

## THE HAMMETT SUBSTITUENT CONSTANTS AND EFFECTS OF MEDIUM

Oldřich PYTELA, Miroslav LUDWIG and Miroslav VEČEŘA

*Department of Organic Chemistry,  
Institute of Chemical Technology, 532 10 Pardubice*

Received October 30th, 1985

The dissociation constants measured earlier for 35 substituted benzoic acids in seven solvents (water, methanol, ethanol, dimethylformamide, acetonitrile, sulpholane, and acetone) have been submitted to the principal components analysis and the factor analysis to produce sets of the Hammett substituent constants. The solvent effects have been evaluated on the dissociation constants of the substituted benzoic acids and, hence, also on the respective substituent constants. The differences have been compared between the substituent constants determined by the principal components analysis and by the factor analysis, the latter being found to be more suitable. The obtained sets of substituent constants have been confronted with literature data, and an excellent agreement has been found between the  $\sigma$  constants derived from the measurements in water with the sets of primary substituent constants and some other sets.

The Hammett equation (1) (refs<sup>1,2</sup>) represents the most widespread and best un-

$$\log k(K) = \log k^0(K^0) + \rho\sigma \quad (1)$$

derstood LFER (ETR) type equation. The  $\sigma$  constant, as a numerical quantity characterizing the given substituent, is of considerable importance exceeding the scope of validity of the Hammett equation<sup>3</sup>. Hammett<sup>2</sup> based the  $\sigma$  scale on the difference of logarithm of dissociation constant of a monosubstituted benzoic acid and logarithm of dissociation constant of benzoic acid in water at 25°C. The values of dissociation constants were taken predominantly from experiments by Dippy<sup>4</sup>. The same way was adopted to obtain the other sets of primary  $\sigma$  constants<sup>5-7</sup>; in ref.<sup>6</sup> the dissociation of benzoic acids in 50% ethanol was used as a secondary standard for some substituents. The statistical  $\sigma$  values satisfying well the maximum possible number of experimental data were used as a basis by Jaffé<sup>8</sup>. The scale denoted as  $\sigma^n$  (ref.<sup>9</sup>) is based on seven selected substituted benzoic acids and eighty selected reaction and equilibrium series. Taft defined the  $\sigma_o$  scale by means of reactions and equilibria of phenylacetic and phenylpropionic acids. Besides that, such sets of substituent  $\sigma$  constants can be encountered for which the way of adjusting is unknown, however, they usually represent compilations of some outstanding sets<sup>6-8</sup>. In this context we are not interested in the substituent constants (e.g.  $\sigma^-$ ,  $\sigma_1$ ,  $\sigma_R$ ) which extend the

scope of validity of the Hammett equation or interpret the principles of the substituent effects.

If substituent constants from various parameters are compared, an overall agreement can be seen between the values given for the most frequent substituents<sup>10</sup>. With less usual substituents the situation is worse, because the  $\sigma$  constants are often determined from the secondary standards in various media, and such a set is then experimentally non-homogeneous. The influence of a change of solvent is usually neglected (except for dissociating or associating substituents), although it is obviously significant with many other substituents (*e.g.* ref.<sup>11</sup>, p. 186, ref.<sup>12</sup>, p. 15). With the primary standards the situation is clear and so is also the scope of validity of the respective  $\sigma$  constants. A transition to another solvent, especially to a medium having different proton-donor or -acceptor properties and also different permittivity and polarizability, can lead (and really leads) to non-proportional changes (as compared with water) in the  $\sigma$  constant values valid in the given medium. The knowledge of these changes is not so important for construction of specific or universal scales of  $\sigma$  constants, but it can serve as a source of new findings about nature of effects of the substituents on the reaction centre<sup>13,14</sup>.

The aim of the present communication is to use the dissociation constants of benzoic acids published by us<sup>15</sup> for a construction of a homogeneous set of primary  $\sigma$  constants and those valid for non-aqueous solvents and to confront these sets with the literature data. Another aim is to adopt the solvent effects on the solvent specific  $\sigma$  constants for an analysis of possible origin of this phenomenon.

## EXPERIMENTAL

The calculations were based on the dissociation constants ( $pK$ ) taken from the previous report<sup>15</sup> except for the substitution derivatives with 4-OC<sub>6</sub>H<sub>5</sub>, 3-SO<sub>3</sub>H, and 4-COOH. These data were treated by the factor analysis using our own programs and an EC 1033 computer and an IQ-151 minicomputer. The missing data were supplemented by 20 short-circuit iterations<sup>16</sup> without reading the means (pseudocovariance matrix) and by 20 short-circuit iterations with reading the means (covariance matrix) in the principal components analysis.

## RESULTS AND DISCUSSION

The dissociation constants taken from ref.<sup>15</sup> were submitted to the correlation analysis of similarity of solvent effects and the results are given in Table I. From the table it follows that the behaviour of the substitution derivatives is different in different solvents. Highly similar are, *e.g.*, water and methanol, whereas water and sulpholane are less similar. This result reflects the solvent effects on the interaction processes between substituents and the reaction centre as well as different degrees of solvation of the substituent proper. The solvation of transmitting groups (*i.e.* carbonyl group in our case) cannot be neglected either.

The above-mentioned effects represent a source of differences between the substituent  $\sigma$  constants, too. They were calculated by two similar ways: the principal components analysis and the factor analysis. In the former case such a vector — the principle component — is sought which shows the maximum correlation with all columns of the source matrix simultaneously, the column being formed, in our case, by the  $(pK - pK_H)$  values in the given solvent. The first principal component (only a single one is considered in our model) represents a sort of "averaged" scale of values proportional to the constants describing the substituent effects. The adjustment to the measure of the Hammett  $\sigma$  constants can be carried out by the regression of logarithms of the dissociation constants in water *vs* elements of the principle component and by calculation of the predicted values of the dependent variable. The substituent constants thus obtained for all the seven solvents used and, moreover, for the set formed by all solvents except water, are summarized in Table II. The factor analysis adopts a more complex model. The scattering is presumed to be formed by a special scattering portion — communality (reflecting the extent of common information which we are interested in — in this case) besides the specific scattering (unicity) and experimental error. The source matrix is decomposed to a product of the so-called loadings matrix and scores matrix to which the error matrix is added. The scores matrix (the scores vector in the case of only one factor) is a quantity analogous to the principle component. The substituent constant values obtained in a way analogous to that of the principle components analysis are summarized in Table II. Finally, the same table also gives the  $\sigma_w$  values obtained according to the Hammett definition from the dissociation constants of benzoic acids in water. The values given in brackets were obtained by the short-circuit procedure (see Experimental). Table III presents the results of correlation analysis of the substituent constants adjusted by the principal components analysis (P), and factor analysis (F) for all the seven solvents (denoted

TABLE I

Correlation coefficients between logarithms of dissociation constants of substituted benzoic acids in various solvents (W — water, MeOH — methanol, EtOH — ethanol, DMF — dimethylformamide, AN — acetonitrile, TMS — sulfolane, AC — acetone)

Solvent	W	MeOH	EtOH	AN	DMF	TMS
MeOH	0.994					
EtOH	0.978	0.991				
DMF	0.965	0.983	0.991			
AN	0.982	0.990	0.986	0.982		
TMS	0.955	0.971	0.973	0.979	0.970	
AC	0.969	0.984	0.986	0.991	0.985	0.976

TABLE II

The substituent constants obtained by the principal components analysis (P) and factor analysis (F) for the set of all the solvents studied (7) and organic solvents (6), the substituent constants determined from the measurements in water (W)

Subst.	$\sigma_W$	$\sigma_{F7}$	$\sigma_{F6}$	$\sigma_{P7}$	$\sigma_{P6}$	Subst.	$\sigma_W$	$\sigma_{F7}$	$\sigma_{F6}$	$\sigma_{P7}$	$\sigma_{P6}$
H	0.00	0.00	0.00	0.00	0.00	3-SH	0.25	0.34	0.32	0.27	0.27
3-CH <sub>3</sub>	-0.06	-0.04	-0.07	-0.11	-0.11	4-SH	(0.06)	0.09	0.07	0.04	0.04
4-CH <sub>3</sub>	-0.14	-0.11	-0.12	-0.16	-0.16	4-SCH <sub>3</sub>	0.01	0.00	0.00	-0.04	-0.04
4-t-C <sub>4</sub> H <sub>9</sub>	-0.15	-0.13	-0.14	-0.19	-0.19	3-SO <sub>2</sub> CH <sub>3</sub>	0.68	0.64	0.61	0.58	0.58
3-CF <sub>3</sub>	0.46	0.48	0.47	0.43	0.43	4-SO <sub>2</sub> CH <sub>3</sub>	0.73	0.66	0.61	0.57	0.56
3-CN	0.62	0.63	0.62	0.59	0.58	3-SO <sub>2</sub> NH <sub>2</sub>	0.53	0.52	0.50	0.47	0.47
4-CN	0.71	0.67	0.63	0.60	0.59	4-SO <sub>2</sub> NH <sub>2</sub>	0.58	0.54	0.48	0.46	0.45
3-COCH <sub>3</sub>	0.35	0.35	0.32	0.28	0.28	3-F	0.33	0.36	0.34	0.31	0.31
4-COCH <sub>3</sub>	0.47	0.42	0.38	0.35	0.34	4-F	0.05	0.13	0.14	0.09	0.10
3-COOH	(0.33)	0.39	0.38	0.35	0.36	3-Cl	0.37	0.42	0.44	0.40	0.40
4-NH <sub>2</sub>	-0.57	-0.63	-0.66	-0.70	-0.71	4-Cl	0.21	0.28	0.27	0.23	0.23
3-NHCOCH <sub>3</sub>	0.15	0.06	0.03	-0.01	-0.01	3-Br	0.35	0.45	0.43	0.40	0.40
4-NHCOCH <sub>3</sub>	-0.09	-0.09	-0.08	-0.12	-0.11	4-Br	0.22	0.27	0.28	0.25	0.25
3-OH	0.12	-0.03	-0.07	-0.09	-0.10	3-I	0.33	0.41	0.38	0.35	0.35
4-OH	-0.38	-0.32	-0.36	-0.39	-0.39	4-I	0.21	0.28	0.27	0.23	0.24
3-OCH <sub>3</sub>	0.09	0.05	0.04	0.01	0.01	3-NO <sub>2</sub>	0.71	0.74	0.72	0.68	0.68
4-OCH <sub>3</sub>	-0.28	-0.22	-0.23	-0.26	-0.26	4-NO <sub>2</sub>	0.81	0.77	0.73	0.69	0.69
3-OC <sub>6</sub> H <sub>5</sub>	0.26	0.30	0.30	0.27	0.27						

by 7), for the same solvent set but without water (6), for aprotic solvents, *i.e.* dimethylformamide, acetonitrile, acetone, and sulpholane (4), for amphiprotic solvents, *i.e.* water, methanol, and ethanol (3), and finally for water (W). Table III clearly shows the similarity between the standard substituent constants determined in water and those in amphiprotic solvents, on the other hand, however, the correlation with the constants determined in aprotic solvents is less close. No significant agreement is observed between the standard  $\sigma$  constants scale determined in water and the constants obtained in organic solvents. This fact (besides the experimental error) can cause the worsening of the Hammett correlations of reactions and equilibria observed in non-aqueous or aqueous-organic solvents, if the standard  $\sigma$  constants are used. On the other hand, however, any extension of the Hammett equation by further specific scales applicable to groups of solvents or even to individual solvents would bring rather complications. Although such extension would improve the correlations, the  $\rho$  reaction constants thus estimated would lose their common basis and would be mutually incomparable. Moreover, the effects of a solvent exercised upon a single (even if a standard) substrate are more or less specific.

The similarity of substituent constants obtained by the principle components analysis and the factor analysis is expressed by the correlation coefficients in Table III. From the table it can be seen that the mutual correlations of the parameter scales determined in different media are obviously close. If, in accordance with the above discussion, no specific scale for a certain group of solvents but the standard scale for water is used, then Table III provides a rough picture of worsening of the correlation.

TABLE III

Correlation coefficients between the substituent constants determined by measurements in water (W), in all the solvents studied (7), in organic solvents (6), in aprotic solvents (4), and in amphiprotic solvents (3) by the principle components analysis (P) and factor analysis (F)

Constant	$\sigma_W$	$\sigma_{F7}$	$\sigma_{F6}$	$\sigma_{F4}$	$\sigma_{F3}$	$\sigma_{P7}$	$\sigma_{P6}$	$\sigma_{P4}$
$\sigma_{F7}$	0.985	—	—	—	—	—	—	—
$\sigma_{F6}$	0.979	0.999	—	—	—	—	—	—
$\sigma_{F4}$	0.972	0.966	0.999	—	—	—	—	—
$\sigma_{F3}$	0.987	0.990	0.982	0.978	—	—	—	—
$\sigma_{P7}$	0.980	0.998	1.000	0.999	0.983	—	—	—
$\sigma_{P6}$	0.978	0.998	1.000	0.999	0.981	1.000	—	—
$\sigma_{P4}$	0.974	0.996	0.999	0.999	0.979	0.999	1.000	—
$\sigma_{P3}$	0.990	0.998	0.996	0.991	0.988	0.995	0.994	0.991

The substituent constants estimated by the principle components analysis and the factor analysis show practically the same good correlation with the standard scale for water. The model of factor analysis, however, is more suitable for interpretation, as it can be documented on the "real error"<sup>16</sup> of the two methods:  $P7 = 0.086$ ,  $F7 = 0.046$ ,  $P6 = 0.089$ ,  $F6 = 0.044$ . The error of the scales determined by the factor analysis is comparable (in the interpretation using all the substituents analyzed and all the media) with the accuracy of validity<sup>3</sup> of the Hammett equation.

It is interesting to relate the substituent constants obtained by evaluation of the measurements in organic solvents to those in water (Table II) for the individual substituents. First of all, there are relatively high values for halogens for which an only slight interaction with solvent can be presumed. In organic solvents halogens behave as stronger electron-acceptors than they do in water. A quite opposite situation is observed with significant acceptors ( $\text{NO}_2$ ,  $\text{CN}$ ,  $\text{CH}_3\text{SO}_2$  groups) which, in addition, show closer values at 3 and 4 positions in organic solvents. This rule is also obeyed, more or less, by methanol and ethanol. As the change in the substituent constants with a change in solvent is observed in both 3 and 4 positions, it seems likely that the reason lies in the inductive effect, in the transmission through the carbonyl bridge (as discussed, *e.g.* by Palm, *ref.*<sup>11</sup> p. 183 ff), or in a specific solvation of the substituent. The study<sup>17</sup> of NMR shifts in various solvents led to the statement that the inductive effect is solvent-independent. If this statement is accepted, the cause of the solvent dependence of substituent constants must be sought elsewhere. Undoubtedly, the transmission coefficient is affected by solvation, the conjugated base of the acid (its stabilization, in fact, determines the substituent-dependent position of the equilibrium) being better solvated in water which can form strong hydrogen bonds. The formation of hydrogen bonds with oxygen atoms of the carboxylate group will lower the electron density and, hence, also the cooperating effect of the substituent. Therefore, all substituents should have weaker effects in water than in organic solvents. In reality, this is only true of inert substituents as, *e.g.*, halogens. Most other substituents, in addition, undergo specific solvation, which causes an opposite effect. These substituents contain atoms with free electron pairs which can be donated during formation of a hydrogen bond. Thereby the electron density is lowered, and the electron-acceptor substituents seem to be stronger in water, whereas the electron-donor substituents seem to be weaker. On the other hand, substituents containing hydrogen atoms able of formation of hydrogen bonds appear in water (due to increased electron density) to be less electron-acceptor or more electron-donor substituents. It is interesting, *e.g.*, to compare the 3-OH and 3-SH groups. In the hydroxyl group the hydrogen atom is little acidic, and the oxygen atom is a good donor for formation of a hydrogen bond — the 3-OH group is an electron acceptor in water and a donor in organic solvents. The thiol group at 3 position to the electron-acceptor carboxyl, on the other hand, can provide its hydrogen in water and appears thus to be a weaker acceptor than it is in organic solvents. Quite unexpected behaviour, in this respect,

is observed with 4-OCH<sub>3</sub> group and, to some extent, also 3-OC<sub>6</sub>H<sub>5</sub> group. Whereas 3-OCH<sub>3</sub> group is, according to expectation, a stronger acceptor in water, the 4-OCH<sub>3</sub> group is a stronger donor, and 3-OC<sub>6</sub>H<sub>5</sub> a weaker acceptor in water. The reason of this phenomenon cannot be given yet.

A comparison of various scales of substituent constants (Table II) with those given in literature is presented in Table IV in the form of the respective correlation coefficients. Generally, the best correlation is obtained for the standard  $\sigma$  constants determined from the measurements in water. These substituent constants agree best with the scale by Exner<sup>3</sup> (Ex), as it is shown in the regression equation

$$\sigma_w = -(4.56 \pm 3.50) \cdot 10^{-3} + (1.00 \pm 0.01) \sigma_{\text{Ex}} \quad (2)$$

(without 3-CO<sub>2</sub><sup>-</sup>)

$$s = 0.017, \quad r = 0.999, \quad n = 34.$$

A somewhat worse dependence (but yet with unit slope and zero intercept) was found for the constants recommended by McDaniel and Brown<sup>6</sup> (DB)

$$\sigma_w = (7.55 \pm 88.10) \cdot 10^{-4} + (1.00 \pm 0.02) \sigma_{\text{DB}} \quad (3)$$

$$s = 0.042, \quad r = 0.992, \quad n = 35.$$

An equally close correlation, but with somewhat lower slope, is obtained with the set by Jaffé<sup>8</sup> (Jf)

$$\sigma_w = (1.26 \pm 1.00) \cdot 10^{-2} + (0.97 \pm 0.02) \sigma_{\text{Jf}} \quad (4)$$

$$s = 0.048, \quad r = 0.992, \quad n = 35.$$

TABLE IV

Correlation coefficients between the substituent constants determined by measurements in water (W), in all the solvents studied (7), in organic solvents (6) by the principle component analysis (P) and factor analysis (F) and between the literature data by Exner<sup>3</sup> (Ex), Mc Daniel and Brown<sup>6</sup> (DB), Jaffé<sup>8</sup> (Jf), and  $\sigma_0$  and  $\sigma^n$  according to Wells<sup>12</sup>

Constant	$\sigma_{\text{Ex}}$	$\sigma_{\text{DB}}$	$\sigma_{\text{Jf}}$	$\sigma_0$	$\sigma^n$
$\sigma_w$	0.999	0.992	0.992	0.980	0.969
$\sigma_{\text{F7}}$	0.986	0.981	0.989	0.982	0.953
$\sigma_{\text{F6}}$	0.979	0.976	0.985	0.974	0.949
$\sigma_{\text{P7}}$	0.980	0.977	0.986	0.965	0.940
$\sigma_{\text{P6}}$	0.978	0.976	0.984	0.963	0.937

The best agreement of the scale determined in organic solvents except for water is found for the data by Jaffé<sup>8</sup> as it is seen in Table IV. This conclusion is not surprising if we consider the way of construction of this scale. Little close correlations are found between the type-different constants  $\sigma_0$  and  $\sigma^n$  taken from the report<sup>12</sup> by Wells, whether they are correlated with the substituent constants derived from the measurements in water or those in organic solvents. The reason can be sought in the somewhat different definition of these constants.

## REFERENCES

1. Hammett L. P.: J. Amer. Chem. Soc. 59, 96 (1937).
2. Hammett L. P.: *Physical Organic Chemistry*, 1st Ed. McGraw-Hill, New York 1940; 2nd Ed. McGraw-Hill, New York 1970.
3. Exner O.: *Korelační vztahy v organické chemii*. Published by SNTL/ALFA, Prague 1981.
4. Dippy J. F. J., Williams F. R.: J. Chem. Soc. 1934, 161.
5. Zollinger H., Wittwer C.: Helv. Chim. Acta 39, 347 (1955).
6. Mc Daniel D. H., Brown H. C.: J. Org. Chem. 23, 420 (1958).
7. Exner O. in the book: *Correlation Analysis in Chemistry: Recent Advances* (N. B. Chapman, J. Shorter, Eds), Chapter 10. Plenum, New York 1978.
8. Jaffé H. H.: Chem. Rev. 53, 191 (1953).
9. Van Bekkum H., Verkade P. E., Wepster B. B.: Rec. Trav. Chim. Pays Bas 78, 815 (1959).
10. Taft R. W.: J. Phys. Chem. 64, 1805 (1960).
11. Palm V. A.: *Osnovy kolichestvennoi teorii organicheskikh reakcii*. Khimiya, Leningrad 1977.
12. Wells P. R.: *Linear Free Energy Relationships*. Academic Press, London 1968.
13. Johnson C. D.: *The Hammett Equation*. Cambridge University Press, Cambridge 1973.
14. Shorter J.: *Correlation Analysis of Organic Reactivity*. Research Studies Press, Wiley, New York 1982.
15. Ludwig M., Baron V., Kalfus K., Pytela O., Večeřa M.: This Journal 51, 2135 (1986).
16. Malinowski E. R., Howery P. G.: *Factor Analysis in Chemistry*. Wiley, New York 1980.
17. Taft R. W., Price E., Fox I. R., Lewis I. C., Andersen K. K., Davis G. T.: J. Amer. Chem. Soc. 85, 709 (1963).

Translated by J. Panchartek.