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COMPILATION AND CRITICAL EVALUATION OF STRUCTURE–REACTIVITY PARAMETERS AND EQUATIONS: PART 2.

Extension of the Hammett σ scale through data for the ionization of substituted benzoic acids in aqueous organic solvents at 25 °C

(Technical Report)

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Compilation and critical evaluation of structure–reactivity parameters and equations: Part 2. Extension of the Hammett σ scale through data for the ionization of substituted benzoic acids in aqueous organic solvents at 25 °C (Technical Report)

Abstract - Data have been compiled for the pK values in certain aqueous organic solvents at 25°C of about 70 *meta*- or *para*-substituted benzoic acids, with a view to proposing values of Hammett constants, σ, in the case of substituents for which values cannot be based on the ionization of substituted benzoic acids in water (Part 1). The emphasis of the work is on the use of data for the apparent pK values of the acids in 1:1-EtOH-H_2O, i.e. a solvent made up of equal volumes of ethanol and water. A calibration equation is derived relating substituent effects measured in this solvent to those measured in water. On the basis of this equation σ values are proposed for 25 substituents, although some of the values are subject to *caveats*, and several further substituents are also discussed.

INTRODUCTION

Even in Hammett's publications [Hammett (1937, 1940)] only a minority of the σ values tabulated were based directly on the ionization of substituted benzoic acids in water at 25°C. In the Table in Chapter 7 of Hammett (1940) the proportion is 17 entries out of 44. Most of the σ values given depended on first applying the Hammett equation to various reactions (e.g. the rates of alkaline hydrolysis of ethyl benzoates in 87.83% ethanol-water at 30°C) by using the data relating to substituents for which σ values based on the ionization of substituted benzoic acids were available, and then applying the established ρ values to the relevant experimental results for other substituents. Thus, right from the start, as pointed out by McDaniel and Brown (1958), there was but a limited number of "primary" σ values; there was a larger number of "secondary" σ values, and even some which might be termed "tertiary", the last-mentioned being based on correlation equations which had been established by using a mixture of primary and secondary σ values. This situation, in fact, led McDaniel and Brown (1958) to suggest that secondary σ values should as far as possible be based on ionization constants of benzoic acids in aqueous organic solvents such as 50% ethanol-water, rather than on rate or equilibrium measurements for a wider range of systems.

In Part 1 of the present project [Shorter (1994)] some 50 recommended σ values, covering 31 substituents, based on the ionization constants of substituted benzoic acids in water at 25°C have been tabulated. The absence of recommended σ_m or σ_p values for some of these substituents is either due to a complete absence of relevant data (probably the limited solubility of the acids in water is largely responsible) or to the unsatisfactory nature of such data as do exist. Data are available, in some cases in substantial quantity, for a further 3 substituents, but there are unsatisfactory aspects which make the tabulation of recommended σ values unwise. The logical next step in extending the benzoic-acid-based σ scale to further substituents is to consider apparent pK_a values in aqueous organic solvents, notably "50% ethanol". Such data are often represented by the symbol pK'_a but throughout the present report they will be described simply as pK values.

The practice of using such data for determining σ values seems to have begun with J.D. Roberts and co-workers (1949) and there are several papers in the *Journal of the American Chemical Society* between 1949 and 1953 which record pK measurements in "50% ethanol" by glass electrode for this purpose. At this point it should be made clear that the "50% ethanol" used by Roberts and various later workers was obtained by mixing equal volumes of ethanol and water, and it thus contains 23.6 mol-% ethanol. We shall refer to this solvent henceforth as 1:1 EtOH-H_2O. It must be carefully distinguished from the 50% ethanol-water used by Wepster and co-workers [Hoefnagel and Wepster (1989,1990)], which was obtained by mixing V dm^3 of ethanol with water and making up to 2V dm^3. This contains 22.4 mol-% ethanol. We will restrict the description 50% EtOH-H_2O to the solvent used by Wepster and colleagues.

Following Roberts, similar work involving p*K* values in 1:1 EtOH-H_2O was done by Bordwell and co-workers in the mid-1950s [Bordwell and co-workers (1952, 1956, 1957)]. As already mentioned, 1:1 EtOH-H_2O was recommended as a solvent by McDaniel and Brown (1958). Extensive measurements involving this solvent were made in the 1960s by Exner and co-workers (1962, 1966, 1970). Many of the σ values in the large compilations are derived from these studies, e.g. Exner (1978).

The first problem in extending the benzoic-acid-based σ scale through glass electrode measurements in 1:1 EtOH-H_2O is that p*K* values are not highly reproducible. Thus Roberts *et al.* (1949) recorded a p*K* value for benzoic acid of 5.75, but a value of 5.80 was found by Roberts and Regan (1953). Correspondingly the value for *p*-toluic acid moved from 5.94 to 6.00. Bordwell and Cooper (1952) recorded 5.73 for benzoic acid , while Exner and Jonás (1962) give 5.54. However, Exner (1966) gives 5.72. Thus measurements of p*K* for substituted benzoic acids in 1:1 EtOH-H_2O are of little worth unless the authors concerned calibrate their method against benzoic acid itself. Exner (1966) recognized this and standardized p*K* values determined by him or taken from the literature to a value of 5.72 for benzoic acid. This procedure is essentially an expression of the hope that Δp*K* values as between benzoic acid and substituted benzoic acids are more reproducible and precise than the absolute values of p*K*. (Δp*K* values are defined as pK_H - pK_X, so that they are positive for substituents X of positive σ values.) Exner (1966) expressed the view that the accuracy of Δp*K* values within a group of related acids would be about ± 0.04 units. There are, however, sometimes marked discrepancies between Δp*K* values for pairs of acids in 1:1 EtOH-H_2O as determined by different authors.

Hammett correlations of Δp*K* values for substituted benzoic acids in 1:1 EtOH-H_2O with σ values based on water solutions are at first sight quite good. Depending on the exact selection of substituents, correlation coefficients which are > 0.99 and often > 0.995 are obtained for regressions involving in the region of 10 to 20 data points. However, values of the standard error of the estimate are in the range 0.03 to 0.06, and this has serious implications for the reliability of σ values based on using the regressions as calibrations. McDaniel and Brown (1958) recognized this and put a figure of 0.1 as an estimated limit of uncertainty on such σ values. In Exner's compilation of 1978 this view appears to be accepted. Unfortunately this extent of uncertainty greatly reduces the worth of such σ values in physical organic chemistry. It also seems certain that these constants are often used by authors who do not appreciate their uncertainty.

There are other aspects of the Hammett treatment of Δp*K* values for substituted benzoic acids in 1:1 EtOH-H_2O which give cause for concern. These become apparent when the regressions are carried out in various different ways: *meta-* and *para*-substituents may be dealt with separately or together and the regression may be "constrained" or "unconstrained". "Constrained" regression means that the line is forced through the X=H origin, i.e. the equation is $\Delta pK = \rho\sigma$. "Unconstrained" regression means that an intercept is permitted, i.e. the equation is $\Delta pK = \rho\sigma + \text{intercept}$. Since we are dealing in these regressions with two very closely related systems, i.e. the same substrates undergoing the same process in two not very different solvents (from a molecular point of view the solvent 1:1 EtOH-H_2O is highly aqueous), it might have been expected that the unconstrained regressions would find only an insignificant intercept, with the H point lying essentially on the line. This appears to be the case when comparable numbers of *meta-* and *para*-substituents are taken in the same regression. [The use of "problem" substituents such as OH and NH_2 must be avoided. See Shorter (1994).] However, this appears to be a cancellation of two opposites, for the *meta*-substituents by themselves give a small negative intercept, while the *para*-substituents give a positive one. Further, the ρ values for the separate unconstrained regressions appear to differ appreciably, the ρ value for the *meta*-substituents being slightly higher than that for the *para*-substituents. The constrained regressions do not yield consistently worse correlations than the unconstrained, whether correlation coefficient or standard deviation of the estimate is taken as the measure of the goodness of fit.

Some tendency towards such dispersion of *meta-* and *para*-substituents may well be not uncommon, since it is by no means certain that the implied assumption of $\rho_m = \rho_p$ for the ionization of substituted benzoic acids in water will apply to other reactions and/or solvents. However, dispersion of this kind is probably usually obscured by the scatter of the data and perhaps by the common current practice of including both *meta* and *para* points in a single regression obtained by a computerized least-squares treatment, without actually plotting the graph.

If regression equations are to be used as calibrations for determining σ values, what form should they take? Constrained or unconstrained? *meta-* and *para*-substituents separately or together? We may recall that van Bekkum *et al.* (1959) suggested that the determination of values should be based largely on the use of *meta*-substituents. McDaniel and Brown (1958) obtained a calibration line by using data for benzoic acid and nine *meta-* or *para*-substituted benzoic acids. Their equation was: $-\mathrm{p}K = 1.522\sigma - 5.761$. Since the p$K$ value used for benzoic acid itself was 5.80 [Roberts and Regan (1953)] the point for the parent acid was about 0.04 off the line, i.e. in an unconstrained regression of $\Delta\mathrm{p}K$ on σ the intercept would be +0.04. In their calculations of σ values from the data for other substituted benzoic acids McDaniel and Brown used the equation in exactly the above form. Subsequently, however, Exner appears to have used the ρ value as obtained by McDaniel and Brown, but to have ignored the 0.04 deviation of the parent acid, i.e. $\Delta\mathrm{p}K$ was divided by 1.522 to calculate σ values regarded as being on the same scale as those calculated from ionization constants of benzoic acids in water. In this way the ρ value was essentially treated as a scaling factor as between the 1:1 EtOH-H_2O and water systems. Bordwell and Cooper (1952) had earlier made the same use of the ρ value of 1.464 as determined by Roberts and co-workers (1949). The latter authors found a pK intercept in the Hammett plot of 5.71, compared with a pK value of 5.75 for benzoic acid. They appear to have made use of this intercept in their calculations of new σ values. As mentioned above, a higher value of pK for benzoic acid was found later; the intercept used was then raised correspondingly to 5.77.

If we are to use the copious data for the pK values of substituted benzoic acids in 1:1 EtOH-H_2O to extend the σ scale, we have to decide on the best way of using the data. This will be done in the next section, but before this, the existence of related data for the ionization of substituted benzoic acids in other aqueous organic solvents must be mentioned.

There are extensive data which have been obtained by glass electrode measurements for benzoic acids in 80% w/w 2-methoxyethanol-water. (This solvent contains 48.6 mol-% of the organic component.) Regression analyses on a selection of data carried out in the same way as those summarized above for 1:1 EtOH-H_2O show very similar features. The *meta* points in unconstrained regression give a line of slightly greater slope than the *para* points do in a similar regression, the former line having a small negative intercept and the latter a positive one. The general quality of the correlations is not so good as in the case of 1:1 EtOH-H_2O. Probably the considerably greater mol-% of organic component introduces solvent effects which exert a specific influence on certain substituents. (2-Methoxyethanol most likely forms clusters at relatively low concentrations in water.) Thus these data, although copious, are less suitable than those for 1:1 EtOH-H_2O to use in the extension of the σ scale.

Hoefnagel and Wepster (1989,1990) have made extensive measurements in 50% EtOH-H_2O (for definition see above), as well as in other aqueous organic solvents, the use of the glass electrode being almost always involved. In Part 1 of the present project [Shorter (1994)] some use was made of these authors' results for solvents containing a very small percentage of ethanol, as well as their results for purely aqueous solutions. Regression analyses as above on a selection of their data for benzoic acids in 50% EtOH-H_2O show the same general features as already noted, i.e. two lines, etc. There is the further point that Hoefnagel and Wepster believe that their results for aqueous organic solvents in general provide evidence for the operation of substituent hydrophobic interactions as a factor influencing acid strength. They propose an extended Hammett equation involving Hansch's hydrophobic substituent constant π [Hansch and Leo (1979,1995)]:

$$\Delta = \rho\sigma + h\,\pi$$

($\Delta = pK_H - pK_X$). The hydrophobic component is not as considerable for substituted benzoic acids in 50% EtOH-H_2O as it is in some aqueous organic solvents, and provided the use of certain substituents is avoided, simple Hammett correlation gives respectable results. Certainly the incorporation of hydrophobic corrections in the case of 50% EtOH-H_2O, or for that matter 1:1 EtOH-H_2O, would not solve the main problems of basing σ values on ionization of benzoic acids in those solvents, as described above. It should be mentioned that Hoefnagel and Wepster (1989,1990) have applied corrections necessary to obtain thermodynamic pK_a values and they claim that substituent effects should be reliable to within 0.02 p*K* units in any of the solvents used. However, the scatter in the Hammett plots is somewhat greater than this. The possibility of using Hoefnagel and Wepster's results for 50% EtOH-H_2O as solvent to extend the Hammett scale is rather restricted by their choice of substituents and it seems more fruitful to concentrate on the results for 1:1 EtOH-H_2O as solvent.

BACKGROUND INFORMATION FOR TABLES AND NOTES

For the present purpose of extending the Hammett σ scale, it seems best to neglect the slight tendency for the plots of Δp*K* values in 1:1 EtOH-H_2O *versus* σ values based on purely aqueous solutions to show dispersion into separate lines for *meta*- and for *para*-substituents. The necessary calibration equation has therefore been established by treating the results for *meta*- and *para*-substituents together. Initially a wide range of data was considered, but after trial regressions the data for certain substituents have been discarded as giving serious deviations. In some cases the deviations can be understood as involving substituents whose electronic effects are likely to be subject to specific influences of solvent. The calibration equation is thus based on data for the following substituents:
(details in Table 2 in Appendix 1):

meta: Me, CF_3, COMe, CN, NHAc, NO_2, OMe, SO_2Me, Br.
para: Me, CN, NHAc, NO_2, SO_2Me, Br.

In applying the Hammett equation through linear regression by the method of least squares, it is usually assumed that the values of the abscissa (σ) are known precisely, while the values of the ordinate (i.e. log *K* or log k) are subject to experimental error. This assumption is obviously not strictly true, although often the experimental errors in the σ values may be much less than those in the ordinate. However, for the purpose of deriving a calibration equation it seems more proper to admit the possibility of experimental error both in Δp*K* determined for benzoic acids in 1:1 EtOH-H_2O and in σ as determined for the same acids in water. A procedure for this has recently been described [Decouzon *et al.* (1994)]. Further, it seems logical to use the Hammett equation in the form $\Delta pK = \rho\sigma$, i.e. to use constrained regression, with no intercept permitted. To use unconstrained regression with intercept would imply that σ values based on the ionization of benzoic acids in 1:1 EtOH-H_2O are being defined in a way different from those based on behaviour in aqueous solution.

We shall assume that the errors in Δp*K* values for solutions in 1:1 EtOH-H_2O are greater than those for σ values based on solutions in water by a factor of 1.5. On this basis and the experimental data for the substituents referred to above, the calibration equation is found to be $\Delta pK = 1.516\ (\pm 0.030)\sigma$, with s = 0.03 and r = 0.9987, and no point deviating significantly. (s = standard deviation of the estimate, r = correlation coefficient.) Δp*K* values for other substituents may therefore be converted to the corresponding σ values by dividing by 1.516. (If equal errors in ordinate and abscissa are assumed, the regression coefficient comes out at 1.517.)

It must be emphasized that for each substituent it is necessary to establish carefully what is the appropriate p*K* value for benzoic acid to be used in association with the p*K* value for the substituted acid. Ideally the authors concerned should themselves have checked the p*K* value for benzoic acid with the same apparatus, procedure, solutions, etc. at the time they studied the particular substituted acid. Unfortunately this is not always the case. There is sometimes reference to a p*K* value for benzoic acid determined in earlier work by the same authors, possibly "with the same apparatus". In other cases a p*K* value for benzoic acid as determined by other authors is quoted, possibly "by the same method", maybe in the form of the intercept at $\sigma = 0.00$ in a Hammett plot. In yet further cases the situation is obscure. This matter has to be considered in connection with assessing the reliability of the calculated σ value for any particular substituent. The details are in the Notes in Appendix 1.

The σ values in Table 1 are the most reliable that can be suggested at present. The substituents are presented in the same order as they appear in Exner (1978) and the values are rounded to two places of decimals. So few of the values are based on repetitive work by two or more research groups, that it is impossible to express the reliability specifically for each value of σ (cf. the situation in Part 1 of this project [Shorter (1994)]). The most one can say is that the uncertainty in most cases should not exceed 0.04, and should be not much worse than in the case of the primary σ values. Of course secondary values from the literature, determined often with calibration equations based on few points (perhaps not well chosen), may be much worse, cf. the uncertainty of 0.1 suggested by McDaniel and Brown (1958), as referred to earlier.

In some cases it seems wise not to include actual values in Table 1, but to refer readers to appropriate Notes in which some serious problem is explained. In certain other cases the inclusion of values in Table 1 seems justified, but with the *caveat* "but see Note...".

Supplementary information has been obtained by analogous treatment of Hoefnagel and Wepster's results for 50% EtOH-H_2O as solvent. The calibration equation based on the same substituents as that for 1:1 EtOH-H_2O above is $\Delta = 1.509\ (\pm 0.025)\sigma$, with $s = 0.0374$ and $r = 0.9981$. (As mentioned above Hoefnagel and Wepster use the symbol $\Delta = pK_H - pK_X$, and it is convenient to use this symbol when discussing their work.) Errors in Δ values for solutions in 50% EtOH-H_2O were assumed to be greater than those for σ values based on solutions in water by a factor of 2.0. If equal errors in ordinate and abscissa are assumed, the regression coefficient comes out at 1.511. Some of the information based on the work of Hoefnagel and Wepster (1989, 1990) is mentioned in the Notes for Table 1. Other such information is discussed in Appendix 2.

TABLE 1. Values of σ_m and σ_p based on the ionization of substituted benzoic acids in 1:1 EtOH-H_2O at 25°C.

Entry and Note Number	Exner Number	Substituent	σ_m	σ_p
1	26	C⋮CH	0.20	0.22
2	49	CH_2Ph	-0.08	-0.11
3	71	CH_2CN	0.15	0.17
4	103	CH_2OH	-	-0.01
5	109	CH_2OMe	0.02	0.03
6	115	CH_2OAc	-	0.05
7	132	CF_3	-	0.53
8	133	CH_2Cl	0.09	0.12
9	136	CH_2Br	0.11	0.12
10	139	CH_2I	0.07	0.09
11	195b	CO_2Et	0.36	0.45
12	251	$SiMe_3$	See Note 12	

Entry and Note Number	Exner Number	Substituent	σ_m	σ_p
13	337	NCS	0.48	0.49
14	343	N_3	0.29	0.18
15	372	$POBu_2$	0.38	0.52
16	373	$POPh_2$	0.44	0.58 (but see Note 16)
17	389	OH	0.05	-0.35 (but see Note 17)
18	390	OMe	See Note 18	
19	391	OEt	See Note 19	
20	401	OCF_3	0.39	0.36 (but see Note 20)
21	408	OAc	0.36	0.28 (but see Note 21)
22	420	OSO_2Ph	0.36	0.33
23	425	SMe	0.13	-0.01
24	435	SCF_3	0.40	0.50 (but see Note 24)
25	453	SOMe	0.50	0.48
26	456	$SOCF_3$	0.67	0.73 (but see Note 26)
27	467	SO_2CF_3	0.80	0.96 (but see Note 27)
28	478	SO_2F	See Note 28	
29	482	SF_5	0.61	0.69 (but see Note 29)

APPENDIX 1

The data in Table 2 were used to establish the calibration equation as set out in the Background Information above. The trial regressions initially included data for *p*-OMe and *p*-COMe, but these showed marked deviations. See discussion of the former in Note 18.

It will be seen from Table 2 that the Δp*K* values for several common and important substituents show considerable variations with source, e.g. *p*-Me, *m*-NO_2, *p*-NO_2, and *m*-Br. No doubt such variations are partly responsible for the scatter in the Hammett plot. At present it does not seem possible to be more selective in the sources used in order to improve the precision of the Δp*K* values used in the regression to establish the calibration equation.

It will also be seen from Table 2 that the values of pK_H vary between 5.72 and 5.80. The earlier (5.75) and the later (5.80) values from Roberts' work and Exner's standardization on a value of 5.72, having earlier obtained a value of 5.54, have already been discussed in the Introduction. Monagle *et al.* (1967)

and Tsvetkov *et al.* (1969) appear to have determined their own values of pK_H as 5.72, and Bordwell *et al.* (1952) determined their own value as 5.73.

TABLE 2. Data used in establishing the calibration equation for calculating σ values.

Substituent X	pK_X	pK_H	ΔpK	σ	Reference
m-Me	5.88	5.72	-0.16		Monagle *et al.* (1967)
	5.90	5.72	-0.18		Exner (1966)
		Mean	-0.17	-0.058	
p-Me	5.94	5.75	-0.19		Roberts *et al.* (1949)
	5.96	5.72	-0.24		Exner (1966)
	5.93	5.72	-0.21		Tsvetkov *et al.* (1969) (a)
	6.00	5.80	-0.20		Roberts and Regan (1953)
		Mean	-0.21	-0.165	
m-CF_3	5.11	5.75	0.64	0.435	Roberts, Webb, and McElhill (1950)
m-COMe	5.21	5.73	0.52	0.368	Bordwell *et al.* (1952)
m-CN	4.85	5.75	0.90	0.623	Roberts and McElhill (1950)
p-CN	4.70	5.75	1.05	0.668	Roberts and McElhill (1950)
m-NHAc	5.52	5.72	0.20	0.165	Exner *et al.* (1970)
p-NHAc	5.81	5.72	-0.09	-0.06	Exner *et al.* (1970)
m-NO_2	4.66	5.75	1.09		Roberts *et al.* (1949)
	4.61	5.72	1.11		Tsvetkov *et al.* (1969) (a)
	4.51	5.72	1.21		Monagle *et al.* (1967)
	4.60	5.72	1.12		Exner (1966)
		Mean	1.133	0.734	
p-NO_2	4.53	5.75	1.22		Roberts *et al.* (1949)
	4.47	5.72	1.25		Tsvetkov *et al.* (1969) (a)
	4.47	5.72	1.25		Monagle *et al.* (1967)
	4.43	5.72	1.29		Exner (1966)
		Mean	1.253	0.777	
m-OMe	5.59	5.72	0.13	0.114	Exner *et al.* (1970)
m-SO_2Me	4.78	5.73	0.95		Bordwell *et al.* (1952)
	4.76	5.72	0.96		Exner (1966)
		Mean	0.955	0.675	

Substituent X	pK_X	pK_H	ΔpK	σ	Reference
p-SO_2Me	4.68	5.73	1.05		Bordwell *et al.* (1952)
	4.61	5.72	1.11		Exner (1966)
		Mean	1.08	0.717	
m-Br	5.22	5.75	0.53		Roberts *et al.* (1949)
	5.11	5.72	0.61		Monagle *et al.* (1967)
	5.15	5.72	0.57		Tsvetkov *et al.* (1969) (a)
		Mean	0.57	0.396	
p-Br	5.53	5.75	0.40		Roberts *et al.* (1949)
	5.27	5.72	0.45		Tsvetkov *et al.* (1969) (a)
		Mean	0.425	0.227	

The pK data are from glass electrode measurements on benzoic acids at 25°C in 1:1 EtOH-H_2O. The σ values are the (unrounded) values for water solutions, taken from Part 1 of this project [Shorter (1994)].

NOTES FOR TABLE 1

Note 1: C⋮CH $\sigma_m = 0.198$ $\sigma_p = 0.224$
Experimental data from Landgrebe *et al.* (1966).
$pK_m = 5.45$ $pK_p = 5.41$ $pK_H = 5.75$ (authors' own value)

Note 2: CH_2Ph $\sigma_m = -0.079$ $\sigma_p = -0.106$
Experimental data from Exner (1966).
$pK_m = 5.84$ $pK_p = 5.88$ $pK_H = 5.72$ (standardized value)
cf. Hoefnagel and Wepster (1990): $\Delta_p = -0.14$; $\sigma_p = -0.093$.

Note 3: CH_2CN $\sigma_m = 0.152$ $\sigma_p = 0.172$
Experimental data from Exner (1966).
$pK_m = 5.49$ $pK_p = 5.46$ $pK_H = 5.72$ (standardized value)

Note 4: CH_2OH $\sigma_p = -0.013$
Experimental data from Exner *et al.* (1962).
$pK_p = 5.56$ $pK_H = 5.54$ (authors' own value)
Hoefnagel and Wepster (1989): $\Delta_m = 0.13$; $\sigma_m = 0.086$, cf. $\sigma_m = 0.07$ quoted in Part 1 [Shorter (1994)].

Note 5: CH_2OMe $\sigma_m = 0.020$ $\sigma_p = 0.026$
Experimental data from Exner (1966).
$pK_m = 5.69$ $pK_p = 5.68$ $pK_H = 5.72$ (standardized value)

Note 6: CH_2OAc $\sigma_p = 0.053$
Experimental data from Exner *et al.* (1962).
$pK_p = 5.46$ $pK_H = 5.54$ (authors' own value)

Note 7: CF_3 $\sigma_p = 0.528$
Experimental data from Roberts, Webb, and McElhill (1950)
$pK_p = 4.95$ $pK_H = 5.75$ (authors' own value)
cf. Hoefnagel and Wepster (1989): $\Delta_p = 0.78$; $\sigma_p = 0.517$

Note 8: CH_2Cl $\sigma_m = 0.086$ $\sigma_p = 0.119$
Experimental data from Exner (1966).
$pK_m = 5.59$ $pK_p = 5.54$ $pK_H = 5.72$ (standardized value)

Note 9: CH_2Br $\sigma_m = 0.106$ $\sigma_p = 0.119$
Experimental data from Exner (1966).
$pK_m = 5.56$ $pK_p = 5.54$ $pK_H = 5.72$ (standardized value)

Note 10: CH_2I $\sigma_m = 0.073$ $\sigma_p = 0.086$
Experimental data from Exner (1966).
$pK_m = 5.61$ $pK_p = 5.59$ $pK_H = 5.72$ (standardized value)

Note 11: CO_2Et $\sigma_m = 0.363$ $\sigma_p = 0.449$
Experimental data from Roberts and Moreland (1953).
$pK_m = 5.20$ $pK_p = 5.07$ $pK_H = 5.75$ (taken from earlier work of the same research group)

Note 12: $SiMe_3$ $\sigma_m = -0.132$ $\sigma_p = 0.00$
Experimental data from Roberts and Regan (1953).
$pK_m = 6.00$ $pK_p = 5.80$ $pK_H = 5.80$ (authors' own value)
cf. Hoefnagel and Wepster (1989): $\Delta_m = -0.22$; $\sigma_m = -0.146$. $\Delta_p = -0.01$; $\sigma_p = -0.007$.

However, according to Hoefnagel and Wepster (1989), the hydrophobic effect of this substituent may well be appreciable in these solvents. Thus these results are of doubtful value in relation to obtaining reliable σ values for $SiMe_3$. See Note 21 of Part 1 [Shorter (1994)].

Note 13: NCS $\sigma_m = 0.482$ $\sigma_p = 0.488$
Experimental data for *m*-NCS from Exner *et al.* (1970).
$pK_m = 4.99$ $pK_H = 5.72$ (standardized value)
Experimental data for *p*-NCS from Bordwell and Boutan (1956).
$pK_p = 4.97$ $pK_H = 5.71$ (authors' own value)

Note 14: N_3 $\sigma_m = 0.290$ $\sigma_p = 0.178$
Experimental data from Exner *et al.* (1970).
$pK_m = 5.28$ $pK_p = 5.45$ $pK_H = 5.72$ (standardized value)

Note 15: $POBu_2$ $\sigma_m = 0.376$ $\sigma_p = 0.515$
Experimental data from Tsvetkov *et al.* (1969) (b).
$pK_m = 5.15$ $pK_p = 4.94$ $pK_H = 5.72$ (authors' own value)

Note 16: $POPh_2$ $\sigma_m = 0.44$ $\sigma_p = 0.58$
These are mean values based on sets of data from two sources which do not agree closely, and should be regarded as giving only a general indication of the electronic effects.
Experimental data from Tsvetkov *et al.* (1969) (a).
$pK_m = 5.11$ $pK_p = 4.88$ $pK_H = 5.72$ (authors' own value)
Experimental data from Monagle *et al.* (1967).
$pK_m = 5.01$ $pK_p = 4.79$ $pK_H = 5.72$ (authors' own value)

Note 17: OH $\sigma_m = 0.05$ (mean value) $\sigma_p = -0.350$
Experimental data from Exner *et al.* (1970).
$pK_m = 5.72$ $pK_p = 6.25$ $pK_H = 5.72$ (standardized value)

and also from Roberts and Moreland (1953).

$pK_m = 5.61$ $pK_H = 5.75$ (taken from earlier work of the same research group)

In view of the poor agreement between the two sources of data for *m*-OH, the value of σ_m must be regarded as unreliable. See Part 1 [Shorter (1994)], and especially Note 26 therein, in which for aqueous solutions the values $\sigma_m = 0.10$ and $\sigma_p = -0.36$ are tabulated.

cf. Hoefnagel and Wepster (1989): $\Delta_m = 0.03$; $\sigma_m = 0.02$.

Hoefnagel and Wepster (1990): $\Delta_p = -0.53$; $\sigma_p = -0.351$.

Note 18: OMe

As indicated in Table 2, experimental data for *m*-OMe were used in establishing the calibration equation. The point lies fairly close to the line, with an effective value of $\sigma_m = 0.086$, compared with 0.114 in water.

For *p*-OMe there are several sources of data:

pK_p	pK_H	ΔpK	Reference
6.07	5.75	-0.32	Roberts *et al.* (1949)
6.12	5.80	-0.32	Roberts and Regan (1953)
6.01	5.72	-0.29	Tsvetkov *et al.* (1969) (a)
6.03	5.72	-0.31	Exner *et al.* (1970)
	Mean	-0.31	

The mean value of ΔpK gives $\sigma_p = -0.204$, cf. $\sigma_p = -0.288$ in aqueous solution. The discrepancy shows why it was desirable to discard *p*-OMe in establishing the calibration equation. It is evident that there is a remarkable specific solvent influence on the electronic effect of *p*-OMe as between water and 1:1 $EtOH-H_2O$. The results of Hoefnagel and Wepster (1989) confirm this situation: $\Delta_p = -0.31$; $\sigma_p = -0.205$. This solvent effect is possibly connected with the cross-conjugation of *p*-OMe and CO_2H. It is necessary to be very cautious about including *p*-OMe in Hammett correlations for processes in aqueous organic solvents.

Note 19: OEt $\sigma_m = 0.059$ $\sigma_p = -0.211$

Experimental data from Exner *et al.* (1970).

$pK_m = 5.63$ $pK_p = 6.04$ $pK_H = 5.72$ (standardized value)

The value for σ_m may be compared with 0.10 given for aqueous solution in Part 1 [Shorter (1994)]. cf. Hoefnagel and Wepster (1989): $\Delta_m = 0.07$; $\sigma_m = 0.046$. No value is available for σ_p in aqueous solution, but it would not be expected to be very different from that for OMe in such solution. Thus the comparable values for σ_p of OMe (Note 18) and OEt almost certainly indicate that both substituents are subject to a specific solvent influence as between water and 1:1 $EtOH-H_2O$.

cf. Hoefnagel and Wepster (1990): $\Delta_p = -0.34$; $\sigma_p = -0.225$.

Note 20: OCF_3 $\sigma_m = 0.390$ $\sigma_p = 0.360$ (mean values)

For this substituent there is a confusion in the literature, which cannot be resolved altogether satisfactorily. Yagupolskii *et al.* (1964) found:

$pK_m = 5.17$ $pK_p = 5.22$

Sheppard (1963) found:

$pK_m = 5.15$ $pK_p = 5.19$

These results are in reasonable agreement, but the problem lies in identifying the appropriate value of pK_H, which was not determined in the same investigations. Yagupolskii *et al.* (1960) had found pK_H to be 5.75. Yagupolskii *et al.* (1964) seem inclined to replace this by 5.71, but this appears to be an intercept term derived from Roberts *et al.* (1949) (see Introduction), who had in fact found $pK_H = 5.75$. If the results of Yagupolskii *et al.* (1964) are related to $pK_H = 5.75$, $\sigma_m = 0.383$ and $\sigma_p = 0.350$. Sheppard (1963) relates his results to the intercept term of 5.71 in Roberts *et al.* (1949), but if instead we again use $pK_H = 5.75$, we obtain $\sigma_m = 0.396$ and $\sigma_p = 0.369$. We combine the results from the two sources to give the mean values above.

Note 21: OAc $\sigma_m = 0.363$ $\sigma_p = 0.277$
Experimental data from Bordwell *et al.* (1956).
$pK_m = 5.16$ $pK_p = 5.29$ $pK_H = 5.71$ (authors' own value)

Exner *et al.* (1970) endeavoured to repeat this work, but were unable to get reproducible results owing to the hydrolysis of the substrates. The above values must be regarded with some caution.

Note 22: OSO_2Ph $\sigma_m = 0.356$ $\sigma_p = 0.330$
Experimental data from Exner *et al.* (1970).
$pK_m = 5.18$ $pK_p = 5.22$ $pK_H = 5.72$ (standardized value)

Note 23: SMe $\sigma_m = 0.132$ $\sigma_p = -0.007$
Experimental data from Bordwell *et al.* (1952).
$pK_m = 5.53$ $pK_p = 5.74$ $pK_H = 5.73$ (authors' own value)

The value for σ_p may be compared with 0.01 given for aqueous solution in Part 1 [Shorter (1994)].

Note 24: SCF_3 $\sigma_m = 0.399$ $\sigma_p = 0.498$ (mean values)

For this substituent there is a confusion in the literature, similar to that encountered in Note 20, the same authors being involved. If we adopt the same solution as proposed in Note 20, the experimental data may be set out as follows:

Yagupolskii *et al.* (1964).
$pK_m = 5.16$ $pK_p = 5.01$ $pK_H = 5.75$
Sheppard (1963):
$pK_m = 5.13$ $pK_p = 4.98$ $pK_H = 5.75$
leading, respectively, to:
$\sigma_m = 0.389$ $\sigma_p = 0.488$
$\sigma_m = 0.409$ $\sigma_p = 0.508$
and to the mean values stated above.

Note 25: SOMe $\sigma_m = 0.501$ $\sigma_p = 0.475$
Experimental data from Bordwell *et al.* (1957).
$pK_m = 4.97$ $pK_p = 5.01$ $pK_H = 5.73$ (authors' own value)

Note 26: $SOCF_3$ $\sigma_m = 0.666$ $\sigma_p = 0.726$
The above values are calculated from the experimental data of Yagupolskii *et al.* (1964):
$pK_m = 4.74$ $pK_p = 4.65$,
assuming $pK_H = 5.75$ (see Note 20).

Note 27: SO_2CF_3 $\sigma_m = 0.798$ $\sigma_p = 0.960$ (mean value)
Experimental data from Yagupolskii *et al.* (1964).
$pK_m = 4.54$ $pK_p = 4.24$
Experimental data from Sheppard (1963).
$pK_p = 4.35$
The above σ values are calculated on the basis of $pK_H = 5.75$ (see Note 20).

Note 28: SO_2F
Experimental data from Kalfus *et al.* (1970).
$pK_m = 4.53$ $pK_p = 4.33$

However, Exner (personal communication, 1995) considers that the solvent used was not precisely of 1:1 EtOH-H_2O composition. It would therefore not be wise to try to apply our calibration equation to these data.

Note 29: SF_5 $\sigma_m = 0.613$ $\sigma_p = 0.693$
These values are calculated from the data of Sheppard (1962):
$pK_m = 4.82$ $pK_p = 4.70$
assuming the value of $pK_H = 5.75$ (see Note 20).

APPENDIX 2

The papers by Hoefnagel and Wepster (1989, 1990) contain much information about Δp*K* values for many substituted benzoic acids in aqueous organic solvents, particularly mixtures of water with ethanol, acetone, or 2-methylpropan-2-ol. Much of the information, however, cannot be interpreted in a simple way in terms of σ and ρ values, because of the intervention of substituent hydrophobic interactions. As already mentioned, the hydrophobic component tends not to be as considerable for substituted benzoic acids in 50% EtOH-H_2O as it is in some aqueous organic solvents, but for certain substituents the hydrophobic component may be appreciable. This solvent is then not suitable for determination of reliable σ values. We give now a few examples of this situation.

One has already been referred to, in Note 12 above, involving $SiMe_3$. For CH_2SiMe_3 Hoefnagel and Wepster (1990) give $\Delta_m = -0.33$ and $\Delta_p = -0.37$. If these values are substituted into the correlation equation we have been using in connection with the work of Hoefnagel and Wepster, we obtain $\sigma_m = -0.219$ and $\sigma_p = -0.245$. However, much of this apparent electron-releasing affect is probably due to substituent hydrophobic interactions, which will undoubtedly be more marked for CH_2SiMe_3 than for $SiMe_3$, so little significance should be attached to these apparent σ values.

In view of the problem regarding the σ_p value of OPh as determined for aqueous solution to be -0.320 [see Shorter (1994), Note 28], experimental results for behaviour in 50% EtOH-H_2O are of interest. Δ = -0.02 [Hoefnagel and Wepster (1990)], giving an apparent σ value = -0.013. This Δ value certainly includes an appreciable acid-weakening hydrophobic component, so that *p*-OPh is indicated to be slightly electron-attracting in character. Hoefnagel and Wepster suggest that a "pseudo-aqueous" σ constant for *p*-OPh would have a value of about 0.04.

The substituent *m*-CEt_3 gives a Δ value of -0.37, corresponding to an apparent σ value of -0.245 [Hoefnagel and Wepster (1989)], i.e. very much more negative than the σ value of *m*-Bu^t at -0.07 [Shorter (1994)]. Undoubtedly there is a strong acid-weakening hydrophobic component in the case of CEt_3.

There are a few cases in which any substituent hydrophobic component may be neglected and the results of Hoefnagel and Wepster (1989, 1990) shed useful light on the behaviour of certain substituents dealt with in Part 1 [Shorter (1994)]. Thus, for CHO Hoefnagel and Wepster (1989) give $\Delta_m = 0.64$ and $\Delta_p = 0.77$. When substituted into our calibration equation for the work of these authors, these values give $\sigma_m = 0.424$ and $\sigma_p = 0.510$. In Part 1 the various available experimental values were not very concordant and the tabulation of recommended σ values was deemed unwise. The above value for σ_m supports the value 0.44 determined through measurements in water by Hoefnagel and Wepster (1989). For *p*-CHO the above value supports the value in Part 1 which was based on measurements in 10% EtOH-H_2O, namely 0.52, rather than the direct determinations on aqueous solutions by certain other authors, which yielded 0.43 and 0.45.

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