EFFECT OF *para* SUBSTITUTION ON DISSOCIATION OF *N*-PHENYLBENZENESULFONAMIDES

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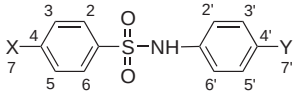
The reaction of substituted anilines and benzenesulfonyl chlorides has been used to prepare 49 substituted *N*-phenylbenzenesulfonamides of general formula 4-X-$C_6H_4SO_2NHC_6H_4$-Y-4′. Their purity was checked by elemental analysis. The substituents X and Y include H, CH_3, CH_3O, Cl, Br, CN, and NO_2. The dissociation constants of all compounds were determined by potentiometric titration in methanol, acetonitrile, *N*,*N*-dimethylformamide, and pyridine. The obtained dissociation constants, pK_{HA}, were correlated with various sets of substituent constants. It was found that the effects of substituents X and Y on the dissociation are best described by using the Hammett equation with σ_p constants and the Yukawa–Tsuno equation with σ_p^- and σ_p constants, respectively. This result confirms the direct conjugation of Y substituent with the reaction centre. The explained variability using the additive model was above 96% in all the solvents used. The data also provided information about the transmission effect of the SO_2 group. The average dissociation constants were further processed by the latent variables methods, principal components and conjugated deviations analyses.
Keywords: Sulfonamides; Dissociation constant; Substituent effects; Transmission effect; Chemometrics; Acidity; Hammett equation.

The validity of the Hammett relationship has already been verified on a large number of various substrates involving benzoic acids, anilines, phenols, naphthoic acids, *N*-phenylsulfonylbenzamides, etc. Another interesting substrate for studies in this area is *N*-phenylbenzenesulfonamide **1** with substituents at positions 4 and 4′.

The reaction centre of this compound (amide nitrogen atom) is connected to two benzene rings – one of them directly and the other through the partly isolating SO_2 group. This enables monitoring of two different ways of substituent affecting in one model system. It can be presumed that the X substituents will affect the dissociation constant less compared with the Y substituents. In addition, there exists a possibility that the negative charge of the conjugated base of *N*-phenylbenzenesulfonamide will be

delocalized by direct conjugation into the Y substituent due to its location at the alternating *para*-position in the benzene ring.



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	Y						
X	OCH_3	CH_3	H	Cl	Br	CN	NO_2
OCH_3	**1aa**	**1ab**	**1ac**	**1ad**	**1ae**	**1af**	**1ag**
CH_3	**1ba**	**1bb**	**1bc**	**1bd**	**1be**	**1bf**	**1bg**
H	**1ca**	**1cb**	**1cc**	**1cd**	**1ce**	**1cf**	**1cg**
Cl	**1da**	**1db**	**1dc**	**1dd**	**1de**	**1df**	**1dg**
Br	**1ea**	**1eb**	**1ec**	**1ed**	**1ee**	**1ef**	**1eg**
CN	**1fa**	**1fb**	**1fc**	**1fd**	**1fe**	**1ff**	**1fg**
NO_2	**1ga**	**1gb**	**1gc**	**1gd**	**1ge**	**1gf**	**1gg**

This communication is not the first to deal with measurement and evaluation of dissociation constants of *para*-substituted *N*-phenylbenzenesulfonamide. However, it tries to approach the problem as systematically as possible. Earlier papers usually covered smaller sets of these compounds or structurally cognate ones. The dissociation constants found are used in those papers as comparison series in studies of tautomeric equilibria[1], studies of substituent effects on p*K* of various compounds[2,3], or they are correlated with kinetic data[4]. More extensive investigation in this field is represented by papers of Dauphin and Kergomard[5–7], who used water and aqueous ethanol of various concentrations as the media for measurements of dissociation constants. Another paper of interest by Javůrková[8] deals with *N*-phenylbenzenesulfonamides with substituents present only in the aniline moiety. The paper[9] by Nádvorník also should be mentioned, since it studies the *ortho*-effect in *N*-phenylbenzenesulfonamide as the substrate and forms a complement to this study.

The chief aim of the present work is to compare the substituent effects from the two benzene rings of model compounds upon the value of dissociation constants. The paper forms a continuation of former studies dealing with various *N*-phenylbenzenesulfonamides[8,9].

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra of the model compounds not yet described in literature were measured on a Bruker AMX 360 apparatus using their 5% solutions in DMSO-d_6 and the chemical shifts (δ, ppm) were referenced to the solvent signal. The purity of sulfonamides was checked by elemental analysis using an automatic analyser EA 1108 (Fisons). The dissociation constants of all the substances at 25 °C in methanol (MeOH), acetonitrile (AN), *N*,*N*-dimethylformamide (DMF), and pyridine (Py) were determined by potentiometric titrations using TITRALAB 3 automatic titrator (Radiometer). The method of measurement and the electrode arrangement used were the same as in our previous paper[10]. Each measurement was repeated three to five times. The solvents used (HPLC purity) were additionally dried over molecular sieves.

Syntheses of Intermediates

4-Cyanobenzenesulfonyl chloride was prepared from 4-aminobenzonitrile by diazotization and decomposition of the diazonium salt with sulfur dioxide in the presence of cuprous chloride (a modification of known procedure[11]). Yield 72%, m.p. 90–103 °C (lit.[12] gives m.p. 110 °C); it was not necessary to purify this compound for next syntheses.

4-Chlorobenzenesulfonyl chloride was synthesized from chlorobenzene by reaction with chlorosulfuric acid (a modification of known procedure[13]). Yield 81%, m.p. 45.5–47.5 °C (lit.[14] gives m.p. 53 °C).

Syntheses of Substituted *N*-Phenylbenzenesulfonamides

The model substances were prepared by the following general procedure: an aniline derivative (0.011 mol) was dissolved in pyridine (1 ml, 0.0125 mol) and benzenesulfonyl chloride (0.01 mol) was added. The reaction mixture was heated on boiling water bath for 5 min and then mixed with dilute hydrochloric acid. The crude product was reprecipitated from its solution in aqueous sodium hydroxide, which was filtered with charcoal and acidified with hydrochloric acid. Then the product was recrystallized from aqueous ethanol (the water content varied depending on the particular product).

The syntheses starting from 4-cyanobenzenesulfonyl chloride had to omit the reprecipitation from sodium hydroxide solution since the CN group is quickly hydrolyzed to $CONH_2$ in the alkaline medium. This fact was confirmed by both elemental analysis and NMR spectroscopy.

The yields, melting temperatures, and elemental analyses of seven model sulfonamides not yet described in literature are given below.

1af: Yield 30%, m.p. 188–191 °C. ^{1}H NMR (DMSO-d_6): 3.81 s, 3 H (H-7); 7.10 d, 2 H (H-2′,6′); 7.31 d, 2 H (H-3,5); 7.72 d, 2 H (H-2,6); 7.84 d, 2 H (H-3′,5′). ^{13}C NMR (DMSO-d_6): 55.9, 105.5, 114.9, 118.6, 119.0, 129.3, 130.8, 133.9, 142.7, 163.1. For $C_{14}H_{12}N_2O_3S$ (288.3) calculated: 58.32% C, 4.20% H, 9.72% N, 11.12% S; found: 58.28% C, 4.22% H, 9.53% N, 10.83% S. **1ef**: Yield 30%, m.p. 186–188 °C. ^{1}H NMR (DMSO-d_6): 7.31 d, 2 H (H-3′,5′); 7.74 d, 2 H (H-2′,6′); 7.80 s, 4 H (H-2,3,5,6). ^{13}C NMR (DMSO-d_6): 106.1, 118.9, 119.1, 127.7, 129.0, 132.9, 134.0, 138.6, 142.2. For $C_{13}H_9BrN_2O_2S$ (337.2) calculated: 46.31% C, 2.69% H, 23.70% Br, 8.31% N, 9.51% S; found: 46.82% C, 2.78% H, 24.15% Br, 8.21% N, 8.75% S. **1fa**: Yield 31%, m.p. 142.5–144.5 °C. ^{1}H NMR (DMSO-d_6): 3.71 s, 3 H (H-7′); 6.85 d, 2 H (H-3′,5′); 7.02 d, 2 H (H-2′,6′); 7.87 d, 2 H (H-3,5); 8.06 d, 2 H (H-2,6). ^{13}C NMR (DMSO-d_6):

55.2, 114.5, 115.2, 117.6, 124.1, 127.5, 129.3, 133.3, 143.5, 157.0. For $C_{14}H_{12}N_2O_3S$ (288.3) calculated: 58.32% C, 4.20% H, 9.72% N, 11.12% S; found: 58.09% C, 4.19% H, 9.71% N, 10.93% S. **1fd**: Yield 30%, m.p. 174–180.5 °C. ^{1}H NMR (DMSO-d_6): 7.15 d, 2 H (H-2′,6′); 7.36 d, 2 H (H-3′,5′); 7.94 d, 2 H (H-3,5); 8.10 d, 2 H (H-2,6). ^{13}C NMR (DMSO-d_6): 115.8, 117.8, 122.5, 127.7, 129.2, 129.6, 133.8, 136.2, 143.4. For $C_{13}H_9ClN_2O_2S$ (292.8) calculated: 53.34% C, 3.10% H, 12.11% Cl, 9.57% N, 10.95% S; found: 53.30% C, 2.77% H, 12.25% Cl, 9.44% N, 10.85% S. **1fe**: Yield 53%, m.p. 205–210 °C. ^{1}H NMR (DMSO-d_6): 7.11 d, 2 H (H-2′,6′); 7.45 d, 2 H (H-3′,5′); 7.96 d, 2 H (H-3,5); 8.05 d, 2 H (H-2,6). ^{13}C NMR (DMSO-d_6): 115.9, 117.3, 117.8, 122.7, 127.7, 132.5, 133.7, 136.7, 143.4. For $C_{13}H_9BrN_2O_2S$ (337.2) calculated: 46.31% C, 2.69% H, 23.70% Br, 8.31% N, 9.51% S; found: 46.35% C, 2.62% H, 24.29% Br, 8.35% N, 9.65% S. **1fg**: Yield 60%, m.p. 193–194.5 °C. ^{1}H NMR (DMSO-d_6): 7.37 d, 2 H (H-2′,6′); 8.06–8.20 m, 6 H (H-2,3,5,6,3′,5′). ^{13}C NMR (DMSO-d_6): 116.0, 117.4, 118.5, 125.4, 127.5, 133.8, 143.0, 143.1, 143.5. For $C_{13}H_9N_3O_4S$ (303.3) calculated: 51.48% C, 2.99% H, 13.85% N, 10.57% S; found: 51.65% C, 2.98% H, 13.80% N, 10.53% S. **1gf**: Yield 45%, m.p. 193–196°C. ^{1}H NMR (DMSO-d_6): 7.33 d, 2 H (H-2′,6′); 7.74 d, 2 H (H-3′,5′); 8.13 d, 2 H (H-2,6); 8.41 d, 2 H (H-3,5). ^{13}C NMR (DMSO-d_6): 106.5, 118.8, 119.4, 125.1, 128.6, 134.0, 141.8, 144.6, 150.4. For $C_{13}H_9N_3O_4S$ (303.3) calculated: 51.48% C, 2.99% H, 13.85% N, 10.57% S; found: 51.74% C, 3.02% H, 13.94% N, 10.72% S.

RESULTS AND DISCUSSION

The values of dissociation constants of the substrates are given as average values $p\bar{K}_{HA}$ (with standard deviations) in Table I. In order to examine the effect of medium on the dissociation process, four solvents were selected for the titration. The choice respected the requirement for using current titration media and rough coverage of the basic types of solvents: amphiprotic methanol, dipolar aprotic protophobic acetonitrile, dipolar aprotic protophilic *N*,*N*-dimethylformamide, and pyridine which additionally has basic properties. The substituents chosen can be classified as ones without any distinct resonance effect (CH_3, H, Cl, Br), those with positive resonance effect (OCH_3), and those with negative resonance effect (NO_2, CN). This choice appeared to be representative sample of substituents in our recent studies.

Mean values of the dissociation constants measured were subjected to calculations by the methods with latent variables. The main goal of these calculations is to isolate significant informations including in data matrices via obtaining individual latent variable vectors. Both methods used, principal components analysis (PCA)[15] and conjugated deviations analysis (CDA)[16], gave comparable results. Therefore, mainly only the results from PCA will be discussed here. The mean values of dissociation constants, $p\bar{K}_{HA}$, were arranged into a matrix ***A*** comprising 4 columns (solvents) and 49 rows (substrates). The calculation on this matrix revealed two latent variables as statistically significant. The first latent variable ***t1A*** explained

TABLE I
Mean values of dissociation constants ($p\bar{K}_{HA}$) and their standard deviations (*s*) of substituted *N*-phenylbenzenesulfonamides **1** in individual solvents at 25 °C

1	MeOH	AN	DMF	Py
1aa	13.58(0.02)	23.99(0.09)	14.45(0.16)	11.83(0.07)
1ab	13.47(0.02)	23.62(0.10)	14.30(0.07)	12.06(0.13)
1ac	13.28(0.03)	23.71(0.08)	13.78(0.07)	11.41(0.05)
1ad	12.75(0.02)	22.75(0.13)	13.06(0.07)	10.55(0.07)
1ae	12.66(0.03)	22.61(0.11)	12.88(0.01)	10.09(0.10)
1af	11.47(0.02)	21.20(0.02)	11.53(0.08)	8.46(0.12)
1ag	11.09(0.06)	20.39(0.04)	10.52(0.06)	7.48(0.05)
1ba	13.52(0.04)	23.86(0.11)	14.15(0.11)	11.98(0.02)
1bb	13.46(0.11)	24.21(0.03)	13.57(0.14)	11.77(0.04)
1bc	13.21(0.03)	23.87(0.12)	13.34(0.11)	11.36(0.18)
1bd	12.63(0.08)	22.58(0.14)	12.67(0.04)	10.40(0.07)
1be	12.64(0.02)	22.81(0.04)	12.68(0.13)	10.27(0.07)
1bf	11.36(0.08)	20.99(0.13)	11.37(0.05)	8.32(0.15)
1bg	10.97(0.01)	20.39(0.04)	10.25(0.06)	7.65(0.14)
1ca	13.50(0.04)	23.36(0.07)	13.21(0.09)	11.78(0.17)
1cb	13.38(0.02)	23.14(0.12)	13.13(0.03)	11.51(0.06)
1cc	13.17(0.02)	23.42(0.10)	12.89(0.07)	10.99(0.02)
1cd	12.61(0.03)	22.57(0.02)	12.53(0.07)	9.94(0.02)
1ce	12.52(0.02)	22.47(0.03)	12.41(0.13)	10.01(0.04)
1cf	11.22(0.03)	20.72(0.05)	11.45(0.08)	7.85(0.01)
1cg	10.76(0.05)	19.93(0.04)	10.11(0.05)	6.98(0.04)
1da	13.12(0.01)	22.85(0.04)	12.97(0.04)	11.10(0.03)
1db	13.11(0.01)	22.83(0.14)	12.71(0.04)	10.58(0.14)
1dc	12.85(0.02)	22.52(0.01)	12.69(0.08)	10.30(0.14)
1dd	12.20(0.01)	21.77(0.10)	12.35(0.03)	9.82(0.11)
1de	12.08(0.03)	21.50(0.11)	12.17(0.08)	9.96(0.07)
1df	10.81(0.04)	20.23(0.13)	11.17(0.04)	7.32(0.02)
1dg	10.37(0.03)	19.38(0.02)	9.50(0.06)	6.46(0.07)
1ea	13.29(0.07)	23.13(0.11)	13.42(0.05)	10.91(0.03)
1eb	13.05(0.04)	23.01(0.10)	13.10(0.11)	10.78(0.12)
1ec	12.84(0.05)	22.63(0.06)	12.81(0.08)	10.49(0.12)
1ed	12.23(0.02)	21.81(0.06)	12.02(0.05)	9.19(0.02)
1ee	12.08(0.05)	21.79(0.10)	12.09(0.08)	9.37(0.08)
1ef	10.81(0.03)	20.10(0.01)	10.68(0.12)	7.79(0.03)
1eg	10.42(0.05)	19.56(0.03)	9.51(0.08)	7.02(0.10)
1fa	12.06(0.02)	22.74(0.09)	12.67(0.04)	10.12(0.05)
1fb	11.85(0.06)	22.41(0.01)	12.47(0.01)	9.83(0.01)
1fc	11.65(0.02)	22.05(0.03)	12.19(0.07)	9.42(0.02)
1fd	11.13(0.06)	21.17(0.04)	11.58(0.03)	8.47(0.03)
1fe	11.12(0.05)	21.13(0.08)	11.52(0.03)	8.41(0.01)
1ff	10.04(0.06)	19.42(0.12)	10.26(0.04)	6.61(0.03)
1fg	9.74(0.02)	18.70(0.03)	8.97(0.06)	5.83(0.01)
1ga	12.56(0.03)	22.59(0.01)	12.59(0.06)	9.85(0.03)
1gb	12.44(0.02)	21.96(0.11)	12.36(0.04)	9.57(0.05)
1gc	12.08(0.07)	21.63(0.12)	12.01(0.05)	9.11(0.06)
1gd	11.47(0.00)	20.79(0.13)	11.25(0.04)	8.11(0.04)
1ge	11.40(0.01)	20.67(0.11)	11.12(0.05)	8.05(0.01)
1gf	10.08(0.02)	19.31(0.06)	9.60(0.05)	6.27(0.02)
1gg	9.67(0.01)	18.41(0.02)	8.80(0.06)	5.35(0.08)

98.24% of variability of the source matrix; the second latent variable describing another 0.99% variability was at the limit of statistical significance. It can be stated that the values of the latent variable ***t1A*** obtained express the combined effect of both substituents, X and Y, on the dissociation of the model substrates free from further effect affecting the extent of dissociation, particularly the solvent effect. Plotting of these data against the substituent constants[17] σ_p provides a better view of relationships between substituents and the dissociation constants. The dependence of ***t1A*** vs σ_p(X) presented in Fig. 1 shows 7 descending series of 7 points each: in each serie there is always a non-variable Y substituent and varying X. Hence we should actually observe seven Hammett straight lines. However, it can be seen, e.g., that the points for X = OCH_3 (σ_p = –0.28) have a lower ***t1A*** value than expected from the linear relationship: this substituent shows thus a weaker donor effect, approaching that of X = CH_3 (σ_p = –0.14). Also, it is obviously not correct to consider comparable substituent effects for X = Cl and Br (both σ_p = 0.22). Clearly, the points corresponding to this substitution do not overlap in the picture, which indicates slightly different effects of Cl and Br substituents from the X position. Figure 2 shows the dependence of ***t1A*** vs σ_p(Y), i.e. each of the descending serie expresses 7 compounds with a constant X substituent and varying Y. Compared with Fig. 1, it can be seen that the individual Hammett straight lines have larger slopes and their distances at the ***t1A*** axis are smaller. This result corresponds to the presumption that the sensitivity of the model substrates to Y substitution is higher and that to X substitution is lower. Moreover, it can be seen

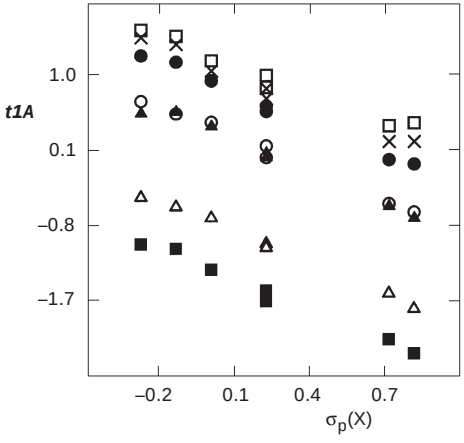

FIG. 1
Dependence diagram of ***t1A*** vs σ_p(X). Y = □ OCH_3, × CH_3, ● H, ○ Cl, ▲ Br, △ CN, ■ NO_2

that all the points with Y = NO_2 (σ_p = 0.81) show lower ***t1A*** values than expected from the linear dependence, which corresponds with the idea of direct conjugation between the substituent and reaction centre; depending on the extent of this conjugation, the substituent constant of nitro group generally assumes the values up to σ_p^- (1.25).

In order to further evaluate the relationship between the type of substitution and the extent of dissociation, the $p\overline{K}_{HA}$ values were arranged into two similar matrices. In the matrix ***XY***, containing 7 rows and 28 columns, the rows represent X substituents and each column represents a substituent Y–solvent combination. The matrix ***YX*** of the same dimensions was arranged analogously: the rows represent various Y substituents, and the columns represent various substituent X–solvent combinations. The PCA calculation on matrix ***XY*** revealed two latent variables as statistically significant, first (***t1XY***) describing 93.18% variability and second (***t2XY***) describing another 3.17% variability of the source matrix. The obtained vector ***t1XY*** expresses the substituent effect of X substituents. The CDA calculation on the same matrix showed that the second latent variable has a high value for X = CN and manifests itself in all the seven columns for MeOH. In methanol, it is possible to observe a higher acidity of derivatives with X = CN compared with those with X = NO_2, which is unusual. Hence it can be presumed that the second variable in matrix ***XY*** will probably describe this phenomenon.

The PCA calculation on ***YX*** matrix gave two statistically significant latent variables ***t1YX*** and ***t2YX***, describing 98.80 and 0.68% variability of the

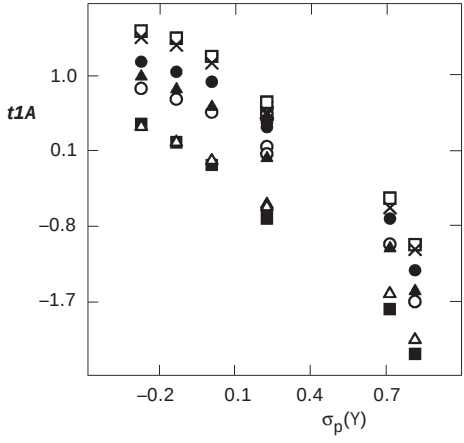

FIG. 2
Dependence diagram of ***t1A*** vs σ_p(Y). X = □ OCH_3, × CH_3, ● H, ○ Cl, ▲ Br, △ CN, ■ NO_2

source matrix, respectively. The obtained vector ***t1YX*** expresses substituent effects of Y substituents. The distinctly highest contribution of the second latent variable is in the column DMF, X = Cl. The physical meaning of this second latent variable was not found; probably it is caused by higher variability of data just in this column. The values of vectors of the individual latent variables, ***t1XY***, ***t2XY***, ***t1YX***, ***t2YX***, are presented in Table II. To make the picture clearer and comparisons of substituent effects from X and Y positions easier, the ***t1XY***, ***t1YX*** vectors were transformed to ***t1XY****, ***t1YX**** by assigning the value of 0 to the substituent H, and the resulting values were given with opposite signs (see Table II).

The correlations of ***t1XY*** and ***t1YX*** vs σ_p, vs σ_p^-, and vs σ_I, σ_R (lit.[17]) were calculated. Relations ***t1XY*** vs σ_p (r = 0.9974) and ***t1YX*** vs σ_p^- (r = 0.9951) were found as the best correlations. This result indicates the manifestation of direct conjugation between Y substituent and the reaction centre, too.

The dissociation constants measured were correlated with various sets of substituent constants to find a model describing the dissociation as close as possible. Following models were tested:

1. $pK = pK^0 - \rho_X\sigma_p - \rho_Y\sigma_p$, Hammett model with substituent constants σ_p for both nuclei

2. $pK = pK^0 - \rho_X\sigma_p - \rho_Y\sigma_p^-$, Hammett model with substituent constants σ_p for X substituents and substituent constants[17] σ_p^- for Y substituents

3. $pK = pK^0 - \rho_X\sigma_{P6} - \rho_Y\sigma_{P6}$, Hammett model with substituent constants σ_{P6} adjusted from processes in non-aqueous media[18]

4. $pK = pK^0 - \rho_{IX}\sigma_I - \rho_{RX}\sigma_R - \rho_{IY}\sigma_I - \rho_{RY}\sigma_R$, Taft model with separated inductive (I) and mesomeric (R) effects of substituents[17]

TABLE II
Values of vectors of latent variables from PCA calculations on matrices ***XY*** and ***YX***

Vector	OCH_3	CH_3	H	Cl	Br	CN	NO_2
t1XY	1.1530	0.9960	0.5604	–0.0966	–0.0301	–1.1950	–1.3880
t2XY	1.0350	0.4989	–1.0690	–1.3550	–0.1717	1.2750	–0.2137
t1YX	1.0100	0.8657	0.6596	0.1027	0.0502	–1.0530	–1.6350
t2YX	–0.3343	–0.7604	–0.1886	0.8115	0.5887	1.4010	–1.5180
t1XY*	0.5929	0.4356	0	–0.6570	–0.5303	–1.7554	–1.9484
t1YX*	0.3504	0.2061	0	–0.5569	–0.6094	–1.7126	–2.2946

TABLE III
Regression characteristics of regression models 1–5

Solvent	Model	pK^0 (*s*)	ρ_X (*s*)	ρ_Y (*s*)	ρ_{IX} (*s*) ρ_{RX} (*s*)	ρ_{IY} (*s*) ρ_{RY} (*s*)	*r* (*s*)	*R* (*s*)
MeOH	1	12.90 (0.02)	1.37 (0.04)	2.52 (0.04)	–	–	–	0.984 (0.197)
	2	13.02 (0.02)	1.38 (0.04)	1.89 (0.03)	–	–	–	0.986 (0.186)
	3	12.88 (0.02)	1.53 (0.06)	2.85 (0.06)	–	–	–	0.974 (0.254)
	4	12.99 (0.03)	–	–	1.76 (0.05) 1.58 (0.07)	3.26 (0.05) 2.87 (0.07)	–	0.989 (0.165)
	5	12.97 (0.02)	1.38 (0.03)	2.19 (0.05)	–	–	0.48 (0.06)	0.989 (0.164)
AN	1	22.94 (0.03)	1.75 (0.06)	3.39 (0.06)	–	–	–	0.980 (0.293)
	2	23.10 (0.03)	1.76 (0.05)	2.56 (0.04)	–	–	–	0.984 (0.264)
	3	22.94 (0.03)	2.02 (0.08)	3.84 (0.08)	–	–	–	0.976 (0.324)
	4	23.23 (0.05)	–	–	2.42 (0.08) 1.63 (0.10)	4.45 (0.08) 3.77 (0.10)	–	0.986 (0.245)
	5	23.05 (0.03)	1.76 (0.05)	2.91 (0.08)	–	–	0.54 (0.08)	0.987 (0.244)
Py	1	10.73 (0.03)	2.12 (0.06)	4.06 (0.06)	–	–	–	0.988 (0.275)
	2	10.91 (0.03)	2.12 (0.05)	3.04 (0.04)	–	–	–	0.990 (0.254)
	3	10.71 (0.04)	2.41 (0.08)	4.61 (0.08)	–	–	–	0.981 (0.347)
	4	10.89 (0.04)	–	–	2.76 (0.07) 2.34 (0.09)	5.25 (0.07) 4.65 (0.09)	–	0.993 (0.211)
	5	10.84 (0.02)	2.12 (0.04)	3.53 (0.07)	–	–	0.48 (0.05)	0.993 (0.211)
DMF	1	13.05 (0.03)	1.55 (0.07)	3.11 (0.07)	–	–	–	0.969 (0.341)
	2	13.20 (0.03)	1.56 (0.06)	2.36 (0.04)	–	–	–	0.979 (0.283)
	3	13.03 (0.04)	1.77 (0.09)	3.53 (0.09)	–	–	–	0.962 (0.378)
	4	13.02 (0.07)	–	–	1.85 (0.10) 1.99 (0.14)	3.97 (0.10) 3.71 (0.14)	–	0.972 (0.325)
	5	13.18 (0.03)	1.56 (0.06)	2.53 (0.09)	–	–	0.74 (0.10)	0.979 (0.279)

5. $pK = pK^0 - \rho_X\sigma_p - \rho_Y[\sigma_p + r(\sigma_p^- - \sigma_p)]$, additive model presuming X substituents to act according to the Hammett relationship with substituent constant σ_p and Y substituent to act according to the Yukawa–Tsuno relationship, where *r* describes the extent of mesomeric effects[19].

In models 1–5 subscripts X, Y correspond accordingly to effects of X or Y substituents. The results of regressions are presented in Table III. When evaluating the quality of regression models by the correlation coefficients (*R*) and residual standard deviations (*s*), we can see that the worst result was provided by model (3) despite the fact that the σ_{P6} substituent constants were adjusted specially for non-aqueous media. In MeOH, AN, and Py the resulting order of success of the models is 3 > 1 > 2 > 4 and the best is model 5; in DMF the order is only slightly different: 3 > 1 > 4 > 2, the best being 5. Hence the best model for describing the dissociation processes of the substrates studied turned out to be the additive model presuming the action of X substituents according to the Hammett relationship and that of Y substituents according to the Yukawa–Tsuno relationship. The result shows larger ability of Y substituents to stabilize conjugated base of model substrate through larger delocalization in comparison with the ability of X substituents and agrees with the conclusion drawn from the treatment of data by the methods with latent variables.

The lower values for ρ_X reaction constants, as compared with ρ_Y, found in all the solvents confirm the presumption that the substrate is less sensitive to the substituents in the ring connected with the reaction centre via the SO_2 group, hence this group acts by its transmission effect, which can be quantified on the basis of the ratio of reaction constants ρ_X/ρ_Y (transmission factor) from model 5. Its values in the individual solvents are 0.63 (MeOH), 0.60 (AN), 0.60 (Py), 0.62 (DMF). The transmission of substituent effects through sulfonyl group (substituents of type X) thus attains roughly 60% of the extent of transmission of effects from type Y substituents. The parameter *r* in regression model 5 appeared to be statistically significant in all the solvents. This confirms the direct conjugation between the reaction centre and Y substituents, in particular NO_2 and CN substituents, stabilizing the conjugated base of *N*-phenylbenzenesulfonamide. The values of reaction constants ρ of all the regression models also quantify the ability of solvent to stabilize the conjugated bases of sulfonamides. The lowest values of ρ are found in MeOH and increase in the order DMF, AN, Py. Hence pyridine is the worst solvent for stabilization of conjugated bases of model substrates, and the substituent effects in this solvent are the most distinct as it is seen from the highest values of the reaction constants.

CONCLUSIONS

The study of acid-base properties of a coherent set of 4,4′-disubstituted *N*-phenylbenzenesulfonamides in four organic solvents showed that the combined effect of both substituents has an additive character. Compared with the effects of Y substituents, the effects of X substituents acting through the sulfonyl group are weakened by the transmission effect of this group, which can be quantified by a transmission coefficient of 0.60. For the regression models tested, the substituent effects on the model substrates are best described by the additive model describing the behaviour of substituents on the basis of the Hammett relationship and that of Y substituents on the basis of the Yukawa–Tsuno relationship. In this way it was found out that direct conjugation of substituent Y with the reaction centre operates in the stabilization of conjugate bases of model substrates. For the acid-base processes, the best solvating effect is exhibited by methanol and, on the other hand, due to worse solvation ability of pyridine, the substituent effects are most distinct in this solvent.

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