ADDITIVITY OF SUBSTITUENT EFFECTS IN *meta*-
AND *para*-SUBSTITUTED BENZOIC ACIDS

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Dissociation constants of 74 mono- and disubstituted benzoic acids were measured in 50% ethanol and in 80% methyl cellosolve. The cumulative substituent effects are generally well represented by the additive scheme. For 3,5-disubstituted acids the additivity holds almost within the experimental error and leaves no place for the theoretically required effect of symmetry on the entropy term; for 3,4-disubstituted acids the deviations from additivity are perceptible and some of them but not all can be explained in terms of current theories of the *ortho* effect. In either series the additive relationship in a constant solvent is more precise than the Hammett equation, which is based in this case on transferring the σ constants from water into a mixed solvent. As far as the material allows to draw conclusions, less irregularities occur in 80% methyl cellosolve than in 50% ethanol.

The additive behaviour is of fundamental importance as the simplest type of dependence of any measurable quantity on structure[1]. If we restrict ourselves to a quantity (y) which is determined only by two factors (i, j), *e.g.* by double substitution, the additivity is expressed by the relationship

$$y_{ij} = x_i + x_j + \varepsilon_{ij} . \qquad (1)$$

In this equation ε is a random variable (error of the correlation equation) and the empirical constants x are determined from a given set of data in order to minimize the sum of squares $\sum \varepsilon^2$.

In the field of structure–energy correlations the additivity is often connected with the Hammett equation[2], or with a generalized relationship[3] of this type. The latter reads for single substitution

$$y_i = \varrho\sigma_i + \varepsilon_i , \qquad (2)$$

where the scale of empirical constants σ is fixed once for all and only the constant ϱ is adjusted in each correlation. In the case of double substitution in equivalent posi-

tions, the Hammett equation is commonly applied in the form[2]

$$y_{ij} = \varrho(\sigma_i + \sigma_j) + \varepsilon_{ij} \tag{3}$$

which includes already the additivity principle. However, this principle and the Hammett equation are *a priori* independent[3] and Eq. (3) does not follow from Eq. (2). A logical consequence of Eq. (2) for double substitution is the relationship[4]

$$y_{ij} = \varrho_1(\sigma_i + \sigma_j) + \varrho_{12}\sigma_i\sigma_j + \varepsilon_{ij} \tag{4}$$

which satisfies the condition of linearity with respect to both σ_i and σ_j separately. Eq. (4) is a particular case of a more general relationship, not involving any fixed scale of constants

$$y_{ij} = y_0 + x_i x_j . \tag{5}$$

Here the terms linear in x_i or x_j, respectively, have been eliminated by a suitable transformation of constants, which in contrast to Eq. (4) are not *a priori* fixed.

Many reaction series have been investigated with the aim to decide whether the behaviour of substituents is additive or not[3]. Quite often, however, the coefficient ϱ_{12} of the cross-term in equation (4) is rather small and of low statistical significance. In addition to the systematic deviation from additivity, as expressed by equation (4), deviations of individual derivatives may be also observed, in particular in the case of adjacent substituents[5−8].

In this paper we have investigated the additive behaviour and possible deviations on the classic example, disubstituted benzoic acids. Owing to their insufficient solubility in water, their pK values were measured in two standard mixed solvents, 50% ethanol and 80% methyl cellosolve. The pK's in water were also measured as far as allowed by the solubulity, but due to their small number these data were not used in the correlations. Although this model system has been studied several times[5−9], we feel that certain points of view have not been paid proper attention. In particular we wanted to compare the correlations according to the additivity principle, Eq. (1), on the one hand and of the Hammett equation (2) on the other hand. Since the scale of constant σ in Eq. (2) has been determined on the same reaction in water[2,3], the Hammett equation in our case relates only to a change of solvent. Another question is whether the additive relationship, Eq. (1), can be significantly exceeded by an equation of the type (5); this problem is dealt with generally and with some computational details elsewhere[10]. Lastly we wanted to estimate in summary the interaction of adjacent substituents by comparing the series of 3,5- and 3,4-derivatives.

The disubstituted benzoic acids chosen for the given purpose are listed in Table I. We considered unremunerative to investigate all the combinations of substituents and preferred to include more substituents than to have a well filled table. Hence

we worked with $40-46\%$ of all possible entries in the individual sets; in the correlations according to Eq. (1) or (5) the number of entries to one empirical constant was $2\cdot4-2\cdot8$. In all sets, hydrogen was also considered as a substituent, so that all bisderivatives always include monoderivatives as well. In order to have comparable data, we redetermined even the pK's of the monoderivatives in this laboratory. Among other substituents also those were included for which deviations are expected in the case of 3,4-derivatives ($e.g.$ NO_2 — steric inhibition of resonance, OH — hydrogen bonds, inhibition of solvation, I — a polarizable, sterically pretentious substituent).

EXPERIMENTAL AND RESULTS

Materials. Several acids were commercial products, most were prepared according to the literature. Since the compounds are well known, most references were omitted. The purity of samples was checked, in addition to the elemental analysis and common physical constants, also by means of the neutralization equivalent.

3-*Nitro-5-methylsulphonylbenzoic acid* (33). 3-Nitro-5-aminobenzoic acid (25 g) was diazotized and reacted with ethyl xanthogenate in an excess of sodium carbonate at 50°C. The precipitate was collected and hydrolyzed in 10% sodium hydroxide; after 1 hour boiling, dimethyl sulphate (19·2 g) was added and the reaction mixture boiled for 1 hour more. After cooling, 3-nitro-5-methylthiobenzoic acid was precipitated with hydrochloric acid, collected, and oxidized by dissolving in acetic acid, adding 10% hydrogen peroxide (150 ml) and evaporating; yield 10 g (30%), m.p. 229—230°C (dilute ethanol). For $C_8H_7NO_6S$ (245·6) calculated: 39·18% C, 2·88% H, 5·71% N; found: 39·02% C, 2·71% H, 5·57% N, neutr. equivalent 245·6.

3-*Bromo-4-cyanobenzoic acid* (45). 3-Bromo-4-aminobenzoic acid (25 g) was diazotized and the filtered solution added slowly to a prepared solution of sodium copper cyanide at 50—60°C. After two hours the solution was acidified to pH 3, cooled, and the product collected; yield 14 g (35%), m.p. 199°C (ethanol). For $C_8H_4BrNO_2$ (226·0) calculated: 43·16% C, 1·79% H, 6·22% N; found: 43·22% C, 1·93% H, 6·05 % N, neutr. equivalent 226·6.

3-*Iodo-4-cyanobenzoic acid* (55) was prepared as above; yield 45%, m.p. 211°C (ethanol). For $C_8H_4INO_2$ (273·0) calculated: 35·19% C, 1·48% H, 5·13% N; found: 35·06% C, 1·42% H, 5·07% N, neutr. equivalent 274·0.

3-*Bromo-4-mercaptobenzoic acid* (46) was prepared from 3-bromo-4-aminobenzoic acid by the procedure described for thiosalicylic acid[11]; yield 32%, m.p. 230°C (ethanol). For $C_7H_5BrO_2S$ (233·1) calculated: 37·40% C, 2·16% H, 13·75% S; found: 37·23% C, 2·01% H, 13·54% S, neutr. equivalent 233·9.

3-*Iodo-4-mercaptobenzoic acid* (51) was prepared from 3-iodo-4-aminobenzoic acid by the procedure described for thiocresol[12]; yield 28%, m.p. 208—210°C (ethanol). For $C_7H_5IO_2S$ (280·1) calculated: 30·00% C, 1·80% H, 11·45% S; found: 29·86% C, 1·67% H, 11·28% S, neutr. equivalent 280·0.

3-*Bromo-4-methylmercaptobenzoic acid* (47) was prepared from 3-bromo-4-mercaptobenzoic acid and dimethyl sulphate in alkaline solution; yield 85%, m.p. 222°C (ethanol). For $C_8H_7BrO_2S$ (247·1) calculated: 38·86% C, 2·85% H, 12·98% S; found: 38·74% C, 2·71% H, 12·80% S, neutr. equivalent 248·0.

Table I

Dissociation Constants of Substituted Benzoic Acids

No	Substituents	M.p., °C	pK (50 A)[a]	pK (80 MCS)[b]	pK (H$_2$O)
		Monoderivatives			
1	H	122	5·73	6·63	—
2	3-Cl	164—166	5·24	5·98	—
3	4-Cl	243	5·27	6·13	—
4	3-Br	155	5·22	5·94	—
5	4-Br	251	5·39	6·10	—
6	3-I	187	5·28	6·03	—
7	4-I	265	5·37	6·15	—
8	3-NO$_2$	141	4·79	5·47	—
9	4-NO$_2$	237—239	4·63	5·29	—
10	3-NH$_2$	173	5·82	6·88	—
11	4-NH$_2$	194—196	6·55	7·70	—
12	3-NH.COCH$_3$	248	5·46	6·40	—
13	4-NH.COCH$_3$	250	5·76	6·66	—
14	3-OH	209—211	5·71	6·69	—
15	4-OH	215	6·09	7·23	—
16	3-OCH$_3$	105	5·62	6·55	—
17	4-OCH$_3$	180	5·93	7·00	—
18	3-SO$_2$CH$_3$	230	4·77	5·71	—
19	4-SO$_2$CH$_3$	267	4·66	5·49	—
20	3-CH$_3$	110	5·92	6·74	—
21	4-CH$_3$	178	6·01	6·83	—
22	3-CN	217	4·85	5·48	—
23	4-CN	219	4·78	5·52	—
		3,5-Bisderivatives			
24	Cl, Cl	182	4·70	5·39	—
25	Br, Br	213	4·66	5·34	—
26	I, I	235	4·83	5·47	—
27	NO$_2$, Cl	147	4·23	4·81	—
28	NO$_2$, Br	161	4·19	4·80	—
29	NO$_2$, I	167	4·30	4·90	—
30	NO$_2$, NO$_2$	204—205	3·80	4·33	—
31	NO$_2$, NH$_2$	211	4·95	5·73	—
32	NO$_2$, NH.COCH$_3$	270	4·50	5·24	—
33	NO$_2$, SO$_2$CH$_3$	229—230	3·85	4·38	—
34	NH$_2$, Cl	216—217	5·48	6·28	—
35	NH.COCH$_3$, Cl	286—288	4·99	5·73	—
36	OH, OH	235—236	5·78	6·73	—
37	OCH$_3$, OCH$_3$	181	5·50	6·37	—

TABLE I

(*Continued*)

No	Substituents	M.p., °C	pK (50 A)[a]	pK (80 MCS)[b]	pK (H$_2$O)
38	CH$_3$, CH$_3$	169	5·98	6·86	—
39	CN, CN	206—207	4·02	4·48	
		3,4-Bisderivatives			
40	Cl, Cl	202—203	4·91	5·63	3·64
41	Cl, OH	170—171	5·69	6·66	4·23
42	Br, NH$_2$	226—228	6·13	7·04	—
43	Br, OH	157—159	5·74	6·66	4·24
44	Br, CH$_3$	203	5·42	6·10	—
45	Br, CN	199	4·35	4·91	3·28
46	Br, SH	230	4·61	5·76	—
47	Br, SCH$_3$	222	5·33	6·12	—
48	Br, SO$_2$CH$_3$	200—202	4·40	5·04	. 3·29
49	I, Cl	215—217	5·02	5·66	—
50	I, OH	173—175	6·09	6·58	—
51	I, SH	208—210	5·01	5·79	—
52	I, SCH$_3$	279—281	5·35	6·16	—
53	I, SO$_2$CH$_3$	208—210	4·26	5·13	—
54	I, NH$_2$	203	6·31	7·09	—
55	I, CN	211	4·31	4·99	—
56	NO$_2$, Cl	181	4·43	5·07	3·33
57	NO$_2$, Br	203	4·54	5·04	3·38
58	NO$_2$, I	214	4·48	5·15	—
59	NO$_2$, OH	187	—	5·88	3·81
60	NO$_2$, SH	278	4·61	5·23	—
61	NO$_2$, NH$_2$	284	5·66	6·62	—
62	NO$_2$, NHCOCH$_3$	221—222	4·79	5·60	—
63	NH$_2$, Cl	212—214	5·50	6·39	4·08
64	NH$_2$, OH	201	6·10	7·32	4·93
65	NH$_2$, NH$_2$	207	—	7·77	—
66	OH, Br	229	5·36	6·25	3·92
67	OH, I	225—228	5·37	6·15	3·88
68	OH, NO$_2$	229	4·58	5·35	3·50
69	CH$_3$, CH$_3$	163	6·04	6·98	—
70	OH, OH	198	—	7·22	4·49
71	OCH$_3$, OH	210	—	7·04	4·51
72	NH$_2$, CH$_3$	164	—	7·13	—
73	NO$_2$, CH$_3$	189	—	5·70	—
74	NO$_2$, NO$_2$	160	3·99	4·34	—

[a] In 50% ethanol; [b] in 80% methyl cellosolve.

3-*Iodo-4-methylmercaptobenzoic acid* (52) was prepared as above; yield 85%, m.p. 279—281°C (ethanol). For $C_8H_7IO_2S$ (294·1) calculated: 32·66% C, 2·40% H, 10·91% S; found: 32·78% C, 2·34% H, 10·72% S, neutr. equivalent 294·8.

3-*Bromo-4-methylsulphonylbenzoic acid* (48) was prepared by oxidation of 3-bromo-4-methyl-mercaptobenzoic acid with 20% hydrogen peroxide in acetic acid solution; yield 86%, m.p. 200—202°C (ethanol). For $C_8H_7BrO_4S$ (279·1) calculated: 34·41% C, 2·53% H, 11·49% S; found: 34·27% C, 2·45% H, 11·24% S, neutr. equivalent 280·2.

3-*Iodo-4-methylsulphonylbenzoic acid* (53) was prepared as above; yield 88%, m.p. 208—210°C (aqueous ethanol). For $C_8H_7IO_4S$ (326·1) calculated: 29·47% C, 2·16% H, 9·58% S; found: 29·35% C, 2·08% H, 9·42% S, neutr. equivalent 327·3.

3-*Nitro-4-mercaptobenzoic acid* (60). 3-Nitro-4-aminobenzoic acid (28 g) was diazotized and the filtered solution added to a sodium polysulphide solution at 20°C. After two hours the disul-phide was precipitated with hydrochloric acid, collected and reprecipitated from a sodium carbon-ate solution. Subsequently, it was reduced by boiling with zinc dust in acetic acid 4 hours; the product was collected by suction and reprecipitated once more; yield 15·3 g (47%), m.p. 278°C (aqueous ethanol). For $C_7H_5NO_4S$ (199·2) calculated: 42·38% C, 2·53% H, 7·03% N; found: 42·27% C, 2·48% H, 6·95% N, neutr. equivalent 198·7.

Measurement of dissociation constants. The apparent dissociation constants in 50% (by volume) ethanol and 80% (by weight) methyl cellosolve were determined by potentiometric titration using a Radiometer PHM 4 millivoltmeter, a glass indication electrode G 200 B and a saturated calomel reference electrode K 100 connected by means of a bridge, filled with a saturated solution of potas-sium chloride in 3% agar-agar. Solutions of the acids ($4 . 10^{-3}$M) were titrated with 0·1M aqueous tetramethylammonium hydroxide; the initial concentration of the solvent was chosen in such a way that the required concentration was reached at the half-neutralization point. The solution was thermostated at $25 \pm 0\cdot1$°C and stirred by a stream of nitrogen, saturated with vapour of the respective solvent.

The dissociation constants were calculated according to Albert and Serjeant[13]. The procedure was checked by repeated determination of the dissociation constant of benzoic acid (pK 5·73 in 50% ethanol, pK 6·63 in 80% methyl cellosolve). All the values given in Table I are related to these standards. The accuracy of the relative values is according to our many years' observa-tion 0·02 pK unit (standard deviation) in 80% methyl cellosolve, in 50% ethanol it is somewhat worse, c. 0·04.

The dissociation constants in water were determined only for acid whose solubility was $3 . 10^{-3}$ M at least. The procedure was the same as above; the primary experimental values were corrected to zero ionic strength according to the Debye–Hückel equation. Hence the values listed in Table I (last column) are thermodynamic dissociation constants.

Calculations: The least square calculations were carried out on a Hewlett–Packard calculator 9820 A. Some details of the programming will be mentioned elsewhere[10]. The statistics are listed in Table II.

DISCUSSION

Let us consider first the 3,5-disubstitution which virtually excludes any interaction between substituents. According to the data of Table II (lines 1 and 3) the substituent

effects are additive with a good precision and no improvement is achieved* using the non-additive relation (5) (lines 2 and 4). Although the fit may be called only "good" according to the statistic[1] ψ, the standard deviation is low and already near to the experimental uncertainty. Hence a certain, not exactly known part of the total scatter must be due to the experimental error and a significantly better fit cannot be achieved by any correlation. A detailed analysis did not reveal any particular substituent with pronounced deviations in the two solvents simultaneously.
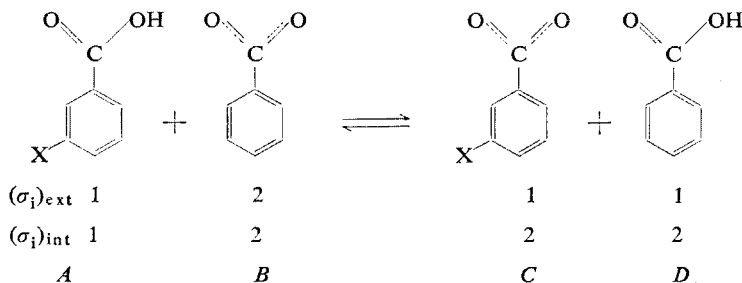
This exact additive behaviour makes it possible to test the theory, considering the influence of symmetry factors on entropy as a part of observed substituent effects[14]. The benzoate anion (B) has a twofold rotation axis and hence the external symmetry number $(\sigma_i)_{ext} = 2$; this axis is lacking in benzoic acid molecule (D) with $(\sigma_i)_{ext} = 1$. The symmetry factors thus should weaken the acidity of benzoic acid by $\log 2 = 0.30$ pK units. In any *meta* or *ortho* substituted benzoic acid the symmetry of the anion (C) is destroyed and it was argued[14] that acid strengthening of 0.30 pK is actually involved in any *meta-* or *ortho*-substituent effect.

However, in the anion of symmetrically 3,5-disubstituted benzoic acids the symmetry is restored; hence the acidity should be again comparable with benzoic acid, *i.e.* lower than in monoderivatives.

In Fig. 1 the relative acidities of 3,5-bisderivatives are plotted against those of 3-derivatives and confronted with the requirement of the symmetry theory as well as with the simple additivity rule. A similar disproval of the mentioned theory may be obtained by comparing data[15] for 3,5- and 3-substituted anilines; in this case even entropy values are directly available.

The complete failure of the theory is, in our opinion, understandable only by referring to internal symmetry numbers $(\sigma_i)_{int}$, connected with the rotation of the

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*   In addition to the comparison of standard deviations also the values of $\log K^0$ reveal that Eq. (5) does not comply. These values are very inaccurate and remote from experimental values to either side; for $\log K$ approaching infinity Eq. (5) reduces to Eq. (1).

COO and COOH groups around the C—C bond. It was recommended[14] to omit these numbers as far as the potential barrier to rotation is higher than 0.5 kcal mol^{-1}. Nevertheless, a compensation between the internal and external symmetry numbers exists and is necessary to account for the observed facts, see formulae $A - D$.
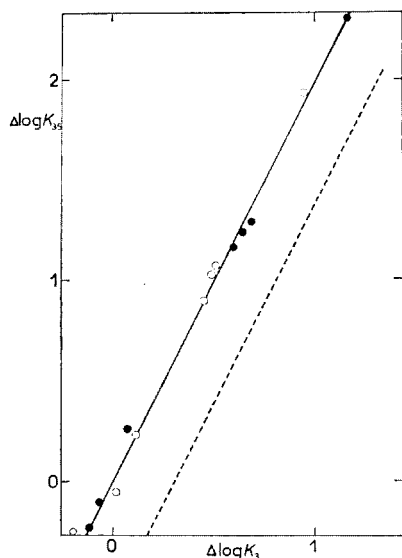

Fig. 1

Comparison of Relative Dissociation Constants of 3-Substituted and 3,5-Disubstituted Benzoic Acids

The full line corresponds to the additivity principle, the broken line is required by external symmetry numbers[14].

If we now proceed to 3,4-bisderivatives, a significantly lowered accuracy of the additive relationship is apparent (Table II, lines 5 and 7). Neither in this case any improvement is achieved with the non-additive relationship (5), see lines 6 and 8. No doubt that it is the proximity effect (*ortho* effect) of the two adjacent substituents which is responsible for this behaviour. A detailed analysis of various kinds of the *ortho* effect was not the proper aim of this paper since we feel that more systematic and more extensive experimental material would be needed. Previous attempts in this direction met also with limited success[5-7]. Nevertheless, we calculated for each derivative the deviation from the additivity (ΔpK) according to the expression

$$\Delta pK_{ij} = pK_{ij} - pK_{i0} - pK_{0j} + pK_{00} , \qquad (6)$$

where the index zero refer to hydrogen.* We searched for some effect postulated

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*   An analysis based on the deviations from Eq. (1) would be less suitable since the constants x of this equation are least-squares values based on all the available data, mono-derivatives and bis-derivatives as well. Hence any deviation from this equation is partly spread to other derivatives sharing this substituent. On the other hand, Eq. (6) relies to the accuracy of measuring mono-derivatives.

in the literature, as far as they are significantly manifested in both solvents and with several derivatives.

The most pronounced deviation is the lowered acidity of 3,4-dinitrobenzoic acid (74). The currently accepted interpretation is the steric inhibition of conjugation; we feel, however, that hindrance to solvation[16] and orientation dependent inductive effect[17] may be of even more importance. According to the values of σ constants in different solvents[18], hydration strengthens the relative electron withdrawing power of the nitro group. An acid weakening effect is also observed with 3-NO$_2$-4-X derivatives, at least for X = halogen; they seem to be somewhat stronger than expected for pure steric inhibition of conjugation in the *meta* position. The latter effect could not be proved in the case of derivatives 3-X-4-NH$_2$ and 3-X-4-OH; instead a somewhat weakened acidity was observed, suggesting rather an explanation based on solvation.

No other kind of proximity effect has been proven in a convincing manner. The derivatives with a hydrogen bond to the nitro group (3-NO$_2$-4-OH, 3-OH-4-NO$_2$, 3-NO$_2$-4-SH, 3-NO$_2$-4-NH$_2$) showed some deviations but no regularity could be detected. The compounds with another type of hydrogen bond, *viz.* between two electron releasing groups (3-NH$_2$-4-OH, 3-OCH$_3$-4-OH, 3,4-(OH)$_2$, 3,4-(NH$_2$)$_2$) show always an enhanced acidity. We expected generally larger deviations for the substituent NH$_2$ owing to the different population of the zwitterionic form, but this was not confirmed. Apparently zwitterions are less represented in mixed solvents than in pure water. No particular deviations were observed for derivatives of iodine in spite of its steric pretensions. Summarizing, many deviations from Eq. (1) remain unexplained in the case of 3,4-disubstituted benzoic acids. A deciding progress in this respect may be probably achieved only by studying the gas phase acidities.

Correlations by the Hammett equation yielded the same general picture as far as the relation between 3,5- and 3,4-derivatives is concerned. The former are correlated (Table II, lines 11 and 12) in either solvent with the same precision, which is almost equal or even somewhat better than in correlations of monoderivatives in the same solvent (lines 9 and 10). Note that this accuracy is not very high; it is evaluated according to the characteristic[1] ψ as "good", although the corresponding correlation coefficient would be denoted[2] as "excellent". The Hammett equation concerns in this case only a change of solvent from pure water, in which the σ constants have been determined, to mixed aqueous solvents; the reaction itself is the same. Hence the accuracy should represent a value which can be expected at best. The reasons why some substituents deviate even in monoderivatives are not easy to recognize. For instance, in 80% methyl cellosolve it is 3-OH as expected, 3-CN and 3-SO$_2$CH$_3$ as could be rationalized, but quite unexpectedly also 3-CH$_3$, 4-Br, and 4-I; in 50% ethanol also 3-OH, 3-CN and 4-Cl, in addition 4-CH$_3$, As to the constants ϱ, our values in 80% methyl cellosolve agree well with the literature[19] (1·68), while the published value[20] in 50% ethanol (1·522) seems to us definitely too high.

3,4-Bisderivatives obey the Hammett equation with a significantly lowered accuracy (Table II, the last two lines), especially in 50% ethanol. This accuracy is only slightly worse than for the additive relationship of the same compounds. The most deviating derivatives are almost the same in the two cases and can be discussed in qualitative terms as attempted above.

TABLE II

Correlations of pK Values of Disubstituted Benzoic Acids

Line	Substitution[a]	Solvent	Relationship	N^b	f^c	s^d	ψ^e	
1	3, 5	80 MCS	additive (1)	26	15	0·038	0·05	—
2	3, 5	80 MCS	non-add. (5)	26	14	0·038	0·05	$\log K^0 \cong -28$
3	3, 5	50 A	additive (1)	26	15	0·040	0·06	—
4	3, 5	50 A	non-add. (5)	26	14	0·041	0·07	$\log K^0 \cong -21{\cdot}5$
5	3, 4	80 MCS	additive (1)	54	33	0·071	0·09	—
6	3, 4	80 MCS	non-add. (5)	54	32	0·069	0·09	$\log K^0 = 11{\cdot}1$
7	3, 4	50 A	additive (1)	47	27	0·111	0·17	—
8	3, 4	50 A	non-add. (5)	47	26	0·110	0·17	$\log K^0 = 2{\cdot}4$
9	mono	80 MCS	Hammett (2)	21	19	0·083	0·13	$\varrho = 1{\cdot}65, r = 0{\cdot}992$
10	mono	50 A	Hammett (2)	21	19	0·068	0·13	$\varrho = 1{\cdot}33, r = 0{\cdot}992$
11	3, 5	80 MCS	Hammett add. (3)	26	24	0·060	0·08	$\varrho = 1{\cdot}69, r = 0{\cdot}997$
12	3, 5	50 A	Hammett add. (3)	26	24	0·061	0·09	$\varrho = 1{\cdot}41, r = 0{\cdot}996$
13	3, 4	80 MCS	Hammett add. (3)	54	52	0·096	0·12	$\varrho = 1{\cdot}57, r = 0{\cdot}993$
14	3, 4	50 A	Hammett add. (3)	47	45	0·126	0·20	$\varrho = 1{\cdot}30, r = 0{\cdot}981$

[a] Series of both 3,5- and 3,4-bisderivatives always include monoderivatives; [b] number of all data; [c] degrees of freedom; [d] root-mean-square difference between experimental and predicted values; [e] $\psi = s/s_0$ is a measure of goodness of fit; $\psi < 0{\cdot}1$ is a "good" fit, $\psi < 0{\cdot}2$ a "fair" fit[1].

We conclude that simple additivity rules in a single solvent are generally obeyed with a better accuracy than the Hammett equation correlating mono- or bisderivatives in variable solvent. The precision of the Hammett equation is thus not affected by combining it with the additivity principle to yield Eq. (3). This statement retains its validity even for 3,4-bisderivatives although the interaction of substituents is reflected in deviations from the additivity principle. If a choice of solvent is to be made, our data suggest that 80% methyl cellosolve could be somewhat more suitable than 50% ethanol.

Elemental analyses were carried out by the staff of Department of Analytical Chemistry, Institute of Chemical Technology, Pardubice.

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