The Separation of Polar, Steric, and Resonance Effects in Organic Reactions by the Use of Linear Free Energy Relationships

By J. Shorter

DEPARTMENT OF CHEMISTRY, THE UNIVERSITY, HULL

1 Introduction. The Scope of the Review

Structural modification of a reactant molecule may influence the rate or equilibrium constant of a reaction through polar, steric, or resonance effects. When a substituent is introduced at a point remote from the reaction centre, only the operation of polar effects need usually be considered, and quite detailed understanding of the influence of structure upon reactivity is possible. Linear free energy relationships, notably the Hammett equation, are very important in this. When the structural modification is close to the reaction centre, our understanding is less advanced. Thus for many years it was impossible to assess the relative importance of different factors contributing, for example, to the '*ortho*-effect' in aromatic systems. About 1952, R. W. Taft suggested a basis for separating polar, steric, and resonance effects by the use of linear free energy relationships, and developed his ideas in detail. Taft's work involved an analysis of the rate coefficients of alkaline and acid-catalysed hydrolysis of esters. Considerable use has been made of this 'Taft analysis' and of the various substituent parameters developed from it.

The present Review seeks to survey the basic assumptions and development of the Taft analysis, and the use which has been made of the various parameters during the last eighteen years.

It is necessary to define the terms used in the title. We consider a reactant molecule RY and an appropriate standard molecule R_0Y. Initially we suppose that Y is not conjugated with either R or R_0. For RY the *polar effect* of the group R comprises all the processes whereby a substituent may modify the electrostatic forces operating at the reaction centre Y, relative to the standard R_0Y. These forces may be governed by charge separations arising from differences in the electronegativity of atoms (leading to the presence of dipoles), the presence of unipoles or electron delocalisation. Field, inductive (through-bond polarisation), and mesomeric effects may in principle be distinguished. Because of the difficulty of distinguishing between field and through-bond effects in practice, the term 'inductive effect' is often used to cover both, and is so used in this Review. The term 'resonance' is sometimes used in connection with the mesomeric effect (*i.e.*, the 'resonance polar effect'; see Section 2) but this is not its ordinary usage in this Review.

When R and R_0 may be conjugated with Y, the above discussion holds but

433

additional influences may arise from the more extensive electron-delocalisation. The mesomeric part of the polar effect will be modified. There will also be the *resonance effect* of R (as in the title) which is concerned with the extent of conjugation of R with Y, relative to the standard R_0Y, and is not part of the polar effect. This distinction is sometimes not clearly made: 'resonance effects' in a wide sense are lumped together and treated as if they are polar in nature (see Section 2). In this Review 'resonance effect' will usually have a narrow connotation as above.

Steric effects are caused by the intense repulsive forces operating when two non-bonded atoms approach each other so closely that such approach involves non-bonded compression energy. The *primary steric effect* of R is the direct result of compression which arises because R differs in structure from R_0 in the vicinity of the reaction centre. A *secondary steric effect* involves the moderation of a polar effect or resonance effect by non-bonded compressions.

In discussing the influence of polar, steric, and resonance effects it is necessary to consider differentially interactions in initial and transition states in the case of rate processes, and in initial and final states in the case of equilibria.[1]

2 Introduction to Linear Free Energy Relationships. The Hammett Equation

Empirical correlations of the reactivities of organic compounds are usually linear relationships involving logarithms of rate or equilibrium constants. At constant temperature the logarithm of a rate constant (k) is proportional to the standard free energy of activation ($\Delta G_{\ddagger}^{\ddagger}$), and that of an equilibrium constant (K) to the standard free energy change of reaction (ΔG^0). The term linear free energy relationship is thus appropriate.[2]

In the early 1930s, Hammett[3] at Columbia and Burkhardt[4] at Manchester, discovered linear relationships involving log k or log K for a number of systems. This work led to the formulation of the Hammett equation (1937), which describes the influence of polar *meta*- or *para*-substituents on the side-chain reactions of benzene derivatives.[5] The Hammett equation takes the forms:

$$\log (k/k_0) = \sigma\rho \tag{1}$$

$$\log (K/K_0) = \sigma\rho \tag{2}$$

where k or K is the rate or equilibrium constant respectively, for a side-chain reaction of a *meta*- or *para*-substituted benzene derivative, and k_0 or K_0 is the constant for the 'parent' compound. The *substituent constant*, σ, measures the polar effect of the substituent (relative to hydrogen), and is, in principle, independent of the nature of the reaction. The *reaction constant*, ρ, depends on the

[1] General account of substituent effects: C. K. Ingold, 'Structure and Mechanism in Organic Chemistry', Bell, London, 2nd edn., 1969.
[2] J. Shorter, *Chem. in Britain*, 1969, **5**, 269, and references therein.
[3] L. P. Hammett, *Chem. Rev.*, 1935, **17**, 125.
[4] G. N. Burkhardt, W. G. K. Ford, and E. Singleton, *J. Chem. Soc.*, 1936, 17.
[5] L. P. Hammett, 'Physical Organic Chemistry', McGraw-Hill, New York, 1940, chap. 7.

nature of the reaction and measures the susceptibility of the reaction to polar effects.

Hammett chose the ionisation of benzoic acids in water at 25 °C as the standard process, for which ρ was defined as $1 \cdot 000$. Values of σ for many substituents, *viz*, $\log (K/K_0)$ were then calculated. The equation was found to apply satisfactorily to all but a few members of fifty-two reaction series. In 1953, Jaffé found data for 371 reaction series to which the equation could be applied with considerable success.[6] By this time, however, a number of exceptions to the uniqueness of the substituent constant had been noted. Indeed, one had been apparent to Hammett: the ionisation of *para*-nitrobenzoic acid gave $\sigma = 0 \cdot 778$ for p-NO_2, but this value proved inapplicable to the reactions of phenol or aniline.[5] In these a value of $1 \cdot 27$ was required. This exalted value was attributed to cross-conjugation of p-NO_2 ($-M$ effect)[1] with OH or NH_2 ($+M$ effect), so that p-NO_2 was effectively more electron-attracting than it was in *para*-nitrobenzoic acid. Jaffé found further examples of this 'duality of substituent constants'.[6] The application of the Hammett equation with increasing refinement has involved the elaboration of this concept.

Brown[7] extended the Hammett equation to highly electron-demanding reactions, notably electrophilic substitution in the aromatic ring, which had previously appeared to be outside the scope of the equation. This involved a new set of substituent constants $\sigma_m{}^+$ and $\sigma_p{}^+$. (Special substituent constants for nucleophilic reactions, *cf.* p-NO_2 above, are designated σ^-.)

In the late 1950s the Hammett equation was re-examined by Wepster and by Taft. Wepster[8] strongly criticised the 'duality of substituent constants'. In his view 'mesomeric *para* interaction' inevitably depends on both the mesomeric effect of the *para*-substituent and of the reaction centre. Thus a 'multiplicity' or 'sliding scale' of σ values would be expected rather than a single exalted constant. Wepster introduced σ^n to designate the normal, unexalted value. Certain σ values, considered to be free from the effects of the above interaction, were taken as primary values, *e.g.* those for m-Cl, m-Me, and m-NO_2. Only these were to be used in evaluating ρ. For other substituents, σ values relevant to particular reaction series were calculated, and σ^n values for such substituents were suggested. The 'sliding scale' was convincingly demonstrated.

Taft's[9] approach was through a quantitative separation of substituent effects into 'inductive' and 'resonance', *i.e.* mesomeric contributions. The inductive contribution was considered to be given by a parameter σ_I based on aliphatic and alicyclic reactivities (see below). The resonance contribution, σ_R, was shown to be reaction-dependent, but an unenhanced resonance parameter, $\sigma_R{}^0$, was defined, by reference to 'insulated reaction series', *i.e.* when the reaction centre is not conjugated with the ring. The values of $\sigma_R{}^0$ and σ_I were appropriately combined to give a normal substituent constant, σ^0.

[6] H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.

[7] H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979, and earlier papers.

[8] H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.

[9] R. W. Taft, *J. Phys. Chem.*, 1960, **64**, 1805, and earlier papers.

3 The Separation of Polar, Steric, and Resonance Effects

A. Introduction to R. W. Taft's Work.—The occurrence of steric as well as polar effects in aliphatic systems and *ortho*-substituted aromatic systems complicates the devising of linear free energy relationships. Little progress was made in this direction until the early 1950s when Taft proposed a procedure (based on a suggestion by Ingold[10]) for evaluating polar and steric parameters in such systems. His analysis essentially involves a quantitative separation of polar, steric, and resonance effects in the total effect of structure upon reactivity in ester hydrolysis.[11]

Taft suggested the following equation for evaluating the polar effect of a substituent R as manifested in the ester $R \cdot CO_2 R^1$:

$$\sigma^* = [\log (k/k_0)_B - \log (k/k_0)_A]/2 \cdot 48 \qquad (3)$$

σ^* is a polar substituent constant for R. The rate constants k refer to reactions of $R \cdot CO_2 R^1$, and k_0 to reactions of $Me \cdot CO_2 R^1$ as a standard. B and A refer to basic and acidic hydrolysis, carried out for the same R^1, solvent, and temperature. The factor $2 \cdot 48$ puts the σ^* values on about the same scale as σ. The equation may also be applied to *ortho*-substituted benzoic esters $o\text{-}X \cdot C_6 H_4 \cdot CO_2 R^1$ with $o\text{-}Me \cdot C_6 H_4 \cdot CO_2 R^1$ as standard. The terms have the following significance: $\log (k/k_0)_B$ gives the sum of the polar, steric, and resonance effects of R (or X); $\log (k/k_0)_A$ gives the sum of the steric and resonance effects of R (or X); the difference gives the polar effect of R (or X). A further equation:

$$E_s = \log (k/k_0)_A \qquad (4)$$

gives a steric substituent constant, E_s, although for systems which are conjugated with —$CO_2 R^1$, E_s contains a resonance contribution.

This procedure is based on three assumptions:
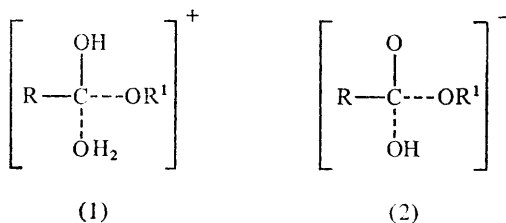(1) the relative free energy of activation may be treated as the sum of independent contributions from polar, steric, and resonance effects;
(2) in corresponding acidic and basic reactions, the steric and resonance effects are the same;
(3) the polar effects of substituents are markedly greater in the basic than in the acidic reaction.

Assumption (1) is by no means self-evident: if the various effects interact, linear analysis is inappropriate. No progress is possible, however, unless such a simplifying assumption is made as a first approximation. Its validity is tested by the usefulness of the results obtained.

Assumption (2) lies at the heart of the analysis. Taft justified it by the following argument. The transition states (having structures closely resembling those of the carbonyl addition intermediates) for the acidic and the alkaline reactions, (1) and (2), differ by two protons.

[10] C. K. Ingold, *J. Chem. Soc.*, 1930, 1032.
[11] R. W. Taft, 'Steric Effects in Organic Chemistry', ed. M. S. Newman, Wiley, New York, 1956, chap. 13. This article summarises Taft's original papers.

$$
\left[\begin{array}{c} \text{OH} \\ | \\ \text{R}\!-\!\!-\!\text{C}\text{-}\text{-}\text{-OR}^1 \\ | \\ \text{O}\,\text{H}_2 \end{array} \right]^{+}
\qquad
\left[\begin{array}{c} \text{O} \\ | \\ \text{R}\!-\!\!-\!\text{C}\text{-}\text{-}\text{-OR}^1 \\ | \\ \text{OH} \end{array} \right]^{-}
$$

$$(1) \qquad\qquad\qquad (2)$$

The small size of these protons makes it reasonable that the steric interaction produced in attaining the transition state should be the same in the two reactions. Further, any resonance effect between R and CO_2R^1 should be the same since both transition states are effectively saturated at the carboxylate carbon. Thus the steric and resonance effects of R relative to Me should be eliminated in equation (3). This assumption will be examined in detail later in this article.

Assumption (3) is supported by the Hammett ρ constants for the reactions of *m*- or *p*-substituted benzoates.[6] For basic hydrolysis ρ values are commonly in the range $+2\cdot2$ to $+2\cdot8$. For acid-catalysed hydrolysis or the related esterification of benzoic acids, ρ values lie close to zero, in the range $-0\cdot2$ to $+0\cdot5$. Thus σ^* may be approximately scaled to σ through a factor $2\cdot48$, the average of the ρ values recorded by Jaffé for basic hydrolysis of benzoates,[6] and the polar contribution to E_s may be neglected.

Taft regards the ultimate justification of the assumptions to be the nature of the results to which they lead. He carried out a careful analysis of a vast amount of data to give σ^* and E_s values, and showed that these could be used to interpret reactivity in other reactions. For any wide range of substituents the conditions regarding constancy of solvent and R^1 could not be completely met. Further, Taft used data from acid-catalysed esterification to supplement those from acid-catalysed hydrolysis. He justified this by pointing out the similarity of the transition states for the two processes. For some substituents R or X, for which there were plenty of data, it appeared that $\log (k/k_0)_A$ or $\log (k/k_0)_B$ did not depend much on solvent or R^1, and that $\log (k/k_0)_A$ was approximately the same for hydrolysis and esterification. Supposedly equivalent $\log (k/k_0)$ values, where available, were averaged, Taft holding that 'the use of average values appears desirable on the basis that small specific effects and experimental errors will be reduced'.[12]

Selected values of σ^* and E_s, are shown in Tables 1 and 2. For a full discussion of the substituent constants for numerous groups, the reader should consult Taft's articles.[11] These include a limited quantity of data for variation of the group R^1 in the ester $R\cdot CO_2R^1$. While the E_s values in Taft's Tables are always based on the original defining reaction, many of the σ^* values are not directly based on the alkaline hydrolysis of esters, but are based on the application of the original σ^* values to other reactions. Table 1 contains two examples of this.

[12] R. W. Taft, *J. Amer. Chem. Soc.*, 1952, **74**, 2729.

Table 1 *Steric and polar parameters for aliphatic systems[a]*

R	E_s	σ^*
H	+1·24	+0·49
Me	0·00	0·00
Et	−0·07	−0·10
Pr^j	−0·47	−0·19
Bu^t	−1·54	−0·30
Pr^n	−0·36	−0·115
Bu^n	−0·39	−0·13
Bu^i	−0·93	−0·125
neopentyl	−1·74	−0·165[b]
$ClCH_2$	−0·24	+1·05
ICH_2	−0·37	+0·85[c]
Cl_2CH	−1·54	+1·94
Cl_3C	−2·06	+2·65
$MeO·CH_2$	−0·19	+0·52
$PhCH_2$	−0·38	+0·215
$Ph(CH_2)_2$	−0·38	+0·08
$MeCH{=}CH$	(−1·63)[d]	+0·36
Ph	(−2·55)[d]	+0·60

[a]R. W. Taft, 'Steric Effects in Organic Chemistry', ed. M. S. Newman, Wiley, New York, 1956, chap. 13; [b]From sulphation of alcohols; [c]From ionisation of carboxylic acids; [d]For significance see text.

Table 2 *Steric and polar parameters for* ortho-*substituents in benzoates[a]*

X	E_s	σ_o^*	σ_o	σ_p[b]
H	—	—	0·00	0·00
OMe	+0·99	−0·22	−0·39	−0·27
Me	0·00	0·00	−0·17	−0·17
F	+0·49	+0·41	+0·24	+0·06
Cl	+0·18	+0·37	+0·20	+0·23
Br	0·00	+0·38	+0·21	+0·23
I	−0·20	+0·38	+0·21	+0·27
NO_2	−0·75	+0·97	+0·80	+0·78

[a]R. W. Taft, 'Steric Effects in Organic Chemistry', ed. M. S. Newman, Wiley, New York, 1956, chap. 13; [b]D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, 23, 420.

Taft regards the values of σ^* as agreeing with 'the qualitative English school theory' of the polar effect.[11] He points out that σ^* and E_s are quite different functions of structure, *e.g.* the series Me, Et, Pr^i, Bu^t shows an additive effect for the polar influence of successive methyl groups, whereas the values of E_s 'telescope'. E_s values in general conform well with qualitative assessment of 'steric hindrance' by means of molecular models. For $\alpha\beta$-unsaturated substituents R, however, the E_s value is often governed mainly by the conjugation of R

with CO_2R^1 in the initial state, and is thus not a measure of the steric effect (see last two entries in Table 1).

When Taft's σ_o* values are changed to a σ_o scale with hydrogen as the standard, by assuming $\sigma_o = \sigma_p$ for Me, it is seen that in various other cases $\sigma_o \sim \sigma_p$. This apparently means that the polar effects of substituents operate equally from the *ortho-* and *para*-position, but as a general rule this seems unlikely.

Values of $\sigma*$ are of importance in the analysis of σ values in terms of σ_I and σ_R (see above).[9] For a few substituents an inductive parameter σ' was based on the reactions of 4-substituted-bicyclo[2,2,2]octane-1-carboxylic acids and esters.[13] The bicyclo-octane system was considered to provide a good model for the transmission of the non-mesomeric part of the polar effect through the benzene ring. It was found that the σ' values for X were proportional to $\sigma*$ for CH_2X.[11] A new inductive parameter for substituents in general was therefore defined as $\sigma_I = 0\cdot45\,\sigma*$.

B. Applications of the Taft Parameters to the More General Understanding of the Reactivities of Organic Compounds.—At this stage we discuss mainly the contributions of Taft and his colleagues. Later we shall consider a variety of examples of the uses made of these parameters by other authors.

(i) *The linear free energy—polar energy relationship.*[11] Taft found that the rate or equilibrium constants for a wide variety of reactions of RY conformed respectively to equation (5)

$$\log\left(k/k_0\right) = \sigma*\,\rho* \tag{5}$$

or the corresponding equation for equilibrium constants, where $\sigma*$ is the polar substituent constant for R and $\rho*$ is a reaction constant analogous to the Hammett ρ constant. A few reactions of *ortho*-substituted aromatic systems $o\text{-}X\cdot C_6H_4\cdot Y$ also obey these equations. Examples are given in the Figure.

Conformity to these equations clearly implies that all effects other than polar remain nearly constant throughout each reaction series. Notably this means either the complete absence of steric effects of substituents or that they are approximately the same as the steric effect of a methyl group within the range considered. The predictive power of these equations is thus limited: deviations may occur if substituents markedly different from those involved in the initial correlation are considered. For many of the reactions the minor rôle of steric effects is readily understood: some involve no change in bond angles at the reaction centre; in others the reaction centre is somewhat remote from the substituent, or the reagent involved is very small.

Deviations from equation (5) were used by Taft to assess other effects quantitatively. A good example of the assessment of steric effects is provided by the application of the modified equation

$$\Delta\Delta H_a = (\Sigma\sigma*)\rho* \tag{6}$$

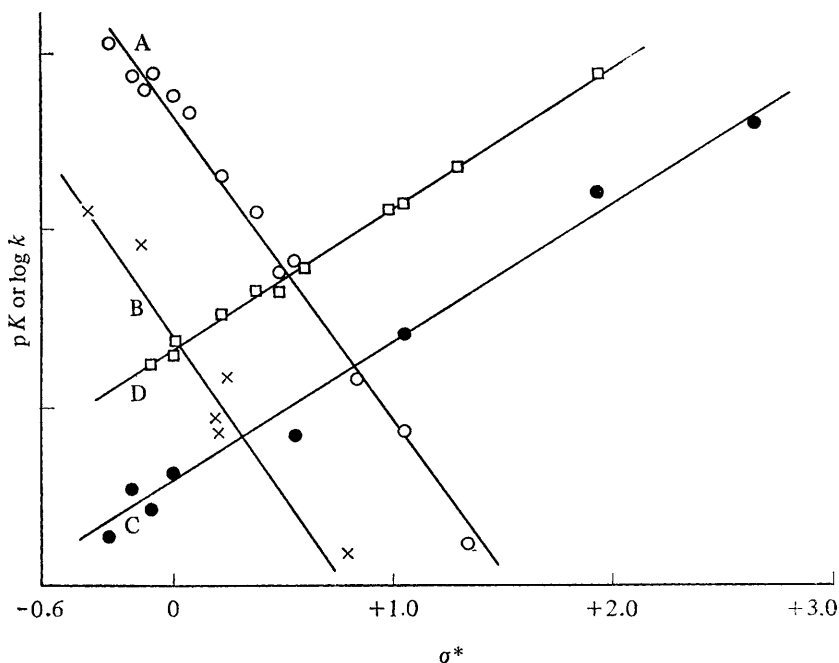[13] J. D. Roberts and W. T. Moreland, *J. Amer. Chem. Soc.*, 1953, **75**, 2167.

Figure *The divisions on the ordinate are* 1·00 *units of* pK *or log* k *apart. The relative positions of the lines* A *to* D *with respect to the ordinate are arbitrary.*
A. pK, *aliphatic carboxylic acids, water,* 25 °C. (J. F. J. Dippy, *Chem. Rev.,* 1939, **25**, 151.)
B. pK, ortho-*substituted benzoic acids, water,* 25 °C. *Abscissa: Taft's* σ_o *values. Benzoic acid deviates markedly.* (J. F. J. Dippy, *Chem. Rev.,* 1939, **25**, 151.)
C. log k, *alkaline hydrolysis of* $[Co(NH_3)_5 \cdot O_2C \cdot R]^{2+}$, *water,* 25 °C. (J. Basolo, J. G. Bergmann, and R. G. Pearson, *J. Phys. Chem.,* 1952, **56**, 22.)
D. log k, *catalysis of dehydration of acetaldehyde hydrate by* $R \cdot CO_2H$, *aqueous acetone,* 25 °C. [R. P. Bell and W. C. E. Higginson, *Proc. Roy. Soc.* (A), 1949, **197**, 141.]

to the enthalpies of dissociation ΔH_d of the addition compounds formed between boron trimethyl and aliphatic amines, $R^1R^2R^3N$.[14] The term $\Sigma\sigma^*$ is the sum of the σ^* values for the groups R^1, R^2, and R^3, so that effectively the parent system is that involving NMe_3. Ammonia and straight-chain primary amines conformed to equation (6), but branched-chain compounds, and secondary or tertiary amines showed marked deviations. Thus Bu^tNH_2 deviated by $-$ 6·6 kcal mol^{-1} (from calculated $\Delta H_d = 19\cdot6$), which was attributed to steric strain in the complex.

The acid-catalysed hydrolysis of diethyl acetals of general formula $R^1R^2C(OEt)_2$ ($R^1 = $ H or Me; R^2 variable) indicated the importance of resonance effects.[15] Application of equation (5), with $\Sigma\sigma^*$ for R^1 and R^2, to the hydrolysis of compounds derived from non-conjugated aldehydes and ketones gave well-separated, parallel straight lines for the two classes of compound, with a number of deviant points. A single straight-line, however, was given by equation (7):

[14] H. C. Brown and G. K. Barbaras, *J. Amer. Chem. Soc.,* 1953, **75**, 6, and earlier papers.
[15] M. M. Kreevoy and R. W. Taft, *J. Amer. Chem. Soc.,* 1955, **77**, 5590.

$$\log (k/k_0) = (\Sigma\sigma^*)\rho^* + (n - 6)h \tag{7}$$

where n is the number of α-hydrogen atoms in R^1 and R^2, *i.e.* $(n - 6)$ is the decrease in the number of such atoms compared to the six in acetonal ($R^1 = R^2 = $ Me), and h is a proportionality constant. The term $(n - 6)h$ is interpreted as a contribution from hyperconjugation in stabilising the transition state [resembling an oxo-carbonium ion, $R^1R^2C(OEt)^+$] relative to the initial state (which is saturated). Some compounds did not conform to equation (7), *e.g.* the acetal with $R^1 = $ Me and $R^2 = $ neopentyl shows clear signs of steric acceleration due to the bulky substituent. A number of other reaction series are correlated by equation (7).[16]

(ii) *The linear free energy—steric energy relationship.*[11] Taft found that a number of reactions conformed to the equation

$$\log (k/k_0) = \delta E_s \tag{8}$$

where δ is a steric susceptibility constant. In such reactions the polar effects of substituents must be very small. Several of the reactions are closely related to acid-catalysed ester hydrolysis, *e.g.* the acid-catalysed hydrolysis of *ortho*-substituted benzamides, but others are very different, *e.g.* methyl iodide reacting with 2-monoalkyl pyridines. For examples of the latter type equation (8) tends to be of rather limited applicability; deviations occur when the range of substituents is extended.

(iii) *The combined linear free energy—polar energy and steric energy relationship.* Pavelich and Taft[17] suggested that the equation:

$$\log (k/k_0) = \sigma^*\rho^* + \delta E_s \tag{9}$$

would be found to be of wider applicability than equations (5) or (8). It implies that the relative free energy of activation may be regarded as a sum of independent contributions from polar and steric effects.

Equation (9) was found by Pavelich and Taft to correlate the results for acid-[18] or base-catalysed[17] methanolysis of $(-)$ -menthyl esters, $R \cdot CO_2C_{10}H_{19}$, in methanol at 30 °C. Biechler and Taft [19] found it also applied in a modified form to the basic hydrolysis of anilides.

C. Further Analysis of Steric Effects in Ester Reactions.—By applying transition state theory Taft[11] accomplished a separation of the overall steric effect of a substituent, as measured by E_s, into 'steric strain' and 'steric hindrance of motions'. For an account of the procedures, Taft's articles should be consulted.

From a series of more than twenty alkyl groups it appears that small groups give only small steric strain, but the hindrance of motions is considerable. The

[16] R. W. Taft and M. M. Kreevoy, *J. Amer. Chem. Soc.*, 1957, **79**, 4011.
[17] W. A. Pavelich and R. W. Taft, *J. Amer. Chem. Soc.*, 1957, **79**, 4935.
[18] W. A. Pavelich, Thesis, Pennsylvania State University, 1955.
[19] S. S. Biechler and R. W. Taft, *J. Amer. Chem. Soc.*, 1957, **79**, 4927.

5

latter rapidly comes to a limit with increasing size and branching of the alkyl group, while steric strain continues to increase. Steric hindrance of motions shows little solvent dependence, suggesting that steric inhibition of solvation is not a factor contributing to this.

Taft showed that the estimates of steric strain in $Me_3B \cdot NR^1R^2R^3$ addition compounds (see above) were related to the estimates of steric strain caused by $R^1R^2R^3C$ in ester reactions. The addition compound and the ester transition state show structural similarities, so the relationship is reasonable. There is no relationship to E_s.

4 Application of Taft's Polar and Steric Parameters
The parameters have been used to correlate a wide range of phenomena, in nature often far removed from the systems from which the parameters were derived. A selection of material is presented to show the great variety of applications.

A. Ionisation of Acids.—Taft correlated the strengths of aliphatic carboxylic acids through the appropriate form of equation (5). Charton[20] has suggested that this system should be a basis for defining σ_I values ($\sigma_I = 0.45\,\sigma^*$); this is doubtless satisfactory for fairly small substituents. However, for a series of arylaliphatic carboxylic acids with bulky substituents Bowden, Chapman, and Shorter,[21] and Bowden and Young[22] correlated the pK values by means of the Pavelich–Taft[17] equation; a significant term in E_s indicated steric inhibition of solvation of the carboxylate ion.

The application of σ^* to many series of non-carboxylic acids has been examined. These are of interest because the substituent is often attached to an element other than carbon. The largest amount of work has been done on the ionisation of the conjugate acids of nitrogen bases. For non-aromatic amines Hall[23] applied equation (5) in the form (10):

$$\text{p}K_a = \rho^* \Sigma\sigma^* + \text{p}K_0 \tag{10}$$

where $\rho^* = -3.14$, -3.23, and -3.30, and p$K_0 = 13.23$, 12.13, and 9.61 for primary, secondary, and tertiary amines respectively (in water). Tertiary amines conformed well; certain secondary and primary amines showed deviations which were attributed to steric effects. The results indicated the importance of solvation of the alkylammonium ion through the N—H bonds, and of steric inhibition of this. Folkers and Runquist[24] reported that Hall's data conformed to one line given by equation (11):

$$\text{p}K_a = \text{p}K_0 - 3.23\Sigma\sigma^* + 1.12\,(n) \tag{11}$$

[20] M. Charton, *J. Org. Chem.*, 1964, **29**, 1222.
[21] K. Bowden, N. B. Chapman, and J. Shorter, *J. Chem. Soc.*, 1963, 5239; 1964, 3370.
[22] K. Bowden and R. C. Young, *Canad. J. Chem.*, 1969, **47**, 2775.
[23] H. K. Hall, *J. Amer. Chem. Soc.*, 1957, **79**, 5441.
[24] E. Folkers and O. Runquist, *J. Org. Chem.*, 1964, **29**, 830.

where n is the number of hydrated NH groups in the alkylammonium ion. The 1·12 (n) term gives an acid-weakening effect of hydration of the NH groups. The above ideas have been developed further by Condon,[25] with regard to statistical effects and to hydration both of free base and of ammonium ion.

Henderson and Streuli[26] have correlated the basicities of substituted phosphines with $\Sigma\sigma^*$. Hall[27] found equation (5) of little relevance to the nucleophilic reactivity of amines, but Henderson and Buckler[28] were more successful with that of phosphines.

B. Heterogeneous Catalysis.—Kraus[29] has reviewed the recent development of linear free energy relationships for heterogeneous reactions. Values of σ or σ^*, based on reactions in solution at room temperature or a little above, have proved applicable to the rates of reaction of substrates on catalysts up to 500° C. This is very surprising since complex interactions between catalyst and substrate might well modify reactivity in a way quite unrelated to polar effects in solution. The correlations involving σ^* are often good. For example, results on the elimination of water from five alkanols over Al_2O_3 at 380 °C are well correlated by σ^*. However, it is often necessary to exclude certain substituents from the correlation. Bu^t is prominent among these, which suggests that steric effects must not be ignored. This has been emphasised by Mochida and Yoneda,[30] and by Ruzicka and his colleagues,[31] who have used the Pavelich–Taft[17] equation (9). Work on linear free energy relationships in this field is hampered by the difficulty of using a wide range of substituents.

C. Polymerisation.—Taft's polar and steric parameters have been found relevant to polymerisation. Otsu and his colleagues[32] have copolymerised various alkyl methacrylates or acrylates, M_2, with styrene or β-chloroethyl methacrylate, M_1. The relative reactivities $1/r_1$, of M_2 towards attack by the polymer radicals were examined in terms of a Pavelich–Taft equation.[17] The correlation with σ^* was good, but there was no significant relationship to E_s. On the other hand Chikanishi and Tsurata[33] reported that for the attack of polystyryl radicals on methyl α-alkylacrylates there was significant correlation with E_s but not σ^*. No doubt the steric effect here is due to the alkyl groups being directly attached to the reacting vinyl bond. For the same system, however, Cameron and Kerr[34] claim that correlation with σ^* as well as E_s is significant.

[25] F. E. Condon, *J. Amer. Chem. Soc.*, 1965, **87**, 4481 *et seq.*
[26] W. A. Henderson and C. A. Streuli, *J. Amer. Chem. Soc.*, 1960, **82**, 5791.
[27] H. K. Hall, *J. Org. Chem.*, 1964, **29**, 3539.
[28] W. A. Henderson and S. A. Buckler, *J. Amer. Chem. Soc.*, 1960, **82**, 5794.
[29] M. Kraus, *Adv. Catalysis*, 1967, **17**, 75.
[30] I. Mochida and Y. Yoneda, *J. Catalysis*, 1968, **11**, 183.
[31] V. Ruzicka, L. Cerveny, and J. Pachta, *Coll. Czech. Chem. Comm.*, 1969, **34**, 2074.
[32] T. Otsu, T. Ito, and M. Imoto, *J. Polymer Sci., Part C, Polymer Symposia*, 1967, 2121, and references therein.
[33] K. Chikanishi and T. Tsurata, *Makromol. Chem.*, 1964, **73**, 231.
[34] G. G. Cameron and G. P. Kerr, *European Polymer J.*, 1967, **3**, 1.

D. Optical Spectra.—σ^* Values have been much used in the correlation of i.r. data, and such correlations have been used to estimate new σ^* values. I.r. frequencies are related to force constants of bonds, whereas intensities are governed by the rate of change of dipole moment with respect to bond length. Polar effects of substituents may influence both of these, although sometimes one is influenced much more than the other. Frequencies, ν, have been correlated with σ^*, while integrated intensities, A, have also been variously correlated in the forms: log A, A, and $A^{1/2}$. T. L. Brown[35] has argued that the use of $A^{1/2}$ is theoretically sound. Earlier, however,[36] he had successfully correlated A for the OH stretching frequency of aliphatic alcohols $R^1R^2R^3C{\cdot}OH$ with $\Sigma\sigma^*$. Deviations were observed where internal hydrogen bonding appeared possible. Rao[37] showed that the OH stretching frequency in eleven carboxylic acids gave excellent correlation with σ^*.

The CO stretching band has been much examined. For example, O'Sullivan and Sadler[38] found good correlation of ν with σ^* for $R{\cdot}CO{\cdot}Me$, with R as a variety of heteroatom groups, while Morcillo *et al.*[39] have correlated A with σ^* for $R{\cdot}CO{\cdot}Ph$.

Various studies of aromatic compounds involve using Taft's σ_o values to place *ortho*-substituted compounds on the same plot as *meta-* and *para*-derivatives. Weigmann and Malewski[40] do this for various bands in aromatic sulphonyl chlorides, with mixed success. Correlation is quite good for the antisymmetrical stretching frequency of $-SO_2-$.

Correlations involving σ^* values and u.v. spectra are much more limited. Polar effects operating in the formation of electronically-excited molecules will not necessarily be closely related to those influencing rate or equilibrium constants. However, Gosavi and Rao[41] found a fairly good linear relationship to $\Sigma\sigma^*$ for ν_{max} of the $n \longrightarrow \pi^*$ CS band in thioureas $R^1R^2N(CS)NR^3R^4$.

E. Nuclear Magnetic Resonance.—Various aspects of n.m.r. have been correlated with σ^*, but the situations are rarely simple. Kan[42] correlated the chemical shifts of the CH_3 or CH_2 protons of acetates or succinates respectively with σ^* values for the alkyl group of the alkoxy-substituent of the ester. The correlation was not very good, deviations being particularly marked for bulky substituents. This behaviour was considered due to steric inhibition of resonance involving the canonical form $X-\overset{-}{C}O=\overset{+}{O}-R$.

[35] T. L. Brown, *J. Phys. Chem.*, 1960, **64**, 1798.
[36] T. L. Brown, *J. Amer. Chem. Soc.*, 1958, **80**, 6489.
[37] C. N. R. Rao and R. Venkataraghavan, *Canad. J. Chem.*, 1961, **39**, 1757.
[38] D. G. O'Sullivan and P. W. Sadler, *J. Chem. Soc.*, 1957, 4144.
[39] J. Morcillo, E. Gallego, R. Madronero, and A. R. Trabazo, *Anales de Quím. (Madrid)* Ser. B, 1964, **60**, 199.
[40] H.-J. Weigmann, and G. Malewski, *Spectrochim. Acta*, 1966, **22**, 1045.
[41] R. K. Gosavi and C. N. R. Rao, *Canad. J. Chem.*, 1967, **45**, 1897.
[42] R. O. Kan, *J. Amer. Chem. Soc.*, 1964, **86**, 5180.

Proton chemical shifts in aromatic systems have been related to σ values for *meta*- and *para*-substituents, and to Taft's σ_o values for *ortho*-substituents. This has been done for the —NH_2 shifts in aniline.[43] Alternatively such correlations have been made the basis of σ_o values, *e.g.* Tribble and Traynham's work on the OH shifts in phenols, leading to σ_o^- values said to be useful in correlating *ca.* thirty reaction series.[44]

Chemical shifts for ^{14}N, ^{19}F, and ^{31}P, coupling constants, and nuclear quadrupole resonance frequencies have also been related to σ^*.

F. Biological Activity.[45]—Linear free energy relationships are increasingly used in the interpretation of biological activity. The problem is complex and certain special parameters have been developed, *e.g.* Hansch's 'partition coefficient' factor, π, which measures the 'hydrophobic bonding' character of a drug, a property which has received little attention in mechanistic chemistry. Polar and steric effects of substituents often play only a subsidiary rôle, but sometimes their part is important. In various systems different types of substituent constant have proved relevant, including σ^* and E_s. Thus results for the esterase activity of human serum using a series of six *p*-nitrophenyl esters, $R \cdot CO_2C_6H_4NO_2$, are well correlated by π and E_s, with the addition of a term in σ^* making a slight improvement. It is of interest that steric parameters are sometimes needed even when the substituent is remote from the functional group responsible for the drug activity. This is presumably connected with a steric effect on the interaction of the drug molecule as a whole with the biological site.

5 Further Consideration of the Steric Parameter

Taft[11] recognised that, even for substituents incapable of normal conjugation with a carboxylic function, there might be a contribution to E_s from a resonance interaction, *i.e.* a hyperconjugative effect of α-hydrogen atoms. In Hancock's[46] view this should be allowed for in the derivation of a 'corrected steric substituent constant', E_s^c in the equation:

$$E_s^c = E_s - h(n - 3) \tag{12}$$

where h is a reaction constant for hyperconjugation and n is the number of α-hydrogen atoms. Quantum mechanical calculations by Kreevoy and Eyring were used as a basis for taking h as -0.306. Selected E_s^c values are shown in Table 3. Hancock[46] showed that the use of E_s^c values could lead to significant improvement in the correlation of certain reactions. The following relationships were found to hold for the saponification of nine esters, $R \cdot CO_2Me$, in 40% aqueous dioxan at 35 °C:

[43] B. M. Lynch, B. C. Macdonald, and J. G. K. Webb, *Tetrahedron*, 1968, **24**, 3595.
[44] M. T. Tribble and J. G. Traynham, *J. Amer. Chem. Soc.*, 1969, **91**, 379.
[45] C. Hansch, *Accounts Chem. Res.*, 1969, **2**, 232, and many references therein.
[46] C. K. Hancock, E. A. Meyers, and B. J. Yager, *J. Amer. Chem. Soc.*, 1961, **83**, 4211.

$$\log k = 1.31 + 1.54\sigma^* + 0.709\,E_s \tag{13}$$

$$\log k = 1.36 + 1.48\sigma^* + 0.471\,E_s^c \tag{14}$$

$$\log k = 1.25 + 1.75\sigma^* + 0.848\,E_s^c - 0.383\,(n-3) \tag{15}$$

For equation (13) the multiple correlation coefficient, R, and standard deviation, s, are 0.992 and 0.076 respectively, *i.e.* the correlation is fairly good because hyperconjugation is involved in E_s and in $\log k$. Equation (14) is poor ($R = 0.970$, and $s = 0.149$) because in E_s^c hyperconjugation has been eliminated. Equation (15) is excellent ($R = 0.998$, $s = 0.043$) because it incorporates proper consideration of both steric and hyperconjugative effects.

Table 3 *Taft's[a] E_s and Hancock's[b] E_s^c for R in* $R\cdot CO_2R^1$

R	E_s	E_s^c
Me	0.00	0.00
Et	−0.07	−0.38
Pr^i	−0.47	−1.08
Bu^t	−1.54	−2.46
Pr^n	−0.36	−0.67
Bu^n	−0.39	−0.70
Bu^i	−0.93	−1.24

[a]Table 1; [b]C. K. Hancock, E. A. Meyers, and B. J. Yager, *J. Amer. Chem. Soc.*, 1961, **83**, 4211.

Hancock[47] has also shown the importance of 'change in the six-number'. Newman[48] showed that the number of atoms in position 6, from the carbonyl-oxygen as 1, makes a large contribution to the steric effect. When a given group is considered both as R and R^1 in $R\cdot CO_2R^1$ there may be a change in the six-number, $\Delta 6$, as between R and R^1, *e.g.* for Me, Et, Pr^i, and Bu^t, $\Delta 6 = 0$, -3, -6, and -9 respectively. Hancock[47] uses $\Delta 6$ as another structural parameter. For the saponification of nine acetates $Me\cdot CO_2R^1$ in 40% dioxan at 35 °C:

$$\log k = 1.40 + 1.34\sigma^* + 0.730\,E_s^c \tag{16}$$

with $R = 0.980$ and $s = 0.161$, the E_s^c values being for the substituents as R. When $\Delta 6$ is included:

$$\log k = 1.35 + 0.688\sigma^* + 0.664\,E_s^c + 0.0477\Delta 6 \tag{17}$$

with $R = 0.997$ and $s = 0.070$, which is a much improved correlation.

Hancock's views do not appear to have achieved the notice they deserve. Bowden, Chapman, and Shorter[21] regarded the improved correlations with some scepticism. P. D. Bolton,[49] however, regards E_s^c and $(n-3)$ as relevant to

[47] C. K. Hancock, B. J. Yager, C. P. Falls, and J. O. Schreck, *J. Amer. Chem. Soc.*, 1963, **85**, 1297.
[48] M. S. Newman, *J. Amer. Chem. Soc.*, 1950, **72**, 4783.
[49] P. D. Bolton, *Austral. J. Chem.*, 1966, **19**, 1013.

the acid- or base-catalysed hydrolysis of aliphatic amides and has obtained significantly better correlations than with E_s.

Modified steric parameters have also been developed by Palm,[50] who considers the contribution of both C—H and C—C hyperconjugation to E_s. Equation (18) is proposed, where n_H is the number of α-C—H bonds and n_C is the number of α-C—C bonds. E_s^0 is described as a 'purely steric constant', and, linked with proper consideration of hyperconjugation, has been much used by Palm and by other authors in the U.S.S.R.[50]

$$E_s^0 = E_s + 0.33\,(n_H - 3) + 0.13\,n_C \tag{18}$$

6 The Significance of σ^*, particularly for Alkyl Groups

There seems little doubt that σ^* values measure the polar effects of substituents when these are substantial, but the significance of small σ^* values has been questioned. This applies to the values for all alkyl groups, which lie mainly between 0 and -0.3. Such small values might arise from an imperfect cancelling of steric effects in the Taft analysis (see below). While Taft[11] asserted that σ^* and E_s are completely different functions of structure, this is not strictly true for alkyl groups: Koppel[51] has shown that for twenty primary, secondary, or tertiary alkyl groups ($\sigma^* = 0$ to -0.4; $E_s = 0$ to -4) with $R = 0.956$ and $s = 0.292$,

$$E_s = 0.88 + 27.78\sigma^* - 1.90\,(n - 3) \tag{19}$$

where n is the number of α—C—H bonds. For electronegative substituents no such relationship was applicable.

Ritchie[52] holds that σ^* values for alkyl groups are not consistent with those for other substituents, since different damping factors for interposing methylene groups are required for the two classes. By symmetry considerations developed for the Hammett equation by Hine, Ritchie shows that the damping factor should be the same for all substituents. He argues that σ^* values of alkyl groups do not really measure the polar effects of the groups and that σ^* is properly zero for all alkyl groups. Ritchie claims that data for various systems conforming to equation (5) are as well correlated by taking $\sigma^* = 0$ for all alkyl groups as by using Taft's values, although this is not properly substantiated by statistical procedures. He also concludes that the hyperconjugative interpretation of acetal hydrolysis (see earlier)[15] is fallacious. The Taft σ^* values for alkyl groups are considered to arise from interaction between the various types of substituent effects in ester hydrolysis, *i.e.* Taft's assumption (1) is erroneous, cross-terms making an appreciable contribution.

Most physical organic chemists, however, continue to believe that the electron-releasing properties of alkyl groups in aliphatic systems increase with chain-

[50] Numerous papers are in the issues of *Reaktsionnaya sposobnost organicheskikh Soedinenii* (with English summaries), ed. V. A. Palm, commencing 1964, and available in English translation as *Organic Reactivity* (Consultants Bureau) from 1966.
[51] I. A. Koppel, *Reakts. spos. org. Soedinenii*, 1965, **2** (2), 26.
[52] C. D. Ritchie and W. F. Sager, *Progr. Phys. Org. Chem.*, 1964, **2**, 323, and references therein.

length and -branching and to use σ^* values as a measure of this. It may be statistically satisfactory to submerge the alkyl groups as a cluster of points at $\sigma^* = 0$ in a sea of highly polar substituents, but this ignores small but well-established structural effects which agree with the σ^* values. It is not clear how these effects are to be explained if $\sigma^* = 0$ for all alkyl groups.

Palm[53] was also aware of the problem posed by the damping factors, but concludes that this indicates the operation of different electrical effects: hydrogen and alkyl groups exert their influence by the through-bonds inductive effect, while the field effect is more important for highly polar substituents. Thus the σ^* values for the two classes of substituent may really be on different scales. Mai[54] has shown that σ^* values may be correlated with ionisation potentials and electron affinities of substituents, but alkyl groups and highly polar substituents require different forms of relationship.

T. L. Brown[55] has discussed the possible rôle of polarisability effects in the σ^* values of alkyl groups. In the transition state for alkaline ester hydrolysis dispersion forces between R and the remainder of the system will stabilise the transition state to a greater extent than in that for acidic ester hydrolysis. σ^* is thus a resultant of polarisability and inductive effects acting in opposite directions. The values are often applied, however, to systems in which these effects act in the same direction. This may be the case in the hydrogenation of aldehydes and ketones, for which Taft and Kreevoy's[16] separation of hyper-conjugative effects through applying equation (5) is therefore probably fallacious.

Much of the literature merits re-examination in the light of the ideas summarised above.

7 The Ortho-Effect. The Work of M. Charton[56]

Steric phenomena have long been recognised as playing a major part in the peculiar effects of *ortho*-substituents.[1] Primary steric effects of various kinds, including steric hindrance to solvation or to the approach of the reagent, and secondary steric effects have been invoked. In certain systems hydrogen-bonding and other intramolecular interactions have been postulated. The main approach to understanding the *ortho*-effect has been the attempt to separate steric effects from polar and other effects; the application of Taft's procedure to aromatic ester hydrolysis and the use of the steric and polar parameters thus derived is the best known of these attempts.

Some authors have approached the problem in a different way. Whereas Taft's analysis estimates the steric effect (E_s) and then eliminates it from a reaction in which both steric and polar effects are known to occur, other authors have selected a reaction believed to be free from the steric effects of *ortho*-

[53] V. A. Palm, *Russ. Chem. Rev.*, 1961, **30**, 471.
[54] L. A. Mai, *Organic Reactivity*, 1967, **4**, 220.
[55] T. L. Brown, *J. Amer. Chem. Soc.*, 1959, **81**, 3229.
[56] M. Charton, *J. Amer. Chem. Soc.*, 1969, **91**, 624, 6649 and papers referred to therein. Professor Charton has also written a summary article to appear in *Prog. Phys. Org. Chem.*

substituents and have derived a scale of σ_o values by assuming $\rho_o = \rho$ for this reaction. The σ_o values have then been used to interpret other reactions.

For instance McDaniel and Brown[57] believed that the pK_a values of 2-substituted-pyridinium ions provided a basis for σ_o values. Usually, however, systems in which the reaction centre is somewhat removed from the ring have been chosen, *e.g.* the dissociation of phenylpropiolic acids. σ_o Values have also been based on spectroscopic data. Charton has compiled available data.[56]

There is often poor agreement between the various values determined for a given substituent. This has prompted a search for the 'true' *ortho*-substituent constant. Several authors have claimed peculiar virtues for their favourite reactions, *e.g.* G. G. Smith[58] argues that interactions with solvent are responsible for the difficulty of determining satisfactory σ_o values. Hence 'true' σ_o values should be determined in the absence of solvent. Thus gas-phase ester pyrolysis, much studied by Smith and his colleagues,[58] is the ideal reaction.

The value to be taken of ρ_o for the standard reaction presents a problem. Each author takes $\rho_o = \rho$ for his favourite reaction, but when the derived σ_o values are applied to other reactions, ρ_o is not in general equal to ρ.

The Reviewer has recently stated that 'the complexity of the influence of *ortho*-substituents on reactivity may make the search for a single, generally applicable scale of σ_o values quite fruitless'.[2] Charton has expressed the same view and has marshalled much evidence in support of it.[56]

Charton has compiled and analysed a vast amount of data on the *ortho*-effect. This work merits much closer examination than can be given here; some of his findings and conclusions are very remarkable. Charton's work is based on the separation of the electronic effect of a substituent X into inductive (non-mesomeric) and resonance (mesomeric) contributions through the equation:

$$\sigma_X = \lambda\sigma_{I,X} + \delta\sigma_{R,X} \tag{20}$$

The factors contributing to E_s values are examined through the equation

$$E_{s,X} = \alpha\sigma_{I,X} + \beta\sigma_{R,X} + \psi r_{V,X} + h \tag{21}$$

λ and δ, or α and β are constants defining the relative importance of inductive and resonance effects. $r_{V,X}$ is related to the size of the substituent. Depending on the shape of the substituent $r_{V,X}$ values are assessed from van der Waals radii in various ways. ψ gives the contribution of steric effects thus specified; h is a constant.

For substituents in aliphatic systems the contribution of the $\sigma_{I,X}$ and $\sigma_{R,X}$ terms was insignificant, and $E_{s,X}$ could be regarded largely as a function of substituent size, *i.e.* E_s is indeed a steric parameter.

For the $E_{s,X}$ values of *ortho*-substituents, however, the $\sigma_{I,X}$ and $\sigma_{R,X}$ terms proved significant while the $r_{V,X}$ term did not, *i.e.* the E_s values of *ortho*-substituents have little to do with steric effects.

[57] D. H. McDaniel and H. C. Brown, *J. Amer. Chem. Soc.*, 1955, **77**, 3756.
[58] D. A. K. Jones and G. G. Smith, *J. Org. Chem.*, 1964, **29**, 3531, and earlier papers.

The approach is extended to the analysis of a vast amount of data. In (21) $E_{s,x}$ is replaced by Q_x, the value of an observed property under the influence of *ortho*-X. Q may be log k, log K, ν *etc*. The $r_{v,x}$ term generally makes little contribution. Charton concludes that steric effects play a minor rôle in the *ortho*-effect. Different contributions of resonance and inductive effects, *i.e.* β/α, account mainly for the variety of phenomena.

Charton's work is undoubtedly a valuable contribution but some of his conclusions are so much at variance with long held ideas that they merit searching examination. His data sets frequently lack substituents whose steric effect is expected to be substantial. Often the necessary items are not available but sometimes bulky groups, *e.g.* Bu^t or I, are admitted not to conform. It is possible that exclusion of data relating to bulky groups may distort the picture for the less bulky substituents appearing in the correlation. Another awkward matter is the frequent need to exclude the parent compound as showing a marked deviation.

The correlation of data made possible by computers is valuable, but one must not lose sight of the chemistry in a welter of statistics. Real effects can be obscured by good correlation coefficients and high confidence levels.

8 Critique of the Taft Analysis

The earlier parts of this Review have shown that the Taft analysis achieved considerable empirical success and led to a deeper understanding of the influence of structure upon reactivity in a wide variety of processes. Nevertheless, as Sections 5, 6, and 7 have shown, there are questions about the significance of the polar and steric parameters. The present Section continues this examination, with particular reference to the fundamental assumptions of Taft's procedure.

In several papers Chapman, Shorter, and their colleagues have made extensive use of the Taft analysis and its parameters, while remaining alert to possible weaknesses. They have drawn attention to the paucity of data relating to acidic and basic ester hydrolysis *in the same solvent*. Attempts to remedy this met with only limited success: at temperatures necessary for studying acidic hydrolysis, aqueous organic solvents often 'crack'. It is much easier to study acid-catalysed esterification of carboxylic acids.

In studying conformation and reactivity, Chapman, Shorter, and Toyne[59] obtained results which cast doubt on Taft's assumption (2) regarding the equality of steric effects in acid- and base-catalysed reactions. The use of a Bu^t group or a $(CH_2)_4$ bridge (*trans*-decalin system) to lock the conformation of cyclohexane compounds enables the reactivity of a functional group to be studied in both the equatorial and the axial disposition. The steric interactions in the two configurations are different and the procedure provides a means of changing steric effects without changing polar effects. For methyl *trans*- and *cis*-4-t-butylcyclohexane carboxylates in 1:3 dioxan–water at 90 °C, $k_{eq}/k_{ax} \sim 4\cdot8$ in acidic hydrolysis and $\sim 8\cdot3$ in alkaline hydrolysis, indicating a difference in

[59] N. B. Chapman, J. Shorter, and K. J. Toyne, *J. Chem. Soc.*, 1961, 2543; N. B. Chapman, A. Ehsan, J. Shorter, and K. J. Toyne, *J. Chem. Soc. (B)*, 1967, 570; 1968, 178.

steric effects in the two reactions. In acid-catalysed esterification in methanol at 30 °C, *trans*-decalin-2β- and 2α-carboxylic acids gave $k_{eq}/k_{ax} \sim 25$. Alkaline hydrolysis of the corresponding methyl esters gave ratios between 18 and 22 in various mixtures of water with methanol or dioxan. It appears that Taft's assumption (2) may be more closely fulfilled as between alkaline hydrolysis in aqueous organic solvents and acid-catalysed esterification in methanol.

Chapman, Shorter, and Utley[60] studied acidic and basic hydrolysis of methyl *ortho*-substituted benzoates in the same aqueous organic solvents. Various features of this and related work led them to criticise Taft's assumption (2) for neglecting the rôle of the solvent: since the transition states of the acidic and basic reactions carry opposite charges it is unlikely that the solvation patterns will be so similar that the steric interactions in the two systems will be the same. By considering the thermodynamics of ions in solution, R. M. Noyes[61] concluded that there are extreme differences in solvent structure around cations and anions, and warned that 'Taft's treatment may not have separated steric effects as cleanly as was hoped.'

Chapman, Rodgers, and Shorter[62] studied the acid-catalysed esterification of *ortho*-substituted benzoic or phenylacetic acids in methanol. Their results, in conjunction with those on related systems, suggested a dependence of steric effects on solvent and the occasional importance of a polar contribution to log $(k/k_0)_A$. Bowden, Chapman, and Shorter[21] examined the Taft analysis and the application of polar and steric parameters in the reactions of arylaliphatic carboxylic acids and esters. A Taft analysis of alkaline hydrolysis led to σ^* values with inconsistencies, and not agreeing well with a set based on the reaction of carboxylic acids with diazodiphenylmethane. Criticism of Taft's assumption (2) was repeated.

A rather different approach to examining the validity of assumption (2) is to study the application of polar and steric parameters to reactions bearing a close resemblance to acid- and base-catalysed ester hydrolysis. Ester exchange provides a very suitable system, *e.g.* the methanolysis of $(-)$-menthyl esters, $R \cdot CO_2 C_{10}H_{19}$, in methanol at 30 °C, studied by Pavelich and Taft.[17,18] Equation (9) was applied to give $\rho_A^* = 0.626$, $\delta_A = 1.549$ for the acid-catalysed reaction, and $\rho_B^* = 2.702$, $\delta_B = 1.301$ for the base-catalysed process, *i.e.* the steric susceptibility constants differ by 18%. Pavelich[18] attributes this to the steric effects ceasing to be equivalent when they are considerably greater than those operating in ester hydrolysis ($\delta = 1$). Howsoever interpreted the results are disturbing to assumption (2). Note also the appreciable polar effect in acid-catalysed exchange.

P. D. Bolton[49] has studied the acidic and basic hydrolysis of aliphatic amides, whose mechanisms closely resemble those of the corresponding ester reactions. The results are best interpreted in terms of a Pavelich–Taft equation (9), modified to use E_s^c values[46] and to include a hyperconjugative term (see above). The

[60] N. B. Chapman, J. Shorter, and J. H. P. Utley, *J. Chem. Soc.*, 1963, 1291.

[61] R. M. Noyes, *J. Amer. Chem. Soc.*, 1964, **86**, 971.

[62] N. B. Chapman, M. G. Rodgers, and J. Shorter, *J. Chem. Soc. (B)*, 1968, 157, 164.

steric susceptibility constant $\delta_A = 0.858$, and $\delta_B = 1.08$, *i.e.* the values differ but in the opposite sense from that found in ester exchange.

On the other hand, support for assumption (2) has come from a variant of this approach. I. V. Talvik[63] interpreted acidic and basic ester hydrolysis in *water* in terms of σ^* and E_s^0 values (based on the usual measurements in aqueous organic solvents), with appropriate hyperconjugative terms. She finds $\delta_A \sim \delta_B \sim 0.80$.

The situation regarding the supposed equality of steric effects in acid- and base-catalysed reactions is thus obscure and deserves attention. There is room for well-designed experimental work. Taft's other assumptions likewise require investigation, particularly assumption (3) which is the basis for ignoring polar effects in the acid-catalysed reactions. A widespread disbelief in assumption (1) regarding the approximate separation of polar, steric, and resonance effects in a linear way would stultify the field. However, it would be appropriate to investigate possible contributions from interaction terms in certain systems. The inclusion of cross-terms in correlations frequently improves them, but often their physical significance is obscure.

Taft's papers in 1952 and 1953 represented a great achievement in dealing with a vast body of data. Our continued dependence on the consequences of the averaging procedures which he found necessary is unsatisfactory, particularly since some of the data are disparate and of doubtful reliability. Further, new values of σ^* and E_s do not have this character: they are based on the behaviour of individual systems, *e.g.* a new E_s value is derived from acid-catalysed esterification in methanol, or a new σ^* value by interpolation in a spectroscopic correlation. There is too little attention paid by many organic chemists to the considerations in Sections 5 and 6 and there is much rather woolly application of E_s and σ^*, with insufficient attention to an adequately wide range of substituents (a point emphasised by Taft[11]) and to proper statistical assessment of correlations. In general the Taft analysis, its equations and parameters are in need of the kind of refinement to which the Hammett equation was subjected in the late 1950s.[8,9]

APPENDIX

Table 4 *Substituent constants*

Symbol	Nature	References
σ	Original Hammett constant	5, 6
σ^+	Constant for electron-demanding reactions (Brown)	7
σ^-	Constant for electron-releasing reactions	5, 6, 64
σ^n	Unexalted Hammett constant (Wepster)	8
σ^0	Unenhanced Hammett constant (Taft)	9
σ_I, σ_R^0	Inductive and resonance parameters used for analysis of σ^0	9
σ_R	Resonance parameter (reaction-dependent)	9

[63] I. V. Talvik, *Reakts. spos. org. Soedinenii*, 1964, **1** (2), 241.
[64] R. W. Taft, *J. Amer. Chem. Soc.*, 1957, **79**, 1045.

Symbol	Nature	References
σ^*	Aliphatic polar substituent constant	11
σ_o^*	Polar constant for *ortho*-substituents (Taft), relative to methyl	11
σ_o	Polar constant for *ortho*-substituents (general)	56
σ'	Polar constant for alicyclic reactivity (Roberts)	13
E_s	Steric parameter (Taft)	11
E_s^c	Steric parameter corrected for C—H hyperconjugation (Hancock)	46
E_s^0	Steric parameter corrected for C—H and C—C hyperconjugation (Palm)	50
n	Number of relevant bonds in correlations allowing for hyperconjugation (subscripts may be attached)	15, 46, 50
$\Delta 6$	Change in the six-number (additional steric parameter, Hancock)	47
π	Hydrophobic bonding constant in biological activity (Hansch)	45