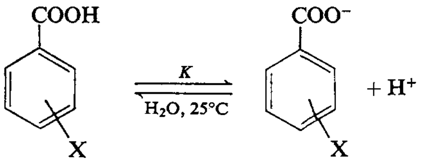
1 The Hammett $\sigma\rho$ relationship

1.1. Introduction. The student of organic chemistry is introduced early to the theory of two distinct and apparently mutually independent modes for transmission of electronic effects, namely induction and resonance (mesomerism). Even if their exact origin and manner of propagation remain uncertain in anything but very simple terms, their terminology at least becomes extremely familiar: moreover, such concepts, despite their limitations, are seen to be the foundation-stones of theoretical interpretation of the mechanisms of organic reactions. Proximity effects and steric interactions can confuse the issue, but although these are exceedingly intricate in origin, the possibility of their intervention is apparent from consideration of the stereochemistry of the molecules involved. In their absence, the effect of a given substituent on reaction rates or equilibrium constants, in terms of its inductive and resonance interaction, is effectively consistent, *qualitatively* at least, through the whole spectrum of reaction types.

The basic aim of the Hammett equation is to evaluate the degree of this consistency in *quantitative* terms. This involves elucidating the contribution of inductive and resonance effects to free energy changes on going from one side to the other of an equilibrium or from the ground state to the transition state of a reaction. Such free energy changes will be proportional to the logarithms of rate or equilibrium constants.

1.2. The Hammett equation. The effect of substituents in the benzene nucleus on the acidity of benzoic acid expressed in terms of $\mathrm{p}K_a$, and the explanation of such effects in terms of induction and resonance, forms a specific example of the ideas generally expressed above. It is also particularly convenient in that, for *m*- and *p*-substituted benzoic acids, electronic factors are very unlikely to be complicated by steric interactions between substituent and reaction site. A quantitative measure of these electronic effects is thus given by the difference between the $\mathrm{p}K_a$ value of the substituted benzoic acid and that of benzoic acid itself. A parameter σ, the *substituent constant*, may then be defined by (1.1) for the equilibrium [*1.1*], which is a measure of the size of such effects for a given substituent in this case. K is the equilibrium constant for the substituted benzoic acid and K_0 is the equilibrium constant for benzoic acid. Since pK_a values are affected by both solvent and temperature, we



[*1.1*]

$$\sigma_x = \log K - \log K_0 = -\mathrm{p}K_a + (\mathrm{p}K_a)_0 \qquad (1.1)$$

arbitrarily define σ as referring to aqueous solution at 25 °C. Table 1.1 gives the pK_a values for *m*-nitro-, *p*-nitro-, *m*-methyl-, and *p*-methylbenzoic acids, and benzoic acid itself, from which by use of (1.1), σ_m and σ_p for these two groups have been calculated.

TABLE 1.1 pK_a *values of some benzoic acids* (H_2O, 25 °C)

X	pK_a (*meta*)	pK_a (*para*)	σ_m	σ_p
NO_2	3.50	3.43	0.71	0.78
CH_3	4.28	4.38	−0.07	−0.17

(The pK_a of benzoic acid is 4.21.)

Electron-withdrawing groups, such as NO_2, increase the equilibrium constant K of [*1.1*] because they stabilise the carboxylate anion; thus the pK_a is numerically smaller than that for benzoic acid, and σ is consequently *positive*. Electron-donating groups, CH_3 for example, decrease the equilibrium constant, and so their σ values are *negative*.

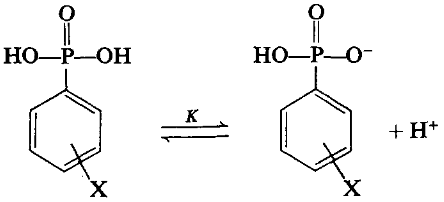
In table 1.2 are shown substituent constants calculated from (1.1) for a variety of common groups (Jaffé, 1953; McDaniel & Brown, 1958).

We must now examine whether such σ values are really constant; that is, do they correctly predict substituent effects on other side chain reactions or equilibria of benzenoid molecules? In many instances they do, and this is illustrated by the following two examples.

TABLE 1.2 *Substituent constants for common groups*

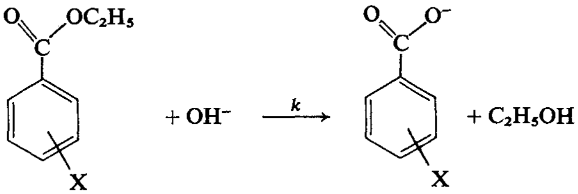
Substituent	σ_m	σ_p	Substituent	σ_m	σ_p
$N(CH_3)_2$	−0.21	−0.83	NH_2	−0.16	−0.66
OCH_3	0.12	−0.27	OCH_2CH_3	0.10	−0.24
CH_3	−0.07	−0.17	CH_2CH_3	−0.07	−0.15
$CH(CH_3)_2$	−0.07	−0.15	$C(CH_3)_3$	−0.10	−0.20
F	0.34	0.06	Cl	0.37	0.23
Br	0.39	0.23	I	0.35	0.28
$COOC_2H_5$	0.37	0.45	$COCH_3$	0.38	0.50
CN	0.56	0.66	NO_2	0.71	0.78
$\overset{+}{N}(CH_3)_3$	0.88	0.82			

The first is the acid dissociation of phenylphosphonic acids (Jaffé, Freedman & Doak, 1953):



[*1.2*]

The second is the alkaline hydrolysis of ethyl benzoates (Ingold & Nathan, 1936; Evans, Gordon & Watson, 1937):



[*1.3*]

Data for the two reactions are recorded in table 1.3, while figs. 1.1 and 1.2 show the graphs of log K/K_0 for the acid dissociations against σ, and log k/k_0 for the hydrolyses against σ, respectively. Both of these graphs show good linearity for *m*- and *p*-substituents. As fig. 1.2 reveals, however, *o*-substituents do not fall on, or even near, the line defined by the other substituents; this demonstrates that steric interactions between substituent and reaction centre, masking electronic factors, vary from

TABLE 1.3 *Selected equilibria and reaction data*

Acid dissociation constants of phenylphosphonic acids (H_2O, 25 °C)

Substituent	pK_a	Substituent	pK_a
H	1.83	*p*-Br	1.60
m-NO_2	1.30	*m*-Cl	1.55
p-NO_2	1.24	*p*-Cl	1.66
m-Br	1.54	*p*-CH_3	1.98

Specific rate constants for alkaline hydrolysis of ethyl benzoates (85 % *aq. ethanol*, 25 °C)

Substituent	$10^5\ k/\mathrm{l\ mol^{-1}\ s^{-1}}$	Substituent	$10^5\ k/\mathrm{l\ mol^{-1}\ s^{-1}}$
o-OCH_3[a]	7.8	*p*-Cl	267
p-OCH_3	13	*o*-NO_2[a]	541
m-CH_3	43	*m*-NO_2	4290
p-CH_3	28	*p*-NO_2	7200
H	62.1	*o*-Cl[a]	139
m-Cl	477		

[a] The relevant values of σ_o ($\log K - \log K_o$) for the *o*-substituted benzoic acids are 0.29 for *o*-CH_3, 0.26 for *o*-Cl, and 1.03 for *o*-NO_2.

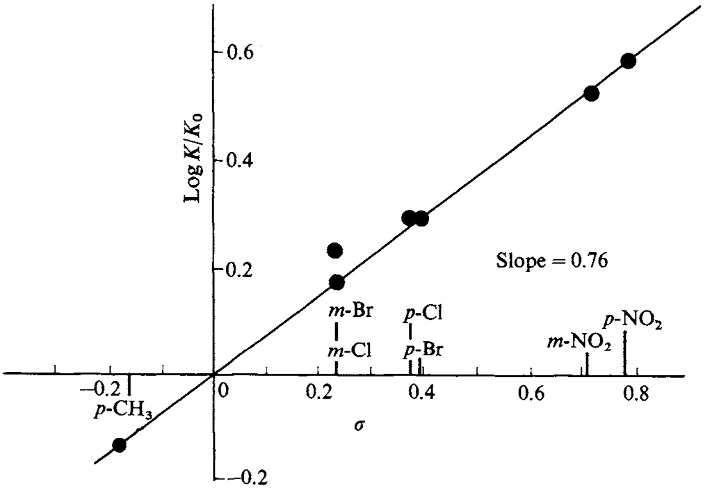


Fig. 1.1. Log K/K_0 *vs*. σ, dissociation of phenylphosphonic acids.

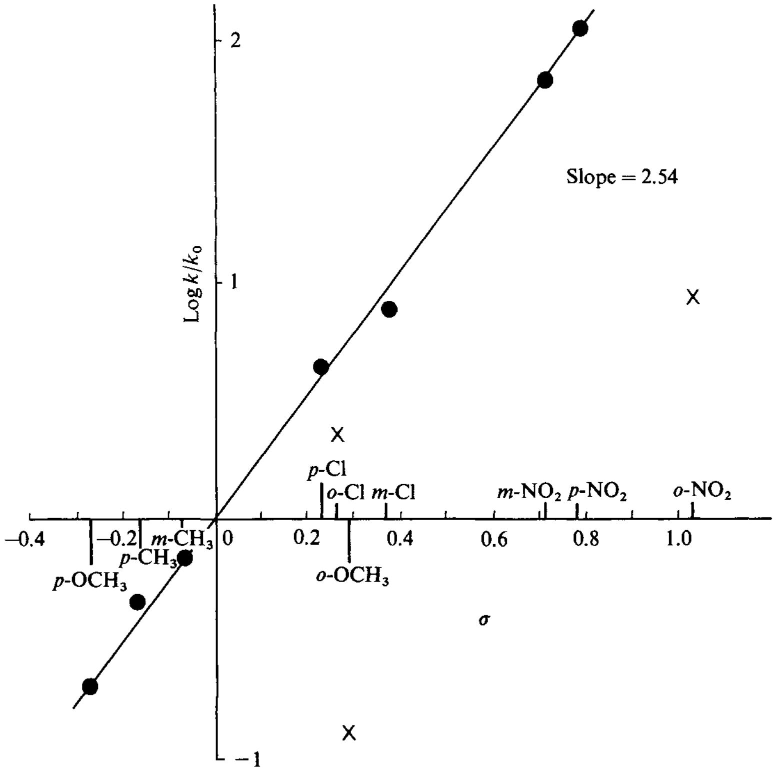


Fig. 1.2. Log k/k_0 *vs.* σ, alkaline hydrolysis of ethyl benzoates; σ_m and σ_p, ●; σ_o, × .

one reaction type to another, and *o*-substituents must be left out of the reckoning, at least for the present.

The linearity of these plots for the remaining substituents reveals that the dissociation of benzoic acids, the dissociation of phenylphosphonic acids, and the alkaline hydrolysis of ethyl benzoates respond in the same manner to the influence of *m*- and *p*-substituents. The slope of the correlation line, 0.76 and 2.54, for the latter two respectively, is referred to as ρ, the *reaction constant*. It is a measure of the sensitivity of the reaction or equilibrium to electronic substituent effects, being by definition 1.00 for the dissociation of benzoic acids in water at 25 °C. In both of the examples chosen, ρ is also positive. This means, for the acid–anion equilibrium, that electron-donating groups decrease the extent of dissociation, while electron-withdrawing groups increase it,

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as can be readily argued from their effect on the stability of the anion. Similarly, electron donor substituents retard the rate of the hydrolysis reaction, while electron acceptors accelerate it; the carbon atom of the carbonyl group of an ester will become more reactive towards nucleophiles with electron-withdrawing groups present.

Generally, therefore, side chain reactivity of *m*- and *p*-substituted benzenes correlates linearly with σ values. For a reaction we can thus write the equation

$$\log k/k_0 = \sigma\rho \qquad (1.2)$$

where k is the rate constant for the side chain reaction of a *m*- or *p*-substituted benzene derivative, and k_0 is the rate constant for the unsubstituted compound. The analogous equation for a side chain equilibrium will be

$$\log K/K_0 = \sigma\rho \qquad (1.3)$$

Equations (1.2) and (1.3) are known collectively as the Hammett equation (Hammett, 1940) which, since it correlates energy changes in reactions or equilibria with those in benzoic acid dissociations, represents a *linear free energy relationship*. It is useful here to summarise the general sign convention for (1.2) and (1.3), discussed above for particular examples, which follows from the definition of the sign of σ from (1.1). *If ρ for a side chain reaction is positive, that reaction is accelerated by electron-withdrawing substituents, and slowed down by electron-donating substituents; if it is positive for an equilibrium, electron-withdrawing substituents favour the right-hand side of the equation defining K for the equilibrium, relative to electron-donating substituents which favour the left-hand side*. A negative ρ value obviously implies the opposite of this for reactions and equilibria.

It is worth noting that all acid dissociations, of general form

$$\mathrm{BH}^{n+} \rightleftharpoons \mathrm{B}^{(n-1)+} + \mathrm{H}^{+} \qquad (1.4)$$

will have positive ρ values whether n is positive, negative, or zero, because the base $\mathrm{B}^{(n-1)+}$ will be stabilised by electron-withdrawing substituents relative to the acid BH^{n+}.

Alternative forms of (1.2) and (1.3) are

$$\log k = \sigma\rho + \log k_0 \qquad (1.5)$$

and

$$\log K = \sigma\rho + \log K_0 \qquad (1.6)$$

Plotting log k or log K against σ should give a straight line with intercept log k_0 or log K_0 on the ordinate. This procedure involves less work than plots of (1.2) and (1.3), as the reader can verify if the data of table 1.3 are plotted in this manner, and it will be employed here subsequently. Another expedient is to multiply rate constants by a uniform factor (e.g. 10^5 in table 1.3) to avoid negative logarithms; clearly this will neither alter the degree of correlation nor the value of ρ. Notice also that, if pK_a values are plotted directly, *the* ρ *value is the negative of the measured slope.*

Finally, before considering the significance of ρ and σ in detail, a brief note with regard to the general accuracy of the Hammett correlation is appropriate. For certain sets of data relating to reactivities of benzene side chains, deviations from the simple Hammett equation may be observed which are large, uniform, and confined to distinct classes of substituents in the *p*-position. Such deviations imply a breakdown in the basic assumptions of the equation; they are mechanistically significant, and will be considered later. At this stage, we are concerned rather with small random deviations, such as can be seen in figs. 1.1 and 1.2 where, although the correlation is good, there are some slight deviations from the line. These have their origin in either experimental inaccuracies, which are generally much larger than the particular workers concerned estimate them to be, or second order irregularities in behaviour of individual substituents. Indeed, the experimental values recorded for the pK_a's of substituted benzoic acids, fundamental to the evaluation of σ, vary quite considerably from one worker to the next, even though measured under the same conditions. This is illustrated very clearly, for example, in McDaniel & Brown's work (1958). Considerations of this sort lead to the conclusion that the third decimal place in σ or ρ is absolutely meaningless. Even deductions putting emphasis on the second place should be treated with some reservation.

1.3. The reaction constant ρ. Table 1.4 gives ρ values for a few reactions and equilibria. Later, references will be made to many further reaction constants. Those in the table serve as simple examples from which several general points can be made. Firstly, it should be noted that all the equilibria chosen are acid dissociations, and consequently the ρ values are positive.

The reaction constant ρ has been interpreted as a measure of the susceptibility of the reaction or equilibrium to substituent effects; a large ρ value for an equilibrium thus implies a large charge *change* at

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TABLE 1.4 *Some typical reaction constants*

	Equilibria		ρ
[*1.4*]	$XC_6H_4COOH \rightleftharpoons XC_6H_4COO^- + H^+$	(H_2O, 25 °C)	1.00
[*1.5*]		(50% aq. C_2H_5OH, 25 °C)	1.60
[*1.6*]		(C_2H_5OH, 25 °C)	1.96
[*1.7*]	$XC_6H_4CH_2COOH \rightleftharpoons XC_6H_4CH_2COO^- + H^+$	(H_2O, 25 °C)	0.49
[*1.8*]	$XC_6H_4CH_2CH_2COOH \rightleftharpoons XC_6H_4CH_2CH_2COO^- + H^+$	(H_2O, 25 °C)	0.21
[*1.9*]	$XC_6H_4CH{=}CHCOOH \rightleftharpoons XC_6H_4CH{=}CHOO^- + H^+$	(H_2O, 25 °C)	0.47
[*1.10*]	$XC_6H_4\overset{+}{N}H_3 \rightleftharpoons XC_6H_4NH_2 + H^+$	(H_2O, 25 °C)	2.77
[*1.11*]		(30% aq. C_2H_5OH, 25 °C)	3.44
[*1.12*]	$XC_6H_4OH \rightleftharpoons XC_6H_4O^- + H^+$	(H_2O, 25 °C)	2.11
[*1.13*]	$XC_6H_4PO(OH)_2 \rightleftharpoons XC_6H_4PO.OH.O^-$	(H_2O, 25 °C)	0.76
[*1.14*]		(50% aq. C_2H_5OH, 25 °C)	0.99
	Reactions		
[*1.15*]	$XC_6H_4COOC_2H_5 + OH^- \rightleftharpoons XC_6H_4COO^- + C_2H_5OH$	(85% aq. C_2H_5OH, 25 °C)	2.54
[*1.16*]	$XC_6H_4CH_2OCOCH_3 + OH^- \rightleftharpoons XC_6H_4CH_2OH + CH_3COOH$	(60% aq. $(CH_3)_2CO$, 25 °C)	0.47
[*1.17*]	$XC_6H_4N(CH_3)_2 + CH_3I \rightleftharpoons XC_6H_4N^+(CH_3)_3I^-$	(90% aq. $(CH_3)_2CO$, 35 °C)	−3.30
[*1.18*]	$XC_6H_4NH_2 + C_6H_5COCl \rightleftharpoons XC_6H_4NHCOC_6H_5 + HCl$	(C_6H_6, 26 °C)	−2.78

the atom of the side chain attached directly to the ring carbon atom from one side of the equilibrium to another. Therefore interposition of a methylene unit between the side chain and the ring results in considerable decrease in ρ. This is illustrated by the sequence of dissociations of benzoic, phenylacetic and phenylpropionic acids [*1.4*], [*1.7*] and [*1.8*]. There is however an increase in ρ value from equilibrium [*1.8*] (phenylpropionic acid) to [*1.9*] (cinnamic acid). This is due to the additional mode of communication, in the latter case, of the substituent effect at the ring carbon atom to the reaction centre by conjugation through the double bond.

Varying the solvent will also affect the size of ρ. This is shown by sequences [*1.4*], [*1.5*] and [*1.6*], and [*1.13*] and [*1.14*]. As the solvent is changed from water (dielectric constant 79) to ethanol (dielectric constant 24) there is a decreasing degree of charge stabilisation by solvation of the acid anion relative to the neutral acid function. This results in greater susceptibility of the dissociation to substituent effects, and thus ρ increases.

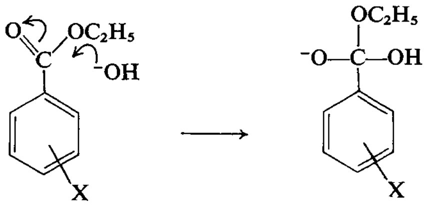
When we turn our attention to the irreversible reactions [*1.15*], [*1.16*], [*1.17*] and [*1.18*], we must remember that such reactions can be interpreted as equilibria between the reactants and the transition state (TS) of the reaction

$$\text{Reactants} \overset{K^{\ddagger}}{\rightleftharpoons} \text{TS} \xrightarrow{k^{\ddagger}} \text{Products} \tag{1.7}$$

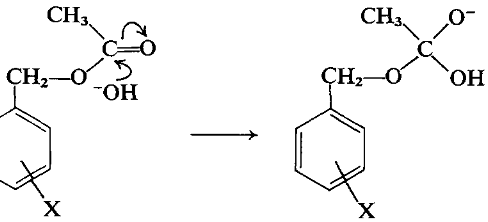
$$K^{\ddagger} = [\text{TS}]/[\text{Reactants}] \tag{1.8}$$

This notion is considered in some detail in chapter 5, but at this stage it must be noted that for interpretation of the relevant σ values, the charge difference between the ground state reactant molecule and the transition state (or the reaction intermediate, if one occurs, which for our purpose will be a close enough approximation) is considered. This is illustrated in detail for reactions [*1.15*] and [*1.17*] in fig. 1.3.

When the formation of the transition state involves electron capture by the reaction site, acceleration is produced by electron acceptor substituents and ρ is positive, e.g. [*1.15*] and [*1.16*].



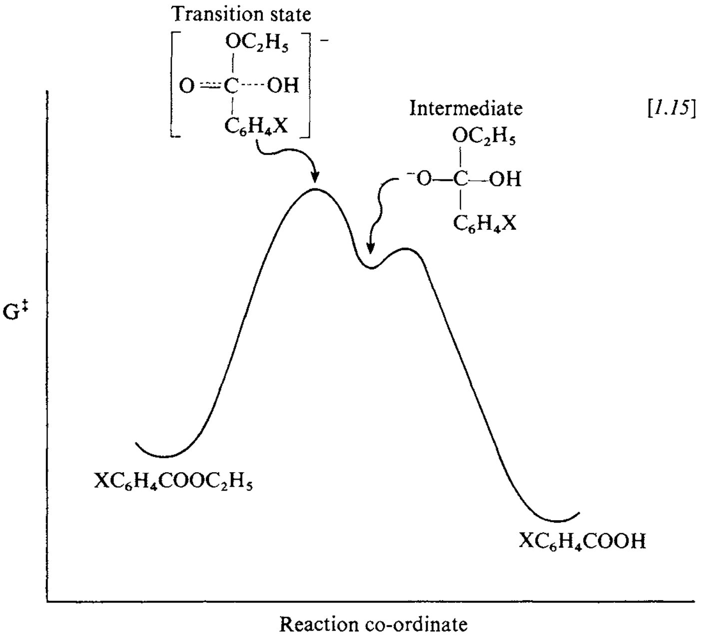
[*1.15*]



[*1.16*]

Alternatively, when formation of the transition state involves donation of electrons from the reaction site, the reaction is accelerated by electron donors, and ρ is consequently negative, e.g. [*1.17*] and [*1.18*].

The size of ρ is an indication of the extent of charge development at the atom of the reacting side chain adjacent to the ring in passing from ground to transition state. In three of the examples shown ([*1.15*], [*1.17*], [*1.18*]) this atom is directly involved in the bond making and



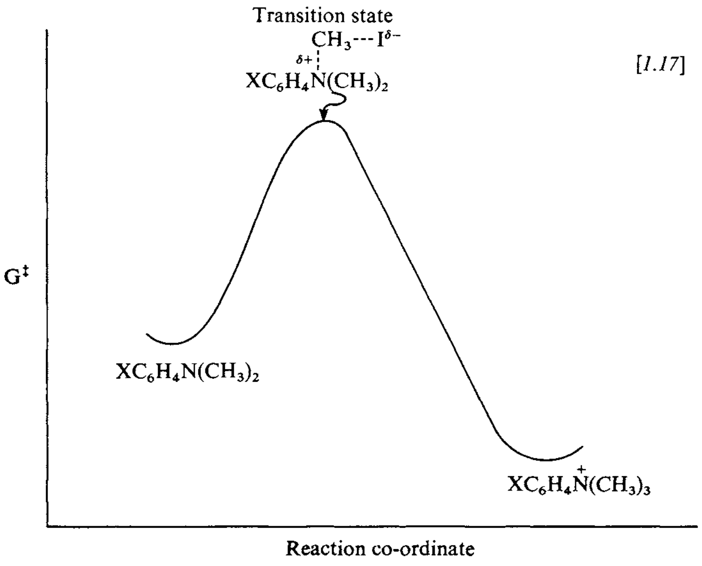


Fig. 1.3. Free energy profiles for reactions [*1.15*] and [*1.17*].