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The Substituent Effect. IV. Proton NMR Chemical Shifts of Phenols

Yuho Tsuno, Mizue Fujio, Yoshio Takai, and Yasuhide Yukawa
Institute of Scientific and Industrial Research, Osaka University, Yamada-kami, Suita, Osaka

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NMR chemical shifts of the hydroxyl proton of *m*- and *p*-substituted phenols were determined in aprotic DMF and DMSO solutions. The effect of substituents on the hydroxy chemical shift was correlated much more excellently with our LArSR relationship, $\Delta\delta=\rho(\sigma^0+r\Delta\bar{\sigma}_R^-)$, than with simple Hammett equation, $\rho\sigma^0$ or $\rho\sigma^-$. The correlation resulted in $\rho=1.655$ and $r=0.639$ in DMF with correlation coefficient 0.9992 and $\rho=1.530$ and $r=0.673$ in DMSO with a correlation coefficient 0.9990. Anisotropy effect of any substituent was not significant. The deviations of particular substituents were ascribed to the modification of the electronic characters of substituents due to strong substituent-solvent interactions in DMF (or DMSO). The inductive and resonance substituent constants, $(\sigma_i)_{\text{DMF}}$ and $(\Delta\bar{\sigma}_R^-)_{\text{DMF}}$, were determined, on the basis of the assumption that the solvent-modification of a given substituent is practically the same at both *meta* and *para* positions.

As described in foregoing papers,[1,2] it had been established that the *Linear Aromatic Substituent-Reactivity* (LArSR) *relationship* (1) could be generally applicable to the substituent effect on both the chemical reactivities, $\log k/k_0$, and physical properties, $P-P_0$, of *meta*- and *para*-substituted benzene derivatives.

$$\begin{aligned}\log (k/k_0) \text{ or } P - P_0 &= \rho\bar{\sigma}\\ &= \rho(\sigma^0+r^+\Delta\bar{\sigma}_R^+ + r^-\Delta\bar{\sigma}_R^-) \qquad (1)\end{aligned}$$

σ^0 is the standard substituent constant which does not involve any additional π-electronic interaction with the reaction center. $\Delta\bar{\sigma}_R^+$ and $\Delta\bar{\sigma}_R^-$ are the resonance substituent constants describing the capabilities for π-electron delocalization (resonance) of conjugatively electron releasing ($-R$) and electron attracting ($+R$) *para* substituents respectively. r^+ and r^- are the resonance reaction constants measuring the extents of effectively exalted resonance interactions of $-R$ and $+R$ substituents in a given system.

This equation implies that the apparent substituent constant $\bar{\sigma}$ can be given by the combination of three terms in bracket at right hand, when a unique ρ value is determined for a given system. Either of the two additional terms plays a significant role in the chemical reactivities in which the benzene conjugation system could be extended fully or partially to the reaction center. In general chemical reactivities, r^+ and r^- are not necessarily equivalent in a given system but are usually independent of each other. The requirement of independent r^+ and r^- values is a characteristic of our LArSR relationship, which subsequently requires the separate statistical applications to conjugatively electron releasing and attracting *para* substituents respectively.

It is believed that the generality of the LArSR Eq. (1) to the effect of electron releasing substituents in electrophilic exalted conjugation reactions, *i.e.*, the applicability of the second term in bracket, has been examined well by ourselves[2-4] and also by many investigators.[2,5-7] Whereas, practical role of the third term for the electron attracting substituent in nucleophilic exalted conjugation systems has not yet been examined enough, for the lack of appropriate data covering over a wide variety of substituents.[2,8] It has been thus highly desirable to obtain the reactivity data and physical data which would enable further testing of the applicability of the last term in the Eq. (1).

In the course of our continuing study of the substituent effect in aromatic derivatives, we have treated several series of NMR chemical shifts of *meta* and *para*-substituted benzene side-chain protons in terms of Hammett-type substituent parameters.[9] The treatment by means of Eq. (1) has appeared to be generally successful for existing data. However, it is rather common that the Hammett-type correlation of proton NMR chemical shifts suffers from the difficulties due to relatively significant role of specific magnetic effects from particular substituents. Our previous results were

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also not quite free from these effects enough to permit the critical test of the applicability of Eq. (1). Our recent data on the chemical shift of ring protons of substituted benzenes in various solvents were correlated with Eq. (1) satisfactorily, but several nagging qualitative problems have still remained.[10]

Among a number of recent communications on the subject, Ouellette[11] reported that the hydroxyl proton resonance of *meta* and *para*-substituted phenols in dimethylsulfoxide solution exhibited remarkably magnified substituent chemical shifts and pointed out that the substituent chemical shifts were linearly correlated by Hammett σ^- constants with impressive accuracy. However, upon the Hammett-type treatment including our preliminary data, we arrived at somewhat different conclusions regarding the correlation of substituent contributions in this system. The hydroxyl chemical shifts were not so satisfactorily correlated, as had been reported, with a single set of ordinary σ^- parameters, but were found to be treated much more excellently with an aid of our LArSR Eq. (1).[12] As far as we were aware, this series of substituent chemical shifts appeared to be most precisely described by means of the reactivity substituent parameters. From these facts, we directed our attention to obtain more extensive data for the substituent effect on the NMR chemical shifts of the hydroxyl proton of *meta* and *para*-substituted phenols in various solvents.

The present paper mainly concerns the general treatment based on our LArSR equation of substituent effects on the hydroxyl chemical shifts of phenols in dimethylformamide. Later, Traynham and Tribble have reported a new set of data for phenol-hydroxyl chemical shifts in DMSO solution,[13] and our shift values, in cases where direct comparison is possible, agree well with data reported by these investigators. However, substituents involved in their determination are still insufficient for our purpose. Then, a full set of our data in DMSO are also included in this paper, in order to permit direct comparison of data obtained in a single study.

Experimental

Phenols. All the phenols used were thoroughly purified by repeated fractionations or recrystallizations from appropriate solvents, and for some phenols purification was effected by further sublimations of purified samples. The mps and other physical constants agreed well with established values.

About a half of *m*- and *p*-substituted phenols used in this series of studies were obtained from commercial sources except those given below.

Following phenols were prepared by the usual diazonium method from corresponding anilines available in pure form. Diazonium sulfates were decomposed by dropwise addition to 36% aqueous sulfuric acid solution at about 80°C and the phenols produced were steam-distilled or extracted by appropriate solvents; m-*Bromophenol*, bp 94—96°C/6 mmHg, lit,[14] bp 135—140°C/12 mmHg; m-*Fluorophenol*, bp 90°C/58 mmHg, lit,[14] bp 108°C/70 mmHg; m-*Trifluoromethylphenol*, bp 73—74°C/15 mmHg, lit,[15] bp 85.5—86.5°C/25 mmHg; m-*Phenoxyphenol*, bp 148°C/4 mmHg, lit,[14] bp 150°C/4.5 mmHg; p-*Fluorophenol*, mp 45—45.5°C recrystallized from *n*-hexane, lit,[14] mp 46.5°C; m-*Iodophenol*, mp 38.5—39.5°C recrystallized from benzene - *n*-hexane, lit,[14] mp 40°C; *3,5-Dichlorophenol*, mp 66°C recrystallized from *n*-hexane, lit,[14] mp 68°C.

p-*Trifluoromethylphenol* (bp 60°C/15 mmHg, lit,[16] bp 71.5—72°C/8 mmHg) was obtained from *p*-trifluoromethylaniline, which was prepared according to the direction of Jones[16] by fluorine-exchange of *p*-tribromomethylnitrobenzene with SbF_5 into trifluoromethylnitrobenzene followed by reduction with $SnCl_2$ in ethanol-hydrochloric acid solution.

p-N,N-*Dimethylaminophenol* was derived from *p*-anisidine. Methylation of anisidine with dimethyl sulfate gave dimethylaminoanisole (bp 146°C/38 mmHg), which was demethylated by boiling with conc. hydroiodic acid to the phenol and purified by recrystallizations from ligroin, mp 77°C, lit,[17] mp 77.5—78°C.

m-Aminophenol was converted into m-*Acetaminophenol* by the acetylation in aqueous acetic acid with acetic anhydride and purified by recrystallizations from water, mp 148—149°C, lit,[18] mp 148°C.

p-Aminophenol was converted into p-*Iodophenol* (mp 92.5—93.5°C recrystallized from ligroin, lit,[19] mp 93—94°C), by literature method and also into p-*Cyanophenol* (mp 111—112°C recrystallized from benzene, lit,[20] mp 113°C) by the Sandmeyer reaction of the diazonium salt with cuprous cyanide.

m-*Cyanophenol* (mp 80°C from benzene - *n*-hexane, lit,[21] mp 82°C) was obtained according to the procedure of Clemm by the dehydration of m-*Hydroxybenzaldoxime* (mp 89.5°C from benzene, lit,[21] mp 87.5°C) with acetic anhydride followed by the hydrolysis of the acetate.

p-*Hydroxybenzylidenaniline* was prepared by the condensation of *p*-hydroxybenzaldehyde with aniline in ether solution (mp 197—198°C, recrystallized from ethanol, lit,[22] mp 194—195°C). p-*Benzylidenaminophenol* was similarly prepared from benzaldehyde and *p*-aminophenol, mp 189—190°C, recrystallized from ethanol, lit,[23] mp 181°C.

Hydroxybenzophenones were obtained by the cleavage of the methyl ether of methoxybenzophenones by heating under reflux for 12 hr with hydrobromic acid - acetic acid mixture (3 vol. Ac_2O, 5 vol. AcOH, and 5 vol. 48% aqueous HBr). m-*Hydroxybenzophenone*, mp 117°C from benzene - ethanol and petroleum ether, lit,[14] mp 116°C; p-*Hydroxybenzophenone*, mp 133°C from benzene, lit,[14] mp 130—132°C.

p-*Phenoxyphenol* was obtained in the similar way from *p*-methoxydiphenyl ether and recrystallized from benzene - *n*-hexane, mp 85—86°C, lit,[14] mp 84—85°C.

m-*Methylmercaptophenol* was prepared by the ether-cleavage of *m*-methoxyphenyl methyl sulfide with hydrobromic acid

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in acetic acid solution (bp 141.5°C/8 mmHg, lit,[24] bp 154—156°C/17—18 mmHg). *m*-Methoxyphenyl methyl sulfide was obtained from anisidine by the modification of the direction given by Grice[25] for *m*-methylmercaptobenzoic acid, bp 125.5°C/17 mmHg. Oxidation of *m*-methylmercaptophenyl acetate, mp 39°C (lit,[24] mp 40—41°C), with hydrogen peroxide in acetic acid according to the direction of Bordwell gave *m*-methylsulfonylphenyl acetate, which yielded on hydrolysis with 10% aqueous sodium hydroxide *m-Methylsulfonylphenol*, in good yield (mp 81—82°C recrystallized from benzene - chloroform, lit,[24] mp 83—84°C). *p-Methylsulfonylphenol* was similarly obtained from methylmercaptophenol (mp 85°C from light petroleum, lit,[24] mp 84—85°C) by oxidation of the acetate with hydrogen peroxide in acetic acid, followed by hydrolysis of *p*-methylsulfonylphenyl acetate resulted; mp 92°C from benzene - chloroform mixture, lit,[24] mp 95—96°C.

p-Thiocyanophenol was prepared by the usual procedure given by Bordwell and was purified by recrystallizations from benzene - *n*-hexane, mp 61°C, lit,[26] mp 62—63°C.

Hydroxynitrostyrenes were prepared by condensation of corresponding hydroxybenzaldehydes with nitromethane; *m-Hydroxynitrostyrene*, mp 141—141.5°C from benzene - ethanol, lit,[27] mp 136—137°C; *p-Hydroxynitrostyrene*, mp 166—167°C from benzene - ethanol, lit,[28] mp 165—166°C.

m-Hydroxybenzaldoxime was converted by Field's direction[29] with nickel acetate into *m-Hydroxybenzamide*, mp 171—172°C from benzene - ethanol, lit,[30] mp 169—170°C.

Ethyl p-hydroxycinnamate (mp 76°C recrystallizations from benzene - *n*-hexane) was prepared by the condensation of *p*-hydroxybenzaldehyde with malonic acid, followed by esterification of cinnamic acid produced.[31] *m-Isomer* (mp 66.5—67.5°C, recrystallizations from benzene - *n*-hexane, lit,[32] mp 70—71°C) was also prepared by the similar procedure.[31]

Solvent. Dimethylsulfoxide was dried for 4 days, boiled under reflux for one day over calcium hydride and fractionally distilled under reduced pressure. The middle fraction bp 100.5°C at 39 mmHg was stored over molecular sieve and distilled before use.

Dimethylformamide which had been prepurified by the literature method was treated with molecular sieve and fractionated under reduced pressure, bp 58°C at 25 mm.

NMR Spectra. The proton resonance spectrum of the phenol hydroxyl group was recorded on a Hitachi-Perkin Elmer R-20 spectrometer, operating at 60 MHz. The probe temperature was maintained at 34.0°C. The measurement was made by freshly prepared DMF or DMSO solutions at the concentration in the range 1.0—0.05M. The solvent peak provided a convenient reference signal. The low field ^{13}C–H satellite of DMF or DMSO solvent main peak was utilized as the general internal standard throughout the series of chemical shift measurement. The shift value was determined by direct counting of peak to peak frequency differences from the standard satellite peak, and calibrated to the shift value from TMS in the usual way. At the concentration range studied, the line width of the hydroxyl resonance signal was generally 1.5 Hz or less, but in some cases was a little broader (2—3 Hz). The broad signal of hydroquinone, 7—8 Hz at 0.5M, was the worst case, and appeared to be diffused more on dilution. The shift values were determined repeatedly at least three different concentrations in the range lower than 0.5M, using independently prepared solution. The values were reproducible to ±0.2 Hz at a given concentration for all samples. Resonance position of a given phenol generally tended to shift very slightly toward high field on dilution, but mostly approached to or remained a constant within ±0.2 Hz at the concentration below 0.25M, independent of concentrations covering over more than 4 folds dilution. A minor dilution shift was apparent in 6 derivatives among 50 substituted phenols to an extent of 2.0—2.5 Hz through a wide range of the concentration 0.5—0.05M in either DMF or DMSO solution. To approximate actual chemical shift values at infinite dilution conditions, the measurement was extended to that in high dilute solutions possible

TABLE 1. CHEMICAL SHIFTS OF HYDROXYL PROTONS OF *m*, AND *p*-SUBSTITUTED PHENOLS

No.	Subst.	DMF		DMSO	
		$\Delta\delta_p^{TMS}$	$\Delta\delta_m^{TMS}$	$\Delta\delta_p^{TMS}$	$\Delta\delta_m^{TMS}$
1	NO_2	11.212	10.558	10.963	10.353
2	CN	10.768	10.372	10.540	10.140
3	CHO	10.733	10.053	10.533	9.878
4	SO_2CH_3	10.728	10.330	10.510	10.160
5	$SOCH_3$	10.203		10.010	
6	SO_2NH_2	10.380		10.187	
7	SCN	10.368		10.140	
8	COC_6H_5	10.572	9.955	10.373	9.793
9	$COCH_3$	10.455	9.848	10.250	9.703
10	$COOCH_3$	10.432	9.897	10.257	9.765
11	COOEt	10.418	9.888	10.238	9.737
12	$CONH_2$	10.077	9.718	9.877	9.531
13	CF_3	10.430	10.212	10.220	10.027
14	$CH{=}CHNO_2$	10.567	9.942	10.340	9.716
15	CH=CHCOOEt	10.148	9.730	9.936	9.556
16	$CH{=}NC_6H_5$	10.235		10.068	
17	$N{=}CHC_6H_5$	9.608		9.437	
18	$N{=}NC_6H_5$	10.438		10.247	
19	C_6H_5	9.632		9.480	
20	H	9.392		9.253	
21	I	9.812	9.882	9.613	9.690
22	Br	9.805	10.013	9.623	9.813
23	Cl	9.773	10.005	9.600	9.810
24	F	9.438	9.963	9.288	9.798
25	SCH_3	9.548	9.567	9.370	9.425
26	OC_6H_5	9.447	9.730	9.266	9.527
27	NHAc	9.217	9.385	9.078	9.262
28	NHC_6H_5	9.117	9.282	8.947	9.120
29	*t*-Bu	9.180	9.212	9.038	9.115
30	C_2H_5	9.162		9.021	
31	CH_3	9.138	9.265	9.002	9.140
32	OCH_3	8.945	9.408	8.828	9.295
33	OH	8.683	9.217	8.535	9.077
34	NMe_2	8.643	9.022	8.535	8.928
35	NH_2	8.400	8.875	8.267	8.755
36	$(CH_3)_2$		9.123		9.018
37	Cl_2		10.582		10.358

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to give no further shift exceeding over a measurement error of ±0.2 Hz by additional dilution with an equal volume of solvent. It can be then estimated that in nearly all instances the discrepancy from the infinite dilution value does not exceed ±0.4 Hz, even for the least favorable case. Results are summarized in Table 1.

Result

In either dimethylsulfoxide (DMSO) or dimethylformamide (DMF) solution, phenols carrying various *meta* and *para*-substituents resulted in the stabilized NMR resonance signals of hydroxyl protons. As mentioned by previous workers,[11–13] the concentration dependence of the shift was not significant in these solvents in contrast to the dilution shift as much as 1 ppm observed in carbon tetrachloride solution.[33]

Table 1 lists the chemical shift values of the hydroxyl protons of *meta* and *para*-substituted phenols at approximately infinite dilution in DMF and DMSO solutions. It may be estimated that the uncertainty in the listed values of chemical shifts does not exceed ±0.005 ppm. The hydroxyl chemical shift varies in either solution over a range of 2.7 ppm with respect to substituent changes. Then, the experimental uncertainty is effectively regarded as being negligible in comparison with the divergent chemical shift variation due to substituent changes. The present results in DMSO solution are generally in good agreement with those reported by Traynham[13] and Ouellette.[11] The latter author reported consistently lower (less shielded) values by *ca.* 0.04 ppm than the present data, but the relative substituent chemical shift values agree well with the present values within usual experimental error.

One of the important facts, as seen in the result in Table 1, is the proportionality between the substituent shifts in both DMF and DMSO solvents. The correlation is given by

$$\Delta\delta_{\mathrm{DMSO}} = 0.951\Delta\delta_{\mathrm{DMF}}$$

The precision can be measured by the standard deviation ±0.022 and the correlation coefficient 0.9992. The similar linearity is observed for literature data of the phenol substituent chemical shifts in HMPA (Hexamethylphosphoramide)[35]

$$\Delta\delta_{\mathrm{HMPA}} = 1.1\Delta\delta_{\mathrm{DMF}}$$

In addition, a series of our recent data in acetonitrile can be also correlated linearly to the shift data in DMF with a coefficient of 0.68.[34] The variation of the chemical shift in a series of substituted phenols are appreciably magnified in either of these solvents as compared with those in carbon tetrachloride. The slope of these correlations appears qualitatively to vary in parallel to the low-field shift of hydroxyl resonance position of a given phenol in respective solvents, and the susceptibility of hydroxyl shifts to substituent changes varies dependent upon the solvent basicity or the hydrogen bond acceptor strength of solvents. Nevertheless, it is clear that the apparent substituent constant $\bar{\sigma}$ remains practically the same in either of these solvents, to a precision on the order of experimental error. Any particular effect on substituent constants is not significant among these solvents. Accordingly, the discussion followed will treat the results in DMF solution conveniently as a representative series of the substituent effects on the hydroxyl chemical shift in these solvents.

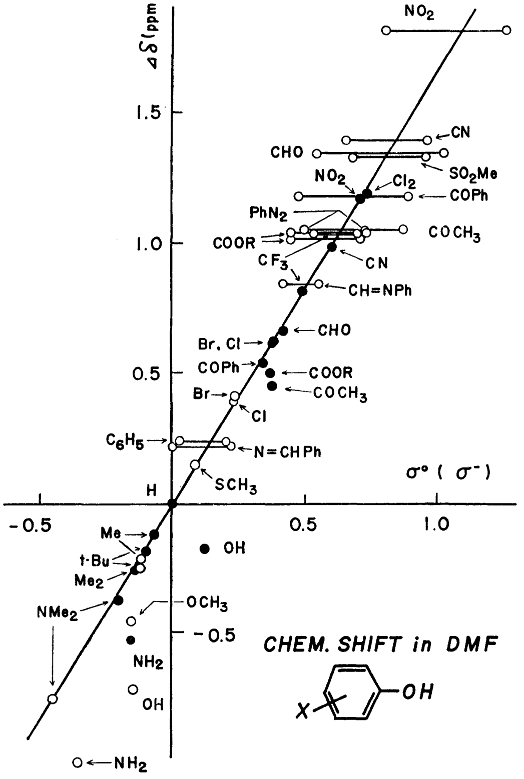

Fig. 1. Hammett plot of hydroxyl chemical shifts of phenols in DMF; open circle for *para* and closed circle for *meta* substituents.

In Fig. 1, the relative substituent chemical shifts of hydroxyl proton are plotted against corresponding σ^0 and σ_p^- constants. Contrary to the results reported by Ouellette[11] considerable scatterings are observed as a whole figure. Deviations from the σ^0 correlation line are more significant in *para* than in *meta*-substituents, while they appear to be rather systematic. The direct employment of any other ordinary set of substituent constants does not improve significantly the overall correlation. However, it should be noticed that most of the *m*-substituent chemical shifts are excellently described by σ_m constants. This is in clear contrast to the behavior of the *meta* ring proton of mono-substituted benzenes which provide apparently a better correlation with σ_p^0 values[10] and the ^{19}F shielding parameters for *meta*-substituted fluorobenzenes[36] which correlate with σ_I constants alone. Among 30 *meta*-substituents examined,

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deviations are obvious only for amino, acetamino, and hydroxy, and detectable to a minor extent for methoxy, acetyl and carboalkoxy groups.[37] These deviations do not appear to be similar to the characteristic deviations observed in the chemical shift of the usual side-chain or ring protons at *meta* position.

TABLE 2. STANDARD SUBSTITUENT CONSTANTS[3b]

Subst.	σ_p^0	σ_m^0	$\Delta\bar{\sigma}_R^-$
NO_2	0.810	0.709	0.455
CN	0.653	0.607	0.309
SO_2CH_3	0.686 (0.749)	*0.64* (0.697)	0.302
SO_2NH_2	*0.65*	0.622	0.246
CHO	*ca. 0.53*	0.415	0.465
COC_6H_5	0.490	0.357 (0.3)	0.387
$COCH_3$	0.491	0.376 (0.30)	0.365
$COOCH_3$	0.460	0.36 (0.32)	0.30
COOEt	0.453	0.38 (0.31)	0.28
$CONH_2$	*0.38*	0.32	0.24
$CH{=}CHNO_2$	*ca. 0.50*	*0.38*	*ca. 0.37*
$CH{=}NC_6H_5$	*0.42*		*0.14*
$N{=}CHC_6H_5$	*0.00*		*0.22*
$N{=}NC_6H_5$	0.40	*0.29*	0.31
CF_3	0.505	0.493, 0.476	0.196
SCN	0.493		0.12
C_6H_5	0.039		0.16
NH_2	−0.36	−0.15	
NMe_2	−0.48	−0.21	
OH	−0.16	0.122	
OCH_3	−0.100 (−0.152)	0.115 (0.06)	
NHAc	0.0	0.12	
CH_3	−0.124	−0.069	
C_2H_5	−0.131		
t-Bu	−0.174	−0.100	
SCH_3	0.083	0.120	
OC_6H_5	0.076	*0.252*	
F	0.212	0.337	
Cl	0.281	0.373	
Br	0.296	0.391	
I	*0.298*	0.352	

Values in bracket are the values to be used for the data in aqueous organic solutions, and given in italic are less reliable.

The hydroxy chemical shift for *meta* substituents diverges along a straight line for σ_m over a range of 1.5 ppm, which will be wide enough to determine the reliable ρ_m-line as a standard for the discussion of substituent effect. The substituent parameter values utilized in the following calculations are listed in Table 2. Nineteen well-behaving *meta*-substituents give a precise straight correlation, on employment of the method of least squares,

$$\Delta\delta_{\mathrm{DMF}}^{\mathrm{OH}} = 1.656\sigma_m - 0.019$$

the standard deviation being ± 0.016 and the correlation coefficient 0.9994. On the basis of this ρ_m value, a set of apparent substituent constants can be determined from this series. They are listed in Table 3. A comparable set can be derived also from the shift data in DMSO solution, where *meta* substituents provide similarly ρ_m value of 1.529 ($s = \pm 0.022$ and $R = 0.9987$), and the apparent $\bar{\sigma}$ values for all *meta* substituents coincide precisely with the values derived from DMF data.

TABLE 3. APPARENT SUBSTITUENT CONSTANTS IN DMF

No.	Subst.	$\bar{\sigma}_p$	$\bar{\sigma}_m$
1	NO_2	1.110	0.716
2	CN	0.843	0.603
3	CHO	0.822	0.411
4	SO_2CH_3	0.819	0.578
5	$SOCH_3$	0.502	
6	SO_2NH_2	0.608	
7	SCN	0.597	
8	COC_6H_5	0.724	0.351
9	$COCH_3$	0.653	0.287
10	$COOCH_3$	0.639	0.316
11	COOEt	0.632	0.312
12	$CONH_2$	0.425	0.209
13	CF_3	0.638	0.507
14	$CH{=}CHNO_2$	0.721	0.344
15	CH=CHCOOEt	0.469	0.243
16	$CH{=}NC_6H_5$	0.520	
17	$N{=}CHC_6H_5$	0.142	
18	$N{=}NC_6H_5$	0.644	
19	C_6H_5	0.156	
20	H	0.011	
21	I	0.265	0.307
22	Br	0.261	0.387
23	Cl	0.242	0.382
24	F	0.040	0.357
25	SCH_3	0.106	0.117
26	OC_6H_5	0.045	0.216
27	NHAc	−0.094	0.007
28	NHC_6H_5	−0.155	−0.055
29	*t*-Bu	−0.117	−0.097
30	C_2H_5	−0.127	
31	CH_3	−0.141	−0.065
32	OCH_3	−0.258	0.022
33	OH	−0.416	−0.094
34	NMe_2	−0.440	−0.212
35	NH_2	−0.587	−0.301
36	$(CH_3)_2$		−0.150
37	Cl_2		0.730

The apparent substituent constants $\bar{\sigma}_p$ for conjugatively electron attracting $(+R)$ *para* substituents all lie in between corresponding σ^0 and σ^- values. The resonance contribution of these *para* substituents to the hydroxyl chemical shift appears to be relatively less effective than that in the phenol dissociation measured by σ^- constants. It may be expected that our LArSR Eq. (1) will enable to correlate the hydroxyl chemical shifts of these groups.

On the least squares application of Eq. (1) to the hydroxyl chemical shifts for these groups including well-behaving *meta*-substituents (total number 31), an excellent linear correlation (Fig. 2) is resulted in

$$\Delta\delta_{\mathrm{DMF}}^{\mathrm{OH}} = 1.655(\sigma^0 + 0.639\Delta\bar{\sigma}_R^-) - 0.016 \qquad (2)$$

The standard deviation from the regression line is ± 0.022 and the correlation coefficient 0.9992. The ρ

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[37] The latter three substituents could be fitted closer to the line by the use of σ_m values given for aqueous organic solution.

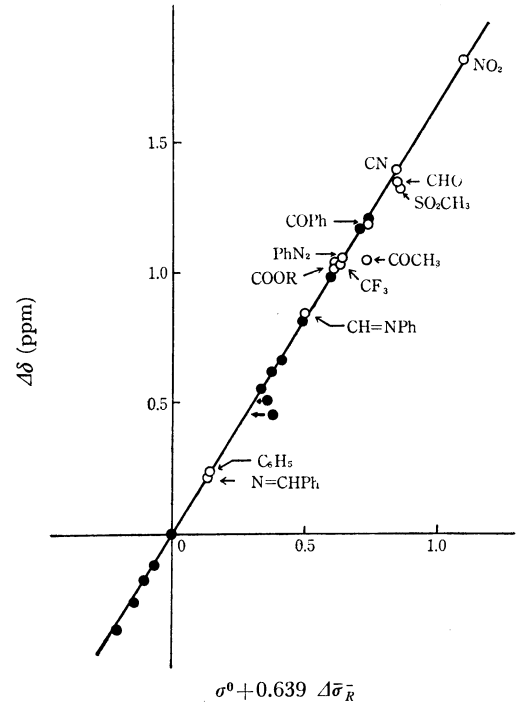

Fig. 2. LArSR plot for hydroxyl proton chemical shifts in DMF; open circle for $+R$ *para* substituents and closed circle for *meta* substituents.

value derived is identical with that obtained from *meta* substituents alone. The same treatment can be applied also to the shifts in the latter solution with analogous precision.[38]

$$\Delta\delta^{\mathrm{OH}}_{\mathrm{DMSO}} = 1.530(\sigma^0+0.673\Delta\bar{\sigma}_R^-) - 0.004$$

It is evident from these results that the hydroxyl chemical shifts of substituted phenols in these solvents can be treated quite successfully by means of our LArSR Eq. (1) in the same way as the general chemical reactivity changes, at least as far as conjugatively electron attracting groups are concerned.

On the other hand, the analogous treatment of conjugatively electron releasing ($-R$) *para* substituents based on Eq. (1), unfortunately, does not appear to be successful. The fit to the Eq. (1) should imply the existence of a certain proportionality between the increments of apparent $\bar{\sigma}_p$ from σ_p^0 values and the corresponding $\Delta\bar{\sigma}_R^+$ parameters throughout a series of *para* $-R$ substituents. However, the apparent enhancement, $\bar{\sigma}_p-\sigma_p^0$, is significant for amino, hydroxy, acetamino, and methoxy groups, but is not significant for the remainder. A contrast is clear in the comparison of the behaviors of *p*-amino and *p*-dimethylamino substituents, in spite of their comparable and potential resonance capabilities in general chemical reactivities. In practice, no clear-cut correlation was observed for these $-R$ substituents between the enhancements $\bar{\sigma}_p-\sigma_p^0$ and the corresponding $\Delta\bar{\sigma}_R^+$ values. It is however to be mentioned that the substituent which gives the anomalous resonance enhancement $\bar{\sigma}_p-\sigma_p^0$ at *para* position does exhibit the anomalous effect, the exalted electron donation, also at *meta* position.

Discussion

It is frequently noted that the substituent effect on the NMR chemical shift is not described so successfully by the ordinary substituent parameters which were derived from chemical reactivities.[9b] Even in chemical reactivities, in general, a single set of Hammett-type substituent constants such as σ, σ^+, and σ^- can not always provide a good description of the actual substituent contribution. The degree of resonance contribution from substituents, relative to their polar or inductive contribution, depends evidently upon the structure of the system and of the detection center and also upon the nature of the detection variables. The susceptibility of the proton NMR chemical shift to the π-electronic (resonance) contribution relative to the σ-electronic (or field) effect from substituents may differ from the relative π-electronic contributions in the reactivity changes of similar structural system. Such the effect should be taken into account, as a first approximation, by the aid of our LArSR relationship or other relevant equations.[39]

A most serious problem we often have encountered with the treatment of substituent effects on proton NMR chemical shifts is the fact that the *meta* substituent chemical shifts do not apparently follow σ_m values, and furthermore, the different ρ-values are often required for respective series of *meta* and *para* substituent chemical shifts. These provide a difficulty in determining unique ρ-value for a given system as generally assumed in the correlation of chemical reactivities. It is then an appreciated feature of the present data that the *meta* substituent chemical shifts can be precisely correlated with σ_m values and most of *para* substituent chemical shifts are described by the combination of σ_p^0 and $\Delta\bar{\sigma}_R^-$ parameters, giving the same ρ value for both series.

Another difficulty in the treatment of substituent chemical shifts is the serious deviations of certain substituents arising from their specific magnetic contributions. Although deviations are significant for several substituents in the present series, the direction and magnitude of deviations are dissimilar to those expected from the nature of anisotropic substituents. The difference in the nature of deviations is evident in the comparison with the α-proton of substituted toluenes. It is clear that any specific magnetic contributions are of little practical consequence and the effects, if present, are relatively unimportant in the chemical shifts of phenol protons in these solvents examined. The hydroxyl chemical shift should be predominantly controlled by the charge produced or the electron density at the hydroxyl oxygen atom, which in turn should be determined by the intramolecular electronic interaction with substituents.

The hydrogen-bonding interaction of the hydroxyl

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[38] Correlation coefficient $R=0.9990$ and standard deviation $s=\pm0.023$.

[39] P. R. Wells, *Chem. Rev.*, **63**, 171 (1963); C. D. Ritchie and W. F. Sager, "Progress in Physical Organic Chemistry," Vol. II, Interscience, New York (1964), p. 323; P. R. Wells, S. Ehrenson, and R. W. Taft, *ibid.*, Vol. IV (1968), p. 147; C. G. Swain and E. C. Lupton, Jr., *J. Amer. Chem. Soc.*, **90**, 4328, (1968); M. J. S. Dewar and P. J. Grisdale, *ibid.*, **84**, 3539 (1962).

function with a hydrogen-bonding acceptor solvent plays evidently an important role in magnifying the substituent chemical shifts and also in fitting to the Hammett-type relationship. The state of phenol molecules reflected on the hydroxyl chemical shift must closely resemble the intermediate state for the acid dissociation of phenols. Intramolecular electronic interactions of substituents with the acquired charge at the phenol oxygen in the present system may be close to those in the phenoxide-ion. The large positive value of ρ and high r-value for conjugatively electron attracting *para* substituents justify the above explanation. What is actually observed in the present system would be the substituent effect on the hydrogen bonding measured by the proton chemical shift as the detection variable. Thus, it is not surprising that the substituent effect in the present system can be treated in the same way as those in the general chemical processes.

In view of the significance of fit to the correlation (2) of well-behaving substituents, dispositions of certain particular substituents, especially of several electron releasing groups, should be significant. The deviations can not be referred to the experimental error, but it is evident that some extraneous effects are operating in these groups. The precision within 0.010 in σ-unit would be high enough to permit the quantitative discussion of the extraneous effects producing significant deviations.

It should be noticed here that the present data are obtained from the measurement in anhydrous aprotic solvents. Several workers have pointed out the importance of the solvent effects on the NMR chemical shift and have offered a variety of rationalizations for the phenomena.40) Most of these rationalizations are based primarily on the intermolecular long range magnetic effect induced from the solvent molecule specifically oriented to solute molecule. It may be expected that the substituent-solvent interaction should take an important part of the solute-solvent interactions in usual aromatic molecules, since the substituent is one of the most polar sites of the solute molecule. The long range magnetic effect might not be so significant from the solvent molecule which coordinates to the substituent located far from the detecting function, while the effect of variation in the electronic nature of particular substituent due to strong interaction with solvent could not be neglected. The parameters of a given substituent should be subject to change by the modification of its electronic characters by the solvent-substituent interaction. Evidence has been accummulated which indicates that substituent effects on aromatic reactivities are not generally independent of solvents.41,42) Since the standard sets of substituent parameters were derived from the measurement in water (or aqueous organic solutions) where donative hydrogen bonding to substituents is highly important, certain deviations of particular substituents might be produced in the correlation of the data in aprotic solvents, upon employment of definite sets of parameters. Thus, it might be plausible to refer the deviations observed in the above correlation primarily to the effect of solvent-modification of substituent effects.

We should examine, first of all, the effect of *meta* substituents where no significant change is expected in the relative contribution of resonance from one series to another. Among a series of *meta* substituents, hydroxyl and amino groups exhibit exceptionally large deviations from the correlation (2); the apparent σ_m values of these groups are more negative than the ordinary σ_m values. It is qualitatively expected that not only these two but all the substituent which possesses a lone electron pair on the α-atom would be more electron releasing in hydrogen-bond acceptor solvents than estimated from the σ values in aqueous solution, from which donative hydrogen-bonding is effective. As a matter of fact, however, this effect does not appear so serious for general $-R$ *meta* substituents (except the above two particular groups) in the present system. Perhaps the small but real deviation of *m*-methoxy group may be referred to this effect. The loss of hydrogen-bond donation in non-aqueous solution can also explain reasonably the deviations of *m*-acetyl and *m*-carboalkoxy groups. Amino and hydroxyl groups, on the other hand, behave as the effective hydrogen-bond donor to DMF and DMSO solvents. The negative charge at hydroxyl oxygen or amino nitrogen due to hydrogen bonding with an acceptor solvent can make these groups further electron releasing, while such an effect would not be significant in aqueous solutions. Ritchie has recently noted the similar behavior of these groups in the dissociation of substituted benzoic acids in DMF solution.43)

From these facts, it appears necessary to utilize the substituent constant characteristic of a substituent in given solvents. It does not appear unreasonable, as a useful approximation, to assume that the apparent substituent constant in a given solvent is to be the ordinary effect characteristic of the "solvent-modified substituent," or of *the existing solvent-coordinated substituent species whose electronic character is effectively modified.* This assumption may be practically useful in view of facts that the modifications of parameters are required only for certain particular substituents and also that finite parameter values can be adopted to these groups for respective solvent classes, since for any particular substituent there is a consistent behavior in the range of solvents.

The effect of the solvent-modification should be operative with the same substituent at *para* position as well as *meta* position. This can be evidently shown in

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40) J. Ronayne and D. H. Williams, *J. Chem. Soc., B*, **1967**, 540; R. J. W. Le Fevre, D. V. Radford, G. L. D. Ritchie, and P. J. Stiles, *ibid.*, **1968**, 148; R. E. Klinck and J. B. Stothers, *Can. J. Chem.*, **40**, 2329 (1962); N. E. Alexandrou and D. Jannakoudakis, *Tetrahedron Lett.*, **1968**, 3841; T. Ledaal, *ibid.*, **1968**, 1683; N, Nakagawa and S. Fujiwara, This Bulletin, **34**, 143 (1961); I. D. Roe and L. K. Dyall, *Aust. J. Chem.*, **19**, 835 (1966); Y. Nomura and Y. Takeuchi, *J. Chem. Soc., B*, **1970**, 956.

41) C. D. Ritchie and G. H. Megerle, *J. Amer. Chem. Soc.*, **89**, 1447 (1967); C. D. Ritchie and R. E. Uschold, *ibid.*, **90**, 3415 (1968); C. D. Ritchie and E. S. Lewis, *ibid.*, **84**, 591 (1962).

42) A. Fischer, G. J. Leary, R. D. Topsom, and J. Vaughan, *J. Chem., Soc. B*, **1967**, 846.

43) C. D. Ritchie and R. E. Uschold, *J. Amer. Chem. Soc.*, **90**, 2821 (1968).

Fig. 1 as the deviations of particular substituents at both *para* and *meta* positions. Either of these substituents brings about the deviations of the same direction and of a comparable order of magnitude from both positions (or of a little greater extent from *para* position). This might partly validate the present discussion based on "solvent-modified substituent." For the correlation of *para* substituents, it is necessary to determine characteristic *r*-values of the system. Conjugatively electron attracting substituents in the present system (in DMF) give an r^- value, 0.639, but it is difficult to determine a unique r^+ value for conjugatively electron releasing substituents as mentioned in Result. However, as apparent substituent constants for most of $-R$ substituents do not differ from their original σ^0 values within the order of experimental uncertainty, excluding the substituents carrying an acidic hydrogen at the α-atom, we may estimate the r^+ value for electron releasing resonance contribution being approximately zero.

Previous investigators[11,13] have employed the standard σ_p values (*i.e.*, more exalted resonance scale, $r^+=0.27$) for *para* substituents instead of σ_p^0 values ($r^+=0.00$). *p*-Amino and *p*-hydroxyl groups fall near the line when they are correlated with σ_p values, while the subsequent deviations are resulted in the other groups, and such the treatment offers a difficulty in explaining why the substituent carrying an active α-hydrogen exerts the enhanced electron donation especially at *meta* position. Since the strongly electron donative detection center $-\overset{\delta-}{\mathrm{O}}\cdots\overset{\delta+}{\mathrm{H}}$ should prevent the additional resonance interaction with *para* $-R$ substituents, no significant resonance exaltation is expected for these *para* substituents. It appears thus more likely to refer the apparent σ-values for $-R$ *para* substituents in the present system to the σ^0, or the substituent parameters closely in the σ^0 scale, of the solvent-modified substituents rather than to the standard σ value.

In contrast to the complicated behaviors of $-R$ substituents, the effect of conjugatively electron attracting *para* substituents can be treated rather successfully as mentioned above. Figure 3 demonstrates the correlation between apparent enhancements, $\bar{\sigma}_p-\sigma_p^0$, of $+R$ *para* substituents in DMF solution and the corresponding $\Delta\bar{\sigma}_R^-$ parameters. Most of substituents fall on or near the straight line with a slope corresponding to the *r* value of 0.64. Carbonyl and sulfonyl derivatives exhibit weaker electron attracting effects than expected from the correlation, and deviations are most serious in $CONH_2$ and SO_2NH_2 groups.

The standard $\Delta\bar{\sigma}_R^-$ parameters ($=\sigma_p^- -\sigma_p^0$), should be the resonance parameters referable to the substituent groups effectively modified by water. To the contrary, the ordinate ($\bar{\sigma}_p-\sigma_p^0$), the apparent enhancement from the standard σ^0, should include the specific effect referable to the change in the solvent-substituent interaction in DMF (or DMSO) from that in water. This effect might cause substantial deviations for particular substituent, while the correlation in Fig. 2 or Fig. 3 is satisfactory for most of substituents, besides some carbonyl and sulfonyl groups which exert weaker electron attracting effect than expected. The reduction observed can be attributed to the fact that in aqueous solution the electron withdrawal of the carbonyl or sulfonyl is enhanced by virtue of its ability to disperse an acquired negative charge into the solvent through hydrogen bonding, but in either DMF or DMSO solution such an effect is inhibited. The consistent fact has been observed in the chemical reactivities.[42] The apparent σ_p^- value of *p*-acetyl group derived from the dissociation of phenols decreases from 0.87 in water to 0.80 in organic solvents, but no significant deduction is observed in σ_p^- of *p*-aldehyde group, in good accordance with the present result. The same effect may be also effective for other substituents. With $CONH_2$ and SO_2NH_2 groups, the similar effect discussed above for amino group could be also operative and hence the overall apparent effect is much more significant in these than the other carbonyl and sulfonyl groups.

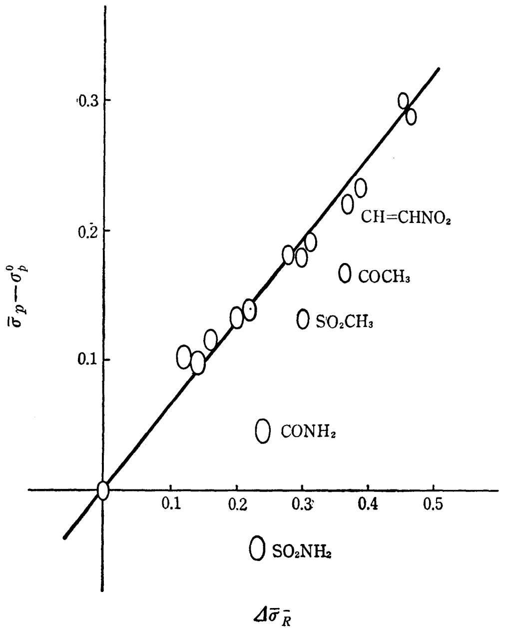

Fig. 3. The plot of the apparent resonance enhancements, $\bar{\sigma}_p-\sigma_p^0$, against standard $\Delta\bar{\sigma}_R^-$ values for $+R$ substituents.

The substituent-solvent interaction might afford the substantial changes in the inductive and then σ^0 parameters as well as in the resonance parameters of respective substituents. Therefore, the apparent enhancements from the standard σ^0 values, $\bar{\sigma}_p-\sigma_p^0$, are not merely referable to the exalted resonance contribution of substituents, but certain reflection of the change in the inductive component of solvent-modified substituents should be taken into consideration for the analysis of these parameters. Although the direct estimations of actual σ^0, inductive substituent constant σ_i, and resonance substituent constant σ_π, for solvent-modified substituents are not immediately possible, the following indirect methods may be applied as a useful approximation.

Inductive and π-Electronic Parameters in DMF

On the statistical analysis of the reaction-dependency of substituent constants, we have emphasized that the substituent effect on benzene reactivities could be separable, to a first approximation, into the inductive σ_i and π-electonic σ_π effects. *Para* and *meta* substituent effects can be expressed generally by a *Linear Substituent Free Energy* (LSFE) *Relationship* (3),[1,3]

$$\log (k/k_0)_p = \rho\bar{\sigma}_p = \rho(\sigma_i + q_r^+\sigma_\pi^+ + q_r^-\sigma_\pi^-) \qquad (3)$$

$$\log (k/k_0)_m = \rho\bar{\sigma}_m = \rho(1.17\sigma_i + 0.50\sigma_\pi^\pm) \qquad (3')$$

σ_i is the inductive substituent constant, independent of the varying contribution of resonance effect. σ_π^+ and $\sigma_\pi{}^-$ are the parameter measuring the capability of substituents to donate or withdraw electron through π-electronic delocalization. σ_π^+ corresponds numerically to 0.42 $\Delta\bar{\sigma}_R^+$ and σ_π^- to 0.73 $\Delta\bar{\sigma}_R^-$ in our LArSR Eq. (1).[44] q_r^+ and q_r^- are the characteristic variables of a given reaction or a given system, measuring the degree of π-electronic interaction with the detection center, and are in general mutually independent. Both q_r^+ and q_r^- are standardized in σ_p^0 scale to be unity; *i.e.*, $\sigma_p^0 = 1.00\ \sigma_i + 1.00\ \sigma_\pi^\pm$. As evident from the reaction-independence of σ_m values, the contribution of σ_π remains a constant, 0.50, in *meta* reactivities regardless of wide variations of reaction type. The fact that the inductive contribution from *meta* substituents is 1.17 times more effective, generally independent of reactions, than that from *para* substituents is a characteristic feature of our LSFE relationship. Combining both equations, can be derived the equations, in which the effect of inductive component is canceled out; for conjugatively electron attracting groups,

$$\log (k/k_0)_p - 0.85 \log (k/k_0)_m = \rho C^-\sigma_\pi^- \qquad (4)$$

and for conjugatively electron releasing groups,

$$\log (k/k_0)_p - 0.85 \log (k/k_0)_m = \rho C^+\sigma_\pi^+ \qquad (4')$$

where $C^\pm$ are practical constants corresponding to $q_r^\pm - 0.425$. Equation (4) is the *linear resonance free energy relationship* which can be practically utilized for the estimation of resonance parameters, without inquiring inductive parameters. If the operation of the same inductive contribution ratio might be assumed for the present system, this equation may be applied for the determination of resonance parameters of solvent-modified substituents. Equation (4) can be modified for ready applications for $+R$ substituents in the form;

$$\begin{aligned} 1/\rho(\Delta\delta_p^{\mathrm{OH}} - 0.85\Delta\delta_m^{\mathrm{OH}}) &= \bar{\sigma}_p - 0.85\bar{\sigma}_m \\ &= C_{\mathrm{M}}^-(\sigma_\pi^-)_{\mathrm{M}} = 0.73C_{\mathrm{M}}^-(\Delta\bar{\sigma}_R^-)_{\mathrm{M}} \qquad (5) \end{aligned}$$

$C_{\mathrm{M}}{}^-$ is a coefficient describing the effective resonance contribution of the system in a given medium M and should remain a constant for all $+R$ substituents. $(\sigma_\pi^-)_{\mathrm{M}}$ or $(\Delta\bar{\sigma}_R^-)_{\mathrm{M}}$ indicates the corresponding resonance parameter of the solvent-modified substituent in M. The same type of equation can be derived for $-R$ substituents; the right hand side of Eq. (5) is given by

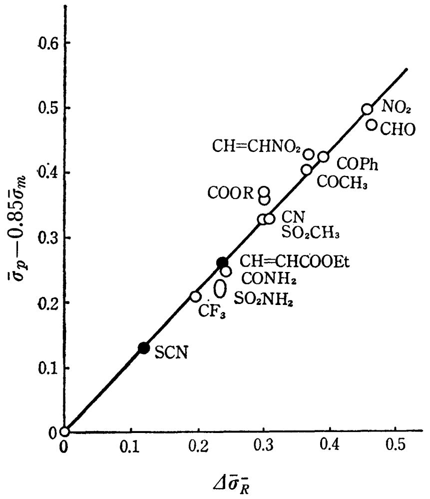

Fig. 4. The plot of the quantities, $\bar{\sigma}_p - 0.85\bar{\sigma}_m$, against standard $\Delta\bar{\sigma}_R^-$ values, for $+R$ substituents.

$$= C_{\mathrm{M}}^+(\sigma_\pi^+)_{\mathrm{M}} = 0.42C_{\mathrm{M}}^+(\Delta\bar{\sigma}_R^+)_{\mathrm{M}} \qquad (5')$$

The coefficient C_{M}^+ is usually not equal to C_{M}^-.

In Fig. 4 the quantities $(\bar{\sigma}_p - 0.85\ \bar{\sigma}_m)$ for $+R$ substituents in DMF solution are plotted against the standard $\Delta\bar{\sigma}_R^-$. The correlation resulted is unexpectedly excellent. The significant deviations of acetyl and methylsulfonyl groups observed in Fig. 3 are not apparent, and it is really surprising that carbamido group just falls on the line. SO_2NH_2 group also appears to satisfy the correlation when the solvent-modified $\bar{\sigma}_m$ value derived from the NH proton chemical shifts of anilines and acetanilides is employed, though we were unable to prepare *m*-sulfonamido-phenol in pure form. The deviations from the line are at most within 0.05 in σ unit. A linear correlation with closely the same order of precision can be obtained for the corresponding quantities in DMSO solution.

It would be then concluded that the solvent-modification of substituent by DMF or DMSO does not affect significantly the resonance parameters so far as are concerned the conjugatively electron attracting substituents. The variation of the apparent substituent constants of these groups in aprotic DMF would be caused predominantly by the solvent-modification of the inductive nature of substituents. On the basis of the apparent slope of the above correlation line 1.09 which corresponds to 0.73 C_{M}^-, $(\Delta\bar{\sigma}_R^-)_{\mathrm{DMF}}$ values can be derived. Since the slope 1.09 should correspond to 0.73 $(q_r^- - 0.425)$, according to Eqs. (3) and (5), $(\sigma_i)_{\mathrm{DMF}}$ can be derived by using Eq. (6).

$$\begin{aligned} (\sigma_i)_{\mathrm{DMF}} &= \bar{\sigma}_p - 0.73q_r^-(\Delta\bar{\sigma}_R^-)_{\mathrm{DMF}} \\ &= \bar{\sigma}_p - 1.40(\Delta\bar{\sigma}_R^-)_{\mathrm{DMF}} \qquad (6) \end{aligned}$$

By the combination of $(\sigma_i)_{\mathrm{DMF}}$ and $(\Delta\bar{\sigma}_R^-)_{\mathrm{DMF}}$, we can calculate a set of $(\sigma^0)_{\mathrm{DMF}}$ for $+R$ substituents modified by DMF solvent. These apparent sets of parameters are summarized in Table 4.

The new parameters for styryl derivative groups appear to be practically useful, even though certain but probably minor solvent-modification should be taken into account. As discussed in the above, the differences of $(\sigma_p^0)_{\mathrm{DMF}}$ from the standard σ_p^0 are signifi-

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[44] $\Delta\bar{\sigma}_R^-$ values given in Table 2 and employed in this study are those derived from the most reliable set of σ_p^- values which have been determined from reliable p*K*a values of phenols, anilines, and dimethylanilines in water. In a previous paper (Ref. 1a) we have noted preliminarily, on the basis of σ_p^- values in the literature, that σ_π^- corresponds to 0.81 $\Delta\bar{\sigma}_R^-$. However, detailed examination of the above new set of σ_p^- values indicates that σ_π^-, the π-electronic effect of $+R$ substituents in σ_p^0 scale should correspond to 0.73 $\Delta\bar{\sigma}_R^-$. Full data and relevant discussions will be published in the near future.

Table 4. Modified substituent parameters in DMF for $+R$ groups

Subst.	$(\Delta\bar{\sigma}_R^+)_{\mathrm{DMF}}$	$(\sigma_i)_{\mathrm{DMF}}$	$(\sigma_p^0)_{\mathrm{DMF}}$
NO_2	0.459	0.467	0.802
CHO	0.434	0.214	0.531
CN	0.303	0.419	0.640
CF_3	0.191	0.371	0.510
$COCH_3$	0.375	0.128	0.402
COC_6H_5	0.391	0.177	0.462
$COOCH_3$	0.339	0.164	0.411
COOEt	0.337	0.160	0.406
SO_2CH_3	0.301	0.398	0.618
$CH{=}CHNO_2$	0.393	0.171	0.458
CH=CHCOOEt	0.240	0.133	0.308
$CONH_2$	0.226	0.109	0.274
SO_2NH_2	0.20	0.32	0.47

cant in carbonyl derivatives and remarkable in amide groups and they are clearly a reflection of the solvent-modification of the inductive components.

Evidences for the solvent-dependence of inductive parameters have been presented on the basis of various studies,[39] among which Taft's study of σ_I using ^{19}F NMR chemical shifts of substituted fluorobenzenes is the most practical and comprehensive.[36] He pointed out that ^{19}F substituent chemical shifts of *m*-substituted fluorobenzenes were correlated linearly with his σ_I parameters, derived from chemical reactivities. This is true in the case of the relative substituent chemical shifts in aqueous methanol, whereas the relative shift in DMF solution does not give so excellent plot against the σ_I.[41] The deviation might primarily arise as a result of solvent-modification in the inductive component of substituents. The analogous variation is expected to be involved in the present DMF system, and in fact $(\sigma_i)_{\mathrm{DMF}}$ are found to correlate linearly with the ^{19}F *m*-substituent chemical shifts in DMF solution. If the substituent chemical shift of *m*-substituted fluorobenzenes, as Taft assumed, being a linear function of inductive parameters is valid, it is then suggested that the present set of $(\sigma_i)_{\mathrm{DMF}}$ evaluates reasonably the inductive effect of the substituents solvated by DMF solvent, and subsequently, this may also offer an evidence justifying the above estimation of resonance parameters in DMF. Even though the test may not yet be regarded as critical, these treatments may have promising applicability to appropriate systems.

For conjugatively electron releasing ($-R$) substituents, the quantities ($\bar{\sigma}_p-0.85\,\bar{\sigma}_m$) are practically not proportional to the standard $\Delta\bar{\sigma}_R^+$ values. However, in view of the significance of the fit of $+R$ substituents to the above treatment (5), the *para/meta* inductive contribution ratio of 0.85 would be assumed for $-R$ substituents. It may be also assumed that the quantities ($\bar{\sigma}_p-0.85\,\bar{\sigma}_m$) for $-R$ groups in DMF solution are proportional to $(\Delta\bar{\sigma}_R^+)_{\mathrm{DMF}}$. In order to practify the separation of substituent effect into σ_i and $\Delta\bar{\sigma}_R^+$ (or σ_π^+) contributions in the present system, it is necessary first to provide the C^+_{DMF} scale of $(\Delta\bar{\sigma}_R^+)_{\mathrm{DMF}}$ contribution. As discussed in the foregoing section, if the present set of apparent $\bar{\sigma}_p$ for $-R$ groups could be referable to the σ_p^0 for solvent-modified substituents in DMF solution, the scale of $(\Delta\bar{\sigma}_R^+)_{\mathrm{DMF}}$ or the C^+_{DMF} value for $-R$ substituents can be estimated to be 0.575 on the basis of *meta/para* σ_π-contribution ratio of 0.50 which is a characteristic of the σ^0 scale. Namely, the resonance contribution of these substituents might be roughly approximated by means of Eq. (7)

$$(\bar{\sigma}_p-0.85\bar{\sigma}_m) = 0.242(\Delta\bar{\sigma}_R^+)_{\mathrm{DMF}} \tag{7}$$

This may lead to the crude estimation of $(\sigma_i)_{\mathrm{DMF}}$ values for $-R$ substituents by

$$\begin{aligned}(\sigma_i)_{\mathrm{DMF}} &= \bar{\sigma}_p - 1.74(\bar{\sigma}_p-0.85\bar{\sigma}_m)\\ &= 1.48\bar{\sigma}_m - 0.74\bar{\sigma}_p\end{aligned}$$

Table 5. Modified substituent parameters in DMF for $-R$ groups

Subst.	$(\Delta\bar{\sigma}_R^+)_{\mathrm{DMF}}$	$(\sigma_i)_{\mathrm{DMF}}$
I	0.02	0.26
Br	−0.28	0.38
Cl	−0.34	0.39
F	−1.09	0.50
SCH_3	−0.03	0.10
OC_6H_5	−0.57	0.29
NHAc	−0.41	0.08
NHC_6H_5	−0.45	0.03
t-Bu	−0.15	−0.06
CH_3	−0.36	0.01
OCH_3	−1.15	0.22
OH	−1.39	0.17
NMe_2	−1.07	0.01
NH_2	−1.37	−0.01

The results are summarized in Table 5. Although the crudeness of derivation does not permit the detailed discussion of these results, Table 5, as a whole, indicates that both $(\Delta\bar{\sigma}_R^+)_{\mathrm{DMF}}$ and $(\sigma_i)_{\mathrm{DMF}}$ derived are considerably modified from the standard values. This fact is in contrast with the result for conjugatively electron attracting substituents (Table 4). The solvent-modification of inductive effect appears serious for OH, NH_2, and $NHCOCH_3$ groups. The exaltation of π-electronic parameter is also most remarkable for these groups. The above treatment stands on the basis that the solvent-modification of substituents could be practically regarded as a minor perturbation as compared with the change in the electronic nature of the detection function, and the apparent nature of the modified substituent might be sufficiently invariable in *meta* and *para* positions in the system of interest. This may generally hold in usual chemical reactivities, while in the present case, especially of hydrogen-bond donor substituents, such as amino, hydroxyl and acetamino groups, the solvent-modification should no longer be a minor perturbation but a change of comparable importance with that of the detection function. There seems to be the possibility for these particular groups to result in the failure of the above treatment. Despite such the possible limitation of application, $(\sigma_i)_{\mathrm{DMF}}$ values for most of $-R$ substituents including these particular groups can be correlated linearly with reasonable precision to $\Delta\Delta\delta^{F}_{m\text{-}X}$ values of *m*-substituted fluorobenzenes in DMF solution. This may suggest that the error induced from this treatment could not be so serious.

Since related facts of interest have been available from our studies of the substituent chemical shifts of phenols and of amino protons of acetanilides and anilines in various aprotic solvents, the further discussion will be presented in accompanying papers.