[Chem. Pharm. Bull. 32(6)2140—2145(1984)]

Studies on ^{13}C Magnetic Resonance Spectroscopy. XVIII.[1] Elucidation of the ^{13}C Substituent-Induced Chemical Shifts of Monosubstituted Benzenes by Means of a Novel Substituent Entropy Constant σ_{s°

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(Received September 7, 1983)

^{13}C Substituent-induced chemical shifts (SCS) of phenyl ring carbons of monosubstituted benzenes and their homologs are well correlated with linear combinations of entropic and enthalpic descriptors, namely $(\sigma_{s^\circ})^2$, σ_{s°, σ_i, σ_π. The novel substituent entropy constant σ_{s° contributes to SCS_{ipso} of an electron-donating group of monosubstituted benzenes and α-substituted toluenes. The effects of magnetic anisotropy in SCS could be represented by σ_{s°.

Keywords——^{13}C NMR; substituent entropy constant σ_{s°; substituent effect; monosubstituted benzene; α-substituted toluene; β-substituted ethyl benzene; magnetic anisotropy; electric field effect

Much attention has been directed to the ^{13}C substituent-induced chemical shifts (SCS) of organic compounds from both theoretical and empirical viewpoints. The interpretation of the SCS of monosubstituted benzenes has been a central topic in relation to the assignment of complex spectra and studies of the substituent effect in the field of physical-organic chemistry. Hitherto, two approaches have been used: quantum chemical and thermodynamic.

In the previous report,[2] the significance of the entropy term in SCS_{ipso} was proposed, based on multiple regression analysis using the Hammett type descriptors σ_i, σ_π and standard entropy difference ΔS°, where ΔS° is the difference between the standard entropy, S°_{298}, of the third law of thermodynamics for a substituted compound and that of the reference.

Recently one of the authors developed the novel substituent entropy constant σ_{s°,[3] defined by Eq. 1,

$$\sigma_{s^\circ} = \log(S^\circ_R/S^\circ_H) \tag{1}$$

where S° means the standard entropy S°_{298} (gas) of the pure compound, and subscripts R and H denote the substituted and the reference compounds, respectively.

In this work, the SCS of monosubstituted benzenes and their homologs have been examined by means of regression analysis using three kinds of descriptors, *i.e.*, σ_i, σ_π and σ_{s°. In addition, the participation of the magnetic anisotropy and electric field effects has been examined.

Experimental

1. ^{13}C SCS of Monosubstituted Benzenes——The set of SCS (referred to benzene) for a selected series of monosubstituted benzenes was taken from the literature.[4] They were all determined in very dilute solution in the inert solvent CCl_4. The selected substituents are as follows: NMe_2, NH_2, OMe, OH, F, Cl, Br, I, *tert*-Bu, iso-Pr, Et, Me, H, CHO, CN, CO_2Me, COMe, COPh, SO_2Me, SOMe, and NO_2 ($n=21$).

2. Other Data Sets——The data sets of ^{13}C SCS of α-substituted toluenes (referred to toluene) and those of ^{13}C SCS of β-substituted ethyl benzenes (referred to ethyl benzene), measured in dilute solution in CCl_4 and/or $CDCl_3$,

were taken from the literature.[5] The selected substituents are as follows:

α-Substituted toluenes: NMe_2, NH_2, OMe, OH, F, Cl, Br, I, SMe, *tert*-Bu, Et, Me, H, CN, COMe, COOH, SO_2Me, SOMe, and NO_2 ($n=19$).

β-Substituted ethyl benzenes: OMe, Cl, Br, Ph, Et, Me, H, CN, COOH, and CHO ($n=10$).

3. Regression Analysis——Regression analyses were carried out using an ACOS 900 system computer at the Computation Center of Osaka University and a PC-8801 personal computer utilizing a library program NEC TSS library TSS/LIB-6 and a program written by us in BASIC.

The standard deviation (SD) is given by $SD=[\sum se/(n-k-1)]^{1/2}$, where n and k mean the numbers of observations and variables, and $\sum se$ denotes the sum of squares of residuals. The superscripts ** and * (in the *F*-test) indicate 99 and 95% confidence levels of the statistical hypothesis.

Equation 2 shows the general form that we applied in the regression analysis.

$$SCS=a\sigma_{s\hat{M}A}+b(\sigma_{s^\circ})^2c\sigma_{s^\circ}+d\sigma_i+e\sigma_\pi+f \qquad (2)$$

The descriptors, substituent entropy constant σ_{s° and the Hammett type substituent constants σ_i and σ_π, are all taken from the literature.[3,6] The values of the magnetic anisotropy correction term, $\sigma_{s\hat{M}A}$ are defined as the squares of σ_{s° for four substituents, *i.e.*, Cl, Br, I and CN, but for the rest are all zero.

All the substituents were first divided into two groups, electron-donating (E.D.) and electron-attracting (E.A.) groups, and regression analyses were carried out on each group separately at every position, using Eq. 2. Thereafter we selected significant descriptors in each regression equation by means of *t* and *F*-tests, and obtained the final results described below. The regression equation for total substituents (T) in each position was obtained by combining the results of the two groups. The descriptors $\sigma_{s^\circ}^+$, $\sigma_{s^\circ}^-$ and σ_π^+, presented in terms of total substituents (T), were thus introduced; the superscript +, for example, means that the electron-donating groups only have the values of origin and the electron-attracting groups have zero or insignificant values.

Results and Discussion

The results of the regression analyses are as follows:

1.a. *ipso* ^{13}C SCS of Monosubstituted Benzenes

E.D. $-7153.36\ \sigma_{s\hat{M}A}+134.88\ \sigma_{s^\circ}+76.19\ \sigma_i+1.31$
$(\pm 425.97)\quad (\pm 23.78)\quad (\pm 8.67)\quad (\pm 2.90)$
$r=0.986,\quad n=13,\quad SD=3.59,\quad F=101.30^{**}$

E.A. $-5244.25\ \sigma_{s\hat{M}A}+39.82\ \sigma_i-0.41$
$(\pm 772.15)\quad (\pm 9.87)\quad (\pm 3.03)$
$r=0.945,\quad n=9,\quad SD=4.06,\quad F=24.94^{**}$

T $-6144.09\ \sigma_{s\hat{M}A}+176.49\ \sigma_{s^\circ}^+ +56.00\ \sigma_i-2.88$
$(\pm 509.27)\quad (\pm 27.09)\quad (\pm 10.08)\quad (\pm 3{,}30)$
$r=0.950,\quad n=21,\quad SD=5.36,\quad F=52.02^{**}$

1.b. *ipso* ^{13}C SCS of α-Substituted Toluenes

E.D. $-792.94\ (\sigma_{s^\circ})^2+136.84\ \sigma_{s^\circ}-16.10\ \sigma_i+0.20$
$(\pm 73.65)\quad (\pm 13.36)\quad (\pm 1.29)\quad (\pm 0.55)$
$r=0.977,\quad n=13,\quad SD=0.58,\quad F=61.62^{**}$

E.A. $-18.37\ \sigma_i-0.11$
$(\pm 2.62)\quad (\pm 0.91)$
$r=0.953,\quad n=7,\quad SD=1.09,\quad F=49.15^{**}$

T $-883.08\ (\sigma_{s^\circ}^+)^2+154.78\ \sigma_{s^\circ}^+-17.35\ \sigma_i-0.38$
$(\pm 66.05)\quad (\pm 10.02)\quad (\pm 1.35)\quad (\pm 0.52)$
$r=0.988,\quad n=19,\quad SD=0.81,\quad F=204.23^{**}$

(E.D.) : electron-donating substituent group
(E.A.) : electron-attracting substituent group
(T): sum of electron-donating and -attracting groups

1.c. *ipso* ^{13}C SCS of β-Substituted Ethyl Benzenes

E.D. $-12.50\ \sigma_i - 1.23$
$(\pm 1.72)\quad (\pm 0.35)$
$r = 0.956,\quad n = 7,\quad SD = 0.71,\quad F = 52.78^{**}$

E.A. $-14.38\ \sigma_i - 0.29$
$(\pm 1.52)\quad (\pm 0.40)$
$r = 0.989,\quad n = 4,\quad SD = 0.45,\quad F = 89.34^{**}$

T $-11.95\ \sigma_i - 1.24$
$(\pm 1.16)\quad (\pm 0.28)$
$r = 0.964,\quad n = 10,\quad SD = 0.58,\quad F = 105.99^{**}$

2. *ortho* ^{13}C SCS of Monosubstituted Benzenes

E.D. $2154.43\ \sigma_{s\hat{M}A} - 24.68\ \sigma_i + 22.25\ \sigma_\pi - 1.01$
$(\pm 231.53)\quad (\pm 4.20)\quad (\pm 3.23)\quad (\pm 0.81)$
$r = 0.982,\quad n = 13,\quad SD = 1.75,\quad F = 82.68^{**}$

E.A. $1111.08\ \sigma_{s\hat{M}A} - 14.40\ \sigma_i + 11.34\ \sigma_\pi + 0.68$
$(\pm 383.38)\quad (\pm 5.42)\quad (\pm 7.30)\quad (\pm 1.77)$
$r = 0.837,\quad n = 9,\quad SD = 2.00,\quad F = 3.89$

T $1835.16\ \sigma_{s\hat{M}A} - 20.19\ \sigma_i + 23.35\ \sigma_\pi - 0.96$
$(\pm 186.72)\quad (\pm 3.22)\quad (\pm 2.05)\quad (\pm 0.76)$
$r = 0.960,\quad n = 21,\quad SD = 2.10,\quad F = 65.90^{**}$

3. *meta* ^{13}C SCS of Monosubstituted Benzenes

E.D. $56.21\ \sigma_{s\hat{M}A} + 3.48\ \sigma_i - 0.87\ \sigma_\pi + 0.07$
$(\pm 27.03)\quad (\pm 0.49)\quad (\pm 0.38)\quad (\pm 0.09)$
$r = 0.971,\quad n = 13,\quad SD = 0.20,\quad F = 48.76^{**}$

E.A. $-57.93\ \sigma_{s\hat{M}A} - 3.91\ \sigma_{s^\circ} + 3.21\ \sigma_i + 0.06$
$(\pm 43.10)\quad (\pm 1.24)\quad (\pm 0.55)\quad (\pm 0.18)$
$r = 0.940,\quad n = 9,\quad SD = 0.20,\quad F = 12.57^{**}$

T $39.32\ \sigma_{s\hat{M}A} - 4.43\ \sigma_{s^\circ}^{-} + 3.24\ \sigma_i - 0.93\ \sigma_\pi^{+} + 0.10$
$(\pm 27.85)\quad (\pm 1.07)\quad (\pm 0.46)\quad (\pm 0.44)\quad (\pm 0.11)$
$r = 0.938,\quad n = 21,\quad SD = 0.25,\quad F = 29.33^{**}$

4.a. *para* ^{13}C SCS of Monosubstituted Benzenes

E.D. $19.60\ \sigma_\pi - 1.05$
$(\pm 1.38)\quad (\pm 0.33)$
$r = 0.974,\quad n = 13,\quad SD = 0.85,\quad F = 201.21^{**}$

E.A. $15.59\ \sigma_\pi - 0.31$
$(\pm 2.06)\quad (\pm 0.50)$
$r = 0.944,\quad n = 9,\quad SD = 0.63,\quad F = 57.12^{**}$

T $20.07\ \sigma_\pi - 0.89$
$(\pm 0.71)\quad (\pm 0.18)$
$r = 0.988,\quad n = 21,\quad SD = 0.81,\quad F = 789.48^{**}$

4.b. *para* ^{13}C SCS of α-Substituted Toluenes

E.D. $7.68\ \sigma_i + 0.49$
$(\pm 0.65)\quad (\pm 0.14)$
$r = 0.962,\quad n = 13,\quad SD = 0.35,\quad F = 138.01^{**}$

E.A. $7.73\ \sigma_i - 0.01$
$(\pm 1.31)\quad (\pm 0.45)$
$r = 0.935,\quad n = 7,\quad SD = 0.54,\quad F = 35.02^{**}$

T 6.91 σ_i+0.50
(±0.62) (±0.17)
r=0.938, n=19, SD=0.45, F=124.63**

4.c. *para* ^{13}C SCS of β-Substituted Ethyl Benzenes

E.D. 3.48 σ_i−0.04
(±0.42) (±0.09)
r=0.965, n=7, SD=0.18, F=67.29**

E.A. 2.70 σ_i−0.13
(±0.70) (±0.18)
r=0.940, n=4, SD=0.21, F=15.10**

T 3.07 σ_i−0.08
(±0.44) (±0.10)
r=0.927, n=10, SD=0.22, F=48.56**

Generally speaking the Hammett-type constants, *e.g.*, σ_i and σ_π, are deduced from the hydrolysis of *meta*- and *para*-substituted benzoic acid esters. Therefore the substituent constants represent the variation of electronic effects due to the substituent and lack the entropy term. As would be expected, they have a good correlation with SCS_{para} or SCS_{meta} of monosubstituted benzenes, where electronic effects of the substituent are predominant, but for the *ipso* position, the effect of the entropy term cannot be neglected. Evidence for the importance of the entropy term in the evaluation of SCS has been obtained in our previous work.[2)]

In addition, the component of electric field Ez, described in the Buckingham equation (SCS=AEz),[7)] is given by Eq. 3.[8)]

$$Ez = 2\mu\cos\theta/r^3 \qquad (3)$$

Ez, in other words, the field intensity, has the dimensions $(erg^{1/2}cm^{3/2})/cm^3 = (erg/cm^3)^{1/2}$, and therefore energy due to the interaction of Ez and an electric dipole can be divided into entropic and enthalpic terms.

As an increment of entropy S_{298} (g) is approximately quadratic with respect to the entropy constant σ_{s°, both $(\sigma_{s^\circ})^2$ and σ_{s° are necessary for the complete expression of the entropy term.

The mutual correlations among the three kinds of descriptors —namely, σ_{s°, σ_i, and σ_π—

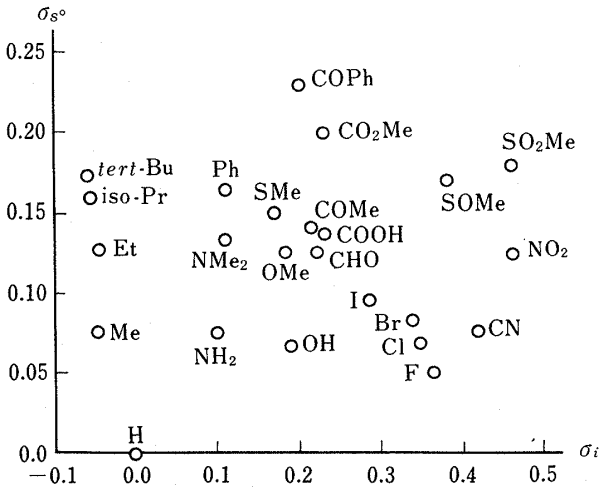

Fig. 1. Plot of σ_i *vs.* σ_{s°
Correlation coefficient=0.015.

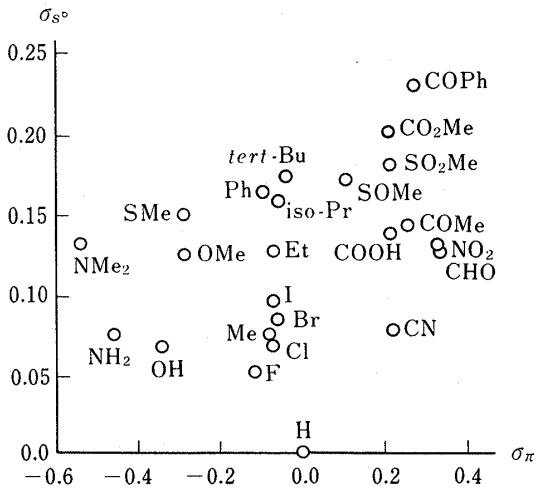

Fig. 2. Plot of σ_π *vs.* σ_{s°
Correlation coefficient=0.347.

are illustrated in Figs. 1 and 2. They are independent of one another. In addition, the linear combination of σ_i and σ_π showed no meaningful correlation with σ_{s°.

$$(\sigma_{s^\circ} = -0.05\ \sigma_i + 0.09\ \sigma_\pi + 0.14 \quad r = 0.372,\ n = 24,\ \mathrm{SD} = 0.05,\ F = 1.69.)$$

The four-parameter, *i.e.*, $(\sigma_{s^\circ})^2$, σ_{s°, σ_i, and σ_π-regression analysis of SCS_{ipso} is not satisfactory because the substituents Cl, Br, I, and CN, known to have strong magnetic anisotropy effects, still deviate greatly from the correlation line. As regards the magnetic anisotropy effect on SCS, the anisotropy of classical susceptibility χ and magnetic shielding anisotropy σ are responsible. χ and σ are expressed by Eqs. 4 and 5.[9]

$$\chi^{\mathrm{d}}_{\mathrm{avg}} = (1/4c^2)\langle r^2 \rangle \tag{4}$$

$$\sigma^{\mathrm{d}}_{\mathrm{avg}} = (1/3c^2)\langle 1/r \rangle \tag{5}$$

As can be seen from the two equations, both $\chi^{\mathrm{d}}_{\mathrm{avg}}$ and $\sigma^{\mathrm{d}}_{\mathrm{avg}}$ could be represented by σ_{s°. The plot of ^{13}C shielding anisotropy $\Delta\sigma$ *vs.* σ_{s° of monosubstituted methanes shows an approximately quadratic relation except for the substituents Cl, Br, I, and CN, and these exceptional points lie on a line bisecting the curve.[1] On the other hand, monohalogenated benzenes gave the following results.

$$\Delta\chi^{9} = 2431.55\ (\sigma_{s^\circ})^2 - 59.75$$

$$r = 0.929,\ \mathrm{SD} = 3.96, \quad F = 18.87^{*}\ (\mathrm{R} = \mathrm{H, F, Cl, Br, I})$$

Consequently, $(\sigma_{s^\circ})^2$ has been adopted as a descriptor of the anisotropy correction factor of the four substituents.

The results of the regression analyses of the two groups do not coincide in terms of dominant parameters and/or regression coefficients even in the same ring carbon atoms. Thus, in the case of the sum of the two groups, an excellent result would not necessarily be expected even if the separate treatments are successful. In general, electron-donating groups afford favorable results, but electron-attracting groups do not. These considerations suggest that it might be more reasonable to treat the groups separately in the elucidation of SCS.

It is assumed that the SCS of *ipso* carbon of monosubstituted benzenes should be the most sensitive to the character of the substituent, particularly the magnetic anisotropy effect. Spiesecke and Schneider reported[10] that the major contributions of the anisotropy effect occurred in the *ipso* position, and the effect was also observed in the *ortho* carbon atoms in monosubstituted benzenes. The present work shows that the anisotropy correction term $\sigma_{s\mathring{\mathrm{M}}\mathrm{A}}$ is large in the *ipso* position, followed by the *ortho* position, but is small in the *meta*, and negligible in the *para* carbon atoms of monosubstituted benzenes. Signs of $\sigma_{s\mathring{\mathrm{M}}\mathrm{A}}$ are the same in the *ipso* and *ortho* positions of the two groups, but opposite in the *meta* position even though the regression coefficients are almost the same. At the ring carbons of α-substituted toluenes and β-substituted ethyl benzenes, the anisotropy contributions are absent.

The entropy term σ_{s° contributes in the electron-donating groups of the *ipso* positions of the benzenes and the toluenes, and in the electron-attracting group of the *meta* carbon atoms of the benzenes.

The descriptor σ_i is significant in all three systems except for SCS_{para} of monosubstituted benzenes, and it is noticeable that SCS_{ipso} and SCS_{para} of the ethyl benzenes correlate well with σ_i.

Results on the SCS_{para} of the benzenes are consistent with those given in previous reports,[4,10,11] *i.e.*, they are mainly controlled by σ_π. As mentioned above, in the toluenes and the ethyl benzenes, resonance effects are absent, and the descriptor σ_i becomes a predominant factor.

Conclusion

1. The SCS of monosubstituted benzenes and their analogs could be expressed by linear combinations of entropic and enthalpic descriptors, namely, $(\sigma_{s^\circ})^2$, σ_{s°, σ_i, σ_π.

2. As for the contribution of the magnetic anisotropy and electric field effects, the former could be represented by σ_{s°, and the latter by linear combinations of σ_i, σ_π, and σ_{s°.

3. The fall-off factors of the weight of σ_i at the *ipso*, *ortho*, *meta*, and *para* positions of monosubstituted benzenes are $1 : -1.66 : 2.37 : 0.15$.

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