

THE *META* VERSUS *PARA* SUBSTITUENT EFFECT IN THE GAS PHASE: SEPARATION OF INDUCTIVE AND RESONANCE COMPONENTS

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Substituent effects of acceptor groups were measured for the gas-phase basicities of some substituted benzonitriles, methyl benzoates and acetophenones, and for gas-phase acidities of some substituted benzoic acids. Substituents considered were NO₂, CN, SO₂CH₃, SO₂F, CF₃, CH₂Cl, COCH₃ and COOCH₃, always in the *meta* and *para* positions. By combination with the literature data, a general conclusion is drawn that the substituent effects are proportional in the two positions and almost equal (the *para*:*meta* ratio is 1.06). No sign of any resonance effect was detected within the accuracy of the approach. The substituent effects in solution were recalculated statistically and the result was similar with a higher ratio, 1.09–1.19. It follows that the conjugation of acceptor groups, particularly of NO₂ as a typical example, has been overestimated by current theories when compared with the much stronger conjugation of typical donors. Moreover, the inductive effect is propagated more effectively from the *para* than from the *meta* position. Many correlations in the literature, neglecting this situation, have been in fact controlled by the more complex, and more striking, behaviour of donors, which has obscured the simpler and more monotonous effect of acceptors, usually less represented in the sample.

INTRODUCTION

Classical theory of substituent electronic effects distinguishes two main mechanisms,¹ inductive (later with the preferred term field effect)‡ and mesomeric (otherwise conjugative or resonance), although a more detailed classification has also been advanced.² Quantitative separation of these effects was pioneered by Taft and co-workers:³ numerous later attempts^{4,5} proceeded essentially along the same lines and brought only slightly different results. An important role in the separ-

ation was given to *meta* and *para* derivatives of benzene. The total substituent effect may be expressed by equations (1), in which Taft's dual substituent parameters (DSP),³ σ_I and σ_R , are measures of the inductive and resonance effect, respectively; the reaction constants ρ express the sensitivity towards these effects.

$$\log k_m - \log k^0 = \rho_I^m \sigma_I + \rho_R^m \sigma_R \quad (1a)$$

$$\log k_p - \log k^0 = \rho_I^p \sigma_I + \rho_R^p \sigma_R \quad (1b)$$

When the reactions investigated also obey the Hammett equation, it follows that all the ρ values must be proportional. Expressing the total substituent effect by the Hammett constants σ_p and σ_m , we obtain

$$\sigma_m = \sigma_I + \alpha \sigma_R \quad (2a)$$

$$\sigma_p = \lambda \sigma_I + \sigma_R \quad (2b)$$

There are therefore two assumptions involved in the model: additivity of the two effects and constancy of their ratio in various reactions. The constant α (0.33 or 0.5, according to the exact definition^{3a} of σ_R) is reasonably constant, excluding compounds with direct

‡ Prompted by a referee's comment, we are obliged to stress here that we shall not deal with the questions which of the terms 'field' or 'inductive' is more appropriate or which of the underlying models is more efficient. We use the traditional term 'inductive' and an operational definition: it is the substituent effect operative in a rigid molecule without multiple bonds. The different models were discussed recently.^{1d,e} In our opinion, the nature of the effect can hardly be described in terms of such simple models in accordance with quantum chemical laws; the discussion of which model is better is essentially useless.

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resonance between the substituent and the reaction centre ('through-resonance' as in 4-nitroaniline). Compounds with this through-resonance can be treated using special values^{3a,c,d} of σ_R (σ_R^+ or σ_R^-), or variable values^{3b} of α , or an additional term⁶ in equations (1). Our attention will be focused on normal cases without through-resonance. The second constant, λ , was originally taken as unity.³

Various statistical procedures for determining σ_I and σ_R on the basis of equations (1) have been analysed⁷ concerning the combined effects of experimental uncertainty and of various presumptions. Most reliable seem to be calculations in which σ_I values are based on separate measurements on aliphatic compounds.^{3d,4a} Then σ_R , ρ_I^+ and ρ_R^- are obtained together by least-squares treatment; the *meta* derivatives are in this case less important and can be treated separately. In a less reliable procedure, all σ and ρ values are obtained at once by a principal component analysis.^{4d} In all statistical methods there are excessive degrees of freedom which must be removed by arbitrary constraints, for instance by giving fixed values to certain substituents.^{4a,d,8,9} By relaxing these constraints the results can change dramatically.⁷ Still another kind of evaluation proceeds in terms of $\sigma_{m,p}$ and equations (2): it seems simple if σ_I are known but a problem arises with adjusting the two empirical constants, σ_p and σ_I , to the same scale.^{4c,5,10} In particular, the adjustment reported by Charton^{4c} is erroneous from the purely mathematical point of view (see the footnote in the Conclusions section).

For these reasons, an attempt was made to solve the problem in a simpler and more convincing way.⁵ If it were possible to find (even empirically) a subset of substituents without resonance effect ($\sigma_R = 0$), λ could then be obtained from a plot of σ_p vs σ_m , and scaling of σ_I could be accomplished from a plot of σ_I vs σ_m . It is evident from any collection⁸ of σ_I and σ_R values that the resonance effects of donors (σ_R negative) may be combined in different substituents with variable inductive effect, while acceptor groups are less variable. Typical acceptors have inductive and resonance component of the same sign (both σ_I and σ_R positive), and the former is dominant in most cases.¹¹ ('Nature has endowed us with a variation of donors whereas the common acceptors form a cluster-like group with less discriminating abilities'^{11a}). Actually we previously obtained a linear dependence⁵ (slope $\lambda = 1.14$) by plotting pK values of substituted benzoic acids in mixed solvents, *para* vs *meta*. The mathematical expression is equation (3), or in terms of σ constants, equation (4). The intercept ϵ , near to zero, is added here only for the purpose of later mathematical discussion (see Appendix).

$$(\log k_p - \log k^0) = \lambda(\log k_m - \log k^0) + \epsilon \quad (3)$$

$$\sigma_p = \lambda\sigma_m + \epsilon \quad (4)$$

It should be stressed that equations (3) and (4) hold

only for non-conjugated substituents; a more detailed enumeration will be given later. The substituents originally used⁵ were both strong and weak acceptors: NO_2 , CN , SO_2X , CHal_3 and CH_2X , and including even some neutral groups such as $\text{CH}_2\text{C}_6\text{H}_5$ and CH_2OCH_3 . Slight deviations were observed for carbonyl substituents, COCH_3 , COC_6H_5 , COOH and COOC_2H_5 . The plots were later complemented by more recent data and similar plots were constructed.^{7,12} The conclusions originally drawn were the following.

(a) Many substituents on the benzene ring, practically all groups without a lone electron pair in the α -position, act essentially by a single mechanism, whatever it may be termed. When it was called⁵ provisionally an inductive effect, this term need not correspond exactly to the definition given in the earlier footnote.

(b) The effect of these substituents is propagated through the benzene nucleus more effectively from the *para* than from the *meta* position. This statement does not depend on whether the inductive or field model is accepted. In this particular case, participation of π -electrons in the transmission was suggested and called the π -inductive effect.^{2,5}

(c) When this definition of the inductive effect is retained, it follows that many popular substituents are much less conjugated with the benzene nucleus than often assumed (through-resonance excluded): for many experimental quantities the contribution from conjugation may be unascertainable.^{5,13}

These conclusions were not accepted by Taft, Palm, Charton and others,^{3d,4c,14} mainly with the belief that resonance effects must be present but they are simply proportional to the inductive effects. Attention was also drawn to the possible influence of the solvent.^{3d} However, studies with various solvent systems gave the same result.^{7,15} Recently, conclusion (c) was repeatedly confirmed, particularly on nitrobenzene.¹⁶ Conclusion (b) also received support.¹⁷ Principal component analysis showed fundamental differences between the action of donors and acceptors,^{15b} in agreement with conclusion (a). In later papers, Taft and colleagues admitted that σ_R of acceptors may be effectively zero in certain circumstances,¹⁸ and used the modified values for gas-phase acidities.¹⁹ However, the most recent analysis⁸ accepts only non-zero values of σ_R for acceptors and assumes again $\lambda = 1$.

In this paper, we report on gas-phase acidities and basicities of benzene derivatives substituted in *meta* and *para* positions with acceptor groups; they were measured by Fourier transform ion cyclotron resonance (FT-ICR). The gas-phase measurements are directed against the objection^{3d} that the value $\lambda > 1$ is due only to solvent effects. They also have the merit of including reaction series which cannot be investigated in solution. The reactions chosen by us do not give any opportunity for through-conjugation; further, we tried to avoid compounds in which the site of protonation is uncertain. Finally, the selection of compounds was res-

tricted by their volatility. The authoritative review by Taft and Topsom¹⁹ lists 15 pairs of compounds satisfying these conditions, and an additional pair was found in the literature.²⁰ However, these examples were restricted to three substituents: NO₂, CN and CF₃. We investigated here mainly some less common groups: SO₂CH₃, SO₂F and CH₂Cl, and in addition also COCH₃ and COOCH₃, for which some deviation from equation (3) could be expected.⁵ The correlation of gas-phase acidities was carried out by Taft and Topsom¹⁹ by regression against σ_I and σ_R , but the few acceptor groups often had only a small influence on the results. In contrast, we performed the analysis only on acceptor substituents and used direct comparison according to equation (3).

EXPERIMENTAL

Materials. 3-Methoxycarbonylbenzenesulphonyl fluoride and 4-methoxycarbonylbenzenesulphonyl fluoride were described recently.^{21a} The remaining compounds are known and were characterized in previous work.²¹

Physical measurements. The general method for the determination of gas-phase proton transfer equilibria by FT-ICR has been described.²² As the aim of this work was the comparison of rather similar values, we used as far as possible the same set of reference compounds for a given pair of *meta* and *para* isomers. Therefore, the measured differences in acidity or basicity are highly significant and not loaded by scaling errors.

During our measurements we found some discrepancies between our experimental data and the current basicity scale.²³ For this reason, the *GB* value for dibutyl ether was revised. The *GB* value for acetophenone²³ was also not consistent with our data; in our opinion this should be corrected according to the data in Table 1.

The equilibrium constants were measured at a cell temperature of 338 K. If we neglect the heat capacity effects, the temperature correction of the Gibbs energy of proton transfer to 298 K can be written as

$$\Delta G(T_0) = \Delta G(T_1) + (T_1 - T_0) \Delta S$$

The entropy change is mainly due to the change in symmetry number of the species involved in the proton transfer ($\Delta S_{\text{rot}} = -R \ln \sigma$). In most cases $\Delta S \approx 0$. For bases having two identical functions $\Delta S = \Delta S_{\text{rot}} = -R \ln 2$, hence a correction of $-0.23 \text{ kJ mol}^{-1}$ was applied to ΔGB (see footnote f in Table 1). The results are given in Tables 1 and 2.

RESULTS AND DISCUSSION

Let us examine successively the three conclusions⁵ (a)–(c) given in the Introduction.

Substituent effects of acceptors

The relative acidities and basicities of benzene *meta* and *para* derivatives collected in Tables 1 and 2 represent 10 pairs. They can be combined with literature data^{19,20} to give altogether 26 pairs with eight different substituents in seven reaction series. All the data can be represented in a single plot (Figure 1), since equation (3) does not involve any particular constant characteristic of the reaction series. A statistical treatment must take into account that each variable is loaded with an experimental error and that the point for the unsubstituted compound has a particular position. The necessary statistics are explained in the Appendix and the results are given in Table 3, line 1. The standard deviation from the regression line is comparable to the assumed experimental error. Unexplained is the deviation of the point for C₆H₄(CN)₂ (Figure 1), but omitting this point does not improve the fit markedly (Table 3, line 1A). The salient feature is the general character of the effect of acceptors, irrespective of their different structures and also being in different series. This is in agreement with principal component analysis;^{15b} generally the behaviour of *meta* derivatives was simple (with a smaller number of terms in the correlation equation) than that of *para* derivatives, but when the substituents were restricted to acceptors, one term was sufficient for both series.

Using the same statistics, we are now able to recalculate the solution data which were previously treated only graphically.^{5,7,12,15a} In Table 3 attention was paid to selecting data comparable in both character and accuracy. For instance, the constants σ from a recent review⁸ are of variable reliability and in a plot similar to Figure 1 the regularity could disappear in the noise. Therefore, we examined separately groups of substituents (Table 3, lines 7–10) and some data were eliminated as outliers by virtue of their deviations (see footnotes to Table 3). For this reason, more important are the results obtained on homogeneous series of directly measured dissociation constants (Table 3, lines 2–6), in which no available data have been omitted. The series 2 in Table 3, represented also in Figure 2, is only a slight extension of the published plot.^{12c} In general, the results obtained in the gas phase and in solution are very similar, disproving the objection^{3d} that the validity of equation (3) is due only to solvent effects.

Taking together the available evidence, equation (3) seems to be one of the best experimentally supported empirical relationships in the field of common linear free energy relationships; it is valid for acceptors of different structure under different conditions. Particular attention was given to substituents of the CH₂X type, which could show at most a slight hyperconjugation, compared with substituents such as NO₂ or CN, for which resonance structures are possible. When the two groups were treated separately (series 3 and 4 in Table 3), the results were the same. In our opinion, these

Table 1. Gas-phase basicities (in kJ mol^{-1}) of *meta* and *para* derivatives of benzene

<i>meta</i> - and <i>para</i> -substituted compound (B)	Reference compound (Ref.)	$GB(\text{Ref.})^a$	ΔGB^c	$GB(B)^s$
<i>Benzonitriles</i>				
3-CH ₂ Cl	<i>c</i> -PrCN	784.9	+3.7	787.8
	PhCN	787.8 ^b	-0.9	
4-CH ₂ Cl	<i>c</i> -PrCN	784.9	+5.1	789.3
	PhCN	787.8 ^b	+0.8	
3-CF ₃	EtCHO	760.7	+6.4	768.2
	<i>n</i> -PrCHO	768.6	+0.7	
4-CF ₃	EtCHO	760.7	+5.0	765.9
	<i>n</i> -PrCHO	768.6	-2.5	
3-CN	MeCN	754.8 ^b	+1.9 ^f	757.5
	EtCHO	760.7	-2.4 ^f	
4-CN	MeCN	754.8 ^b	+2.4 ^f	759.3
	EtCHO	760.7	+0.4 ^f	
3-SO ₂ Me	HCO ₂ Et	775.3	+1.1	777.0 ^h
	<i>n</i> -PrCN	777.0	+0.5	
4-SO ₂ Me	HCO ₂ Et	775.3	+0.3	776.2 ^h
	<i>n</i> -PrCN	777.0	-0.3	
3-NO ₂	MeCN	754.8 ^b	+1.8	757.6
	EtCHO	760.7	-2.1	
4-NO ₂	MeCHO	747.3 ^b	+6.3	753.3
	MeCN	754.8 ^b	-2.3	
	EtCHO	760.7	-6.9	
<i>Methyl benzoates:</i>				
3-CO ₂ Me	(<i>n</i> -Pr) ₂ O	813.8	+4.9 ^f	818.5
	<i>c</i> -PrCO ₂ Me	816.3 ^b	+2.0 ^f	
4-CO ₂ Me	Et ₂ O	805.0 ^b	+11.1 ^f	816.1
	(<i>n</i> -Pr) ₂ O	813.8	+1.6 ^f	
3-SO ₂ Me	<i>c</i> -PrCO ₂ Me	816.3 ^b	+0.5 ^f	804.5
	MeCO ₂ Me	795.0 ^b	+9.1	
4-SO ₂ Me	Cyclopentanone	801.2	+3.2	801.7
	Et ₂ O	805.0 ^b	0.0	
3-SO ₂ F	MeCO ₂ Me	795.0 ^b	+6.1	781.8
	Cyclopentanone	801.2	+0.4	
4-SO ₂ F	Et ₂ O	805.0 ^b	-2.6	778.3
	HCO ₂ Et	775.3	+6.0	
3-SO ₂ F	<i>c</i> -PrCN	784.9	-2.1	781.8
	<i>t</i> -BuCN	786.2 ^b	-4.9	
4-SO ₂ F	HCO ₂ Et	775.3	+2.4	778.3
	<i>c</i> -PrCN	784.9	-5.5	
	<i>t</i> -BuCN	786.2 ^b	-8.4	
<i>Acetophenones:</i>				
3-COMe	(<i>n</i> -Pr) ₂ O	813.8	+9.6 ^f	824.5
	(<i>n</i> -Bu) ₂ O	821.2 ^c	+4.3 ^f	
4-COMe	PhCOMe	(825.9) ^d	-5.5 ^f	823.3
	<i>c</i> -PrCO ₂ Me	816.3 ^b	+6.8 ^f	
	(<i>n</i> -Bu) ₂ O	821.2 ^c	+2.3 ^f	
	PhCOMe	(825.9) ^d	-7.5 ^f	

^a Ref. 23, unless stated otherwise.

^b Additions and corrections to Ref. 23, personal communication, 1987.

^c Revised value; (*n*-Bu)₂O was found here to be a stronger base than (*n*-Pr)₂O and *c*-PrCO₂Me by 7.0 and 5.3 kJ mol^{-1} in GB , respectively.

^d This value reported in Ref. 23 is not consistent with our measurements.

^e Measured at 338 K and estimated to be valid at 298 K unless there is no symmetry change during proton exchange; see footnote f.

^f A correction of $-\Delta TR \ln 2 = -0.2 \text{ kJ mol}^{-1}$ has been applied to equilibria involving compounds with a symmetry number of 2.

^g Average values from the individual measurements as given in preceding columns.

^h Protonation of these compounds may possibly occur on the sulphonyl group instead of the cyano group. Since this concerns both the *meta* and *para* derivative, the conclusions would be little changed.

Table 2. Gas-phase acidities (in kJ mol^{-1}) of *meta*- and *para*-substituted benzoic acids

AH (benzoic acid)	Ref.H (reference compound)	$\Delta_{\text{acid}}G^\circ(\text{Ref.H})^a$	$\Delta\Delta_{\text{acid}}G^\circ$	$\Delta_{\text{acid}}G^\circ(\text{AH})$
3- CH_2Cl	4- CF_3 -phenol	1381.3	-1.3	1380.0
	3- CF_3 -phenol	1390.8	-10.6	
4- CH_2Cl	4- CF_3 -phenol	1381.3	-3.3	1377.9
	3- CF_3 -phenol	1390.8	-12.8	

^a Ref. 24.

findings make untenable the objections^{3d,14} that all these groups are in fact conjugated but their mesomeric effects are approximately proportional to their inductive effects. One must rather accept that the acceptor groups are simply less diversified,¹¹ and their simpler behaviour has been obscured in most correlations by the more conspicuous behaviour of donors.^{15b}

In conclusion to this section, one should define

exactly the substituents for which equation (3) is valid. Our original statement was that it is valid for groups without an unshared electron pair and without an electron sextet in the α -position.⁵ This definition can now be examined more closely. Certainly equation (3) holds even for substituents with multiple bonds if these groups are sufficiently strong acceptors [NO_2 , CN , $\text{N}=\text{NC}_6\text{H}_5$, $\text{C}_6\text{H}_2(\text{NO}_2)_3$], even a triple bond itself is sufficient in $\text{C}\equiv\text{CH}$ or $\text{C}\equiv\text{CC}_6\text{H}_5$. However, groups with a $\text{C}=\text{C}$ double bond without further electron-attracting substitution act as donors and deviate downwards in plots such as those in Figures 1 and 2 ($\text{CH}=\text{CHC}_6\text{H}_5$, C_6H_5). Groups with an α lone electron pair also deviate downwards,^{12a} usually very distinctly (OR , SR , NR_2 , halogens). When such substituents bear electron-attracting atoms or groups, their total mesomeric effect diminishes and the points in the graph approach the line pertinent to the acceptors.^{12a} In the limiting case the mesomeric effect is near to zero and the substituent is controlled by equation (3) [SCF_3 , SCOCH_3 , SOCF_3 , SeCF_3 , $\text{N}(\text{CF}_3)_2$]; in contrast, the electron-attracting power of the fluorine atoms in OCF_3 is not sufficient to overcome the conjugation. Insufficient data are available concerning unsubstituted alkyl groups which can possibly act as hyperconjugative donors in addition to their strong polarizability and to solvent effects. In mixed solvents, the point for unsubstituted methyl does not deviate⁵ but in water and in the gas phase¹⁹ alkyl groups behave as weak donors. Another question still unanswered is whether some substituents actually act as acceptors by resonance, deviating upwards in plots such as those in Figure 1 or 2. (The cases of through-resonance with a donor as reaction centre are excluded.) Such evident acceptors were $\text{B}(\text{OH})_2$ ⁵ and BBr_2 ,^{16b} but no further evidence has since been obtained. Concerning the carbonyl substituents (COCH_3 , COC_6H_5 , COOH , COOCH_3), the opinion was offered⁵ that their resonance constants are positive and just detectable within the framework of the correlation analysis (0.03–0.05 in σ units). In individual plots, their deviation may appear to be negligible or just detectable.^{5,12a,b,15a} Also some polyfluorinated substituents seem to deviate,^{5,12a} but also at the limits of accuracy.

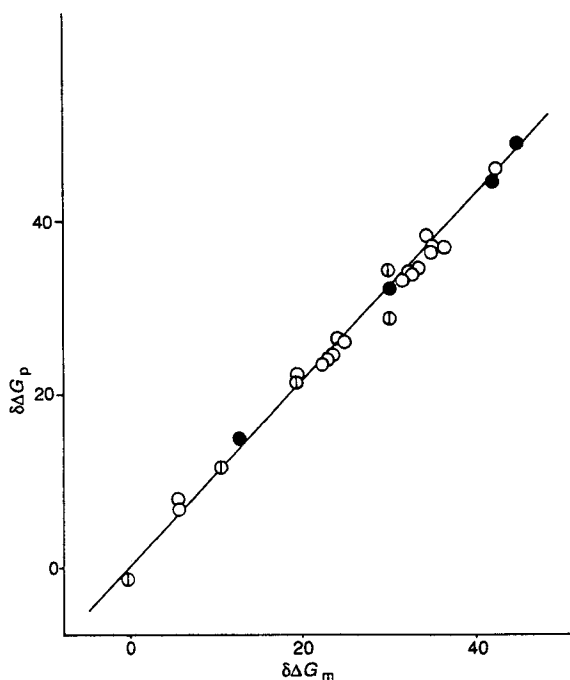


Figure 1. The *meta-para* plot for the Gibbs energies (kJ mol^{-1}) of the gas-phase ionization of various aromatic compounds: (●) acidities of substituted benzoic acids; (○) basicities of substituted benzonitriles; (○) basicities of various carbonyl compounds. Substituent used were only groups: CH_2Cl , CF_3 , COCH_3 , COOCH_3 , CN , NO_2 , SO_2CH_3 and SO_2F . Experimental data from this work and Refs 19 and 20

Table 3. Substituent effects of acceptors at the *meta* and *para* positions, correlated by equation (3)

Reaction	Medium	Quantity	b^a s_b^b	$s^{a,b}$	r^a	N^c
1 Protonation of ArCOOCH ₃ , ArCN, ArCOCH ₃ , ArCHO, ArCONMe ₂ , deprotonation of ArCOOH	Gas phase	ΔG°	1.058 0.009	0.94	0.9990 0.9985	26
1A Series 1 without C ₆ H ₄ (CN) ₂	Gas phase	ΔG°	1.062 0.008	0.81	0.9993 0.9989	25
2 Deprotonation of ArCOOH ^d	50% EtOH or 80% MCS	pK	1.155 0.009	0.028	0.9984 0.9991	49
3 Deprotonation of ArCOOH, only CH ₂ X substituents from series 2	50% EtOH or 80% MCS	pK	1.162 0.028	0.017	0.9941 0.9984	21
4 Deprotonation of ArCOOH, only substituents except CH ₂ X	50% EtOH or 80% MCS	pK	1.155 0.012	0.034	0.9986 0.9970	28
5 Deprotonation of ArCOOH ^e	Water, aqueous and non-aqueous solvents	pK	1.127 0.008	0.040	0.9985 0.9966	59
6 Deprotonation of nitrobenzoic acids ^f	Aqueous and non-aqueous solvents	pK	1.106 0.011	0.030	0.9993 0.9971	15
7 Constants σ , non-conjugated carbon substituents ^{g,h}	Various solvents and unspecified conditions	σ	1.086 0.016	0.027	0.9936 0.9973	58
8 Constants σ ; Si, Ge and Sn substituents ^{g,i}	Various solvents and unspecified conditions	σ	1.156 0.025	0.026	0.9937 0.9977	29
9 Constants σ ; sulphur substituents ^{g,j}	Various solvents and unspecified conditions	σ	1.137 0.009	0.024	0.9992 0.9981	28
10 Constants σ ; phosphorus substituents ^{g,k}	Various solvents and unspecified conditions	σ	1.187 0.021	0.039	0.9957 0.9943	28
11 Series 7–10 together		σ	1.142 0.008	0.030	0.9965 0.9981	143

^a See Appendix for the exact meaning of the statistics; the two values of r correspond to equations (A9) and (A10), respectively.

^b Standard deviation from the regression line in kJ mol⁻¹, pK units or σ units as appropriate.

^c The number of points corresponds to the number of substituents (without hydrogen) in lines 1–4 and 6–10, or to the number of solvents in line 5.

^d Substituents COX excluded; with seven points concerning these substituents the results are practically unchanged; data from Refs 5, 12a and 15a and references cited therein.

^e Including substituents COX but not CH₂X; data as in series 2 and in addition from Ref. 25.

^f Data from Ref. 25.

^g Data of various origins, sometimes estimated, Ref. 8.

^h Without pure alkyls; substituents CHMeOH, CMe₂OOH and CH₂P(O)Ph₂ excluded *a posteriori* as outliers, $s = 0.037$ if included.

ⁱ Substituents SnPh₃ and SiPh₃ excluded as outliers, $s = 0.050$ if included.

^j Only substituents with sulphur in a higher oxidation state, mainly SO₂X, sulphoxides only with electron attracting groups; two Se analogues included; substituent SO₂Cl excluded as outlier, $s = 0.042$ if included.

^k Only substituents with phosphorus in a higher oxidation state or with electron-attracting substituents, simple phosphines excluded; substituents P(O)PhTol and P(S)PhTol excluded as outliers, $s = 0.017$ if included.

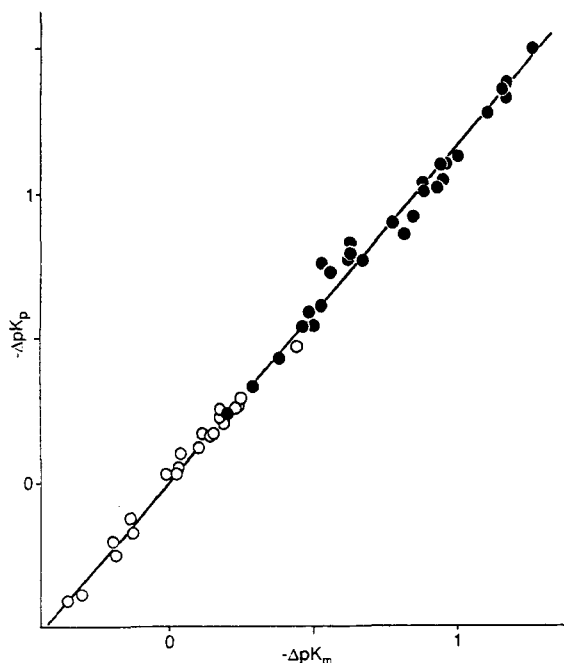


Figure 2. The *meta-para* plot of pK values of substituted benzoic acids in two mixed solvents (50% ethanol and 80% 2-methoxyethanol). (○) substituents CH_2X ; (●) acceptor substituents. Experimental data from Refs 12a and 25

Transmission through the benzene ring

Another result from Figures 1 and 2 and Table 3 is the values of slopes. For the gas phase, the slope $\lambda = 1.06$ is just significantly greater than unity; for the pK values in solution it is between 1.11 and 1.16. In the literature, λ was often taken as unity, either on *a priori* grounds^{3d,14a,b,26} or as an approximate assumption which cannot be disproved.^{4e,8} Even values lower than unity were sometimes claimed.^{14c} In one case,^{4c} the reason was omitting the important point (0, 0); this is a fatal mistake with few points. In other cases complex calculations were carried out,^{3d,4c} usually related to the principal component analysis.^{4a,d,f} We have shown previously⁷ that these calculations are never unambiguous; the resulting set of σ_I and σ_R can be transformed without affecting the condition of the best fit. For instance, any set of σ_I and σ_R can be replaced by new values σ_I^* and σ_R^* according to equations (5) with an arbitrary value of c . After this substitution, equations (2) retain their validity with an unchanged fit. However, λ is changed from $\lambda = 1$ to $\lambda = 1 + c - \alpha c$. In this way λ can assume any value.

$$\sigma_I = (1 - \alpha c)\sigma_I^* \quad (5a)$$

$$\sigma_R = \sigma_R^* + c\sigma_I^* \quad (5b)$$

To remove this ambiguity, some constraints were usually accepted. Popular was the constraint^{4a,d} $\sigma_R(\text{NMe}_2^+) = 0$, which was heavily criticized.^{8,9,11} We conclude that statistical procedures are unable to yield a value of λ as reliable as that obtained by a direct plot (see Figures 1 and 2 and similar relationships in particular cases).¹⁷

The value $\lambda > 1$ could be interpreted in terms of a more effective propagation of the inductive effect from the *para* position than from the *meta* position if we were able to define exactly what the pure inductive effect is. In aliphatic compounds an operational definition is evident,^{1c} for instance referring to the popular framework of bicyclo[2,2,2]octane, but the effect is largely independent of the model compounds chosen.^{1c,4c,8} To extend the definition to aromatic systems one must assume that there are at least some substituents which cannot be conjugated (say CCl_3 or CH_2X); the two hypotheses, $\lambda > 1$ and $\sigma_R(\text{CH}_2\text{X}) = 0$, then support each other.

Conjugation of the acceptor groups with the benzene ring

At this point, our previous opinion⁵ has received the strongest support from recent investigations. Practically all the reasoning was centred on the negligible conjugation in nitrobenzene¹⁶ and will not be discussed here.

Interaction of a general substituent with the benzene ring can be also expressed by an isodesmic reaction [equation (6)]. Of course, this interaction can be different in nature and cannot be equated with the resonance or conjugation terms.



Nevertheless, ΔH^0 values for equation (6), calculated for acceptors ($\text{X} = \text{NO}_2, \text{CHO}, \text{COCH}_3, \text{COOH}$), are lower in absolute values (-15 to -29 kJ mol^{-1}) than those for typical donors ($\text{X} = \text{OH} - 52.8, \text{NH}_2 - 47.5 \text{ kJ mol}^{-1}$). The validity of this comparison is somewhat compromised by the small number of available enthalpies of formation²⁷ and also by their relatively low accuracy.

CONCLUSIONS

The results in this paper give further support to the ideas of different behaviours of donor and acceptor substituents in correlation analysis,^{5,11} and of the negligible conjugation of acceptors (at least with the benzene ring). These results also contribute to the problem of the separation of inductive and resonance effects. However, the latter problem is very difficult and a quantitative solution can probably not be obtained with the desirable accuracy. In our opinion, the inductive effect can be estimated with some reliability from systems

other than benzene derivatives. The resonance effect obtained as a difference is not accurate and too variable.^{1c} The latest scheme with four different sets of σ_R constants,^{3d,8} all only for benzene derivatives, is merely a confession that a general separation is unattainable.^{1c} It appears that benzene derivatives are not the best model since the effects in *meta* and *para* positions are too similar; the solution of equations (1) or (2) with the unknowns σ_I and σ_R is then mathematically unstable. Note that perfect separation of inductive and resonance effects in the σ_I and σ_R values would be of theoretical importance, but does not affect the use of these constants in correlations according to equations (1); any of their linear combinations would give the same statistical fit.*

* This evident mathematical feature was neglected in the attempted separation which started with adjusting σ_I and σ_p to the same scale.^{4c} This adjustment was carried out repeatedly, and σ_I were scaled successively by a systematically increasing factor. In each case a set of σ_I and σ_R was calculated and tested on several series of (insufficiently differing) data. Evidently the fit must be the same, independent of the value of the variable factor; the best value cannot be found in this way.

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APPENDIX

Statistical procedure

Equation (3) requires a special kind of regression when the slope λ is to be estimated from a set of experimental values: $\log k_{p,i}$, $\log k_{m,i}$ and $\log k^0$. We assume here that the equation is valid and the deviations are caused only by experimental errors in these three quantities, which all possess the same distribution with zero expected value and variance δ^2 . We consider three possibilities as to how the experimental data have been obtained:

- (1) All values of $\log k_{p,i}$, $\log k_{m,i}$ and $\log k^0$ are available from a common source with the same accuracy.
- (2) All $\log k_{p,i}$ and $\log k_{m,i}$ have the same accuracy, but $\log k^0$ was obtained by repeated measurements and is much more accurate.
- (3) Always a subset of three values of $\log k_{p,i}$, $\log k_{m,i}$ and $\log k_i^0$ is available from the same source; this means that each value of $\log k_i^0$ is used only together with the $\log k_{p,i}$ and $\log k_{m,i}$ values to which it belongs.

In case (3), the actual variables are $(\log k_p - \log k^0)_i$ and $(\log k_m - \log k^0)_i$ and the regression is forced through the origin: $\epsilon = 0$ in equation (3). In case (2), the regression also passes through the origin with a good approximation. In case (1), the experimental value of $\log k_0$ constitutes a unique additional point with the coordinates (0, 0) and ϵ means the second parameter to be estimated. If, however, the slope λ is near unity, this estimation would be ineffective and the regression line is better assumed to pass through the origin. This is seen from the graphical representation: when the experimental points are pictured as small circles, the point for $\log k^0$ is represented by a given line at an angle of 45° to the coordinate axes. Therefore, we used the regression line passing through the origin [equation (A1)] in all cases. The least-squares condition for equal experimental errors in either coordinate is equation (A2). In geometrical terms it means that deviations are minimized in the perpendicular direction to the regression line.²⁸

$$y = bx \tag{A1}$$

$$SS_R = \frac{1}{1 + b^2} \sum_i (y_i - bx_i)^2 = \min \tag{A2}$$

By introducing $b = \tan \beta$ we obtain the solution in a convenient form [equation (A3)]. The residual sum of squares is given by equation (A4). The standard deviation from the regression line [equation (A5)] represents an estimate of δ in case (1) or (2) or of $\sqrt{2}\delta$ in case (3).

$$\tan 2\beta = \frac{2b}{1 - b^2} = 2 \sum_i x_i y_i \left/ \left(\sum_i x_i^2 - \sum_i y_i^2 \right) \right. \tag{A3}$$

$$RSS = \sum_i y_i^2 - b \sum_i x_i y_i \tag{A4}$$

$$s^2 = RSS / (n - 1) \tag{A5}$$

The statistical distribution of b was not examined here. Its standard deviation is given approximately by equation (A6) (for another approximation, see Ref. 28).

$$s_b = \frac{sb}{\sum_i x_i y_i} \sqrt{\sum_i x_i^2 + \sum_i y_i^2} \tag{A6}$$

All regressions in this paper have been calculated according to equations (A1)–(A6).

A problem may arise when we want to define a ‘correlation coefficient’ comparable to that used in the literature in the case of common regression. One starts better from the term coefficient of determination, which is defined by either equation (A7) or (A8).

$$r^2 = \frac{\left[\sum_i (\hat{y}_i - \bar{y})(y_i - \bar{y}) \right]^2}{\left[\sum_i (\hat{y}_i - \bar{y})^2 \sum_i (y_i - \bar{y})^2 \right]} \tag{A7}$$

$$1 - r^2 = \frac{\sum_i (y_i - \hat{y}_i)^2}{\sum_i (y_i - \bar{y})^2} \tag{A8}$$

In the case of common regression these two definitions yield the same well known expression for r . In our case, the results are different. From equation (A7) we obtain equation (A9) whether we use equation (A7) as it is written or replacing y by x in it:

$$r^2 = \frac{\left(\sum_i x_i y_i \right)^2}{\left(\sum_i x_i^2 \sum_i y_i^2 \right)} \tag{A9}$$

With equation (A8) it is not clear what should be substituted for the denominator; we propose a preliminary definition as in the equation

$$1 - r^2 = \frac{RSS}{\left[\sum_i (x_i - \bar{x})^2 + \sum_i (y_i - \bar{y})^2 \right]} \tag{A10}$$

The correlation coefficient does not have the same meaning in the two definitions. In equations (A8) and (A10) it can be understood in terms of information entropy; it is the ratio of entropy (uncertainty) after the

regression has been applied to the entropy before the regression, when only the mean values of x and y were known. Equations (A7) and (A9) represent the angle of two vectors in the polydimensional space; the angle is

small when the correlation is close. We hope to examine this mathematical problem more closely.²⁹ In Table 3 the values of r according to the two definitions are given; the differences in these examples are negligible.