center.

Assignment and Inspection of Spectra

All spectra were analysed by the first order rule and inspected by T. Hirashima's dispersion method[6] except 1-CH_3 derivative, in which ring ^{1}H afforded nearly singlet structure. The results are summarized as below (*cf.* Table II). The calculated dispersion Δ calcd. agrees well with experimental dispersion Δ exp. within <0.1 cps, which supports the correct analysis.

1) PartIII: Y. Sasaki and M. Suzuki, *Chem. Pharm. Bull.* (Tokyo), **16**, 1187 (1968). This paper constitutes a part of series entitled "Studies on the Nuclear Magnetic Resonance Spectra in Aromatic Systems" by Y. Sasaki.
2) Location: *Toneyama, Toyonaka, Osaka.*
3) Y. Sasaki, M. Suzuki, T. Hibino, and K. Karai, *Chem. Pharm. Bull.* (Tokyo), **15**, 599 (1967).
4) ρ calcd.=π-electron charge density from simplified LCAO MO method.
5) Y. Sasaki and M. Suzuki, *Chem. Pharm. Bull.* (Tokyo), **15**, 1429 (1967); *ibid.*, **16**, 1187 (1968).
6) T. Hirashima, T. Kameo, O. Manabe, and H. Hiyama, The Abstract Papers in the 19th Annual Meeting of the Chemical Society of Japan, Vol. 1, 94 (1966); *Bull. Chem. Soc. Japan*, in press.

Table I. Observed and Calculated Ring ^1H, Side Chain ^1H Chemical Shifts and Coupling Constants in 1-Substituted-3,4-dimethoxybenzene Series

Substituent	Ring ^1H (ppm) H_2 obs.	H_2 calcd.	H_5 obs.	H_5 calcd.	H_6 obs.	H_6 calcd.	Side chain ^1H (ppm) OCH_3	J (cps) 2,6	J (cps) 5,6
NH_2	+1.09	+1.23	+0.69	+0.67	+1.17	+1.17	3.76 3.80	2.4	8.2
OCH_3	+0.80	+0.90	+0.56	+0.51	+0.96	+0.84	3.62 3.64 3.67	2.7	8.6
CH_3	+0.62	+0.64	+0.62	+0.60	+0.62	+0.58	3.65		
H	+0.47[a]	+0.47	+0.47	+0.47	+0.47	+0.41		1.2	7.8
Br	+0.35	+0.25	+0.63	+0.55	+0.31	+0.19	3.66	2.2	8.7
CHO	−0.11	−0.11	+0.39	+0.26	−0.05	−0.17	3.76	1.7	8.1
$COOCH_3$	−0.28	−0.27	+0.50	+0.37	−0.35	−0.33	3.73	1.8	8.3
NO_2	−0.37	−0.48	+0.45	+0.26	−0.52	−0.54	3.87	2.4	8.6

a) J.S. Martin and B.P. Dailey, *J. Chem. Phys.*, **39**, 1722 (1963).

Table II. Results of Dispersion Method (cps)

Substituent	Δ expt.	Δ calcd.	dif.
NH_2	4.38	4.38	0.00
OCH_3	3.49	3.54	0.05
Br	3.16	3.15	0.01
CHO	4.64	4.58	0.06
$COOCH_3$	7.65	7.68	0.03
NO_2	8.49	8.49	0.00

Result and Discussion

1) Chemical Shift

In the previous papers,[3] the author has examined the application of the simple sum rule using substituent's shielding parameters proposed by 3 groups of workers, Martin and Dailey,[7] Spiesecke and Schneider,[8] and Diehl.[9] In this work, discussion about 1-substituted-3,4-dimethoxybenzene series was carried out using Schneider and Spiesecke's parameter.

Plots of δH_2 and δH_6, the experimental chemical shift at *ortho* position of substituent (R) in 1-substituted-3,4-dimethoxybenzene series, *versus* d_o (R)[10] and δH_5, chemical shift at *meta* position of substituent (R), *versus* d_m(R) give good straight lines with slopes as below (*cf.* Fig. 1).

$$\delta H_2 = 0.89 d_o(R) + 0.45$$

$$\delta H_5 = 0.64 d_m(R) + 0.55$$

$$\delta H_6 = 1.00 d_o(R) + 0.47$$

7) J.S. Martin and B.P. Dailey, *J. Chem. Phys.*, **39**, 1722 (1963).
8) H. Spiesecke and W.G. Schneider, *J. Chem. Phys.*, **37**, 731 (1961).
9) P. Diehl, *Helv. Chim. Acta*, **45**, 829 (1961).
10) d_o (R), d_m (R), d_p (R) = shielding parameter at *ortho*, *meta* and *para* position in mono-substituted benzene series. R = substituent.

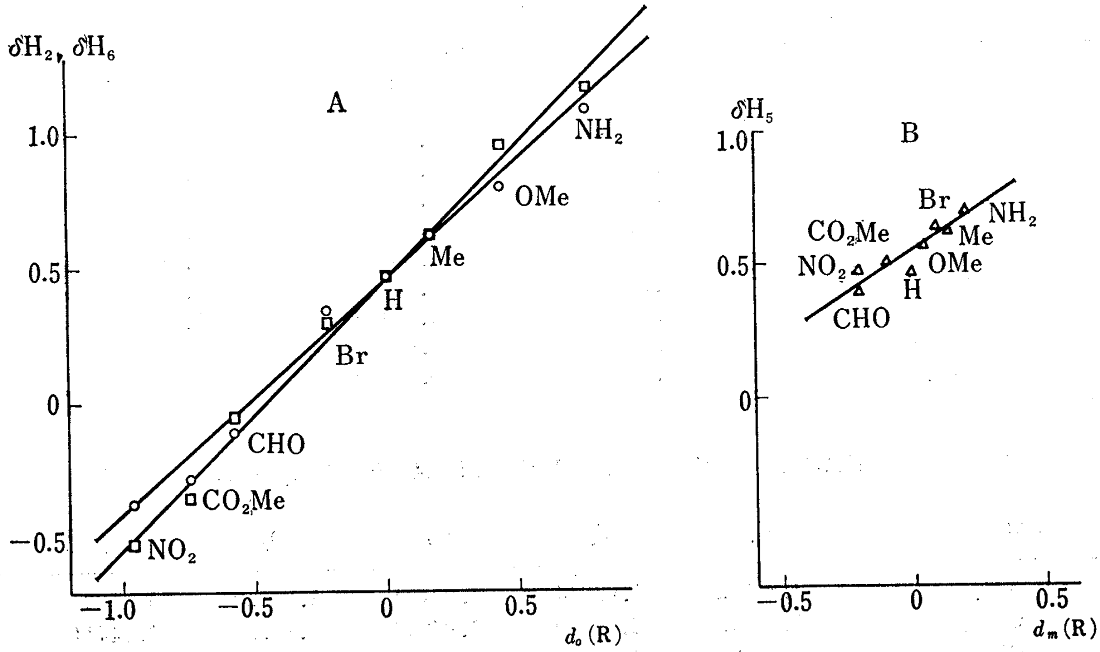

Fig. 1

A : —○— δH_2, —□— δH_6 in 1-substituted-3,4-dimethoxybenzene series/d_o(R)
B : —△— δH_5 in 1-substituted-3,4-dimethoxybenzene series/d_m(R)

Otherwise, from simple sum rule, the calculated ring ^{1}H chemical shifts (*cf.* Table I) are shown as below:

$$\delta H_2 = d_o(\mathrm{R}) + d_o(\mathrm{OCH_3}) + d_m(\mathrm{OCH_3}) = d_o(\mathrm{R}) + 0.47$$

$$\delta H_5 = d_m(\mathrm{R}) + d_o(\mathrm{OCH_3}) + d_m(\mathrm{OCH_3}) = d_m(\mathrm{R}) + 0.47$$

$$\delta H_6 = d_o(\mathrm{R}) + d_p(\mathrm{OCH_3}) + d_m(\mathrm{OCH_3}) = d_o(\mathrm{R}) + 0.41$$

Slope of the experimental value in δH_6 is unity which corresponds to slope of calculated chemical shift, and rather samll in δH_6 which has substituents at both *ortho* positions. It shows that the mutual resonance of the three substituents in 1-substituted-3,4-dimethoxybenzene series—namely the deviation from simple sum rule—is small. Slope from the experimental value in δH_5 is far from unity. It may be that owing to small magnitude of $d_m(\mathrm{R}) \lesssim 0.3$ ppm, the deviation from simple sum rule $\lesssim 0.1$ ppm affects serious influence.

2) π-Electron Charge Density Calculation

In the present study, the ρ clacd. values have been calculated from simplified LCAO MO method using Streitwiesers parameter.[11] The results are summarized as below:

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11) Streitwieser's parameter for HMO calculation

Element	Coulomb integral	Bond integral
N	$h_{\dot{N}}=0.5$	$k_{C-N}=0.8$
	$h_{\ddot{N}}=1.5$	$k_{CN}=1.0$
O	$h_{\dot{O}}=1.0$	$k_{C-O}=0.8$
	$h_{\ddot{O}}=2.0$	$k_{C=O}=1.0$
Cl	$h_{Cl}=2.0$	$k_{C-Cl}=0.4$
Br	$h_{Br}=1.5$	$k_{C-Br}=0.3$
CH_3	$h_C=-0.1$	$k_{C-Y}=0.8$
(C–Y–Z)	$h_Z=-0.5$	$k_{Y-Z}=0.3$

Auxiliary inductive parameter$=0.1\,h_X$ except $\ddot{O}$,$\ddot{N}$; 0.05 for $h_{\ddot{O}}$, $h_{\ddot{N}}$

Table III.[11] HMO Calculations of Monosubstituted Benzene Series

Substituent	*ortho*	*meta*	*para*
NH_2	1.03700	0.99826	1.02928
OCH_3	1.02528	0.99888	1.01960
CH_3	1.00452	0.99988	1.00326
Cl	0.979	1.001	0.987
Br	0.98400	1.00104	0.99040
CN	0.96462	1.00098	0.96886
CHO	0.93458	1.00148	0.94140
$COOCH_3$	0.94028	1.00160	0.94768
NO_2	0.94106	0.99766	0.93194

Table IV. HMO Calculations of 1-Substituted-3,4-dimethoxybenzene Series[11]

Substituent	C_2	C_5	C_6	O_3	O_4
NH_2	1.06192	1.02244	1.05400	1.94220	1.94520
OCH_3	1.05012	1.02330	1.04248	1.94236	1.94414
CH_3	1.02952	1.02448	1.02224	1.94224	1.94252
H	1.02482	1.02482	1.01794	1.94228	1.94228
Br	1.00906	1.02580	1.00194	1.94226	1.94106
CHO	0.96320	1.02434	0.95068	1.94254	1.93066
$COOCH_3$	0.96840	1.02468	0.95682	1.94290	1.93220
NO_2	0.97316	1.01710	0.95114	1.94100	1.92232

As illustrated in the previous communication,[5] the ring ^1H chemical shift has been divided mainly into two parts, one is the contribution from ρ value, the other is that from magnetic anisotropy effect, *etc.* Accordingly the simple sum rule should also be held in ρ

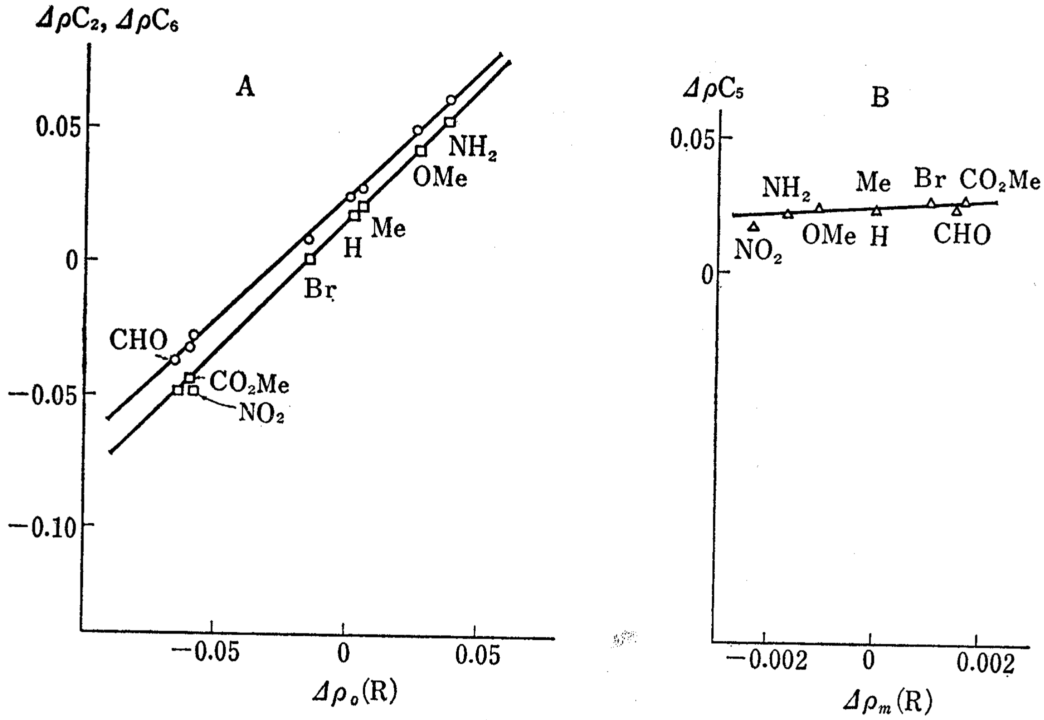

Fig. 2

A: —○— $\Delta\rho C_2$, —□— $\Delta\rho C_6$ in 1-substituted-3,4-dimethoxybenzene series/$\Delta\rho_o$ (R)
B: —△— $\Delta\rho C_5$ in 1-substituted-3,4-dimethoxybenzene series/$\Delta\rho_m$ (R)

value estimation. Plots of $\Delta\rho C_2$ and $\Delta\rho C_6$ *versus* $\Delta\rho_o(R)$,[12] $\Delta\rho_{C5}$ *versus* $\Delta\rho_m$ (R) give good straight lines with slopes as below (*cf.* Fig. 2).

$$\Delta\rho C_2 = 0.95\Delta\rho_o(R) + 0.0258$$

$$\Delta\rho C_5 = 1.46\Delta\rho_m(R) + 0.0236$$

$$\Delta\rho C_6 = 1.03\Delta\rho_o(R) + 0.0166$$

From the simple sum rule, following relations are estimated (*cf.* Table V).

$$\Delta\sigma C_2 = \Delta\rho_o(R) + \Delta\rho_o(OCH_3) + \Delta\rho_m(OCH_3) = \Delta\rho_o(R) + 0.0242$$

$$\Delta\rho C_5 = \Delta\rho_m(R) + \Delta\rho_o(OCH_3) + \Delta\rho_m(OCH_3) = \Delta\rho_m(R) + 0.0242$$

$$\Delta\rho C_5 = \Delta\rho_o(R) + \Delta\rho_p(OCH_3) + \Delta\rho_m(OCH_3) = \Delta\rho_o(R) + 0.0185$$

TABLE V. Local Excess Charges of 1-Substituted-3,4-dimethoxybenzene Series calculated by Simple Sum Method of ρ Value

Substituent	C_2	C_5	C_6
NH_2	0.06116	0.02242	0.05548
OCH_3	0.04944	0.02304	0.04376
CH_3	0.02868	0.02404	0.02300
H	0.02416	0.02416	0.01848
Br	0.00816	0.02520	0.00248
CHO	−0.04126	0.02564	−0.04694
$COOCH_3$	−0.03556	0.02576	−0.04124
NO_2	−0.03478	0.02182	−0.04046

Slopes of ρC_2 and ρC_6 in both groups are in good correspondence except ρC_5 which shows just the same aspect as chemical shift.

3) Ring ^1H Chemical Shift and π-Electron Charge Density

Previously, Schaefer and Schneider[13] have correlated the ring ^1H chemical shift with ρ calcd. value and proposed following relation.

TABLE VI. Simple Sum of Revised Shielding Parameter and ρ_{nmr} in 1-Substituted-3,4-dimethoxybenzene Series

Substituent		δ rev. ppm	ρ_{nmr}	Substituent		δ rev. ppm	ρ_{nmr}
NH_2	2	1.12	1.105	Br	2	0.59	1.055
	5	0.63	1.059		5	0.53	1.050
	6	1.03	1.096		6	0.50	1.047
OCH_3	2	0.94	1.088	CHO	2	0.09	1.008
	5	0.59	1.055		5	0.43	1.040
	6	0.85	1.079		6	0.00	1.000
CH_3	2	0.63	1.059	$COOCH_3$	2	0.18	1.017
	5	0.54	1.050		5	0.45	1.042
	6	0.54	1.050		6	0.09	1.008
H	2	0.51	1.048	NO_2	2	0.02	1.002
	5	0.51	1.048		5	0.42	1.039
	6	0.42	1.039		6	−0.07	0.993

12) $\rho_o(R)$, $\rho_m(R)$, $\rho_p(R) = \rho$ values at *ortho*, *meta* and *para* position in mono substituted benzene series, respectively. $\Delta\rho$ = local excess charge.

13) T. Schaefer and W.G. Schneider, *Can. J. Chem.*, **41**, 966 (1963).

$$\delta = k \cdot \Delta\rho$$

δ = chemical shift ppm

$k = 10.7 \pm 0.2$ ppm/e

$\Delta\rho$ = excess charge density

This relation is somewhat unfavorable to *ortho* ^{1}H shift in substitued C_6H_6 series, where the contributions other than ρ value afford serious contribution. In the previous paper of this series,[5] the revised shielding parameter corresponding to π-electron charge density has been estimated. Now the ρnmr values, estimated from the relation between the simple sum of the revised shielding parameter and excess charge $\sum[d \text{ rev. } (\text{R})]i = k \cdot \Delta\rho$, have been compared with ρ calcd. from simplified LCAO MO method (*cf.* Table VI). In general, ρ calcd. values are smaller than those of ρ nmr, because the former calculated from Streitwieser's parameter are somewhat underestimated in the electron releasing and overestimated in the electron attracting substituent group. These discrepancies have been observed in the correlation between π-electron charge density and $\sigma\pi$[14] (*cf.* Fig. 3, 4) and will be settled by more refined calculation in the near future.

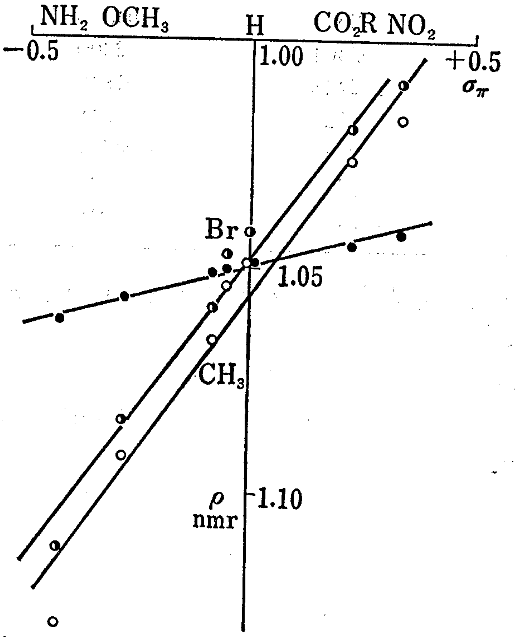

Fig. 3. Correlation between ρ_{nmr} and σ_π

—○— ρC_2 —●— ρC_5 —◑— ρC_6

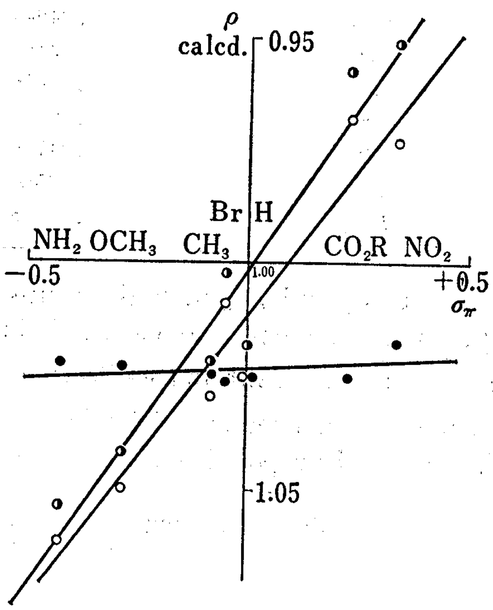

Fig. 4. Correlation between ρ calcd. and σ_π

—○— ρC_2 —●— ρC_5 —◑— ρC_6

4) Side Chain ^{1}H Chemical Shift and σ_π Value of the Substituent R

In 1-substituted-3,4-dimethoxybenzene series, two or three side chain signals were observed in NH_2, OCH_3 groups and one in the electron attracting substituent group, but the difference between ρO_3 and ρO_4 (*cf.* Table IV) was relatively large in electron attracting group and showed reverse trend with the side chain signals. It has been described by Marcus[15] that the electronic transmission between the substituent R and the terminal proton is enhanced, in the type R–C_6H_4–T–H, when T is conjugated with the benzene ring, *e.g.*, T=O, N, and C≡C. So the correlation between $\sigma\pi$ of substituent R and ^{1}H chemical shift of methoxy group was examined. When R=CH_3O, CH_3, Br, CHO and $COOCH_3$, the correlation mentioned above was satisfactory.

14) Y. Yukawa and Y. Tsuno, *Nippon Kagaku Zasshi*, **86**, 873 (1965).
15) S. Marcus, W. F. Reynolds, and S. Miller, *J. Org. Chem.*, **31**, 1872 (1966).

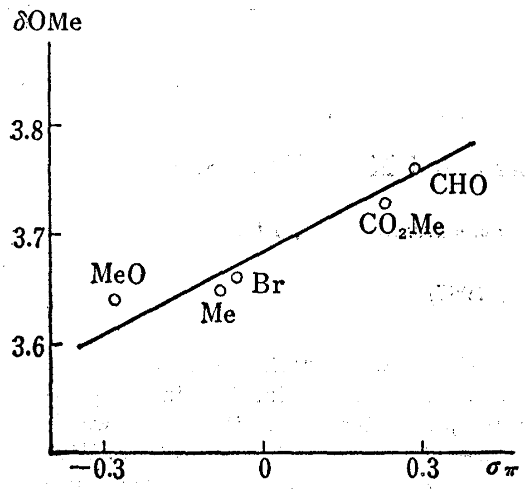

Fig. 5. Correlation between σ_π and Side Chain Proton Chemical Shift.
Chemical shift of $R=OCH_3$ is the mean value.

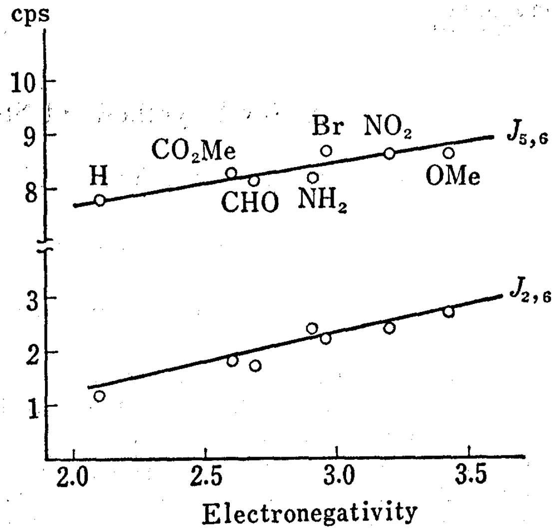

Fig. 6. Correlation between Coupling Constant and Electronegativity of the Substituent Groups

5) Coupling Constant

As shown in Fig. 6, coupling constants were linear with electronegativity of the substituent group.[16,17]

Conclusion

Simple sum rule of substituent's shielding parameter is shown to be almost reliable within 0.1 ppm in 1-substituted-3,4-dimethoxybenzene series, and above rule is also compatible with ρ clacd. value estimation. The correlations between coupling constant and electronegativity of the substituent group, OCH_3 ^1H chemical shift and $\sigma\pi$ are satisfactory.

In the present step, considerable deviations are observed between ρ nmr and ρ clacd., although general trends are very similar. This problem will be studied in the following paper.

Acknowledgement The author expresses her deep thanks to Assoc. Prof. Dr. Y. Sasaki, Faculty of Pharmaceutical Sciences, Osaka University, for his generous encouragement throughout this work.

16) J.R. Cavanaugh and B.P. Dailey, *J. Chem. Phys.*, **34**, 1099 (1961).
17) D.H. McDaniel and A. Yingst, *J. Am. Chem. Soc.*, **86**, 1334 (1964).