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Further Investigations on Polar Substituent Effects on the NMR Chemical Shifts of *N*-Acylanilines and Related Compounds. Correlation Analytical Approach and Solvent Effects

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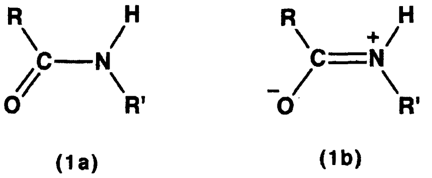
The ^{1}H, ^{13}C, and ^{15}N chemical shifts of various substituted anilides of the carboxylic and sulfonic acids $ZNHC_6H_4Y$ ($Z=C_6H_5CO$, CH_3CO, CF_3CO, and CH_3SO_2) and related compounds were correlated with σ and related substituent constants. The ρ-values from the Hammett type plots of the chemical shifts were shown to provide some important information concerning the polarization of the amide chromophore. The solvent effect on ρ showed the fact that the local π-polarization of an amide is strengthened in polar or hydrogen-donating solvents.

The amide linkage constitutes the framework of peptide, protein, and other bio-molecules and is important in the manifestation of biological activity. In addition, many aromatic and heterocyclic amides were synthesized in anticipation of pharmaceutical and other biological activities. Structures of these natural and artificial amides have been elucidated rather extensively by spectroscopic and X-ray crystallographic methods. NMR spectroscopy is one of the most versatile tools in this field.[1,2] The structure and the characteristic properties of amides were studied by usual one-dimensional and two-dimensional ^{1}H, ^{13}C, and ^{15}N NMR spectroscopy. A large collection of chemical shifts and coupling constant data have been accumulated.[3—5] In addition, dynamic NMR experiments are extremely useful to shed light on the rotational barrier about the C–N bonds of amides.[6] The rotational barrier is normally between 15 and 20 kcal mol^{-1} and is considerably higher than other single bonds. The fact that the C–N bond of the amide moiety has a high rotational barrier should reflect the partial double bond character of this bond. X-Ray crystallographic studies[7,8] on one hand and the theoretical calculations[9,10] on the other showed the planarity of the amide group. These facts have been explained by the concept of so-called "amide resonance", which means a rather strong conjugation through the N–C=O system constituting the amide group. This concept can be described by the resonance between the two canonical structures given below (Chart 1).

In our previous investigations,[11—13] the substituent effects on the rotational barriers of a series of benz- and salicylamides were correlated with their ^{15}N chemical shifts. We also reported that the ^{1}H and ^{13}C chemical shifts of substituted benzanilides $XC_6H_4CONHC_6H_4Y$ could be correlated well with σ (σ^{-}).[14] In contrast to the good δ^{1}H and δ^{13}C vs. σ plots, the δ^{15}N vs. σ^{-} plots did not give any good correlation.[15] In the latter plots, the plotted points of *p*-substituted anilides tend to separate from those of *m*-substituted anilides.[16] This finding was interpreted by assuming competition between the local π-polarization within a strongly conjugated amide group[17,18] and electron-donating mesomerism in the anilino group.



(1a) **(1b)**

Chart 1.

In this paper, we wish to provide some supporting evidence for the participation of the above-mentioned competition from the Hammett type and DSP correlation analyses on several anilides. The solvent dependency of the ρ-value was useful to characterize the hydrogen bond interaction involved. The stability and the interaction with other chromophores of locally polarized amide chromophores in *N*-acylanilines were discussed on the basis of these experiments.

Results and Discussion

To clarify the characteristic feature of the amide functional group in anilides, the ^{1}H, ^{13}C, and ^{15}N NMR spectra of a series of *N*-acyl-*m*- and *p*-substituted acylanilines (**2a**—**2c**) and related compounds were measured in several solvents. Results on ^{13}C and ^{1}H spectra are given, respectively, in Tables 1 and 2, together with those of related compounds. ^{15}N Spectra were reported separately in relation to the peculiar separation of the plotted points of *p*-substituted derivatives from those of *m*-substituted derivatives in their δ^{15}N vs. σ plots.[16]

To evaluate the polar substituent effect as impartially as possible, six each of substituted anilides carrying the same substituents at the *m*- and *p*-positions were chosen. The selected substituents (Y) on the anilino aromatic ring are methoxyl, methyl, chloro, acetyl, cyano, and nitro groups. Two *p*-substituted derivatives (*p*-NMe_2 and *p*-OH) were added to the plot after examination showed that the added points did not affect the ρ-values considerably. In the case of benzanilides, the effect of substituent (X) on the benzoyl group was also

Table 1. The Carbonyl ^{13}C Chemical Shifts[a)] of Various *m*- and *p*-Substituted Anilides $RNHC_6H_4Y$ in Various Solvents

Y	Solvent	R			$XC_6H_4CONHC_6H_5$
		C_6H_5CO **2a**	CH_3CO **2b**	CF_3CO **2c**	**4**
p-NMe_2	Py	166.33	168.39	155.54	166.70
	Me_2CO	165.58	168.28	155.04	166.06
	MeOH	168.66	171.23	156.31	168.69
	MeCN	166.32	169.09	155.51	166.49
	DMSO	164.75	167.33	153.92	165.29
p-OH	Py	166.48	168.69	155.72	166.86
	Me_2CO	165.79	168.98	155.35	165.86
	MeOH	168.73	171.35	156.67	168.69
	MeCN	166.50	169.38	155.81	166.15
	DMSO	165.08	167.53	154.19	165.18
p-OMe	Py	166.54	168.64	155.81	166.36
	Me_2CO	165.90	168.57	155.42	165.70
	MeOH	168.75	171.34	156.64	168.60
	MeCN	166.54	169.38	155.78	166.15
	DMSO	165.24	167.76	154.36	164.88
p-Me	Py	166.70	168.82	155.88	166.79
	Me_2CO	166.08	168.73	155.51	166.20
	MeOH	168.84	171.48	156.67	168.89
	MeCN	166.67	169.45	155.88	166.63
	DMSO	165.46	168.03	154.50	165.30
m-Me	Py	166.87	168.98	155.97	167.03
	Me_2CO	166.17	168.93	155.53	166.38
	MeOH	168.91	171.59	156.75	169.14
	MeCN	166.80	169.67	155.97	167.14
	DMSO	165.67	168.17	154.60	165.51
H	Py	166.61	169.05	155.99	166.61
	Me_2CO	166.31	168.98	155.71	166.31
	MeOH	168.93	171.62	156.80	168.93
	MeCN	166.77	169.74	156.02	166.77
	DMSO	165.55	168.26	154.66	165.55
m-OMe	Py	166.91	169.11	156.00	166.77
	Me_2CO	166.33	169.04	155.67	166.06
	MeOH	168.93	171.64	156.75	168.69
	MeCN	166.76	169.84	155.97	166.47
	DMSO	165.63	168.35	154.62	165.27
p-Cl	Py	166.92	169.11	155.95	165.86
	Me_2CO	166.37	169.09	155.75	165.18
	MeOH	168.85	171.62	156.75	167.67
	MeCN	166.80	169.75	156.01	165.70
	DMSO	165.62	168.44	154.70	164.35

examined. To specify the substituents on benzoyl and anilino groups, the anilides were named as *N*-(X-substituted benzoyl)-Y-substituted aniline, whenever necessary. Hereafter, X and Y denote the substituent on the benzoyl-aromatic ring and on the anilino-aromatic ring, respectively.

$RCONHC_6H_4Y$ $CH_3SO_2NHC_6H_4Y$ $XC_6H_4CONHC_6H_5$
$R = C_6H_5$ (**2a**) (**3**) (**4**)
$R = CH_3$ (**2b**)
$R = CF_3$ (**2c**)
$Y = OMe, Me, H, Cl, COMe, CN, NO_2,$ *p*-NMe_2, and *p*-OH

At most of the anilides were only sparingly soluble in less polar solvents, five perdeuterated solvents, namely pyridine-d_5, acetone-d_6, methanol-d_4, acetonitrile-d_3, and dimethyl-d_6 sulfoxide, were used in the experiments. The chemical shifts of several of these anilides, mostly *p*-substituted, were reported previously.[19,20)] These data agreed with our results in most cases.

The substituent effect on their chemical shifts was first analyzed by the correlation analytical approach using the Hammett equation (Eq. 1).[21)] These obtained ρ-values were used as a measure for the transmission of polar substituent effect. Influence of the polarity of the solvent on the transmission was discussed on the basis of solvent dependency of the ρ-values.

$$\delta = \rho\sigma + \delta_0. \qquad (1)$$

Table 1. (Continued)

Y	Solvent	R			$XC_6H_4CONHC_6H_5$
		C_6H_5CO **2a**	CH_3CO **2b**	CF_3CO **2c**	**4**
m-Cl	Py	167.08	169.25	156.06	165.39
	Me_2CO	166.47	169.29	155.88	164.87
	MeOH	168.94	171.73	156.82	167.24
	MeCN	166.96	170.04	156.10	165.56
	DMSO	165.89	168.68	154.82	164.16
m-CN	Py	167.14	169.49	156.23	164.88
	Me_2CO	166.71	169.61	156.11	164.35
	MeOH	168.93	171.91	157.02	166.43
	MeCN	167.05	170.22	156.29	165.05
	DMSO	166.00	168.96	155.01	163.61
p-CN	Py	167.24	169.63	156.20	165.24
	Me_2CO	166.76	169.67	156.09	164.87
	MeOH	169.00	172.43	156.96	166.97
	MeCN	167.14	170.29	156.26	165.52
	DMSO	166.05	169.14	155.05	164.05
m-NO_2	Py	167.19	169.68	156.34	164.64
	Me_2CO	166.76	169.70	156.22	164.14
	MeOH	169.03	172.00	157.08	166.28
	MeCN	167.17	170.33	156.39	164.91
	DMSO	166.00	169.07	155.14	163.29
p-NO_2	Py	167.41	169.74	156.32	165.03
	Me_2CO	166.83	169.81	156.20	164.60
	MeOH	169.01	172.06	157.05	166.75
	MeCN	167.23	170.42	156.35	165.07
	DMSO	166.21	169.36	155.16	163.83
m-COMe	Py	167.08	169.23	156.13	—
	Me_2CO	166.52	169.14	155.93	—
	MeOH	168.95	171.13	156.93	—
	MeCN	167.01	169.93	156.22	—
	DMSO	165.64	168.51	154.66	—
p-COMe	Py	167.24	169.49	156.08	—
	Me_2CO	—	—	155.95	—
	MeOH	—	—	156.88	—
	MeCN	—	—	156.16	—
	DMSO	165.91	168.86	154.71	—

a) Downfield chemical shifts from TMS.

In correlating NMR chemical shifts with the polar substituent constant, the choice of an appropriate substituent constant fitted to the nature of the observed nucleus becomes very important so as to obtain a good correlation. ^{13}C Chemical shifts of carbon atoms bonded directly to an aromatic ring are generally correlated best with σ_I and other inductive parameters of substituents.[22—24] However, the effect of the anilino substituent Y on $\delta^{13}C$ of amide carbonyl group could be correlated best with the Hammett σ constant. The ^1H and ^{19}F chemical shifts showed a good performance when they were plotted against σ, or its substitutes, σ^+ and σ^-, when the relevant atom can participate in the direct resonance with the substituent. In the case of ^{15}N chemical shifts of the anilide nitrogen atom, the best results were obtained when we used σ^- constant[25] as a measure for the polar substituent effect. Even when we used the σ^-, the correlation as a whole assembly including both *m*- and *p*-substituted derivatives was only fair due to the separation of the Hammett plots for the *m*- and the *p*-substituted derivatives.[16] To examine subtle differences in the substituent effect, the polar effects of *m*- and *p*-substituted derivatives were evaluated individually.

The Hammett ρ constant and the δ_0 values obtained by correlating the chemical shifts with an appropriate σ constant are given in Table 3; where δ_0 is the best fit chemical shift of unsubstituted compound calculated as the intercept of the regression line. The correlation coefficients (r) for the linear regression to Eq. 1 are also given in the last column of the same table. Here, ρ, ρ_m, and ρ_p refer to the gradients of the plots including all (*meta* and *para*, together), *m*-substituted, and *p*-substituted anilides, respectively. The X and Y in the parentheses following ρ refer to the substituent effect by substituent X on the benzoyl group and by substituent Y on the anilino group, respectively.

Carbonyl ^{13}C chemical shifts were measured in five

Table 2. The Amide ^1H Chemical Shifts[a)] of Various *m*- and *p*-Substituted Anilides $RNHC_6H_4Y$ in Various Solvents

Y	Solvent	R				$XC_6H_4CONHC_6H_5$
		C_6H_5CO **2a**	CH_3CO **2b**	CF_3CO **2c**	CH_3SO_2 **3**	**4**
p-NMe$_2$	Py	10.77	10.47	12.19	10.91	10.59
	Me$_2$CO	9.29	8.97	9.97	8.03	9.22
	MeCN	8.53	8.15	9.00	—	8.52
	DMSO	9.97	9.65	10.98	9.09	9.91
p-OH	Py	10.88	10.64	12.33	11.05	10.78
	Me$_2$CO	9.36	9.13	10.08	8.15	9.35
	MeCN	8.59	8.20	8.70	—	8.62
	DMSO	10.02	9.68	11.02	9.18	10.03
p-OMe	Py	10.86	10.59	12.36	11.18	10.88
	Me$_2$CO	9.44	9.08	10.14	8.25	9.39
	MeCN	8.65	8.29	9.07	—	8.63
	DMSO	10.19	9.80	11.15	9.35	10.11
p-Me	Py	10.87	10.62	12.39	11.34	10.90
	Me$_2$CO	9.46	9.11	10.18	8.40	9.47
	MeCN	8.71	8.28	9.10	—	8.70
	DMSO	10.23	9.85	11.19	9.54	10.19
m-Me	Py	10.85	10.61	12.36	11.42	10.88
	Me$_2$CO	9.45	9.14	?	8.47	9.50
	MeCN	8.75	8.38	9.20	—	8.76
	DMSO	10.22	9.86	11.20	9.65	10.30
H	Py	11.00	10.74	12.48	11.54	11.00
	Me$_2$CO	9.58	9.20	10.26	8.58	9.58
	MeCN	8.77	8.45	9.15	—	8.77
	DMSO	10.27	9.94	11.28	9.72	10.27
m-OMe	Py	10.99	10.71	12.44	11.51	11.02
	Me$_2$CO	9.53	9.19	10.22	8.77	9.53
	MeCN	8.74	8.52	9.13	—	8.74
	DMSO	10.26	9.93	11.24	9.78	10.23
p-Cl	Py	10.95	10.82	12.61	11.70	11.11
	Me$_2$CO	9.66	9.31	10.38	8.71	9.60
	MeCN	8.79	8.40	9.23	—	8.76
	DMSO	10.41	10.09	11.40	9.90	10.32

solvents. In the case of ^{13}C chemical shifts, the separation of the *meta*- and the *para*-plotted points are slight and barely exceeds the experimental error.

In the case of ^1H, the separation of the *p*-plotted points from the *m*-plotted points became a little larger but not so obvious as for ^{15}N chemical shifts. On the whole, the reliability (*r*-value) is higher when δ^1H of the whole assembly comprising both *m*- and *p*-Y-substituted derivatives were plotted against their σ^- constant. In other words, ρ is more reliable than the corresponding ρ_m or ρ_p in many cases.

In contrast, the plotted points of *p*-substituted anilides separate clearly from those of *m*-substituted anilides in the $\delta^{15}N$ vs. σ^- plots; the ρ_p value is always more positive than ρ_m. The correlations were considerably improved in the separate $\delta^{15}N$ vs. σ_m and $\delta^{15}N$ vs. σ_p (σ^-) plots in every series of anilides examined.[16)]

Separation of Inductive and Resonance Effects by DSP Analysis. To measure the contributions of inductive and resonance effects separately, the regression to the Taft's dual substituent parameter (DSP) equation[22,23)] was carried out.

$$\delta = \rho_I\sigma_I + \rho_R\sigma_R + \delta_0. \tag{2}$$

The results are given in Table 4. As expected from the general trend of ^{13}C chemical shifts, the carbonyl $\delta^{13}C$ is governed largely by the inductive effect of the benzoyl substituent X. The minus signs of the both ρ_I and ρ_R could be attributed to the local π-polarization of the CONH group induced by the dipole in XC_6H_4 group. The effects on $\delta^{13}C$ from anilino substituent Y contain a larger resonance contribution, probably because the nitrogen atom located in between is more susceptible to the resonance effect, especially when an electron-withdrawing substituent Y occupies the *para*-position of the anilino ring.

DSP analysis on the substituent effects on δ^1H showed that the resonance and the inductive effects contribute comparably to the chemical shifts in both series of X- and Y-substituted anilides. Except in the case of *m*-Y-substituents, the resonance effect predominates a little over the inductive effect.

The similar analysis on ^{15}N chemical shifts showed a very large contribution (more than 80%) of the res-

Table 2. (Continued)

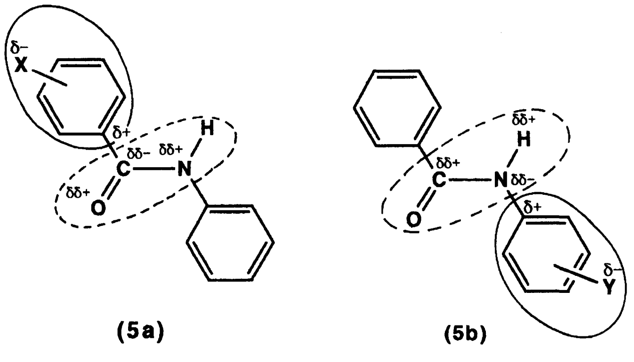
Y	Solvent	R				$XC_6H_4CONHC_6H_5$
		C_6H_5CO	CH_3CO	CF_3CO	CH_3SO_2	
		2a	**2b**	**2c**	**3**	**4**
m-Cl	Py	11.07	10.89	12.66	11.81	11.02
	Me_2CO	Broad	9.31	10.40	8.82	9.64
	MeCN	8.89	8.62	9.21	—	8.82
	DMSO	10.45	10.15	11.44	10.02	10.41
m-CN	Py	11.26	11.04	12.81	11.93	11.23
	Me_2CO	9.84	9.52	10.56	9.03	9.73
	MeCN	8.98	8.64	9.13	—	9.05
	DMSO	10.60	10.29	11.59	10.22	10.45
p-CN	Py	11.35	11.12	12.83	Broad	11.24
	Me_2CO	Broad	9.58	10.61	9.25	9.78
	MeCN	9.06	8.65	9.25	—	8.91
	DMSO	10.72	10.39	11.65	10.51	10.50
m-NO_2	Py	11.31	11.18	12.87	11.97	11.38
	Me_2CO	9.98	9.62	10.67	9.15	9.91
	MeCN	9.10	8.72	9.15	—	9.04
	DMSO	10.71	10.43	11.71	10.38	10.59
p-NO_2	Py	11.51	11.37	12.47	Broad	11.36
	Me_2CO	10.08	9.74	10.75	9.45	9.85
	MeCN	9.14	8.79	9.24	—	9.02
	DMSO	10.83	10.56	11.79	10.76	10.57
m-COMe	Py	11.19	11.00	12.71	11.79	—
	Me_2CO	9.73	9.37	10.43	8.81	—
	MeCN	8.94	8.52	9.18	—	—
	DMSO	10.48	10.16	11.47	10.00	—
p-COMe	Py	11.32	11.11	12.84	12.05	—
	Me_2CO	—	—	10.53	9.20	—
	MeCN	—	—	9.24	—	—
	DMSO	10.59	10.29	11.56	10.36	—

a) Downfield chemical shifts from TMS.

onance effect. This is in accord with the anomalous Hammett plots for $\delta^{15}N$.[16)]

Local π-Polarization in Amide Chromophores. In the series of X-substituted benzanilides, the ρ (X) of $\delta^{13}C$ vs. σ_I plot is negative irrespective of the nature of solvents. The negative ρ values for the carbonyl $\delta^{13}C$ vs. σ_I plot has been reported on substituted benzoyl and cinnamoyl derivatives and interpreted in terms of local π-polarization mechanism.[16—18)] The local polarization can be expected to occur in a system in which two chromophores are weakly coupled. In such a system, the two chromophores are fairly independent and close to each other. In these circumstances, the field effect due to the polarity (dipole moment) of the first chromophore (XC_6H_4 or YC_6H_4) induces the subsidiary polarization of π-electrons in the second chromophore (NHC=O). The local polarization induced by the local dipoles in benzoyl (XC_6H_4) and anilino (YC_6H_4) aryl groups can be described by **5a** and **5b**, respectively (Chart 2), in which the permanent dipoles generated by the introduction of a polar substituent (X or Y) are denoted by $\delta+$ or $\delta-$ and the secondarily induced charge separations are denoted by the symbols $\delta\delta+$ or $\delta\delta-$.

After all, the magnitude of the negative ρ-value on the atom connecting two (weakly coupled) chromophores should be a measure for the strength of local polarization. On the other hand, the degree of extended polarization has been measured by the magnitude of positive ρ-value on the atom attached to the aromatic ring and at the end opposite to the substituent in the mesomeric system, i. e. carbonyl O atom to the *p*-X substituent (**6a**) and amide N atom to the *p*-Y substituent (**6b**) (Chart 3). Hereafter, the local and extended polarization will be discussed by these criteria.



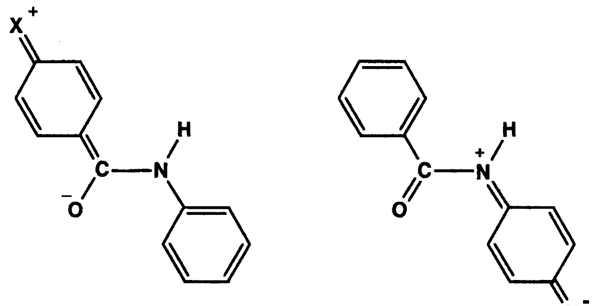
(5a) **(5b)**

Chart 2.

In the cases of *N*-acylanilines investigated, the $\rho_m(Y)$ for $\delta^{15}N$ vs. σ plots becomes negative in all series. In analogy with the carbonyl $\delta^{13}C$ chemical shifts discussed above, reversed sign of the $\rho_m(Y)$-values for

Table 3. The ρ-Values for the Hammett Plots (Eq. 1) of Chemical Shifts of Various *m*- and *p*-Substituted Anilides and Related Compounds $RNHC_6H_4Y$

Compound	σ	Solv.	All			*meta*			*para*		
			δ_0	ρ	r	$\delta_{0,m}$	ρ_m	r	$\delta_{0,p}$	ρ_p	r
^{15}N											
$XC_6H_4CONHPh$	σ	Py	128.64	3.368	0.941	129.35	1.061	0.988	128.44	3.115	0.957
(**4**)		Me_2CO	131.29	3.601	0.949	131.89	2.331	0.980	131.20	3.713	0.959
		DMSO	133.46	3.347	0.955	134.10	1.354	0.892	133.45	3.767	0.991
$PhCONHC_6H_4Y$	σ^-	Py	127.47	4.560	0.839	129.49	−1.624	0.925	127.44	5.361	0.927
(**2a**)		Me_2CO	131.37	0.773	0.563	132.37	−1.429	0.842	129.49	1.061	0.988
		DMSO	132.47	3.850	0.838	134.16	−0.916	0.714	132.34	4.423	0.991
$CH_3CONHC_6H_4Y$	σ^-	Py	133.75	1.789	0.680	134.60	−2.233	0.865	134.01	2.478	0.917
(**2b**)		DMSO	139.22	2.288	0.848	139.95	−0.639	0.884	139.36	2.765	0.950
$CF_3CONHC_6H_4Y$	σ^-	Py	127.59	0.915	0.632	128.12	−1.317	0.863	127.70	1.265	0.854
(**2c**)		DMSO	132.90	0.888	0.662	133.46	−1.209	0.867	132.96	1.208	0.891
$CH_3SO_2NHC_6H_4Y$	σ^-	Py	121.08	5.689	0.947	122.09	2.318	0.860	121.12	6.091	0.966
(**3**)		DMSO	126.08	5.547	0.954	127.10	2.062	0.919	126.13	5.978	0.976
$PhCH{=}NC_6H_4Y$	σ^-	DMSO	333.23	11.17	0.928	333.42	6.370	0.674	333.95	12.33	0.977
$H_2NC_6H_4Y$	σ^-	DMSO	64.74	12.49	0.944	64.84	7.755	0.990	64.34	16.29	0.997
$Cl^-H_3N^+C_6H_4Y$	σ	D_2O	51.37	1.892	0.781	52.09	0.281	0.930	50.83	2.892	0.924
^{13}C											
$XC_6H_4CONHPh$	σ_I	Py	166.98	−3.050	0.914	166.95	−3.352	0.933	166.87	−2.508	0.910
(**4**)		Me_2CO	166.34	−2.893	0.949	166.42	−3.377	0.962	166.26	−2.409	0.984
		MeOH	169.12	−3.799	0.935	169.14	−4.275	0.958	169.03	−3.201	0.941
		MeCN	166.82	−2.672	0.962	166.99	−3.162	0.978	166.67	−2.222	0.985
		DMSO	165.53	−2.838	0.940	165.62	−3.323	0.958	165.64	−2.386	0.967
$PhCONHC_6H_4Y$	σ	Py	166.79	0.662	0.966	166.80	0.598	0.874	166.78	0.687	0.971
(**2a**)		Me_2CO	166.20	0.821	0.989	166.25	0.732	0.982	166.20	0.824	0.988
		MeOH	168.86	0.218	0.921	168.92	0.102	0.752	168.85	0.223	0.942
		MeCN	166.75	0.569	0.985	166.77	0.516	0.962	166.74	0.575	0.989
		DMSO	165.51	0.853	0.975	165.62	0.588	0.938	165.49	0.889	0.990
$CH_3CONHC_6H_4Y$	σ	Py	169.01	0.874	0.987	169.02	0.853	0.984	169.01	0.873	0.985
(**2b**)		Me_2CO	169.01	0.938	0.962	168.97	0.942	0.989	169.01	0.923	0.952
		MeOH	171.61	0.633	0.908	171.60	0.523	0.976	171.64	0.692	0.910
		MeCN	169.70	0.866	0.986	169.74	0.846	0.999	169.68	0.848	0.982
		DMSO	168.22	1.303	0.987	168.25	1.197	0.997	168.23	1.332	0.984
$CF_3CONHC_6H_4Y$	σ	Py	155.94	0.477	0.978	155.97	0.459	0.954	155.93	0.459	0.983
(**2c**)		Me_2CO	155.63	0.746	0.992	155.62	0.833	0.980	155.63	0.714	0.996
		MeOH	156.74	0.416	0.960	156.75	0.419	0.922	156.73	0.401	0.961
		MeCN	155.96	0.517	0.982	155.97	0.535	0.952	155.95	0.497	0.988
		DMSO	154.57	0.768	0.990	154.61	0.692	0.974	154.57	0.768	0.990



(**6a**) (**6b**)

Chart 3.

these $\delta^{15}N$ vs. σ plots were rationalized by assuming the local π-polarization of amide group (**5b**).[16]

Anomalous ρ_P Values in $\delta^{15}N$ vs. σ^- Plots. The ρ_p values for $\delta^{15}N$ tend to increase in the series of benzanilides which have aromatic rings at both ends of the molecule. Their $\rho_p(X)$ and $\rho_p(Y)$ are larger than the $\rho_p(Y)$ of acet- and trifluoroactanilides. This phenomenon is peculiar to $\delta^{15}N$; no such anomaly was observed with the ρ-values of other nuclei. The π-chromophore of benzanilide that extends throughout the ArCONHAr′ system might contribute to mobilize electrons in the chromophore and is expected to facilitate the transmission of the substituent effect.

Influence of Solvents on the Substituent Effects. If we compare the $\rho(X)$-values for the carbonyl $\delta^{13}C$ in various solvents, it becomes the most negative in methanol, which means that the local π-localization is strongest in this solvent. The magnitude of $\rho(X)$ increases approximately in the increasing order of donor

Table 3. (Continued)

Compound	σ	Solv.	All			*meta*			*para*		
			δ_0	ρ	r	$\delta_{0,m}$	ρ_m	r	$\delta_{0,p}$	ρ_p	r
^1H											
$XC_6H_4CONHPh$ (**4**)	σ	Py	10.97	0.469	0.976	10.94	0.537	0.931	10.98	0.462	0.994
		Me_2CO	9.53	0.411	0.980	9.52	0.451	0.935	9.53	0.396	0.991
		MeCN	8.75	0.331	0.949	8.75	0.414	0.913	8.74	0.296	0.978
		DMSO	10.24	0.421	0.980	10.26	0.393	0.919	10.24	0.416	0.992
$PhCONHC_6H_4Y$ (**2a**)	σ^-	Py	10.98	0.396	0.958	10.94	0.543	0.957	10.99	0.377	0.970
		Me_2CO	9.56	0.440	0.972	9.51	0.623	0.976	9.56	0.403	0.990
		MeCN	8.77	0.341	0.972	8.75	0.451	0.963	8.75	0.316	0.990
		DMSO	10.29	0.459	0.976	10.24	0.633	0.986	10.28	0.435	0.985
$CH_3CONHC_6H_4Y$ (**2b**)	σ^-	Py	10.75	0.464	0.967	10.68	0.686	0.974	10.76	0.436	0.985
		Me_2CO	9.22	0.411	0.968	9.16	0.602	0.971	9.23	0.386	0.987
		MeCN	8.40	0.347	0.954	8.44	0.383	0.948	8.37	0.320	0.978
		DMSO	9.95	0.499	0.974	9.90	0.713	0.989	9.95	0.468	0.986
$CF_3CONHC_6H_4Y$ (**2c**)	σ^-	Py	12.48	0.310	0.778	12.42	0.657	0.979	12.46	0.252	0.775
		Me_2CO	10.27	0.420	0.978	10.20	0.632	0.973	10.26	0.393	0.996
		MeCN	9.09	0.164	0.651	9.17	−0.026	0.230	9.08	0.182	0.701
		DMSO	11.27	0.441	0.970	11.23	0.641	0.980	11.27	0.409	0.987
$CH_3SO_2NHC_6H_4Y$ (**3**)	σ^-	Py	11.47	0.759	0.983	11.49	0.734	0.977	11.46	0.748	0.982
		Me_2CO	8.53	0.765	0.987	8.57	0.789	0.971	8.54	0.755	0.991
		DMSO	9.68	0.885	0.989	9.70	0.922	0.994	9.67	0.873	0.998

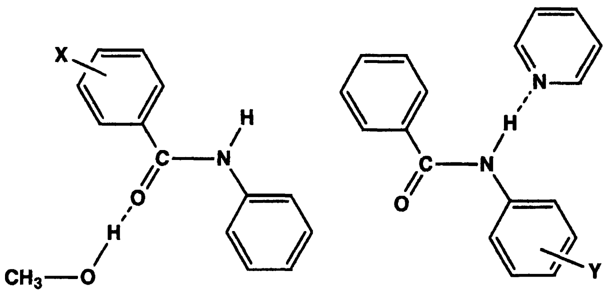
Table 4. Dual Substituent Parameter (DSP) Analysis of the Polar Substituent Effect on the NMR Chemical Shifts of Benzanilides $XC_6H_4CONHC_6H_4Y$

	Solvent	ρ_I	ρ_R	δ_0	I(%)	R(%)	r
^{15}N							
X(all)	DMSO	+2.304	+4.905	133.4	32.0	68.0	0.875
X(*m*)		+1.428	+0.340	134.1	80.1	19.9	0.911
X(*p*)		+3.315	+6.370	133.8	33.8	67.0	0.989
X(all)	Acetone	+2.062	+5.849	132.0	26.1	73.9	0.892
X(*m*)		+2.337	+0.733	131.9	76.1	23.9	0.972
X(*p*)		+1.760	+7.664	132.1	18.7	81.3	0.992
X(all)	Pyridine	+2.133	+5.160	129.2	29.2	70.8	0.868
X(*m*)		+1.084	+0.304	129.3	78.1	21.9	0.988
X(*p*)		+2.928	+6.953	129.2	29.6	70.4	0.991
Y(all)	DMSO	+1.093	+7.992	134.1	12.0	88.0	0.748
Y(*m*)		−0.522	−1.562	133.9	25.0	75.0	0.917
Y(*p*)		+2.709	+11.518	134.1	19.0	81.0	0.958
^{13}C							
X(all)	DMSO	−2.545	−0.750	165.32	77.2	22.8	0.959
X(*m*)		−3.064	−1.424	165.41	68.3	31.7	0.993
X(*p*)		−2.253	−0.349	165.36	86.6	13.4	0.974
Y(all)	DMSO	+0.608	+1.275	165.63	32.3	67.7	0.914
Y(*m*)		+0.574	+0.268	165.63	68.2	31.8	0.946
Y(*p*)		+0.704	+1.542	165.59	31.3	68.7	0.993
^1H							
X(all)	DMSO	+0.331	+0.643	10.29	34.3	65.7	0.953
X(*m*)		+0.323	+0.336	10.30	49.0	51.0	0.947
X(*p*)		+0.355	+0.700	10.27	33.6	66.4	0.994
Y(all)	DMSO	+0.587	+0.704	10.30	45.5	54.5	0.973
Y(*m*)		+0.569	+0.416	10.28	57.8	42.2	0.997
Y(*p*)		+0.628	+0.810	10.31	43.7	56.3	0.982

Table 5. The ρ-Values for the Hammett Plots (Eq. 1) of Chemical Shifts of Benzanilides Bearing Substituents (X,Y) on Both Rings $XC_6H_4CONHC_6H_4Y$

Compound	σ	Solv.	δ_0	ρ	r
^{13}C					
$XC_6H_4CONHC_6H_4OMe$	σ_I	Py	166.58	−2.701	0.981
		DMSO	165.03	−2.455	0.979
$XC_6H_4CONHC_6H_5$	σ_I	Py	166.78	−2.470	0.968
		DMSO	165.41	−2.366	0.986
$XC_6H_4CONHC_6H_4NO_2$	σ_I	Py	167.29	−2.388	0.989
		DMSO	166.04	−2.032	0.980
$MeOC_6H_4CONHC_6H_4Y$	σ	Py	166.31	0.563	0.985
		DMSO	164.85	0.910	0.993
$C_6H_5CONHC_6H_4Y$	σ	Py	166.78	0.677	0.968
		DMSO	165.51	0.870	0.992
$O_2NC_6H_4CONHC_6H_4Y$	σ	Py	165.01	0.814	0.992
		DMSO	163.76	1.196	0.991
^1H					
$XC_6H_4CONHC_6H_4OMe$	σ	Py	10.935	0.417	0.983
		DMSO	10.129	0.423	0.992
$XC_6H_4CONHC_6H_5$	σ	Py	10.985	0.456	0.995
		DMSO	10.244	0.404	0.997
$XC_6H_4CONHC_6H_4NO_2$	σ	Py	11.527	0.470	0.994
		DMSO	10.789	0.423	0.992
$MeOC_6H_4CONHC_6H_4Y$	σ^-	Py	10.912	0.319	0.973
		DMSO	10.135	0.415	0.995
$C_6H_5CONHC_6H_4Y$	σ^-	Py	10.986	0.379	0.964
		DMSO	10.308	0.431	0.997
$O_2NC_6H_4CONHC_6H_4Y$	σ^-	Py	11.440	0.361	0.969
		DMSO	10.582	0.434	0.999

number. Similarly, amide ^1H chemical shifts and the gradients $\rho(X)$ of δ^1H vs. σ plots of *N*-(X-substituted benzoyl) anilines also vary in the order of the donor numbers of solvents. Needless to say, δ^1H shifts downfield as the donor number increases. Simultaneously, $\rho(X)$ and $\rho_p(X)$ for δ^1H vs. σ plots increase in the same order. This implies the fact that the substituent effect from the benzoyl group tends to be better transmitted to the amide group when the solvent is more electron-donating and, hence, more strongly hydrogen-bonded to the NH group. The absolute values of $\rho(X)$ from the $\delta^{13}C$ vs. σ_I plots increase in nearly the same order as the $\rho(X)$ from the δ^1H vs. σ plots. Opposite signs of the gradients imply that ^{13}C and ^1H are at the opposite ends of the dipole induced by the local polarization. From the observed ρ-values, both the OH···O hydrogen bonding between methanol and the carbonyl oxygen (**7a**) and the NH···X hydrogen bonding between the amide NH and the hydrogen-accepting solvents (pyridine, dimethyl sulfoxide, and acetone) (**7b**) must favor the local polarization by stabilizing the local amide chromophore (Chart 4). Thus, the whole amide group must become more susceptible to the effect of benzoyl substituent X when the NH group is involved in stronger hydrogen bonding. Methanol can act as a hydrogen acceptor, but must be a considerably weaker acceptor than pyridine or dimethyl sulfoxide.



(7a) **(7b)**

Chart 4.

Hydrogen bonding is known to favor the polar mesomeric structure (**1b**) of amides, increasing the rotational barrier about the amide C–N bond. The rotational barriers of *N*,*N*-dimethylbenzamides increase in the following order of solvents: $C_5D_5N < (CD_3)_2SO < CD_3OD$.[12,13] This implies that both the general polarity effect and the hydrogen bond effect cooperate in increasing the induced polarity of amide group. The presence of a hydrogen bond between the carbonyl oxygen and methanol was supported by the high field shifts of ^{17}O NMR in the cases of *N*,*N*-dimethylbenzamides.[13] The effect on $\delta_0(^{13}C)$ was obscured, probably because the carbon atom is not involved in the hydrogen bonding.

In the series of *N*-acylanilines **2a**—**c**, the ρ (also ρ_m and ρ_p) in the $\delta^{13}C$ vs. $\sigma(Y)$ plots was smallest in methanol, which forms hydrogen bonds with carbonyl groups. This fact does not conflict with the above conclusion on the local π-polarization, since it can be an indication of lesser contribution of **6b**.

Benzanilides Bearing Substituents (X,Y) on Both Rings. To discover clear the details of the mechanism of the transmission of the substituent electronic effect in the amide system, the effects due to the substitution on the both aromatic rings were examined. Thus, the effects of the substituent (X) on benzoyl group were evaluated using a series of disubstituted benzanilides $XC_6H_4CONHC_6H_4Y$, in which the substituent (Y) on the anilino group was fixed, and vice versa. The results are given in Table 5. When we compared the three series of *N*-benzoyl-Y-substituted anilines, the common tendency that $\rho(Y)$ is the largest for *N*-(*p*-nitrobenzoyl)-Y-substituted anilines and the smallest for the *N*-(*p*-methoxybenzoyl)-Y-substituted anilines was observed.

The perturbation on ρ_p by the substituent on the aromatic rings can be interpreted in terms of the cross conjugation effect. In the case of *N*-(X-substituted benzoyl)-*p*-nitroanilines, for example, the conjugation through the *p*-nitroanilino chromophore (**6b**) should compete with the amide resonance perturbed by the X-substituted benzoyl group. As the *p*-nitro group strengthens the anilino conjugation, the local polarization of CONH group was attenuated, resulting in less negative $\rho(X)$-value of carbonyl carbon atom. On the other hand, an electron-donating methoxyl group on the anilino ring should attenuate the resonance effect from the anilino aromatic ring judging from the more negative $\rho(X)$.

When we compared *N*-(*p*-nitrobenzoyl)-, *N*-benzoyl-, and *N*-(*p*-methoxybenzoyl)anilines, ^{13}C chemical shifts of *N*-(*p*-nitrobenzoyl)anilines are the most susceptible to the substituent effect from the Y-substituents. This is seen by fact that the carbonyl $\delta^{13}C$ is affected by the anilino substituent Y considerably. The effects of Y-substituents are attenuated when the electron-donating mesomeric effect by the benzoyl substituent (X) increases. This finding suggests that the carbonyl carbon is involved in cross-conjugation. The conjugation through the substituted benzoyl chromophore XC_6H_4 must be the one component and the other might be the amide resonance perturbed indirectly by the anilino substituent (Y). This sort of effect is obscured with the ^1H chemical shifts of the amide NH group.

Conclusion. From the more elaborate examination of the polar substituent effects on the chemical shifts of *N*-acylanilines, the amide chromophore (CONH) was shown to be locally polarized and only weakly interacted with aryl group attached to either or both ends (carbonyl carbon and amide nitrogen) except for anilides bearing an electron-accepting substituent at the *para*-position. Judging from more negative ρ-values in solvents capable of forming hydrogen bonds, the amide chromophore seemed to be stabilized by the hydrogen bonding interactions both with the carbonyl oxygen and with the amide hydrogen, which enhance the so-called amide resonance.

Experimental

All anilides used in this investigation are known compounds and were prepared by the reaction of the corresponding acyl chloride or benzenesulfonyl chloride with substituted anilines. The crude anilides were purified by repeated recrystallization. The purity was checked by comparing their melting points with those in literature.

^1H and ^{13}C NMR spectra were measured using a JEOL EX-270 spectrometer. The sample for the measurements were prepared by dissolving about 100 mg of an anilide in about 0.6 ml of solvent. The ^1H and ^{13}C chemical shifts were given in ppm downfield from TMS (internal reference). The accuracy for ^1H was +0.08 Hz (3×10^{-4} ppm) and for ^{13}C +0.3 Hz (1×10^{-3} ppm).

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