LINEAR FREE ENERGY RELATIONSHIPS

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I. INTRODUCTION

A. THE NATURE AND UTILITY OF THE RELATIONSHIPS

An understanding of the dependence of reactivity upon the many reaction variables, particularly substrate structure, reagent structure and reaction medium, is one of the primary aims of chemistry. In qualitative terms the more important features of the main reaction types have been recognized, and the finer details of many individual reactions have been clarified. The quantitative prediction from theory of the result, velocity and extent of even the simplest processes is, however, still an objective for the future. With this aim in view current investigations seek to place on a quantitative basis well-established qualitative concepts as a necessary stepping stone to more precise theories.

During the past three decades the steady accumulation of rate and equilibrium data has led to the formulation of a number of empirical correlations. These promise to simplify the theoretical problem by permitting attention to be focused on only one or two of the reaction variables, while the others are held essentially constant.

The general form of these correlations is a linear relationship between the logarithms of the rate or equilibrium constants for one reaction (A) and those for a second reaction (B) subjected to the same variations of reactant structure or reaction conditions. (Each set of rate or equilibrium constants is termed a reaction series.) The relationship may be expressed by equation 1

$$\log k_B = m \log k_A + c \qquad (1)$$

where k_B and k_A are the corresponding rate or equilibrium constants,[1] m is the slope and c the intercept of the straight line obtained.

Since the logarithm of an equilibrium constant (K) is proportional to the standard free-energy change (ΔF^0) accompanying the reaction

$$\log K = -(\Delta F^0/2.3RT) \qquad (2)$$

and the logarithm of a rate constant (k), according to the transition state theory (*cf.* 91a), is proportional to the standard free-energy of activation (ΔF^*)

$$\log k = \log \frac{RT}{Nh} - \frac{\Delta F^*}{2.3RT} \qquad (3)$$

Equation 1 is equivalent to a linear relationship between standard free-energy changes and can be represented also by equation 4[1]

$$F_B = m'\Delta F_A + c' \qquad (4)$$

The formal similarity of equations 2 and 3 provides an explanation for the correlation of both equilibrium and rate data. This might have been unexpected since the former are independent and the latter completely dependent upon the reaction path between reactants and products.

From the existence of these relationships it may be inferred that the reaction variable in question operates upon each reaction series in the same manner. This means that is is without any function specific for one series or individual members of a series, that the reaction mechanism does not change throughout each reaction series, and that parameters derived from the relationship can provide a quantitative measure of the variable and its effect. The task of surveying the over-growing body of reactivity data can thus be considerably simplified. Furthermore, a well established relationship permits the prediction of unknown reactivities. There is thus theoretical and practical utility in these correlations, particularly when their range of validity is clearly defined.

B. THE COVERAGE OF THIS REVIEW

In a general manner the thermodynamic and kinetic requirements for the appearance of a linear free-energy relationship have been investigated previously, at least for structural changes in the substrate (*cf.* 242a). This is extended to set up a generalized relationship from which it is possible to assess the expected ranges of application of the individual equations and their interdependences.

Correlations of structural changes in the substrate, structural changes in the reagent and changes in the reaction medium provide three divisions within which the individual relationships are examined. There is considerable overlap in general and in particular between the second and third sections where solvolyses are concerned.

The review by Jaffé (134) in 1953 of the Hammett equation is the most extensive of any of these relationships. Only the substituent parameters have been subjected to subsequent review (244). The accumulation of further reactivity data, its attempted extension beyond the restrictions originally imposed and changes in the method of computation of the parameters necessitate a re-examination.

The Brønsted equation, being the earliest empirical correlation of reactivity, has received considerable attention. Recent discussions (11a,e, 14a) do not however specifically treat the equation as an example of a general linear correlation of free energy changes.

No independent reviews have been published concerning the other relationships discussed here, although Taft (242, 244) has examined in some detail the various equations associated with his name.

Brief comments on all of these relationships appear in recent texts on physical organic chemistry (*cf.* 99, 121).

II. THEORETICAL IMPLICATIONS OF THE RELATIONSHIPS

A. GENERALIZED RELATIONSHIPS

Following an analysis similar to that used by Glasstone, Laidler and Eyring (94) for the influence of external parameters on reactivity, the standard free-energy change (ΔF^A) of a reaction A may be considered as a function of a number of independent variables, x, y, etc. Variations of the standard free-energy change can then be expressed, at constant temperature, by equation 5

$$d\Delta F^A = \left(\frac{\partial \Delta F^A}{\partial x}\right)_T dx + \left(\frac{\partial \Delta F^A}{\partial y}\right)_T dy + \dots \qquad (5)$$

For a finite change in x from some arbitrary standard value x_0 to x_i while the other variables are held constant, the free-energy change will be given by eq. 6

$$\Delta F_i^A - \Delta F_0^A = (\partial \Delta F^A/\partial x)_T(x_i - x_0) \qquad (6)$$

which is a linear relationship between ΔF_A and x, and hence between $\log k$ and x, provided that

$$(\partial \Delta F^A/\partial x)_T = g_x^A \qquad (7)$$

remains constant within the range of variation of x.

In combination with equations 2 and 3, equations 8 and 9 can be applied to the influence of the same change in the variable x on two reactions A and B.

$$\log (k_i/k_0)_A = g_x^A(x_0 - x_i)/2.303RT_A \qquad (8)$$

$$\log (k_i/k_0)_B = g_x^B(x_0 - x_i)/2.303RT_B \qquad (9)$$

where k represents a rate or equilibrium constant, and the g-terms are the partial differentials of a standard free-energy of activation or a standard free-energy change during reaction as appropriate.

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(1) Throughout this review k will be used to represent a specific rate *or* equilibrium constant and ΔF a standard free energy of activation *or* of reaction as applicable where correlations cover both reaction rates and equilibria.

The combination of equations 8 and 9 leads to a linear free-energy correlation between reaction series A and B, equivalent to the generalized equation 1.

$$\log (k_i/k_0)_B = \frac{g_x^B T_A}{g_x^A T_B} \times \log (k_i/k_0)_A \qquad (10)$$

By selecting one reaction series as a standard, *e.g.*, A, equation 10 may be considered composed of two parts

$$\log (k_i/k_0)_A \equiv X_i \qquad (11)$$

dependent only on the change in the variable x, and

$$g_x^B T_A / g_x^A T_B = G_x^{AB} \qquad (12)$$

dependent only on the nature of and the conditions employed for reaction series B and its susceptibility to changes in x relative to that for the standard reaction series A.

The relative rate constants of reaction B will be linearly correlated by the two-parameter eq. 13

$$\log (k_i/k_0)_B = X_i G_x^{AB} \qquad (13)$$

provided that all other variables but x remain constant, and the ratio g_x^B/g_x^A remains constant throughout the range of variation of x. Note that g_x^A and g_x^B need not be individually constant, so that part of the range of application of eq. 13 may result from parallel variations in these terms.

Relative reactivity data may still be accommodated by a simple equation even when these conditions are not fulfilled.

In particular: (a) I. Although the other variables do not remain constant, provided they are independent, their individual contributions may be summed as in equation 5. Using the same arbitrary zero for the variables x and y and standard reaction series A and A′, respectively, there results for simultaneous variations

$$\log (k_i/k_0)_B = X_i G_x^{AB} + Y_i G_y^{A'B} \qquad (14)$$

which is one generalized form of the four-parameter equations. In this case the ratios g_x^B/g_x^A and g_y^B/g_y^A must remain constant within the range of variation of *both* x and y.

Equation 14 is the simplest expression correlating multiple variations. It results from the use of a common chosen zero for the parameters measuring the variables. A more general treatment is described by Miller (182).

II. One special case of the simultaneous variation of x, y, z, etc., occurs when they are not independent but change in proportion to x, *i.e.*

$$dy = a_{xy}dx,\ dz = a_{xz}dx, \text{ etc.}$$

This situation is indistinguishable from that of variations in x alone since

$$dx + dy + dz + \ldots = dx(1 + a_{xy} + a_{xz} + \ldots) \qquad (15)$$

and the result will be the introduction of another proportionality constant into the g-terms. In other circumstances the interdependence of the variables will lead to the failure of equation 14 and any more complex expression of the same type that seeks to account for multiple variations.

(b) As will be noted later, the non-constancy of the g-terms though causing a failure of the simple equations 13 and 14 may in some cases be accounted for by a correcting term.

While such corrections are empirical, it is possible in special cases to provide a theoretical basis for the modification. Similarly, the incursion of additional factors in certain members of several reaction series can be accommodated by a modification of the X_i-term in equation 13. Equation 16 then seeks to account, for example, for the variation of X_i with y, as

$$\log (k_i/k_0) = \left[X_i + \left(\frac{\partial X_i}{\partial y}\right)_B \times (y_B - y_A)\right] G_x^{AB} \qquad (16)$$

One result of the addition of correcting terms is the improved precision with which the modified equation reproduces experimental data. Such terms have no theoretical value unless their origin can be identified. It is preferable that the necessary parameters be obtained from an independent source.

B. PREDICTED RANGE OF APPLICATION AND LIMITATIONS

The development of the generalized relationships represented by equations 13 and 14 already has necessitated a series of restrictions. From these and a number of other factors it is possible to assess in general terms the conditions expected to lead to failures.

To be useful a large number of values for the parameter X_i must be provided by the measurements defining them; *i.e.*, $\log (k_i/k_0)_A$, and, for subsequent theoretical utilization of the parameter, the measured variable (or variables) x must be known. This places severe restrictions on the choice of standard reactions. One for which extremely precise data are available, but whose mechanism is unknown, would be unsuitable. Furthermore neither the zero for the measure of the variable nor the standard reaction series should be selected from those showing extreme behavior. A reaction series in which changes in mechanism occur would clearly be unsatisfactory (see (a) below).

Assuming a satisfactory choice of defining conditions, the correlation of a large number of reaction series by equation 13 will be expected to fail when: (a) The factor $g_x^{AB} = (\partial \Delta F^B/\partial x)$ does not remain constant throughout the normal range of variation of x. Changes in mechanism within reaction series would be common causes of variations (sometimes abrupt) in the g-terms. If the reaction series can be divided clearly between two (or more) markedly different mechanisms, both sets of data may be satisfactorily correlated separately (*cf.* sections III-A-3, III-B-2, IV-A-2).

TABLE I

LINEAR FREE ENERGY RELATIONSHIPS

Equation	Correlation of relative reactivity	X_i	G_x^{AB}	Y_i	G_y^{AB}	Correcting term
Hammett	Substituents in *m*- and *p*-aromatic substrates	σ	ρ	—	—	—
Modified Hammett		σ^+ or σ^-	ρ	—	—	—
Taft	Substituents in aliphatic and *o*-aromatic substrates	σ^*	ρ^*	—	—	—
Modified Taft	Inclusion of steric and resonance effects	σ^*	ρ^*	—	—	ψ
		σ^*	ρ^*	E_s	δ	—
Hansson	Substituents in both reactants	$s_1 + s_2$	r	—	—	t
Grunwald–Winstein	Ion solvating power and nucleophilicity of solvent	Y	m	—	—	—
Modified Grunwald–Winstein		Y	m	N	l	—
Brønsted	Acid and base catalytic power	$\log K_a$	α	—	—	—
Swain–Scott	Electrophilicity and nucleophilicity of solvents and reagents	e	s	n	s'	—
Swain–Mosely–Bown		d_1	c_1	d_2	c_2	—
Edwards	Basicity and polarizability of reagents	P	A	H	B	—

Identification of Variables

σ ≡ electrostatic and electronic effect of a subst. rel. to –H
σ^* ≡ electrostatic and electronic effect of a subst. rel. to $-CH_3$
E_S ≡ steric effect of a subst. rel. to $-CH_3$
s_1, s_2 ≡ substrate structural parameters
Y ≡ ionizing power of solvent rel. to 80% aq. ethanol
N ≡ nucleophilicity of solvent rel. to 80% aq. ethanol
e, d_1 ≡ electrophilicity of reagent (solvent) rel. to water
n, d_2 ≡ nucleophilicity of reagent (solvent) rel. to water
P ≡ polarizability of reagent rel. to water
H ≡ basicity of reagent rel. to water
ψ ≡ resonance correction
t ≡ steric correction

(b) The ratio $(x_i - x_0)_B/(x_i - x_0)_A$ does not remain constant. This means that the X_i-parameter as defined is inadequate to describe the variable in reaction series B, where presumably it is operating in a unique manner. Redefined sets of parameters or zero conditions have been used in attempts to correlate data of this type (*cf.* sections III-A 2, 4, 5 and 6; III-B-3 and 4; IV-A-2).

(c) The ratio g_x^B/g_x^A does not remain constant. Equation 13 will be successful even though the individual g-terms are not constant provided their variations are proportional.

(d) Other variables are not constant nor are their changes linear functions of the changes in x.

As pointed out above the situation (d) is taken into account by either an empirical correcting factor or by equation 14.

In addition to (a), (b) and (c) above, which in this case apply to both x and y, equation 14 fails when: (e) The ratios g_x^B/g_x^A and $g_y^B/g_y^{A'}$ are not constant within the range of variation of *both x and y*. This places exceptionally large restrictions on the data that can be correlated and on the choice of standard reaction series in setting up the four parameter equations (*cf.* Sections III-A-9, III-B-3, V-B, V-C).

The relative standard free energy change is a composite quantity. It may be factored thermodynamically into relative enthalpy and relative entropy changes.

$$\Delta F = \Delta H - T\Delta S$$

$$\therefore (\partial\Delta F/\partial x)_T = (\partial\Delta H/\partial x)_T - T(\partial\Delta S/\partial x)_T \qquad (17)$$

In general it is to be expected that $(\partial\Delta H/\partial x)$ and $(\partial\Delta S/\partial x)$ will be completely different functions of the variable x in the various reaction series. The criteria of (a), (c) and (e) require therefore that either

$(\partial\Delta S/\partial x)_T = 0$, *i.e.*, the series is isoentropic, or
$(\partial\Delta H/\partial x)_T = 0$, *i.e.*, the series is isoenthalpic, or
$(\partial\Delta S)\partial x)_T$ and $(\partial\Delta H/\partial x)_T$ are linearly related

These features are discussed in detail as they affect the application of the Hammett equation (section III-A-3) (*cf.* 30, 166, 252), but will apply quite generally to linear free energy relationships. Note that a limited correlation will result whenever $(\partial\Delta H/\partial x)_T$ is very much greater or less than $T(\partial\Delta S/\partial x)_T$, which could be due solely to the temperature employed.

The alternative analysis of free energy changes in terms of potential energy changes and quotients of the appropriate partition functions does not lead to experimentally determinable quantities. Although these are ultimately the theoretical quantities that are desired, the present discussion is not advanced by their use. Nevertheless it is usually presumed that, with the exception of steric corrections, the variables studied operate solely upon the potential energy.

Theoretical developments based on these empirical correlations will always be hampered by uncertainty as to the authenticity of the selected measure of variable in question and the possible presence of proportional contributions from other variables. The Hammett and Taft equations appear the least subject to doubts. The lack in many cases of even a restricted correlation involving various physical quantities has halted purely theoretical treatments of reactivity. These two types of treatment approach one another in the Edwards equation and certain series correlated by the Hammett and Taft equations.

In all cases continuous variables are correlated by means of essentially discontinuous parameters. Certain discontinuous variations (*cf.* III-B) are also accommodated. Some variables, particularly steric effects, although modifying the free energy change in a distinctly non-linear manner, are still measurable by virtue of the deviations from linearity and the magnitude of the required correcting term. The question of authenticity is, however, more serious in these cases.

The success or failure of a particular correlation can be judged graphically. However, none of the relationships is to be regarded as exact and all the data examined will contain experimental error to a greater or lesser degree. Thus statistical assessment of attempted correlations is generally carried out by the least squares method (*cf.* 134i). Jaffé (134h) has suggested that two-parameter correlations be described in terms of correlation coefficients: $r > 0.99$ excellent, $r > 0.95$ satisfactory, $r > 0.90$ fair fit, but has pointed out the significance of other statistical quantities and the dangers of judgment in terms of correlation coefficients alone. Three- and four-parameter equations yield related quantities through multiple regression methods but their assessment is more difficult. A statistic termed "goodness of fit" also has been employed (235).

III. CORRELATION OF STRUCTURAL CHANGES IN THE SUBSTRATE

A. THE HAMMETT EQUATION

1. General Discussion

The history of the Hammett equation and its place among the many attempts during the past thirty years to analyze the influence of substituents on reactivity has been discussed in other places. It suffices to say that it was proposed in 1937 (109) as an empirical correlation representing a more sophisticated extension of the Hixon–Johns approach (126).

As originally proposed

$$\log k - \log k_0 = \sigma\rho \qquad (18)$$

where k and k_0 are rate or equilibrium constants for reactions of *m*- and *p*-substituted and unsubstituted benzene derivatives, respectively, σ is a parameter dependent only on the substituent and its position and ρ is a parameter dependent only upon the nature of the derivative, the reaction and conditions under which it takes place. The equation sought only to correlate reactions occurring in a side chain and was found not to be applicable to *o*-substituted benzene derivatives nor to aliphatic compounds.

In 1940, Hammett (110) was able to correlate 52 reactions while by 1953 Jaffé (134) was able to list 204 reactions, many under different temperature and solvent conditions, correlated with a median precision of ±15%.

The restriction of substituent location to *meta* and *para* in benzene and the general failure of the unmodified equation in the case of reaction at nuclear positions clearly indicate that the variable correlated derives from the polar effect of the substituent, steric effects and direct resonance interactions being absent. On the basis of an electrostatic theory of reactivity the variable x has been identified with the relative charge density at the ring carbon atom to which the reacting side chain is bonded.

In terms of the generalized equation

$$X_i = \sigma_i \equiv \log (k_i/k_0)_A \qquad (19)$$

where A, the ionization constants of benzoic acids in water at 25°, is the reaction series defining σ

$$G_X^{AB} = \rho_B = \frac{T_A\,(\partial\Delta F/\partial x)_B}{T_B\,(\partial\Delta F/\partial x)_A} = \frac{T_A\,(\partial\Delta F/\partial\sigma)_B}{T_B\,(\partial\Delta F/\partial\sigma)_A} \qquad (20)$$

in which T_A and $(\partial\Delta F/\partial x)_A$, or its equivalent $(\partial\Delta F/\partial\sigma)_A$ are constants determined by the defining reaction series.

It was originally proposed that the Hammett equation would only be applicable to isoentropic series since structural variations in enthalpy and entropy would not be expected to be the same. But there appear to be more series where entropy varies than where it remains constant. The situation has been examined by Leffler (166), who finds for numerous reaction series a linear relation between enthalpy and entropy, or activation energy and pre-exponential factors. Taft (242h) also recognizes that such a relationship should exist if the Hammett equation is followed and interprets such entropy variations as having their origin in polar effects. Only for a small number of the reaction series correlated by the Hammett equation are data available to examine for linear enthalpy–entropy relationships or constant entropy changes. While these features may generally be applicable, there are cases for which relative activation energies but not log rate constants (*i.e.*, relative free energy changes) are correlated with sigma (70). Some reaction series correlated by the Hammett equation are to be expected where entropy factors are dominant. This is the case for the hydrolysis of aryl acid succinates and glutarates (93) and for the acid dissociation of some phenols (86). At least one reaction series has been observed in which log k is linear with sigma although neither ΔH^* nor ΔS^* is (272).

Numerous extensions of the equation have been suggested to cover reactions and systems originally excluded. One of the main sources of failure is found in reactions where there can be direct conjugation between reaction center and substituent, particularly reactions of anilines, phenols and in nuclear substitutions. Attempts to accommodate such reaction series by means of unique enhanced sigma-values are discussed in sub-sections 5 and 6. The rigidity and other geometric features of the benzene system that leave the *m*- and *p*-positions free from steric effects are present in other aromatic and heterocyclic systems as well as in certain alicyclic and acyclic systems. The limited data on substituent effects in these systems are presented in sub-sections 7 and 8.

It was the empirical observation of Hammett that the influence of both *m*- and *p*-substituents could be correlated with the sigma-values by the *same* straight line. The many subsequent data have been analyzed in terms of a single rho value for each reaction series, and deviations, which appear more often for *p*-substituents, have been interpreted in terms of enhanced resonance effects. However, Hine (122, 123) has argued that in general there should be different proportionality factors appertaining to *meta* and *para* series. The reasons and implications for this suggestion are dealt with in sub-section 3 on rho-values. Statistical analysis by Jaffé (138) suggests this may indeed be the case, but only in a few more cases than would arise by chance. It is thus not a serious factor for the majority of reactions so far examined.

Initially the prime purpose of the Hammett equation was for the storage of data and the prediction of new data. For this purpose a generally applicable sigma-value for each substituent was required. From these values unknown rate constants could be computed and rho-values for new reaction series used in mechanistic interpretations. Jaffé (134a) thus computed sigma-values for all but a few substituents to give the best statistical fit for all data available. This procedure makes both the sigma-values and rho-values dependent upon the body of data known at any particular time. More seriously from the point of view of current theoretical trends, all but large systematic deviations tend to be obscured. McDaniel and Brown (172) recommended a return to the original definition using the dissociation of the substituted benzoic acids. It has been pointed out, however, that this scale of values still contains some which include contributions due to direct conjugation. One recommendation (10) is the use of a restricted set of "primary" sigma values based on the defining reaction series. The reviewer has adopted this approach, although a decision has still to be made for each reaction series whether direct conjugation occurs or not. It is theoretically more sound to use as a defining reaction series one where the side chain is "insulated" from the benzene ring (*cf.* 245). Such a scale, based for example on the phenylacetic acids, is less satisfactory, however, since the reduced sensitivity to substituent effects leads to a reduced precision in the sigma-values. In any case the "insulated" reaction series are correlated excellently by the "primary" sigma-values so that there is in practice little choice between the two definitions.

A fundamental requirement for the appearance of a linear free energy relationship is a constancy of mechanism throughout each reaction series. In the extreme, an abrupt change in mechanism results in a difference response of log *k* to substituent polar effects and hence a sharp discontinuity in the usual Hammett log *k* *versus* σ plot (as in Fig. 1). One application of the Hammett application is in the recognition of mechanistic changes. More usual, and less readily identified unless a large number of substituents are examined, are curved log *k* *versus* σ plots (illustrated by Fig. 2). For the extremes a and b it may be considered that the reaction mechanism is different. Throughout the series, however, there would appear to be a continuous change in mechanism from one extreme to the other. Such cases may be resolvable into two straight lines, albeit poorly correlated, in which case the results could still be divided into two mechanistic categories.

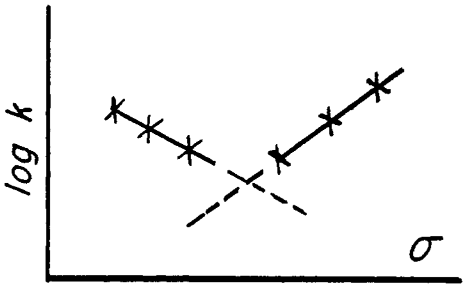


Figure 1.

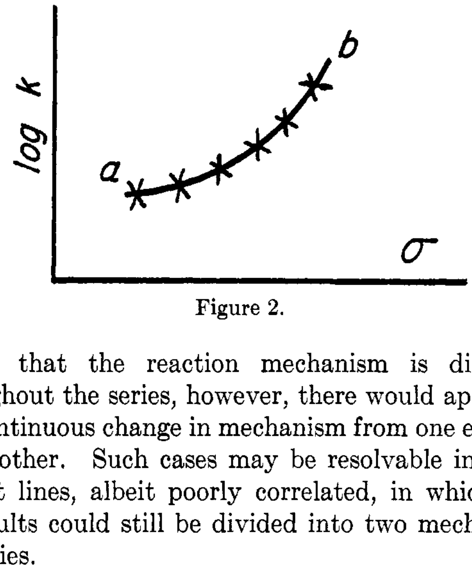


Figure 2.

This more common type of deviation of the Hammett equation, exemplified by the curved correlation of phenol with benzoic acid dissociation constants (*cf.* Fig. 2 of ref. 243) could be interpreted in terms of a dependence, linear or otherwise, of σ upon ρ (see also sub-section 5), *i.e.*, by various enhancements of the σ-value in various reaction series. The alternative view, discussed in detail by Swain and Langsdorf (231), is that the ρ-value depends on the substituent. In other words, different substrates react through more or less different mechanisms between the two extremes. The likelihood of *both* types of behavior makes analysis of non-linear Hammett "correlations" uncertain. An interesting example of this type of behaviour is found in the solvolysis of benzyl tosylates (153), the mechanism of which has been a matter of considerable discussion. Pronounced curvature of the log k *versus* σ plot for *p*-substituents indicates the inadequacy of the unmodified Hammett relationship for this reaction series. Failure of the sigma-values alone would not seem to be the answer here since the *m*-substituents are accommodated by a different line. The corresponding *m*-substituted chlorides are well correlated by the "primary" sigma-values, while Okamoto and Brown (189) report that the σ^+-scale accounts for the enhanced rates for electron-releasing *p*-substituents. The interpretation by the latter in terms of a *sharp* mechanistic change appears insecure in view of the previous statements and the examination in sub-section 5 of the σ^+-parameter.

Extreme cases of curvature in log k *versus* σ plots with maxima and, more commonly, minima have been observed. Such is often the case for free radical reactions where *all* substituents irrespective of polarity may facilitate reaction. In ionic reactions this behavior has been observed in the hydrolysis of substituted benzoyl chlorides (118) and of substituted benzenesulfonyl chlorides (27). A minimum for the unsubstituted compound is especially noticeable in the case of the stability of the platinum–styrene complexes (144).

In the case of complex reactions having no single step rate-determining, the Hammett relationship may fail for the over-all rate constant, despite excellent correlations for the individual steps. This situation may arise whenever the observed rate constant contains a sum or difference of the rate constants for individual steps (186A). However other, often more satisfying, explanations of the resultant curvature can be provided as in the case of the acid-catalyzed oximation of benzophenones (70).

Similar non-linearity of log k_{obs} with σ has been observed for semicarbazone formation in nearly neutral solution (2). Here a prior equilibrium and the subsequent reaction of a complex are both correlated with almost equal but opposite ρ-values such that under certain conditions the over-all rate shows only a small random variation with substituent changes.

Certain substituents, classified as $\pm$M, can facilitate reactions by electron release or withdrawal. These cannot be defined by a single σ-value independent of reaction. Examples are the phenyl and nitroso groups. Reaction centers can similarly be "amphoteric" as in the acidity of substituted 1-hydroxypyridinium cations (137) where enhanced σ-values for both +M and −M groups are required to produce a linear correlation.

2. *The Substituent Parameters*

In the equation originally proposed and examined by Hammett (109) the sigma-values were *defined* in terms of the relative acidities of the benzoic acids. Correlations were based in the main on sixteen such values, nine of which were for *p*-substituents, and five further values (four *para*) derived from ethyl benzoate saponification data. There resulted thirty-four sigma values (110) that formed the basis for Jaffé's re-examination (134). From the correlation of 371 reaction series involving four or more markedly different substituents, those having $r > 0.95$ gave a further 73 sigma-values (31 from more than one reaction series). Subsequent workers have added to this listing.

Jaffé's treatment is equivalent to a redefinition of sigma as the value of the parameter which best fits all the available experimental data. This definition, while useful in the accommodation of a large number of reaction series, creates some difficulties, particularly in the understanding of deviations. Investigations concerned with the latter feature have led to a return to the original defining reaction series for sigma.

Powerful direct conjugative interactions between *p*-substituents and some reaction centers were recognized by Hammett as a major cause of failure of the equation. In the case of −M substituents this was found to lead to an enhanced parameter, designated σ^*. (For the designation of the direction of substituent interactions by a conjugative mechanism −M signifies electron withdrawal.) No such dual scale was at first found for +M substituents for which however there were many reaction series where serious deviations were registered. Subsequent investigations of reaction series having powerful resonance requirements and the investigations of aliphatic and alicyclic systems have yielded a number of specialized sigma values such that decisions regarding nomenclature became urgent. Table II summarizes the convention adopted together with four further symbols made necessary by later work.

TABLE II

SIGMA VALUE NOMENCLATURE

Reaction Mechanisms Conference, Swarthmore, Pa., September, 1956

Symbol	Range of application
σ	Ordinary Hammett value
σ^+	Enhanced value for direct conjugation in an electron-demanding reacn.
σ^-	Enhanced value for direct conjugation in an electron-releasing reacn.
σ^*	Value appropriate to *o*-phenyl and aliphatic derivs.
σ'	Value appropriate to 4-bicyclooctane derivatives
σ^n	"Normal" values of Bekkum, Verkade and Wepster
σ^0	Direct conjugation interaction free values of Taft and Lewis
σ_I	That part of the value attributed to inductive effects
σ_R	That part of the value attributed to resonance effects

The existence of direct conjugation between the carboxyl group of the benzoic acids and +M substituents in the *p*-position means that the originally defined set of substituent parameters contains enhanced values for these substituents. Bekkum, Verkade and Wepster (10) suggest therefore a limited set of eight sigma-values defined by the relative ionization constants of the *m*-substituted benzoic acids (1–8 in Table III) with two *p*-substituents (9 and 10) to be used only when direct resonance interactions are clearly absent. With these "primary" sigma-values available data on 88 reaction series were correlated as compared with almost five times this number processed by Jaffé (134). This reduction is due to the scarcity of data covering *m*- as compared with *p*-substituents. Of 56 reaction series common to both treatments, Bekkum, Verkade and Wepster find 34% having correlation coefficients better than 0.998, 77% better than 0.99 and 89% better than 0.98; while Jaffé, for these reaction series, finds 29% better than 0.99, 59% better than 0.98, but none better than 0.998, in fact only 6% of the 371 reactions covered show this high precision. That this marked improvement is due to the removal of deviations due to variable *p*-substituent influences is shown by the computation of sigma-values for other *m*-substituents (Table IV, numbers 11–19). The standard deviations obtained are no larger than might be expected and do not greatly exceed those for substituents "H" and "*p*-NO$_2$" (Table V) calculated from reaction series correlated using the primary values of these substituents. There appear to be no significant variations for *m*-substituents although the small magnitude of the sigma-values for amino-, hydroxy and related groups gives them a disproportionate uncertainty and hence a very limited utility.

TABLE III

"PRIMARY" SIGMA VALUES

Substituent	σ^a	σ^{0b}	Substituent	σ^a	σ^{0b}
1. *m*-CH$_3$	−0.069	−0.07	6. *m*-I	0.352	0.35
2. H	.000	.00	7. *m*-COCH$_3$	.376	.34
3. *m*-F	.337	.35	8. *m*-NO$_2$	.710	.79
4. *m*-Cl	.373	.37	9. *p*-COCH$_3$	.502^c	(.46)^d (.40)^e
5. *m*-Br	.391	.38	10. *p*-NO$_2$	.778^c	(.82)^d (.73)^e

[a] $\sigma \equiv \log (k/k_0)$ of reaction series 1a of Table IX (10). [b] $\sigma^0 = \sigma_I + \sigma_R{}^m$ (243). [c] For reactions not involving direct conjugation. [d] For reactions in water and aqueous solvent mixtures. [e] For reactions in non-hydroxylic media.

Turning their attention to *p*-substituents, Bekkum, Verkade and Wepster then computed σ^n ("normal")-values based on well correlated reaction series ($r >$ 0.98) considered to exhibit no direct conjugation interactions between substituent and reaction center. These values are listed in Table V (numbers 28–42). To illustrate the choice of reaction series, those used for all substituents were the dissociation of the phenylacetic and phenylpropionic acids; those used only for +M substituents included acid dissociation of phenols and thiophenols and nucleophilic displacements by substituted phenolate ions; those used only for −M-substituents included benzoic acid, benzoyl chloride and benzoate ester reaction series, carbonium ion reactions and electrophilic aromatic substitutions. Several reaction series were excluded from both categories on the basis of uncertain mechanism or possible enhancements with both types of substituent. Also included in Tables III and IV are sigma-values for other substituents (20–27 and 43–49) calculated in much the same way but with less rigid restrictions in choice of reaction series, where a choice exists.

Calculated sigma-values based on all reaction series show an appreciable spread, especially those for *p*-substituents with marked mesomeric effects. It is to be expected that different reaction centers having different conjugative possibilities and requirements will lead to different degrees of enhancement of *para*-sigma values, *i.e.*, continuous range of values as opposed to dual or triple values are represented by σ^+ and σ^-. This is borne out by the "continuous" population of the ranges for these sigma-values, with no indication of grouping (10).

If it is concluded that the "normal" sigma-values measure inductive and resonance polar effects (see below) and that enhanced values are due to differences in direct conjugation between initial and final (or transition) states, then *para* resonance energy

$$\Delta\Delta F_p = -2.303RT(\sigma - \sigma^n)\rho \tag{21}$$

is suggested as a better measure of the latter effect than $(\sigma - \sigma^n)$ which will vary with temperature and with ρ even though the same extent of resonance interaction may be involved. (An alternate measure would be $(\sigma - \sigma^n)/\sigma^n$.)

Within the range $1 \leq \rho \leq 2$ there appears no relationship between $\Delta\Delta F_p$ and ρ; outside this range $\Delta\Delta F_p$ increases markedly with ρ since reaction series with high rho-values involve reactions at nuclear positions or on centers strongly conjugated with the aromatic system. There are again no indications of grouping of the $\Delta\Delta F_p$ values. Some examples are given in Table VI.

Reactions of anilines were excluded from the determination of σ^n-values since it was expected that "saturation" effects might enter whereby two +M-groups in *para* disposition would prevent full operation of normal resonance polar effects of each other. But since phenol and thiophenol reactions were not excluded, Taft (243) suggests that the σ^n-values for +M-groups are still too low.

TABLE IV

SECONDARY SIGMA VALUES (*meta*)

Substituent	σ^{n}[a]	σ^{0}[b]	σ (J)[c]	σ(McD. B.)[d]
11. *m*-OH	0.095 ± 0.025	. .[e] (0.04)[f]	−0.002 ± 0.106	0.121
12. *m*-OCH$_3$	.076 ± .041	.13[g] (0.06)[h]	.115	.115
13. *m*-NH$_2$	− .038 ± .035	− .14[e]	− .161	− .16
14. *m*-N(CH$_3$)$_2$	− .049 ± .092	− .15[e]	− .211	. .
15. *m*-CO$_2$CH$_3$	.317 ± .038	.36	.315 ± 0.036	0.37
16. *m*-CF$_3$	.467 ± .071	.42	.415	.43
17. *m*-CN	.613 ± .035	.62	.678	.56
18. *m*-SO$_2$CH$_3$	.678 ± .044	.66	.649 ± 0.043	.60
19. *m*-N(CH$_3$)$_3^+$	.855 ± .093	. .[i]	.904	.88
20. *m*-C$_2$H$_5$	(− .072)[i,k]	. .	− .043	.07
21. *m*-*i*-C$_3$H$_7$	(− .068)[i,k]	. .	. .	. .
22. *m*-*t*-C$_4$H$_9$	(− .067)[i,k]	. .	−0.120	0.10
23. *m*-Si(CH$_3$)$_3$	(− .053 ± 0.060)[k]	. .	− .121	−0.04
24. *m*-CO$_2$H	(.348 ± .018)[k]	0.36	.355	. .
25. *m*-CO$_2^-$	(.069 ± .108)[k]	. .	.104 ± 0.076	−0.1
26. *m*-SCH$_3$	(.225 ± .018)[k]	0.13[e]	.144 ± 0.031	0.15
27. *m*-S(CH$_3$)$_2^+$	(1.032)[i,k]	. .	. . .	1.00

[a] Mean of all calculated values (10). [b] $\sigma^0 = \sigma_I + \sigma_R^m$ (243, 243A). [c] Values of Jaffé (134g). [d] Values of McDaniel and Brown (172). [e] Solvent dependence too great to permit evaluation. [f] For reactions in non-hydroxylic solvents. [g] For reactions in pure aqueous solutions. [h] For reactions in solvents other than pure water. [i] Treatment not applied to charged groups. [j] Only reaction series 1010 (Table IX) suitable. [k] Not listed in ref. 10. [l] For "benzoic" (type A) reactions only (*cf.* Table IX).

TABLE V

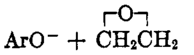
SECONDARY SIGMA VALUES (*para*)

Substituent	σ^{n}[a]	σ^{0}[b]	σ(J)[c]	σ(Mc.D.B)[d]
(H	0.003 ± 0.022[e])			
28. *p*-OH	− .178 ± .036[f]	. .[g] (−0.13)[h]	−0.357 + 0.104	−0.37
29. *p*-OCH$_3$	− .111 ± .021[f]	− .12[i] (− .16)[j]	− .268	− .268
30. *p*-NH$_2$	− .172 ± .026[f]	− .38	− .660	− .66
31. *p*-N(CH$_3$)$_2$	− .127 ± .076[f]	− .44	− .600 ± 0.213	− .83
32. *p*-CH$_3$	− .129 ± .037	− .15	− .170	− .170
33. *p*-F	(.056 ± .025)	.17	.062	.062
34. *p*-Cl	.238 ± .032	.27	.227	.227
35. *p*-Br	.265 ± .033	.26	.232	.232
36. *p*-I	.299 ± .030	.27	.276	.18
37. *p*-CO$_2$H	.406 ± .039	. .	.265 ± 0.126	(.45)
38. *p*-CO$_2$CH$_3$	.463 ± .022	0.46	.636 ± 0.080	.45
39. *p*-CF$_3$	.532 ± .077	. .	.551	.54
40. *p*-CN	.674 ± .042	0.69[k] (0.63)[l]	.628 ± 0.132	.660
41. *p*-SO$_2$CH$_3$	.686	. .	.728	.72
(*p*-NO$_2$	.788 ± 0.028[e])			
42. *p*-N(CH$_3$)$_3^+$	.800 ± .093	. .[m]	0.859 ± 0.149	0.82
43. *p*-C$_2$H$_5$	(− .117 ± .033)[n]	. .	− .151	− .151
44. *p*-*i*-C$_3$H$_7$	(− .098 ± .033)[n]	. .	− .151	− .151
45. *p*-*t*-C$_4$H$_9$	(− .136 ± .031)[n]	. .	− .197	− .197
46. *p*-Si(CH$_3$)$_3$	(.011 ± .030)[n]	. .	− .072	− .07
47. *p*-CO$_2^-$	(.120 ± .084)[n,o]	. .[m]	.132 ± 0.050	.0
48. *p*-SCH$_3$	(.220)[n]	. .	− .047	.00
49. *p*-S(CH$_3$)$_2^+$	(1.199)[n]	. .[m]	. . .	.90

[a] Based only on well correlated reaction series not involving resonance interactions (10). [b] Derived from "insulated" reaction series (243). [c] Values of Jaffé (134g). [d] Values of McDaniel and Brown (172). [e] Calculated value from reactions correlated using this primary substituent. [f] Reactions of anilines and aniline derivatives also excluded. [g] Value extremely variable for reactions in aqueous solvents. [h] For reactions in non-hydroxylic solvents. [i] For reactions in pure aqueous solutions. [j] For reactions in non-aqueous and mixed aqueous solvents. [k] For reactions in aqueous solvent mixtures. [l] For reactions in non-hydroxylic solvents. [m] Treatment not applied to charged substituents. [n] Not listed in ref. 10. [o] All involve formation of a dianion or a doubly negative charged transition state.

TABLE VI

$\Delta\Delta F_p$-VALUES (KCAL./MOLE)

No.	Reaction	$-N(CH_3)_2$	$-NH_2$	$-OCH_3$	$-CH_3$	$-Cl$	ρ
1a	$ArCO_2H \rightleftarrows ArCO_2^-$	0.90	0.67	0.21	0.06	0.02	1.000
15a	$ArPO_3H^- \rightleftarrows ArPO_3^-$	0.40	0.35	.16	.02	(− .09)	1.105
47g	$ArCO_2Et + OH^-$	1.48	1.61	.50	(− .04)	(− .07)	2.545
47j	$ArCO_2Et + OH^-$	1.54	1.35	.26	.00	(− .15)	2.468
141d	$2ArCHO \rightarrow ArCH_2OH + ArCO_2H$	4.7	..	.80	.19	(− .07)	4.019
1006	$Ar_3C \rightleftarrows Ar_3COH$	6.4	5.6	2.8	0.74	0.83	3.968
		NO_2	$COCH_3$	CN	SO_2CH_3	CO_2CH_3	ρ
23c	$ArOH \rightleftarrows ArO^-$	−1.87	−0.88	..	..	−0.82	2.687
23d	$ArOH \rightleftarrows ArO^-$	−0.63	− .75	..	..	− .79	3.141
25a	$ArSH \rightleftarrows ArS^-$	− .85	− .84	..	−0.56	− .99	2.453
25d	$ArSH \rightleftarrows ArS^-$	− .17	− .68	..	..	− .86	3.024
77	 $ArO^- + \overset{\ulcorner O \urcorner}{CH_2CH_2}$	.53	..	0.25	..	..	−1.115
26a	$ArNH_3^+ \rightleftarrows ArNH_2$	−1.68	−1.34	−1.26	−1.56	..	2.941

Tables I–IV compare Bekkum, Verkade and Wepster's values with Jaffé's values and McDaniel and Brown's values, and with the σ^0-values (see below) which are also presumed free from direct conjugative enhancements. The differences for +M-substituents are quite marked.

In essence Bekkum, Verkade and Wepster's procedure for the analysis of substituent effects is: (1) Fit the experimental data to the primary sigma values as

$$\log k = \log k_0 + \sigma\rho$$

excluding substituents 9 and 10 where direct resonance interactions with −M-substituents appear possible. This determines the ρ-value and $(\log k_0)_{\text{calcd.}}$ (2) Compute σ-values from the remaining data by Jaffé's method (134i). (3) Compare calculated σ-values with tabulated σ^n-values and check for enhancements by means of equation 21. Negative values of $\Delta\Delta F_p$ signify that the product (or transition state) is favored over the initial state.

Assuming no resonance interaction between the NO_2 and NH_3^+– groups the $\Delta\Delta F_p$ value of −1.7 kcal./mole derived from the dissociation of *p*-nitroanilinium cation in water must measure the direct interaction of the NO_2 and NH_2 groups in *p*-nitroaniline. Other resonance interaction energies may be computed similarly.

Maki and Geske (176) have examined the effect of substituents on the polarographic reduction of nitrobenzenes. Analysis in terms of σ^n or σ^0 are both satisfactory for the *m*-substituted nitrobenzenes while for the *p*-compounds changes in conjugation are demonstrated. In the case of the amino-group, σ^n leads to a $\Delta\Delta F_p$ value of 2.9 kcal./mole (*cf.* above) which is certainly too large, while σ^0 gives a more reasonable value of 1.45 kcal./mole. This seemingly verifies the overcompensation of the σ^n-values for powerful +M-substituents.

It also has been suggested (185) that the sigma-values for the *m*-nitro, *p*-nitro and *p*-acetyl groups derived from reactions of benzoic acids are not normal since these powerful −M-groups will prevent the full operation of resonance between the carboxyl group and the ring (saturation effect). Recalculation using only insulated reaction series leads to σ_G-values which for *m*-nitro and *p*-nitro groups are lower than the σ^n-values. Although the procedure is essentially that employed by Taft and Lewis (248) to compute σ^0-values, the two scales show disturbing differences. The σ_G-values computed from electrophilic substitutions (see sub-section 5) are also different (152). While the σ_G and σ^n-values for the *p*-methoxy group compare favorably, the σ_G-value for *p*-nitro is *ca.* 10% lower than the σ^n-value and, most surprising, a 20% lowering is required for the *m*-nitro group.

Taft and Lewis (247, 248, 249) have approached the use of *m*- and *p*-substituent parameters as measures of polar effects by means of a separation into inductive (I) and resonance contributions (R). If these effects are quantitatively separable then

$$\log (k/k_0)_m = I_m + R_m \tag{22}$$

$$\log (k/k_0)_p = I_p + R_p \tag{23}$$

and setting

$$I_m = I_p = I$$

$$R_m = \alpha R_p = \alpha R$$

gives

$$I = \left(\frac{1}{1-\alpha}\right) \{\log (k/k_0)_m - \alpha \log (k/k_0)_p\} \tag{24}$$

as a means of computing inductive effects of all substituents for which both *meta* and *para*-reactivity data are available. Equation 24 is as precise and less dependent upon the reaction type than is the Hammett equation.

These inductive effects then were fitted to a "linear inductive energy relationship"

$$I = \sigma_I\rho_I \tag{25}$$

where σ_I is an inductive parameter obtainable from studies of aliphatic and alicyclic reactivities (see Taft equation, section III-B). While it has been found possible to set up a fixed scale of inductive effects covering all reaction types, analysis of the resonance contributions by

$$R = \sigma_R \rho_I \tag{26}$$

gave widely scattered values of σ_R in accord with the findings of Bekkum, Verkade and Wepster. For *m*-substituents generally and for *p*-substituents in "insulated" reaction series, where the reaction center is separated from the ring by one or more methylene groups, an unenhanced $\sigma_R{}^0$-value is obtainable from which are derived

$$\sigma^0 = \sigma_I + \mathrm{n}_R{}^0 \tag{27}$$

These σ^0-values should be the same within their uncertainties as the σ^n-values except, as already discussed, where resonance interactions in the latter have been overcompensated. Taft has drawn attention, however, to variations of σ^0 with solvent presumably responsible for some of the spread in the σ^n-values. Highly polarizing side chains may also modify the σ^0-values.

The analysis of experimental data utilizing the σ^0-values follows precisely the procedure recommended by Bekkum, Verkade and Wepster except that enhancements are assessed in terms of $(\sigma_R - \sigma_R{}^0)$; *para*, and presumably *meta*, resonance energies can also be computed utilizing the σ^0-values.

This treatment contains a number of assumptions that merit careful examination, especially in view of the potential theoretical value of substituent parameters (σ_I and $\sigma_R{}^0$).

(1) *The effect of structural changes on reactivity can be expressed as the sum of independent inductive, resonance and steric contributions:* This analysis is the basis of all attempts, both qualitative and quantitative, to understand reactivity-determining factors (*cf.* 31a). Its usefulness as a close approximation may be inferred from the successes already achieved.

(2) *Steric effects absent for m- and p-substituted phenyl relative to the phenyl group:* A most reasonable assumption in view of the geometry of these systems.

(3) *A set of σ_I-values can be derived from studies of aliphatic and alicyclic systems that is applicable to aromatic systems:* This requires, amongst other things, that the balance of direct electrostatic interactions and interactions induced through the bond system remain essentially constant in all systems. The requirements of this assumption have been examined (259) and do not appear likely. Furthermore, quantitative comparisons of aromatic and aliphatic substituent parameters are, as yet, uncertainly based (*cf.* 260).

(4) *Inductive effects in m- and p-positions are essentially equal that is*

$$\left.\begin{aligned} I_m &= \sigma_I \rho_I{}^m \\ I_p &= \sigma_I \rho_I{}^p \end{aligned}\right\} = I = \sigma_I \rho_I \tag{28}$$

Empirically it is found that setting $I_m/I_p = \gamma$ (a further adjustable parameter) does not significantly improve the correlations, but a difference exceeding ±20% produces a significant decrease in the precision of equation 24. For most reaction series and most substituents (which are dipolar) this may arise from the approximate balancing of the lower I_p due to increased path for induction and lower I_m due to the angle of the dipole vector (259). Such balancing would be expected to fail for substituents carrying unit charge and probably also for nuclear substitutions. That failure is in fact observed in just these cases is not surprising. With these exceptions, and the selection of a precision level of 0.03 sigma unit, failure of this assumption may be unimportant.

(5) $R_m/R_p = \alpha$, a unique proportionality constant measuring the extent of relayed mesomeric interactions from the *m*-position: The assumption of $\alpha = {}^1/_3$ for normal reaction series and $\alpha = {}^1/_{10}$ when the *p*-substituent is employing direct conjugation was abandoned, despite the good correlations achieved, in favor of a variable parameter for each reaction series. This follows the findings of Roberts and Jaffé (211) that the improvement in correlation achieved by permitting α to be an adjustable parameter is highly significant and is presumably to be attributed to general and variable *p*-resonance interactions throughout all reaction series.

For insulated reaction series (upon which $\sigma_R{}^0$ is based) there are no *para* enhancements and α should have its maximum value since the *meta–para* difference must be at a minimum. (The value 0.6 has been estimated (243)). However Taft and Lewis (248) compute $\alpha = 0.50$ and 0.60 for the dissociation of $ArCH_2CO_2H$ and $ArCH_2CH_2CO_2H$, respectively, which are no larger than the values required to correlate the dissociation of $ArCO_2H$ in ethanol, propanol and butanol solutions (0.61, 0.62, 0.62) and a number of other reactions where direct conjugation might be expected. The variation in α (0.45 to 0.60) required for reactions correlated by the σ^0-values is greater than might have been expected.

(6) *The same ρ-value is applicable to both meta and para series.* This assumption is examined in detail later (sub-section 3). It is noteworthy that ρ_I-values approximately the same as the Hammett ρ-values are obtained inevitably since aliphatic σ^*-values, and hence σ_I, already have been adjusted to the Hammett σ-value scale.

It would appear then that although the separated σ_I and $\sigma_R{}^0$-values reproduce qualitatively substituent polar effects as required by theory, their utility as quantitative parameters is not without question. The σ^0-values, on the other hand, like the σ^n-values, represent a considerable improvement on the original sigma-values for correlative purposes and investigations of

TABLE VII

σ_I VALUES (243A)

Estimated standard error ± 0.03

1. NMe_3^+	$+0.90^a$	19. OH	$+0.30^c$
2. SO_2F	+ .84	20. CH_3CO	$+ .28^b$
3. NO_2	+ .63	21. $NHCOCH_3$	$+ .27^b$
4. CH_3SO_2	+ .62	22. OCH_3	+ .26, $+0.30^b$
5. NH_3^+	$+ .60^a$	23. SH	$+ .23^c$
6. CH_3SO	$+ .56^a$	24. SCH_3	+ .19
7. CN	+ .56	25. CH_2Cl	+ .17
8. SF_5	+ .56	26. NH_2	$+ .13^c$
9. F	+ .52	27. NMe_2	$+ .10^b$
10. Cl	+ .47	28. C_6H_5	+ .10
11. Br	+ .45	29. $CH{=}CH_2$	+ .05
12. CF_3	+ .42	30. H	.00
13. I	+ .40	31. CO_2^-	$.00^a$
14. $OCOCH_3$	$+ .39^b$	32. CH_3	− .05
15. NO	+ .39	33. C_2H_5	− .05
16. OC_6H_5	+ .38	34. Me_3C	− .07
17. CHO	$+ .31^b$	35. Me_3Si	− .11
18. CO_2Et	$+ .30^b$	36. O^-	$- .12^a$

[a] Value for aqueous solution; applicability probably limited (precision uncertain). [b] Value for aqueous solutions. [c] Value for aprotic solvents.

deviations. The most recent compilation of σ_I-values is given in Table VII (243A).

The σ^0 and σ^n-values of Tables III, IV and V are in agreement with theoretical assessments of substituent effects. An examination of the standard deviations, however, reveals that these parameters provide no answer to the question of relative effects of alkyl groups. The effect of alkyl groups on reactivity could be accommodated over-all by one *meta* and one *para* σ-value. This situation presumably arises from the use of an approximately equal number of reaction series showing the "inductive" order and the "hyperconjugative" order of substituent effects. The difference between chloro and bromo substituents is similarly within the uncertainty of the σ-values.

For the finely detailed analysis of substituent effects recourse must be taken to selected reaction series, for otherwise minor differences will be smoothed out. Comparisons may still be made in terms of calculated sigma values since this permits an assessment of the relative magnitudes of deviations. Thus in connection with the much discussed influence of alkyl groups in reactivity (*cf.* 25) a variation of sigma for the *p*-methyl group with solvent is reported (151), its absolute value falling with decreased water content and polarity. Variations with increased branching of *p*-alkyl groups are explained variously by steric inhibition of ring solvation (215), steric inhibition of bond shortening (55) and by hydrogen bonding effects on hyperconjugation (217).

Considerable interest has been shown in the sigma-values correlating charged substituents. Hine's attempt (122, 123) (see sub-section 3) to assess rho-values in terms of sigma-values requires parameters for charged substituents because these are almost the only reaction centers for which realistic equilibrium data are available. It seems that the basic requirements for the appearance of a linear free energy relationship may not be met in this case of extreme substituent effect. Excessive polarization of the system is possible, although this feature will apply in all equilibria involving charged reaction centers close to the ring. Despite these misgivings, many reaction series of this type are well correlated, although the parameters show appreciable solvent sensitivity.

Numerous attempts have been made to account for substituent effects by electrostatic and electronic theories. These fall into two broad groups, one in which the substituent character is derived from some other empirical quantity, particularly dipole moments, and the other utilizing quantum mechanical calculations. Both suffer from the present lack of precise knowledge of transition state detail and certain essential parameters and integrals. Equilibria thus offer the best testing ground for theories since the structures of initial and final states can in principle be determined exactly. Direct electrostatic interactions due to substituent charge or dipole require fewer assumptions in their calculation although intramolecular dielectric constants are uncertain. It has been possible however to assess approximately the contribution of this effect to the relative free energy change and thence examine contributions by other effects (259).

Jaffé (133) has pointed out that the sigma-values provide the most exact source of information available for the computation of the quantities, *e.g.*, coulomb and resonance integrals, that appear in the molecular orbital method. Consistent results have been obtained in the semi-empirical calculation of reactivity by these methods, although much further work needs to be done (*cf.* for example 198).

Following the treatment of inductive effects on acid dissociation developed by Branch and Calvin (31b), McGowan (173, 174, 175) has suggested the simple equation 29 for the free energy of ionization of a substituted acid

$$\Delta F = -RT \ln K = -RT \ln K_H + BQ \qquad (29)$$

where K_H is the dissociation constant of the unsubstituted acid, Q is a number signifying the "effective charge" due to the substituent and B (in kcal./mole) is equated to $14/2^n$, where n depends upon the structure of the acid. In the absence of steric and resonance effects n is simply the number of atoms between the position of substitution and the dissociating proton.

In these terms the Hammett equation becomes

$$\log (K/K_0) = \sigma_X\rho = -B(Q_0 - Q_x)/2.3RT \qquad (30)$$

where Q_0 and Q_x are the effective charges of the $C_6H_5^-$ and $XC_6H_4^-$ groups, respectively.

McGowan (174) further observes that

$$Q_x = Q_0 + 0.25\sigma_x$$

Hence

$$\rho = 54.7B/T = 2.5/2^n \text{ at } 25° \quad (31)$$

The treatment thus predicts that the rho-value for a particular reaction will be found in one or other of a few distinct groups. In Table VIII the validity of equation 31 is examined for acid dissociations in water at 25°. Equation 32

TABLE VIII

PREDICTED RHO VALUES

Dissociating acid	Calcd. (eq. 31)	Calcd. (eq. 32)	Observed[a]
$XC_5H_4NH^+$	5.0	5.8	6.11[b]
XC_6H_5OH	2.5	2.6	2.26
$XC_6H_5NH_3^+$	2.5	2.6	2.94
$XC_6H_4CO_2H$	1.25	1.16	1.00
$XC_6H_4CH_2CO_2H$	0.325	0.52	0.56
$XC_6H_4CH_2CH_2CO_2H$	0.16	0.23	0.24

[a] See Table 8, sub-section 3. [b] See sub-section 7.

$$\rho = 0.184B/\alpha^n \quad (32)$$

where $B = 14.1$ and $\alpha = 0.223$ derived from a least squares analysis of the variation of $\log \rho_{\text{obsd}}$ with n, is also examined. It is essentially only in the value of α that equations 31 and 32 differ.

Evidently these simple equations are able to reproduce experimental data with remarkable precision. Taft (243) has made the similar observation that

$$\rho = (2.8 \pm 0.5)^{1-i}$$

where i is the number of "saturated" bonds between the benzene ring and the atom upon which there is a unit charge change on ionization, and the rho-values apply to dissociations in water of selected *m*-substituted acids.

Important recent work on the correlation of substituent effects with various physical quantities is discussed separately in sub-section 10. The use of extra-kinetic data in the analysis of reaction rate-determining factors is most important theoretically. The greater potential control, precision and understanding of fundamental molecular quantities cannot but assist the examination of reaction processes. One notable example is the suggested use of substituent effects on shielding parameters obtained from the n.m.r. spectra of the fluorobenzenes to measure inductive and resonance polar effects (243).

3. *The Reaction Parameters*

The meaning attached to the magnitude and sign of the Hammett rho-value depends upon the interpretation given to the sigma-values. The relationship simply yields the reaction parameter as a proportionality factor depending upon the response of a particular reaction series to substituent changes relative to that of the standard reaction.

Reaction parameters computed by the method of Bekkum, Verkade and Wepster (BVW) (10) are listed in Table IX. The numbering system used by Jaffé (134b) is employed here, with new reaction series accommodated by numbers greater than 1000. References to the original experimental data are only given for reactions not examined by Jaffé. Included also for references is the numbering system of Taft and Lewis (248) which serves to classify the reaction types. Statistical quantities are presented for the BVW rho-values only. The comparison (10) between these and Jaffé's tabulation has been briefly discussed in sub-section 1. The rho-values of Jaffé and of McDaniel and Brown (172) are also presented for comparison as are the corresponding ρ_I-values (248).

Table IX includes most of the reaction series examined both by Bekkum, Verkade and Wepster and by Taft and Lewis. In addition there are several reaction series (marked *) covering temperature and solvent variations.

Identification of the sigma-values with measures of substituent polar effects permits the identification of the rho-value as the relative susceptibility of a particular reaction series to electrostatic and electronic effects. As such, the following generalizations are evident from the definition of the sigma-values: (a) Reactions facilitated by electron withdrawal, *i.e.*, by acid-strengthening substituents, will have positive rho-values. (b) Reactions more susceptible, irrespective of direction, to electrical effects than the dissociation of the benzoic acids in water will have rho-values of absolute magnitude greater than unity. It will appear below that there are limitations even to these generalizations.

From the standpoint of the generalized relationship of section II the reaction parameter for some reaction series A is given by

$$\rho_A = G_x{}^A = \frac{T_0}{T_A} \times \frac{(\partial \Delta F^A/\partial x)_T}{(\partial \Delta F^0/\partial x)_T} \quad (33)$$

or replacing the variable x by its experimental measure σ

$$\rho_A = \frac{T_0}{T_A} \times \frac{(\partial \Delta F^A/\partial \sigma)_T}{(\partial \Delta F^0/\partial \sigma)_T} = \frac{G_0}{T_A} \times \left(\frac{\partial \Delta F^A}{\partial \sigma}\right)_T \quad (34)$$

where the various terms have the significance discussed in section II and G_0 is a constant dependent only upon the chosen standard reaction.

One immediate expectation based on equation 34 is that the rho-value should decrease with increase in temperature and more specifically, if $(\partial \Delta F^A/\partial \sigma)$ is temperature invariant

$$\rho_{A1}/\rho_{A2} = T_2/T_1 \quad (35)$$

TABLE IX

HAMMETT REACTION PARAMETERS

Reaction no.	Classification[a]	Reaction series	Solvent	T°, C.	ρ	r[b]	s[c]	n[d]	(log k_0)[e]	ρ (J) (134)	ρ_I (248)	Notes
		Acid dissociations										
1a	A1			25	1.000							
1b	A1			15	0.999	0.995	0.025	6	−0.019[f]	0.954	..	*
1c	A1			20	1.010	.992	.030	6	− .016[f]	.958	1.00	*
1d	A1			25	1.011	.994	.030	6	− .013[f]	.958	1.00	*[g](0.766)[h]
1e	A1		H_2O	30	1.019	.996	.028	6	− .005[f]	.961	..	*
1f	A1			35	1.016	.996	.037	6	− .008[f]	.961	..	*
1g	A1			40	1.029	.994	.031	6	− .004[f]	.968	..	*
1h	A1			45	1.029	.994	.027	6	+ .001[f]	.969	..	*
1j	A9	$ArCO_2H$	CH_3OH	25	1.761	.984	.102	8	− .041[f]	1.537	1.55	*
1k	A9		40% EtOH	25	1.972	.964	.244	5	−5.311	1.668	..	*
1m	A2		50% EtOH	25	1.851	.993	.099	5	−5.652	1.601	1.50	*(1.431)[h]
1n	A2		70% EtOH	25	1.989	.993	.110	5	−6.293	1.738	..	*
1o	A2		80% EtOH	25	2.045	.993	.112	5	−6.651	1.791	..	*
1p	A2		90% EtOH	25	2.144	.991	.128	5	−6.999	1.869	..	*
1q	A2		95% EtOH	25	2.243	.993	.124	4	−7.029	1.890	..	*
1r	A10		EtOH	25	2.278	.993	.123	5	−7.362	1.957	1.67	*
1u	A11		n-C_3H_7OH	25	1.546	.997	.038	10	+0.012[f]	...	1.65	*
1s	A12		n-C_4H_9OH	25	1.502	.996	.044	8	−0.001[f]	1.476	1.56	*
1v	A5		26.5 w. % dioxane	25	1.480	.998	.025	7	−4.942	...	1.23	(79, 80 147, 149)
1w	A6		43.5 w. % dioxane	25	1.667	.997	.032	7	−5.624	...	1.33	
1x	A7		73.5 w. % dioxane	25	1.568	.999	.026	6	−7.087	...	1.42	
3a	A3		1% EtOH	20	1.248	.978	.084	6	−3.920	1.430	..	
3b	A3	$2CH_3ArCO_2H$	50% EtOH	25	1.773	.989	.122	5	−5.819	1.673	1.64	
6b	A4	2,6-$(CH_3)_2ArCO_2H$	50% EtOH	25	1.400	.998	.031	4	−5.185	...	..	*(209)
8	B1	$ArCH_2CO_2H$	H_2O	25	0.562	.982	.039	5	−4.335	0.489	0.46	
9	B2	$ArCH_2CH_2CO_2H$	H_2O	25	.237	.997	.003	4	−4.663	0.212	0.24	
10	A18	$ArCH{=}CHCO_2H$	H_2O	25	.418	.995	.019	4	−4.430	0.466	0.47	
1001b	A21	$ArC{\equiv}CCOOH$	50% EtOH	24	.625	1.000	.007	4	3.396	...	0.65	(22)
13	B7	$ArB(OH)_2$	25% EtOH	25	2.177	1.000	.015	7	−9.697	2.146	2.15	(2.152)[h]
14a	B5	$ArPO_3H_2$	H_2O	25	0.754	1.000	.008	5	−1.831	0.755	0.73	
15a	B6	$ArPO_3H^-$	H_2O	25	1.105	0.998	.028	5	−7.080	0.949	1.19	
23a	C1		H_2O	25	2.262	0.997	.054	7	−9.947	2.113	2.36	(2.446)[h] (2.281)[h]
23b	C1	ArOH	30% EtOH	25	2.522	1.000		4	−10.818	3.197	..	
23c	C2		49% EtOH	21	2.687	0.984	0.116	6	−11.258	2.545	2.70	
23d	C3		95% EtOH	21	3.141	.980	.157	6	−12.766	2.364	2.90	
25a	C4	ArSH	49% EtOH	21	2.453	.994	.062	6	−7.798	2.236	2.70	
25b	C5	ArSH	95% EtOH	21	3.024	.986	.120	6	−9.334	2.847	2.91	
26a	C9		H_2O	25	2.941	.999	.046	7	−4.658	2.767	2.90	(2.934)[h] (2.921)[h]
26b	C9	$ArNH_3^+$	30% EtOH	25	3.186	.995	.062	5	−4.107	3.435	..	
26aA	C11		CH_3OH	25	4.027	.999	.058	5	−0.054[f]	3.016	4.00	
26bA	C12		EtOH	25	4.496	.999	.084	5	−0.002[f]	3.535	4.75	
27c	(C13)	$ArN(CH_3)_2H^+$	H_2O	20	3.557	1.000	.018	3	−5.172	...	3.34	
27d	C13		20% dioxane	20	3.942	1.000	.042	3	−4.833	...		
27e	C13		45% dioxane	20	4.196	0.998	.118	3	−4.134	...		(263)
		Other reactions										
32	C14	$ArNH_2 + HCOOH \rightarrow ArNHCHO + H_2O$	67% C_5H_5N	100	−1.301	.997	.040	5	+0.582	−1.429	−1.47	
40a	C14		CH_3OH	25	−0.577	.988	.025	7	−3.695	−0.229		
40b	C14	$ArCOOH + CH_3OH + \rightarrow ArCOOCH_3$		40	− .585	.991	.022	7	−3.201	− .216		*
40c	C14			50	− .622	.985	.031	7	−2.858	− .209		*
40d	C14			60	− .615	.987	.028	7	−2.575	− .213		*
43	A14	$ArCOOH + (C_6H_5)_2CN_2$	EtOH	30	.979	1.000	.025	3	−1.763	.940	1.00	(0.962)[h]
45	A14		EtOH	30	.887	1.000	.010	5	−1.795	.946		
46a	A14	$ArCOOCH_3 + OH \rightarrow ArCOO^-$[g]	60% $(CH_3)_2CO$	0	2.535	0.992	.117	5	−3.113	2.460		*
46b	A14			15	2.452	.990	.123	5	−2.520	2.299		
46c	A14			25	2.382	.991	.118	5	−2.144	2.229		
46d	A14			40	2.274	.992	.108	5	−1.626	2.128		*
47d	A14	$ArCOOC_2H_5 + OH^- \rightarrow ArCOO^-$	85% EtOH	25	2.547	.999	.054	4	−3.211	2.537		
47e	A14			35	2.458	.999	.054	4	−2.781	2.464		
47f	A14			50	2.130	1.000	.000	4	−2.197	2.322		*
47g	A16		88% EtOH	30	2.545	0.998	.053	8	−3.110	2.431	2.50	(2.188)[h]
47h	A16		60% $(CH_3)_2CO$	0	2.656	.996	.081	7	−3.613	2.443		*
47i	A16			15	2.527	.996	.083	7	−2.982	2.353		*
47j	A15			25	2.468	.996	.080	7	−2.622	2.265	2.33	
47k	A15			40	2.378	.995	.081	7	−2.105	2.181		*
55	A19	$ArCH{=}CHCOOC_2H_5 + OH^-$	EtOH	30	1.233	.994	.041	5	−2.712	1.329	1.29	(1.282)[h]
65a	D15	$ArCOCl + C_2H_5OH$	EtOH	0	1.735	.996	.052	7	−4.107	1.542	1.90	
70b	D15	$ArCONH_2 + OH^- \rightarrow ArCOO^-$	60% EtOH	52.8	1.399	.998	.041	4	−5.115	1.364		*

TABLE IX (*Continued*)

Reaction no.	Classification[a]	Reaction series	Solvent	$T°$, C.	ρ	r^b	s^c	n^d	$(\log k_0)^e$	ρ (J) (134)	ρ_I (248)	Notes
70c	D15			64.5	1.305	.996	.054	4	−4.679	1.273		*
70d	D15			80.3	1.169	.999	.031	4	−4.154	1.146		*
70e	D15			100.1	1.153	.994	.062	4	−3.541	1.100		*
71b	D15	$ArCONH_2 + H^+ \rightarrow ArCOOH$	60% EtOH	52.4	−0.502	.996	.022	4	−5.597	−0.483		*
71c	D15			65	− .310	.983	.029	4	−5.069	− .310		*
71d	D15			79.5	− .310	.852	.094	4	−4.411	− .298		*
71e	D15			99.6	− .230	.889	.058	4	−3.704	− .222		*
77	C7	$ArO^- + \overset{\ulcorner O \urcorner}{CH_2CH_2}$	98% EtOH	70	−1.115	.991	.068	4	−4.217	− .947	−1.00	
80	C6	$ArOH + CH_3OSO_3^-$	H_2O	100	−0.650	.998	.014	5	−4.132	− .813	−0.66	
90a	C6	$ArCH_2OCOCH_3 + OH^- \rightarrow ArCH_2OH$	EtCO	0	.858	.996	.043	4	−2.025	.818		*
90b	C6			15	.790	.996	.041	4	−1.496	.762		*
90c	B14			25	.745	.996	.038	4	−1.183	.743		*
90d	B14			40	.731	.997	.032	4	−0.748	.725		*
94d	D5	$ArCH_2Cl + H_2O$	50% $(CH_3)_2CO$	60	−1.309	.964	.126	7	−5.211	−1.688	−1.43	
100	D6	$ArCH(C_6H_5)Cl$ Solv.	EtOH	25	−4.029	.996	.135	5	−4.249	−5.090	−4.00	
112a	C16	$ArNH_2 + C_6H_5COCl$	C_6H_6	25	−3.207	.999	.048	5	−1.119	−2.781	−3.20	
114d	C17	$ArNH_2$ + DNCB	EtOH	100	−2.785	1.000	.037	4	−2.323	−2.415	−2.87	
200	D11	$ArH + NO_2^+ \rightarrow ArNO_2$	$(CH_3CO)_2O$	25	−7.292	0.988	.290	5	+0.003[f]	−5.926	−6.70	
201	D9	$ArB(OH)_2 + Br_2 \rightarrow ArBr$	20% CH_3COOH	25	−3.819	.995	.176	4	−2.209	−4.504	−3.62	
1002	D2	$(ArN{=}NAr^1)H^+$	20% EtOH	25	2.549	.998	.110	8	+2.839	...	2.41	(139, 274)
1006	D1	$Ar_3C^+ + H_2O \rightleftarrows Ar_3COH + H^+$	H_2O–H_2SO_4	25	3.968	.997	.316	6	+6.757	...		(66, 67)
1009a	C8	$ArOSi(C_2H_5)_3 + OH^-$	51% EtOH	25	1.987	.999	.013	3	+0.145	...	1.85	(1)
1010	D3	$ArC(CH_3)_2Cl + H_2O$	90% $(CH_3)_2CO$	25	−4.479	.998	.091	8	−3.953	...	−4.34	(38, 40, 189)
1012	D14	ArN_2^+ + 2,6-H_2N–$C_{10}H_6SO_3H$	H_2O	20	4.091	.998	.129	5	+0.310	...	4.15	(280)

[a] Reference: A, benzoic reactivities; B, miscellaneous reactivities; C, nucleophilic reactivities; D, electrophilic reactivities. [b] Correlation coefficient. [c] Standard deviation of experimental, measurements from the regression line. [d] Number of substituents employed. [e] Intercept of regression line at $\sigma = 0$. [f] Correlation using log (k/k_0). [g] Data from source other than that used to define sigma. [h] ρ_I-values calculated by Roberts and Jaffé (211). * Not listed in ref. 10.

should and has been used to account quantitatively for reaction series differing only in temperature (242b).

An examination of this feature is summarized in Table X. Essentially the same conclusions may be drawn as were reported by Jaffé (134f), but in addition the results may be compared with the application of the isokinetic relationship of Leffler (166).

TABLE X

VARIATION OF ρ WITH $1/T$

Reaction series	Relationship	Application of isokinetic relationship
1b-h	Scattered decrease	Electron withdrawing substituents only (H changes small)
40a-d	Scattered decrease	Isokinetic
41a-d	Linear increase	Isokinetic
46a-c	Linear increase	Isoentropic
46Aa-c		Isoentropic
47a-c		Isoentropic
47d-f	Precise linear increase	Isoentropic
47h-k	Precise linear increase	Isoentropic
49a-d		Isoentropic
70b-c	Linear increase	Isokinetic
71b-c	Linear increase	Isokinetic
82a-d	Precise linear increase	
84a-d	Linear decrease	Isoentropic
90a-d	Precise linear increase	Isoentropic
91a-d	Linear (?)	No significant variation
121c-e	Linear increase	
155a-d	Steep linear decrease	
188a-d	Rapid increase	Isokinetic

It is more usual among reaction series correlated by the Hammett equation that

$$\left(\frac{\partial \Delta F^A}{\partial \sigma}\right)_T = \left(\frac{\partial \Delta H^A}{\partial \sigma}\right)_T - T \times \left(\frac{\partial \Delta S^A}{\partial \sigma}\right)_T \tag{36}$$

is not temperature invariant, *i.e.*, the essential requirement for the simple equation 35 is not fulfilled.

Three broad types of behavior have been observed (*cf.* Table 10): (a) *Isoentropic series* $(\partial \Delta S/\partial \sigma)_T = 0$: The outstanding example of this type is the saponification of substituted benzoate esters (reaction series 46 and 47) for which equation 35 is applicable with high precision.

(b) *Isokinetic series*, ΔH and ΔS are linearly related

$$\Delta H^A = \Delta H_0{}^A + \beta_A \Delta S^A \tag{37}$$

where β_A is the slope of the isokinetic line and $\Delta H_0{}^A$ is the intercept independent of σ (generally of no physical significance).

$$\therefore \left(\frac{\partial \Delta F^A}{\partial \sigma}\right)_T = \left(1 - \frac{T}{\beta_A}\right) \left(\frac{\partial \Delta H^A}{\partial \sigma}\right)_T \tag{38}$$

The majority of reactions correlated by the Hammett equation that can be tested have been found to be of this type. Many reaction series not following the Hammett relationship show isokinetic behavior. Among these are several for which other linear free energy relationships are applicable (*cf.* the Taft equation, section III-B, and the Grunwald–Winstein equation, section IV).

(c) *Series with ΔH and ΔS apparently independent:* Two reaction series of this type have been recorded.

One of these is the standard reaction, where isokinetic behavior is only observed for the dissociation of the benzoic acids substituted with electron-withdrawing groups. Throughout the reaction series 1b-h ΔH changes are small in comparison with changes in ΔS. These are then essentially *isoenthalpic* reaction series for which

$$\rho_A = \frac{G_0}{T_A}\left(\frac{\partial \Delta F^A}{\partial \sigma}\right)_T = -G_0 \times \left(\frac{\partial \Delta S^A}{\partial \sigma}\right)_T \qquad (39)$$

As expected, the observed change in rho with temperature is barely significant.

Reaction series 91a-d has rho linear with $1/T$ but with virtually a zero slope (apparently isoenthalpic). Applicability of the isokinetic relationship could not be tested since variations in ΔH and ΔS are quite small and possibly random.

The reaction series for which variations of rho with temperature or isokinetic behavior can be examined represent a relatively small sample of the total encompassed by the Hammett equation. Many of those of unknown character are clearly not isoentropic so that equation 35 has very limited utility. Indeed, among those examined are several for which rho increases with temperature. Nevertheless, in view of the fact that markedly different responses by ΔH and ΔS to substituent changes will cause a failure of the Hammett equation, the isokinetic relationship must be widely applicable.

Taking equation 38 to be general (isoentropic series excluded), it is clear that rho may change in sign with change in temperature and become zero at $T = \beta_A$, without there being any change in $(\partial \Delta H//\partial \sigma)$. It follows that mechanistic discussions in terms of the sign of rho are dangerous, especially when its magnitude is small. Similarly, a small rho value need not characterize a reaction with little ionic character.

Further restrictions must be added to those of subsection 2 for the safe application of the Hammett equation. In order to use the rho-values obtained through the "primary" sigma value or the σ^0-value analysis, the reaction series should be examined at least at two temperatures remote from the isokinetic point ($T = \beta_A$).

Table IX contains several reaction series differing only in solvent. The most thoroughly examined has been the dissociation of the benzoic acids for which Kilpatrick (147) reports

$$\log (K/K_0) = \log (K/K_0)_{D=\infty} + L/D \qquad (40)$$

where D is the dielectric constant of the solvent, L is characteristic of the substituent, and $\log (K/K_0)_{D=\infty}$ is the "intrinsic" relative dissociation constant (273). Equation 40 is followed for water, ethylene glycol, methanol and ethanol but not for 1-propanol and 1-butanol nor for mixtures of dioxane and water. In terms of rho-values, equation 40 becomes

$$\rho_A = \rho_0 + (L'/D_A) \qquad (41)$$

where $L'(= L/\sigma)$ is independent of the substituent, and ρ_0 is the reaction parameter applicable to a solvent of infinite dielectric constant. The only other reaction series (26a, 26aA and 26b-A) that can be tested for pure solvents concern the acidity of the anilinium cations in water, methanol and ethanol. Equation 41 correlates these data quite satisfactorily (*cf.* 148).

Although correlations of rho-values with $1/D$ and $(D - 1)/(2D + 1)$ have been reported for mixed solvents (*cf.* 92), the range of permissible solvent variation is generally small and it is more typically observed that these functions do not adequately describe the ionic properties of solvent mixtures. The effect of reaction medium on reactivity is discussed in detail in section IV of this review.

A corollary of equation 41, examined in detail for the case of the relative dissociation of the benzoic acids in water by Hammett (108), is that rho-values will be temperature dependent by virtue of variations in dielectric constant. Equation 40 is in fact equivalent to an analysis of the relative free energy change into a component due to electrostatic interactions through space and a component independent of the medium (inductive and resonance effects). Both of these components will in general be operative as potential energy changes, yet the former will be temperature variant. Thus an entropy change will be observed whenever the direct field effect makes an appreciable contribution to the total substituent effect. The converse, that isoentropic series have negligible direct field effects, need not necessarily be true.

The extent of transmission of polar effects from the aromatic ring to the reaction center will be some function of the intervening side chain. It has been supposed that these factors might be independent of the nature of the reaction center and an attempt has been made to compute on this basis ratios of rho-values from molecular orbital theory (135). Comparisons of calculated and observed ratios are in moderate agreement (134e), but there are indications that the dependence of these ratios on the nature of the reaction (*e.g.*, acid dissociation or ester saponification) is considerable (221).

Since the reaction parameter depends largely upon the electrostatic and electronic properties of the initial and final (or transition) states of the reacting side chain, a dependence would be expected on the sigma values of these states when functioning as substituents. Hine (122) has developed an expression for this by considering the equilibria of equation 42.

If the unmodified Hammett equation is applicable to the equilibria $ArX_1 \rightleftarrows ArX_2$ with Y_1 and Y_2 as sub-

$$\begin{tikzcd}
X_1C_6H_4Y_1 \arrow[r, shift left, "K^{Y}_{X_1}"] \arrow[d, shift right, "K^{X}_{Y_1}"'] & X_1C_6H_4Y_2 \arrow[l, shift left] \arrow[d, shift left, "K^{X}_{Y_2}"] \\
X_2C_6H_4Y_1 \arrow[r, shift left] \arrow[u, shift right] & X_2C_6H_4Y_2 \arrow[l, shift left, "K^{Y}_{X_2}"] \arrow[u, shift left]
\end{tikzcd} \qquad (42)$$

stituents and $ArY_1 \rightleftarrows ArY_2$ with X_1 and X_2 as substituents, then

$$\begin{aligned} \log(K_{X_1}{}^{Y}/K_{X_2}{}^{Y}) &= (\sigma_{X_1} - \sigma_{X_2})\rho^{Y} \\ \log(K_{Y_1}{}^{X}/K_{Y_2}{}^{X}) &= (\sigma_{Y_1} - \sigma_{Y_2})\rho^{X} \end{aligned} \qquad (43)$$

But since

$$(K_{X_1}{}^{Y}/K_{X_2}{}^{Y}) = (K_{Y_1}{}^{X}/K_{Y_2}{}^{X})$$

then

$$\rho^{Y}/(\sigma_{Y_1} - \sigma_{Y_2}) = \rho^{X}/(\sigma_{X_1} - \sigma_{X_2}) = \tau \qquad (44)$$

where τ is a constant depending only upon the reaction conditions (temperature and solvent) of the equilibria, and the relative disposition of substituent and reaction center in XC_6H_4Y. If the common assumption is followed, namely, that the same rho-value applies to both *m*- and *p*-derivatives, then

$$\frac{\sigma_{m\text{-}Y_1} - \sigma_{m\text{-}Y_2}}{\sigma_{p\text{-}Y_1} - \sigma_{p\text{-}Y_2}} = \frac{\tau_m}{\tau_p} = \frac{\sigma_{m\text{-}CO_2H} - \sigma_{m\text{-}CO_2^-}}{\sigma_{p\text{-}CO_2H} - \sigma_{p\text{-}CO_2^-}} \qquad (45)$$

for all pairs of substituents which can be initial and final (or transition) states of reactions correlated by the unmodified Hammett equation. Hine points out that the sigma-values listed by McDaniel and Brown (172) do not conform to equation 45, and suggests the assumption of equal ρ_m and ρ_p-values is responsible. However the basic assumptions and physical significance of this analysis require further examination. Clearly only equilibria can be discussed in the present context since sigma-values for groups acting as transition states have no meaning in the Hammett equation. Secondly, consultation of a list of groups for which sigma-values have been determined reveals that the majority of pairs correspond to unrealistic equilibria that if possible would involve nuclear substitutions. The unmodified Hammett equation is not applicable in these cases. Of reaction series that are suitable for this treatment only three pairs, CO_2H/CO_2^-, OH/O^- and NH_3^+/NH_2, have sigma-values reported. Even if charged substituents are permissible in the Hammett equation there are still only two (*m*-CO_2H and *p*-CO_2H) of the twelve required sigma-values known with certainty.

In terms of individual substituents and reacting side chains Hine's suggestions are untestable. A statistical examination has, however, been carried out (138). It is found that out of 336 reaction series the number for which rho-values correlating *m*- and *p*-derivatives are different is significantly greater than would be expected purely by chance. In some 85% of the series the differences are not significant, and it is suggested that only a few series show serious differences. Included in the examination were many *p*-substituents having enhanced sigma-values that may in part be responsible for the observed result.

Concerning the test of equation 45 with existing sigma-values, if analyzed into inductive and resonance contributions (*cf.* 248), then

$$\begin{aligned} \frac{\tau_m}{\tau_p} &= \frac{(\sigma_I{}^{p} + \sigma_R)_{Y_1} - (\sigma_I{}^{p} + \sigma_R)_{Y_2}}{(\sigma_I{}^{m} + \alpha\sigma_R)_{Y_1} - (\sigma_I{}^{m} + \alpha\sigma_R)_{Y_2}} \\ &= \frac{\Delta\sigma_I{}^{p} + \Delta\sigma_R}{\Delta\sigma_I{}^{m} + \alpha\Delta\sigma_R} \simeq \frac{\Delta\sigma_I{}^{p}}{\Delta\sigma_I{}^{m}} \simeq 1 \end{aligned} \qquad (46a)$$

where $\Delta\sigma_I = (\sigma_I)_{Y_1} - (\sigma_I)_{Y_2}$, the difference in inductive effects of the side chain in initial and final (or transition) states, and $\Delta\sigma_R = (\sigma_R)_{Y_1} - (\sigma_R)_{Y_2}$, the resonance effect difference which must be small (hence $\Delta\sigma_R/\Delta\sigma_I \simeq 0$) for the unmodified Hammett equation to be valid.

This approach and subsequent developments (123) of it are potentially useful to an understanding of reaction parameters through the separation of intrinsic electrical character of the reacting side chain from factors due to reaction conditions. Precise data on equilibria between uncharged products and reactants and corresponding substituent parameters are essential to its fulfillment.

A somewhat similar treatment of reaction parameters in terms of the polar character of the reacting side chain in initial and final (or transition) states has been presented recently by Sager and Ritchie (214). A more fundamental approach is adopted in which polar character is expressed in terms of intrinsic electronegativities and an attempt is made to allow in the reaction parameters for inductive and electrostatic modes of interaction. At present the treatment is essentially empirical and has been applied particularly to the Taft equation. Further developments may indicate the utility of this approach that can in principle be applied to all linear free energy relationships.

4. The Correlation of Free Radical Reactions

The theoretical implications of the Hammett relationship in terms of substituent polar effects require that free radical reactions will not be correlated. Variations of rate with substitution are expected whenever the radical formed can be stabilized by delocalization. Hence essentially no variation of rate with *m*-substituents and some enhancement of rate with both −M- and +M-*p*-substituents should be the result.

Experimentally, non-random variations of log *k* with sigma are observed, but generally with small and hence uncertain rho-values. However, careful investigation reveals (236) that the above statements are over-simplifications and that there are major electronic changes in the transition states of radical reactions leading to a dependence upon polar effects. Certain radical reactions involve considerable resonance stabilization effects, *e.g.*, *m*-substituents can provide enhanced contributions in the polarographic oxidation of anilines to radical ions (245A).

Side chain chlorination of substituted toluenes shows a marked dependence on substituent having $\rho = -1.5$ (119). This has led to the suggestion that the electronegativity of the attacking radical is the important factor. However Russell (212) has found smaller rho-values for the oxidation of substituted cumenes *via* peroxy radicals (also highly electronegative), and the data of Johnston and Williams (143) on aromatic substitution by *t*-butoxy radicals indicate that other factors are involved. Indeed the value $\rho = -0.76$ for the photo-chlorination of substituted toluenes draws attention to the complexities in this type of reaction series (255). In keeping with the dependence of radical stability on delocalization some radical reactions are found to be better correlated by means of enhanced sigma-values, *e. g.*, σ^+ (128, 213). This is not, however, general since aromatic substitutions by *t*-butoxy radicals follow the normal sigma-values well but the σ^+-values poorly (254).

Small rho-values need not indicate a reaction without ionic character. As outlined in sub-section 1, different steps in the over-all reaction process may have almost equal but opposite ρ-values. Multi-center reactions, even those involving heterolytic bond making and breaking steps, often show many characteristics of free radical reactions. One example is the Diels–Alder reaction for which $\rho = -0.6$ correlates the effect of substituents in the diene (271) and $\rho = +0.27$ substituents in the dienophile (8).

The *ortho*-Claisen rearrangement of *p*-substituted allyl phenyl ethers is an interesting example of a multi-center reaction in which the substituent operates on both the breaking and the forming bond. Various correlations in terms of both processes have been achieved in support of the currently accepted mechanism, but it has been pointed out that the success of the resultant four-parameter equations may be illusory (96, 262).

The Curtius rearrangement of benzazides in toluene solution follows the Hammett equation for *m*-substituents, but *p*-substituents have very little effect (275, 276). Similarly, all *p*-substituents tend to retard slightly the piperidine-catalyzed condensation of substituted benzaldehydes with diethyl malonate in kerosene solution (187). These reactions normally show a marked polar effect, but in low dielectric solvents undoubtedly new mechanisms are operating. Hammett rho-values *alone*, however, do not serve to place these in the free radical category.

5. The Correlation of Electrophilic Aromatic Substitutions

It has been stressed on several occasions that the Hammett equation correlates substituent effects on *side chain* reactivity. Pearson, Baxter and Martin (196) appear to have been the first to examine in detail its application to nuclear substitutions and similar reactions. They, and subsequently several groups of workers, observed that the original set of sigma values were inadequate for *p*-substituents of the +M-type although generally satisfactory for the *m*-compounds (177, 210). This type of failure has since become fairly common and is considered to be due to the existence of considerable direct resonance between the substituent and the reaction center, in this case a nuclear carbon atom.

Brown and Nelson (37) examined a series of substitution reactions of toluene and observed a proportionality

$$\log p_f = c \log (p_f/m_f) = cS_f \tag{46b}$$

between the "activity" of the reagent as measured by the logarithm of partial rate factor for *p*-substitution ($p_f = k_p/k_0$) and its "selectivity" (S_f) as measured by the logarithm of the ratio of partial rate factors for *p*- and *m*-substitution. It was realized that such a proportionality would be a consequence of the application of a modified Hammett relationship

$$\log (k_p/k_0) = \log p_f = \sigma_p{}^+\rho^+, \text{ etc.} \tag{47}$$

hence,

$$c = \sigma_p{}^+/(\sigma_p{}^+ - \sigma_m{}^+) \tag{48}$$

where the σ^+-values are a new scale applicable to reactions particularly facilitated by electron-releasing groups, and ρ^+ are the corresponding reaction parameters.

The determination of the factor *c* in the "Selectivity" relationship and the setting of $\sigma_{m\text{-Me}}{}^+ = \sigma_{m\text{-Me}}$ permitted the calculation of $\sigma_{p\text{-Me}}{}^+$, hence of ρ^+ for a number of reactions, *e.g.*, nitration $\rho^+ = -5.92$, and further σ^+-values for other groups. However, this procedure was considered to have such a high susceptibility to error that a standard reaction was sought. Solvolysis of the substituted phenyldimethylcarbinyl chlorides was selected (38) since the transition state for this reaction, having considerable carbonium ion character, should resemble closely the transition states for electrophilic reactions at aromatic carbon atoms and other atoms conjugating strongly with the aromatic system. For *m*-substituents this reaction is correlated well by the Hammett sigma values.

Table XI lists some of the substituent parameters derived in this manner and compares them with the σ_n-values (38, 39).

Table XII lists some of the reaction parameters and statistical data for correlations employing the σ^+-values.

The solvolysis of other aryl substituted alkyl halides were examined in terms of the σ^+-values (189). Despite the fact that Table XII already contains reaction

TABLE XI

ELECTROPHILIC SUBSTITUENT PARAMETERS
(BROWN AND OKAMOTO)

Substituent	$\sigma_m{}^n$	$\sigma_m{}^+$	$\sigma_p{}^n$	$\sigma_p{}^+$
$N(CH_3)_2$	...	...	−0.127	(−1.7)[a]
OCH_3	0.076	0.047	− .111	−0.778
CH_3	− .069	− .066	− .129	− .311
F	.337	.352	.056	− 0.73
Cl	.373	.399	.238	.114
Br	.391	.405	.265	.150
I	.352	.359	.299	.135
$CO_2C_2H_5$	(.317)[b]	.366	(.463)[b]	.482
CF_3	.467	.520	.532	.612
CN	.613	.562	.674	.659
NO_2	.710	.674	.778	.790
$N(CH_3)_3{}^+$	.855	.359	.800	.408

[a] Value derived from other reactions correlated. [b] Value for CO_2CH_3 group.

TABLE XII

ELECTROPHILIC REACTION PARAMETERS
(BROWN AND OKAMOTO)

Reaction	ρ^+	r^a	s^b	b^c
Solvol. of $ArCMe_2Cl$ in 90% aq. acetone at 25°	−4.62	0.980	0.274	8[d]
Bromination by Br_2 in HOAc at 25°	−12.14	.987	.604	8
Chlorination by Cl_2 in HOAc at 25°	−8.06	.987	.190	9
Bromination by (Br^+) in aq. MeOH at 25°	−5.78	.798	.076	7
Nitration in CH_3NO_2 or Ac_2O at 0° or 25°	−6.22	.980	.287	13
Protonolysis of $ArSiMe_3$ in HOAc	−4.60	.980	.248	14
Brominolysis of $ArSiMe_3$ in HOAc	−6.04	.990	.175	14
Brominolysis of $ArB(OH)_2$ in aq. HOAc	−4.44	.992	.114	16
$Ar_3COH \rightleftarrows Ar_3C^+$ in aq. H_2SO_4	−3.64	.995	.512	12
$Ar_3CCl \rightleftarrows$ ion pairs in liq. SO_2	−3.73	.981	.234	15

[a] Correlation coefficient. [b] Standard deviation of experimental data from the regression line. [c] Number of substrates employed in the regression. [d] Correlation of *m*-substituted compounds with McDaniel and Brown σ-values.

series believed to involve reaction center–substituent resonance interactions to widely differing extents, the marked deviation of *p*-MeO for the trityl halides, and of all +M-*p*-substituents for the benzhydryl halides were attributed to differences in carbonium ion character and hence resonance interactions in the transition state. It is noteworthy that a discontinuity that appears in the log *k versus* σ^+ plot for the benzyl halides is attributed to a change in mechanism (*cf.* subsection 1).

The success of this treatment, and of the activity-selectivity relationship also, is surprising in view of the expectation of widely varying resonance contributions (244). The apparent constancy of enhanced substituent parameters could arise, as pointed out by Brown and Okamoto themselves (39), through the correlation of data predominantly involving *p*-substituents. Thus the ρ^+-values themselves are accommodating some of the variations in the effect of each substituent. Reaction parameters derived from *m*-substituted compounds alone could reveal this, were such data of the required accuracy available. Excellent correlations of substitution data on anisole (222) by means of the Selectivity relationship appear to indicate that the σ^+-value for the powerfully conjugating *p*-methoxy group is valid, or at least varies linearly with the σ^+-value for the *m*-methoxy group.

The reactions considered in the σ^+-treatment all have exceptionally high electron-withdrawing resonance requirements, perhaps all of a magnitude similar to that of the aryldimethyl-carbinyl chloride solvolysis. Certainly on considering all reaction series ranging from small to large resonance requirements von Bekkum, Verkade and Wepster (10), as discussed in sub-section 2, found a continuous range of sigma-values required when rho-values were based on *m*-substituted compounds. Similarly Taft and Lewis (248) were unable to set up a generally applicable scale of σ_R-values measuring resonance polar effects. It is interesting to observe that $\sigma_R{}^+$-values derived by subtracting Taft's σ_I-values from σ^+ have been found (204) to be linearly related

$$\sigma_R{}^+ = 1.91\sigma_R - 0.03$$

with σ_R obtained from McDaniel and Brown's sigma-values. The precision is not, however, high. No such relationship can be found between $\sigma_R{}^0$ and $\sigma_R{}^+$, nor, of course, for $\sigma_R{}^0$ and the widely varying σ_R-values given by Taft.

As reported by Okamoto and Brown (189) and by Deno and Evans (66) a number of reactions are not well correlated by the above set of σ^+-values and other sets have been devised. One example is the cleavage of mercury diaryls by hydrochloric acid where $^1/_2(\sigma + \sigma^+)$ is required (69). This again argues against a unique set of σ^+-values. It has been shown from variations of the ratio $\log f_x/\log f_{p\text{-Me}}$ that if the *p*-methyl group has a unique σ^+-value then *p*-phenyl, α-naphthyl and β-naphthyl cannot have unique values (65, 73).

Yukawa and Tsuno (277, 278, 279) have examined the various scales of σ^+-values in terms of a separation of inductive and resonance effects by permitting the latter to be variable

$$\sigma^+ - \sigma = \sigma_R{}^+ - \sigma_R \equiv G(R) \qquad (49)$$

where σ is derived from Jaffé's compilation. It was found that there is a linear relationship

$$(\sigma_A{}^+ - \sigma) = r(\sigma_B{}^+ - \sigma) \qquad (50)$$

that accommodates the various sets of σ^+-values (38, 39, 66, 67, 180, 191, 196, 197). Using the Brown and Okamoto set as standards ($\bar{\sigma}^+$), as in equation 51

$$\sigma^+ = \sigma + r(\bar{\sigma}^+ - \sigma) = \sigma + r\Delta\sigma_R^+ \tag{51}$$

thirty-five reaction series, including many for which the unmodified equation using the Brown and Okamoto σ^+-values fails, are correlated well by

$$\log k = \rho(\sigma + r\Delta\sigma_R^+) + \log k_0 \tag{52}$$

Equation 52 will inevitably correlate the data better than the original Hammett equation, with or without σ^+-values, since an additional adjustable parameter (r) has been introduced to compensate for variations. Bearing this in mind, it is found that $\Delta\sigma_R^+$ remains essentially constant with variations of rho from -12 to -0.6 and of r from 2.3 to 0.2. The rho-values obtained agree well with values computed from m-substituted compounds alone; hence r appears a valid measure of the direct resonance requirements of the reaction center. Reactions which satisfactorily follow the σ^+-values of Brown and Okamoto are found to have r-values between 0.7 and 1.3, outside this range σ^+ is either too large or too small compared with Yukawa and Tsuno's values (examples in Table XIII) and the values correlating m-substituents indicating, as suggested above, that ρ^+ serves to compensate for variations in the substituent effect. There appears to be no relationship between r and ρ^+. Recent investigations of the electrophilic cleavage of organic compounds of silicon, tin, lead and germanium are well correlated by equation 52 (73A, 73B).

TABLE XIII

ELECTROPHILIC REACTION PARAMETERS (YUKAWA AND TSUNO)

Reaction	ρ_H	r	s[a]	n[b]
Solvolysis $ArCMe_2Cl$, 90% aq. acetone, 25°	-4.518	1.000	0.093	21
Solvolysis Ar_2CHCl, i-PrOH, 25°	-4.004	1.350	.070	6
$Ar_3COH \rightleftarrows Ar_3C^+$, H_2SO_4, 25°	-11.73	0.764	.335	10
Halogenation, in HOAc, 25°	-8.82	1.660	.414	15
Bromination, (Br^+), 50% aq. diox., 25°	-5.276	1.145	.080	7
Nitration in CH_3NO_2 or HOAc, 25°	-6.377	0.897	.327	12
Brominolysis of $ArB(OH)_2$, 20% HOAc, 25°	-3.84	2.29	.313	16
Protonolysis of $ArSiMe_3$, 72% aq. MeOH, 50°	-5.597	0.727	.125	13

[a] Standard deviation of experimental data from the regression line. [b] Number of data used in the regression.

The Yukawa–Tsuno treatment can be applied equally well to reactions involving a loss of resonance interaction during activation. Several derivatization reactions of aryl ketones and aldehydes are of this type (70).

After verifying the experimental results that the p-fluoro-substituent deactivates the benzene ring toward a few reactions, *e.g.*, nitration, but weakly activates toward others, and that p-alkyl-substituents stand in the "inductive order" for nitration, but in the "Baker-Nathan" order for most other reactions, Knowles, Norman and Radda (152) also conclude that a unique set of σ^+-values is not possible. Examination of σ^+-values calculated to correlate six reactions led them to suggest, in contrast to several other workers, that the absolute magnitude of σ^+ increases with increasing absolute value of ρ^+. A modified Hammett equation then was set up for p-substituents

$$\log (k/k_0) = \sigma_G\phi + \sigma_R\phi \tag{53}$$

where σ_G measures the "ground state electron density" *para* to the substituent relative to that in benzene (presumably proportional to Taft's σ^0-value), σ_R measures the direct resonance interaction and ϕ measures the "demand of the reagent for electrons in the transition state." The parameter σ_R then was examined in terms of

$$\sigma_R = \sigma_P f(\phi) = \sigma_P\phi^n \tag{54}$$

σ_P measuring the ability of the substituent to supply electrons (polarizability) and $f(\phi)$ being some function of the reaction parameter (ϕ), assumed for simplicity of the form ϕ^n. By assuming that the t-butyl substituent is not polarizable, ϕ can be determined and hence n from

$$\log [\log (k/k_0) - \sigma_G\phi] = \log \sigma_P + (n + 1) \log \phi \tag{55}$$

by plotting the left-hand side of equation 55 against log ϕ using the p-phenyl substituent with $\sigma_G = -\sigma_{\text{Hammett}}$. (Opposite signs were given to σ_G and σ_P as compared with the usual scales to facilitate mathematical handling.) This choice, an unfortunate one in view of the uncertainty of $\sigma_{p\text{-Ph}}$, was dictated by the limited data available. The well-documented p-methyl group was rejected because of its very low polarizability. From this plot $n = 1$, hence

$$\log (k/k_0) = \sigma_G\phi + \sigma_P\phi^2 \tag{56}$$

For several substituents σ_G- and σ_P-values were determined from plots. After iterative adjustment of the three parameters, equation 56 satisfactorily reproduces the substitution data particularly a minimum in the log (k/k_0) *vs.* ϕ plot at $\phi = -\sigma_G/2\sigma_P$ which leads to deactivation by the p-fluoro-substituent in nitration but activation in other reactions.

Equation 56 has an uncertain derivation in a number of respects. Particularly disturbing are the choice as starting points of the t-butyl and phenyl groups, whose sigma-values are imprecise, and also the doubly logarithmic plot of equation 55 which determines the most important value n.

From a comparison of equations 52 and 56 and their derivation it would be expected that: $\phi \simeq \rho$, $\sigma_G \simeq \sigma^n = \sigma^0$ and $\sigma_P\phi \simeq r\ \Delta\sigma_R^+$. Comparisons are made in

TABLE XIV

KNOWLES, NORMAN AND RADDA PARAMETERS

A. Substituent parameters

Subst.	$-\sigma_G$	σ^n[a]
p-MeO	−0.27	(−0.111)
p-Me	− .19	− .129
Ph	.01	(.2 to −0.3)
p-F	.10	(.056)
p-Cl	.22	.238
p-Br	.235	.265

B. Reaction parameters

Reaction	$-\phi$	ρ
1. Protonol. of $ArSiMe_3$	−6.04	−5.60
2. Bromin. by Br^+	−8.07	−5.28
3. Nitration	−9.54	−6.38
4. Chlorination	−13.71	−8.82
5. Bromination	−14.62	

C. Direct resonance contributions (regardless of sign)

Reaction number	*p*-MeO		*p*-Me		*p*-F		*p*-Cl	
	$\sigma_P\phi$	$r\Delta\sigma_R{}^+$	$\sigma_P\phi$	$r\Delta\sigma_R{}^+$	$\sigma_P\phi$	$r\Delta\sigma_R{}^+$	$\sigma_P\phi$	$r\Delta\sigma_R{}^+$
1	0.15	0.365	0.01	0.095	0.07	0.095	0.08	0.07
2	.20	.57	.015	.15	.09	.15	.11	.09
3	.24	.45	.02	.12	.105	.12	.13	.07
4	.36	0.83	.03	0.215	.15	0.215	.19	0.13
5	.38		.03		.16		.20	

[a] Values in parentheses have considerable uncertainty.

Tables XIVA, B and C from which it is clear that the values compared do not have the same significance. Since Yukawa and Tsuno's parameters are closely related to other parameters derived by means of the Hammett relationship and to the familiar inductive and resonance effects, it would appear then that the treatment of Knowles, Norman and Radda, if valid, has resulted in a remixing of these contributors to the total substituent effect instead of a separation.

Once again attention must be drawn to the introduction of adjustable parameters upon which there is no external check.

6. The Correlation of Nucleophilic Aromatic Substitutions

It was for reactions of the nucleophilic type, although not ring substitutions, that a possible duality of sigma-values was first encountered. Hammett (110) observed that a new parameter, σ^*, now termed σ^- (see Table II), was required to correlate the effect of *para*-electron withdrawing groups on reactions of anilines and phenols. It appeared that for the three reactions studied the new scale precisely accommodated direct resonance interactions.

Berliner and Monack (26) report the first study of a nuclear substitution, the reaction of 4-substituted-2-nitrobromobenzenes with piperidine, for which even electron-releasing substituents, especially the dimethylamino group, were only moderately well correlated by Hammett's sigma-values. It was suggested therefore that the new scale should encompass all *para* substituents and not only strongly conjugative electron-withdrawing ones.

Four of the reactions listed in Table XV were examined by Jaffé (134c). The correlations obtained using two sigma-values were significantly less precise than those for the majority of reaction series. Since a constant activating substituent, as in the *o*-nitrohalobenzenes, is generally essential to obtain measurable reaction rates, few *m*-substituted compounds were examined. (A *m*-substituent must perforce be *ortho* or *para* to the activating nitro group and can potentially interact with it.) Such data being absent, the procedures of van Bekkum, Verkade and Wepster (10) and of Taft and Lewis (248) cannot be applied; therefore no nucleophilic aromatic substitutions appear in their compilations.

Ample data have been provided on reactions of anilines and phenols, especially acid–base equilibria (see Table IX, sub-section (3) from which "true" ρ-values can be computed. Calculated σ^--values for a number of groups are presented in Table XV. Again the results indicate that a unique set of σ^--parameters can-

TABLE XV

NUCLEOPHILIC AROMATIC SUBSTITUTIONS

Substrate	Reagent	Solvent	Temp., °C.	ρ	Reference
$X\text{-}C_6H_4F$	CH_3O^-	CH_3OH	0	9.20	180
$X\text{-}C_6H_4Br$	$C_5H_{10}NH_2$	C_6H_6	99	4.871[a]	53
$4X\text{-}2\text{-}NO_2C_6H_3F$	$C_2H_5^-$	C_2H_5OH	25	4.071[a]	28
$4X\text{-}2\text{-}NO_2C_6H_3Cl$	CH_3O^-	CH_3OH	25	3.941[a]	52
$4X\text{-}2\text{-}NO_2C_6H_3Br$	$C_5H_{10}NH_2$	$C_5H_{10}NH_2$	35	4.918[a]	26
$4X\text{-}2\text{-}NO_2C_6H_3I$	CH_3O^-	CH_3OH	50	3.874	181
$4X\text{-}2\text{-}NO_2C_6H_3I$	N_3^-	CH_3OH	50	3.118	181
$4X\text{-}2\text{-}NO_2C_6H_3I$	SCN^-	CH_3OH	50	5.046	181
$4X\text{-}2,6(NO_2)_2C_6H_2Cl$	CH_3O^-	CH_3OH	0	3.80	180

[a] Computed by Jaffé.

not be derived to correlate all reaction series of this type. The limited success achieved by Miller (181) through this approach no doubt results from the close similarity of the reactions in Table XV that he utilized.

TABLE XVI

NUCLEOPHILIC SUBSTITUENT PARAMETERS

	σ^--Values			
Substituent	Phenols[a]	Anilines[b]	Ring subst.[d]	σ^n
p-N_2^+	2.9[c]	3.15	1.87	(2.0)[c]
p-$S(CH_3)_2^+$	1.20	. .	1.41	1.12
p-$N(CH_3)_3^+$	0.73	0.70	1.11	0.800
p-NO_2	1.26	1.20	1.27	.778
p-CN	0.91	0.99	0.86	.674
p-CHO	1.10	.98	.89	.23)
p-F	0.05	.06	− .015	(.056)
p-OCH_3	−0.11	− .25	− .6	(− .111)

[a] Reaction series 23a of Table IX; $\rho = 2.26$. [b] Reaction series 26a of Table IX; $\rho = 2.94$. [c] *Cf.* Lewis and Johnson (168). [d] Reaction series of Table XV due to Miller (180, 181).

7. *The Extension to Other Aromatic Systems*

All aromatic and heterocyclic systems, being planar and rigid, have substituent-reaction center dispositions like the *m*- and *p*-positions in benzene derivatives. Since proximity effects are absent, the Hammett equation should in principle be valid for these systems, although in practice certain difficulties are encountered in its application and in the comparison of results between systems.

One approach, adopted by Hammett (110) and by Jaffé (134), is to regard the system as a substituted benzene, whence β-naphthyl is treated as the 3,4-benzo-substituent. α-Naphthyl and similar systems which will show steric factors not present in benzene cannot be treated in this way, but substituent parameters have been derived for β-naphthalene, 2-phenyl-3,4-methylenedioxy, hydrindene and tetralin derivatives.

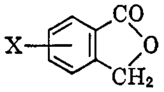


Figure 3.

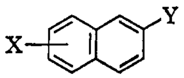


Figure 4.

Other means have been suggested (3, 136) for the handling of more complex substrates when the reacting side chain or the substituent may be considered to be attached to the benzene ring in two positions. In the first case, *e. g.*, reactions of substituted phthalides

$$\log (k/k_0) = \sigma_1\rho_1 + \sigma_2\rho_2 \qquad (57)$$

where $\sigma_1\rho_1$ and $\sigma_2\rho_2$ refer to the points of attachment of the reacting side chain, *i.e.*, 1 and 2, respectively, of Fig. 3. Conversely the 6- and 7-X-substituted naphthalene derivatives (Fig. 4) may be considered benzene derivatives containing the 3,4-CHCXCHCH-substituent.

$$\log (k/k_0) = \sigma_{(\mathrm{CHCXCHCH})}\rho$$

where ρ is the reaction parameter correlating "normal" phenyl substrates. Both procedures might be applied to heterocyclic substrates by regarding the heteroatom as a substituent as opposed to regarding the heterocyclic ring as a whole as the substituent. Substrates of the α-naphthyl type might also be accommodated, but the ρ-value in this case will embody the effect of a constant *o*-substituent.

It is more satisfactory, however, to select as a new standard substrate the unsubstituted parent compound of the series. Investigations of substituent effects in the naphthalene system have commenced along these lines (*cf.* 261). Examination of the existing data, see Table XVII, has permitted the evaluation of a tentative list of σ_N-values based on acid dissociation and ester hydrolysis data, applicable to the napthalene system which may be compared with the corresponding benzene parameters (σ^n) (258).

Some useful conclusions concerning electronic relay through the naphthalene system and steric effects due to *peri*-hydrogen can be derived from the above computations, but exact comparison of substituent parameters between the benzene and naphthalene systems is precluded by the absence of reaction constants for the latter. When these become available σ_N-values on the benzene scale can be determined accurately and use can be made of the greater diversity of substituent-reaction center dispositions.

Bryson's (49) investigations of substituent effects on

TABLE XVII

SUBSTITUENT PARAMETERS FOR THE NAPHTHALENE SYSTEM

Substituent[a]	σ_N	σ_m	Substituent	σ_N	σ_p
3α-NO_2	0.674	0.710	4α-NO_2[b]	0.691	.0778
3α-Cl	.354	.373	4α-Cl[b]	.233	.238
3α-Br	.354	.391	4α-Br	.246	.265
3α-CH_3	− .069	− .069	4α-CH_3	− .156	− .129
5α-NO_2[b]	.488	. . .	4α-F	.110	.06
5α-Br	.255	. . .	4α-OCH_3	− .264	. . .
6α-NO_2	.467	. . .	4α-$N(CH_3)_2$	− .229	. . .
7α-Cl[c]	.114				

[a] For numbering system see Wells and Ward (261). [b] Values of greatest certainty derived from data of both Price (203) and Vaughan (87, 88, 89). [c] Derived from data of Price only; all other values from the data of Vaughan.

the naphthylamines also illustrate significant differences between the effects of a given substituent in formally similar positions of different aromatic systems. Examined in terms of inductive and resonance contributions using Taft's parameters

For anilines $\sigma_m = 1.05\sigma_I + 0.33\sigma_R$
For naphthylamines $\sigma_{3\alpha} = 0.95\sigma_I + 0.12\sigma_R$
$\sigma_{4\beta} = 0.78\sigma_I + 0.40\sigma_R$

The value $\rho = 2.82$ was used throughout so that the "absolute value" of Bryson's sigma values is probably incorrect. The different relative contributions of the two factors (inductive and resonance) will remain whatever corrections are made to $\sigma_{3\alpha}$ and $\sigma_{4\beta}$.

Two other carbocyclic systems that have been examined are fluorene and anthracene. Regarding 2- and 3-substituents as *meta* and *para*, respectively, correlation of the reactivity of 9-bromofluorenes is successful only to a limited extent (71). The reacting side chain in the 10-substituted anthracene-9-carboxylic acids and esters (186) suffers proximity effects of the same type but far greater than those due to the *peri*-hydrogen in α-naphthyl derivatives. The rates of ester hydrolysis in this system are very slow. Substituent effects on acid strength are correlated moderately well by σ_p-values with the exception of the nitro group which is estimated to be twisted some 85° out of plane.

Heterocyclic substrates have been examined in terms of the ring and its heteroatom as a substituent. However the sigma-values derived from pyridine, quinoline, isoquinoline (78), furan and thiophene (202, 203), carboxylic acids and esters, like those for the phenyl and naphthyl groups are variable and of little value. A more rewarding approach appears to be through regarding the system as a "new" one, as in the case of naphthalene derivatives, when the heteroatom becomes either the reaction center or a constant substituent. Pyridine is thus a substituted benzene and quinoline a substituted naphthalene.

The acidity of the pyridinium cations, in keeping with the situation of the reaction center as a nuclear atom, shows the greatest susceptibility to substituent effects of any acid–base equilibrium series yet studied. Correlation by means of the σ^n-values of the data collected by Bryson (50) pertaining to the pyridinium cations in water at 25° gives $\rho = 6.114$ with a correlation coefficient of 0.992, and the quinolinium cations (using σ_N-values of Table XIV) gives $\rho = 5.759$ (correlation coefficient 0.996), which are significantly different. Using $\rho = 6.00$, Bryson analyzes these data in terms of Taft's parameters to yield

3-Substituted pyridines $\sigma = 1.02\sigma_I + 0.40\sigma_R$
3-Substituted quinolines $\sigma = 0.93\sigma_I + 0.23\sigma_R$
4-Substituted isoquinolines $\sigma = 0.95\sigma_I + 0.38\sigma_R$

suggesting, once again, that there are differences in relative contributions from inductive and resonance effects in different systems.

8. The Extension to Other Cyclic Systems

The most important system of this category is the group of 4-substituted bicyclo[2,2,2]octane-1-derivatives (208) upon which Taft has based his list of inductive sigma-values. The system is rigid and of such geometry that the 4-substituent is essentially the same distance from a reaction site, *e. g.*, a carboxyl group, as is a *p*-substituent in benzene, although separated from it by a different σ-bond structure and a different intramolecular medium. Steric effects again are absent so that the linear free energy correlation

$$\log (k/k_0) = \sigma'\rho' \qquad (58)$$

should be, and is, followed in this system. The values of log (k/k_0) are of the same order of magnitude for both the bicyclooöctane and benzene systems despite the absence in the former of a π-electron path for relay of substituent effects. If the factors computed by Waters (246) for relay of inductive effects by way of saturated bonds are adopted, this mode of substituent interaction is negligible in the system and the direct electrostatic effect would seem to be almost solely responsible. Other calculations are indecisive but indicate that this could be the case.

The σ'-values (for OH, $CO_2C_2H_5$, Br and CN substituents) were derived using $\rho' = \rho$ (Hammett) from the benzoic acid dissociation under the same conditions. This must be an approximation in view of the changes in susceptibility of reactions to substituent polar effects with changes in reaction center environment. It may be a reasonable approximation in view of the success of the σ_I-scale discussed more fully in sub-section 2.

The *trans*-4-substituted cyclohexane-1-carboxylic acid system shares with the above system the absence of π-electronic interactions, the remoteness of substituent and reaction center, and, if restricted to the diequatorial conformation, essentially the same geometry. This, and the related *cis*-3-substituted cyclohexane system, have been studied by Siegel and Komarmy (218) in terms of σ'' and ρ''-values. Assuming, as above, that for the ρ''-value the approximate Hammett parameter can be used, σ'' is consistently 30% lower than σ'. This has been explained in terms of direct electrostatic interactions.

Ethylenic and acetylenic bonds also possess the geometrical requirements believed to be essential for the application of a linear free energy relationship to substituent changes. The 3-substituted *trans*-acrylic acids (60, 124) and propiolic acids (59) are more satisfactorily discussed in terms of the Taft relationship (section IIIB). In the present context, however, it is of interest that both series are reported to be correlated by the σ_p-values of Jaffé.

9. *The Correlation of ortho-Substituent Effects*

Taft's method for the evaluation of polar effects in aliphatic substrates by the elimination of steric effects (see section IIIB), has been applied by him to *o*-substituted benzene derivatives. As illustrated in Table XVIII the substituent parameters (σ_0) obtained closely resemble the corresponding σ_p-values. The major discrepancies are for the methoxy group, whose $\sigma_p{}^n$-value is uncertain, and the fluoro group for which, like the unsubstituted compound, the steric effect correction may not be applicable. Such a close correspondence is surprising in view of the expectation of greater inductive effects from the *ortho* than from the *para* position. This scale of sigma-values is based on the assumption that the saponification of *p*- and *o*-substituted ethyl benzoates has the same susceptibility to substituent polar effects. It leads to a rho-value of 1.787 for the dissociation of *o*-substituted benzoic acids in water at 25° which appears to be excessively large. This means that the σ_0-values may be considerably too small (*cf.* 260).

TABLE XVIII

o-SUBSTITUENT PARAMETERS (RELATIVE TO H)

Substituent	σ_0	$\sigma_p{}^n$	Substituent	σ_0	$\sigma_p{}^n$
F	0.24	(0.056)	OCH_3	−0.39	(−0.111)
Cl	.20	.238	CH_3	− .17	− .129
Br	.21	.265	NO_2	.80	.778
I	.21	.299			

A number of reaction series has been examined to yield purely polar effects where steric interactions between *o*-substituents and the reaction center might be negligible. For the phenylpropiolic acid system (184, 207) this is partially the case. Some success also has been achieved in the case of the 2-substituted pyridinium cations where Brown and McDaniel (35, 36) have suggested that the usual effects of steric inhibition of resonance (of substituent and of reacting side chain), steric inhibition of solvation, steric inhibition of reagent approach and hydrogen bonding may be relatively small. Such factors will vary from reaction to reaction for any given substituent. Charton (58) has examined a number of reaction series with extended side chains using *para*-sigma values to measure *ortho*-polar effects. Satisfactory correlations are obtained when the side chain is composed of at least two atoms, *e.g.*, $-CH_2CH_2-$, $-CH{=}CH-$, and $-OCH_2-$, yielding ρ_0-values which differ substantially from the normal rho-values. These differences must be attributed both to different substituent effects *and* different susceptibilities to substituent effects.

Farthing and Nam (85) have defined an electronic parameter (σ_E) and a steric parameter (σ_S) for *o*-substituents using the benzoic acid dissociation in water at 25° as the standard reaction series; thus

$$\log (K/K_0)_{ortho} = \sigma_O = \sigma_E + \sigma_S$$
$$\log (K/K_0)_{para} = \sigma_E$$

The four parameter equation

$$\log (k/k_0) = \sigma_E\rho_E + \sigma_S\rho_S \qquad (59)$$

was then examined for forty-five reaction series through the correlation of log $(k/k_0)/\sigma_S$ with σ_E/σ_S; 40% of these series have correlation coefficients greater than 0.99 and only two gave poor correlations, although *o*-methyl and methoxy deviated in sixteen series and were excluded from the statistical analysis. No subsequent discussion or extension of this approach, essentially equivalent to that of Taft (see section IIIB), has been reported.

When σ_S (or ρ_S) is zero, equation 58 reduces to the Hammett equation with σ_p accounting for *ortho*-polar effects. A plot of the ρ_E-values against the Hammett rho-values is reported to be fairly linear.

10. *The Correlation of Non-reactivity Data*

Twenty-three correlations of substituent effects on physical data, chiefly infrared frequencies, are reported by Jaffé (134d) for which the Hammett equation is satisfactory but rarely good. This approach to the measurement of polar effects as opposed to the use of reactivity data is a potentially powerful theoretical tool. While the details of reaction processes and the definition of transition states are beyond present capabilities, the "static" properties of molecules may not be.

Several further series of polarographic data can be added to Jaffé's list, namely, the reduction of iodobenzenes (62), the reduction of benzaldehydes and acetophenones (63) the reduction of 6-substituted quinoxalines (225) and the oxidation of *p*-substituted phenylferrocenes (179). The ionization potentials of free radicals have been suggested (146) as a measure of "absolute Lewis base strength." Since only inductive and resonance effects would appear to be involved here, such measurements may be of great value. For *m*- and *p*-substituted benzyl radicals these potentials are well correlated by the σ^+-values (112A).

Although resultant dipole moment changes are not readily accommodated by the sigma-values, individual bond dipoles should show a correlation if they could be determined accurately. Infrared absorption is, however, dependent upon changes in dipole moment during vibration so that correlations of this type are to be expected. Plots of frequency (ν) or relative frequency shift ($\nu - \nu_0/\nu_0$) against sigma-values have generally been employed (*cf.* 42,250) and some use has been made of the deviations observed (90).

Improvements in methods of determining infrared intensities have shifted the emphasis toward their correlation. Brown (45) has discussed a simple molecular orbital model for bond dipole moments in conjunction with an expression for the change in dipole moment and the square root of the intensity (A). For the benzonitriles and the acetophenones $A^{1/2}$ shows a very good correlation with σ^+ (see sub-section 5). The normal sigma-values correlate $A^{1/2}$ for substituted phenols, anilines and methylanilines. A number of deviations are observed that have proved difficult to interpret.

The logarithms of the relative intensities of the O–H stretching vibration in phenols are linearly related to the relative dissociation constants of the corresponding benzoic acids (41). Similarly, log A *versus* σ correlates substituent effects in the benzonitriles, while $\delta\nu$ *versus* σ does not (251). Rao and Venkataraghavan (206A) have carried out a statistical analysis of the correlation of infrared frequency shifts and intensity changes. Hammett σ-values and σ^+-values are equally successful in producing fair to moderate fits. The standard deviations from regression are, however, quite large, always exceeding 10% of the maximum possible value of the $\sigma\rho$-product. The sign and magnitude of the rho-values correlating log A accord with the nature of the bond or group involved in vibration.

Correlations of ultraviolet and visible spectral data have not been particularly successful. The azomethine dye system has been examined in three solvents, cyclohexane, butyl acetate and methanol (34). The scatter about a linear $1/\lambda_{\max}$ *versus* σ plot increases with increased polarity of solvent. Considerable use has been made by Schubert (*cf.* 215, 216) of ultraviolet spectral changes, particularly with varying solvent in the investigation of substituent character.

Nuclear magnetic resonance data recently have provided some correlations of a novel type (*cf.* 245). Pecularities were first observed for chemical shifts in the F^{19}-resonance in the fluorobenzenes where *m*- and *p*-substituents were correlated by two lines (106). In terms of inductive and resonance factors the shielding parameters

$$\delta^{F} = 10^{6}(H_{C_6H_5F} - H_{ArF})/H_{C_6H_5F}$$

where H is the field strength at which resonance occurs, follow equations 60 and 61 with remarkable precision.

$$\delta_m{}^{F} = 6.1\sigma_I - 0.5 \text{ (av. dev. } \pm 0.35) \qquad (60)$$

$$\delta_p{}^{F} = 9.0\sigma_I - 30.6\sigma_R{}^0 - 0.8 \text{ (av. dev. } \pm 0.35) \qquad (61)$$

Of particular interest is the absence of influence by resonance effects from the *m*-position in comparison with the powerful effect from *para*. Modifications of equations 60 and 61 have also been employed successfully, particularly the correlation of $\delta_p^F - \delta_m^F$ with $\sigma_R{}^0$ alone (243). The apparently differing response to inductive effects from *m*- and *p*-positions is not considered to be conclusive (243A).

B. THE TAFT EQUATION

1. General Discussion

The Hammett equation successfully correlates a wide variety of reactivity and other data and provides a quantitative measure of substituent polar effects (electronic and electrostatic interactions) by virtue of the limitations placed upon the choice of reactant geometry, in particular substituent and reaction site location. With a relaxation of these limitations, linear free energy correlations can still be observed provided other restrictions are imposed. Thus the Brønsted equation (section VA) deals with reagent changes in the limited class of acid- and base-catalyzed reactions.

By limiting the type of reaction to esterifications and ester hydrolyses, correlations of substituent effects in aliphatic and *o*-substituted substrates become possible. Thus Taft (237) observed that

$$\log (k/k_0) = fA \qquad (62)$$

would accomplish this. In equation 62, k is the rate constant for any ester (or acid) in a given reaction series; k_0 the rate constant for the corresponding acetate (for substituent changes in the acyl portion of the ester), methyl ester (for alkyl portion changes) or *o*-toluate (for *o*-substituents in the benzoic series) as appropriate; f is a proportionality constant: and A = log (k/k_0) for the appropriate standard reaction series ($f = 1$).

Equation 62 is in reality *six* correlations, each with a differently defined scale of A-values set up for acid- or base-catalyzed reactions involving substituent changes in the acyl portion, the alkyl portion or the *o*-position of benzoic acids or esters. These six scales are different, the individual A-values showing no proportionality, so that it may be inferred that a given substituent is operating in a different manner in the various reaction types. For a given type (*e.g.*, variations in the acyl component for acid-catalyzed esterifications or hydrolyses) equation 62 indicates the role of the substituent, both polar and steric, to be the same throughout. However, the success of equation 62 must at least in part be attributed to the small variations of log (k/k_0) observed, leading to f-values close to unity except in the case of variations of the alkyl component in base-catalyzed reactions. In half the reactions of each of the other types f was set equal to unity to define the A-values. In all reactions f changes little with structure, reagent or solvent.

From a consideration of the nature of the transition states of acid- and base-catalyzed reactions of esters, the application of equation 62 and the A-values obtained are readily rationalized. Furthermore, as suggested by Ingold (131), the ratio of rate constants for otherwise equivalent base- and acid-catalyzed reactions (k_B/k_A) should be principally a function of substituent polar effects. Taft (238, 239) has utilized this to set up equation 63

$$\log (k/k_0)_B - \log (k/k_0)_A = 2.48\sigma^* \qquad (63)$$

correlating, by σ^*, substituent polar effects relative to methyl in aliphatic and *o*-substituted aromatic substrates. Basically it is assumed that $\log (k/k_0)_A$, the relative rate constant for an acid-catalyzed esterification or hydrolysis, is governed almost completely by steric and resonance effects (polar effects negligible) and that the relative rate constant for the otherwise equivalent base-catalyzed reaction has quantitatively the same steric and resonance components. Hammett ρ-values (Table IX) support the contention that the acid-catalyzed reactions are insensitive to polar effects. Relative rate constants for reactions differing only in the type of catalysis are not generally available, but by the use of equation 62 the appropriate $(k/k_0)_B$ and $(k/k_0)_A$ data can be deduced. Most of the available ester hydrolyses and esterification data are correlated by equation 62 using $f = 1$; hence the σ^*-scale was set up essentially by using averaged (k/k_0)-values. The proportionality factor 2.48 attempts to set the σ^*-values on the same scale as the Hammett σ-values although based on the methyl group as standard. It was derived (239) on the assumption that the susceptibility to substituent polar effects of the same reaction of aliphatic and *o*-substituted benzene derivatives would be equal; σ^*-values for *o*-substituents were deduced by the use of Hammett ρ-values pertaining to the corresponding reactions of *m*- and *p*-substituted benzene derivatives. Two reaction series studied not involving esters were common to both the aliphatic and the *o*-benzoate sets of data permitting an average conversion factor (2.48 ± 0.09) to be calculated applicable to the hydrolysis and esterification data of equation 63. This then becomes the defining equation for the σ^*-values, which utilizes average values of $\log (k/k_0)$ from, for acidic reactions (the hydrolysis of ethyl esters in 70% aqueous acetone and 60% aqueous acetone, and the esterification of carboxylic acids in methanol, ethanol and cyclohexanol) and for basic reactions (the hydrolysis of ethyl esters in 70% aqueous acetone, 85% aqueous ethanol and 60% aqueous ethanol all at 25°). It is noteworthy that the average Hammett rho-values for these series are, for the acid reactions, -0.015 ± 0.26, and the basic reactions, 2.48 ± 0.06. The difference corresponds closely to the factor deduced.

Thirty-seven aliphatic and four *o*-substituted benzene derivative reactions and sets of physical data subsequently were correlated by the Taft eq. 64 (239, 242e)

$$\log (k/k_0) = \sigma^*\rho^* \qquad (64)$$

using the σ^*-values as defined above. A sample of these reaction series is listed in Table XIX with their statistical data. These are additional to the five reaction series, including that defining the σ^*-values, which are accommodated by various proportionality factors in equation 63.

The most interesting feature of equation 64 is the absence of any term correcting for steric and resonance effects. This may be taken to imply that steric factors are closely similar throughout these series and in fact approximate to the steric effect of the methyl group. Excessively bulky substituents lead as expected to failure. For similar reasons the excessively small substituent —H cannot serve as a standard and the *o*-fluoro substituent deviates in some cases. Such a con-

TABLE XIX

CORRELATIONS BY EQUATION 64

Reaction	Solvent	Temp., °C.	ρ^*	s[a]	n[b]
	Aliphatic substrates (RY relative to CH_3Y)				
$RCO_2H \rightleftarrows RCO_2^-$	Water	25	$+1.721 \pm 0.025$	0.06	16
$RCH_2CH(OC_2H_5)_2 + H^+$	50% dioxane	25	$-3.652 \pm .085$	.08	7
$RCO_2H + (C_6H_5)_2CN_2$	Ethanol	25	$+1.175 \pm .043$	.06	12
$RCH_2OH \rightleftarrows RCH_2O^-$	Isopropyl alc.	27	$+1.364 \pm .09$	.09	8
$CH_3CH(OH)_2$–$H_2O(RCO_2H)$[c]	Acetone	25	$+0.801 \pm .015$	.02	13
$CH_3COCH_3 + I_2(RCO_2H)$[c]	Water	25	$+1.143 \pm .022$	.02	5
NH_2NO_2 decomp. (RCO_2^-)[c]	Water	25	$-1.426 \pm .035$	.07	7
Hyd. $CH_2(OR)_2$ by acid	Water	25	$-4.173 \pm .150$	.05	7
Solv. $R_1R_2R_3CCl$	80% ethanol	25	-3.29	.22	13[d,e]
Solv. $RCH_2OSO_2C_7H_7$	Ethanol	100	-0.742	.03	6[e]
$RCH_2Br + C_6H_5S^-$	Methanol	20	-0.606	.02	5[e]
	o-Aromatic substrates (relative to o-toluene derivative)				
$ArCO_2H \rightleftarrows ArCO_2^-$	Water	25	$+1.787 \pm 0.13$	0.15	7
$CH_3CH(OH)_2$–$H_2O(ArCO_2H)$[c]	Acetone	25	$+0.771 \pm .019$	.02	5
$ArNH_3^+ \rightleftarrows ArNH_2$	Water	25	$+2.898 \pm .15$	.19	5
$ArNH_2 + C_6H_5COCl$	Benzene	25	$+2.660 \pm .22$	.28	4

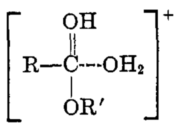
[a] Standard deviation of the experimental data from the regression line. [b] Number of substituents employed. [c] Catalysis by various acids (reaction series 1 requires all reactions following the Brønsted catalysis law will follow the Taft equation). [d] Number of different $R_1R_2R_3$ combinations, standard $(CH_3)_3CCl$. [e] Reference 223.

stancy of steric effects can be expected in but a few reaction series so that equation 64 will have only limited utility. Changes in resonance interaction during reaction (or activation) must also be negligible.

Esterification and ester hydrolysis, being the most intensively studied and probably best understood reactions subject to both acid and base catalysis, are the most satisfactory standard reactions in the aliphatic series. Although entropy changes are generally small, the activation process is always accompanied by a considerable steric effect. On the other hand, many of the reaction series listed in Table XIX show marked entropy changes, despite the conclusion that steric effects are negligible. As in the case of the Hammett equation isoentropy is not essential for correlations by equation 64.

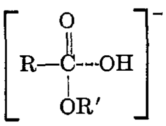
The basic assumptions of this approach to substituent effects in aliphatic substrates are: (a) The relative free energy change is separable into independent components due to polar, steric and resonance effects. (b) Steric effects are cancelled out and resonance effects are either absent or are cancelled out in the difference log $(k/k_0)_B - \log (k/k_0)_A$ of eq. 63.

Assumption (a) already has been discussed in section III-A-2. For ester hydrolysis assumption (b) requires that the transition states (A) for the acid-catalyzed reaction and (B) for the base-catalyzed reaction be of such configurations along the reaction path that the reacting carbon atoms are close to tetrahedral and have essentially the same steric environments about them.



$$\left[\begin{array}{c} \text{OH} \\ \| \\ \text{R---C---OH}_2 \\ | \\ \text{OR}' \end{array}\right]^+$$

A



$$\left[\begin{array}{c} \text{O} \\ \| \\ \text{R---C---OH} \\ | \\ \text{OR}' \end{array}\right]^-$$

B

This would seem to be a reasonable assumption in view of the small size and remoteness of the two protons by which A and B differ. The markedly greater sensitivity of the base-catalyzed reaction is then to be attributed to the highly polarizing nature of the localized charge on the hydroxide ion in contrast to the dispersed charge on the protonated ester. (Both reactions involve a neutral molecule and an ion as reactants.)

Reaction series conforming to the restrictions required by expressions of the same type as equation 63 are rare, particularly that of a closely similar mechanism for acid- and base-catalyzed reactions. More reaction series have been found that can be correlated by equation 64 for which the major restriction is constancy in steric interactions during reaction or activation. Although such requirements severely limit the range of application of these equations, their value in mechanistic investigations is enhanced. Notably, as with all the simple linear free energy relationships, reaction mechanism must remain constant throughout the reaction series (*cf.* 240) and that mechanism must involve only small changes in bond angles about the reaction center, and the abstraction or attachment of relatively small groups.

The data available and, in several cases, the nature of the reactions correlated had dictated that the majority of substituents processed by the Taft equation be alkyl groups. In many cases, almost all in the case of the correlation of physical data, alkyl groups have been the only ones studied. The inability of the Hammett equation to distinguish between the effects of different alkyl groups has been discussed in section III-A-2. Significantly different σ^*-values are possible because of the greater susceptibility of aliphatic reactions to the polar effects of substituents closer to the reaction site. The potential utility and searching test of equation 64 will only be fully realized by the examination of a wider range of substituents.

Taft (242g) has examined the precision of equation 64 and assessed both its ability to predict substituent polar effects and to demonstrate the incursion of other variables. It is suggested that factors whose contribution to the log (k/k_0) values are less than 10% are unlikely to be detected. Vertical deviations from the correlation line exceeding $0.16\rho^*$ log unit (an arbitrary but reasonable choice) can be considered due to some other variable (or variables).

Among correlations to equation 64 subsequently reported the base strengths of aliphatic amines (107) and phosphines (120) are noteworthy in that they assist in the evaluation of factors influencing acid–base strength.

Amines	RNH_2	$pK_a = 13.23 - 3.14\sigma^*$
	R_1R_2NH	$= 12.13 - 3.23\Sigma\sigma^*$
	$R_1R_2R_3N$	$= 9.61 - 3.30\Sigma\sigma^*$
Phosphines	RPH_2	$pK_a = 2.46 - 2.64\sigma^*$
	R_1R_2PH	$= 5.13 - 2.61\Sigma\sigma^*$
	$R_1R_2R_3P$	$= 7.85 - 2.67\Sigma\sigma^*$

Within each series deviations due to steric effects are slight and susceptibilities to polar effects are essentially constant. The basicity order $NH_3 > RNH_2 > R_2NH > R_3N$ is attributed to steric inhibition of solvation while changes in the state of hybridization of phosphorus are held responsible for the reverse order $R_3P > R_2PH > RPH_2$.

2. Reaction and Substituent Parameters for Polar Effects

Bearing in mind that steric effects and polar effects are distinctly different functions of structural changes in the substrate, the success of equation 64 in correlating relative reactivities for reactions of varying types is the best evidence that polar effects alone are being measured. Expressed in the form of the generalized equation of section II

$$\left(\frac{\partial \log k}{\partial \sigma^*}\right)_Z = \rho_Z^* = \frac{T_0}{T_Z} \times \frac{(\partial \Delta F/\partial \sigma^*)_Z}{(\partial \Delta F/\partial \sigma^*)_0} \qquad (65)$$

the Taft equation provides a set of parameters, σ^*, resembling the Hammett sigma-values, that measure the electronic and electrostatic effects of substituents relative to the methyl group. Table XX illustrates the values of the parameter applicable to aliphatic substrates. Table XVIII of section III-A-9 summarizes the values for *o*-substituents (σ_0^*).

TABLE XX

ALIPHATIC SUBSTITUENT POLAR PARAMETERS

Substituent	σ^*	Substituent	σ^*
1. Cl_3C	+2.65	13. $ClCH_2$	+1.05
2. CH_3O_2C	+2.00	14. CF_3CH_2	+0.92[a]
3. CH_3CO	+1.65	15. CH_3COCH_2	+ .60
4. C_6H_5	+0.60	16. CH_3OCH_2	+ .52
5. H	+ .49	17. $C_6H_5CH_2$	+ .215
6. CH_3	.00	18. $NO_2(CH_2)_2$	+ .50[a]
7. C_2H_5	− .10	19. $Cl(CH_2)_2$	+ .385[a]
8. *i*-C_3H_7	− .19	20. $CF_3(CH_2)_2$	+ .32[a]
9. *t*-C_4H_9	− .30	21. $C_6H_5(CH_2)_2$	+ .08
10. $(CH_3)_3N^+CH_2$	+1.90	22. *n*-C_3H_7	− .115
11. $CH_2SO_2CH_2$	+1.32[a]	23. *n*-C_4H_9	− .13
12. $CNCH_2$	+1.30	24. cyclo-C_6H_{11}	− .15[a]

[a] Derived other than from defining relationship (equation 62).

It is important to note that the σ^*-values are determined by direct electrostatic and inductive effects of the group *when attached to a saturated carbon atom.* The Hammett sigma-values concern the group attached to an aromatic carbon atom in a system with which it can also engage in resonance interactions (resonance polar effects). The Taft equation fails when the substituent enters into resonance with the reaction center to different extents in the initial and final (or transition) states.

The factor 2.48 was introduced into equation 63 in an attempt to place the σ^*-values on the same scale as the Hammett sigma-values. Basically it has been assumed that the reacting side chain will show the same susceptibility to substituent effects irrespective of the nature of the system, aliphatic, *o*-substituted aromatic or aromatic with free *o*-positions, to which it is attached. Examination of (a) the relative magnitudes of ρ^*, ρ_0^* and ρ-values calculated based on this initial assumption; (b) Hammett rho-values for reaction series involving constant *o*-substituents and (c) alternative methods of producing a common scaling of Hammett and Taft parameters, suggest that there is no foundation for the assumption (260).

The fact that the two sets of substituent parameters are on different scales in no way affects their utility *within their individual ranges of application.* Their use in combination for theoretical purposes is, however, seriously handicapped. This is particularly true when, as discussed in section III-A-3, the assumption of equal rho-values is used to compute aromatic inductive parameters through the effect of 4-substituents in the bicyclo[2,2,2]octane-1-derivatives. The value of the parameters in the Taft equation is to be judged on the method of their derivation, their consistency with theory and their reliability in the prediction and interpretation of results completely independent of the Hammett equation.

Not only are the σ^*-values in accord with qualitative polarities of alkyl groups predicted on theoretical grounds, (*cf.* 132, 257), but precise additive relationships are observed that are to be expected, at least to a limited extent, from the presumed mode of operation of polar effects. (Such additivity would not be expected and indeed has not been observed for steric and resonance effects.) Some of these relationships are illustrated in Table XXI.

TABLE XXI

ADDITIVITY OF σ^*-VALUES

Substituent	σ^*	Ratio	Substituent	σ^*	Sum
CH_3CO	1.65	2.75	$2C_6H_5CH_2$	0.215	0.43
CH_3COCH_2	0.60		*cf.* $(C_6H_5)_2CH$		.405
$ClCH_2$	1.050	2.73			
$Cl(CH_2)_2$	0.385		$C_6H_5CH_2$	0.215	
CF_3CH_2	.92	2.9	C_2H_5	−0.100	.115
$CF_3(CH_2)_2$	.32	2.7	*cf.* $C_6H_5(CH_3)CH$		.105
$CF_3(CH_2)_3$	.12				
C_6H_5	.60	2.8	$C_6H_5CH_2$	0.215	.77
$C_6H_5CH_2$	.215	2.7	$HOCH_2$	0.555	
$C_6H_5(CH_2)_2$	.080		*cf.* $C_6H_5CHOHCH_2$		.765
$CH_3CH{=}CH$	.360	2.8			
$CH_3CH{=}CHCH_2$	.13				

Taft (242e) has made use of the reduction factor of 1/2.8 (= 0.36) corresponding to the interposition of a methylene group to compute σ^*-values for X–CH_2 groups not otherwise available. It has been pointed out that a factor of 1/3 was proposed many years ago by Derick (68). A similar factor appears in the treatment due to McGowan, discussed in section III-A-3. Suitable σ^*-values have not been determined from which an assessment for the relay of polar effects across other groupings can be made, but the separation of inductive and resonance polar effects in aromatic systems (section IIIA3) suggests a factor of 0.5 to 0.6, appropriate to two aromatic carbon atoms.

3. Reaction and Substituent Parameters for Steric Effects

Having achieved a quantitative scale of substituent polar effects applicable to *o*-aromatic and aliphatic systems, it becomes possible to separate steric contributions from the log (k/k_0) values (by subtracting $\sigma^*\rho^*$) *provided these are the only additional variables.* Taft (238) has carried out this separation in the case of *o*-substituted benzene substrates using the σ_0^*-values of Table XVIII of section III-A and the Hammett rho-values. For base-catalyzed ester hydrolysis reactions the steric parameters (E_S) relative to methyl obtained are given in Table XXII. The steric parameters in no way parallel the polar effects of these substituents

TABLE XXII

STERIC PARAMETERS FOR *o*-SUBSTITUTED BENZOATES

Substituent	E_S	Substituent	E_S
C_6H_5	−0.90	OCH_3	+0.97 ± 0.00
NO_2	− .71 ± 0.11	OC_2H_5	+ .86 ± .04
I	− .20 ± 0.07	Cl	+ .18 ± .08
CH_3	.00	Br	+ .01 ± .17

(measured by σ_0^* or σ), but are in agreement with their relative van der Waals radii and the requirements of atomic models (242d). The unsubstituted and *o*-fluoro compounds fit the Hammett equation and would correspond to E_S-values of +0.49. No comment has been made on the E_S-values for the methoxy and ethoxy groups which imply steric *facilitation.* Presumably hydrogen-bonding effects are involved here.

From the mode of obtaining the σ^*-values, the above procedure is equivalent to assuming (quite reasonably as indicated by Hammett rho-values) that acid-catalyzed esterifications and ester hydrolyses are insensitive to polar effects. Or, as a modification of equation 63

$$\delta E_S \equiv \log (k/k_0)_B - \sigma^*\rho^* \equiv \log (k/k_0)_A \qquad (66)$$

where δ, unity for benzoate reactions at 25°, accounts for other reactions having different susceptibilities to steric effects.

One other reaction series, where *o*-substituents appear to operate solely through their steric effects, the acid-catalyzed hydrolysis of benzamides has been correlated by equation 66 (241). The δ-value (0.812 ± 0.032) and the existence of the correlation are compelling evidence that ethyl benzoates and benzamides are hydrolyzed by very similar mechanisms.

By means of equation 66 using rho-values for unhindered *m*- and *p*-benzoates, an estimate has been made of the polar ($\sigma^* = -0.026$ relative to H) and steric ($E_S = -0.402$ relative to CH_3) effects of the 2,3-benzo substituent (192). *peri*-Interactions in α-naphthyl substrates are thus large, being intermediate between the steric effects of iodo and nitro groups.

Unlike the aromatic series, there are few aliphatic reactions in which steric effects do not play an important role in reactivity determination. (Hence the limitations of the Hammett and simple Taft equations.) Thus it is in the aliphatic series where the examination of steric effects has been most fruitful, although once again the range of substituents is dominated by alkyl groups. For a number of acid-catalyzed reactions, and a few others, the "*linear steric energy relationship,*" equation 66, is applicable (238, 241). However, the precision is generally lower, the number of assumptions required greater and the range of permissible structural variations less certain than the "*linear polar energy relationships,*" equations 63 and 64. Equation 63 remains valid if the transition states for ester hydrolysis and esterification still contain resonance interactions provided their reduction has been essentially the same in both acid- and base-catalyzed reactions. Equation 66 requires that $\log (k/k_0)_A$ contains no resonance contribution, and since this has been used to define the E_S-scale there is no certainty that the parameters do not contain some non-steric components. Some steric parameters, from references 238 and 242d, are listed in Table XXIII. No additive relationships are observed. Increasing substituent bulk has a "telescoping" effect.

TABLE XXIII

STERIC PARAMETERS FOR ALIPHATIC SUBSTRATES

Substituent	E_S	Substituent	E_S
CH_3	0.00	n-C_3H_7	−0.36
C_2H_5	− .07	n-C_4H_9	− .39
i-C_3H_7	− .47	n-C_5H_{10}	− .40
t-C_4H_9	−1.54	cyclo-C_4H_7	− .06
neo-C_5H_{11}	−1.74	cyclo-C_5H_9	− .51
CF_3	−1.16	cyclo-C_6H_{11}	− .79
CCl_3	−2.06	cyclo-C_7H_{13}	−1.10
CBr_3	−2.43		

Steric (S) and polar (P) effects are completely different functions of structure and may originate from independent variables (resonance interactions are *not* independent of steric effects). Both variations may be

$$\mathrm{d} \log k = \left(\frac{\partial \log k}{\partial P}\right)_S \times \mathrm{d}P + \left(\frac{\partial \log \mathrm{k}}{\partial S}\right)_P \times \mathrm{d}S, \textit{ or}$$

$$\log (k/k_0) = \sigma^*\rho^* + \delta E_S \qquad (67)$$

examined by a four-parameter equation utilizing a common standard (CH_3–). As discussed in section II, although equation 67 has a greater potential range of application than equations 64 and 66 it suffers more restrictions. The simple application of this modified Taft equation to the base-catalyzed transmethylation of *l*-menthyl esters (195) yields

$$\log (k/k_0) = (2.702 \pm 0.067)\sigma^* + (1.301 \pm 0.055)E_S$$

The pseudo-first order rate constants

$$k_1 = k_2[OH^-] + k_3[OH^-]^2$$

for the hydrolysis of N-methylanilides ($C_6H_5N(CH_3)$-COR) have also been examined (29). The correlation

$$\log (k_3/k_2) = 1.575\sigma^* + 0.713E_S + 0.43$$

is observed, but correlations of $\log (k_2/k_0)$ and $\log (k_3/k_0)$ are of considerably lower precision. Some of the attempts to accommodate the effect of *o*-substituents by the Hammett equation (section II-A-9) lead to expressions of essentially the same form as equation 67.

4. The Estimation of Other Effects Causing Deviations

A large body of reactivity data still can not be correlated by the Taft equation despite the introduction of a term to account for steric effects. There can be many reasons for this as implied by the assumptions discussed above, but in a few cases it is suggested that the deviations may be used as measures of other variables, particularly resonance effects and non-classical bonding interactions.

It has been assumed that any resonance interactions between the carbonyl group and the substituent, especially powerful when α,β-unsaturated, are completely lost in the formation of the ester reaction transition states, whether acid or base catalyzed. This may be true, but it is certainly not the case in several other reaction series. Ionization of the carboxylic acids, where for example benzoic and acrylic acids are abnormally weak, is certainly one of these (238). Another is the acid dissociation of mercaptans (157).

Twenty-four diethyl acetals and ketals of the type $R_1R_2C(OC_2H_5)_2$, where R_1 and R_2 were mostly alkyl groups, yield a partial correlation to equation 64 (158, 159). Several of the substituents that could not be correlated, *e.g.*, those with α,β-unsaturated substituents, were clearly involved in resonance interactions. Excluding these, two parallel lines for the acetals and the ketals were obtained, with some scatter that appears to be related to the number of α-hydrogen atoms (n_H) in the groups R_1 and R_2. Taft and Kreevoy (246) suggest *C–H* and to a lesser extent *C–C hyperconjugative effects* are responsible.

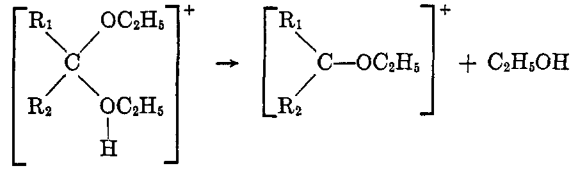
Two equations have been utilized

$$\log (k/k_0) = 3.60\Sigma\sigma^* + 0.54(n_H - 6) \qquad (68)$$

$$\log (k/k_0) = 3.60\Sigma\sigma^* + 0.62n_H + 0.24n_C \qquad (69)$$

where k_0 in equation 68 applies to acetonal and in eq. 96 to formal with the σ^*-values of R_1 and R_2 suitably based; n_C, the number of α-carbon–carbon bonds, accounts to *C–C hyperconjugation.*

It is claimed on the basis of mechanistic studies (188) that in the rate-determining step



the substrate suffers essentially no change in steric interactions but large changes in resonance interactions (but *cf.* acid-catalyzed esterification and ester hydrolysis where both interactions change considerably). Nevertheless the neopentyl and *t*-butyl methyl ketals deviate markedly so that the identification of deviations from log (k/k_0) *versus* $\sigma^*\rho^*$ as purely hyperconjugative is not without question. It is doubtful whether the precision of equation 68 or 69 with one and two adjustable correcting factors, respectively, can by themselves justify this identification. The best support for this treatment is perhaps that a number of similar correlations of non-reactivity data have been observed (see sub-section 5), although no indication of hyperconjugative effects is observed in other reaction series correlated by the Taft equation where changes in resonance interactions occur. There are without doubt electronic effects due to alkyl groups other than induction measured by σ^* (*cf.* 44). Whether these are solely or even partially explained by hyperconjugation, as it is commonly understood, continues to provoke discussion.

More outstanding are the deviations from the Taft equation caused by neighboring group participation (anchimeric assistance). Streitwieser (223) has applied equation 64 to the acetolysis of secondary carbinyl brosylates (*p*-bromobenzenesulfonate) and observed that $k_{obs.}/k_{calcd.}$ for the *trans*-4-X-cyclohexyl compounds has the values 320 ($X = CH_3COO$), 450 ($X = Br$) and 1.5×10^6($X = I$). Deviations in the case of the solvolyses of tertiary halides in aqueous ethanol though considerably smaller provide also evidence of steric accelerations. Primary sulfonates yield a satisfactory linear correlation.

5. The Correlation of Non-reactivity Data

As in the case of the Hammett equation there are a number of series accommodated by the Taft equation that concern some physical property of a single state. Such correlations provide in principle a means of exact definition of the σ^*-values and ultimately their prediction from theory.

The dipole moments of the alkyl chlorides, iodides, cyanides and amines provide four such series of high precision with widely varying ρ^*-values. The alkyl–hydrogen bond energies in the lower paraffins are also well correlated (242f).

Correlations of spectroscopic data are particularly interesting from the theoretical standpoint since in this sphere mathematical electronic theory and experiment make their closest approach. Taft (242f) reports that the quadrupole coupling constants of C–Cl bonds in RCl are well correlated by equation 64, but the C–O stretching frequencies in the infrared spectra of alcohols are less satisfactory. Subsequently Brown (43) has found that the intensity (A) of this C–O vibration shows a more precise linear dependence on Taft's substituent parameters. Several workers (*e.g.*, 42, 170, 190) have investigated σ^*-dependence of a variety of infrared absorptions both in terms of frequency shifts and intensity changes. While vibrational transition will in many cases lead to changes in steric interactions (*cf.* 18), the Franck–Condon principle should prohibit such changes in electronic transitions (but *cf.* 215). For the most part, however, attempted correlations of ultraviolet spectral data have not been successful, although the $n \rightarrow \pi^*$ transitions of aliphatic nitro compounds (7) and carbonyl compounds (205) seem to be exceptions. In these series resonance effects due to alkyl groups have been estimated in terms of C–H and C–C hyperconjugation.

Certain equilibria although dependent not upon a single state but upon energy differences between two states are conveniently mentioned in this sub-section. Oxidation-reduction potentials of substituted ferrocenes (160), the enthalpies of olefin hydrogenation (246) and the free energies of ketone hydrogenation (246) are correlated using the σ^*-values but with deviations. Taft and Kreevoy (246) account for these deviations by hyperconjugative parameters in the manner described in sub-section 4. Brown (44), however, has pointed out that while inductive and dispersion effects of alkyl groups oppose each other in the system used to define σ^* they probably act in the same direction in ketone hydrogenation. Thus the identification of alkyl group deviations is ambiguous.

C. THE HANSSON EQUATION

The correlation of multiple variations has been discussed in general terms in section II and more specifically as modifications of the Hammett and Taft equations. The simultaneous variations of structural features is a special case that may profitably extend the utility of these "basic" equations. Multiple substitutions in one reactant are readily accommodated in the absence of mutual interactions by the additive nature of substituent parameters. Structural variations in two reactants lead to a four-parameter equation.

Consider the reactions

$$RX + RY \rightarrow \text{products } (k_{12})$$
$$R_0X + R_0Y \rightarrow \text{products } (k_{00})$$

where the second is considered as the standard member of a series obtained by variations of R in both RX and RY (*e.g.*, R_1X and R_2Y). Two approaches to the relative rate constants k_{12}/k_{00} are possible if the Taft equation, for example, is applicable to the four individual reaction series.

$$\begin{aligned}\log (k_{12}/k_{00}) &= \log (k_{12}/k_{10}) + \log (k_{10}/k_{00}) \\ &= \sigma_2^*\rho_{X_1}^* + \sigma_1^*\rho_{Y_0}^* \qquad (70)\end{aligned}$$

$$\begin{aligned}\log (k_{12}/k_{00}) &= \log (k_{12}/k_{02}) + \log (k_{02}/k_{00}) \\ &= \sigma_1^*\rho_{Y_2}^* + \sigma_2^*\rho_{X_0}^* \qquad (71)\end{aligned}$$

where σ_1^* and σ_2^* are substituent parameters for R_1 and R_2, ρ_{X_1} and ρ_{X_0} are reaction parameters for R_1X and R_0X respectively, with any RY and ρ_{Y_1} and ρ_{Y_0} are reaction parameters for R_2Y and R_0Y, respectively, with any RX.

Equations 70 and 71 provide measurements of the same quantity and are valid provided *all* four individual Taft correlations are valid. It follows then that

$$(\rho_{X_1}^* - \rho_{X_0}^*)/\sigma_1^* = (\rho_{Y_2}^* - \rho_{Y_0}^*)/\sigma_2^* = q \qquad (72)$$

where q is independent of the substituents involved and the nature of the reaction centers but depends upon environmental conditions (*cf.* the τ-parameters of Hine (122, 123) discussed in section III-A-3).

From equations 70, 71 and 72

$$\log (k_{12}/k_{00}) = \sigma_1^*\rho_{Y_0}^* + \sigma_2^*\rho_{X_0}^* + \sigma_1^*\sigma_2^*q \qquad (73)$$

correlates structural changes in both reactants by means of a four-parameter equation (q is determined by the other four parameters) alternative to equations 70 and 71.

For $q = 0$, *i.e.*, structural changes in one reactant leave the susceptibility of the reaction to substituent changes in the second reactant unchanged, then all three equations reduce to a simplified form as equation 74.

$$\log (k_{12}/k_{00}) = \sigma_1^*\rho_Y^* + \sigma_2^*\rho_X^* \qquad (74)$$

For $q \neq 0$, the situation normally to be expected (*cf.* 260), mean reaction parameters

$$\bar{\rho}_X^* = \frac{1}{n}\,\Sigma\rho_{X_i}^*;\quad \bar{\rho}_Y^* = \frac{1}{m}\,\Sigma\rho_{Y_j}^*$$

could be utilized, in which case

$$\log (k_{12}/k_{00}) = \sigma_1^*\bar{\rho}_Y^* + \sigma_2^*\bar{\rho}_X^* + \delta_{12} \qquad (75)$$

where

$$\delta_{12} = \left(\sigma_1^*\sigma_2^* - \frac{\sigma_1^*}{n}\,\Sigma\sigma_j^* - \frac{\sigma_2^*}{m}\,\Sigma\sigma_i^*\right) q$$

depends upon δ and the differences between σ_1^*, σ_2^* and the mean σ^*-values for substituents in these positions.

A simple expression correlating variations in two substituents will thus be unexpected. It is therefore surprising that Hansson (115) has been able to account for structural variations in both reactants for the additions of amines to epoxides by means of equation 76.

$$\log (k/k_0) = r(s_a + s_0) + t \qquad (76)$$

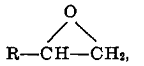
where

k_0 applies to the reaction of ammonia with ethylene oxide
k applies to "any" amine and epoxide
r (= 1, for the reaction of amines with epoxides in water at 20°) depends only upon the reaction
s_a (= 0 for ammonia) and s_0 (= 0 for ethylene oxide) depend only upon the structure of the amine and epoxide, respectively
t is a correcting factor attributed to steric effects added to account for the failure of trimethylamine and triethylamine in almost all cases (t = 0 for ethylene oxide).

The structural parameters listed in Table XXIV were obtained for s_a by averaging the log (k/k_0) values for each of the amines reacting with ethylene oxide, propylene oxide, glycidol and epichlorohydrin, and for s_0 by averaging the log (k/k_0) values for each epoxide reacting with the eight amines.

TABLE XXIV

STRUCTURAL PARAMETERS FOR EQUATION 76

Amine	s_a	Amine	s_a	 R=	s_0
NH_3	0.00	$C_2H_5NH_2$	0.74	H	0.00
CH_3NH_2	0.94	$(C_2H_5)_2NH$	.63	CH_3	− .02
$(CH_3)_2NH$	1.47	$(C_2H_5)_3N$	.36	CH_2OH	− .04
$(CH_3)_3N$	2.23	Pyridine	.14	CH_2Cl	.51

With some additional rate data for the propylene oxide reactions Hannson (116) was able to derive s_a-values for two other tertiary amines and report an excellent correlation for their dissociation constants by means of equation 76 using $r = -0.54$, $s_0 = 0$ and $t = 0$. Primary and secondary amines were not examined in this way although a correlation with the Brønsted equation (section V-A) is reported (116). It already has been noted however (section III-B-1) that the Taft equation gives three separate but essentially parallel regression lines for the primary, secondary and tertiary amine basicities (107). Using the s_a-values for $R_1R_2R_3N$, the solvolyses of tertiary alkyl iodides ($R_1R_2R_3CI$) in aqueous alcohol are poorly correlated by equation 76 using $r = -0.34$. Regarding other epoxide reactions, there is a satisfactory correlation of their base-catalyzed cleavage in water at 25° using $r = 1.03$ and $s_a = 0$ although a slightly modified set of s_0-values is required. Thus tests of equation 76 for other reaction series are too few to permit any judgment on its generality.

With the correcting factor t omitted, equation 76 is clearly a form of equation 75 with

$$s_a \cong \sigma_1{}^*\bar{\rho}_Y{}^* \text{ and } s_0 \cong \sigma_2{}^*\bar{\rho}_X{}^*$$

where

$\sigma_1{}^* = \Sigma\sigma^*$ for substituents in the amine (based on $\sigma_H{}^* = 0$)
$\sigma_2{}^*$ applies to the substituent in the epoxide (based on $\sigma_H{}^* = 0$)
$\bar{\rho}_Y{}^*$ applies to the addition of various amines to an "average" epoxide
$\bar{\rho}_X{}^*$ applies to the addition of an 'average' amine to various epoxides and adjustments have been made in s_0 and s_a such that $\delta_{12} \simeq 0$.

Parker and Isaacs (193) have drawn attention to the fact that in examining structural effects on epoxide reactions attention must be paid to the direction of ring opening. Equation 76 presumes that attack occurs exclusively at the same site in all four epoxides. Only a few limited Taft correlations of reactions of epoxides with base have been reported.

It is found that the Hansson equation apparently correlates the basicity of amines well but the solvolysis of tertiary alkyl iodides poorly, whereas the Taft equation cannot correlate the former by a single line (107) but the tertiary alkyl chlorides (223) form a satisfactory series.

Contributions from steric factors would be expected in all the epoxide–amine reactions above. On examination of the reaction of a series of methylpyridines with propylene oxide calculated s-values showed no additive relationships and the t-term as a correction for steric factors was shown to be invalid (117).

IV. THE CORRELATION OF CHANGES IN THE REACTION MEDIUM

A. THE GRUNWALD-WINSTEIN EQUATION

1. *General Discussion*

The understanding of the influence of reaction medium on reactivity is difficult even at the qualitative level. The problem resolves itself to one of recognizing the precise functions of the solvent molecules both individually and collectively, and of devising some means of measuring these functions. Various properties of pure and mixed solvents are readily measured with high precision, but the relationship between these properties and the required functions are complex and little understood.

For reactions involving ions, ionic intermediates or transition states the principle of Hughes and Ingold (127), that increases in ion solvating power favor the creation and concentration of charge, provides the basis for further developments. For each solvent, and each component of a solvent mixture, account must be taken of changes in electrostatic free energy of ions due to bulk dielectric properties, ion solvation, solvation and other association effects of neutral molecules, and covalent bonding interactions between the substrate and the solvent, or component thereof, acting as a reagent.

Numerous theoretical treatments of solvent effects in terms of the bulk dielectric constant (D) have been suggested. The most fruitful of these apply to equilibria, for example the logarithms of relative acid strength which are linear with $1/D$ (183), particularly in single component solvents. Although the Kirkwood model (150) leads to a $(D - 1)/(2D + 1)$ term, which has been examined (*cf.* 164), at high values of D, this treatment for rates or equilibria can lead to a linear dependence of $\log k$ on $1/D$ (125, 165). Empirical correlations of $\log k$ and activation energies for Michael addition reaction (145) and of activation energies for solvolyses of sulfonic esters (129, 130) in mixed solvents with the dielectric constant itself are somewhat surprising. The bulk dielectric constant, especially for mixed solvents, is not the quantity appropriate to the molecular level although the "true" value may show a simple dependence upon it.

The composition of a mixed solvent in the vicinity of the solute may be different from that of the over-all solution (*cf.* 219). These differences can arise at one extreme from differences in weak attractive forces and at the other extreme from complex formation irrespective of whether the solute is ionic or neutral. Such effects can be considered under the general heading of solvation for which one solvent component may be preferred. A further extreme may be distinguishable (*cf.* 112) in which one component of the solvent is acting as a reagent in a step which is rate determining. It has proved difficult to decide at what stage specific solvation becomes covalent bonding with a reagent.

Attempts to assess the various solvent influences by empirical relationships may be considered in terms of (a) dielectric constant mentioned above, (b) mole fraction of a particular component, (c) solvating power, and (d) effectiveness as a reagent. Mole fraction (N) correlations form part of equation 77 due to Hyne and Robertson (130)

$$E_a = -47.18(D - \alpha + 1.43[N_{H_2O}(M.V.)_{H_2O} + N_{ROH}(M.V.)_{ROH}]) + 25{,}580 \quad (77)$$

which reproduces moderately well the activation energies (E_a) for the solvolyses of methyl benzenesulfonate ($\alpha = 0$) in water–alcohol (ROH) mixtures. The molecular volume (M.V.) of each component is also included. A number of other investigators have observed a limited dependence of log k on mole fraction, or activity of one solvent component, often in opposite direction to that expected from changes in dielectric constant (*cf.* 112). The Grunwald–Winstein solvent parameters also show this (sub-section 2). Solvating power is presumed to be the property assessed through the present linear free-energy relationship and some deviations from it are attributed to the solvent operating as a reagent. Reagent effectiveness is the subject of section V where the Swain equations overlap considerably the Grunwald–Winstein equation.

2. The Correlation of Solvolysis Rates

The mechanisms of substitution at a saturated carbon atom where the solvent functions as reagent cannot be resolved by kinetics in terms of unimolecular or bimolecular (or other) processes. However, the two mechanistic categories postulated are expected (95) to show such markedly different changes in reactivity with solvent changes that solvent effects have been suggested as diagnostic of mechanism. Grunwald and Winstein (103) have reasoned that in the S_N1 or "*limiting*" mechanism, which has a rate determined by the ionization of the substrate, ion solvating power will be the dominant factor. This factor, and certain specific factors such as hydrogen bonding tendency and electrophilic catalysis, should then be measurable as a parameter, Y, by the effect of solvent changes on log k^0 for some arbitrarily chosen standard substrate (*e.g.*, *t*-butyl chloride) reacting by this mechanism, *i.e.*

$$\mathbf{Y}_A - \mathbf{Y}_B \equiv \log k_A{}^0 - \log k_B{}^0 \quad (78)$$

where $k_A{}^0$ and $k_B{}^0$ are the specific rate constants for the solvolysis of *t*-butyl chloride in solvents A and B, respectively. Selecting as standard solvent B (*i.e.*, $\mathbf{Y}_B = 0$) 80% v./v. aqueous ethanol, the Grunwald–Winstein equation (79) was set up to correlate the

$$\log k_A - \log k_0 = m\mathbf{Y}_A \quad (79)$$

solvolysis rate (k_A) for any substrate reacting by the S_N1 or "*limiting*" mechanism in any solvent (A) relative to its rate in the standard solvent (k_0) in terms of the "*ionizing power*" ($\mathbf{Y}_A$) defined by equation 78 and a proportionality factor, m, independent of the solvent. A selection of the **Y**-values from the compilation of Fainberg and Winstein (81) is given in Table XXV. These differ significantly from the original listing (103) following the redetermination of some of the rate constants for *t*-butyl chloride. A greater range of solvent mixtures and compositions is covered.

TABLE XXV

Y-VALUES (25°)[a]

Components (by volume)

% A	A = Ethanol B = Water	Methanol Water	Dioxane Water	Acetone Water	Acetic[b] acid Water	Formic[b] acid Water	Acetic[b] acid Formic acid
100	−2.033	−1.090	...	...	−1.639	2.054	−1.639
95	−1.287[c]	...	...	−2.76[d]	...	2.163	...
90	−0.747[c]	−0.301	−2.030	−1.856	...	2.222	−0.929[c]
80	.000	.381	−0.833	−0.673	...	2.318	...
70	.595	.961	0.013	0.130	...	...	...
60	1.124	1.492	0.715	0.796	1.519	...	...
50	1.655	1.972	1.361	1.398	1.938	2.644	0.757
40	2.196	2.391	1.945	1.981	2.312	...	...
30	2.721	2.753	2.455	2.482	...	...	...
25	2.908	...	...	2.689	2.843	3.100	1.466
20	3.051	3.025	2.877	2.913	...	...	...
10	3.312	3.279	3.217	3.230	...	...	1.862
0	3.493	3.493	3.493	3.493	...	...	2.054

Acetic acid–water[b]		Dioxane–formic acid[b]		Other solvents	
M.H$_2$O	**Y**	% Dioxane	**Y**	Solvent	**Y**
0.50	−1.400	80	−2.296[c]	Formamide	0.604
2.00	−0.863	60	−0.677	n-$C_3H_7CO_2H$	1.7[e]
4.00	− .404	40	0.402	*i*-Propyl alc.	−2.73[e]
8.00	.193	20	1.291	*t*-Butyl alc.	−3.26[d]
16.00	.984			Acetic acid[f]	−1.675

[a] From ref. 81. [b] All solutions containing 0.065–0.068 m lithium acetate and/or formate. [c] Estimated from data at 50° and 75°. [d] Estimated from data on *t*-butyl bromide. [e] Estimated from data on α-phenylethyl chloride. [f] Estimated value at zero salt concentration.

Although the original **Y**-values served to correlate satisfactorily through equation 79 the solvolyses of six substrates besides *t*-butyl chloride, the data of benzhydryl chloride in aqueous acetone required modified values that were used also for α-phenylethyl chloride (103). Thus a unique set of **Y**-values (or a unique *m*-value for each substrate) was questionable from the start, although not at that stage serious.

Subsequently (270) the application of equation 79 to primary substrates, which may react by the S_N2 or *nucleophilic* (N) mechanism, and secondary substrates showing borderline behavior was examined. Linear plots of log *k* versus **Y** were obtained for primary aryl sulfonates in alcohol–water mixtures, but in acidic solvents *k* is several hundredths smaller than the **Y**-value requires. For primary halides the log *k versus* **Y** plots are significantly curved to give low log *k* values at high **Y**. Examining the "borderline" isopropyl and benzyl substrates, equation 79 gave a fairly satisfactory correlation for alcohol–water solvents with deviations smaller than in the case of primary substrates. Since both of these types of substrate are also dependent upon the nucleophilic power of the solvent, the parameter *m*, supposedly independent of the solvent, must contain a component proportional to **N**/**Y**, where **N** is a measure of solvent nucleophilicity. In the range of solvent compositions and types correlated this component must have remained fairly constant.

The first test of the suitability of the *t*-butyl chloride based **Y**-values and of the utility of equation 79 (270) was limited in the range of solvent types. The solvolyses of *trans*-2-bromo- and *trans*-2-methoxycyclohexyl brosylates and 2,2,2-triphenylethyl tosylate (*p*-toluenesulfonate), placed with certainty in the S_N1 or *limiting* category by virtue of neighboring group participation, were found to be well correlated. Subsequent investigations covering a wider range of binary solvent mixtures (82, 83, 84, 269) produced poor correlations covering all solvent types, but were improved to follow equation 79 with high precision by treating each binary solvent mixture separately. The **Y**-values are thus retained as a measure of solvent function and specific effects are accommodated to some extent by the *m*-values and in the main by $(\log k_0)_{\text{calcd}}$.

Table XXVI lists some of the *m*-values and other relevant quantities. The improvement in the correlation of the solvolyses of *t*-butyl bromide by omitting acidic solvents can be seen. Treating each binary solvent separately gives mean probable errors of fit of 0.015 at 0° and 0.010 at 25°. The major modification in parameters occurs in $(\log k_0)_{\text{calcd}}$; that is, a dispersion of approximately parallel lines is obtained. The most precise correlation observed for α-phenylethyl chloride and bromide is that in aqueous acetic acid solutions, where the probable error of fit (*r*) has about the same magnitude as the estimated error in log *k*. For the

TABLE XXVI

m-VALUES FOR S_N1 OR "LIMITING" SOLVOLYSES

Substrate	Temp., °C.	Solvents	u^a	m	$(\log k_0)^b$ calcd.	r^c	Source
t-Butyl chloride	25	All solvents	..	1.000	...	...	81
t-Butyl bromide	0	All solvents	27	1.001	4.918	0.166	83
	25		28	0.924	3.494	.155	83
	0	All except acidic solvents	23	.953	4.821	.090	83
	25		22	.917	3.383	.044	83
t-Butyl nitrate	25	All solvents	5	.839	3.442	.046	83
t-Amyl chloride	25	Aq. ethanol	2	.87	4.82	...	83
t-Amyl bromide	25	Methanol and aq. ethanol	2	.862	3.233	0.026	83
α-Phenylethyl chloride	25	All solvents	35	1.056	5.094	0.190	82
	50		29	0.974	3.843	.200	82
	50	Aq. acetic acid^d	6	1.045	3.887	.005	82
α-Phenylethyl bromide	0	All solvents	25	1.123	5.415	.321	83
	25		26	1.031	3.955	.294	83
	25	Aq. acetic acid^d	5	1.245	4.364	.003	83
Neophyl chloride	50	All solvents		0.835^e	...	.030^f	84
	75			.821^e	...		84
Neophyl bromide	50			.821^e	...	.013^f	84
	75			.756^e	...		84
Benzhydryl chloride	25	All solvents	24	.927	3.062	.408	269
Benzhydryl bromide	25	Aq. acetic acid^d	4	1.687	2.017	.008	269
	25	Aq. dioxane	3	0.954	2.442	.008	269
Benzhydryl fluoride	25	Aq. ethanol	2	0.98	6.56	...	269
Trityl benzoate	25	Aq. acetone	2	0.79	4.02	...	269
Trityl thiocyanate	25	Aq. acetone	3	0.261	3.076	0.010	269

[a] Number of data used in correlation. [b] Intercept of regression line at Y = 0. [c] Probable error of fit, $r = 0.6745\sqrt{d^2/(n-2)}$ where *d* are the differences between observed and calculated log *k* values. [d] Aqueous acetic acid solvents all contain *ca.* 0.07 *M* lithium acetate. [e] Average of the various *m*-values for several solvent pairs. [f] Average of probable errors of separate correlation for several solvent pairs.

correlation of separate solvent pairs the data on α-phenylethyl chloride gives mean probable errors of fit of 0.045 at 25° and 0.032 at 50°. The two separate correlations for benzhydryl bromide yield the greatest divergence of m-values observed; but in general the variations in m are slight. Separate correlations of benzhydryl chloride have an average r of 0.002.

In several cases curvature of the log k *versus* **Y** plots for particular solvent pairs is evident. In other cases curvature, at least at high water concentrations, must occur since all lines for aqueous solvents must pass through the point for pure water. For α-phenylethyl chloride this curvature was assessed by means of a power series in **Y** with terms greater than $\mathbf{Y}^2$ neglected, *i.e.*

$$\log k = a + b\mathbf{Y} + c\mathbf{Y}^2 \qquad (80)$$

Equation 80 gives an improved correlation (average r = 0.009) since an additional adjustable parameter (c) has been introduced. The significance of the equation is uncertain, having $a \simeq (\log k_0)_{\text{calcd}}$ and $b \simeq m$ of equation 79, while c never exceeds 5% of b (82).

In terms of the generalized relationship (equation 13 of section II)

$$X_{\text{i}} = Y_{\text{i}} = \log k_{\text{i}}^{t\text{-BuCl}} - \log k_0^{t\text{-BuCl}} = -(\Delta F_{\text{i}}^* - \Delta F_0^*)_{t\text{-BuCl}}/2.3RT \qquad (81)$$

and (A = t-BuCl, T = 25° throughout)

$$G_{\text{x}}^{\text{AB}} = m_{\text{AB}} = (\partial\Delta F^{\text{B}}/\partial x)/(\partial\Delta F^{\text{A}}/\partial x) = (\partial\Delta F^{\text{B}}/\partial Y)/(\partial\Delta F^{\text{A}}/\partial Y) \qquad (82)$$

Equations 81 and 82 provide the basis for assessing the correlations and dispersions discussed above.

If the reaction series correlated by the Grunwald–Winstein equation are, as is supposed, dependent solely on the ionization of the substrate, a unimolecular process, then the rate constant k_{i}, in a particular solvent i, may be expressed in terms of *degenerate activity coefficients* of the reactant (f) and transition state (f_*) by reference to 80% v./v. aqueous ethanol as the standard state. Thus

$$\mathbf{Y}_{\text{i}} = \log k_{\text{i}}^{\text{A}} - \log k_0^{\text{A}} = \log (f^{\text{A}}/f_*^{\text{A}})_{\text{i}} \qquad (83)$$

$$\therefore\ m_{\text{AB}}\mathbf{Y}_{\text{i}} = \log (f^{\text{A}}/f_*^{\text{A}})_{\text{i}}/\log (f^{\text{B}}/f_*^{\text{B}})_{\text{i}} \qquad (84)$$

where f^{A} is the degenerate activity coefficient of A(t-butyl chloride) and f_*^{A} is the degenerate activity coefficient of the transition state for its ionization in the solvent i.

If the solvolysis of t-butyl chloride (*cf.* 54) is anything but unimolecular, a more complicated expression than equation 83 will result. However, even in this "simple" case the **Y**-parameter has to account for changes in activity of both the substrate, a neutral molecule and the transition state, a partially ionized configuration. While the latter may depend in the main on "ionizing power," there is no reason to suppose this to be the major factor controlling the former. There have been few investigations of substrate activity under the conditions of solvolysis. It has been found, however, that for the alkyl chlorides and bromides *both* substrate and transition state activities change markedly between 24% and 1% aqueous ethanol (61). There are indications (101) that large organic cations, anions and neutral molecules interact with solvent molecules to similar extents. In addition, other specific factors such as hydrogen bonding between the solvent and the leaving group cast doubt upon the identification of the variable measured by the **Y**-values. Separate correlations for different binary solvent mixtures could be attributed not only to variable m-values, but also to the inadequacy of a unique set of **Y**-values.

In acidic solutions of high dielectric constant a condition more stringent than equation 84 is required by Hammett and Deyrup (111) to set up the H_0-acidity function (*cf.* 194). In its definition and its use in investigations of acid-catalyzed reactions the activity coefficient ratios must remain constant for a particular medium and "acidity" for all uncharged bases unlike equation 84 which accommodates substrate variations by means of m_{AB}. In solvent mixtures to which the Grunwald–Winstein equation is applied the H_0-function loses its original meaning. Grunwald, Berkowitz, Gutbezahl and Marshall (100, 102, 104, 105, 178) have made extensive studies of solvent effects on acidity and basicity which are discussed in sub-section 3.

Fainberg and Winstein (81) have examined the **Y**-values of various solvents in considerable detail. The observations of Cropper, Speith and Olson (64) that the solvolysis of t-butyl chloride in various aqueous solvents is linear with mole fraction of water over limited ranges on further examination appears to be due to inflections in the **Y** *versus* $N_{\text{H}_2\text{O}}$ curves. For the various solvent pairs a power series may be used to express **Y** in terms of $N_{\text{H}_2\text{O}}$.

$$\mathbf{Y} = a + bN_{\text{H}_2\text{O}} + cN_{\text{H}_2\text{O}}^2 + dN_{\text{H}_2\text{O}}^3 + eN_{\text{H}_2\text{O}}^4 \qquad (85)$$

The coefficients were determined by multiple regression so that equation 85 can be used to predict **Y**-values at intermediate compositions with high precision. No theoretical or interpretative significance can, however, be attached to this equation. Several functions of the bulk dielectric constant were examined, but a linear dependence of **Y** was observed only over very small ranges. A different curve was described for each binary solvent. This is all evidence of the variety of functions contributing to the **Y**-values.

As in the case of the Hammett equation (section III-A) the free energy changes encompassed by the linear correlations are composite quantities which may be factored into enthalpy (ΔH) and entropy (ΔS) terms. These factors would be expected to be different functions of solvent changes but from equation 82

$$m_{\text{AB}} = \frac{(\partial\Delta H^{\text{B}}/\partial\mathbf{Y}) - T(\partial\Delta S^{\text{B}}/\partial\mathbf{Y})}{(\partial\Delta H^{\text{A}}/\partial\mathbf{Y}) - T(\partial\Delta S^{\text{A}}/\partial\mathbf{Y})} \qquad (86)$$

Both $(\partial \Delta H/\partial \mathbf{Y})$ and $\partial \Delta S/\partial \mathbf{Y})$ must be constant to satisfy equation 86 and hence either (a) $(\partial \Delta S/\partial \mathbf{Y}) = 0$, *i.e.*, isoentropic; (b) $(\partial \Delta H/\partial \mathbf{Y}) = 0$, isoenthalpic; or (c) ΔS and ΔH are linearly related, *i.e.*, isokinetic. Leffler (166) reports a number of isokinetic series covering solvent changes. In pure solvents the solvolysis of *t*-butyl chloride, and hence the **Y**-values, are determined principally by enthalpy changes with the exception of water, a unique solvent in many other solvolyses (*cf.* 129, 130), for which ΔS is some 15 entropy units higher than the average (2.9 ± 0.6 e.u.) (268). In binary solvents, while **Y**, and hence ΔF, shows a smooth, in parts essentially linear, curve when plotted against mole fraction of water, ΔH and ΔS *versus* N_{H_2O} plots are very complex, showing pronounced curvature and abrupt changes of curvature. Isokinetic behavior is observed only over small ranges of variation of composition of binary solvents. Using Henry's law constants determined at various temperatures the effect of solvent on ΔF, ΔH and ΔS for both the reactant, *t*-butyl chloride, and the transition state can be estimated. Both states are found to be subject to important modifications. Whether these changes are dominant in the entropy or enthalpy change depends upon the solvent and the substrate (268).

In addition to the uncertainty as to the variables measured by the **Y**-values, the correlation of different substrates by various *m*-values for different binary solvents places the full responsibility for deviations on the substrate. It has been pointed out (23) that most substrates reacting by the S_N1 or *limiting* mechanism are sterically hindered to bimolecular attack by nucleophiles. Steric inhibition of solvation should be an important factor in such cases and will vary from substrate to substrate and from solvent to solvent. On this basis variable **Y**-values are to be expected.

Even if ionizing power were the only factor requiring consideration, its influence on the rate of ionization of the substrate is only observed indirectly through the rate of solvolysis due to "ion pair return" (*cf.* 267). Thus

$$k_{\text{observed}} = k_{\text{ionization}} \times F$$

where F is the fraction of ions produced that are converted immediately to product.

The wide range of application of equation 79 is thus surprising in view of the variety of factors operating, although for most substrates it is noticeable that m differs little from unity. Apparently a number of variable contributors to the **Y**-values are mutually compensating yielding an essentially constant quantity for each solvent although of uncertain origin. Swain and Mosely (233) have raised the further point that the standard substrate may not be an ideal representative of the S_N1 "limiting" mechanism. They suggest trityl (triphenylmethyl) fluoride as a better choice and their modifications of the Grunwald–Winstein equation are discussed in section VB. It is notable that the solvolyses of trityl fluoride are poorly correlated by the **Y**-values.

Wilputte-Steinert and Fierens (264) have examined a number of features of the Grunwald–Winstein equation. While finding the correlations useful as a diagnosis of mechanism, they consider the **Y**-values so dependent upon the choice of standard substrate as to have limited utility. An extended expression has been developed (266), to accommodate both substituent changes, *i.e.*, series following the Hammett equation, and solvent changes for both the S_N1 limiting mechanism and the other extreme termed "*S_N2 lim.*" This linkage between the Hammett and Grunwald–Winstein equations cannot be fully realized for solvolysis reactions but suitable data, discussed in sub-section 3, are available for acid dissociations. Nucleophilic contributions to solvent effects on borderline solvolyses have been assessed by means of deviations from a linear log k *versus* **Y** plot (265). As indicated above, a satisfactory correlation may result, however, from nucleophilic contributions that remain essentially constant or proportional to the "ionizing power" of the solvent if the solvent variation examined is limited.

3. The Correlation of Other Reactivity Data

Solvent effects on acidity and basicity have been examined by Grunwald and Berkowitz (102) using a treatment running parallel to the application of the Grunwald-Winstein equation to solvolytic reactions. Considering the change in thermodynamic dissociation constants of an acid (HA) with solvent change in terms of degenerate activity coefficients

$$\Delta pK_A \equiv pK_A - pK_A^W = \log f_H + \log (f_A/f_{HA}) \quad (87)$$

where pK_A and pK_A^W are the pK_a values for infinitely dilute solutions in the solvent and in water, respectively, and f_H, f_A and f_{HA} are activity coefficients based on infinitely dilute aqueous solution as the standard state. It was then postulated that for systems of the type $AZ \rightleftarrows AZ'$ and $BZ \rightleftarrows BZ'$, where Z and Z′ are functional groups, that

$$(1/m_A) \times \log (f_{AZ}/f_{AZ'}) = (1/m_B) \times \log (f_{BZ}/f_{BZ'}) = Y_{Z,Z'} \quad (88)$$

This is the same requirement that is necessary for the Grunwald–Winstein equation and more general than the requirement, that $m_A = m_B = 1$, needed to set up the acidity functions (*cf.* 111). $Y_{Z,Z'}$, termed the *activity function*, depends upon the solvent and the change $Z \rightleftarrows Z'$ but, if equation 88 is generally valid, is independent of the radicals A, B, etc.

A set of **Y**-values, so designated for their correspondence with the H_--function (194), was computed for aqueous ethanol solvents (S_a, S_b, etc.) by the method of least squares using equation 89

$$(\Delta pK_{HA} - \Delta pK_{HOAc})_{S_a} = (Y_a/Y_b)(\Delta pK_{HA} - \Delta pK_{HOAc})_{S_b} \quad (89)$$

comparing ΔpK for some acid (HA) with ΔpK for acetic acid (HOAc). By arbitrarily setting $\mathbf{Y}_- = 1.000$ for pure ethanol, a scale differing from that of the Grunwald–Winstein, $\mathbf{Y}_-$-values are obtained as illustrated in Table XXVII; $(m_{HA} - m_{HOAc})$ values then are obtainable from equation 90.

$$\Delta pK_{HA} - \Delta pK_{HOAc} = (m_{HA} - m_{HOAc})\mathbf{Y}_- \quad (90)$$

By an analogous procedure $\mathbf{Y}_0$-values (104), corresponding to the H_0-acidity function (194), were based upon the conjugate acids of uncharged nitrogen bases and scaled upon $\mathbf{Y}_0 = -1.000$ for pure ethanol. Compared in Table XXVII the $\mathbf{Y}$- and $\mathbf{Y}_0$-scales show no correspondence in absolute magnitude showing their greatest sensitivity to changes in solvent composition at opposite ends of the scale. For the 82% w. dioxane in water $\mathbf{Y}_0 = -0.635$ was chosen to set the scale for this binary solvent (178). In this way $\mathbf{Y}_0$-values for aqueous ethanol, aqueous dioxane and aqueous methanol showed a precise correspondence and were essentially equal to $-(1 - w)^2$; where w is the weight fraction of water in the solvent. Thus the $\mathbf{Y}_0$-values apparently are dependent only upon the water content and independent of the other component of a binary solvent.

TABLE XXVII

$Y_{Z,Z'}$-VALUES

Aqueous ethanol (% w. ethanol)	$\mathbf{Y}$[a,c]	Y_0[d]	Aqueous dioxane (% w. dioxane)	$\mathbf{Y}_0$[e]
100	1.000[b]	−1.000[b]	82	−0.635[b]
95	..	−0.882	70	− .522
80	0.964	− .570	45	− .230
65	.924	− .379	20	− .052
50	.816	− .266	0	.000[b]
35	.596	− .136		
20	.349	− .057		
0	.000[b]	− .000[b]		

[a] Estimated precision of $\mathbf{Y}$, ±0.010 for pure ethanol and ±0.02 for aqueous ethanol. [b] By definition. [c] Reference 102. [d] Reference 104. [e] Reference 178.

Table XXVIII lists the proportionality factors $\Delta m = m - m_0$, where m_0 pertains to the standard acid, appropriate to equation 90 or the corresponding expression in $\mathbf{Y}_0$. For the carboxylic acids m decreases with increasing polarity of the substituents in the acid. For the conjugate acids of the amines in aqueous ethanol the same polarity effect may be present but the dominant factor appears to be associated with the number of substituents on the nitrogen atom. However, the Δm-values derived from the data in aqueous ethanol and aqueous dioxane show no correspondence. As in the case of the application of the Grunwald–Winstein equation to solvolyses the m-term carries the burden of general correlation failures.

Hammett rho-values (section III-A) show a solvent dependence that can be rationalized in terms of the Grunwald–Winstein equation (102, 104, 266). When both linear free energy relationships are valid for the reaction series AZ ⇄ AZ′ then

$$(\rho - \rho^0)/\mathbf{Y}_{Z,Z'} = (m - m^0)/\sigma = \beta_{Z,Z'} \quad (91)$$

where ρ and ρ^0 are the Hammett reaction parameters for the reaction taking place in a solvent having $Y_{Z,Z'}$ and the standard solvent, respectively; m and m^0 are substrate parameters for the AZ–AZ′ pair having a substituent, characterized by σ, and no substituent, respectively; $\beta_{Z,Z'}$ is a parameter characteristic of the reaction under consideration and the temperature, but independent of substituents and solvents.

TABLE XXVIII

$(m_A - m_0) = \Delta m$-VALUES

Acid	Δm[a]	r[b,c]	Acid (BH), B =	Δm[d,e]	r[b,f]	Δm[d,g]	r[b,h]
Formic	−0.270	0.017	Ammonia	−0.134	0.018	−1.650	0.015
Acetic	.000	...	Methylamine	.697	.014		
Propionic	.225	0.013	Ethylamine	.454	.020		
Butyric	.317	.010	Dimethylamine	.942	.017		
Isovaleric	.472	.014	Trimethylamine	1.507	.027	−0.402	0.015
Chloroacetic	.024	.013	Aniline	0.000	...	0.000	...
Cyanoacetic	− .189	.015	*o*-Toluidine	.209	0.014		
Glycolic	− .095	.040	*m*-Toluidine	.189	.017		
Lactic	− .175	.018	*p*-Toluidine	− .109	.014	−0.189	0.010
Malonic	− .312	.089	*p*-Anisidine	...	...	− .662	.015
Succinic	− .016	.036	Methylaniline	1.025	0.021	.755	.020
Glutaric	.038	.035	Dimethylaniline	1.873	0.023	1.318	.010
Benzoic	.536	.028					
Salicylic	− .101	.036					

[a] $\Delta m = m_{HA} - m_{HOAc}$ based on $\mathbf{Y}_-$ correlation for aqueous ethanol. [b] r = probable error of fit of eq. 90; *cf.* Table XXVII. [c] Mean value 0.023. [d] $\Delta m = m_{BH} - m_{C_6H_5NH_3}$. [e] Based on $\mathbf{Y}_0$ correlation for aqueous ethanol. [f] Mean value 0.018. [g] Based on $\mathbf{Y}_0$ correlation for aqueous dioxane. [h] Mean value 0.015.

It is reported that the Hammett rho-values for the ionization of substituted benzoic acids in aqueous alcohols (102) and for the ionization of substituted anilines in aqueous ethanol (104) are linearly dependent on $\mathbf{Y}_-$ and $\mathbf{Y}_0$, respectively, with satisfactory precision. It is interesting, but probably coincidental, that $\beta_{\mathrm{CO_2H-CO_2^-}}$ ($= 0.63$) and $\beta_{\mathrm{NH_3^+-NH_2}}$ ($= -0.57$) have similar magnitudes. An adequate test of equation 91 cannot at present be made due to an insufficiency of $\mathbf{Y}_{Z,Z}$-values. In any case the Hammett rho-values change with solvent by amounts which in many cases barely exceed their uncertainties so that success or failure of equation 91 may have little significance.

Several uses to which the activity functions ($\mathbf{Y}_{Z,Z}$) can be put have been suggested by Gutbezahl and Grunwald (104, 105). The H_- and H_0-acidity function can only be useful if the $\mathbf{Y}_-$ and $\mathbf{Y}_0$-values are close to zero or the m-values of the acids studied are identical. In other cases, particularly solvent mixtures of low dielectric constant, the activity functions may assist in the examination of acid–base systems where acidity functions are not applicable. The activity postulate itself has led to estimates of degenerate activity coefficients of single ions, of liquid junction potentials and of ion solvation energies. In a manner resembling the use of acidity functions, the $\mathbf{Y}_0$-values have been used to investigate the mechanism of the specific acid-catalyzed rearrangement of phenylpropenylcarbinol (105), of the racemization of 3-*p*-menthene (163) and of the hydrolysis of substituted *o*-benzoate esters (161).

4. The Correlation of Spectral Data

Although the quantitative aspects of solvent effects on a number of physical properties, such as refractive index (9) and infrared frequencies (17, 19), have been examined, successful correlations have only been achieved for shifts in ultraviolet and visible spectra. These have, however, such an exceptional precision that it is suggested (46, 154, 155, 156) that these measurements provide an independent and accurate means of determining solvent parameters.

Kosower (154, 155, 156) has examined the charge transfer spectra of 1-ethyl-4-carbomethoxypyridinium iodide in a number of aqueous ethanol, methanol and acetone solvents. The absorption maxima can be determined with an accuracy of *ca.* 0.2%. When converted to transition energies (by $E = h\nu$) these measures are termed **Z**-values (in kcal/mole). Excellent linear correlations between the **Z** and **Y**-values (81) are obtained

$$\begin{array}{ll} \text{Methanol–water} & \mathbf{Y} = 0.4163\mathbf{Z} - 35.88 \\ \text{Ethanol–water} & \mathbf{Y} = 0.3534\mathbf{Z} - 29.95 \\ \text{Acetone–water} & \mathbf{Y} = 0.2989\mathbf{Z} - 24.76 \end{array} \tag{92}$$

The regression lines all converge on the point for pure water and cover a range in **Y**-values from $+0.8$ to -3.0 and in **Z**-values from 85 to 73 kcal./mole. With secondary standards, for example the pyridine-N-oxides, it is suggested that **Z**-values for a much wider range of solvents can be determined. Other spectral data and some reactivity data follow the **Z**-values, either linearly or by smooth curves, with satisfactory precision.

Brownstein (46) has extended the treatment by defining S-values for the solvents examined by Kosower as the shift of the absorption maximum of 1-ethyl-4-carbomethoxypyridinium iodide relative to its value in ethanol ($S = 0$). Solvent effects on spectral shifts, reaction rates and equilibrium constants are then expressed by equation 93.

$$\log k_{\mathrm{solv}} - \log k_{\mathrm{EtOH}} = SR \tag{93}$$

where R is dependent only upon the process under examination. Fifty-eight S values from Kosower's work were used to compute R-values for nine "reactions." Continuation of this procedure, employing always at least nine points to determine new R-values, permitted the tabulation of one hundred and fifty-eight S-values and seventy-eight R-values. The data processed were composed of thirty-three series of infrared frequencies, twenty-nine reaction rate or equilibrium series, sixteen series of ultraviolet or visible absorptions and nine series of nuclear magnetic resonance data. In keeping with the observations of Kosower, correlations of solvolysis reactions have the precision of the original Grunwald–Winstein equation. No other reaction or equilibrium studied shows an acceptable correlation. It is noteworthy that electronic and vibrational spectral data show good to moderate correlations, whereas nuclear magnetic resonance spectra show either a poor correlation or no correlation. It appears that the use of equation 92 should be restricted to processes closely resembling that of the defining reaction series, a comment that could be made concerning linear free energy relationships in general.

V. THE CORRELATION OF CHANGES IN THE REAGENT

A. THE BRØNSTED CATALYSIS EQUATION

The earliest known linear free energy relationship is the correlation of acid and base strength with effectiveness as catalysts in reactions subject to general acid–base catalysis (33). Developed empirically from studies of the decomposition of nitramide, the relationship may be expressed by equations 94 and 95.

$$\log k_{\mathrm{A}} = \log G_{\mathrm{A}} + \alpha \log K_{\mathrm{A}} \tag{94}$$

$$\log k_{\mathrm{B}} = \log G_{\mathrm{B}} - \beta \log K_{\mathrm{A}} \tag{95}$$

where k_{A} and k_{B} are the catalytic constants in some process for acid (A) and base (B) catalysis, respectively; K_{A} is the dissociation constant of the acid (A) or the conjugate acid of the base (B); and G_{A}, G_{B}, α and β are "constants" which depend upon the reaction process and the conditions of temperature and solvent.

For specific acid or base catalysis in the same solvent in which K is determined (usually water), α and $\beta = 1$. As α and β tend to zero, catalysis by the solvent swamps all other, and acid–base catalysis can no longer be demonstrated. In reactions subject to general catalysis α and β are positive and less than unity.

Statistical corrections are required in correlating the effect of catalysts of differing types. Brønsted (32) modified his original expressions to the ones now commonly used

$$k_A/p = G_A(qK/p)^\alpha \tag{96}$$

$$k_B/q = G_B(p/qK_A)^\beta \tag{97}$$

where p is the number of equally bound dissociable protons of the acid catalyst (or the conjugate acid of the base catalyst) and q is the number of equivalent sites for protonation in the base catalyst (or the conjugate base of the acid catalyst). Certain ambiguities that remain have been conventionally removed by Bell (11b) by allowing the statistical factors p and q to apply only to protons on different atoms. Thus $p = 1$ for NH_4^+ (not 4) and $q = 1$ for RCO_2^- whereas $p = 2$ for $HO_2C(CH_2)_nCO_2H$ and $q = 2$ for H_2NNH_2. Benson (24) has discussed the general question of statistical corrections in terms of symmetry numbers for reactants and products (or transition states). In many cases, however, the range of variation in k_A (or k_B), K_A and other sources of deviation are such that the statistical correction is a relatively trivial factor.

The decomposition of nitramide is at the same time the most studied and best correlated general base-catalyzed reaction. Equation 97 is adequate to cover an extremely wide range of bases, but only shows high precision when the catalysts are examined separately according to charge type. Even so, bases of the type B^{++} are poorly correlated. Bell (11c) reports the parameters of Table XXIX for aqueous solution at 15°. Within each charge type the bases are all structurally similar. Thus B^- contains fourteen carboxylic anions, primary phosphate and hydroxyl ion. The latter deviates considerably.

The most intensively studied acid-catalyzed reaction is the dehydration of acetaldehyde hydrate in acetone (14b, 16). Forty-five carboxylic acids and phenols are correlated by equation 96 having $\alpha = 0.54$ with a mean deviation of 0.1 log unit.

TABLE XXIX

BRØNSTED CORRELATIONS OF NITRAMIDE DECOMPOSITION IN WATER

Base type	Example	G_B	β	Number of catalysts
B^{--}	Succinate	2.07×10^{-5}	0.87	5
B^{++}	$[Co[NH_3)_5OH]^{++}$	7.8×10^{-3}	.82	7
B^-	Acetate	7.2×10^{-5}	.80	16
B°	Aniline	1.70×10^{-4}	.75	8

Other well studied examples of general base catalysis, *e.g.*, the mutarotation of glucose, and general acid catalysis, *e.g.*, the iodination of acetone, are discussed by Bell (11d). Sufficient data for each of several charge types or structural types have rarely been obtained so that separate correlations have not been attempted. A recent study of the hydrolysis of *p*-nitrophenylacetate catalyzed by a series of bases indicates different correlations of similar slope for negatively charged oxygen bases, anilines, pyridines and imidazoles in order of increasing catalytic power (47). The decomposition of substituted benzoyl peroxides in benzene solution (167) is noteworthy for a change in mechanism from a radical process to one showing general acid catalysis that follows the Brønsted equation. Mechanistic problems in the case of the acid-catalyzed hydrolysis of substituted methyl *o*-benzoates have been examined through Hammett, Grunwald–Winstein and Brønsted correlations (161).

By selecting some acid (or base) as a standard and considering *relative* catalytic constants and acidities, equation 94 can be expressed as a two-parameter equation of the general type previously considered

$$\log (k_A/k_A^0) = \alpha \log (k_A/k_A^0) \tag{98}$$

where $\log (K_A/K_A^0)$, which could be represented by some symbol, *e.g.*, R_A, is a reagent parameter measured by relative acidity and α is a reaction parameter measuring the susceptibility of the catalysis of the process to the changes in relative acidity.

The distinction between reagent and substrate is an arbitrary one. Viewing the variable catalyzing acid (or base) as the substrate, equation 98 is simply a Hammett correlation (section III-A) when the catalysts are *m*- and *p*-substituted aromatic compounds, and a Taft correlation (section III-B) in other cases. As a Hammett series, when the catalysts are substituted benzoic acids and the reaction takes place in water at 25° α and ρ are identical since

$$\log (K/K_0) \equiv \sigma$$

by definition. For other aromatic acids (and for aromatic bases) and other conditions

$$\alpha = \rho_R/\rho_A$$

where ρ_A applies to the ionization of the acids (or bases) and ρ_R applies to the catalyzed reaction as a Hammett series. In reactions that follow the Taft equation (with $\rho_R{}^*$) catalyzed by acids (or bases) that also follow the Taft equation (with $\rho_A{}^*$)

$$\log (k_A/k_A^0) = \rho_R{}^*/\rho_A{}^*\sigma^*$$

Consider two substrates whose reactions involving a wide variety of catalysts are correlated by the Brønsted equation with exponents α_1 and α_2. (The reactions of α-chloroacetate and α-bromoacetate with anionic bases (220) are good examples). Some of these acids (or bases) may constitute a Hammett series and some others a Taft series, hence

$$\alpha_1 = \sigma\rho_{R_1}/\rho_A = \sigma^*\rho_{R_1}{}^*/\rho_A{}^*$$

and

$$\alpha_2 = \sigma\rho_{R_2}/\rho_A = \sigma^*\rho_{R_2}{}^*/\rho_A{}^*$$

$$\therefore \alpha_1/\alpha_2 = \rho_{R_1}/\rho_{R_2} = \rho_{R_1}{}^*/\rho_{R_2}{}^* \qquad (99)$$

Although, as indicated in section III-B, ρ_{R_1} and ρ_{R_2} are not necessarily the same as $\rho_{R_1}{}^*$ and $\rho_{R_2}{}^*$, respectively, equation 99 shows that their ratios are equal when a widely applicable Brønsted correlation can be found. Conversely, the failure of equation 99 can provide a reason for limitations of the Brønsted equation.

The general limitations and conditions of linear free energy relationships discussed in section II, particularly those concerning substituent effects, will apply to the Brønsted equation. However, with the restriction of reaction type to those involving proton transfers a number of correlations are observed for which the broader Hammett and Taft equations fail. Limitation of structural variations is still important. Deviations from a wide correlation for the dehydration of acetaldehyde hydrate have been identified as due to abnormal resonance stabilization in the anions of "pseudo-acids" not present in carboxylate and phenolate anions (12, 16). Imidazole and hydroxylamine prove to be exceptional in the general base catalysis of the aminolysis of phenyl acetate (140), probably because functions other than base strength are involved. Similarly, carboxylic acids function as general acid catalysts in the isomerization of 4α,6α-dibromocholestane following the Brønsted equation but phenols are not correlated, appearing in the kinetic expression as a second-order term (162).

Hammett correlations of acid and base strength are obtained for a variety of solvents (cf. section III-a). It is to be expected then that the Brønsted equation will still be applicable irrespective of the solvents in which k_A (or k_B) and K_A are determined. Table XXX illustrates the parameters obtained for the decomposition of nitramide in a variety of media correlated with the conjugate acid strength of catalyzing amine bases from aqueous solution measurements (56, 57).

TABLE XXX

NITRAMIDE DECOMPOSITION IN VARIOUS SOLVENTS

Solvent	Dielectric constant	β	$10^6 G_B$
Water	78.5	0.75	36
Nitrobenzene	34.8	.67	2.9
m-Cresol	11.8	.84	17
Isopentyl alcohol	5.7	.92	0.80
Anisole	4.3	.64	1.1
Benzene	2.3	.7	1.3

No parallel appears between dielectric constant and either β or G_B, and the somewhat modified β-values for the correlation of anionic bases parallel neither the amine β-values nor the dielectric constant. Bender (20) has suggested a "Selectivity" relationship should be observed between the exponents (α or β) of the Brønsted equation and the intercepts (*i.e.*, log G_A or log G_B). The data of Table XXX show no indications of linear variations of β with log G_B.

Variations in substrate, reaction medium and catalyst structure all affect the magnitude of the α-, β- and G-values. All present little can be said concerning the magnitude of these parameters unless the correlations are of the Hammett type. Specific catalysis in an inert medium has no meaning, there being no conjugate acid and base of the solvent, so that under these conditions there is in principle no limit on the values of α and β to be expected.

Bell (13a, 14a) and also Frost and Pearson (91b) have discussed the mechanisms of acid-base catalysis and the significance of the Brønsted equation. For single proton transfer reactions, as in

$$S + HA_i \underset{-1}{\overset{1}{\rightarrow}} SH + Bi$$

$$SH \overset{2}{\rightleftarrows} \text{Products}$$

for the acid-catalyzed reaction, general catalysis is usually observed when $k_A{}^i$ (the catalytic constant observed) $= k_1{}^i$ for any acid (HA_i) ($k_1{}^i$ *etc.*, refer to the steps in the postulated reaction mechanism). This suggests that the rates of ionization of acids (proton transfer to a reference base, *e.g.*, solvent water) should be linearly related to their ionization constants. A number of slowly ionizing weak acids for which this rate can be measured show such a parallel. For the more complex two-proton transfer reactions, as in

$$S + HA_i \underset{-1}{\overset{1}{\rightleftarrows}} SH + B_i$$

$$SH + B_i \overset{2}{\rightarrow} \text{Products}$$

again for the acid-catalyzed reaction, the normal result for general catalysis has $k_A{}^i = k_2{}^i K_i/K_{HS}$ where K_i and K_{HS} are the customary (*i.e.*, relative to water) ionization constants of the catalyzing acid (HA_i) and the protonated substrate (HS). The second step is of the type leading to a Brønsted correlation of single proton transfers, hence

$$k_A{}^i = GK_i{}^{1-\beta}/K_{HS} = G'K_i{}^{\alpha'}$$

Additional mechanisms of reaction can be envisioned, especially in poorly ionizing media, through hydrogen bonded complexes between the substrate and acids or bases. This situation has been examined by Gordon (98) who reports a linear correlation between hydrogen bonding and acid strength that will result in correlations by the Brønsted equation for these processes also. A rate-determining decomposition of substrate–acid or substrate–base complex by base or acid, respectively, can lead to general catalysis by acids and bases simultaneously (13b). Such a two-step process may be kinetically indistinguishable from a concerted mechanism (*cf.* 226).

Specific base catalysis is generally treated in terms of proton transfers, but the same kinetic form is observed in reactions involving reversible addition of hydroxyl ions as in ester hydrolyses. The basic action of a reagent is one example of its nucleophilicity, albeit a very special one meriting a separate treatment. Nucleophilic catalysis can thus be expected to follow the Brønsted equation and this is indicated for the solvolysis of the chloroacetate and bromoacetate anion catalyzed by a large number of anionic bases (220). Although no independent evidence for intermediate formation could be adduced, this type of catalysis of the hydrolysis of acetic anhydride by heterocyclic amines has been suggested (97). Correlation by the Brønsted equation leads to an exponent $\beta = 0.925$. Ester hydrolysis itself has been found subject to general base catalysis although this is properly called nucleophilic catalysis since a proton transfer to the base is not envisioned. Thus, for esters containing a good leaving group, *e.g.*, substituted phenyl acetates and ethyl thioacetate, the Brønsted equation correlates the catalysis by heterocyclic bases, including imidazole, with an exponent of $\beta = 1.62$ (21). (The restriction of β-values in the range zero to unity is no longer applicable when the Brønsted equation is used for nucleophilic catalysis.) Trimethylamine deviates markedly from this correlation due to steric factors, and the hydroxyl ion can only be brought into the correlation by a β-value of *ca.* 0.4. For catalysis of the hydrolysis of *p*-nitrophenyl acetate by substituted imidazoles (essentially a Hammett correlation) the Brønsted exponent $\beta = 0.67$ is observed (48). Activation of the acyl portion of esters can also lead to the observation of general base catalysis (142). It is suggested that in this case nucleophilic catalysis is not involved. The Brønsted equation, with $\beta = 0.47$, accommodates a wide variety of catalysts including water, formate, aniline, phosphate and imidazole, all of which operate in accordance with their proton acceptor capabilities. In contrast, the action of a wide range of nucleophiles on *p*-nitrophenyl acetate does not satisfactorily parallel basicity (141). A detailed discussion of catalysis of reactions of acid derivatives has been given by Bender (20).

B. THE SWAIN EQUATIONS

Unless there is a close parallel between basicity and nucleophilicity the Brønsted equation will only be applicable to displacement reactions of hydrogen, *i.e.*, proton transfer reactions. Such a parallel is not generally observed for reactions involving displacements on other atoms, although some examples of Brønsted correlations have been found (*cf.* section V-A). Swain and Scott (235) have suggested that in general the action of both nucleophilic and electrophilic reagents needs to be considered if all reactions are regarded as involving concerted processes. A four-parameter equation

$$\log (k/k^0) = sn + s'e \qquad (100)$$

might then serve to correlate polar displacement reactions of all types. In eq. 100, k/k_0 is the specific rate constant for the displacement reaction relative to some arbitrarily chosen standard condition of nucleophilicity and electrophilicity, n and e are reagent parameters measuring, respectively, nucleophilic and electrophilic power and s and s' are parameters measuring the power of the substrate to discriminate between various nucleophiles (N) and electrophiles (E), respectively. If the s and s' parameters are considered to be determined solely by the nature of the substrate, then the n and e parameters will vary with temperature and reaction medium (other than N and E character).

Equation 100 without further definitions represents a general four-parameter linear free energy relationship of which special cases already have been discussed. Applied to displacements on hydrogen, a fixed nucleophile (n constant) leads to the Brønsted equation for acid catalysis with

$$\alpha \log (K_A/K_A{}^0) = s'(e - e^0) \qquad (101a)$$

and with a fixed electrophile (e constant) the Brønsted equation for base catalysis having

$$-\beta \log (K_A/K_A{}^0) = s(n - n^0) \qquad (101b)$$

When the substrate is modified simply by substituent changes, then for Hammett series

$$s = a\sigma \text{ and } s = b\sigma$$

$$\therefore \log (k/k_0) = (an + be)\sigma \qquad (102a)$$

and for Taft series similarly

$$\log (k/k_0) = \sigma^*(an^* + be^*) \qquad (102b)$$

For the special case of displacement reactions of the S_N1 or "limiting" type having a negligible susceptibility to nucleophilic attack (*i.e.*, $s \simeq 0$) then the Grunwald–Winstein equation is obtained correlating the electrophilic power of solvents (A and B)

$$\log (k_A/k_B) = s'(e_A - e_B) = m(\mathbf{Y}_A - \mathbf{Y}_B)$$

The same result will be obtained if the substrate is susceptible to nucleophilic attack but the compared solvents (A and B) have equal n-values.

At the other extreme, the special case of nucleophilic displacements in a medium of constant electrophilicity (water at 25°) leads to the equation

$$\log (k/k_0) = sn \qquad (103)$$

TABLE XXXI

NUCLEOPHILIC PARAMETERS ($n_{H_2O} \equiv 0.00$)

Nucleophile	n	Nucleophile	n	Nucleophile	n
$NO_3^{=}$	1.03[a]	$C_6H_5O^-$	3.5[f]	SCN^-	4.41[d,e]
$2,4,6\text{-}(NO_2)_3C_6H_2O^-$	1.9[b]	Br^-	3.53[d,e]	$C_6H_5NH_2$	4.49[d]
$ClCH_2CO_2^-$	2.2[c]	C_5H_5N	3.6[b]	I^-	5.04[d,e]
$HOCH_2CO_2^-$	2.5[c]	HCO_3^-	3.8[b]	HS^-	5.1[b]
$SO_4^{=}$	2.5[b]	$H_2PO_4^-$	3.8[b]	$SO_3^{=}$	5.1[b]
Cl^-	2.70[d,e]	N_3^-	4.00[g]	CN^-	5.1[h]
$CH_3CO_2^-$	2.72[d]	$(NH_2)_2CS$	4.1[b]	$S_2O_3^{=}$	6.36[d]
HCO_2^-	2.75[c]	HO^-	4.20[d]	$HPSO_3^{=}$	6.6[b]

[a] From the correlations of reactions of glycidol (no. 4) and epichlorohydrin (no. 3) (199). [b] From the correlation of reactions of mustard cation (no. 9) (235). [c] From the correlation of reactions of chloro- and bromoacetate (220). [d] Based on the correlation of three or more substrates of Table XXXIII (235). [e] Corrected values of Petty and Nichols (199). [f] From the correlation of reactions of iodoacetate (114). [g] Defined by reaction with methyl bromide (235). [h] From correlation of reactions of iodoacetate and methyl iodide (114).

where the parameters are measured relative to $n \equiv 0$ for water at 25° and $S \equiv 1.000$ for methyl bromide. (Essentially the same expression has been suggested by Hine (121c) and, for deviations from the Grunwald–Winstein equation, by Wilputte–Steinert and Fierens (265).

Table XXXI lists nucleophilic parameters and Table XXXII substrate parameters appropriate to equation 103. While there is in general no parallel between the n-values and the basicity of nucleophiles, a second set of values (signified by n_H) could be derived to correlate displacements on hydrogen (*cf.* 235). In this case equation 103 reduces to equation 101.

There are two examples in Table XXXII of displacements at a sulfur as opposed to a carbon atom. The mustard cation (no. 9), is moderately well correlated by equation 103 covering nucleophiles of three charge type (N^0, N^- and $N^{=}$) although the hydroxide ion shows exceptionally high reactivity. Benzenesulfonyl chloride, on the other hand, shows a generally poor correlation. This suggests that a different set of n-values is required according to the atom upon which displacement is occurring. Indeed the poor correlation of, amongst others, trityl fluoride might be taken to indicate that additional sets are required for carbon in various states of hybridization and substitution. Discrimination by this substrate between various nucleophiles would be expected to be quite low and possibly dominated by factors normally making only small contributions to the n-values. For similar reasons the failure of the Grunwald–Winstein equation for this substrate is not surprising (233).

TABLE XXXII

SUBSTRATE PARAMETERS FOR NUCLEOPHILIC ATTACK

* Shows ring opening reactions.

Substrate	s	Number[a]	Reference
Methyl bromide	1.00[b]	6	235
Methyl iodide	1.15	3	114
1-Chloro-2,3-epoxypropane*	1.00[c]	7	235
2,3-Epoxypropanol*	0.96[c]	7	235
Chloroacetate	1.0	3	220
Bromoacetate	1.1	4	220
Iodoacetate	1.33	5	114
β-Propionolactone*	0.77[d]	7	235
Ethylene-β-chloro-ethylsulfonium ion*	0.95[e]	7	235
Benzyl chloride	0.87	3	235
Ethyl tosylate	0.66	5	235
Benzoyl chloride	1.43[f]	4	235
Benzenesulfonyl chloride	1.25[g]	3	235
Trityl fluoride	0.61[g]	8	235

[a] The number of reactions employed in the correlations. [b] Defining reaction series. [c] Corrected s-values of Petty and Nichols (199). [d] Correlation improved using corrected n-values (199). [e] Reactivity of hydroxide underestimated by n-value. [f] Reactivity of acetate overestimated by n-value. [g] Correlation of low precision.

Equation 103 has been applied to nucleophilic aromatic substitutions (51) but poor correlations are obtained. The deviations are not, however, as large as those ascribable to mechanistic changes, and the n-values retain some usefulness in the diagnosis of such changes (169).

Difficulties in interpretation arise when this treatment is extended to solvolysis reactions and a new equation was suggested instead of equation 100 (234). In equation 104

$$\log (k/k_0) = c_1d_1 + c_2d_2 \qquad (104)$$

c_1 and c_2 are substrate parameters defined by $-c_1 = c_2 = 1.00$ for t-butyl chloride, $c_1 = 3.00c_2$ for methyl bromide, $c_2 = 3.00c_1$ for trityl fluoride, and d_1 and d_2 are solvent parameters whose scale is set at zero for 80% aqueous ethanol. This procedure is made necessary by the fact that when the solvent acts as both electrophile and nucleophile the parameters of equation 104 can no longer be specified by a single standard substrate (*cf.* 99e). The parameters d_1 and d_2 although not precisely equivalent to n and s are by their mode of definition intended to measure nucleophilic and electrophilic character.

Streitwieser (224) has discussed the utility and failings of equation 104. By setting the c_1, c_2 scales with *t*-butyl chloride having equal dependence on nucleophilic (d_1) and electrophilic (d_2) character exactly intermediate between trityl fluoride and methyl bromide, completely artificial and inconsistent reagent parameters are obtained. Thus methyl, ethyl and *n*-butyl bromides are found less sensitive to nucleophilic attack than *t*-butyl chloride or benzhydryl chloride. Moreover, the solvolysis of 1-bromobicyclo[2.2.2]octane, whose structure precludes nucleophilic participation from the rear, is found (72) to parallel that of *t*-butyl chloride in various solvents. Streitwieser suggests $c_2 = 0.00$ and $c_1 = 1.00$ for *t*-butyl chloride might provide a better scale of reagent parameters. This would make the d_1 and the Grunswald–Weinstein **Y**-values almost identical. With this change equation 104 becomes a modified Grunwald–Winstein equation containing a correcting term c_2d_2 and thus inevitably leads to improved correlations (229, 230, 232). (The presence of four parameters in equation 100 accomplishes this anyway.) For substrates utilizing nucleophilic functions this correcting term is essentially the δ_N correction of Wilputte–Steinert and Fiernes (265) or the **lN**-term of Winstein, Fainberg and Grunwald (269). For substrates structurally dissimilar or reacting by a mechanism "more limiting" than that of *t*-butyl chloride the correcting term accounts for the inadequacies of the **Y**-values. One such inadequacy may be due to the fact that **Y** for hydroxylic solvents measures both "ion solvating power" and "H-bonding electrophilic assistance" from which different leaving groups will require different relative contributions (232).

The troublesome trityl substrates have been examined by Hawthorne and Cram (113) in terms of equation 102 for the reaction of trityl chloride in benzene solution with substituted benzyl alcohols. Assuming the alcohol fills both the role of electrophile and nucleophile (its concentration appears in the kinetic expression as a second-order term), then the rho-value obtained for the series is identical with $(as + bs')$. Adding phenol, which should act as the only electrophile, leads to a rho-value of essentially zero which implies that as is negligible. The c_1-parameter for trityl chloride would not suggest a negligible dependence on nucleophilicity. The effect of phenols on the reaction of *t*-butyl bromide with pyridine (substitution and elimination) in nitromethane solution has been correlated with their acid strength suggesting that the *e*-values of the Swain–Scott equation might be derived from acidity measurements (200).

A third equation, 105, was suggested by Swain and Dittmer (227) and subsequently further examined (228).

In equation 105, k/k_0 is the specific rate constant for solvolysis of substrates A or A_0 in any solvent relative to that in 80% aqueous ethanol, A is any chloride or bromide, A_0 is a standard compound, methyl bromide, a is characteristic only of the substrate and b only of the solvent. Superficially a two-parameter equation (*cf.* the Taft equation 63, section III-B), equation 105 is restricted to structurally similar substrates with similar leaving groups and seeks to cancel out common solvent dependences, thus focusing attention on differences. Setting $a = 0.00$ for methyl bromide (A_0), $a = 1.00$ for *t*-butyl chloride and $b = 0.00$ for 80% aqueous ethanol, fifteen halides ranging from picryl and *p*-nitrobenzoyl chloride ($a \simeq -0.4$) through benzyl chloride ($a = 0.2$) and isopropyl bromide ($a = 0.4$), to *t*-butyl halides were examined in nineteen solvents including triethylamine, aniline, aqueous alcohols and acetone, water, acetic and formic acids. The relative rate constants are reproduced with an average error of a factor of 1.5 in the rate constants which vary by 10^6.

$$\log (k/k_0)_A - \log (k/k_0)_{A_0} = ab \tag{105}$$

Large negative values for amines and positive values for acids indicate that the *b*-values are some measure of acid strength or electrophilicity, but it is not clear what common factors have been cancelled out and what factors remain.

C. THE EDWARDS EQUATION

Correlations of nucleophilic catalysis by the Brønsted equation have been mentioned in section V-A, and discussed by Bender (20). Their restrictions to families of reagents having the same nucleophilic atom (*cf.* 47) suggests reagent basicity and polarizability are being examined as independent variables with the latter constant. Edwards (76) has sought to account for these two functions by means of extra-kinetic quantities in equation 106

$$\log (k/k_0) = \alpha E_n + \beta H \tag{106}$$

where k/k_0 is the rate or equilibrium constant for reaction with some reagent relative to that for reaction with water (k_0), E_n is a parameter characteristic of the reagent measuring nucleophilicity or Lewis base strength, H is a parameter characteristic of the reagent measuring conventional (Lowry–Brønsted) base strength, α and β are substrate parameters determined by the substrate's discrimination between reagents and dependence upon nucleophilicity and basicity.

The E_n-value for a reagent (N^-) was determined by the electrode potential (E) for the oxidative dimerization (to N:N) relative to that for water by

$$E_n = E^0 + 2.60 \tag{107}$$

the potential for the standard reagent, water ($E_n^0 = 0.00$), being an adjustable parameter. This scale thus resembles the "absolute Lewis base strengths" of Kaufman and Koski (146) based on the ionization potentials of free radicals.

TABLE XXXIII

REAGENT PARAMETERS (EDWARDS)

Reagent	E_n[a]	P	H[b]	Reagent	E_n[a]	P	H[b]
ClO_4^-	0.00[c]		−9.0	$C_6H_5NH_2$	1.78		6.28
F^-	− .27	−0.150	4.9	SCN^{-}*	1.83		(1.00)
NO_3^-	.29		(0.40)	NH_3*	1.84		11.22
$SO_4^{=}$	.59*		3.74	$(CH_3O)_2POS^{-}$*	2.04		(4.00)
$ClCH_2CO_2^-$	.79		4.54	$C_2H_5S_2O_3^{-}$*	2.06		(−5.00)
$CH_3CO_2^-$	.95		6.46	I^{-}*	2.06	0.718	(−9.00)
C_5H_5N	1.20		7.04	$(C_2H_5O)_2POS^{-}$*	2.07		(4.00)
Cl^-	1.24*	0.389	(−3.00)	$C_7H_7S_2O_3^{-}$*	2.11		(−6.00)
$C_6H_5O^-$	1.46		11.74	$(NH_2)_2CS$	2.18		0.80
Br^-	1.51*	0.539	(−6.00)	$S_2O_3^{=}$*	2.52		3.60
N_3^-	1.58		6.46	$SO_3^{=}$*	2.57		9.00
OH^-	1.65*	0.143	17.48	CN^-	2.79		10.88
NO_2^-	1.73*		5.09	$S^{=}$*	3.08		14.66
$CO_3^{=}$	1.1		12.1				

[a] E_n-values marked with asterisk are derived from electrode potential measurements, others from correlations of Table XXXIV. [b] H-values in parentheses are estimates through correlations of Table XXXIV. [c] Calculated $E_n = -0.73$ through equation 109.

The H-values were determined by the acidities in water of the conjugate acids of the reagents relative to water by

$$H = pK_a + 1.74 \qquad (108)$$

Table XXXIII lists reagent parameters and Table XXXIV substrate parameters for a number of reactions conducted in aqueous solution at 18–25° covering a wide variety of reaction centers.

In all cases, except for displacements on hydrogen, the first term dominates the βH contributes in only a minor fashion to log (k/k_0). For displacements on carbon and sulfur, equation 106 and Swain–Scott equation are essentially the same except that the former permits slight corrections to be made and these are spread over four instead of two parameters. Correlation is thus improved.

The relative magnitudes of α and β suggest that the E_n-parameter retains the main contributions paralleling base strength so often observed qualitatively. Negative β-values furthermore do not conform with the nature of the reaction processes involved. Thus equation 109 was subsequently suggested (77).

$$\log (k/k_0) = aP + bH \qquad (109)$$

in which relative polarizabilities (P) measured by molar refraction (R) were used instead of oxidative dimerization potentials.

$$P \equiv \log (R_\infty/R_\infty^{H_2O})$$

These values are also listed in Table XXXIII. It was found that

$$E_n = 3.60P + 0.0624H$$

for seven simple nucleophiles (monatomic anions and hydroxyl) so that comparing equations 106 and 109

$$a = 3.60\alpha \text{ and } b = \beta + 0.0624\alpha$$

and the contribution due to conventional base strength is increased somewhat and is in fact always positive.

TABLE XXXIV

SUBSTRATE PARAMETERS (EDWARDS)

Substrate	Displacement on	n[a]	α	β
Ethyl tosylate[b]	C	5	1.68	0.014
β-Propionolacetone[b]	C	7	2.00	.069
Diazoacetone[c]	C	4	2.37	.191
1-Chloro-2,3-[b]epoxypropane	C	6	2.46	.035
Methyl bromide[b]	C	6	2.50	.006
2,3-Epoxypropanol[b]	C	6	2.52	.000
Iodoacetate[d]	C	6	2.59	− .052
Benzyl chloride[b]	C	3	3.53	− .128
Benzoyl chloride[b]	C	4	3.56	.008
Ethylenimine[e]	N	5	2.12	.026
Ethylene-β-chloroethyl[b] sulfonium cation	S	12	2.45	.074
Benzenesulfonyl chloride[b]	S	3	2.56	.046
H_3O^+ (base strength in water)	H	..	0.00	1.000
Mutarotion of glucose[b]	H	6	−0.41	0.471
Oxidations by[f] H_2O_2	O	5	6.31	− .394
	O	5	5.20	− .279
Ag^+[g]	Ag	..	3.08	− .078
AgN_2^+ formation[h]	Ag	15	7.14	− .226
Zn^{++}[g]	Zn	..	1.32	.206
ZnN_4^{++} formation[h]	Zn	11	5.94	.650
Cd^{++}[g]	Cd	..	2.18	.071
CdN_4^{++} formation[h]	Cd	12	6.98	.255
Hg^{++}[g]	Hg	..	6.57	− .137
HgN_2^{++} formation[h]	Hg	10	12.92	− .099
I_2N formation[i]	I	4	3.04	.000
IN^+ formation[i,j]	I	3	6.85	.162

[a] Number of reagents correlated. [b] *Cf.* ref. 235. [c] Ref. 171. [d] Ref. 4, 5, 6 and 253. [e] Ref. 201. [f] Ref. 75. [g] Mn^+ + nucleophile salt (Lewis acid strength). [h] Complex formation constants (K_f) correlated. [i] Iodine complex formation. [j] Ref. 15.

In comparison with the Swain–Scott equation (103) and the Swain–Mosely–Bown equation (104) discussed in section V-B, equation 106 or 109 appears to correlate a wider range of reaction types and provide an independent means of parameter determination. For displacements on carbon the major improvement achieved by the Edwards equation is the correlation of the hydroxyl anion (*cf.* 47). Despite the wide applicability reported for equation 106, there are some notable exceptions. Neither the E_n-value for the P-value for the cyanide ion correlate its nucleophilicity either because of resonance interactions within the cyanogen molecule (*cf.* 114) or, a general feature of polyatomic nucleophiles, the polarizability of more than one atom needs to be considered (77). Nucleophilic catalysis of ester reactions is poorly correlated (141), and the parallel with reagent basicity is considerably underestimated. On the other hand, the correlation of displacement reactions on protonated ethylenimines are satisfactory despite the fact that all the other correlations of displacements on carbon atoms are for neutral substrates (74). However, the Swain–Scott equation is more satisfactory for these substrates although less so for the similar mustard cation. For reaction of protonated ethylenimines with substituted benzoates precise Hammett correlations are observed (201). High rho-values (1.5–1.7) suggest a greater parallel with basicity than implied by the β-value (see Table XXXIV).

Were a large number of electrode potentials accurately known or reliable polarizability values for a wide variety of nucleophiles available, equations 106 and 109 might be powerful tools for mechanistic investigations. Even so it is not clear that the oxidative dimerization process is a valid model for acceptor–donor interactions in displacement reactions. Basicity is only one special case of nucleophilicity and factorization of total reactivity into nucleophilicity and basicity seems unrewarding. Possibly the most outstanding feature of displacements on hydrogen is the low steric requirement, a feature not yet assessed by any reagent correlation.

VI. CONCLUSIONS

A number of equations that seek to correlate variations in substrate, reagent and reaction medium have been examined. All are of the type that suppose free energies changes to be linearly dependent on the variables concerned. Where these variables can be identified the derived parameters are useful theoretical quantities; otherwise the equations serve to store and predict reactivity data.

The most stringent restrictions of variation lead to the most satisfactory relationship, namely, that due to Hammett. Intensive studies of recent years have led to extensions and modifications, adding considerably to its original value. With less rigid restrictions, the more limited Taft equation may be applicable.

For a few reaction types, parameters measuring the function of the solvent and the reagent have been obtained. Attempts to extend these equations are only achieved by the use of further adjustable parameters, a knowledge of whose origin is at best imprecise.

New correlations will certainly be developed, and a fruitful venture may be the analysis of the Hammett reaction parameters in terms of solvent and reagent variations. It is to be hoped that the inherent limitations and dangers of the linear free energy relationship approach, particularly the disarming success of multiparameter equations, will not blunt this useful theoretical tool.

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VII. REFERENCES

(1) Akermann, E., *Acta Chem. Scand.*, **11**, 373 (1951).
(2) Anderson, B. M., and Jencks, W. P., *J. Am. Chem. Soc.*, **82**, 1773 (1960).
(3) Anderson, E., Birkhimer, E. A., and Bak, T. A., *Acta Chem. Scand.*, **14**, 1899 (1960).
(4) Backer, H. J., and van Mels, W. H., *Rec. trav. chim.*, **49**, 177 (1930).
(5) Backer, H. J., and van Mels, W. H., *Rec. trav. chim.*, **49**, 363 (1930).
(6) Backer, H. J., and van Mels, W. H., *Rec. trav. chim.*, **49**, 457 (1930).
(7) Balasubramanian, A., and Rao, C. N. R., *Chemistry & Industry*, 1025 (1960).
(8) Barnstorff, H. D., and Meek, J. S., Abstracts of Papers, 125th Natl. A.C.S. Meeting, Kansas City, Mo., March 23–April 1, 1954.
(9) Bayliss, N. S., Cole, A. R. H., and Little, L. H., *Austral. J. Chem.*, **8**, 26 (1955).
(10) van Bekkum, H., Verkade, P. E., and Wepster, B. M., *Rec. trav. chim.*, **78**, 815 (1959).
(11) Bell, R. P., "*Acid-base Catalysis*," Clarendon Press, Oxford, Eng., 1941: (a) Chapter V, (b) p. 85, (c) pp. 86–87, (d) pp. 88–91, (e) pp. 107–111.
(12) Bell, R. P., *J. Phys. Chem.*, **55**, 885 (1951).
(13) Bell, R. P., "Advances in Catalysis," Vol. 4, Academic Press Inc., New York, N.Y., 1952: (a) pp. 174–210, (b) pp. 188–191.
(14) Bell, R. P., "The Proton in Chemistry," Methuen and Co. Ltd., London, 1959: (a) Chapter X, (b) p. 158.
(15) Bell, R. P., and Gelles, E., *J. Chem. Soc.*, 2734 (1951).
(16) Bell, R. P., and Higginson, W. C. E., *Proc. Roy. Soc.* (London), **A197**, 141 (1949).
(17) Bellamy, L. J., *Spectrochim. Acta*, **14**, 216 (1959).
(18) Bellamy, L. J., and Williams, R. L., *J. Chem. Soc.*, 863 (1957).
(19) Bellamy, L. J., and Williams, R. L., *Trans. Faraday Soc.*, **55**, 14 (1959).
(20) Bender, M. L., *Chem. Rev.*, **60**, 53 (1960).
(21) Bender, M. L., and Turnquest, B. W., *J. Am. Chem. Soc.*, **79**, 1656 (1957).
(22) Benghiat, S. I., and Becker, E. I., *J. Org. Chem.*, **23**, 885 (1958).
(23) Bensley, B., and Kohnstam, G., *J. Chem. Soc.*, 4747 (1957).

(24) Benson, S. W., *J. Am. Chem. Soc.*, **80**, 5151 (1958).
(25) Berliner, E., *Tetrahedron*, **5**, 202 (1959).
(26) Berliner, E., and Monack, L. C., *J. Am. Chem. Soc.*, **74**, 1574 (1952).
(27) Berger, G., and Olivier, S. C. J., *Rec. trav. chim.*, **46**, 516 (1927).
(28) Bevan, C. W. L., *J. Chem. Soc.*, 665 (1953).
(29) Biechler, S. S., and Taft, R. W., Jr., *J. Am. Chem. Soc.*, **79**, 4927 (1957).
(30) Blackadder, D. A., and Hinshelwood, C., *J. Chem. Soc.*, 2728 (1958).
(31) Branch, G. E. K., and Calvin, M., "The Theory of Organic Chemistry," Prentice–Hall Inc., New York, N.Y., 1941: (a) Chapter VI, (b) pp. 203–211.
(32) Brønsted, J. N., *Chem. Rev.*, **5**, 322 (1928).
(33) Brønsted, J. N., and Pederson, K. J., *Z. physik. Chem.*, **108**, 185 (1924).
(34) Brown, G. H., Figuras, J., Gledhill, R. J., Kibler, C. J., McCrossan, F. C., Parmenter, S. M., Nottum, P. W., and Weissberger, A., *J. Am. Chem. Soc.*, **79**, 2919 (1957).
(35) Brown, H. C., and McDaniel, D. H., *J. Am. Chem. Soc.*, **77**, 3752 (1955).
(36) Brown, H. C., and McDaniel, D. H., *J. Am. Chem. Soc.*, **77**, 3756 (1955).
(37) Brown, H. C., and Nelson, K. L., *J. Am. Chem. Soc.*, **75** 6296 (1953).
(38) Brown, H. C., and Okamoto, Y., *J. Am. Chem. Soc.*, **79**, 1913 (1957).
(39) Brown, H. C., and Okamoto, Y., *J. Am. Chem. Soc.*, **80**, 4979 (1958).
(40) Brown, H. C., Okamoto, Y., and Ham, G., *J. Am. Chem. Soc.*, **79**, 1906 (1957).
(41) Brown, T. L., *J. Phys. Chem.*, **61**, 820 (1957).
(42) Brown, T. L., *Chem. Rev.*, **58**, 581 (1958).
(43) Brown, T. L., *J. Am. Chem. Soc.*, **80**, 6489 (1958).
(44) Brown, T. L., *J. Am. Chem. Soc.*, **81**, 3229 (1959).
(45) Brown, T. L., *J. Phys. Chem.*, **64**, 1798 (1960).
(46) Brownstein, S., *Can. J. Chem.*, **38**, 1590 (1960).
(47) Bruice, T. C., and Lapinski, R., *J. Am. Chem. Soc.*, **80**, 2265 (1958).
(48) Bruice, T. C., and Schmir, G. L., *J. Am. Chem. Soc* **79**, 1663 (1957).
(49) Bryson, A., *J. Am. Chem. Soc.*, **82**, 4862 (1960).
(50) Bryson, A., *J. Am. Chem. Soc.*, **82**, 4871 (1960).
(51) Bunnett, J. F., and Bassett, J. Y., Jr., *J. Am. Chem. Soc.*, **81**, 2104 (1959).
(52) Bunnett, J. F., Draper, F., Jr., Rynson, P. R., Noble, P., Jr., Tonkyn, P. G., and Zahler, R. F., *J. Am. Chem. Soc.*, **75**, 642 (1953).
(53) Bunnett, J. F., and Levitt, A., *J. Am. Chem. Soc.*, **70**, 2778 (1948).
(54) Bunton, C. A., and Nayak, B., *J. Chem. Soc.*, 3854 (1959).
(55) Burawoy, A., Jr., and Spinner, E., *J. Chem. Soc.*, 3752 (1954).
(56) Caldin, E. F., and Peacock, J., *Trans. Faraday Soc.*, **51**, 1217 (1955).
(57) Callender, D. D., Fergusson, W. D., Fellis, G. C., and Trotman-Dickinson, A. F., *J. Chem. Soc.*, 3834 (1960).
(58) Charton, M., *Can. J. Chem.*, **38**, 2493 (1960).
(59) Charton, M., *J. Org. Chem.*, **26**, 735 (1961).
(60) Charton, M., and Merslich, H., *J. Am. Chem. Soc.*, **80**, 5940 (1958).
(61) Clement, R. A., and Rice, M. R., *J. Am. Chem. Soc.*, **81**, 326 (1959).
(62) Colichman, E. L., and Liu, S. K., *J. Am. Chem. Soc.*, **76**, 913 (1954).
(63) Coulson, D. M., Crowell, W. R., and Tendick, S. K., *J. Am. Chem. Soc.*, **79**, 1354 (1957).
(64) Cropper, W. H., Spieth, F., and Olson, A. R., *J. Am. Chem. Soc.*, **76**, 6248 (1954).
(65) Deans, F. B., Eaborn, C., and Webster, D. E., *J. Chem. Soc.*, 3031 (1959).
(66) Deno, N. C., and Evans, W. L., *J. Am. Chem. Soc.*, **79**, 5804 (1957).
(67) Deno, N. C., and Schriesheim, A., *J. Am. Chem. Soc.*, **77**, 3051 (1955).
(68) Derick, C. G., *J. Am. Chem. Soc.*, **33**, 1181 (1911).
(69) Dessy, R. E., and Kim, J-Y., *J. Am. Chem. Soc.*, **82**, 686 (1960).
(70) Dickinson, J. D., and Eaborn, C., *J. Chem. Soc.*, 3036 (1959).
(71) Dickinson, J. D., and Eaborn, C., *J. Chem. Soc.*, 3641 (1959).
(72) Doering, W. E., and Finkelstein, M., reported by Streitwieser, ref. 224.
(73) Eaborn, C., Lasocki, Z., and Webster, D. E., *J. Chem. Soc* 3034 (1959).
(73A) Eaborn, C., and Pande, K. C., *J. Chem. Soc.*, 3715 (1961).
(73B) Eaborn, C., and Waters, J. A., *J. Chem. Soc.*, 542 (1961).
(74) Earley, J. E., O'Rourke, C. E., Clapp, L. B., Edwards, J. O., and Lawes, B. C., *J. Am. Chem. Soc.*, **80**, 3458 (1958).
(75) Edwards, J. O., *J. Phys. Chem.*, **56**, 279 (1952).
(76) Edwards, J. O., *J. Am. Chem. Soc.*, **76**, 1541 (1954).
(77) Edwards, J. O., *J. Am. Chem. Soc.*, **78**, 1819 (1956).
(78) Elderfield, R. C., and Siegel, M., *J. Am. Chem. Soc.*, **73**, 5622 (1951).
(79) Elliott, J. H., *J. Phys. Chem.*, **46**, 221 (1942).
(80) Elliott, J. H., and Kilpatrick, M., *J. Phys. Chem.*, **45**, (454) (1941).
(81) Fainberg, A. H., and Winstein, S., *J. Am. Chem. Soc.*, **78**, 2770 (1956).
(82) Fainberg, A. H., and Winstein, S., *J. Am. Chem. Soc.*, **79**, 1597 (1957).
(83) Fainberg, A. H., and Winstein, S., *J. Am. Chem. Soc.*, **79**, 1602 (1957).
(84) Fainberg, A. H., and Winstein, S., *J. Am. Chem. Soc.*, **79**, 1608 (1957).
(85) Farthing, A. C., and Nam, B., Abstracts of Papers Presented to the Chemical Society Symposium on Steric Effects in Conjugated Systems, Hull, England, July, 1958, pp. 131–140.
(86) Fernandez, L. P., and Hepler, L. G., *J. Am. Chem. Soc.*, **81**, 1783 (1959).
(87) Fischer, A., Fountain, H. M., and Vaughan, J., *J. Chem. Soc.*, 1310 (1957).
(88) Fischer, A., Mitchell, W. J., Ogilvie, G. S., Packer, J., and Vaughan, J., *J. Chem. Soc.*, 1426 (1958).
(89) Fischer, A., Murdoch, J. D., Packer, J., Topsom, R. D., and Vaughan, J., *J. Chem. Soc.*, 4358 (1957).
(90) Freedman, H. H., *J. Am. Chem. Soc.*, **82**, 2454 (1960).
(91) Frost, A. A., and Pearson, R. G., "Kinetics and Mechanism," John Wiley and Co., Inc., New York, N.Y., 1961: (a) p. 99, (b) pp. 213–231.
(92) Fuchs, R., and Nisbet, A., *J. Am. Chem. Soc.*, **81**, 2371 (1959).
(93) Gaetjens, E., and Morawetz, H., *J. Am. Chem. Soc.*, **82**, 5328 (1960).
(94) Glasstone, S., Laidler, K. J., and Eyring, H., "The Theory of Rate Processes," McGraw–Hill Book Co., Inc., New York, N.Y., 1941, pp. 464–468.
(95) Gleave, J. L., Hughes, E. D., and Ingold, C. K., *J. Chem. Soc.*, 236 (1935).
(96) Goering, H. L., and Jacobson, R. R., *J. Am. Chem. Soc.*, **80**, 3277 (1958).

(97) Gold, V., and Jefferson, E. G., *J. Chem. Soc.*, 1409 (1953).
(98) Gordon, J. E., *J. Org. Chem.*, **26**, 738 (1961).
(99) Gould, E. S., "Mechanism and Structure in Organic Chemistry," Holt, Rinehart and Winston, New York, N.Y., 1960: (a) pp. 107–118, (b) pp. 113–114, (c) pp 220–230, (d) pp. 299–303, (e) p. 300.
(100) Grunwald, E., *J. Phys. Chem.*, **55**, 881 (1951).
(101) Grunwald, E., Baughman, G., and Kohnstam, G., *J. Am. Chem. Soc.*, **82**, 5801 (1960).
(102) Grunwald, E., and Berkowitz, J., *J. Am. Chem. Soc.*, **73**, 4939 (1951).
(103) Grunwald, E., and Winstein, S., *J. Am. Chem. Soc.*, **70**, 846 (1948).
(104) Gutbezahl, B., and Grunwald, E., *J. Am. Chem. Soc.*, **75**, 559 (1953).
(105) Gutbezahl, B., and Grunwald, E., *J. Am. Chem. Soc.*, **75**, 565 (1953).
(106) Gutowsky, H. S., McCall, D. W., McGarvey, B. R., and Meyer, L. H., *J. Am. Chem. Soc.*, **74**, 4809 (1952).
(107) Hall, H. K., Jr., *J. Am. Chem. Soc.*, **79**, 5441 (1957).
(108) Hammett, L. P., *J. Chem. Phys.*, **4**, 613 (1936).
(109) Hammett, L. P., *J. Am. Chem. Soc.*, **59**, 96 (1937).
(110) Hammett, L. P., "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N.Y., 1940, p. 184 ff.
(111) Hammett, L. P., and Deyrup, A. J., *J. Am. Chem. Soc.*, **54**, 2721 (1932).
(112) Hammond, G. S., Reeder, C. E., Fang, F. T., and Kochi, J. K., *J. Am. Chem. Soc.*, **80**, 568 (1958).
(112A) Harrison, A. G., Kebarle, P., and Lossing, F. P., *J. Am. Chem. Soc.*, **83**, 777 (1961).
(113) Hawthorne, M. F., and Cram, D. J., *J. Am. Chem. Soc.*, **76**, 3451 (1954).
(114) Hawthorne, M. F., Hammond, G. S., and Graybill, B. M., *J. Am. Chem. Soc.*, **77**, 486 (1955).
(115) Hannson, J., *Svensk Kem. Tidskr.*, **66**, 351 (1954).
(116) Hannson, J., *Acta Chem. Scand.*, **8**, 365 (1954).
(117) Hannson, J., *Svensk Kem. Tidskr.*, **67**, 246 (1955).
(118) Hedlund, I., *Arkiv Kemi*, **14A**, 1 (1940).
(119) van Helden, R., and Kooyman, E. C., *Rev. trav. chim.*, **73**, 269 (1954).
(120) Henderson, W. M., Jr., Streuli, C. A., and Buckler, S. A., *J. Am. Chem. Soc.*, **82**, 5791 (1960).
(121) Hine, J., "Physical Organic Chemistry," McGraw–Hill Book Co., Inc., New York, N.Y., 1956: (a) pp. 69–76, (b) pp. 134–136, (c) pp. 137–138, (d) p. 142, (e) p. 158, (f) pp. 192–194, (g) pp. 276–282.
(122) Hine, J., *J. Am. Chem. Soc.*, **81**, 1126 (1959).
(123) Hine, J., *J. Am. Chem. Soc.*, **82**, 4877 (1960).
(124) Hine, J., and Bailey, W. C., Jr., *J. Am. Chem. Soc.*, **81**, 2075 (1959).
(125) Hironi, K., *Bull. Chem. Soc. Japan*, **33**, 1251 (1960).
(126) Hixon, R. M., and Johns, I. B., *J. Am. Chem. Soc.*, **49**, 1786 (1927).
(127) Hughes, E. D., and Ingold, C. K., *J. Chem. Soc.*, 244 (1935).
(128) Huyser, E. S., *J. Am. Chem. Soc.*, **82**, 394 (1960).
(129) Hyne, J. B., and Robertson, R. E., *Can. J. Chem.*, **34**, 863 (1956).
(130) Hyne, J. B., and Robertson, R. E., *Can. J. Chem.*, **34**, 931 (1956).
(131) Ingold, C. K., *J. Chem. Soc.*, 1032 (1930).
(132) Ingold, C. K., "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N.Y., 1956, pp. 67–92.
(133) Jaffé, H. H., *J. Chem. Phys.*, **20**, 279 (1952).
(134) Jaffé, H. H., *Chem. Rev.*, **53**, 191 (1953): (a) p. 195, (b) p. 198, (c) pp. 212–213, (d) p. 214, (e) p. 216, (f) p. 218, (g) p. 222, (h) p. 236, (i) pp. 253–254.
(135) Jaffé, H. H., *J. Chem. Phys.*, **21**, 415 (1953).
(136) Jaffé, H. H., *J. Am. Chem. Soc.*, **76**, 4261 (1954).
(137) Jaffé, H. H., *J. Org. Chem.*, **23**, 1790 (1958).
(138) Jaffé, H. H., *J. Am. Chem. Soc.*, **81**, 3020 (1959).
(139) Jaffé, H. H., and Gardner, R. W., *J. Am. Chem. Soc.*, **80**, 319 (1958).
(140) Jencks, W. P., and Carriuolo, J., *J. Am. Chem. Soc.*, **82**, 675 (1960).
(141) Jencks, W. P., and Carriuolo, J., *J. Am. Chem. Soc.*, **82**, 1778 (1960).
(142) Jencks, W. P., and Carriuolo, J., *J. Am. Chem. Soc.*, **83**, 1743 (1961).
(143) Johnston, K. M., and Williams, G. H., *J. Chem. Soc.*, 1446 (1960).
(144) Joy, J. R., and Orchin, M., *J. Am. Chem. Soc.*, **81**, 306 (1959).
(145) Kamlet, M. J., and Glover, D. J., *J. Am. Chem. Soc.*, **78**, 4556 (1956).
(146) Kaufmann, J. J., and Koski, W. S., *J. Am. Chem. Soc.*, **82**, 3262 (1960).
(147) Kilpatrick, M., *Chem. Rev.*, **30**, 159 (1952).
(148) Kilpatrick, M., and Arenberg, C. A., *J. Am. Chem. Soc.*, **75**, 3812 (1953).
(149) Kilpatrick, M., and Eanes, R. D., *J. Am. Chem. Soc.*, **65**, 589 (1943).
(150) Kirkwood, J. G., *J. Chem. Phys.*, **2**, 351 (1934).
(151) Kloosterziel, H., and Backer, H. J., *J. Am. Chem. Soc.*, **74**, 5806 (1952).
(152) Knowles, J. R., Norman, R. O. C., and Radda, G. K., *J. Chem. Soc.*, 4885 (1960).
(153) Kochi, J. K., and Hammond, G. S., *J. Am. Chem. Soc.*, **75**, 3445 (1953).
(154) Kosower, E. M., *J. Am. Chem. Soc.*, **80**, 3253 (1958).
(155) Kosower, E. M., *J. Am. Chem. Soc.*, **80**, 3261 (1958).
(156) Kosower, E. M., *J. Am. Chem. Soc.*, **80**, 3267 (1958).
(157) Kreevoy, M. M., Harper, E. T., Duval, R. E., Wilgens, H. S., and Ditsch, L. T., *J. Am. Chem. Soc.*, **82**, 4899 (1960).
(158) Kreevoy, M. M., Morgan, C. R., and Taft, R. W., Jr., *J. Am. Chem. Soc.*, **82**, 3064 (1960).
(159) Kreevoy, M. M., and Taft, R. W., Jr., *J. Am. Chem. Soc.*, **77**, 5590 (1955).
(160) Kuwana, T., Bublitz, D. E., and Hoh, G., *J. Am. Chem. Soc.*, **82**, 5811 (1960).
(161) Kwart, H., and Price, M. B., *J. Am. Chem. Soc.*, **82**, 5123 (1960).
(162) Kwart, H., and Weisfeld, L. B., *J. Am. Chem. Soc.*, **78**, 635 (1956).
(163) Kwart, H., and Weisfeld, L. B., *J. Am. Chem. Soc.*, **80**, 4670 (1958).
(164) Laidler, K. J., and Eyring, H., *Ann. N.Y. Acad. Sci.*, **39**, 303 (1940).
(165) Laidler, K. J., and Landskroener, P. A., *Trans. Faraday Soc.*, **52**, 200 (1956).
(166) Leffler, J. E., *J. Org. Chem.*, **20**, 1202 (1955).
(167) Leffler, J. E., and Petropoulos, C. C., *J. Am. Chem. Soc.*, **79**, 3068 (1957).
(168) Lewis, E. S., and Johnson, M. D., *J. Am. Chem. Soc.*, **81**, 2070 (1959).
(169) Lewis, E. S., and Johnson, M. D., *J. Am. Chem. Soc.*, **82**, 5408 (1960).
(170) Lunn, W. H., *Spectrochim. Acta*, **16**, 1088 (1960).
(171) Macauley, C. E., and King, C. V., *J. Am. Chem. Soc.*, **74**, 6221 (1952).
(172) McDaniel, D. H., and Brown, H. C., *J. Org. Chem.*, **23**, 420 (1958).
(173) McGowan, J. G., *Chemistry & Industry*, 632 (1948).

(174) McGowan, J. G., *J. Soc. Chem. Ind.* (London), **68**, 253 (1949).
(175) McGowan, J. G., *J. Appl. Chem.*, **10**, 312 (1960).
(176) Maki, A. H., and Geske, D. H., *J. Am. Chem. Soc.*, **83**, 1852 (1961).
(177) de la Mare, P. B. D., *J. Chem. Soc.*, 4450 (1954).
(178) Marshall, H. P., and Grunwald, E., *J. Am. Chem. Soc.*, **76**, 2000 (1954).
(179) Mason, J. G., and Rosenblum, M., *J. Am. Chem. Soc.*, **82**, 4206 (1960).
(180) Miller, J., *Austral. J. Chem.*, **9**, 61 (1956).
(181) Miller, J., *J. Am. Chem. Soc.*, **79**, 93 (1957).
(182) Miller, S. I., *J. Am. Chem. Soc.*, **81**, 101 (1959).
(183) Minnick, L. J., and Kilpatrick, M., *J. Phys. Chem.*, **43**, 259 (1939).
(184) Newman, M. S., and Merrill, S. H., *J. Am. Chem. Soc.*, **77**, 5552 (1955).
(185) Norman, R. O. C., Radda, G. K., Brimacombe, D. A., Ralph, P. D., and Smith, E. M., *J. Chem. Soc.*, 3247 (1961).
(186) Norman, R. O. C., and Ralph, P. D., *J. Chem. Soc.*, 2221 (1961).
(186A) Noyce, D. S., Bottini, A. T., and Smith, S. G., *J. Org. Chem.*, **23**, 752 (1958).
(187) Ogata, Y., and Tsuchida, M., *J. Am. Chem. Soc.*, **81**, 2092 (1959).
(188) O'Gorman, J. M., and Lucas, H. J., *J. Am. Chem. Soc.*, **72**, 5489 (1950).
(189) Okamoto, Y., and Brown, H. C., *J. Org. Chem.*, **22**, 485 (1957).
(190) O'Sullivan, D. G., and Sadler, P. W., *J. Chem. Soc.*, 4144 (1957).
(191) Packer, J., Vaughan, J., and Wilson, A. F., *J. Org. Chem.*, **23**, 1215 (1958).
(192) Packer, J., Vaughan, J., and Wong, E., *J. Org. Chem.*, **23**, 1373 (1958).
(193) Parker, R. E., and Isaacs, N. S., *Chem. Rev.*, **59**, 766 (1959).
(194) Paul, M. A., and Long, F. A., *Chem. Rev.*, **57**, 1 (1957).
(195) Pavelich, W. H., and Taft, R. W., Jr., *J. Am. Chem. Soc.*, **79**, 4935 (1957).
(196) Pearson, D. E., Baxter, J. F., and Martin, J. C., *J. Org. Chem.*, **17**, 1511 (1952).
(197) Pearson, D. E., and Burton, J. D., *J. Org. Chem.*, **19**, 957 (1954).
(198) Peters, D., *J. Chem. Soc.*, 2654 (1957).
(199) Petty, W. L., and Nichols, P. L., Jr., *J. Am. Chem. Soc.*, **76**, 4385 (1954).
(200) Pocker, Y., *J. Chem. Soc.*, 1179 (1959).
(201) Power, D. H., Jr., Schatz, V. B., and Clapp, L. B., *J. Am. Chem. Soc.*, **78**, 907 (1956).
(202) Price, C. C., and Dudley, E. A., *J. Am. Chem. Soc.*, **78**, 68 (1956).
(203) Price, C. C., Mertz, E. C., and Wilson, J., *J. Am. Chem. Soc.*, **76**, 5131 (1954).
(204) Rao, C. N. R., and Goldman, G. K., *Can. J. Chem.*, **36**, 1596 (1958).
(205) Rao, C. N. R., Goldman, G. K., and Balasubramanian, A., *Can. J. Chem.*, **38**, 2508 (1960).
(206) Rao, C. N. R., and Verkataraghavan, R., *Can. J. Chem.*, **39**, 1757 (1961).
(207) Roberts, J. D., and Carboni, R. A., *J. Am. Chem. Soc.*, **77**, 5554 (1955).
(208) Roberts, J. D., and Moreland, W. T., Jr., *J. Am. Chem. Soc.*, **75**, 2167 (1953).
(209) Roberts, J. D., and Regan, C., *J. Am. Chem. Soc.*, **76**, 939 (1954).
(210) Roberts, J. D., Sandford, J. K., Sixma, F. L. J., Cerfontain, H., and Zagt, R., *J. Am. Chem. Soc.*, **76**, 4525 (1954).
(211) Roberts, J. L., and Jaffé, H. H., *J. Am. Chem. Soc.*, **81**, 1635 (1959).
(212) Russell, G. A., *J. Am. Chem. Soc.*, **78**, 1047 (1956).
(213) Russell, G. A., *J. Org. Chem.*, **23**, 1407 (1958).
(214) Sager, W. F., and Ritchie, C. D., *J. Am. Chem. Soc.*, **83**, 3498 (1961).
(215) Schubert, W. M., Craven, J. M., Minton, R. G., and Murphy, R. B., *Tetrahedron*, **5**, 194 (1959).
(216) Schubert, W. M., Steadley, H., and Craven, J. M., *J. Am Chem. Soc.*, **82**, 1353 (1960).
(217) Shiner, V. J., and Verbanic, C. J., *J. Am. Chem. Soc.*, **79**, 373 (1957).
(218) Siegel, S., and Kormany, J. M., *J. Am. Chem. Soc.*, **82**, 2547 (1960).
(219) Smith, B. B., and Leffler, J. E., *J. Am. Chem. Soc.*, **77**, 2509 (1955).
(220) Smith, G. F., *J. Chem. Soc.*, 521 (1943).
(221) Stecher, E. D., Dunn, F., and Gelblum, E., *J. Am. Chem. Soc.*, **79**, 4748 (1957).
(222) Stock, L. M., and Brown, H. C., *J. Am. Chem. Soc.*, **82**, 1942 (1960).
(223) Streitwieser, A., Jr., *J. Am. Chem. Soc.*, **78**, 4935 (1956).
(224) Streitwieser, A., Jr., *Chem. Rev.*, **56**, 637 (1956).
(225) Strier, M. P., and Cavagnol, J. C., *J. Am. Chem. Soc.*, **80**, 1565 (1958).
(226) Swain, C. G., *J. Am. Chem. Soc.*, **72**, 4578 (1950).
(227) Swain, C. G., and Dittmer, D. C., *J. Am. Chem. Soc.*, **75**, 2647 (1953).
(228) Swain, C. G., Dittmer, D. C., and Kaiser, L. E., *J. Am. Chem. Soc.*, **77**, 3737 (1955).
(229) Swain, C. G., Kaiser, L. E., and Knee, T. E. C., *J. Am. Chem. Soc.*, **80**, 4092 (1958).
(230) Swain, C. G., Knee, T. E. C., and McLachlan, A., *J. Am. Chem. Soc.*, **82**, 6101 (1960).
(231) Swain, C. G., and Langsdorf, W. P., Jr., *J. Am. Chem. Soc.*, **73**, 2813 (1951).
(232) Swain, C. G., and McLachlan, A., *J. Am. Chem. Soc.*, **82**, 6095 (1960).
(233) Swain, C. G., and Mosely, R. B., *J. Am. Chem. Soc.*, **77**, 3727 (1955).
(234) Swain, C. G., Mosely, R. B., and Bown, D. E., *J. Am. Chem. Soc.*, **77**, 3731 (1955).
(235) Swain, C. G., and Scott, C. B., *J. Am. Chem. Soc.*, **75**, 141 (1953).
(236) Swain, C. G., Stockmayer, W. H., and Clarke, J. T., *J. Am Chem. Soc.*, **72**, 5426 (1950).
(237) Taft, R. W., Jr., *J. Am. Chem. Soc.*, **74**, 2729 (1952).
(238) Taft, R. W., Jr., *J. Am. Chem. Soc.*, **74**, 3120 (1952).
(239) Taft, R. W., Jr., *J. Am. Chem. Soc.*, **75**, 4231 (1953).
(240) Taft, R. W., Jr., *J. Am. Chem. Soc.*, **75**, 4237 (1953).
(241) Taft, R. W., Jr., *J. Am. Chem. Soc.*, **75**, 4538 (1953).
(242) Taft, R. W., Jr., "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N.Y., 1956, Chapter 13: (a) pp. 565–570, (b) p. 581, (c) p. 598, (d) p. 601, (e) pp. 607–610, (f) p. 614, (g) p. 621, (h) p. 660 ff.
(243) Taft, R. W., Jr., *J. Phys. Chem.*, **64**, 1805 (1960).
(243A) Taft, R. W., Jr., personal communication.
(244) Taft, R. W., Jr., Deno, N. C., and Skell, P. S., *Ann. Rev. Phys. Chem.*, **9**, 287 (1958).
(245) Taft, R. W., Jr., Ehrenson, S., Lewis, I. C., and Glick, R. E., *J. Am. Chem. Soc.*, **81**, 5352 (1959).
(245A) Taft, R. W., Jr., Fox, I. R., and Lewis, I. C., *J. Am. Chem. Soc.*, **83**, 3349 (1961).
(246) Taft, R. W., Jr., and Kreevoy, M. M., *J. Am. Chem. Soc.*, **79**, 4011 (1957).
(247) Taft, R. W., Jr., and Lewis, I. C., *J. Am. Chem. Soc.*, **80**, 2436 (1958).

(248) Taft, R. W., Jr., and Lewis, I. C., *J. Am. Chem. Soc.*, **81**, 5343 (1959).
(249) Taft, R. W., Jr., and Lewis, I. C., *Tetrahedron*, **5**, 210 (1959).
(250) Thompson, H. W., Needham, R. W., and Jameson, D., *Spectrochim. Acta*, **9**, 208 (1957).
(251) Thompson, H. W., and Sted, G., *Trans. Faraday Soc.*, **52**, 1421 (1956).
(252) Venkataraman, H. S., and Hinshelwood, C., *J. Chem. Soc.*, 4977 (1960).
(253) Wagner, C., *Z. physik. Chem.*, **A115**, 121 (1925).
(254) Walling, C., and Jacknow, B. B., *J. Am. Chem. Soc.*, **82**, 6113 (1960).
(255) Walling, C., and Miller, B., *J. Am. Chem. Soc.*, **79**, 4181 (1957).
(256) Waters, W. A., *J. Chem. Soc.*, 1554 (1933).
(257) Waters, W. A., "Physical Aspects of Organic Chemistry," D. Van Nostrand, Inc., New York, N.Y., 1950, Chapter 11.
(258) Wells, P. R., paper presented before the 35th A.N.Z.A.A.S. Congress, Section B, Brisbane, Australia, May, 1961.
(259) Wells, P. R., and Adcock, W., to be published.
(260) Wells, P. R., and Pritchard, I. E. M., *J. Am. Chem. Soc.*, in press.
(261) Wells, P. R., and Ward, E. R., *Chemistry & Industry*, 528 (1958).
(262) White, W. N., Gwynn, D., Schli, R., Girard, C., and Fife, W., *J. Am. Chem. Soc.*, **80**, 3271 (1958).
(263) Willi, A. V., *Helv. Chim. Acta*, **40**, 2019 (1957).
(264) Wilputte-Steinert, L., and Fierens, P. J. C., *Bull. soc. chim. Belg.*, **64**, 308 (1955).
(265) Wilputte-Steinert, L., and Fierens, P. J. C., *Bull. soc. chim. Belg.*, **65**, 719 (1956).
(266) Wilputte-Steinert, L., Fierens, P. J. C., and Hannaert, H., *Bull. soc. chim. Belg.*, **64**, 628 (1955).
(267) Winstein, S., Clippinger, E., Fainberg, A. H., and Robinson, G. C., *J. Am. Chem. Soc.*, **76**, 2597 (1954).
(268) Winstein, S., and Fainberg, A. H., *J. Am. Chem. Soc.*, **79**, 5937 (1957).
(269) Winstein, S., Fainberg, A. H., and Grunwald, E., *J. Am. Chem. Soc.*, **79**, 4146 (1957).
(270) Winstein, S., Grunwald, E., and Jones, H. W., *J. Am. Chem. Soc.*, **73**, 2700 (1951).
(271) de Witt, E. J., Lester, J. T., and Ropp, G. A., *J. Am. Chem. Soc.*, **80**, 3271 (1958).
(272) de Wolfe, R. H., *J. Am. Chem. Soc.*, **82**, 1585 (1960).
(273) Wynne-Jones, W. F. K., *Proc. Roy. Soc.* (London), **A140**, 440 (1933).
(274) Yeh, S-J., and Jaffé, H. H., *J. Am. Chem. Soc.*, **81**, 3287 (1959).
(275) Yukawa, Y., and Tsuno, Y., *J. Am. Chem. Soc.*, **79**, 5530 (1957).
(276) Yukawa, Y., and Tsuno, Y., *J. Am. Chem. Soc.*, **81**, 2007 (1959).
(277) Yukawa, Y., and Tsuno, Y., *Bull. Chem. Soc. Japan*, **32**, 960 (1959).
(278) Yukawa, Y., and Tsuno, Y., *Bull. Chem. Soc. Japan*, **32**, 965 (1959).
(279) Yukawa, Y., and Tsuno, Y., *Bull. Chem. Soc. Japan*, **32**, 971 (1959).
(280) Zollinger, H., *Helv. Chim. Acta*, **36**, 1730 (1953).