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Carbon-13 Nuclear Magnetic Resonance Spectroscopy. V.[1] Studies on Carbon-13 Magnetic Resonance Spectra in Aromatic and Heteroaromatic Systems. (1). Mono- and Disubstituted Benzene Derivatives[2]

Goh Miyajima,[3a] Yoshio Sasaki and Miyoko Suzuki[3b]

Naka Works, Hitachi Ltd.[3a] *and Faculty of Pharmaceutical Sciences, Osaka University*[3b]

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Numerous carbon-13 chemical shifts of monosubstituted, *meta*- and *para*-disubstituted benzene derivatives as well as symmetrically and unsymmetrically substituted toluene and chlorobenzene homologs were measured to test the reliability of the simple sum rule from monosubstituted benzene derivatives. The chemical shifts of *meta*- and *para*-disubstituted benzene derivatives were examined with respect to the substituent constants σ_I and σ_π.

Introduction

Recently, there have been numerous papers[4] on theoretical and experimental work on carbon-13 magnetic resonance spectroscopy. And, for the practical utility, the reliability of the simple sum rule of carbon-13 chemical shifts for monosubstituted benzene derivatives was confirmed for polysubstituted benzene derivatives, and the wide application for the structural determination of organic compounds[5a,b] was suggested. In this work, the carbon-13 magnetic resonance chemical shifts of monosubstituted benzenes were determined with reference to benzene by the normal technique together with the proton decoupling technique, and the reliability of the simple sum rule for the above parameters was examined with numerous *meta*- and *para*- disubstituted benzenes, *etc.*

Experimental

Carbon-13 spectra are measured in an Hitachi Perkin-Elmer Type R-20A High Resolution NMR Spectrometer equipped with a 15.085 MHz transmitter and a thermostatically controlled permanent magnet, with a proton external lock mode, which guarantees field and resolution stabilities over a long period. For normal scanning, the R-206C Carbon Attachment and A-1600A Time Averaging Computer are used, and for the proton decoupling technique, the R-201 Spin Decoupler and R-208 Proton Wide Band Decoupler are operated at the same time. The phase rotation of a signal is not observable because of the radio-frequency sweep system. The signal positions read out from the A-1600A Time Averaging Computer are calibrated as chemical shifts using the frequency counter in the frequency unit, or are taken directly from a precalibrated chart. Solid materials are made into solution, while liquid are examined directly with or without dilution. The fluids are placed in a normalized pyrex galss tube (8.0 mm *o.d.* and 7.0 mm *i.d.*), employing a plastic turbine driven by compressed air. Under these conditions, deviations in chemical shifts due to the sample tube are in the order of $\lesssim \pm 0.05$ ppm, even when an external reference is used. In this work, carbon-13 enriched MeI and C_6H_6, which are 213.3 ppm and 65.2 ppm higher field shift than the CS_2 external reference, respectively, are used as reference compounds. The solvent effects observed in dimethylsulfoxide (DMSO) and CCl_4 are $\lesssim 1.0$ ppm. All materials used were of J.I.S. grade, and were obtained from Tokyo Kasei Chemical Co. Ltd. Several spectra are shown in Fig. 1—4.

1) Part IV: G. Miyajima, Y. Sasaki and M. Suzuki, *Chem. Pharm. Bull.* (Tokyo), **18**, 1498 (1970).
2) This work was presented at the 9th NMR Symposium in Japan, at Kanazawa, in October, 1970.
3) Location: *a*) *Katsuta, Ibaragi*; *b*) *Toneyama 6-1-1, Toyonaka, Osaka.*
4) J.W. Emsley, J. Feeney and L.H. Sutcliffe, High Resolution Nuclear Magnetic Resonacne Spectroscopy, Vol. 2 Chapter 12, Section 2, Pergamon, 1966.
5) *a*) P.C. Lauterbur, *J. Am. Chem. Soc.*, **83**, 1838 (1961); **83**, 1846 (1961); *idem*, *J. Chem. Phys.*, **38**, 1406 (1963); **38**, 1415 (1963); **38**, 1432 (1963); *b*) K.S. Dhami and J.B. Stothers, *Can. J. Chem.*, **43**, 498 (1965); **43**, 510 (1965); **43**, 521 (1965); **43**, 479 (1965).

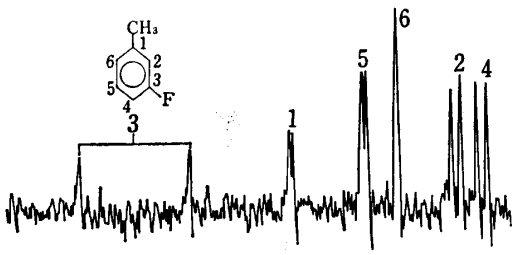

Fig. 1. Proton Decoupled *meta*-Fluorotoluene (Undiluted Liquid)

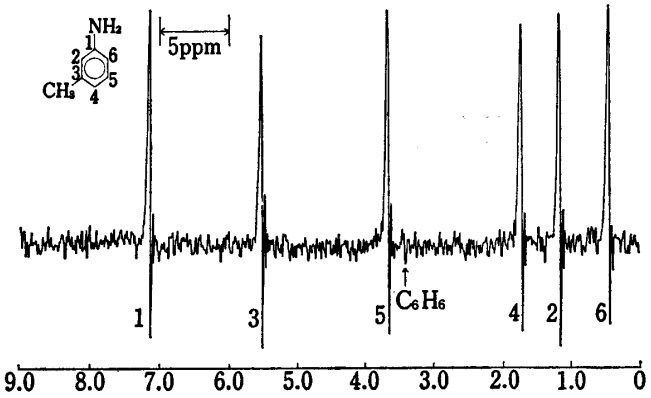

Fig. 2. Proton Decoupled *meta*-Toluidine (Undiluted Liquid)

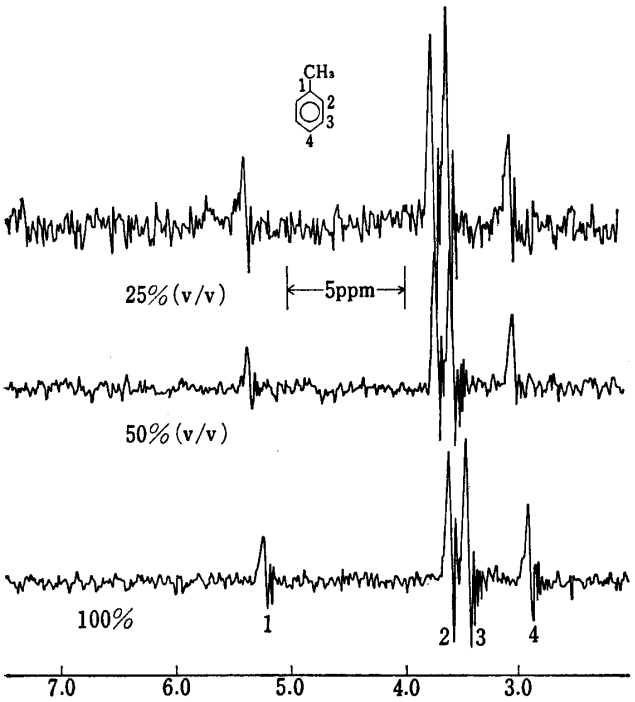

Fig. 3. Solvent Effect on Proton Decoupled Toluene
solvent: dimethylsulfoxide

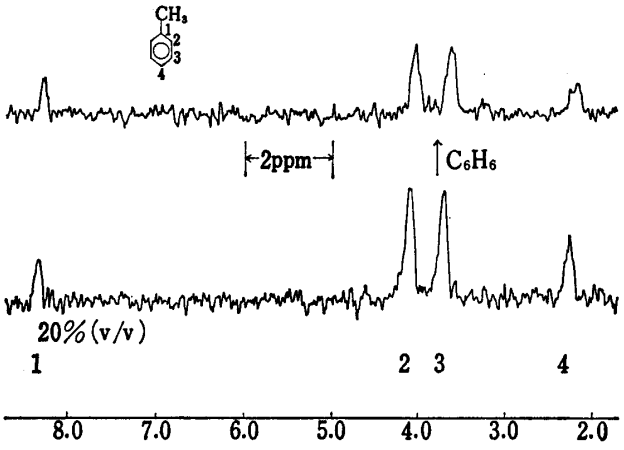

Fig. 4. Solvent Effect on Proton Decoupled Toluene
solvent: carbon tetrachloride

Result and Discussion

Monosubstituted Benzene Derivatives

The carbon-13 chemical shifts of monosubstituted benzene derivatives relative to benzene, used as reference, are summarized in Table I. These data differ somewhat from those presented by Spiesecke and Schneider,[6] probably due to the improvements of the experimental conditions.

Disubstituted Benzene Derivatives

1,3-Disubstituted Benzene Derivatives——The results obtained for 1,3-disubstituted benzene derivatives are summarized in Table II, where the observed shifts are compared with the sum of the parameters summarized in Table I. The table shows the correspondence between observed values and calculated ones.

These series contain two substituents on the C-1 and C-3 carbon atoms, respectively. Formerly, it was suggested that the substituent effect at the *meta* position had an inductive

6) H. Spiesecke and W.G. Schneider, *J. Chem. Phys.*, **35**, 731 (1961).

TABLE I. C-13 Magnetic Resonance Chemical Shifts of Monosubstituted Benzene Derivatives (PPM) (undiluted liquid)

X	1	2	3	4	
NMe_2	−22.76	+15.31	−0.99	+11.53	
NHMe	−21.74	+15.51	−1.26	+11.20	
NH_2	−19.29	+12.73	−1.46	+ 9.81	
OH	−27.11	+12.33	−1.86	+ 6.83	
OMe	−32.15	+14.05	−1.53	+ 7.36	
Me	− 9.21	− 0.73	+0.13	+ 2.85	
Et	−15.71	− 0.33	+0.33	+ 2.58	
F	−35.13	+13.00	−1.52	+ 4.04	
Cl	− 6.36	− 0.46	−1.59	+ 1.72	
Br	+ 5.17	− 3.76	−2.25	+ 1.00	
I	+32.35	−10.08	−2.85	0	
C_6H_5	−13.10	+ 0.66	−1.60	+ 0.13	DMSO
NO_2	−19.82	+ 5.10	−1.13	− 6.36	
CHO	− 8.62	− 1.33	−0.80	− 5.97	
COMe	− 9.21	− 0.27	−0.27	− 4.71	
COEt	− 9.02	+ 0.33	−0.33	− 4.51	
SO_2NH_2	−16.04	+ 1.72	−1.66	− 5.10	DMSO
CN	+15.71	− 3.98	−1.19	− 4.71	
CF_3		+ 3.65	+0.13	− 2.92	
CO_2Me	− 2.25	− 1.26	−0.07	− 4.51	

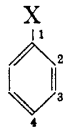

TABLE II. C-13 Magnetic Resonance Chemical Shifts of 1,3-Disubstituted Benzene Derivatives (PPM)

R_1	R_3		1	2	3	4	5	6	
Me	CN	obs	−11.6	− 4.6	+15.8	− 1.6	−1.6	− 6.1	
		calcd.	−10.4	− 4.7	+15.8	− 1.1	−1.1	− 5.4	
		Δ	− 1.2	+ 0.1	0	− 0.5	−0.5	− 0.7	
Me	F	obs	−12.1	+11.9	−35.0	+16.1	−1.3	+ 3.5	undiluted
		calcd.	−10.7	+12.3	−35.0	+15.9	−1.4	+ 3.3	
		Δ	− 1.4	− 0.4	0	+ 0.2	+0.1	+ 0.2	
Me	OMe	obs	−11.7	+12.5	−33.3	+16.5	−1.6	+ 6.0	
		calcd.	−10.7	+13.3	−32.0	+16.9	−1.4	+ 6.6	
		Δ	− 1.0	− 0.8	− 1.3	− 0.4	−0.2	− 0.6	
OMe	Br	obs	−33.2	+10.3	+ 5.0	+ 4.0	−3.6	+14.3	
		calcd.	−34.5	+10.3	+ 3.7	+ 3.6	−3.8	+15.1	
		Δ	+ 1.3	0	+ 1.3	+ 0.4	+0.2	− 0.8	
OMe	OMe	obs	−33.5	+27.1	−33.5	+21.5	−2.1	+21.5	
		calcd.	−33.7	+28.2	−33.7	+21.5	−3.0	+21.5	
		Δ	+ 0.2	− 1.1	+ 0.2	0	+0.9	0	
OH	Cl	obs	−29.7	+11.6	− 7.0	+ 7.2	−3.1	+13.4	
		calcd.	−28.7	+11.8	− 8.3	+ 6.3	−3.5	+14.0	
		Δ	− 1.0	− 0.2	+ 1.3	+ 0.9	+0.4	− 0.6	
OH	CO_2Me	obs	−30.1	+11.4	− 1.9	+ 7.0	−3.6	+ 7.0	
		calcd.	−27.2	+11.1	− 4.1	+ 5.8	−1.9	+ 7.8	
		Δ	− 2.9	− 0.3	+ 2.2	+ 1.2	−1.7	− 0.8	

R_1	R_3		1	2	3	4	5	6
NH_2	OMe	obs	−21.5	+27.0	−33.3	+24.3	−2.5	+20.0
		calcd.	−20.8	+26.8	−33.7	+23.9	−3.0	+20.1
		Δ	− 0.7	+ 0.2	+ 0.4	+ 0.4	+0.5	− 0.1
NH_2	Me	obs	−18.8	+11.2	−10.7	+ 8.3	−1.4	+14.7
		calcd.	−19.2	+12.0	−10.7	+ 9.1	−1.3	+15.6
		Δ	+ 0.4	− 0.8	0	− 0.8	−0.1	− 0.9
NH_2	Br	obs	−21.4	+10.0	+ 4.5	+ 7.0	−3.5	+13.5
		calcd.	−21.6	+ 8.9	+ 3.7	+ 6.0	−3.8	+13.7
		Δ	+ 0.2	+ 1.1	+ 0.8	+ 1.0	+0.3	− 0.2
NH_2	I	obs	−22.1	+ 4.1	+31.7	+ 1.5	−3.8	+12.9
		calcd.	−22.2	+ 2.6	+30.9	− 1.3	−4.4	+12.7
		Δ	+ 0.1	+ 1.5	+ 0.8	+ 2.8	+0.6	+ 0.2
NH_2	OEt	obs	−21.8	+26.4	−32.6	+24.0	−2.3	+19.9
		calcd.	−20.8	+26.8	−33.7	+23.9	−3.0	+20.1
		Δ	− 1.0	− 0.4	+ 1.1	+ 0.1	+0.7	− 0.2
NH_2	CF_3	obs	−20.0	+17.0		+13.9	−1.9	+ 9.8
		calcd.	−19.4	+16.4		+13.5	−1.4	+ 9.8
		Δ	− 0.6	+ 0.6		+ 0.4	−0.5	0
NH_2	Ac	obs	−21.4	+14.1	−10.5	+11.0	−1.9	+ 8.4
		calcd.	−19.6	+12.4	−10.7	+ 9.5	−1.8	+ 8.0
		Δ	− 1.8	+ 1.7	+ 0.2	+ 1.5	−0.1	+ 0.4
Ac	Cl	obs	−11.0	− 0.1	− 6.6	− 5.0	−2.4	+ 1.3
		calcd.	−10.8	− 0.8	− 6.7	− 5.2	−1.9	+ 1.4
		Δ	− 0.2	+ 0.7	+ 0.1	+ 0.2	−0.5	− 0.1
Ac	Br	obs	−15.4	− 3.5	+ 5.0	− 8.2	−3.5	− 0.2
		calcd.	−11.5	− 3.5	+ 4.9	− 8.5	−2.6	+ 0.7
		Δ	− 3.9	0	+ 0.1	+ 0.3	−0.9	− 0.9
NO_2	OMe	obs	−21.3	+19.3	−32.4	+ 6.8	−2.5	+12.5
		calcd.	−21.3	+19.2	−33.3	+ 7.7	−2.6	+12.5
		Δ	0	+ 0.1	+ 0.9	− 0.9	+0.1	0
NO_2	OEt	obs	−21.2	+19.2	−31.6	+ 7.4	−2.0	+13.0
		calcd.	−21.4	+19.2	−33.3	+ 7.7	−2.7	+12.5
		Δ	+ 0.2	0	+ 1.7	− 0.3	+0.7	+ 0.5
NO_2	Cl	obs	−21.2	+ 4.2	− 7.4	− 7.0	−3.8	+ 5.7
		calcd.	−21.4	+ 4.6	− 7.5	− 6.9	−2.7	+ 6.8
		Δ	+ 0.2	− 0.4	+ 0.1	− 0.1	−1.1	− 1.1
NO_2	Br	obs	+21.2	+ 1.4	+ 5.0	−10.4	−4.2	+ 5.0
		calcd.	+22.1	+ 1.3	+ 4.1	−10.2	−3.4	+ 6.1
		Δ	− 0.9	+ 0.1	+ 0.9	− 0.2	−0.8	− 1.1
NO_2	CO_2Me	obs	−20.4	+ 4.0	− 3.9	− 7.6	−2.9	0
		calcd.	−19.9	+ 3.8	− 3.4	− 7.6	−1.2	+ 0.6
		Δ	− 0.5	+ 0.2	− 0.5	0	−1.7	− 0.6
NO_2	CF_3	obs	−20.3	+ 7.7		− 4.4	−2.9	+ 1.3
		calcd.	−19.7	+ 8.8		− 2.7	−1.0	+ 2.2
		Δ	− 0.6	− 1.1		− 1.7	−1.9	− 0.9
NO_2	Ac	obs	−20.5	+ 5.3	−10.5	− 6.6	−2.9	+ 0.3
		calcd.	−20.1	+ 4.8	−10.3	− 6.7	−1.4	+ 0.4
		Δ	− 0.4	+ 0.5	− 0.2	+ 0.1	−1.5	− 0.1

solvent: dimethylsulfoxide

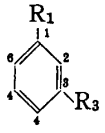

TABLE III. C-13 Magnetic Resonance Chemical Shifts of 1,4-Disubstituted Benzene Derivatives (PPM)

R_1	R_4		1	2	3	4	
NH_2	OH	obs	−13.1	+11.2	+11.2	−21.5	
		calcd.	−12.5	+10.8	+10.8	−17.3	
		Δ	− 0.6	+ 0.4	+ 0.4	− 4.2	
NH_2	OMe	obs	−14.3	+11.7	+12.7	−24.1	
		calcd.	−11.9	+11.2	+12.6	−22.4	
		Δ	− 2.4	+ 0.5	+ 0.1	− 1.7	
NH_2	Me	obs	−18.2	+12.7	− 2.0	+ 2.2	
		calcd.	−16.4	+12.8	− 2.2	+ 0.6	
		Δ	− 1.8	− 0.1	+ 0.2	+ 1.6	
NH_2	Cl	obs	−19.4	+11.5	− 1.3	+ 6.6	
		calcd.	−17.6	+11.1	− 2.0	+ 3.4	
		Δ	− 1.8	+ 0.4	+ 0.7	+ 3.2	
NH_2	CO_2Me	obs	−25.9	+14.3	− 4.0	+10.5	
		calcd.	−23.8	+12.0	− 2.7	+ 7.6	
		Δ	− 2.1	+ 2.3	− 1.3	+ 2.9	
NH_2	Ac	obs	−26.3	+14.6	− 3.4	+ 2.0	
		calcd.	−24.0	+12.4	− 1.8	+ 0.6	
		Δ	− 2.3	+ 2.2	− 1.6	+ 1.4	
NH_2	NO_2	obs	−28.0	+14.8	+ 1.2	− 9.0	
		calcd.	−25.7	+11.6	+ 3.6	−10.0	
		Δ	− 2.3	+ 3.2	− 2.4	+ 1.0	
OMe	OH	obs	−25.3	+12.7	+11.5	−23.6	
		calcd.	−25.4	+12.2	+10.8	−19.7	
		Δ	+ 0.1	+ 0.5	+ 0.7	− 3.9	
OMe	OMe	obs	−26.1	+12.7	+12.7	−26.1	
		calcd.	−24.8	+12.6	+12.6	−24.8	
		Δ	− 1.3	+ 0.1	+ 0.1	− 1.3	
OMe	CN	obs	−35.5	+12.4	− 6.6	+24.3	
		calcd.	−36.9	+12.9	− 5.5	+23.1	
		Δ	+ 1.4	− 0.5	− 1.1	+ 1.2	
OMe	Ac	obs	−35.8	+13.8	− 2.9	− 2.9	undiluted
		calcd.	−36.9	+13.8	− 1.8	− 1.8	
		Δ	+ 1.1	0	− 1.1	− 1.1	
OMe	NO_2	obs	−37.3	+13.1	+ 1.9	−13.3	
		calcd.	−38.6	+13.0	+ 3.6	−12.4	
		Δ	+ 1.3	+ 0.1	− 1.7	− 0.9	
Me	OH	obs	− 2.3	− 2.3	+12.5	−25.0	undiluted
		calcd.	− 2.4	− 2.6	+12.4	−24.2	
		Δ	+ 0.1	+ 0.3	+ 0.1	− 0.8	
Me	OMe	obs	− 1.9	− 2.3	+13.9	−30.5	
		calcd.	− 1.9	− 2.3	+14.2	−29.3	
		Δ	0	0	− 0.5	− 1.2	
Me	F	obs	− 5.4	− 2.1	+13.4	−33.3	undiluted
		calcd.	− 5.2	− 2.2	+13.1	−32.2	
		Δ	− 0.2	+ 0.1	+ 0.3	− 1.1	
Me	Ac	obs	−15.7	− 1.3	− 0.5	− 7.1	
		calcd.	−13.9	− 1.0	− 0.2	− 6.3	
		Δ	− 1.8	− 0.3	− 0.3	− 0.8	
Me	NO_2	obs	−18.8	− 2.3	+ 4.4	−18.2	
		calcd.	−15.6	− 1.8	+ 5.0	−16.9	
		Δ	− 3.2	− 0.5	− 0.6	− 1.3	
Ac	OH	obs	− 1.7	− 3.3	+12.0	−34.9	
		calcd.	− 2.4	− 2.2	+12.0	−31.8	
		Δ	+ 0.7	− 1.1	0	− 3.1	

solvent: dimethylsulfoxide

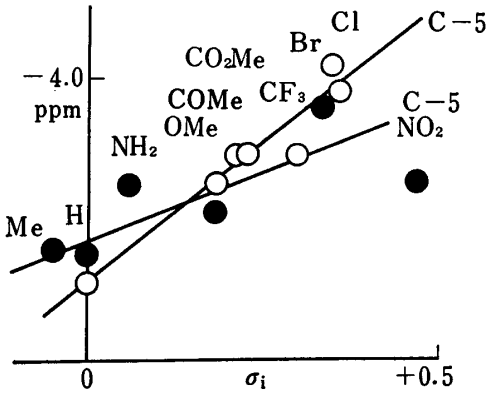

Fig. 5a ○: *meta*-substituted nitrobenzene
●: *meta*-substituted anisole

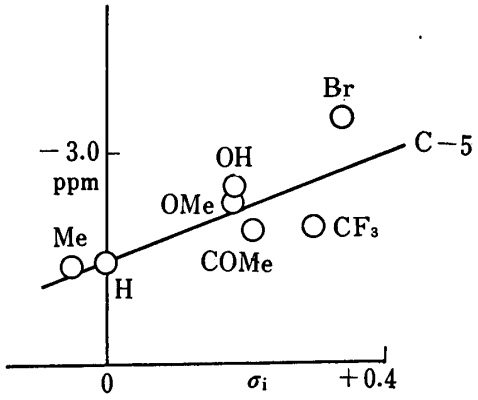

Fig. 5b ○: *meta*-substituted aniline

character, and then, in these series, the inductive effects of two substituents on the C-5 position should be additive. In the present work, the observed shifts were divided into several groups, namely those of *meta*-substituted nitrobenzene, anisole, aniline, toluene, chloro- and bromobenzene series, and compared with the substituent constant σ_i.[7]

As shown in Fig. 5a—c, for the *meta*-substituted nitrobenzene, aniline and anisole series, the C-5 chemical shifts are linearly related with σ_i. Similar results were observed for *meta*-substituted chloro- and bromobenzene derivatives, but the result for the toluene series did not show a clear linear relation by the want of data.

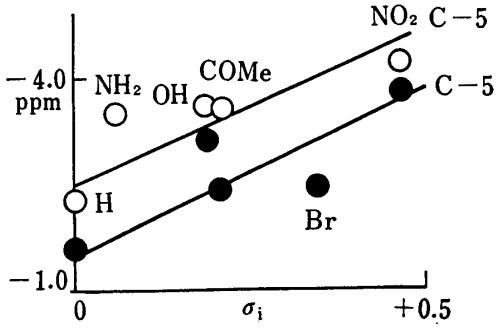

Fig. 5c ●: *meta*-substituted chlorobenzene
○: *meta*-substituted bromobenzene

1,4-Disubstituted Benzene Derivatives——The reliability of the simple sum rule was confirmed for *para*-substituted aniline, anisole and toluene derivatives (Table III). The discrepancies between the observed and calculated shifts are somewhat exaggerated when the substituents have a strong mesomeric character. Thus, the C-2 chemical shifts of the aniline derivatives showed a linear relation with the substituent constant σ_π because the influence of the mesomeric interaction between the substituent groups was strong. However, the C-2 chemical shifts of toluene series were linearly related with the substituent

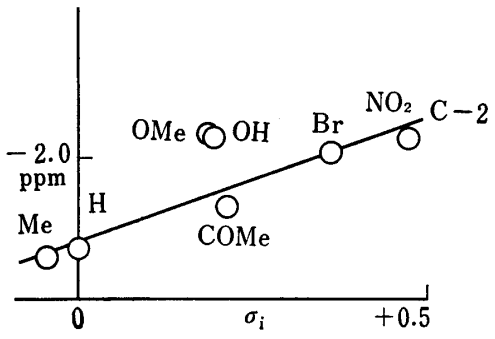

Fig. 6a ○: *para*-substituted toluene

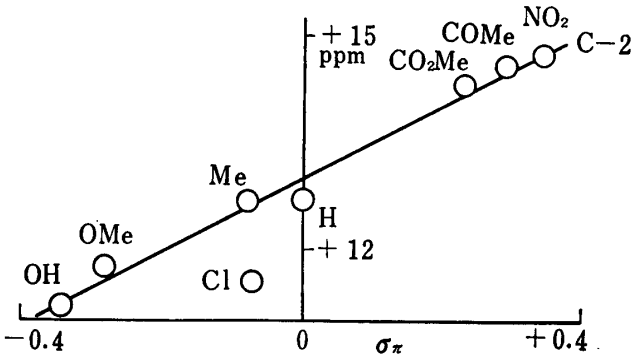

Fig. 6b ○: *para*-substituted aniline

7) Y. Yukawa and Y. Tsuno, *Nippon Kagaku Zasshi*, **86**, 873 (1965).

constant σ_i, because of the weak electronic effect of Me group. (Fig. 6a—b) With anisole derivatives there was neither definite relation with σ_i nor σ_π, because of the intermediate electronic effect due to OMe group.

Symmetrically and Unsymmetrically Substituted Toluene and Chlorobenzene Homologs

As shown in Table IV, the carbon-13 chemical shifts of symmetrically and unsymmetrically substituted toluene and chlorobenzene homologs were found to conform to the simple sum rule. Table IV shows that differences between the observed and calculated values were negligible in toluene series. With chlorobenzene homologs the differences were somewhat larger, due to the mesomeric character of the chlorine atoms.

TABLE IV. C-13 Magnetic Resonance Chemical Shifts of Toluene and Chlorobenzene Homologs (PPM) (undiluted liquid)

		1	2	3	4	5	6	
1,2-di Me	obs	−7.8	−7.8	−1.4	+2.5	+2.5	−1.4	
	calcd.	−9.9	−9.9	−0.6	+3.0	+3.0	−0.6	
	Δ	+2.1	+2.1	−0.8	−0.5	−0.5	−0.8	
1,3-di Me	obs	−9.1	−1.6	−9.1	+2.1	+0.1	+2.1	
	calcd.	−9.1	−1.5	−9.1	+2.1	+0.3	+2.1	
	Δ	0	0.1	0	0	−0.2	0	
1,4-di Me	obs	−6.1	−0.6	−0.6	−6.1	−0.6	−0.6	
	calcd.	−6.4	−0.6	−0.6	−6.4	−0.6	−0.6	
	Δ	+0.3	0	0	+0.3	0	0	
1,3,5-tri Me	obs	−8.9	+1.3	−8.9	+1.3	−8.9	+1.3	
	calcd.	−8.6	+1.4	−8.6	+1.4	−8.6	+1.4	
	Δ	−0.3	−0.1	−0.3	−0.1	−0.3	−0.1	
1,2-di Cl	obs	−4.7	−4.7	−2.5	+0.2	+0.2	−2.5	
	calcd.	−6.8	−6.8	−2.1	+0.1	+0.1	−2.1	
	Δ	+2.1	+2.1	−0.4	+0.1	+0.1	−0.4	
1,3-di Cl	obs	−7.4	−0.8	−7.4	+1.1	−2.4	+1.1	
	calcd.	−8.0	−0.9	−8.0	+1.3	−3.2	+1.3	
	Δ	+0.6	+0.1	+0.6	−0.2	+0.8	−0.2	
1,4-di Cl	obs	−4.8	−2.3	−2.3	−4.8	−2.3	−2.3	
	calcd.	−4.6	−2.1	−2.1	−4.6	−2.1	−2.1	
	Δ	−0.2	−0.2	−0.2	−0.2	−0.2	−0.2	
1,3,5-tri Cl	obs	−8.0	0	−8.0	0	−8.0	0	DMSO
	calcd.	−9.5	+0.8	−9.5	+0.8	−9.5	+0.8	
	Δ	+1.5	−0.8	+1.5	−0.8	+1.5	−0.8	
1,2,4-tri Cl	obs	−3.8	−6.1	−2.9	−5.7	−0.5	−3.8	
	calcd.	−5.1	−8.0	−2.5	−6.3	−0.3	−2.7	
	Δ	+1.3	+1.9	−0.4	+0.6	−0.2	−1.1	
1,2,3-tri Cl	obs	−6.2	−6.2	−6.2	−1.5	−1.5	−1.5	DMSO
	calcd.	−8.4	−7.3	−8.4	+0.3	−1.5	+0.3	
	Δ	+2.2	+1.1	+2.2	−1.8	0	−1.8	