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Studies on ^{13}C Magnetic Resonance Spectroscopy. X.[1] ^{13}C Nuclear Magnetic Resonance Chemical Shifts of 2-Substituted Naphthalenes and Their 6-Methoxy Derivatives

HITOSHI TAKAI, AKIRA ODANI, and YOSHIO SASAKI

Faculty of Pharmaceutical Sciences, Osaka University[2]

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^{13}C chemical shifts of 2-substituted naphthalenes and their 6-methoxy derivatives were determined by the aids of the additivity of the substituent effect and the selective H-D exchange reaction. The reliability of the additivity of the shielding parameters of monosubstituted benzenes for the above naphthalene series were acknowledged, and the linear relations between the chemical shifts and shielding parameters or substituent constants were confirmed.

Keywords——^{13}C magnetic resonance; chemical shift; assignment; 2-substituted naphthalenes; 2-substituted-6-methoxynaphthalenes; additivity rule; H-D exchange reaction

Introduction

In the previous report,[1] the relationship between ^{13}C magnetic resonance chemical shift and the electronic character of the substituent, and the reliability of the additivity of the substituent effect were confirmed for substituted benzene series. In this work, we extended our discussions to naphthalene series, and in order to exclude the *peri* interaction and appreciate the resonance contribution, 2-substituted naphthalene (**1**) and their 6-methoxy (**2**) derivatives were examined.

On the assignments of the ring carbons of substituted naphthalenes several reports[3] are already published, but some of their data are ambiguous and the wide varieties of substituents are not incorporated. This work was undertaken to complete the assignment of the ^{13}C chemical shifts of **1** and **2** with the aid of the H–D exchange reaction, and the observed data were tried to correlate with the substituent constants σ_i and σ_π[4] or their linear combinations.

Experimental

Measurements of Spectra

The details of the ^{13}C NMR measurements are all the same as described in the previous report.[1] ^{1}H NMR spectra were taken in $CDCl_3$ or CCl_4 solution on a Hitachi R-22 type spectrometer. Line positions are calibrated from the internal reference Me_4Si with an accuracy of ± 1.0 Hz.

Materials

2-Nitro- and 2-iodonaphthalenes were prepared from 2-naphthylamine by the authentic methods, other 2-substituted naphthalenes were commercially available, and their 6-methoxy derivatives are prepared from 2-napthol by the authentic methods given in Chart 1. The chemical transformations of the deuterated compounds obtained fron the selectively deuterated materials are compiled in Chart 2. The positions of the H-D exchange reaction were confirmed by the ^{1}H NMR signal intensity or ^{13}C signal peak height.

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[1] Part IX: H. Takai, K. So, and Y. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **26**, 1303 (1978).

[2] Location: *Yamadakami 133-1, Suita, Osaka 565, Japan.*

[3] W. Kitching, M. Bullpitt, D. Gartshore, W. Adcock, T.C. Khor, D. Doddrell, and I.D. Rae, *J. Org. Chem.* **42**, 2411 (1977); and references cited therein.

[4] Y. Yukawa and Y. Tsuno, *Nippon Kagaku Zasshi*, **86**, 873 (1965).

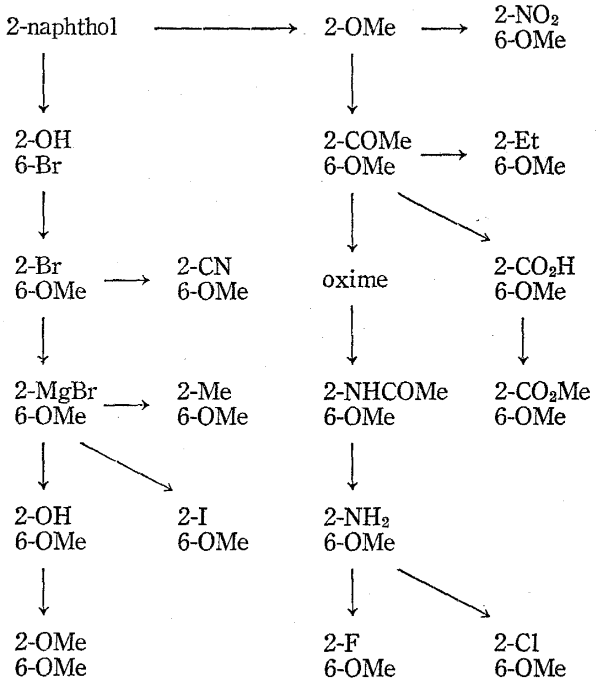
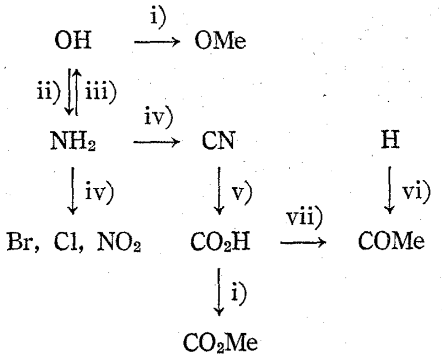


Chart 1. Preparative Methods of 2-Substituted-6-methoxynaphthalenes



i) methylation by CH_2N_2

ii) Bucherer reaction
N. L. Drake, "Organic Reactions," Vol. 1, John Wiley and Sons, Inc., New York, 1963, p. 120. This reaction accompanies the scattering of D at C-1 and C-3.

iii) *via* diazonium salt

iv) Sandmeyer reaction

v) alkaline hydrolysis

vi) Friedel–Crafts acylation
S. Yura, Y. Yamamoto, H. Hara, and R. Oda, *Kogyo Kagaku Zasshi*, **45**, 575 (1942). This reaction accompanies a partial scattering of D at α-position, where the content of D altered from ~70% to ~50% before and after the reaction.

vii) haloform reaction
M.S. Newman and H.L. Holmes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., 1966, p. 428.

Chart 2. Method of Chemical Transformation

H-D Exchange Reaction

The H-D exchange reaction used in this work are as follows:

a) **Grignard Method**——2-Methoxynaphthalene-1-d or 2-Methoxynaphthalene-6-d: Grignard reagents prepared in anhydrous THF from 1-bromo- (3 g) or 6-bromo-(5 g) derivatives of 2-methoxynaphthalene were decomposed by D_2O. The product obtained by the ordinary method was recrystallized from MeOH, mp 72°. Yields are almost quantitative. The extent of the H-D exchange at C-1 or C-6 was ~90%.

b) **Desulfonation by Acid**——2-Aminonaphthalene-1-d: 2-Aminonaphthalene-1-sulfonic acid (2 g) in 5% DCl/D_2O was heated in a sealed tube at 105° for 12 hr. The reaction mixture was alkalized by 10% NaOH and extracted by $CHCl_3$. The $CHCl_3$ layer thus obtained was dried over anhydrous $MgSO_4$, and the solvent was removed. The deposited crystals are recrystallized from $CHCl_3$-n-C_6H_{14}, mp 111°, yield 0.6 g (47%). The extent of the H-D exchange at C-1 was ~90%.

2-Bromo- and 2-Chloronaphthalene-1-d: The products obtained from 2-aminonaphthalene-1-sulfonic acid (4.2 g) by the Sandmeyer reaction[5] were heated in an acidic D_2O (20% D_2SO_4 for bromo and 10% DCl for chloro compound, respectively) at 105° in a sealed tube for 1 hr. The product was extracted by n-C_6H_{14} and the organic layer thus obtained was dried over anhydrous $MgSO_4$. After the solvent was removed, the residue was purified by n-C_6H_{14}-SiO_2 column chromatography. Yield of the bromo compound is 1.8 g (46%), and 1.4 g (46%) for the chloro compound. The extents of the H-D exchange at C-1 are~ 90%, respectively.

c) **Desulfonation by Raney-Ni and Alkali**——2-Aminonaphthalene-8-d: 2-Aminonaphthalene-8-sulfonic acid (2 g) was desulfonated by Raney-Ni (2.5 g) in 20% $NaOH/D_2O$ (1.5 ml) according to the modified Schwenk's method,[6] yield 0.2 g (16%). The extent of H-D exchange at C-8 was ~70%. The scattering of D to C-3 is facilitated by heating for a long time.

2-Aminonaphthalene-5-d: The same procedure described above afforded 2-aminonaphthalene-5-d (0.2 g, yield 31%) from 2-aminonaphthalene-5-sulfonic acid (1 g). The extent of the H-D exchange de-

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5) A.I. Vogel, "Textbook of Practical Organic Chemistry," Longmans, Green and Co. Ltd., 1966, p. 604.

6) E. Schwenk, D. Papa, B. Whitman, and H. Ginsberg, *J. Org. Chem.*, **9**, 1 (1944).

termined by the ^{1}H NMR and mass spectra was $\sim$30%. The scattering of D to C-3 and C-6 is facilitated by heating for a long time.

d) **Acid Catalized H-D Exchange Reaction**——2-Hydroxynaphthalene-3,6,8-d$_3$: 2-Hydroxynaphthalene (2 g) dissolved in 6% DCl/D$_2$O (3.5 ml) was heated in a sealed tube at 120° for 12 hr. The product was purified by the ordinary method, mp 120°, yield 1.8 g (90%). This process is accompanied by the redistribution of D at C-1 and C-3, namely, D at C-1 completely disappeared and remained a little at C-3. The extents of the H-D exchange at C-6 and C-8 were $\sim$90%.

Naphthalene-1,4,5,8-d$_4$[7]: Naphthalene (4 g) dissolved in AcOD (11 g) +97% D$_2$SO$_4$ (2.7 g) was heated at 120° in a sealed tube with occasinoal agitation. After heating for 4 hr, the mixture was diluted with H$_2$O, and product was extracted by n-C$_6$H$_{14}$. After organic layer was dried over anhydrous MgSO$_4$, solvent was removed. To promote the H-D exchange, same process was repeated for the avove product. The extents of the H-D exchange are $\sim$70% at α and 25% at β, respectively. The combination of CF$_3$CO$_2$D and D$_3$PO$_4$ instead of AcOD and D$_2$SO$_4$ gave a similar result.

e) **PtO$_2$ Catalized H-D Exchange Reaction**——2-Aminonaphthalene-1,3,6,7,8-d$_5$: The mixture of 2-aminonaphthalene hydrochloride (1 g) and a small amount of PtO$_2$ suspended in 4% DCl (5 ml) was heated in a sealded tube at 130° for 24 hr. The mixture was diluted by H$_2$O, and alkalized by 10% Na$_2$CO$_3$, and the product was extracted by CHCl$_3$. After the oragnic layer thus obtained was dried over anhydrous MgSO$_4$, solvent was removed. The residue was purified by C$_6$H$_6$–Al$_2$O$_3$ column chromatography. The extents of the H-D exchange at C-1, -3, -6, -7 and -8 positions are 30—50%, and D content fluctuates by the reaction condition.

Results and Discussion

Assignment of ^{13}C Chemical Shift (*cf.* Table I and II)

Various techniques are now available for the assignment of ^{13}C chemical shifts of the substituted aromatics. In the favorable case, signals are assigned on the bases of their characteristic behaviours. In this work, the shifts of **2** with two substituents in the molecule spread over a wide range, and are readily assigned refering the substituent chemical shift (S.C.S.) of monosubstituted benzenes. Assignments of **1** are achieved by comparing the observed S.C.S. of **2** with the calculated shift from the additivity of the S.C.S. of **1** and 6-methoxynaphthalene (*cf.* Chart 3).

TABLE I. ^{13}C Chemical Shifts of 2-Substituted Naphthalene Derivatives[a]

Substituent	Carbon No.									
	1	2	3	4	5	6	7	8	9	10
N(CH$_3$)$_2$	106.50	148.46	116.33	128.62	127.30	121.91	126.04	126.04	134.97	126.82
NH$_2$	108.54	144.02	118.19	129.10	127.66	122.39	126.22	125.74	134.91	127.96
NHCOCH$_3$	116.87	135.39	120.05	128.56	127.48	124.90	126.34	127.48	133.77	130.66
OCH$_3$	105.72	157.51	118.41	129.22	127.48	123.41	126.16	126.58	134.49	128.92
OH	109.50	153.13	117.59	129.76	127.66	123.53	126.28	126.40	134.50	128.92
OCOCH$_3$	118.49	148.46	121.13	129.34	127.72	125.62	126.52	127.72	133.87	131.55
CH$_3$	126.70	135.09	127.90	127.54	127.42	124.73	125.62	127.06	133.60	131.62
CH$_2$CH$_3$	125.50	141.69	127.00	127.72	127.48	124.90	125.74	127.36	133.65	131.92
H	127.72	125.62	125.62	127.72	127.72	125.62	125.62	127.72	133.42	133.42
F	110.79	160.54	116.15	130.24	127.78	125.02	126.76	127.18	133.52	129.94
Cl	126.59	131.50	126.76	129.48	127.79	126.10	127.05	126.88	134.04	131.56
Br	129.88	119.75	129.16	129.46	127.78	126.16	126.40	126.82	134.55	131.80
I	136.47	91.34	134.19	129.22	127.66	126.28	126.46	126.46	134.85	131.91
COCH$_3$	130.03	134.50	123.87	128.34	127.72	128.34	126.72	129.50	132.50	135.58
COOCH$_3$	130.90	127.18	125.14	128.02	127.60	128.02	126.46	129.22	132.45	135.45
CN	133.95	109.38	126.16	129.04	127.90	128.26	127.48	128.86	132.16	134.55
NO$_2$	124.36	145.16	119.15	129.33	127.78	129.51	127.78	129.81	131.85	135.69

[a] In ppm downfield from internal TMS.

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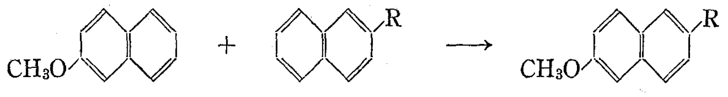
[7] Y. Kawazoe, M. Araki, S. Sawaki, and M. Ohnishi, *Chem. Pharm. Bull.* (Tokyo), **18**, 381 (1970).

Table II. ^{13}C Chemical Shifts of 2-Substituted-6-methoxynaphthalene Derivatives[a)]

Substituent	Carbon No. 1	2	3	4	5	6	7	8	9	10
NH_2	109.20	142.22	118.67	127.84	106.20	155.35	118.85	127.24	130.24	128.68
$NHCOCH_3$	117.29	133.47	120.71	127.36	105.78	157.15	119.15	129.04	129.64	131.74
OCH_3	106.20	156.25	118.91	128.14	106.20	156.25	118.91	128.14	129.88	129.88
OH	109.74	151.75	118.01	128.38	106.14	156.01	119.21	127.72	129.82	129.70
$OCOCH_3$	118.37	146.72	121.43	127.96	105.90	157.57	119.39	128.98	128.98	132.58
CH_3	126.52	132.87	128.44	126.46	105.66	156.97	118.49	128.62	129.16	132.63
CH_2CH_3	125.38	139.53	127.48	126.64	105.73	157.09	118.55	128.86	129.22	132.94
H	127.48	123.41	126.16	126.58	105.72	157.51	118.41	129.22	128.92	134.49
F	110.72	159.28	116.33	128.88	105.90	157.08	119.62	128.49	129.07	131.37
Cl	126.28	129.01	127.03	128.11	105.76	157.75	119.66	128.38	129.43	132.79
Br	129.52	116.93	129.52	128.32	105.24	157.81	119.63	128.32	129.94	132.99
I	136.17	87.98	134.67	128.26	105.72	157.99	119.45	128.26	130.60	133.29
$COCH_3$	129.86	132.55	124.54	126.93	105.73	159.68	119.53	130.94	127.70	137.18
$COOCH_3$	130.72	125.20	125.86	126.70	105.73	159.49	119.51	130.72	127.84	137.07
CN	133.59	106.68	126.94	127.72	105.96	159.97	120.53	129.88	127.72	136.35
NO_2	124.42	143.72	119.87	127.72	105.96	160.68	120.89	131.38	127.06	137.73

a) In ppm downfield from internal TMS.



1 2

Chart 3

The assignment by the additivity alone is not always reliable, and to achieve an unequivocal assignment the more reliable methods——deuterium exchange, selective decoupling and nondecoupling—were used. For fluorine compounds one to four bond C–F couplings are utilized.

Formerly, Tormyshev and Mamatyuk[8)] prepared the selectively ^{13}C enriched methylnaphthalenes valuable for the study of the solvent effect.[9)] The preparations of the above compounds are expensive, then we used mainly H–D exchange reaction as a complemental aid. For example, the correct assignments of C-1 and C-3 shifts of 2-methoxynaphthalene, the previous assignment of which involves some discrepancies—namely, one assigned the signal at the highest field to C-1[10)] and the other to C-3[11)]—are determined unambigously (*cf.* Table III). 1-Deuterio-2-methoxynaphthalene prepared from 1-bromo-2-methoxynaphthalene by the Grignard method supports that the signal at the highest field must be assigned to C-1, and 2-methoxynaphthalenes deuterated at additional positions–for example, 6-deuterio compound prepared from 6-bromo-2-naphthol, and 3,6,8-trideuterio and 3,6,7,8-tetradeuterio from the corresponding 2-naphthols–also confirmed the above conclusion. The methods of the chemical transformation of the deuterated compounds are compiled in Chart 2.

The H–D exchange reactions used in this work are summarized as follows: a) debromination by the Grignard reaction, b) desulfonation in acidic media, c) desulfonation in basic media, d) acid-catalized H–D exchange reaction, and e) PtO_2 catalized H–D exchange reaction.

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8) V.M. Tormyshev and V.M. Mamatyuk, *Izv. Sib. Otd. Akad. Nauk SSSR, Ser. Khim. Nauk.*, **1976**, 107.
9) M. Mishima, *Ph.D. Thesis*, Osaka University (1976).
10) L. Ernst, *Chem. Ber.*, **108**, 2030 (1975).
11) R.J. Highet and J.M. Edwards, *J. Magn. Reson.*, **17**, 336 (1975).

Table III. ^{13}C Chemical Shifts of 2-Methoxynaphthalene

Carbon No. 1	Carbon No. 3	Reference
105.82	118.71	Ernst[10]
118.7	105.7	Highet and Edwards[11]

In ppm downfield from internal TMS.

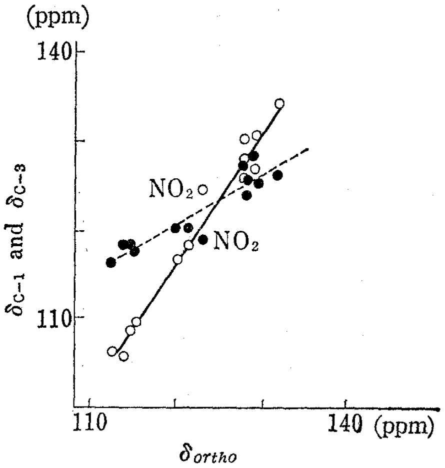

Fig. 1. Correlations between Chemical Shifts of 2-Substituted Naphthalenes [C-1 (○) and C-3 (●)] and Chemical Shifts at *ortho* Positions of Monosubstituted Benzenes

Method a) is excellent for the deuterium content of the reaction product, but suitable bromo compounds are not always available. In the present step, as the several 2-aminonaphthalene sulfonic acids are commercially available, so method b) is hopeful when the desulfonation occurs readily as in the case of 2-aminonaphthalene-1-sulfonic acid, but this reaction sometimes facilitates the scattering of D to other positions. Further, to distinguish the α- and β-carbon of 2-acetonaphthone, the shifts of which distribute in a narrow range, 1,4,5,8-tetradeuterionaphthalene prepared by method d) was acylated by the Friedel-Crafts method to 2-acetonaphthone deuterated dominantly at α-positions.

The correlations between C-1 or C-3 chemical shifts induced by the substituents and δ_{ortho} (S.C.S.[12] of the *ortho* positions of monosubstituted benzenes) showed a serious deviation of the nitro compound (*cf.* Fig. 1). To settle this deviation, the selective decoupling

Table IV. Differences[a] between Calculated and Observed Chemical Shifts of 2-Substituted-6-methoxynaphthalene Derivatives[b]

Substituent	Carbon No. 1	2	3	4	5	6	7	8	9	10
NH_2	−0.90	−0.41	+0.06	+0.12	−0.54	−1.07	+0.16	0	+0.17	+0.35
$NHCOCH_3$	−0.66	−0.29	−0.12	+0.06	−0.30	−0.36	−0.02	−0.06	−0.37	−0.01
OCH_3	−0.72	−0.95	+0.04	−0.06	−0.72	−0.95	+0.04	−0.06	+0.11	+0.11
OH	−0.48	−0.83	+0.12	+0.24	−0.48	−0.59	−0.14	+0.18	+0.18	+0.29
$OCOCH_3$	−0.12	−0.47	+0.24	+0.24	−0.18	−0.06	−0.08	+0.24	+0.39	+0.04
CH_3	−0.06	+0.01	0	−0.06	−0.24	−0.35	−0.08	−0.06	−0.06	+0.06
CH_2CH_3	−0.12	−0.05	+0.06	−0.06	−0.25	−0.30	−0.02	0	−0.07	+0.05
F	−0.17	−0.95	+0.36	+0.22	−0.12	−0.17	−0.07	+0.19	−0.05	−0.36
Cl	+0.07	+0.28	+0.27	+0.23	+0.03	+0.24	+0.18	0	+0.11	−0.16
Br	+0.12	+0.59	+0.18	0	+0.54	+0.24	−0.44	0	+0.11	−0.12
I	+0.06	+1.15	+0.06	−0.18	−0.06	+0.18	−0.20	−0.30	−0.25	−0.31
$COCH_3$	−0.07	−0.26	−0.13	+0.27	−0.01	+0.55	−0.02	+0.06	+0.30	−0.53
$COOCH_3$	−0.06	−0.23	−0.18	+0.18	−0.13	+0.42	−0.26	0	+0.11	−0.55
CN	+0.12	+0.49	−0.24	+0.18	−0.06	+0.18	−0.26	+0.48	−0.06	−0.81
NO_2	−0.30	−0.77	−0.18	+0.47	−0.18	+0.72	−0.32	−0.07	+0.29	−0.97

a) (Calculated–observed) values.
b) In ppm.

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[12] Defined as the shifts of a carbon in the substituted system minus the shifts of the same carbon in the parent system.

was used, where the decoupling power was supplied at a gradual step of ±20 Hz around 750 Hz (799 Hz for H-1 and 732 Hz for H-3 from TMS at 90 MHz), and the sharpness of the signal supported our assignment.

^{13}C NMR Data Treatment and Results

The ^{13}C shifts of **2** are calculated from the sum of the S.C.S. of **1** and the corresponding shifts of 6-methoxynaphthalene, and the differences (Δ-values) between the calculated and observed shifts are compiled in Table IV. The maximums of the deviations are within 1.1 ppm, so we are able to conclude that the additivity of the chemical shift holds satisfactorily for this series. The validity of this empirical rule is evaluated by the correlation coefficients of the chemical shifts of **2** *vs.* those of **1** at the corresponding positions (*cf.* Table V). A poor correlation of C-5 is attributed to the fact that induced shift by the substituent is too small to correlate with any parameters.

TABLE V. Correlation Coefficients between Corresponding Chemical Shifts of **1** and **2**

Carbon No.	Correlation coefficient (r^2) **1** *vs.* **2**
1	1.000
2	1.000
3	0.999
4	0.958
5	0.003
6	0.988
7	0.945
8	0.980
9	0.963
10	0.994

TABLE VI. Correlation Coefficients between Chemical Shifts of **1** and Some Parameters

Carbon No.	Correlation for	Correlation coefficient (r^2)
1	δ_{ortho}	0.968
2	δ_{ipso}	1.000
3	δ_{ortho}	0.903
4	δ_{meta}	0.846
5	δ_{meta}	0.189
6	δ_{para}	0.972
7	δ_{meta}	0.195
	σ_i	0.850
	$4.23\sigma_i-0.26\delta_{meta}$	0.891
8	δ_{para}	0.821
	σ_π	0.907
9	δ_{meta}	0.168
	σ_π	0.887
	$-7.37\sigma_i+1.75\delta_{meta}$	0.912
10	δ_{para}	0.980

$\delta_{ipso}, \delta_{ortho}, \delta_{meta}, \delta_{para}$: Chemical shifts of monosubstituted benzenes.

The correlation coefficients of the chemical shifts of **1** *vs.* empirical parameters are summarized in Table VI. Except C-10 carbon, those with the substituent groups are correlated with the S.C.S. of monosubstituted benzenes. The shifts of C-9, adjacent to the two carbons—C-8 and C-10—with σ_π character, are linear with $-\sigma_\pi$, and those of C-6 and C-8 remote from the substituent groups are also correlated with the substituent constants σ_π, whereas C-7 carbons are linear with σ_i.

These results will be settled by the molecular orbital treatment in the due time.