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Proton NMR Studies of Substituent Effects. The Hammett-type Relationship in *meta*- and *para*-Substituted Formanilides[*1]

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The spectral analyses of 23 *meta*- and *para*-substituted formanilides in dimethyl sulfoxide have proved that they exist in an equilibrium of *cis*- and *trans*-forms of restricted rotational isomers in the solvent. The chemical shifts of the protons on the formanilides are strongly dependent on the polar nature of the substituent. In the *cis*-form, the chemical shifts of both the imino and the formyl protons correlate with the Hammett σ^0. In the *trans*-form, a plot of the chemical shifts of the formyl protons against the σ^0-constants reveals a good correlation in the case of *meta*-derivatives, but serious deivations for the *para*-substituents, both for the electron-releasing conjugative substituents and for the electron-withdrawing conjugative substituents. The deviations for both types of substituents are in the direction to be anticipated for any important extra conjugative interaction between the *para*-substituent and the side-chain. The Yukawa-Tsuno equation is precisely applicable to these shifts when we assume that this system has the same r-value for both types of substituents; the relation is expressed as:

$$\Delta\delta = -12.0(\sigma^0 + 1.12\Delta\bar{\sigma}_R) + 0.5.$$

where $\Delta\bar{\sigma}_R=\sigma^+-\sigma^0$ for the electron-releasing conjugative substituents and where $\Delta\bar{\sigma}_R=\sigma^--\sigma^0$ for the electron-withdrawing conjugative substituents ($r=0.993$, $s=0.8$). From the solvent effect on the substituents, such as NH_2, OH, and COOH, their σ^0-values in dimethyl sulfoxide are proposed. It is also deduced that this solvent effect affects principally the part of the inductive contribution in the overall substituent effect.

It has been extensively verified that the respective Yukawa-Tsuno equation, either (1) or (2), can be applied to the electrophilic or the nucleophilic reaction of the side-chain derivatives of benzene whenever the opportunity arises for a strong conjugative interaction between the substituent

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and the reaction site:[1)]

$$\log k/k_0 = \rho(\sigma^0 + r\Delta\bar{\sigma}_R^+) \qquad (1)$$

where $\Delta\bar{\sigma}_R^+ = \sigma^+ - \sigma^0$, or:

$$\log k/k_0 = \rho(\sigma^0 + r\Delta\bar{\sigma}_R^-) \qquad (2)$$

where $\Delta\bar{\sigma}_R^- = \sigma^- - \sigma^0$. Yukawa and Tsuno[1)] have also suggested that if the σ^+- and σ^--values[2),3)] are used as a common reference of the substituent constants in a series of side-chain derivatives, Eqs. (1) and (2) will turn to:

$$\log k/k_0 = \rho(\sigma^0 + r\Delta\bar{\sigma}_R) \qquad (3)$$

where $\Delta\bar{\sigma}_R = \sigma^+ - \sigma^0$ and $\sigma^- - \sigma^0$.

Meanwhile, in NMR studies, a number of correlations have been noted between the reactivity parameters and the chemical shifts of the protons on benzene derivatives. In such a situation, it has been reported that Eq. (1) or (2) can be precisely applied to the side-chain derivatives.[4),*2] However, no work has been reported on the series of compounds in which Eq. (3) commonly holds both for the electron-releasing conjugative substituent and for the electron-withdrawing conjugative substituent.

In the present study, we have measured the chemical shifts of protons on the side-chain of 23 *meta*- and *para*- substituted formanilides dissolved in dimethyl sufoxide, where they exist in an equilibrium of *cis*- and *trans*-forms of restricted rotational isomers. This paper will describe how the substituent effect on the chemical shifts of protons on each isomer has been investigated from the viewpoint of the Hammett-type relationship. Especially, we will reveal that the Yukawa-Tsuno equation (3) is commonly applicable to the chemical shifts of the formyl proton of the *trans*-form for both types of substituents mentioned above when we assume that this system has the same *r*-value for the above substituents, and we adopt the σ^+- and σ^--values as a common reference of the substituent constants.

Moreover, from the investigation of the solvent effect on the substituents, such as NH_2, OH, and COOH, which form a strong hydrogen bonding with dimethyl sulfoxide, their σ^0-values in this solvent will be proposed. We will also discuss which part of the inductive and mesomeric contributions of the overall substituent effect this solvent effect has an influence on.

Experimental

Materials. *The substituted and the unsubstituted formanilides* used in the present study were prepared from formic acid[*3] and the appropriate substituted anilines[*4] according to the literature methods. The *p*-aminoformanilide was prepared by reducing *p*-nitroformanilide by iron dust in diluted formic acid. All the melting points or the boiling points of the formanilides, except for the compounds described below, agreed with the value described in the literature. *m*-Hydroxy derivative, mp: 112.7—113.2°C; *m*-Fluoro derivative, mp: 61.0—62.0°C; *p*-Fluoro derivative, mp: 66.0—66.5°C; *m*-Acetyl derivative, mp: 98.5—99.5°C; *p*-Acetyl derivative,

TABLE 1. VALUES OF THE CHEMICAL SHIFTS OF THE PROTONS OF *meta*- AND *para*-SUBSTITUTED FORMANILIDES (in cps relative to the unsubstituted compound)

	Substituent	*cis*-Form		*trans*-Form
		-NH-	-CHO	CHO[a)]
1	*p*-NH_2	29.2	9.1	22.7
2	*p*-$N(CH_3)_2$	18.6	5.1	15.2
3	*p*-OH	18.5	5.0	16.3
4	*m*-OH	8.6	2.2	1.8
5	*p*-CH_3O	8.4	3.5	12.0
6	*m*-CH_3O	0.6	−1.0	−1.6
7	*p*-CH_3	5.1	1.9	4.8
8	*m*-CH_3	4.5	0.3	1.5
9	H	0.0	0.0	0.0
10	*p*-F	−5.1	−0.4	4.6
11	*m*-F	−13.7	−2.7	−3.5
12	*p*-Cl	−7.2	−1.4	−0.6
13	*m*-Cl	−11.8	−2.5	−2.8
14	*p*-Br	−8.9	−1.3	−1.0
15	*m*-Br	−10.0	−1.9	−3.4
16	*p*-$COCH_3$	−16.9	−3.9	−9.4
17	*m*-$COCH_3$	−11.5	−3.0	−4.0
18	*p*-COOH	−18.0	−5.0	−8.7
19	*m*-COOH	−8.4	−0.8	−2.6
20	*p*-CN	−26.6	−6.7	−12.6
21	*m*-CN	−22.0	−5.1	−6.4
22	*p*-NO_2	−34.7	−6.8	−13.9
23	*m*-NO_2	−26.9	−6.3	−9.4

a) The chemical shift of this proton was calculated according to the typical AB-system.

b) The values of the coupling constants in the case of all the formanilides were 2.1±0.5 cps for the *cis*-proton and 11.0±0.5 cps for the *trans*-proton respectively, the substituent effect on which was not detected.

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1) Y. Yukawa and Y. Tsuno, *Nippon Kagaku Zasshi* (*J. Chem. Soc. Japan, Pure Chem. Sect.*), **86**, 873 (1965); Y. Yukawa, Y. Tsuno and M. Sawada, This Bulletin, **39**, 2274 (1966).

2) H. C. Brown and Y. Okamoto *J. Am. Chem. Soc.*, **79**, 1913 (1957).

3) H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

4) Y. Yukawa and H. Yamada, *Nippon Kagaku Zasshi* (*J. Chem. Soc. Japan, Pure Chem. Sect.*), **85**, 501 (1964).

[*2] For example the unpublished data by the present author: $\Delta\delta = -17.2(\sigma^0 + 0.32\Delta\bar{\sigma}_R^+)$ for the chemical shifts of the formyl protons of *m*- and *p*-substituted benzaldehydes in dimethyl sulfoxide.

[*3] Product of the Katayama Kagaku Kogyo Co., Ltd.

[*4] Products of the Tokyo Kasei Kogyo Co., Ltd.

TABLE 2. THE SUBSTITUENT CONSTANTS

Substituent	σ^0	$\Delta\bar{\sigma}_R^+$ and $\Delta\bar{\sigma}_R^{-}$ [a]	σ_i [a]	σ_π^+ and σ_π^- [a]
1 *p*-NH_2	−0.36[c]	−1.00	0.06	−0.42
2 *p*-$N(CH_3)_2$	−0.48[a]	−1.30	0.06	−0.54
3 *p*-OH	−0.16[a]	−0.82	0.19	−0.34
4 *m*-OH	0.121[b]	—	—	—
5 *p*-CH_3O	−0.100[a]	−0.678	0.185	−0.281
6 *m*-CH_3O	0.115[b]	—	—	—
7 *p*-CH_3	−0.124[a]	−0.187	−0.045	−0.078
8 *m*-CH_3	−0.069[b]	—	—	—
9 H	0.00	0.00	0.00	0.00
10 *p*-F	0.212[a]	−0.285	0.363	−0.118
11 *m*-F	0.337[b]	—	—	—
12 *p*-Cl	0.28[a]	−0.167	0.348	−0.070
13 *m*-Cl	0.37[b]	—	—	—
14 *p*-Br	0.30[a]	−0.15	0.337	−0.054
15 *m*-Br	0.39[b]	—	—	—
16 *p*-$COCH_3$	0.46[c]	0.41[e]	0.21	0.29
17 *m*-$COCH_3$	0.376[b]	—	—	—
18 *p*-COOH	—	(0.28)[d]	—	—
19 *m*-COOH	—	—	—	—
20 *p*-CN	0.66[b]	0.34[c]	0.41	0.25
21 *m*-CN	0.62[c]	—	—	—
22 *p*-NO_2	0.82[c]	0.45[c]	0.47	0.34
23 *m*-NO_2	0.71[b]	—	—	—

a) Cited from the paper by Yukawa and Tsuno.[1]
b) Cited from the paper by McDaniel and Brown. D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958).
c) Cited from the paper by Taft. R. W. Taft, Jr., *J. Phys. Chem.*, **64**, 1805 (1960).
d) The $\Delta\bar{\sigma}_R^-$-value for *p*-COOR.
e) $\Delta\bar{\sigma}_R^- = \sigma^- - \sigma^0$. The σ^--value are cited from Ref. 3.

mp: 106.0—107.0°C. These compounds were confirmed by elemental analysis and by a study of the IR spectra.

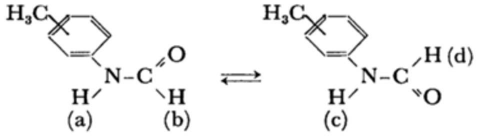
Dimethyl Sulfoxide.[*4] This was distilled under reduced pressure after having been refluxed with calcium hydride for a few hours, avoiding any uptake of atmospheric moisture, and was stored over Linde-3A molecular sieves[5] (bp: 61°C/3 mmHg).

All the sample solutions were left standing for about 48 hr at room temperature after the sample tube had been sealed, so as to reach equilibrium completely.

Measurement of NMR Spectra. All the spectra were obtained on a JNM C-60 spectrometer. The prove temperature was maintained at 20.0±0.5°C. The chemical shift was measured by relating it to the resonance peak of 0.5 mol% benzene added as an internal reference by the side-band technique. Since, in every case, the signal of benzene appeared 159.7±0.5 cps down field from the low-field ^{13}C–H satellite of dimethyl sulfoxide, it was confirmed that benzene could be utilized as an internal reference. The proton signals were independent of the concentration, ranging from 5 to 0.5 mol%, and of addition of a small amount of water. In Table 1 the chemical shifts of the protons of 23 *meta*- and *para*-substituted formanilides at a 5 mol% concentration are given relative to formanilide itself. The precision of the measurement was within about ±0.5 cps for the chemical shifts of the formyl protons, while, within about ±0.8 cps for the imino protons.

Results and Discussion

Analyses of Spectra of *meta*- and *para*-Substituted Formanilides. From the observation of near-infra-red absorption spectrum and the measurement of apparent dipole moment of formanilide in carbon tetrachloride solution, Mizushima *et al.*[6] have indicated that it exists in two forms—*cis*- and *trans*-forms of restricted rotational isomers, which are caused by a partial double-bond character of the C-N bond. Recently, inspecting the NMR spectra of formtoluidides in carbon tetrachloride, measured at 60 Mc and 100 Mc, Nishiyama and Yamada[7] proved that the *cis*- and *trans*-forms of the formtoluidide existed in an equilibrium:



(I) *cis*-Form (II) *trans*-Form

On the basis of the above informations, we analysed the spectra of *meta*- and *para*-substituted formanilides at several concentrations in carbon tetrachloride, benzene, acetone, and dimethyl sulfoxide. The formanilides, except for the formtoluidides and the unsubstituted formanilide, were too sparingly soluble in such non-polar solvents as carbon tetrachloride and benzene for the spectra to be examined. As an example, the spectra of form-*p*-toluidide at 5 mol% in carbon tetrachloride and dimethyl sulfoxide are shown in Figs. 1 and 2.

The spectrum of Fig. 1 shows the same pattern as that obtained by Nishiyama and Yamada,[7] and it reveals that the formtoluidide exists in the *cis*- and *trans*-forms in carbon tetrachloride. They were assigned by comparing, with each other, the coupling constants between the imino and the formyl protons of them. The resonance signals, (a) and (c), were assigned to the imino protons of the two forms, because their line width may be broadened due to a relaxation phenomenon involving the ^{14}N

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5) R. J. Ouellette, *Can. J. Chem.*, **43**, 707 (1963).

6) I. Suzuki, M. Tsuboi, T. Shimanouchi and S. Mizushima, *Spectrochim. Acta*, **16**, 471 (1960).

7) T. Nishiyama and F. Yamada, *Nippon Kagaku Zasshi (J. Chem. Soc. Japan, Pure Chem. Sect.)*, **89**, 979 (1968).

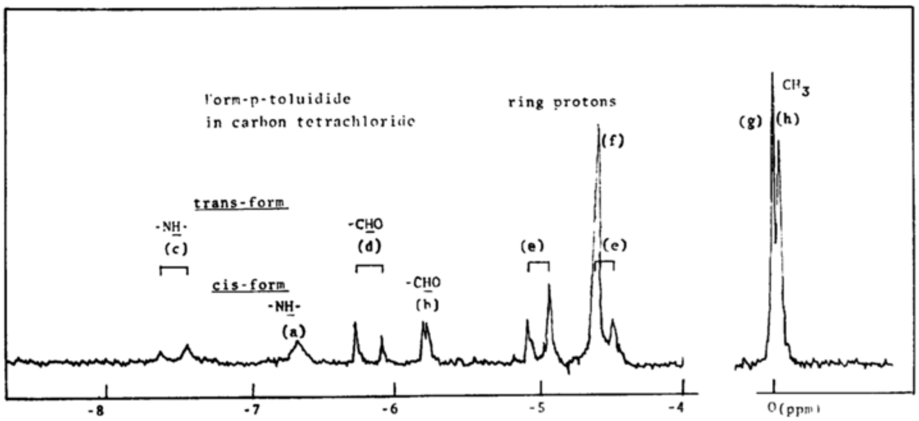

Fig. 1. Proton resonance spectrum (60 Mc/sec) of form-*p*-toluidide at 5 mol% in carbon tetrachloride at 20.0±0.5°C. The chemical shifts shown are relative to the methyl group of the *cis*-form.

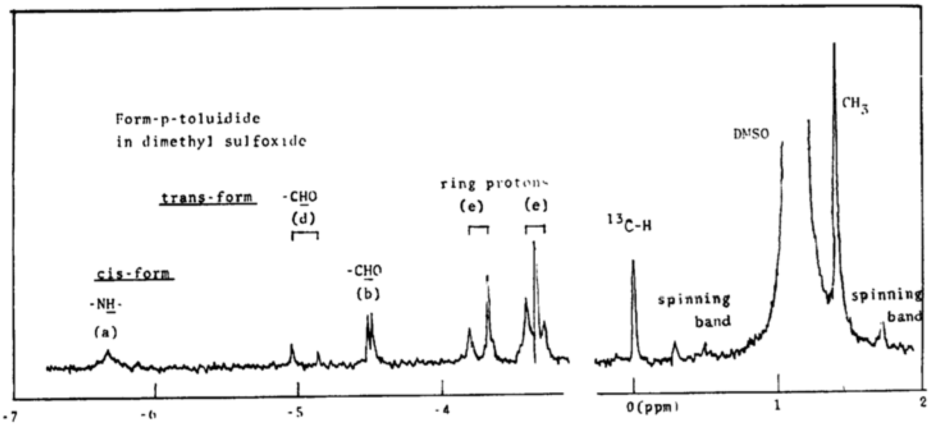

Fig. 2. Proton resonance spectrum (60 Mc/sec) of form-*p*-toluidide at 5 mol% in dimethyl sulfoxide at 20.0±5°C. The chemical shifts are shown relative to the low-field ^{13}C–H satellite of dimethyl sulfoxide.

quadrupole.[8] The signal (a) also shifted variably depending on the kind of solvents. The resonance signals, (b) and (d), were assigned to the formyl protons of the two forms, because they gave sharp resonance lines and the shift by variation of solvents little occured. The signal (a) of the imino proton was ascribed to belong to the *cis*-form, and the signal (b), to arise from the proton of the formyl group in the *cis*-form, which was a doublet due to the spin-spin coupling with the imino hydrogen. The value of the coupling constant was 2.2 cps, which was consistent with that obtained for the *cis*-proton of some kinds of amides ($J_{cis}=2.1$ cps for formamide[9] and $J_{cis}=1.8$ cps for formtoluidide[7]). The signals, (c) and (d), were assigned to belong, respectively, to the imino and the formyl protons of the *trans*-form, because they were the doublet due to the spin-spin coupling between the *trans*-protons, and the value of the coupling constant was 11.3 cps ($J_{trans}=11.4$ cps, both for formamide[9] and for formtoluidide[7]).

Figure 2 shows the spectrum of the form-*p*-toluidide in dimethyl sulfoxide. All the resonance signals, except for that of the imino proton of the *trans*-form, correspond with those in carbon tetrachloride solution. When a small amount of dimethyl sulfoxide was added in the carbon tetrachloride solution of the formtoluidide, the signal (a) of the imino proton of the *cis*-form shifted to the lower field, whereas that of the *trans*-form, (c), remained almost constant. As the concentration of the dimethyl sulfoxide increased, the signal (a) approached to the signal (c). Accordingly, in dimethyl sulfoxide, the signal (c) may be concealed behind the signal (a). The low-field shift

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[8] J. A. Pople, W. G. Schneider and H. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill, New York (1959), p. 102.

[9] L. H. Piette, J. D. Ray and R. A. Ogg, *J. Mol. Spectroscopy*, **2**, 66 (1958).

of the signal (a) by the addition of dimethyl sulfoxide may be due to the hydrogen bonding between the imino hydrogen of the *cis*-form and the molecule of dimethyl sulfoxide. The independence of the concentration of the dimethyl sulfoxide in the case of the chemical shift of the imino proton of the *trans*-form may be ascribed to that the associated molecules of the *trans*-form make the ring dimer (See Fig. 11).

Although Figs. 1 and 2 do not so distinctly the doublet of the resonance signals of the ring protons, the spectrum of form-*p*-anisidide shows the typical AB-type doublet of the protons on the *para*-disubstituted benzene ring (Fig. 3). The signal (e) was ascribed to belong to the *cis*-form, while the signal (f), to the *trans*-form, from their relative intensities. In Fig. 1 the two resonance signals, (g) and (h), of the methyl protons, which appeared at slightly different positions, corresponded with the *cis*- and *trans*-forms respectively.

When the spectra in carbon tetrachloride (Fig. 1) and benzene are compared with those in dimethyl sulfoxide (Fig. 2) and acetone, the intensities of all resonance signals of the protons of the *trans*-form in the latter solvents are much smaller than those of the *cis*-form. This shows that the *cis*- and *trans*-forms exist in an equilibrium, and that the equilibrium inclines toward the *cis*-form in the polar solvent. The effect of varying the concentrations in carbon tetrachloride showed that the equilibrium favored the *cis*-form as the concentration increased.*5 The substituent effect on the

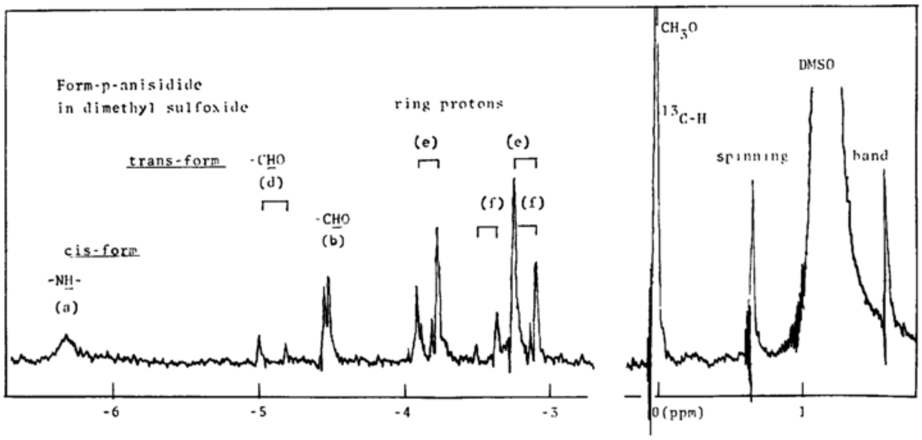

Fig. 3. Proton resonance spectrum (60 Mc/sec) of form-*p*-anisidide at 5 mol% in dimethyl sulfoxide at 20.0±0.5°C. The chemical shifts shown are relative to the low-field ^{13}C–H satellite of dimethyl sulfoxide.

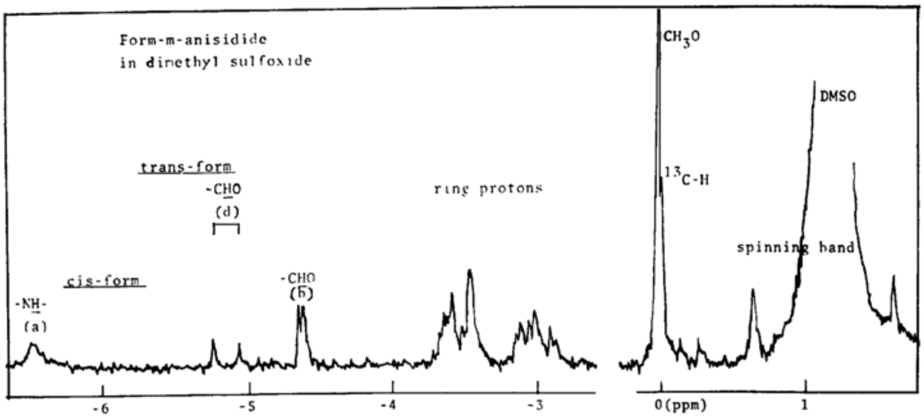

Fig. 4. Proton resonance spectrum (60 Mc/sec) of form-*m*-sanisidide at 5 mol% in dimethyl sulfoxide at 20.0±0.5°C. The chemical shifts are relative to the low-field ^{13}C–H satellite of dimethyl sulfoxide.

[*5] With higher concentrations, the asymmetric polarized structure is favored by a dipoler-type interaction, as has been indicated for *N,N*-disubstituted formamide. (Ref. 10).

10) T. Yonezawa and I. Morishima, This Bulletin, **39**, 2346 (1966).

equilibrium in dimethyl sulfoxide showed a trend that the *trans*-form was favored by the electron-releasing substituent. These results may be all explained by assuming an asymmetric polarized structure for the *cis*-form (Fig. 7), while, a non-polarized structure for the *trans*-form (Fig. 11), as will be discussed in detail later. The representative spectra of *meta*- and *para*-substituted formanilides in dimethyl sulfoxide are shown in Figs. 3 and 4.

Substituent Effect on the *cis*-Form. (*i*)*Correlation of the Chemical Shift of the Imino Proton with the σ^0-Constant.* Although the ^{14}N quadrupole makes the measurement of accurate chemical shifts difficult by broadening the imino proton signal, this disadvantage is offset by the wide range of the chemical shifts observed (about 70 cps). This enhanced sensitivity of the substituent effect on the imino proton signal can be understood in terms of hydrogen bonding to the solvent molecule.

In Fig. 5, the relative chemical shifts of the imino protons are plotted against the σ^0-values. The correlation is expressed by Eq. (4), which was derived from a least-squares fit of the data:

$$\Delta\delta = -40.3\sigma^0 + 2.1 \qquad (4)$$

for all the 18 substituents except five: p-NH$_2$, m-OH, p-OH, m-COOH and p-COOH. The correlation coefficient and the standard deviation have the respective values of 0.988 and 2.1. The plots for p-COOH and m-COOH are excluded from the figure, for their σ^0-values have not been established. The plots for such substituents as p-NH$_2$, p-OH, and m-OH deviate greatly above the correlation line. These substituents, whether in the *meta*-position or the *para*-position, are apparently much more electron-releasing than the ordinary σ^0-values predict. The effect may be a reflection of the alteration of the substituent by the specific solvation. The σ^0-values of these substituents in dimethyl sulfoxide, calculated from the regression line, are: -0.67 for p-NH$_2$, -0.41 for p-OH, -0.16 for m-OH, 0.50 for p-COOH, and 0.11 for m-COOH. The reliability of these σ^0-values will be examined in the succeeding sections.

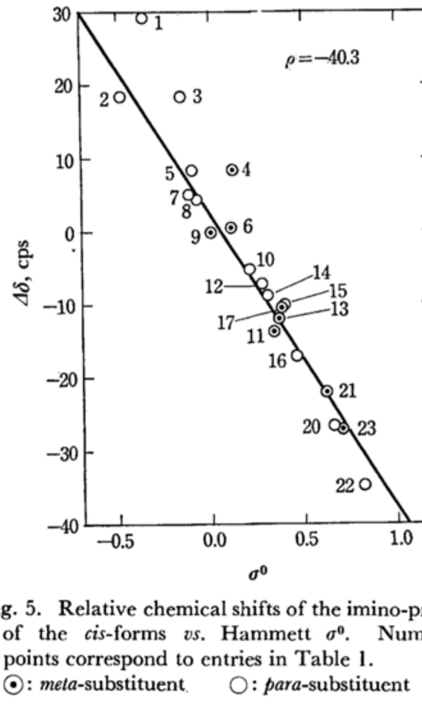

Fig. 5. Relative chemical shifts of the imino-protons of the *cis*-forms *vs.* Hammett σ^0. Numbered points correspond to entries in Table 1.
⊙: *meta*-substituent ○: *para*-substituent

This aspect of the substituent effect on the imino proton reveals that there is no extra conjugative interaction between the substituent and the side-chain in the *cis*-form. This result suggests that, the amide group not in the plane of the aromatic ring, can not interact with the aromatic *pi*-electron system. When we assume an asymmetric polarized structure for the *cis*-form, the departure from planarity can be explained as due to the steric repulsion between the hydrogen of the aryl group, in the ortho position shown, and the C–O$^-$ group,*[6] The molecule of the *cis*-form is shown schematically in Fig. 7.

(*ii*) *Correlation of the Chemical Shift of the Formyl Proton with the σ^0-Value.* It is expected that the

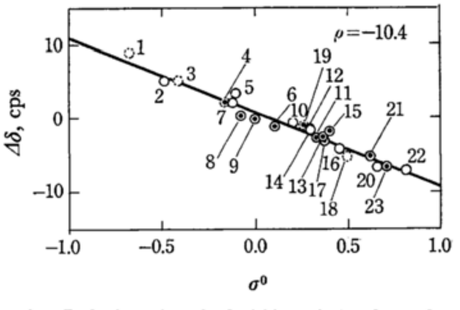

Fig. 6. Relative chemical shifts of the formyl-protons of the *cis*-forms *vs.* Hammett σ^0. Numbered points correspond to entries in Table 1. Substituents, NH$_2$, OH and COOH are shown by dotted circles.
⊙: *meta*-substituent ○: *para*-substituent

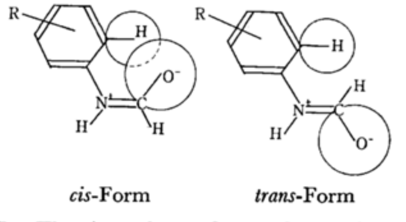

Fig. 7. The *cis*- and *trans*-forms of *m*- and *p*-substituted formanilides. The radii of the circles correspond to the van der Waals' radii of the atoms.

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*[6] This type of steric repulsion has been suggested for formanilide by Mizushima *et al.* (Ref. 6).

chemical shifts of the formyl protons correlate with the σ^0-values, because even those of the imino protons exhibit no significant conjugative interaction between the substituent and the imino group. Thus, as is shown in Fig. 6, the relative chemical shifts can be expressed as:

$$\Delta\delta = -10.4\sigma^0 + 1.0 \tag{5}$$

for all the 18 substituents except for five substituents mentioned above. The values of r*7 and s*7 were 0.974 and 0.8 respectively. This lack of good correlation is to be expected since the formyl protons of all the formanilides have a small spread of total chemical shift (about 16 cps). When the σ^0-values in dimethyl sulfoxide are used for the substituents mentioned above, all their plots fall close to the correlation line, as is shown by the dotted circles in the figure.

Substituent Effect on the *trans*-Form. Application of the Yukawa-Tsuno Equation to the Chemical Shift of the Formyl Proton. In the *trans*-form, a plot of the chemical shifts of the formyl protons against the Hammett σ^0-constants reveals a good correlation in the case of the *meta*-derivatives, as is shown in Fig. 8. This relation can be expressed as:

$$\Delta\delta_m = -12.0\sigma^0 + 0.5 \tag{6}$$

In this case, too, the plots for *m*-OH and *m*-COOH fall close to the *meta*-correlation line when their σ^0-values in dimethyl sulfoxide are used. The ρ-value is compatible with the ρ-value (−10.4) in the case of the formyl proton in the *cis*-form, as is to be expected from the fact that the distance between the substituent and the proton observed is not very different in the two cases. As is shown in Table 1, however, the formyl protons of all the *trans*-forms have quite a large spread of total chemical shift (about 37 cps) compared with the case of the formyl proton of the *cis*-form. This must be a reflection of a strong extra conjugative interaction between the substituent and the side-chain in the *trans*-form.

It is characteristic that all the plots for the electron-releasing conjugative substituents at the para-position, such as p-NH_2, p-$N(CH_3)_2$, and p-CH_3, deviate seriously from the *meta*-correlation line in the direction to be predicted by the σ^+-value,[2] whereas those for the electron-withdrawing con-

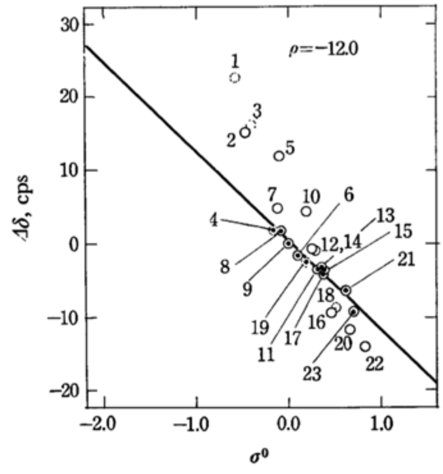

Fig. 8. Relative chemical shifts of the formyl protons in the *trans*-form *vs.* Hammett σ^0. Numbered points correspond to entries in Table 1. Substituents, NH_2, OH, and COOH are shown by dotted circles.
⊙: *meta*-substituent ○: *para*-substituent

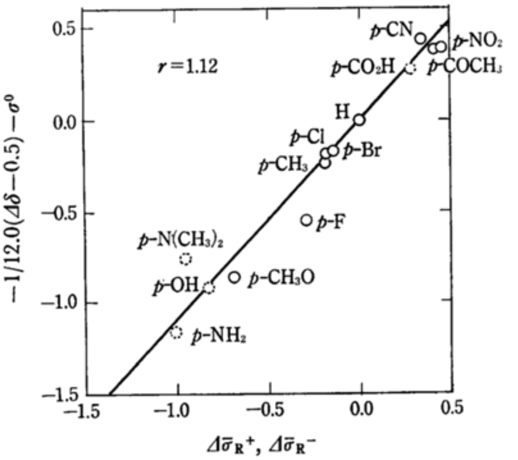

Fig. 9. Determination of the r-value for the chemical shifts of the formyl protons of the *trans*-forms.

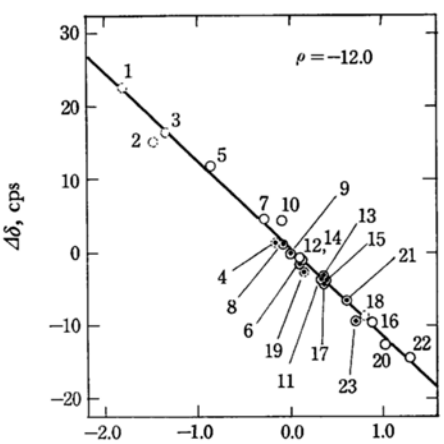

Fig. 10. Correlation of the chemical shifts of the formyl protons of the *trans*-forms with the Yukawa-Tsuno equation. Numbered points correspond to entries in Table 1. Substituents, $N(CH_3)_2$, NH_2, OH, and COOH are shown by dotted circles.
⊙: *mreta*-substituent ○: *para*-sbustituent

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*7 r: the correlation coefficient; s: the standard deviation of experimental results from the regression line.

jugative substituents, such as *p*-$COCH_3$, *p*-CN, and *p*-NO_2, deviate considerably in the direction of the σ^--value.[3)] When the σ^+-values are used for the former substituents and the σ^--values for the latter, all the plots except that for *p*-$N(CH_3)_2$ fall near the correlation line, but the correction seems yet to be insufficient. This result suggests that the Yukawa-Tsuno equation (3) may be applicable to the chemical shifts of the formyl protons if we adopt the σ^+-values for the former substituents and the σ^--values for the latter as a common reference of substituent constants, and if we assume that this system has the same r-value for both types of substituents. Thus, a good correlation is obtained as:

$$\Delta\delta = -12.0(\sigma^0 + 1.12\Delta\bar{\sigma}_R) + 0.5 \qquad (7)$$

for the 16 substituents, as is shown in Fig. 10. The values of r[*7] and s[*7] were 0.993 and 0.8 respectively. A plot for the *p*-fluoro derivative deviates somewhat above the correlation line, as has been observed by Yukawa and Yamada.[4)] in the chemical shifts of the ethynyl protons in *meta*- and *para*-substituted phenylacetylenes.

When the σ^0-values in dimethyl sulfoxide and the ordinary $\Delta\bar{\sigma}_R$-values[*8] are used, the plots for *p*-NH_2, *p*-OH, and *p*-COOH[*9] fall close to the correlation line. Only the plot for *p*-$N(CH_3)_2$ deviates greatly down from the correlation line. Yukawa and Tsuno[10)] have indicated a good correlation between the chemical shifts of *para*-protons on monosubstituted benzenes and the $\Delta\bar{\sigma}_R$-values, but in this case, too, the plot for *p*-$N(CH_3)_2$ deviates considerably from the correlation line. From the correlation line, the $\Delta\bar{\sigma}_R^+$-value for *p*-$N(CH_3)_2$ is calculated as -0.93. When this value is used in the present case, the plot for *p*-$N(CH_3)_2$ falls near the correlation line, as is shown by dotted circle, (2), in Fig. 10. The origin of the difference between the two $\Delta\bar{\sigma}_R^+$-values, one of which has been derived from the reactivity data and the other from the NMR data, is not yet evident.

The characteristic aspect of the substituent effect in the case of the *trans*-form is in contrast to the situation in the *cis*-form, and it implies that the aryl and the amide groups constitute a expanded conjugated system over the whole molecule. When we assume an asymmetric polarized structure for the *trans*-form (Fig. 7), this is explained as follows. First, in the *trans*-form, the aromatic ring and the amide groups lies in the same plane, because of the lack of the steric interaction between the aryl and the amide groups. Second, as is shown schematically in Fig. 11, the molecules of the *trans*-form associate to make the ring dimer.[*10] All of these effects may cause that the formal charges on the nitrogen atom of the imino group and the oxygen atom of the C–O group are distributed along the bonds in the molecule, and that the composite *pi*-electron systems are delocalized along the entire body of the planar molecule.

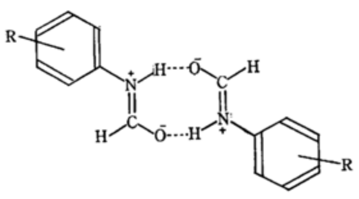

Fig. 11. The ring dimer of the molecules of the *trans*-form of *m*- and *p*-substituted formanilides.

Solvent Effect on Three Substituents, NH_2, OH, and COOH. Equation (7) shows that the normal $\Delta\bar{\sigma}_R$-values can also be applied in dimethyl sulfoxide to the substituents, such as NH_2, OH, and COOH, which form a strong hydrogen bonding with the solvent molecule. This result suggests that this specific solvation does not affect the term of the conjugative interaction. On the other hand, their σ^0-values in dimethyl sulfoxide differ remarkably from their normal σ^0-values. Which, then, the inductive or the mesomeric contribution of the σ^0-constant, does this solvation influence? We will now attempt to answer this question.

The σ^0-constant separated by Yukawa and Tsuno[1)] is shown in Eq. (8):

$$\sigma^0 = \sigma_i + \sigma_\pi \qquad (8)$$

where the σ_i and σ_π terms are called the *sigma*-inductive and *pi*-electronic effects respectively. When the σ_i-and σ_π-values[*11] are used, Eq. (3) generally turns to:

$$\log k/k_0 = \rho(\sigma_i + \mathbf{r}\sigma_\pi) \qquad (9)$$

where $\sigma_\pi = \sigma_\pi^+$[*12] and $\mathbf{r} = 1 + 2.4r$ for the electron-releasing conjugative substituent, and $\sigma_\pi = \sigma_\pi^-$[*12] and $\mathbf{r} = 1 + 1.2r$ for the electron-withdrawing conjugative substituent. Here, we will assume that this solvation affects only the term of the inductive effect by forming hydrogen bonding with the substituent group. Then. Eq. (8) can be expressed as:

$$\sigma^0_{(\mathrm{DMSO})} = \sigma_{i(\mathrm{DMSO})} + \sigma_\pi \qquad (10)$$

From Eq. (10), the σ_i-values in dimethyl sulfoxide are calculated to be: -0.25 for *p*-NH_2, -0.07 for

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[*8] See Table 2.

[*9] Although the $\Delta\bar{\sigma}_R^-$ value for *p*-COOH has not been established, there may be little difference between the $\Delta\bar{\sigma}_R^-$ values for *p*-COOH and *p*-COOR. Therefore, the $\Delta\bar{\sigma}_R^-$ value for *p*-COOR (0.28) is used in this case.

11) Y. Yukawa and Y. Tsuno, "Jikken Kagaku Koza" (Handbook of Chemical Experiments), Supplemental Vol. 12, ed. by the Chem. Soc. Japan, Maruzen Co., Tokyo (1967), p. 462.

[*10] The presence of the ring dimer for formanilide has been suggested by Mizushima *et al.* (Ref. 6).

[*11] See Table 2.

[*12] $\sigma_\pi^+ = 0.415\Delta\bar{\sigma}_R^+$ and $\sigma_\pi^- = 0.81\Delta\bar{\sigma}_R^-$ (Ref. 1). If $0.415\Delta\bar{\sigma}_R^-$ is adopted, the plots for *p*-CN, *p*-$COCH_3$, *p*-COOH, and *p*-NO_2 fall on the correlation line.

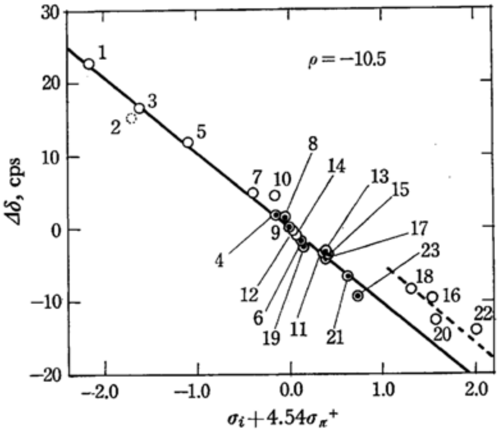

Fig. 12. Correlation of the chemical shifts of the formyl protons of the *trans*-forms with the equation, $\Delta\delta=\rho(\sigma_i+r\sigma_\pi)$. Numbered points correspond to entries in Table 1.
⊙: *meta*-substituent ○: *para*-substituent

p-OH, and 0.27 for *p*-COOH. If Eq. (9) holds for all the *para*-substituents which are electron-releasing conjugative, the use of these σ_i-values will prove the above assumption to be appropriate.

Figure 12 shows that Eq. (9) fits well for all the substituents mentioned above; the relation can be expressed as:

$$\Delta\delta = -10.5(\sigma_i + 4.54\sigma_\pi^+) \qquad (11)$$

In view of the error in the measurement of each chemical shift, we are probably justified in concluding that this ρ-value is almost equal to the ρ-value (-12.0) for the *meta*-derivatives. When the σ_π^--values are used for the electron-withdrawing conjugative substituents, *p*-COCH$_3$, *p*-CN, *p*-COOH, and *p*-NO$_2$, their plots fall on the other line. However, this result may be reasonable in view of the definition of the σ_π^--value.*[12] This fact does not essentially affect the above discussion. Accordingly, it may be concluded that this type of solvation influences not the mesomeric contribution but the inductive contribution of the substituent effect.

We wish to express our indebtedness to Mr. Mitsuru Yamazaki of Nagoya University for the measurement of the NMR spectra. Thanks are also due to Mr. Shozo Masuda of Tokyo University for his elemental analyses of the samples.