THE DISSOCIATION CONSTANTS OF MONOCARBOXYLIC ACIDS; THEIR MEASUREMENT AND THEIR SIGNIFICANCE IN THEORETICAL ORGANIC CHEMISTRY

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I. INTRODUCTION

Measurements of the dissociation constants of monocarboxylic acids in aqueous solution have contributed very materially to our knowledge of the polar effects of substituent atoms and groups in organic molecules. For the most part the organic chemist is concerned with qualitative considerations, and hence usually takes into account only the relative strengths of acids. Nevertheless, it is imperative that dissociation constant data should be the outcome of work providing a high degree of accuracy, and therefore the old less-reliable data must be superseded by the modern values whenever these are available. The experimental technique and methods of computation have undergone rapid development in recent years, and, as a consequence, dissociation constants of organic acids in aqueous solution can now be determined with considerable accuracy.

The writer has for the last eight years been engaged in the measurement of the strengths of monobasic organic acids in water at 25°C. by a semi-precision conductivity method, and the work has now reached a stage at which a review of the whole will be advantageous. The entire series of dissociation constants are discussed in relation to each other and in the light of recent contributions to the subject of the polarity of groups.

A brief account is given of those aspects of the conductivity method with which the organic chemist may be unfamiliar, and, in addition, arguments are advanced in favor of the use, in organic discussions, of dissociation constant data relating to aqueous solutions and a fixed temperature.

II. MEASUREMENT OF ACID STRENGTHS

A. Early attempts at comparison

It is interesting to trace the early efforts directed at the determination of the acid strengths or "avidities," as they were then abstractly designated. Julius Thomsen, in 1854, attempted to compare, by a thermochemical method, the avidities of two acids competing for a limited quantity of base in aqueous solution, and some twenty years later the investigation was extended by Wilhelm Ostwald, who resorted to a variety of procedures in an attempt to ascertain more accurately the competing avidities. Perhaps the best known of these methods is that of comparing the effects of various acids on the hydrolysis rates of well-known organic compounds, such as methyl acetate and acetamide (this investigation has also the distinction of having marked the beginning of the systematic study of homogeneous catalysis).

In seeking a different method of procedure Ostwald turned his attention to the possibilities of the electrical conductivity of acid solutions (138), and the first experiments concerned hydrochloric, acetic, dichloroacetic, and certain other acids. Kohlrausch had already established the experimental procedure, and by means of it discovered two fundamental laws governing the conductance of salts in aqueous solution (*viz.*, the square-root law and the law of the independent migration of ions). It should be noted that these earlier results were expressed as molecular conductivities (μ), defined as the product of the specific conductance and the number of cubic centimeters containing 1 gram-molecule of the solute, although, later, molecular conductivity was replaced by equivalent conductivity (Λ), which relates to 1 gram-equivalent of the solute. Moreover, the Siemens unit was then the unit of resistance, and hence the values of Λ in the older literature appear lower than those deduced on the present basis of the ohm; these conductivity data may be converted to the present standard by multiplying by the factor 1.066.

The electrical conductivity method proved of great use to Ostwald, for he succeeded in obtaining molecular conductivities at fixed concentrations which presented a relative order completely in harmony with the sequence of avidities arrived at by other methods of comparison; furthermore, a satisfactory explanation of these conductivity results was soon forthcoming.

A year prior to this Arrhenius (2) had published his far-reaching theory of the ionic dissociation of electrolytes. This hypothesis, which accounted so strikingly for the abnormalities in Raoult's cryoscopic measurements, soon led to a means of representing the strength of an acid, and in consequence of its application in this connection the concept became greatly enhanced in value.

It was pointed out by the antagonists of the ionic hypothesis that in the case of strong electrolytes the mass action law did not appear to govern the equilibrium which was supposed to exist between molecules and ions. To counter this, Arrhenius suggested that a better test of the theory would be provided by electrolytes in which dissociation varies over a wider range upon dilution. Experimental data for this class of electrolyte were furnished by Ostwald, who in a short space of time examined about two hundred and forty organic acids in aqueous solution (140). The results proved that the law of mass action was obeyed reasonably well here, and, furthermore, led to the familiar dilution law expression which serves to connect K (dissociation or ionization constant), α (degree of dissociation), and c (molecular concentration). The equation is

$$K = \frac{\Lambda_c^2 \cdot c}{\Lambda_0 \left(\Lambda_0 - \Lambda_c\right)}$$

where Λ_c and Λ_0 are the equivalent conductivities at concentration c and at infinite dilution, respectively. It was found to hold good for further weak acids (18, 164), for phenols (5), and for amines (25), and since that time, i.e., for the past forty years, an ever-increasing body of evidence of this kind has been accumulating.

B. *Thermodynamic dissociation constants*

Until recent years the Ostwald constant had been accepted as a quite satisfactory means of expressing acid strength. For weak acids, although strictly incorrect, it is certainly an approximation, and is now referred to as the classical dissociation constant ($K_{cl.}$). With the elucidation of the anomaly of strong electrolytes, the problem of weak electrolytes has also undergone further scrutiny, and it has become evident that the Ostwald method of computing acid strengths has its shortcomings.

Firstly, it was wrongly assumed that ion mobility is independent of concentration; the Arrhenius degree of ionization, $\alpha = \Lambda_c/\Lambda_0$, must be replaced by Λ_c/Λ_x where Λ_x, although referring to complete dissociation, ascribes to the ions the mobilities obtaining at concentration c. The means of deducing Λ_x from the experimentally determined Λ_0 is provided by Onsager (136), who has modified the Debye–Hückel treatment. Banks (11) has produced a simplified form of the Onsager expression which renders the process of calculation less laborious, *viz.*,

$$\Lambda_x = \sqrt{\Lambda_0^2 - 2b(\Lambda_0\, \Lambda_c\, c)^{1/2}}$$

where b is the Onsager slope, which, for an aqueous solution at 25°C., is $(0.2271\Lambda_0 + 59.78)$.

Secondly, in the mass action equation activities must take the place of stoichiometric concentrations, i.e.,

$$K = \frac{a_{\mathrm{H}} \cdot a_{\mathrm{X}}}{a_{\mathrm{HX}}}$$

Since a, the activity, is given by $c \times f$ (where f is the activity coefficient), the equilibrium constant becomes

$$K = \frac{c_i f \times c_i f}{c_u}$$

where $c_i (= c\alpha)$ and $c_u (= c(1 - \alpha))$ represent the concentrations of ionic and undissociated species, respectively. By taking logarithms and substituting the Debye–Hückel expression, $-\log f = A\sqrt{c_i}$, the above equation becomes

$$\log K = \log \frac{c_i^2}{c_u} - 2A\sqrt{c_i}$$

where $2A$ is a constant which has been evaluated as 1.01 (for details see reference 35). All dependable dissociation constants are calculated on this basis and are called "true" or "thermodynamic" constants ($K_{th.}$).[1] The vast majority of organic acids studied so far possess strengths ranging from 10^{-5} to 10^{-3}, and here the values of $K_{th.}$ are invariably less than those of $K_{cl.}$.

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[1] The terms $K_{\mathrm{th.}}$ and $K_{\mathrm{cl.}}$ are further contractions of the terms $K_{\mathrm{therm.}}$ and $K_{\mathrm{class.}}$ employed in previous papers.

Examination of results for a given acid will show, where the accuracy is great enough, that $K_{cl.}$ falls as dilution increases, in contrast to $K_{th.}$ which remains constant, until finally, at high dilution, the former approaches the value of the latter, as is to be anticipated on theoretical grounds. This feature is illustrated by the data (for aqueous solutions at 25°C.) shown in table 1.

In the case of acids the dissociation constants of which do not fall below 10^{-5} no allowance is made for the conductance of the water used in making the solutions, since these acids are, relatively, so very much stronger than carbonic acid as to depress almost completely the ionization of the latter. For investigations of ordinary organic acids, therefore, the specific conductance of the conductivity water is measured simply to ensure that the specimen is acceptable.

TABLE 1

Variation in $K_{cl.}$ and $K_{th.}$ with dilution

ACETIC ACID (126)			*dl*-MANDELIC ACID (12)		
10^3C	$10^5K_{cl.}$	$10^5K_{th.}$	10^3C	$10^4K_{cl.}$	$10^4K_{th.}$
5.91153	1.801	1.748	6.2307	4.094	3.877
3.44065	1.792	1.749	4.1414	4.060	3.874
2.41400	1.788	1.750	2.9045	4.047	3.880
1.36340	1.785	1.752	2.2938	4.027	3.866
1.02831	1.779	1.750	2.1454	4.030	3.883
0.21844	1.770	1.750	1.4006	3.996	3.873
0.15321	1.766	1.750	1.3190	3.987	3.863
0.11135	1.768	1.753	0.73771	3.936	3.850
0.028014	1.759	1.752	0.22647	3.869	3.866

C. Limiting equivalent conductivities and ion mobilities

In order to determine Λ_0, separate experiments must be made on solutions of a soluble salt of the monobasic acid. The sodium salt is invariably employed for this purpose, since it is a strong electrolyte (uni-univalent) and yields results which may be extrapolated to zero concentration in the plot of Λ_c against $\sqrt{c}$. Actually, in the extrapolation process Kohlrausch's square-root equation is superseded by Onsager's equation, meaning that the plot of $\Lambda_c/\sqrt{c}$ should not only be linear, but the slope should approach the theoretical value (($0.2271\Lambda_0 + 59.78$) given by Onsager for aqueous solutions at 25°C., i.e., the conditions applying to most conductivity measurements).

In the case of a salt derived from a strong acid and strong base solvolysis is negligible, and good agreement with Onsager's equation is reached, provided the simple "normal" solvent correction is applied to the measurements, i.e., for aqueous solutions, allowance having been made for the conductivity of the water, which consists in subtracting the specific conductance of the water from that of the given solution. The sodium salts of most organic acids, however, are appreciably hydrolyzed in solution, and here the "normal" solvent correction proves to be excessive. In arriving at the true correction the hydrolysis must also be taken into account, and a means of calculating the combined solvent and hydrolysis correction has been proposed by Ives (97) and by Davies (34). Lately, however, Banks and Davies (12) have succeeded in showing, by a series of precision measurements on sodium mandelate in samples of water differing in quality, that it is incorrect to assume that carbonic acid is the only impurity in ordinary conductivity water; this assumption is implicit in the suggested method of correction and apparently leads to slight overcorrection. If it is agreed, therefore, that there exist traces of various other impurities in the average specimen of conductivity water, it seems that no exact method of correction can be applied to the results from hydrolyzed salts. It is proposed by Banks and Davies that a value of Λ_0 can be obtained in these cases by suitably inserting a line possessing the theoretical Onsager slope. This method resembles the expeditious procedure employed by the present author (as the result of an earlier suggestion

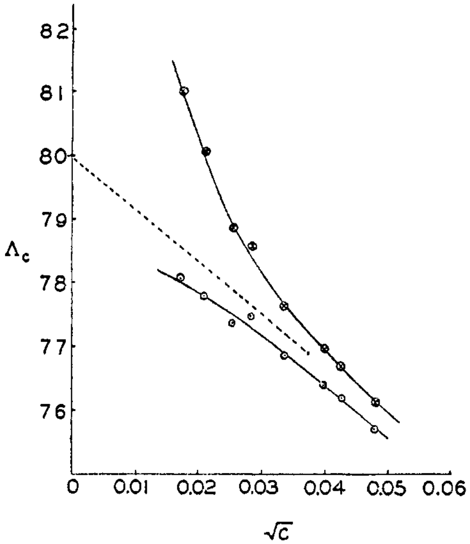


FIG. 1. Plot of Λ_c against $\sqrt{c}$ for sodium *p*-toluate. ⊗, uncorrected; ⊙, "normal solvent" corrected. $\Lambda_0 = 80.0$. The dashed line is the Onsager slope.

by Dr. C. W. Davies), in which values of uncorrected and "normal" corrected Λ_c are both plotted against $\sqrt{c}$, and, where the curves begin to diverge seriously, a straight line is drawn representing the Onsager slope 50, 51) (for all the organic salts studied this line is inclined at an almost constant angle). Figure 1, representing the results for sodium *p*-toluate (due to the author), is typical; it will be seen that the Onsager slope approaches more closely the "normal" solvent-corrected points, agreeing with the observations of Banks and Davies on sodium mandelate. This method provides an accuracy sufficient for the purpose in hand. A divergence of 0.2 unit in Λ_0 affects the dissociation constant of benzoic acid by less than 0.1 per cent, which is negligible, since the constant is expressed, for ordinary purposes, to three significant figures only. Values of Λ_0 obtained in this way have proved reasonably reproducible, and the good agreement with results of other investigators on the sodium salts of acetic, benzoic, and *m*- and *p*-chlorobenzoic acids has given justification for the method (53).

Although most workers apply the square-root relation to their results for aqueous solutions, there exists an alternative method of extrapolation which has also been adopted in modern investigations. This is due to Ferguson and Vogel (59), who employ the formula

$$\Lambda_c = \Lambda_0 - Bc^n$$

where B and n are arbitrary constants estimated by a graphical method for each electrolyte.

In arriving at the value of Λ_0 (acid) from Λ_0 (salt) on the basis of the law of the independent mobility of ions, the data for the limiting mobilities of the hydrogen and sodium ions are used. Computation of actual mobilities involves a knowledge of transport or transference numbers, since the mobility of a specified ion (l) is the product of the equivalent conductivity of an electrolyte containing the ion and the transport number of the ion relating to that electrolyte at the given concentration. Recent and very reliable determinations of transport number by the moving-boundary method (121), coupled with precision measurements of conductivity on aqueous solutions of hydrogen chloride and sodium chloride (154), have led to values of 50.10 and 349.72 for the limiting mobilities of sodium and hydrogen ions, respectively, in water at 25°C. (127). Of course, on the other hand, Λ_0 (salt) can be converted to Λ_0 (acid) simply with a knowledge of $l_{0_{\text{H}}} - l_{0_{\text{Na}}}$, which may be obtained from independent measurements of the limiting equivalent conductivities of suitable electrolytes (e.g., $\Lambda_{0_{\text{HCl}}} - \Lambda_{0_{\text{NaCl}}}$); however, these additional determinations are not necessary now that accurate ion-mobility data are available.

Jeffery and Vogel (101) have published alternative values for the mobilities of the sodium and hydrogen ions, derived from their own conductivity measurements, to which they apply the Ferguson–Vogel formula. It has been pointed out that the use of these mobilities leads to values of Λ_0 (acid) which are 1.4 units (mhos) smaller than those based on the MacInnes–Shedlovsky mobilities, and consequently the values of K are not strictly comparable (40); the latter mobility data appear to be finding the more general acceptance. Until the new data were forthcoming, those of Noyes and Falk (135) and of Kendall (108) were employed.

The mobilities of anions (l_a) derived from various monobasic organic acids vary considerably in magnitude, and some interesting generalizations can be traced upon examination of the data recorded by the present author and his coworkers for some ninety different anions.

In the vast majority of cases the ion mobilities range between 27 and 33 units, and as a rule it can be said that, as the weight and size of the ion increase, the mobility is diminished, and there appears to be no definite limit, which is contrary to the belief held by Ostwald (139) that l_a is not altered further when the ion contains as many as twelve atoms. Nevertheless, it is true that the smaller the ion the greater is the effect of bringing about a given increase in size; this is best illustrated by the following values of l_a for saturated and unsaturated aliphatic acids: acetic, 40.9; *n*-butyric, 35.1; *n*-valeric, 33.4; *n*-hexoic, 30.8; *n*-heptoic, 29.2; *n*-valeric, 28.8; *n*-nonoic, 27.1; *cf.* acrylic, 37.4; vinylacetic, 34.8; allylacetic, 33.0. It has also been noted that in the case of aliphatic monocarboxylic acids, chain branching reduces the speed of migration of the ion, so that for l_a in isomeric ions the order of magnitude is primary > secondary > tertiary, e.g., the anions of *n*-valeric, isovaleric, and trimethylacetic acids possess mobilities of 33.4, 32.7, and 31.9, respectively. A similar conclusion can be drawn from the values of l_a in the cases of *n*-butyric and isobutyric (35.1 and 34.1) and hexoic and diethylacetic (30.8 and 30.4) acids.

In the benzoic and phenylacetic series, the mobilities of the halogen-substituted ions are arranged, for greater part, in the order I < Br < Cl < F (the converse of the order of the halide ions). The effect of a bulky substituent may be distinguished in the *o*-phenyl- and *o*-phenoxy-benzoic ions, which possess mobilities of 23.5 and 23.3, respectively, compared with 33.4 for the benzoic anion. It has been made very clear, however, that bulk and weight are not the only factors influencing the movement of the ion, for it seems that the values of l_a for methyl- and methoxyl-substituted ions are, on the whole, smaller than might be expected when comparison is made with those for halogen- and nitro-substituted anions. Furthermore, examination of the four series (benzoic, phenylacetic, β-phenylpropionic, and cinnamic) shows that the effects of substituting a group in the *o*-, *m*-, and *p*-positions are not identical, although there appears to be no rule as to the change brought about by moving the substituent from one position to another. The mobilities of the anions of *cis*- and *trans*-cinnamic acids are distinctly different (32.6 and 30.4, respectively); the *cis*-form is more compact and possibly is hindered less in its movement. In the aliphatic systems, also, it has been shown that isomeric ions do not possess identical mobilities (99, 41).

D. The conductimetric method of measurement

Although the procedure is still, in principle, that developed by Kohlrausch, vast improvements in equipment and technique have been made since his time.

The induction coil as a source of current is now replaced either by a Vreeland generator (first recommended by Taylor and Acree (160)), or, more commonly, by a thermionic valve oscillator (introduced by Hall and Adams (74)), which produces a constant high-frequency alternating current sensibly free from unidirectional component. Several types of conductivity cell have been introduced from time to time for various purposes; probably the best known are the pipet cells devised by Washburn (165) and the cell of the dipping-electrode type due to Hartley and Barrett (88). Cells of the bottle type have also been used to advantage by numerous workers (100, 50). Silica or borosilicate glass (usually Pyrex or Jena 16 III grade) is used in the construction of the cells, and the electrodes are almost invariably of platinum, greyed or blacked according to requirements. A standard solution of strong electrolyte, conventionally potassium chloride, is employed for calibration of the cell. The first data for such a solution were supplied by Kohlrausch and Holborn (112, 113), although since that time fresh determinations have been made, effecting very small changes, the most recent being due to Jones and Prendergast (107); for cells possessing a relatively low cell constant, the "intermediate cell" method (35) is recommended. In order that reasonable resistances may be measured (the desirable range is 1000 to 50,000 ohms), a variety of cells should be available to cope with solutions covering a wide range of concentration; consequently, judgment must be exercised in the selection of a cell for any given measurement.

Two types of bridge wire are now in general use. There is the straight wire, which is similar to that employed originally by Kohlrausch and by Ostwald, except that the effective length is greatly extended by the attachment of selected resistances at either end of the wire. The second type, namely, the drum-wound form, is compact but is said to have its disadvantages (35). All the standard resistances of the bridge assembly are of the low-inductance quality. It is essential that outside disturbances be eliminated if satisfactory results are to be obtained; thus the current generator must be enclosed by an earthed metal screen. During measurements the balance-point may be obscured somewhat (especially where resistances are high) by capacitance effects arising from the cell, but this difficulty is largely overcome by use of a suitable variable condenser in parallel with the standard resistance. The whole problem of bridge assembly and procedure has been dealt with in detail by Jones and Josephs (106) and by Shedlovsky (154), who suggest numerous refinements.

A telephone of low resistance, tuned to the frequency of the generated current (approximately 1000 cycles per second), is used as detector, sometimes in conjunction with a valve-amplifier, although a loud-speaker device is preferable where difficulty is encountered with the audibility of the note. The greater advantages of a visible indication of balance-point are obvious, and an apparently satisfactory device has now been provided, *viz.*, the null-point indicator ("electric eye"), which embodies a small cathode-ray tube; it is claimed to be extremely sensitive, and doubtless will receive wide application in course of time.

The most satisfactory conductivity water for general use is that described by Kendall (109) and referred to as "equilibrium water." Its chief impurity is carbon dioxide present in such a concentration as to be in equilibrium with atmospheric carbon dioxide; the specific conductivity of this water is 0.8–0.9 gemmho. Various stills have been devised for the preparation of "equilibrium water," although others have been described which are capable of supplying water of even a higher grade. For most conductivity investigations a range of solutions of varying concentration is required; at the present time they are made up by the weight-dilution procedure (proposed by Whetham (171)), as the old method of successive volume-dilution imposed limitations which often led to serious errors. In determining the conductivity of a series of solutions covering a range of concentrations, it is better to make the initial measurement on the strongest solution and to continue through the run with increasing dilution; the adverse effect of adsorption of solute at the electrodes is thus minimized.

The dissociation constants of organic acids recorded in the older literature are less accurate, not only on account of lack of refinements in the procedure but because the purity of the compounds was so frequently open to doubt. This is well illustrated in the fatty acid series, where it has been found that the closest agreement with recent semi-precision measurements (41) is to be found in the determinations of the only investigator (63) who stated consistently the purity of his materials.

It is essential also that precautions should be taken to safeguard the purity of the salts employed in the determinations. These are made from pure acids by titration with sodium hydroxide (carbonate-free), and the solid product is isolated by evaporation and purified by crystallization from alcohol. Successful measurements have been made, however, on the aqueous solutions made directly by titration; in many cases there is no alternative but to proceed in this way, e.g., with nitro-substituted acids and unsaturated aliphatic acids (40).

E. Other methods of measurement

Apart from the conductimetric method there are two other reliable procedures now employed in obtaining the dissociation constants of acids, *viz.*, the potentiometric titration method and the alternative E.M.F. method of Harned. In the former procedure, solutions of the acid are partially neutralized with known quantities of base and the pH of the solutions is determined by means of a suitable electrode made up into a cell with a reference electrode, usually the calomel half-cell. Various electrodes may be used with the solution under investigation; these include the ordinary hydrogen electrode, the glass electrode, and the quinhydrone electrode. Special precautions have to be observed in operating each of these. The following is the choice of electrodes made in the more important investigations of dissociation constant: Branch, Yabroff, and collaborators (178, 23, 24, 19, 179) on substituted phenylboric and the hydroxybenzoic acids (hydrogen electrode); Bennett, Brooks, and Glasstone (14) on substituted phenols (glass electrode); Kuhn and Wassermann (114) on halogeno- and hydroxy-benzoic acids (quinhydrone electrode). It should be realized that the potentiometric method has its shortcomings: briefly, there is doubt regarding the actual potential of the calomel electrode on the hydrogen scale, and, again, uncertainty is introduced by the employment of a liquid junction. Moreover, the experimental accuracy achieved with solutions of sparingly soluble acids compares unfavorably with that obtained in conductimetric measurements.

The alternative cell method has been exploited very successfully by Harned and coworkers (83, 84, 86). In measurements upon four aliphatic acids at temperatures ranging in 5° intervals from 0° to 60°C., they have employed a cell without liquid junction. This consists of a Ag–AgCl electrode and the hydrogen electrode in a solution of the fatty acid and its sodium salt and sodium chloride. From the E.M.F. determined for different concentrations of acid and salt, the thermodynamic dissociation constant is calculated (a concise account of the method of calculation has been given by Glasstone (65)). A high degree of accuracy has been achieved by Harned, and later workers have also used the method to advantage in determining dissociation constants of further acids at a variety of temperatures (see page 162).

F. A survey of the available modern data

All of the dissociation constant data for monobasic organic acids (also for phenols and bases) that have been derived by the modern, more reliable methods are assembled in the appendix to this paper.

Vast numbers of classical constants were published by earlier workers, notably by Ostwald, and they may be used as confirmatory evidence in discussion, especially when a number of them are recorded by a single investigator; nevertheless, no importance must be attached to relatively small differences in such constants. When results are expressed in terms of $K_{cl.}$, there exists the factor introduced by considerations of the concentrations of the acid solutions; it has already been seen that $K_{cl.}$ is not independent of concentration (page 179). If two acids differ widely in solubility, the conductivity measurements might involve solutions differing vastly in dilution, and thus a comparison of the classical constants is rendered invalid. This objection is particularly significant in the fatty acid series.

III. THE EFFECT OF TEMPERATURE AND SOLVENT VARIATION

A. Temperature dependence

Broadly speaking, it can be said that at ordinary temperatures the conductivity of an aqueous solution increases by about 2 per cent per degree rise, although it is possible for temperature elevation to bring about a fall in specific conductivity. With weak electrolytes the temperature coefficient is determined by two factors: namely, the mobilities of the ions, which invariably increase with rising temperature, and the degree of dissociation, which reaches a maximum. At temperatures above this maximum the increase of mobility may not be great enough to offset the effect of decreased dissociation, and with such a state of affairs the measured conductivity may diminish upon elevation of temperature. It is not surprising, therefore, to find that the ionization constants of organic acids have been observed to pass through a maximum (K_m) as the temperature increases. A number of earlier workers, including H. C. Jones, A. A. Noyes, and Schaller, made measurements on organic acids at several temperatures ranging from 5° to 100°C., and although the temperature (θ) of maximum dissociation constant (K_m) was not determined in any case, it was clear that the dissociation constant did not necessarily increase with rise of temperature. In recent years thermodynamic dissociation constants have been recorded for a limited number of acids (formic (84), acetic, propionic (83), *n*-butyric (86), chloroacetic (175), glycolic (134), lactic (128)) at a variety of temperatures, and Harned and Embree (84) show by means of such data that when $\log K_t - \log K_m$ is plotted against

$t - \theta$ (where t is the temperature relating to the dissociation constant K_t), a curve is obtained which approaches parabolic form in the region extending 75°C. on either side of θ, so that for ordinary purposes the following empirical equation satisfactorily connects temperature and the maximum ionization constant,

$$\log K_t - \log K_m = -p(t - \theta)^2$$

where p is a general constant, 5.0×10^{-5} degree^{-2}. Actually, the values of θ and K_m are obtained by plotting $\log K + pt^2$ against t; the slope of the resulting straight line gives $2p\theta$, and the intercept at $t = 0$°C. is $\log K_m - p\theta^2$. This relationship must already be regarded as of great significance.

As a generalization, it may be said that the stronger the electrolyte the lower the temperature of K_m, and it is possible, theoretically, that values of K_t may range themselves in different relative orders according to the temperature. Thus, Harned and Embree have advocated that in a comparison of acid strengths in relation to constitution, it is better to select data for K_m, because then $\Delta H = 0$ in every case, and consequently complications arising from possible differences in heat capacity and entropy effects are eliminated.

Subsequently, both Hammett (78) and Baker (7) also suggested that such complications might affect the relative order of the dissociation constants of acids. The significance of this objection has been considered by the present author (39), who points out that the facts actually indicate, however, that safe conclusions *can* be reached from $K_{th.}$ data relating to a fixed temperature. With evidence of this kind consistent and satisfactory results have been obtained in past discussions, and, moreover, quantitative relationships have been satisfied (see section V); this can scarcely be described as fortuitous. Indeed, it might be anticipated that the differences which are liable to cause complications will be negligible in a series of similar acids (i.e., acids possessing like strengths). The theoretical objection can be tested by taking into account Harned's multi-temperature data for acetic, propionic, and *n*-butyric acids (83, 86). It is seen below that the order is indisputable, no matter whether the values of K relate to a fixed temperature or to θ.

ACID	$K_{10°}$	$K_{25°}$	K_m
Acetic	1.729	1.754	1.76
Propionic	1.326	1.336	1.34
n-Butyric	1.576	1.515	1.57

It is also noteworthy that Pitzer's alternative formula (144), relating K and t, involves the assumption that the entropy change and the change in heat capacity for monobasic acids are constant, and this is given justification by the experimental facts.

It may be concluded, therefore, that evidence goes far to show that accurate values of $K_{th.}$ for acids at 25°C. yield an order of acid strengths acceptable for purposes of discussion, despite the matter of temperature dependence.

B. The effect of changing the solvent

Exceedingly few measurements have been made on solutions of organic acids in non-aqueous solvents, although those which are available make it clear that dissociation in these solvents is substantially less than in water, as might be expected with media of lower dielectric constant. The difficulties encountered in purifying and handling organic solvents are far greater and, moreover, the resistances to be measured are of a higher order. Again, in the case of aqueous solutions of acids, the effect of change in the quality of the solvent upon the conductivity is inappreciable (actually, since carbonic acid is the chief impurity in conductivity water it is unnecessary, in the case of most organic acids, to correct for the solvent conductivity), but with acids in non-aqueous solution the quality of the solvent is a much more important factor (the influence of traces of water is appreciable), and no reasonably reliable method of correction exists; consequently, a grave difficulty is encountered here in interpreting the results. Thus it appears somewhat invidious to attempt to compare the scanty and less trustworthy dissociation constant data for non-aqueous solutions of weak acids with those relating to water.

The bulk of the available data refer to solutions in methyl and ethyl alcohols, and the most extensive conductivity measurements are those of Goldschmidt and collaborators (66) and of Hunt and Briscoe (94). The last-named authors also examined a small number of acids in acetone but did not record any dissociation constants. By using an arbitrary method of correction for the conductivity of the solvent, Goldschmidt obtained constant values of K for alcoholic solutions, but Hunt and Briscoe, by simply deducting the conductivity of the solvent from the measured conductivity, arrived at very irregular values of K. These investigations, together with unpublished work by the present writer on the conductivity of benzoic, phenylpropionic, cinnamic, and other acids in acetone, serve to show that, before wholly satisfactory dissociation constants can be deduced by this method, the problem of true solvent correction needs thorough investigation.

A small number of approximate dissociation constants for organic acids (and bases) in non-aqueous solution have been determined potentiometrically (73, 67, 174, 26, 130a); although it is not certain how reliable these constants may be, they seem to be comparable with the conductimetric data.

Wynne-Jones (176), after a consideration of certain of these results, suggested that organic acids of similar type do not give the same order of strengths in all solvents, and, to exemplify this, he selected a number of constants for aqueous and ethyl alcohol solutions (due to Goldschmidt). In reply to this claim, Burkhardt (28) pointed out that the list of acids in question contained ortho-substituted benzoic acids, which had long been recognized to behave abnormally and therefore should be omitted from a general discussion (compare the findings of Wooten and Hammett (174)). A fuller review of dissociation constants of organic acids in water and in methyl and ethyl alcohols was made later by Wynne-Jones (177), who postulated that dissociation constants will not present the same sequence from solvent to solvent, on account of the varying transfer energies of acids arising from the differing electrostatic conditions in each solvent. From electrostatic considerations he arrived at a relationship connecting dissociation constants in different solvents, and he showed that, for each of the acids under examination, a straight line was given when the values of log K_r (i.e., the logarithmic function of the ratio of the dissociation constant of the acid in question to that of benzoic acid, employed as reference) relating to the three solvents were plotted against the reciprocals of the dielectric constants of the solvents. One aim of the relationship was to provide a means of arriving at a satisfactory

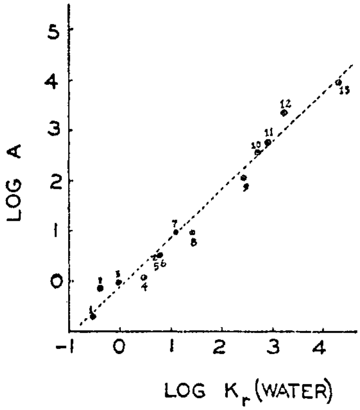


FIG. 2. Plot of log A against log K_r (water) for a number of acids. 1, acetic acid; 2, phenylacetic acid; 3, benzoic acid; 4, formic acid; 5, *m*-nitrobenzoic acid; 6, *p*-nitrobenzoic acid; 7, salicylic acid; 8, 3,5-dinitrobenzoic acid; 9, *o*-nitrobenzoic acid; 10, 2,4-dinitrobenzoic acid; 11, dichloroacetic acid; 12, trichlorobutyric acid; 13, trichloroacetic acid.

comparison of acid strengths, and Wynne-Jones advocated that, in theoretical discussions, his "intrinsic strengths" (A) should be employed; these values refer to a theoretical solvent of infinite dielectric constant and are obtained from the graph by extrapolation, the intercept on the dissociation constant axis giving log A. It is significant, however, that the values of A present the same sequence as that provided by $K_{th.}$ data for the same acids in water (see figure 2), and it is therefore not proved that dissociation constants of acids in water are likely to give an ambiguous relative order.

Lately, Minnick and Kilpatrick (103a) have recorded the relative strengths of a series of acids in water, methyl alcohol, and ethyl alcohol, which give further support for Wynne-Jones' relation (the lack of success experienced with data for certain water–dioxane mixtures seems to indicate that the applicability of the relationship is limited to solvents of dielectric constant > 25). An unaltered sequence of strengths is preserved in all three solvents, the results for *o*-chlorobenzoic acid being excluded, and, again, the intrinsic strengths are in qualitative agreement with the constants for aqueous solutions. It was shown, also, that the strengths of acids in two solvents of equal dielectric constant were the same.

In this connection it should be noted that Wooten and Hammett (174) have shown that with meta- and para-substituted benzoic acids the values of log K_r for butanol and water when plotted yield a straight line (actually, these workers believe that their results as a whole are best interpreted along the lines already discussed by Schwarzenbach and Egli (153a), who take into account, not only the dielectric constant of the solvent for the acid, but the distance separating the reacting group and the substituent and the component of the group dipole acting in this direction). Furthermore, the data provided by Halford (73), Bright and Briscoe (26), and Hixon (67) for alcoholic solutions, and by Griffiths (70) for chlorobenzene solutions (obtained by an indicator method) give, in each case, an order which is precisely the same as that derived from aqueous solutions (after excluding systems which are recognized as abnormal); and Kolthoff, Lingane, and Larson (113a) go so far as to predict the dissociation constants of acids in alcohols from a knowledge of the constants for aqueous solutions.

Apart from this, Wynne-Jones' relationship serves simply to relate K with dielectric constant, although it is known that changes in dielectric constant (and viscosity) do not wholly explain the difference in behavior of electrolytes in passing from solvent to solvent. The factor of chemical affinity, differing vastly with each solvent, is quite important; this point has already been made elsewhere by Hartley *et al.* (89), Hovorka and Simms (93), and others. Bound up with this matter is the problem of true solvent correction, and until this has been elucidated, the strengths in non-aqueous solutions will not be determined (conductimetrically) with an accuracy approaching that which obtains with aqueous solutions.

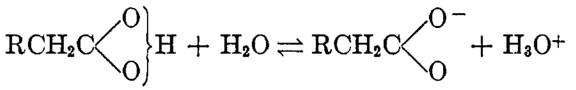
Meantime, in defense of the practice of basing theoretical discussion on a consideration of the relative strengths of acids and bases in water, it may be said that here the solvent possesses a high dielectric constant, and consequently the other factors affecting electrolytic dissociation are rendered comparatively less important; moreover, these are not likely to lead to complications where electrolytes of similar character are being considered. Actually, in any discussion in organic chemistry the acids under review are always of the same type, so that their strengths should be influenced consistently by various factors (13, 174, 170a). The only exceptions are likely to be found in acids containing substituents that affect the strength by some interaction in space, the influence of which may be governed abnormally by the magnitude of the dielectric constant (certain ortho-substituted benzoic acids belong to this category). It has become apparent from the available evidence that, when these systems are excluded, both "intrinsic strengths" and the approximate strengths recorded for various acids in non-aqueous solvents fall into the same sequence as the thermodynamic dissociation constants of these acids in water.

IV. THE EFFECT OF CONSTITUTION ON DISSOCIATION CONSTANTS

A. Generalizations

Ostwald's extensive measurements on carboxylic acids made it clear that substitution of certain groups or atoms gives rise to an increase of strength, whereas other groups lead to a diminution; these were the groups or atoms which had come to be regarded as possessing negative and positive characteristics, respectively. Also, it became evident that the influence of a group was to a great extent determined by its proximity to carboxyl; Wegscheider (170) actually calculated factors representing the influence of the common groups at different positions along the saturated aliphatic chain.

The ionic dissociation of an acid, e.g., of a substituted acetic acid, is governed by the following equilibrium,



$$\mathrm{RCH_2C}\left\langle\begin{matrix}\mathrm{O}\\ \mathrm{O}\end{matrix}\right\}\mathrm{H} + \mathrm{H_2O} \rightleftharpoons \mathrm{RCH_2C}\left\langle\begin{matrix}\mathrm{O}^-\\ \mathrm{O}\end{matrix}\right. + \mathrm{H_3O^+}$$

Thus, when a substituent is introduced into an acid, the influence of the substituent relative to that of hydrogen is expressed by the extent to which the equilibrium is displaced in one direction or the other. When the substituent has the effect of bringing the electrons of the hydrogen–oxygen linkage more under the control of the oxygen, it leads to an enhancement of acid strength, and, conversely, when the substituent causes the opposite movement of electrons, it creates a diminution of strength.

In the substituted acetic acids the extent to which the polarity of the substituent group influences the dissociation constant of the acid is analogous to its effect on the dipole moment (μ) of the corresponding substituted methane. The electron-attractive or electron-repulsive nature of groups is identified with the amount of restraint exercised by the groups over their covalency electrons, and common substituents give the following diminishing order:

$$NO_2 > F > Cl > Br > I > OH > Ph > H > \text{alkyl}$$

The effect of this restraint is transmitted through the molecule and through space, and is likened to electrostatic induction. Flürscheim (61) recognized such an effect, and it has been discussed more precisely in recent years by Lapworth, Robinson, and Ingold, independently, although we are indebted to Lewis (118) for its original electronic interpretation. Throughout this paper the terminology of Ingold is employed; consequently this polar influence in question is referred to as the inductive effect (represented as I), electron repulsion, $R \rightarrow C$, is given a positive sign, and electron attraction, $R \leftarrow C$, is given a negative sign.

In unsaturated conjugate systems there occurs, in addition to the electronic displacement of inductive type, a migration of electrons involving covalency changes as postulated by Lowry (123). It is now understood that this second effect is partly of permanent character and, therefore, like the inductive effect, is reflected in the dipole moment; this permanent component is termed the mesomeric effect (M) and is the outcome of the resonance of the molecule. The total effect, consisting of the permanent and time-variable factors (the latter being brought out on attack of reagents and called the electromeric effect (E)), is designated the tautomeric effect (T) and is represented by curved arrows ($\curvearrowright$).

In interpreting the influence of a substituent in a given position, in benzoic acid, for instance, the changes resulting from the operation of both electronic disturbances must be taken into account.

Full details of the different polar influences, together with accounts of the implications of the conception of quantum-mechanical resonance in theoretical organic chemistry are to be found in recent summaries (147, 96, 167, 168, 104, 142). These principles are assumed in this discussion of the effects of substituent groups on the strengths of acids, which are supported by data for phenols and bases (all the dissociation constants are assembled in the appendix). In the text of the discussion it is frequently more convenient to give the strengths of acids in terms of the unsubstituted acid as unity, i.e., K/K_u. Where the actual dissociation constants are quoted, the values have been multiplied by 10^5 unless otherwise stated, and refer to aqueous solution at 25°C.

B. The influence of alkyl groups[2]

Alkyl groups usually exhibit a weak electron-repulsive character ($+I$); this has been amply demonstrated in various reactions. In the paraffins, however, methyl fails to reveal any polar influence, as shown by the negligible dipole moments of these compounds; this gives ground for the belief that the inductive effect of the alkyl group arises from a stimulation produced by the rest of the molecule (96). When alkyl is directly attached to the aromatic nucleus or to conjugate unsaturated systems generally, electromeric displacements occur; actually this disturbance and the inductive effect both contribute to the dipole moment of toluene.[3]

TABLE 2

Strengths of methyl-substituted aromatic acids

SYSTEM	K/K_u*		
	o-	*m-*	*p-*
Benzoic	1.97	0.87	0.68
Cinnamic	0.87	1.00	0.75
Phenylboric†	0.13	0.71	0.51

* K_u always refers to each appropriate parent acid.

† The tabulated data for substituted phenylboric acids (and phenols) contained in this Section refer to aqueous alcoholic solutions.

The strengths of methyl-substituted aromatic acids reveal that the influence of methyl in the three positions of the nucleus follows the order *o-* and *p-* > *m-* (the abnormal *o*-toluic acid is excluded), as will be seen from table 2. The more effective the substituent the lower the acid strength becomes, and the actual order obtained is a natural consequence of the operation of electromeric displacements from the ortho- and para-positions. A marked diminution of influence is observed in passing from *p*-toluic to *p*-tolylacetic acid (K/K_u, 0.87), and very little further decrease in *p*-methyl-β-phenylpropionic acid (K/K_u, 0.94), although substitution of

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[2] The strengths of aliphatic acids are not discussed here, since they are best dealt with in the light of considerations given in later pages.

[3] Since revision of this article values for the dipole moments of alkylbenzenes and alkylcyclohexanes have been published by Baker and Groves (J. Chem. Soc. **1939**, 1147), and discussed in a further paper dealing with the polar effects of alkyl groups (BAKER: J. Chem. Soc. **1939**, 1150).

p-methyl in cinnamic acid causes a fall nearly as marked as in benzoic acid; this latter change must be attributed to the existence of the conjugate system, which permits the tautomeric transfer of electrons.

Similar conclusions may be drawn from the strengths of methyl-substituted anilines (75), dimethylanilines (36), and benzylamines (30). It must be remembered, of course, that the relative order of strengths of the bases will be the converse of that observed with acids.

Increase of the inductive effect is brought about by extension of the *n*-alkyl chain (110), and also upon progressive substitution of methyl by further methyl groups giving the sequence (96)

$$(CH_3)_3C— > (CH_3)_2CH— > CH_3CH_2— > CH_3—$$

It is noteworthy, however, that the introduction of these homologous groups into aromatic acids indicates the existence of modifying factors; this will be seen from the relative strengths (8) cited below.

ACID	K/K_u			
	CH_3	C_2H_5	*iso*-C_3H_7	*tert*-C_4H_9
p-Alkylbenzoic acid	0.68	0.71	0.71	0.63
p-Alkylphenylacetic acid	0.87	0.87	0.83	0.78

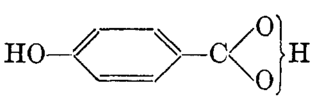
Thus the polar influences of the alkyl substituents, in the benzoic acid series, at least, present a distinctly abnormal order, *viz.*, *tert*-butyl > methyl > ethyl ≈ isopropyl > hydrogen. (It must be borne in mind that this is the order of polar effects, and not of acid strengths.) Anomalies of this kind have been discussed by Baker and Nathan (9), who visualize an electron release of mesomeric type arising from the H—α-C bond, which functions in addition to the inductive effect and decreases in the order methyl ≫ ethyl > isopropyl. It is claimed that this operates only when alkyl is attached to a conjugate system, and that it has its origin in the tendency for electron displacements from the duplet forming the C—H bond in methyl or substituted methyl, i.e., $CH_3CH_2—$ or $(CH_3)_2CH—$; consequently no such effect is associated with *tert*-butyl. This influence when combined with the inductive effect (possessing the same sign but presenting the converse order of magnitudes) might easily lead to a partial or total inversion of the effects of the alkyl groups in question. The strengths of the *p*-alkyl groups quoted here are, therefore, quite in harmony with the Baker–Nathan postulate; it is scarcely to be expected that the anomaly will be detectable in the phenylacetic acid system. The presence of a marked modifying influence in the benzoic acid system only will account for the fact that the differences in strength between various alkylbenzoic acids are no greater than those between the alkylphenylacetic acids.

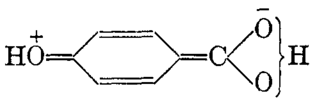
Anomalous behavior of this kind was first observed in the nuclear substitution of *p*-alkyltoluenes which, contrary to expectation, yield a preponderance of the 2-derivative. Kinetic measurements have also furnished examples of this feature, the most recent being provided by studies of the acid-catalyzed prototropy of phenyl alkyl ketones (55) and of the alkaline hydrolysis of saturated aliphatic esters (57).

C. The influence of hydroxyl and alkoxyl groups

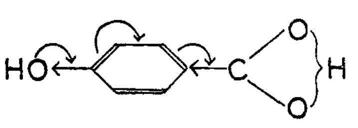
The hydroxyl group has a distinct attraction for electrons ($-I$), but in addition it is capable of releasing unshared electrons from the oxygen atom by the tautomeric mechanism ($+T$) where the system is favorable; thus, for instance, phenols and phenolic ethers give ortho- and para-derivatives on nuclear halogenation and nitration.

In saturated acids substitution of hydroxyl introduces a $-I$ effect only; thus glycolic acid (K/K_u, 8.3) and mandelic acid (K/K_u, 8.0) are stronger than acetic and phenylacetic acids, respectively. Likewise, when hydroxyl occupies the meta-position of benzoic acid, K is increased (K/K_u, 1.32), but *p*-hydroxyl, on the other hand, brings about a fall in strength (K/K_u, 0.46), because here (see formula I) the powerful $+T$ effect (having its origin in resonance between the following structures) successfully opposes $-I$.





For a similar reason *o*-hydroxycinnamic acid (II) is weaker than the parent cinnamic acid (K/K_u, 0.67), although the meta-substituted acid is stronger (K/K_u, 1.10).



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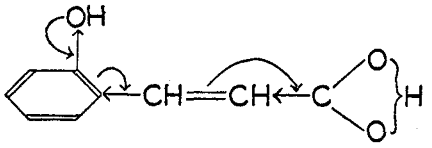


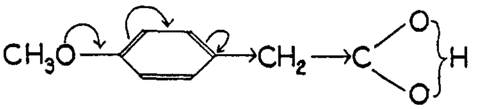
II

Salicylic acid, which exhibits abnormality, will be discussed later.

The influence of alkoxyl is naturally similar to that of hydroxyl. The order of strengths

$$m\text{-RO—} > \text{H} > o\text{- or } p\text{-RO—}$$

is observed in the methoxybenzoic (excluding the ortho-acid), methoxyphenylacetic, methoxy-β-phenylpropionic, methoxycinnamic, and ethoxyphenylboric series, as will be seen from table 3. It has been pointed out elsewhere (49, 46) that the inclusion of phenylacetic and β-phenylpropionic acids would not perhaps have been anticipated, since the transmission of an electromeric effect, as such, is rendered impossible by the intervening methylene linkage (or linkages). The explanation given is that the electromeric displacements initiated by methoxyl proceed to the *p*-(or *o*-)carbon atom, whence the influence of the resulting negative charge is propagated inductively to the carboxyl (III). The substituent is exerting what Robinson (148) has described as "virtually a relayed general or inductive effect."



III

It is noteworthy that the polar influences are most pronounced in the benzoic and cinnamic acids; this is a generalization which applies to all substituent groups and can be attributed to the existence, in those acids, of conjugate systems which greatly facilitate the transfer of polar influences. Also, it is seen that as the substituted benzene nucleus is removed further from the carboxyl, the effect of methoxyl becomes relatively smaller; this is noticeable elsewhere, in the relative effects of other substituents upon benzoic, phenylacetic, and β-phenylpropionic acids.

The contrasting influences of *m*- and *p*-methoxyl (and ethoxyl) groups have been demonstrated in the velocity data for various side-chain reactions, such as the hydrolysis of benzyl bromides (116) and of benzoic and cinnamic esters (111) and the stabilities of potassium hydroxamates (26a); also in the basic strengths of the anilines (75), the dimethylanilines (36), and the benzylamines (30) (see appendix).

A further significant observation is forthcoming from a comparison of the strengths of the hydroxy and corresponding methoxy acids so far determined. Contrary to expectation, methyl, when it displaces hydrogen of the hydroxyl group, causes an *increase* in acid strength (see table 4). On precedent, a definite weakening of the acid would be anticipated upon introduction of methyl, which is regarded as possessing a $+I$ effect. It must be borne in mind, however, that the evidence which indicates this polar influence of methyl refers essentially to methyl attached to carbon. Indeed, it now appears that the sign of the inductive effect is altered when methyl is linked to oxygen, and there exists other evidence to show that the reversal of the normal polar effect is characteristic of methyl in the methoxyl group. It has been shown by Groves and Sugden (72) that phenol possesses a mesomeric moment (1.12) far in excess of that of anisole (0.40); again, it is well known that anisole is attacked by electrophilic reagents far less readily than phenol. Actually, nothing is known of the genesis of the inductive effect of methyl except that its polarity is impressed upon it by the group to which it is attached, and Ingold (96) states that, although "alkyl groups generally function as feebly repelling groups, the possibility of the other type of behaviour can be foreseen."

TABLE 3

Influence of alkoxyl groups on dissociation

ACID	K/K_u		
	o-	*m*-	*p*-
Methoxybenzoic acid	1.29	1.30	0.54
Methoxyphenylacetic acid			0.89
Methoxy-β-phenylpropionic acid	0.72	1.01	0.94
Methoxycinnamic acid	0.94	1.15	0.79
Ethoxyphenylboric acid	0.46	1.55	0.31

TABLE 4

*Strengths of hydroxy- and methoxy-substituted acids**

ACID	K/K_u
Glycolic acid	15
Methoxyacetic acid	33.5
m-Hydroxybenzoic acid	8.3
m-Methoxybenzoic acid	8.1
p-Hydroxybenzoic acid	2.9
p-Methoxybenzoic acid	3.38
o-Hydroxycinnamic acid	2.44
o-Methoxycinnamic acid	3.45
p-Hydroxycinnamic acid	4.00
p-Methoxycinnamic acid	4.21

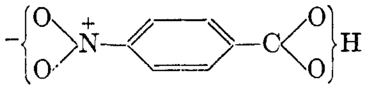
* See references 140, 22, 141, and the appendix.

The change brought about by substituting higher alkyl groups in hydroxy acids is also noteworthy; measurements show that, although introduction of alkyl into glycolic acid always greatly enhances K, the effect diminishes as the group extends (141) (compare the effects of different alkoxyl groups upon halogenation and nitration of the benzene nucleus (105, 146, 31)).

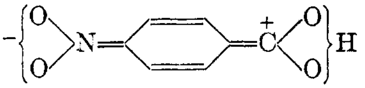
A number of data are available for acids bearing the phenoxyl group. The sequence of strengths for the substituted benzoic acids is m-C_6H_5O— > H > p-C_6H_5O— (see appendix), which is the same as that obtained with methoxybenzoic acids (in this connection it should also be noted that p-phenoxyphenylboric acid is much weaker than the unsubstituted phenylboric acid (19)). It is interesting, however, that in the para-position phenoxyl reduces K more effectively than does methoxyl, whereas in the meta-position it leads to a comparatively greater strength; this latter feature doubtless arises from the inherent electron-attractive character of phenyl as opposed to the electron-repulsion of methyl (see page 169). On the other hand, in the p-phenoxyl group the ambipolar tautomeric character of phenyl ($\pm T$), now capable of exerting itself, apparently gives rise to a greater accession of electrons towards the nucleus than does the inductive effect of methyl. The order m-C_6H_5O— > H is due to the operation of the inductive effect alone; for the same reason (and to a greater degree) phenoxyacetic acid (K/K_u, 42) is very much stronger than acetic acid and, naturally, stronger than methoxyacetic acid (K/K_u, 18.6); this is in harmony with the observation (117) that, in aromatic substitution, the directive power of phenoxyl is small by comparison with that of methoxyl.

D. The influence of the nitroxyl group

The nitro-substituent is powerfully meta-directing in aromatic substitution, indicating a pronounced electron-attractive nature, and consequently it is to be expected that this substituent should increase considerably the strength of an organic acid. For aromatic acids the order of falling strengths is p-NO_2 > m-NO_2 > o-NO_2 > H (excluding the ortho-substituted benzoic acid), as will be seen from table 5. The inductive effect, alone, should lead to the order of strengths m- > p-, but the reverse is actually the case, partly because electromeric displacements ($-T$) occur from the para-position. Numerous examples of the same feature are to be found in the data for reaction velocities of side-chain processes (172) and for classical dissociation constants of phenols (91) and anilines (120a). This additional effect is the outcome of resonance between benzenoid and quinonoid structures (49); with p-nitrobenzoic acid, for example, the following represent the unperturbed structures:

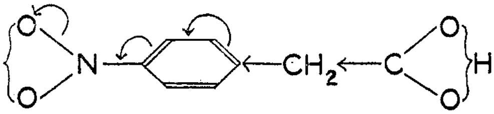


and



This is in contrast to the resonance obtaining in *p*-hydroxybenzoic acid, where the movement of electrons is in the opposite direction (see page 171).

The tautomeric effect is capable of being relayed to some extent through a saturated hydrocarbon chain by the mechanism indicated in formula IV, as shown by *p*-nitrophenylacetic and *p*-nitro-β-phenylpropionic acids, which preserve the normal order (*cf.* the effect of *p*-methoxyl).



IV

It is remarkable that the relative difference between meta- and para-substituted acids is greater in the phenylacetic and β-phenylpropionic acid series than in the benzoic acid series; this is contrary to anticipation, as the tautomeric effect should be far more effective in the latter. The explanation advanced (43) is that in the para series hydrogen ion arises to some extent from the methylene group; this is possible in view of the well-known reactivity of methylene in phenylacetic acid (and in like compounds), and the isolation, by Opolski and Zwislocki (137), of salts of the postulated formula

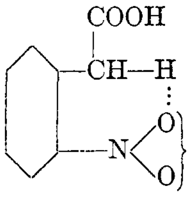
TABLE 5

Strengths of nitro-substituted acids

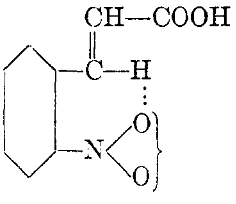
SYSTEM	K/K_u		
	o-	*m*-	*p*-
Benzoic acid	107	5.19	6.00
Phenylacetic acid	2.03	2.21	2.89
β-Phenylpropionic acid	1.44		1.54
Cinnamic acid	1.94	2.08	2.46
Phenylboric acid	2.84	35.0	49.7

$$C_2H_5OCOCH{=}C_6H_4{=}NOOM$$

Moreover, it is noteworthy that the ortho-substituted acids, unlike the para-substituted acids, are not stronger than the meta-substituted acids, although electromeric disturbances should operate from the ortho-position as easily as from the para-position, so as to facilitate ionization of the acid. The suggestion offered by Dippy and Lewis (45, 46) is that nitroxyl in the ortho-substituted acids (phenylacetic (V), β-phenylpropionic, and cinnamic (VI)) is capable of chelating with hydrogen of the methylene group along the lines proposed by Sidgwick and Callow (156) for *o*-nitrotoluene.



V

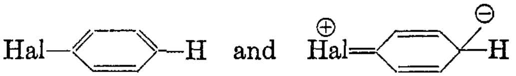


VI

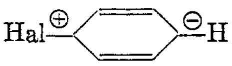
The effect of this chelation is to oppose ionization.

E. The influence of halogens

The inductive effects of the halogens ($-I$) present the sequence F > Cl > Br > I, and the old-established strengths of the halogenoacetic acids are consistent with this. When halogen is attached to the aromatic nucleus, however, its polar effect is considerably modified by an influence of the tautomeric type which diminishes from F to I, thus presenting the same relative order as the inductive effects but possessing the opposite sign. This modifying factor was first recognized by Baddeley and Bennett (4), and it is now generally believed to be a mesomeric effect arising from resonance between benzenoid and quinonoid forms (179, 96), although agreement has not been reached regarding the genesis of this polarization of the aromatic nucleus. Whereas Ingold and Branch attribute it to resonance between structures such as



Bennett and coworkers (14) state that the dipolar unperturbed structure should not involve an actual increase of covalency between halogen and nuclear carbon, if the order F > . . . > I is to be preserved. They overcome the difficulty by proposing the following dipolar structure,



although they admit of a distinct polarizability of the halogen–carbon bond, diminishing in the order I > . . . > F (*cf.* 96, 148). Recently Bird and Ingold (20) have postulated this sequence for the total polarizability effect, which appears to be prominent in aromatic substitution processes (Baker (6) has also been led to this order for the electromeric effects).

The foregoing conflicting influences ascribed to the halogen substituents are in accord with the well-known fact that the halogens, although ortho-para orienting, deactivate the aromatic nucleus (this has been discussed by Bird and Ingold, who have recorded the comparative rates of nitration of monohalogenobenzenes by acetyl nitrate at 18°C.: H, 1; F, 0.15; Cl, 0.03; I, 0.18), and with various dipole moment measurements (most significant in this connection is the sequence of mesomeric moments published by Groves and Sugden (71), *viz.*, C_6H_5F, 1.00; C_6H_5Cl, 0.97; C_6H_5Br, 0.89; C_6H_5I, 0.87).

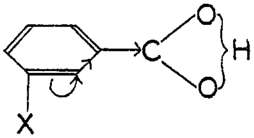
For simplicity the polar effects associated with halogens attached to the benzene ring may be represented as $-I + M$ $(+E)$; the relative influence of these factors upon a particular reaction depends on the system, the nature of the attacking reagent, and external conditions. Thus it happens that halogens in aromatic combination frequently fail to present the inductive order, and sometimes reveal a complete inversion of this order. From the strengths of aromatic acids and of phenols it is seen that, although the inductive effect is the predominant factor (the dissociation constants, with one exception, are distinctly higher than those of the unsubstituted compounds), there is superimposed upon this the opposing mesomeric effect (see table 6). The net polar effect arising from this

TABLE 6

Effect of halogen substitution upon the dissociation of organic acids

POSITION OF SUBSTITUENT	VALUES OF K/K_u			
	F	Cl	Br	I
Benzoic acid series				
o-	8.61	18.2	22.3	21.9
m-	2.18	2.36	2.46	2.25
p-	1.15	1.68	1.71	
Phenylacetic acid series				
o-		1.76	1.81	1.88
m-		1.48		1.42
p-	1.16	1.32	1.33	1.36
Phenylboric acid series				
o-		7.10		
m-	5.58	6.85	7.41	
p-	1.86	3.20	3.68	
Phenol series				
o-	13.4	31.9	30.6	28.5
m-	4.72	15.3	13.7	12.2
p-	0.81	4.13	4.13	6.84

combination of influences has produced, in these acids, partially or completely inverted sequences throughout (the net result of these opposing factors is easily appreciated by reference to the diagrammatic representation by Dippy and Lewis (43)). It will be noted that the *o*- and *p*-fluoro-acids (and *o*- and *p*-phenols) are markedly weaker than the others, indicating a very considerable mesomeric effect in the case of fluorine. Actually this effect appears to predominate in *p*-fluorophenol, the dissociation constant of which is lower than that of phenol. A further important observation is that irregularities extend to the *m*-halogeno-acids; the explanation given (43) is that the disturbance, virtually electromeric, is relayed inductively by the following mechanism (taking, for example, the benzoic acid system (VII)):



VII

Furthermore, it seems, from the data on phenylacetic acid, that the mesomeric effect can be transmitted through a saturated carbon chain (*cf.* the effect of methoxyl).

Comparable data are provided by the halogenoanilines and halogenodimethylanilines (see appendix), where a complete inversion is observed. Additional evidence of the irregularity of the effects of halogens attached to benzene is forthcoming from numerous measurements on reaction velocity (see reference 4 for a summary).

F. The influence of ethenyl and phenyl groups

When the vinyl and phenyl groups are introduced into an aliphatic acid, there is an appreciable increase in strength, as will be seen from the following K/K_u figures:

VINYLACETIC ACID $CH_2{=}CHCH_2COOH$	PHENYLACETIC ACID $C_6H_5CH_2COOH$	DIPHENYLACETIC ACID $(C_6H_5)_2CHCOOH$
2.55	2.78	6.55

This leads inevitably to the conclusion that the ethenyl and phenyl groups possess an intrinsic attraction for electrons (60, 61, 3, 122, 96, 131); for the sake of simplicity Dippy and Lewis (44) refer to this permanent influence as an inductive effect ($-I$). Dipole moment measurements verify the existence of such an effect; in the case of vinyl the following data (in Debye units) due to Höjendahl (161) may be cited as evidence:

Vinyl bromide	1.48	Allyl bromide	1.93	Allyl chloride	1.97
Ethyl bromide	2.09	*n*-Propyl bromide	2.15	*n*-Propyl chloride	2.11

Again, analysis of the dipole moments of substituted benzenes has demonstrated that the aromatic nucleus, on account of its polarizable character, makes a contribution to the measured moment (159, 15).

Although it has still to be understood precisely how this polarization arises, it doubtless has its origin in the unsaturated nature of the groups in question. It is certainly significant that saturation of acids bearing these groups leads to a marked diminution in dissociation constant (see table 7). It will be noticed that the acids containing the cyclohexyl group possess strengths very similar to those of the fatty acids.

TABLE 7

Effect of ethenyl and phenyl groups upon the dissociation of acids

ACID	10^5K
Vinylacetic acid, $CH_2{=}CHCH_2COOH$	4.62
Butyric acid, $CH_3(CH_2)_2COOH$	1.50
Allylacetic acid, $CH_2{=}CH(CH_2)_2COOH$	2.11_5
Valeric acid, $CH_3(CH_2)_3COOH$	1.38
Benzoic acid, C_6H_5COOH	6.27
Cyclohexanecarboxylic acid, $C_6H_{11}COOH$	1.34
Phenylacetic acid, $C_6H_5CH_2COOH$	4.88
Cyclohexylacetic acid, $C_6H_{11}CH_2COOH$	2.36

Comparable results have been obtained with bases upon saturation of the aromatic nucleus, as will be seen from the following data for pK_H obtained by Hall and Sprinkle (75): aniline, 4.6; cyclohexylamine, 10.61; methylamine, 10.64; also *cf.* pyridine, 5.21, and piperidine, 11.31.

It should also be noted that the introduction of a triple bond enhances the strength of an acid much more than does the double bond; this is illustrated by the constants given in table 8. The dipole moment data of Wilson and Wenzke (173) for compounds containing triple bonds likewise indicate that the greater the degree of unsaturation the more pronounced the intrinsic attraction for electrons becomes.

There is ample evidence to show that the so-called inductive effect of the vinyl and phenyl groups can be transmitted along a saturated carbon chain as far as the third member. In table 9 the reference acid in each case is the corresponding saturated acid. Similar conclusions can be drawn from the relative strengths of phenyl-, benzyl-, and phenylethylboric acids (24, 19), and of the phenyl-substituted aliphatic primary amines (30) (see appendix).

When the vinyl and phenyl groups are present in a conjugate unsaturated system, however, a second factor is introduced. It is recognized that these groups, by virtue of their available electrons, are capable of being concerned in electromeric displacements in either direction according to the demand ($\pm T$). This is strikingly illustrated in the relative stabilities of cyanohydrins recorded by Lapworth and Manske (115); phenyl when directly linked to carbonyl acts in the same sense as methyl but causes a 42-fold change in the constant, whereas when phenyl is not conjugated with carbonyl, as in methyl benzyl ketone, no appreciable difference in the constant is noted.

TABLE 8

Effect of a triple bond upon the dissociation of organic acids

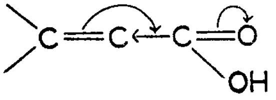
ACID	10^5K
Propionic acid, CH_3CH_2COOH	1.33
Acrylic acid, $CH_2{=}CHCOOH$	5.56
Crotonic acid, $CH_3CH{=}CHCOOH$	2.03
Tetrolic acid, $CH_3C{\equiv}CCOOH$	222.8
Phenylpropiolic acid, $C_6H_5C{\equiv}CCOOH$	590

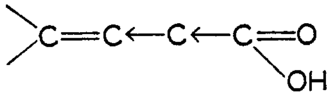
TABLE 9

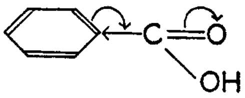
Transmission of effect of vinyl and phenyl groups along a carbon chain

ACID	K/K_u
Acrylic acid, $CH_2{=}CHCOOH$	4.17
Vinylacetic acid, $CH_2{=}CHCH_2COOH$	3.08
Allylacetic acid, $CH_2{=}CH(CH_2)_2COOH$	1.53
Phenylacetic acid, $C_6H_5CH_2COOH$	2.78
β-Phenylpropionic acid, $C_6H_5(CH_2)_2COOH$	1.67
γ-Phenylbutyric acid, $C_6H_5(CH_2)_3COOH$	1.17

This combination of polarization and polarizability effects gives an interpretation to a number of other features apparent in the present data for olefinic and phenyl-substituted acids. In the first place, on comparing acrylic, vinylacetic, and allylacetic acids, it is seen that there is a gradual fall in strength, but the difference between the α,β- and β,γ-unsaturated acids is less than that between the β,γ and γ,δ acids. The operation of the $-I$ effect alone should lead to the order $\alpha,\beta \gg \beta,\gamma > \gamma,\delta$ (comparable to that for halogenated aliphatic acids), but actually in the α,β-acid an opposing electromeric disturbance operates which serves to reduce the dissociation constant (see VIII), even to the extent of producing a different order of strengths among the acids in some instances (*cf.* 99); where the double bond and carboxyl are not included in a conjugate system (IX), only one influence is exerted. A similar reason can be advanced for the anomaly of the first member of the phenyl-substituted series of acids, namely, benzoic acid (X); the difference between the dissociation constants of phenylacetic and β-phenylpropionic acids suggests a constant for benzoic acid far in excess of that actually observed (see appendix).


VIII


IX


X

Examination of the relative strengths of aniline, benzylamine, and β-phenylethylamine discloses a similar feature (appendix).

It has been shown beyond doubt (99) that for *n*-pentenoic and *n*-hexenoic acids the order of strengths is actually $\beta,\gamma > \alpha,\beta > \gamma,\delta$. Evidence of similar significance is provided by the following hydroaromatic acids (32, 149) (K_u relates to the parent saturated acid):

ACID	K/K_u
Δ^1- and Δ^2-tetrahydrobenzoic acid	1.60 and 2.24
Δ^1- and Δ^2-cycloheptenecarboxylic acid	0.76 and 2.20

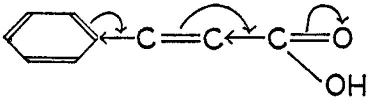
These are instances of the condition indicated above, where the tautomeric effect is great enough to affect the order of strengths. The alternation of dissociation constants in a series, emphasized by earlier workers, is merely incidental and has no meaning beyond that given here.

The influence of alkyl substituents in olefinic acids is much more pronounced than in saturated acids, and this can be attributed to the fact that the system containing the double bond is far more impressionable than one with a saturated carbon chain. Introduction of a methyl or ethyl group into acrylic acid causes the strength to fall by more than one-half, while a second methyl group brings about a further striking diminution of strength, as will be seen from the following results:

SYSTEM	K/K_u		
	CH_3	C_2H_5	$(CH_3)_2$
Acrylic acid	0.37	0.36	0.14
Vinylacetic acid	0.69	0.68	0.56

It is natural, of course, that the influence of alkyl should be less marked in the non-conjugate system.

Phenyl brings about reduction of acid strength when situated in the β-position of an α,β-olefinic acid, e.g., cinnamic acid (K/K_u, 0.66). Doubtless the tautomeric effect of phenyl preponderates here (XI).



XI

In the α-position, however, phenyl has the net effect of enhancing K, as now its inductive influence alone operates (atropic acid: K/K_u, 2.57 (140)).

In contrast to the evidence provided by the phenyl-substituted acids discussed above, there are instances of reactions where the polar influence of phenyl appears to be subordinate to that of methylene; the best known include the ortho-para substitution of diphenylmethane, the relative stabilities of cyanohydrins (115), where introduction of a terminal phenyl group into acetone, methyl ethyl ketone, and methyl *n*-propyl ketone has scarcely any effect upon the thermodynamic constant, and the nitration of guaiacol benzyl ether (1), in which phenyl behaves as though it were conjugated with the aromatic ring in creating a recession of electrons from itself. Thus it is obvious that the individual influences associated with the polarization and polarizability of phenyl are exhibited in varying degree, the priority being determined by the system in which the group is situated and the nature of the reaction.

G. *The ortho-effect*

It is well known that introduction of one or two groups into the ortho-positions of a substituted benzene frequently leads to a marked retardation, or even a complete inhibition, of reaction. Outstanding, of course, are the classical works of Victor Meyer on the esterification rates of organic acids. It was pointed out by Meyer (129, 130) that the abnormality (referred to herein as the "ortho-effect") depends not so much upon the chemical character of the ortho-substituent as upon its size (although no consistent relationship between group size and resultant abnormality was apparent), and it was also shown that behavior was normal when the reacting group was separated from the benzene nucleus by one or more carbon atoms.

The relatively high strengths of ortho-substituted benzoic acids have long been recognized, and this observation has lately been confirmed further by Dippy and Lewis (45) whose measurements are tabulated in table 10 (the constants for phenylacetic acids are included for purposes of comparison). An increase in strength is noted even in the case of substituents which usually have the effect of depressing the dissociation constant.

Meyer's interpretation of the ortho-effect was applied by Flürscheim (61) to explain these high dissociation constants. In modern terms this explanation assumes that in dilute aqueous solution, where the acid is in continuous contact with water, only the reassociation (reverse) process in the equilibrium

$$RCOOH + H_2O \rightleftharpoons RCOO^- + H_3O^+$$

will be affected by steric hindrance; retardation of this process, brought about by the blocking effect of the substituent, leads to an enhanced dissociation constant. Similar views when applied to the equilibrium

TABLE 10

Effect of various substituents on the dissociation of organic acids

POSITION OF SUBSTITUENT	VALUES OF K/K_u						
	CH_3	HO	CH_3O	Cl	Br	I	NO_2
Benzoic acid series							
o-	1.97	15.9	1.29	18.2	22.3	21.9	107
m-	0.87	1.26	1.30	2.36	2.46	2.25	5.19
p-	0.68	0.44	0.54	1.68	1.71		6.00
Phenylacetic acid series							
o-				1.76	1.81	1.88	2.03
m-				1.48		1.42	2.21
p-	0.87		0.89	1.32	1.33	1.36	2.89

$$RNH_2 + H_2O \rightleftharpoons RNH_3^+ + OH^-$$

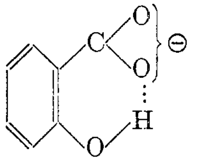
would demand an increase of basic strength in ortho-substituted anilines, for here again only the reverse change should be influenced unfavorably, but actually a marked *decrease* in strength is observed. Straightforward behavior is exhibited by the substituted benzylamines and *N*, *N*-dimethylanilines (appendix), although it is remarkable that the dimethylanilines should contrast with the anilines in this respect.

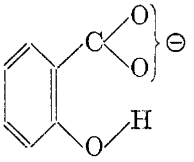
Very few di-ortho-substituted benzoic acids have been examined so far; nevertheless it has become evident that introduction of the second substituent brings about a further large increase in strength.

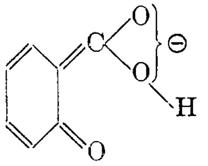
ACID	K/K_u
2,6-Dihydroxybenzoic acid (140)	797
2,6-Dinitrobenzoic acid (157)	1299
2-Methyl-6-nitrobenzoic acid (46)	181

In a survey of the problem of the ortho-effect, Dippy, Evans, Gordon, Lewis, and Watson (42) have pointed out that apparent abnormality is observed in aromatic compounds possessing suitably placed substituents only when the reacting group is a powerful electron-donor, and, in support of this, certain reaction velocity data are cited. Therefore it appears that consideration of the bulk of the ortho-substituent fails to account entirely for the ortho-effect; doubtless, interaction of groups intervenes, and this frequently constitutes the major factor. Thus the present view is that interference with the process of reassociation of the ions of the acid may be effected both by group interaction in space and by bulk (geometrical) influence.

Probably the large bulk of the ortho-substituent is chiefly responsible for the high strengths exhibited by *o*-phenyl- and *o*-phenoxy-benzoic acids; it is seen, for example, that in passing from the latter acid to *o*-methoxybenzoic acid, simple alteration of the hydrocarbon radical causes K to fall to almost one-quarter of its value. On the other hand, the strength of salicylic acid is an order greater than that of *o*-methoxybenzoic acid or of acetylsalicylic acid; obviously the factor intervening here is not of geometrical character. To account for this, Branch and Yabroff (23) have postulated the formation of a hydrogen bond between the hydroxyl and carboxyl groups (compare Sidgwick and Callow's suggestion of chelation in ortho-substituted phenols (156)), whereby reassociation of anion and hydrion is inhibited. It will be seen from formula XII that the groups are favorably situated, and the resonance that renders the bond possible is facilitated by the electronic rearrangements occurring between XIII and XIV (unperturbed structures).

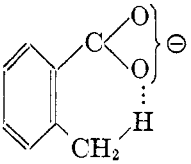

XII


XIII


XIV

This concerns the anion (almost entirely) which will form such a bond more readily than the undissociated acid, since the electron-donating atom here is actually charged. The further large increase in strength exhibited by 2, 6-dihydroxybenzoic acid has been attributed by W. Baker (10) to the formation of hydrogen bonds by both oxygens of carboxyl. Good support for the suggested chelation in phenolic compounds has been forthcoming from infrared absorption spectra (89a, 88a, 175a, 67a); the characteristic OH absorption is found to be absent in certain ortho-substituted phenols, such as salicylaldehyde, *o*-nitrophenol, and salicylic esters, and this is attributed to hydrogen bonding involving the hydroxyl group.

The view has been advanced (42) that a factor of this type contributes substantially to the abnormality of *o*-toluic acid. It is thought probable that a hydrogen bond can be formed between an alkyl group and a suitably placed electron-donating atom; Sidgwick and Callow (**156**) have already postulated chelation in *o*-nitrotoluene (*cf.* Peacock (143) and Evans (55), both of whom have reported similar cases of intramolecular interaction of methyl). Thus the high dissociation constant of *o*-toluic acid may be due to the limited formation of hydrogen bond as shown in formula XV (the explanation offered by Bennett and Mosses (16) refers to an interaction between methyl and carboxyl, but bond formation is not postulated).



XV

On the other hand, an effect of the geometric type may account for the abnormality found in *o-tert*-butylbenzoic acid (K/K_u, 5.58; *p-tert*-butylbenzoic acid, 0.63 (155)).

In the phenylacetic, β-phenylpropionic, and cinnamic acid systems the carboxyl group is too far removed from the ortho-substituent for bulk influences to intervene, and the positions of the atoms are not suitable for chelation; the absence of ortho-effects in these acids can thus be understood. Inspection of the data for substituted phenylboric acids (appendix) does not reveal an ortho-effect, while in the ortho-substituted phenols any enhancement of strength is not ponderable. This latter feature is attributed to the fact that the charged oxygen of the anion in these cases is weakly electron-donating by comparison with the oxygen of the carboxylate ion.[4]

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[4] Jenkins (J. Chem. Soc. **1939**, 1137) has now offered a proof of the non-existence of an ortho-effect in halogeno- and nitro-substituted phenols (and anilines), which goes to show that the inductive effects of the substituents here are very largely responsible for the recorded strengths.

The foregoing views are in harmony with data for the rates of esterification and hydrolysis of ortho-substituted benzoic acids and esters, respectively (see 42, 56). Notably, an ortho-effect is apparent only when the reacting group contains an electron-donating atom.

The case of *o*-methoxybenzoic acid is problematic. Unlike the *p*-isomer, this acid is stronger than the unsubstituted compound; this contrasts also with the behavior of methoxyl in β-phenylpropionic and cinnamic acids. This may be due to the predominance of the inductive effect in the benzoic acid system, where the substituent is situated at such close quarters to carboxyl, meaning that the explanation is an electrostatic one. Very recently, Fox and Martin (62a) have shown, in an infrared spectroscopic investigation, that *p*-methoxybenzoic acid gives the usual carboxylic acid curve, whereas the *o*-methoxybenzoic acid exhibits an additional band of considerable intensity. These authors suggest that the feature may be due to hydrogen-bond formation between OH of carboxyl and the oxygen of methoxyl; it is doubtful, however, whether this would affect the ionization of the acid.

In explanation of the high strengths of *o*-nitro- and *o*-halogeno-benzoic acids it was proposed (42) that oxygen of the carboxylate ion may act as electron-donor in the formation of a coördinate bond with the substituent group. This viewpoint is now rendered unnecessary, however, since Jenkins (102a) (see page 198), by an analysis of the dissociation constants of the isomeric nitro- and halogeno-benzoic acids in the light of classical electrostatic theory and having regard to actual interatomic distances and group moments, has been able to show that these groups behave no less normally when situated in the ortho-position than when placed in the meta- and para-positions, i.e., the large K exhibited by the *o*-nitro- and *o*-halogeno-benzoic acids is simply the outcome of induction, probably occurring largely through space. These groups were selected by Jenkins for analysis because they presented the simplest case from the point of view of calculation, but it so happens that they are the only common groups to show always a predominating inductive effect when substituted in organic acids. In all cases they have the effect of increasing K, no matter whether substituted in aliphatic or aromatic systems. It can be appreciated, therefore, why data for these acids have been capable of interpretation in electrostatic terms. Mesomeric effects are not accounted for by the theoretical treatment, and where these intervene lack of conformity will be evinced; doubtless this factor is responsible for the displacement of *p*-nitrobenzoic acid.

Calculations involving the methyl and hydroxyl groups would have been more complicated, but in any case the dissociation constant data present sequences which are not consistent with an explanation based on electrostatic theory alone. This is due to the fact that with these substituents electromeric effects are much more prominent, e. g., hydroxyl is known to cause an increase *or* decrease in K. Apart from this, there is much more evidence for abnormal behavior of the ortho-substituent in these cases. The effect of methyl in the ortho-position is to increase K, whereas in the meta- and para-positions it reduces K, in accord with normal experience; again, the polar effect of hydroxyl is by no means so different from that of methoxyl as to cause salicylic acid to possess such a vastly superior strength in comparison with *o*-methoxybenzoic acid. Moreover, the explanation offered for the behavior of the methyl and hydroxy acids involves hydrogen-bond formation leading to a six-membered ring with two double bonds, a proposition which contains no novel feature. Indeed, hydrogen-bond formation is regarded as implicit in the suggested resonance of the molecule.

Thus, it now appears that the ortho-effect, with its implication of abnormality, is exhibited in the benzoic acid series only where the ortho-position is occupied either by hydroxyl or methyl substituents or by some particularly bulky group.

Evidence of an ortho-effect in organic acids is not confined to the benzoic acid system. It has already been pointed out (62, 89, 44) that in crotonic acids of *cis*-configuration the substituent group is permanently maintained in a position comparable to that of the ortho-substituent in benzoic acid, and, consequently, a markedly high acid strength is to be anticipated. This is shown below, where it is seen that the *cis*-acids are always much stronger than the *trans*-isomers. The cinnamic acids can be added to this category; allocinnamic acid is about four times as strong as the ordinary (*trans*) acid.

ACID	10^5K	ACID	10^5K
Crotonic acid	2.03	Isocrotonic acid	3.6
α-Chlorocrotonic acid	72	α-Chloroisocrotonic acid	158
Cinnamic acid	3.65	Allocinnamic acid	13.2

The fact that α-naphthoic acid is stronger than β-naphthoic acid doubtless has a similar bearing ($10^5K = 20.4$ and 6.8, respectively (18)). This influence is not reflected in the relative strengths of the naphthylboric acids, but analogy is found in the naphthylamines, where the α-isomer is the weaker base.

It scarcely needs to be emphasized that the problem of the ortho-effect is one of great complexity, and other factors, in addition to the influences which have been discussed, are probably operative. Nevertheless, when a wholly satisfactory explanation of the phenomenon of steric effects is forthcoming, bulk and chelation factors will doubtless prove to be of major significance.

Examination of the classical dissociation constants recorded from time to time for certain 2,3- and 2,5-disubstituted benzoic acids indicates a further factor (quite apart from the ortho-effect) determining the restraint put on the ionization of carboxyl. It is seen that when a meta-substituent is introduced into an ortho-substituted benzoic acid, the effect on K varies according to whether the group is brought into the 3- or the 5-position. In other words, carboxyl is not influenced independently by the two substituents but rather by a resultant effect which is determined, to some extent, by the influence which these groups exert upon each other. From the data in table 11 it is seen that with *o*-nitrobenzoic acid a greater enhancement of strength is brought about by introduction of the meta-substituent into the 5-position, whereas with salicylic and *o*-chlorobenzoic acids greater strength is associated with substitution in the 3-position, although there are cases where the differences are negligible.

TABLE 11

Comparison of the effects of 3- and of 5-substitution upon the dissociation of an orthosubstituted benzoic acid

ACID	10^3K	REFERENCE	ACID	10^3K	REFERENCE
Salicylic acid:			*o*-Chlorobenzoic acid:		
3-Hydroxy-	1.14	(140)	3-Nitro-	8.7	(90)
5-Hydroxy-	1.08		5-Nitro-	6.2	
3-Nitro-	15.7	(140)	*o*-Nitrobenzoic acid:		
5-Nitro-	8.9		3-Chloro-	4.4	(90)
			5-Chloro-	14.2	
o-Chlorobenzoic acid:					
3-Hydroxy-	1.4	(33)	3-Nitro-	14.4	(157)
5-Hydroxy-	1.4		5-Nitro-	26.4	

H. The saturated aliphatic acids

Reliable data are now available for the strengths of the normal series of fatty acids extending from acetic to nonoic acid, together with those of certain analogs. These results are considered separately, because their discussion involves, to some extent, arguments embodied in the interpretation of the ortho-effect.

In the first place, the normal acids, excluding *n*-butyric acid, are found to fall in strength as the series is ascended, and the decrease is most pronounced in passing from acetic to propionic acid. Such behavior is in harmony with our knowledge of the inductive effects ($+I$) of alkyl groups; the sequence of strengths is conveniently represented in figure 3 (for the complete list of constants see the appendix). This compares with the findings of Evans, Gordon, and Watson (57), who studied the alkaline hydrolysis of the ethyl esters of these normal acids; on ascending the series the energy of activation gradually rises, as anticipated in a class B reaction (i.e., one which is facilitated by withdrawal of electrons from the seat of reaction) when the $+I$ effect of the substituent group increases.

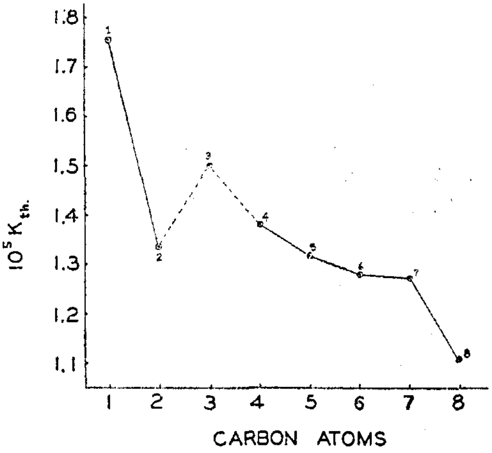
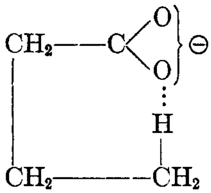


FIG. 3. Plot of the number of carbon atoms in the alkyl chain against values of 10^5K_{th}. 1, acetic acid; 2, propionic acid; 3, *n*-butyric acid; 4, *n*-valeric acid; 5, *n*-hexoic acid; 6, *n*-heptoic acid; 7, *n*-octoic acid; 8, *n*-nonoic acid.

It is evident that *n*-butyric acid behaves anomalously, for its dissociation constant is definitely high. Attention has already been drawn to this by Bennett and Mosses (16), who point out that the terminal methyl group of *n*-butyric acid compares in its situation with the methyl group of *o*-toluic acid, and they postulate, consequently, that the abnormalities exhibited by these acids have a common origin: namely, an interaction of methyl and carboxyl in space. They also state that the abnormality is less marked in the fatty acid because the approach of methyl to the carboxyl group is intermittent here, on account of free rotation of the chain. The conception of hydrogen-bond formation as applied to *o*-toluic acid may supply an interpretation of this spatial interaction in the case of *n*-butyric acid; thus high acid strength would be attributed to the reluctance of hydrion to recombine with the anion in consequence of the following process (41):



Evidence of another kind also shows that the ionization of *n*-butyric acid is affected by some disturbance. Harned and Sutherland (86) record for this acid a value of $\theta = 8°C.$ (temperature of maximum K), whereas with other acids of this order of strength θ lies between 20° and 25°C.

From the data (10^5K) tabulated below (41) it is seen that the dissociation constants of isobutyric and diethylacetic acids are also relatively high; this is to be expected, since these acids also possess the three-carbon alkyl chain. Moreover, the chain branching leads to more frequent approach of the terminal methyl groups to carboxyl, and this would account for the sequence

diethylacetic > isovaleric > *n*-butyric

which is the converse of the order that would arise from operation of inductive effects alone.

Acetic acid........	1.75_5				
Propionic acid....	1.33_5	Isobutyric acid..	1.38	Trimethylacetic acid...	0.891
n-Butyric acid....	1.50	Isovaleric acid...	1.67	Diethylacetic acid.....	1.77_5
n-Valeric acid.....	1.38				

Inspection of figure 3 shows that K for propionic acid is somewhat low by comparison with the succeeding normal acids, and it seems that if all the points representing the higher normal acids were displaced downwards with respect to propionic acid, a perfectly continuous sequence from acetic acid would be revealed. This is probably due to those acids above *n*-butyric acid being involved also, to some extent, in a chelation process. It is a necessary outcome of the view already expressed that hydrogen of γ-methylene should always be capable of forming a bond along the lines suggested. The influence of a chelation factor cannot be traced in the data for unsaturated aliphatic acids, owing, no doubt, to its being masked by the preponderating additional polar effects introduced by the ethenyl grouping.

Chain branching at the α-carbon atom leads to acid strengths which reveal an entirely different problem. From the preceding table it is seen that substitution of a single methyl group in propionic acid at the α-carbon atom does not bring about a fall in K, although with introduction of two methyl groups there is a very appreciable diminution; it is significant that with other acids of the type XCH_2COOH (where X is a substituent other than alkyl) a proportionate fall in K is observed when one methyl group substitutes in the α-position (41).

There is a striking analogy between the relative strengths of *p*-ethyl-, *p*-isopropyl-, and *p*-*tert*-butyl-benzoic acids (10^5K: 4.43_5, 4.43, and 3.98, respectively) and of propionic, isobutyric, and trimethylacetic acids (10^5K: 1.33_5, 1.38, and 0.891, respectively); moreover, it seems as though their interpretations must be identical. The aromatic acids differ from the aliphatic acids only in that a benzene nucleus separates carboxyl from the alkyl group, so that influences arising in the latter will be transmitted readily in both systems. It appears that the partial inversion of the polar effects of ethyl, isopropyl, and *tert*-butyl encountered in the alkylbenzoic acids is being observed once again, and the alternative suggestions due to Baker and Nathan (9) and to the present writer (39, 41) should provide an explanation.

The order of the energies of activation for the alkaline hydrolysis of acetic, propionic, isobutyric, and triethylacetic acids (57) indicates a similar feature (it should be noted that a group which causes a diminution of K in an acid brings about an increase in the energy of activation in a class B reaction). Again, the strengths of the methylamines present the order

$$NH_3 \ll CH_3NH_2 < (CH_3)_2NH \gg (CH_3)_3N$$

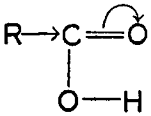
It seems that here an increasing restraint is being put on the inductive effect of methyl as methylation of ammonia proceeds, and this compares with the conclusions drawn above in the case of acids.

It is also interesting to note the changes brought about in basic strengths upon lengthening the alkyl chain. The results of Hall and Sprinkle (75) for the *N*-alkyl- and *N*,*N*-dialkyl-anilines indicate throughout that the ionization is facilitated not in the manner anticipated from operation of the normal inductive effects but always in the order

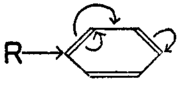
ethyl > *n*-propyl > methyl > hydrogen

meaning that either the ethyl or *n*-propyl group is behaving anomalously.

Finally, formic acid, the first member of the fatty acid series, presents a peculiar problem. It is distinct from its homologs in that its dissociation constant is greater by a power of ten; in other words, introduction of alkyl into formic acid brings about a change of surprising magnitude. It should be kept in mind, however, that introduction of methyl into benzene brings about a striking increase of reactivity in substitution reactions, and there is an analogy between the two processes (cf. 98).



and



I. Sundry substituents

Our knowledge of the influences of other groups upon dissociation constants is not by any means so adequate. Nevertheless, where evidence is forthcoming, it is in harmony with observations regarding the effects of these groups upon other processes.

The acetyl group in aromatic substitution is known to be strongly meta-orienting, and consequently the group is electron-attracting. This would follow from the fact that acetyl, containing carbonyl, presents a positively charged carbon at its point of attachment. Thus, it is to be anticipated that the strength of pyruvic acid will be relatively high ($K = 3.2 \times 10^{-3}$ (21); *cf.* acetic acid, $K = 1.76 \times 10^{-5}$). The enhancing influence of acetyl is only slight, however, when it replaces hydrogen in the hydroxyl group of *m*- and *p*-hydroxybenzoic acids, and the order of strengths

m-acetoxybenzoic acid > benzoic acid > *p*-acetoxybenzoic acid

is preserved, which means that oxygen attached directly to the nucleus is the predominant factor here.

ACID	K/K_u	
	m-	*p*-
Acetoxybenzoic acid (140)	1.58	0.67
Hydroxybenzoic acid (23)	1.32	0.46

Again, the cyano group presents an example of a well-defined electron-attractive substituent (K/K_u for cyanoacetic acid, 205 (140)). Its influence is known to be similar to that of the nitroxyl group, e.g., the dipole moments (*D*) of *p*-tolyl cyanide and nitrobenzene are 4.37 and 4.42, respectively (in benzene solution at 22°C.) (161), and this is also reflected in the following comparison of acid strengths: K/K_u for *p*-cyanobenzoic acid, 4.9 (162); for *p*-nitrobenzoic acid, 6.0 (43).

The influence of the nitrosyl substituent is also noteworthy. It has been shown by Ingold (95) that substitution of nitrosobenzene leads to the para-derivative, and Robinson (145) states that this is to be anticipated. Hammick and Illingworth (82), however, claim that this result is a consequence of the complexity of the reacting molecule under the prevailing conditions, and that when the compound is in unimolecular condition the nitroso group is meta-directing. Introduction of this substituent into an aliphatic acid certainly increases the strength greatly (K/K_u for α-nitrosopropionic acid, 37 (164)), and this is in keeping with the depression of basic strength found in passing from dimethylaniline to *p*-nitrosodimethylaniline (see appendix).

It is convenient to include in this category of miscellaneous acids the few measurements made very recently on certain organic deutero-acids in deuterium oxide as solvent.

Lewis and Schutz (120), employing the minute cell devised by Lewis and Doody (119), have determined conductimetrically the strengths (10^5K) of CH_3COOD and $CH_2ClCOOD$ (0.59 and 63, respectively). As stated by these workers, the differences in zero point energy indicate that proton is bound in the hydro-acid less firmly than deuteron in the deutero-acid, and consequently deutero-acids should be the weaker, as is found to be the case (*cf.* acetic acid, 1.76; chloroacetic acid, 137.8). Moreover, it was also pointed out that the weaker the acid (i.e., the stronger the bond) the greater the relative difference between the strengths of hydro- and deutero-acids (compare Halpern (76)). This is borne out by the foregoing data and by the ratios (K_{D_2O}/K_{H_2O}) for oxalic, formic, and acetic acids recorded by Schwarzenbach, Epprecht, and Erlenmeyer (153) (cf. Hornel and Butler (92)).

V. THE QUANTITATIVE CORRELATION OF DISSOCIATION CONSTANTS

A certain amount of attention has been devoted to the numerical correlation of dissociation constants with other physical characteristics, notably dipole moments, and a summary of the attempts in this direction is given here.

On the grounds that the free energy of ionization of an acid can be expressed as $RT \log_e K$, Derick (37) suggested, several years ago, that the relative polar effects (negativity or positivity) of the radicals in organic acids are best represented quantitatively as $-1000/\log K$ (the negative sign is convenient), and, consequently, the influence of a substituent is given by the ratio

$$-\frac{1000}{\log K}\Big/-\frac{1000}{\log K_u}$$

where K is the dissociation constant of the substituted acid and K_u that of the parent unsubstituted acid. Later Waters (166), also taking the view that the change in free energy of ionization is a measure of the influence of the substituent, endeavored to show that the values of log K for certain substituted benzoic acids (XC_6H_4COOH) were linear functions of the dipole moments (μ, in Debye units) of the corresponding substituted benzenes (XC_6H_5) (a quantity which also expresses the polarity of the molecule). Actually, the strengths of the meta-substituted acids were examined, for here complicating factors such as tautomeric and steric effects were considered to be absent. Indeed, it is reasonable to assume that a quantitative connection between K and μ will exist when the polar influences determining their magnitude are comparable, i.e., when only permanent or "polarization" effects operate in the molecule. Waters' relationship, however, proved to be only very approximate.

The connection between dissociation constant and dipole moment has also been emphasized by Smallwood (158), who has endeavored to show by calculation that the change in the K for an acid, brought about by introduction of a substituent, is determined largely by the magnitude and orientation of the moments of the substituents. From a knowledge of group moments and molecular dimensions, he has estimated values for the changes in energy of ionization, and these agree with experimental figures deduced from actual dissociation constant data (compare the new development due to Kirkwood and Westheimer (111a) connecting K and the electrostatic influence of the substituent group; by means of this mathematical formulation Westheimer and Shookhoff (170a) have accounted for the ratios of the dissociation constants of a few monobasic acids).

A little later, Nathan and Watson (132) succeeded in demonstrating that for the common substituted acetic acids the plot of log K against μ (in Debye units) is a curve of the form

$$\log K = \log K_u - x(\mu + a\mu^2)$$

where x and a are constants for the series. When sufficient accurate data ($K_{\text{th.}}$) for substituted benzoic and phenylacetic acids became available, it was found (47, 48) that the points for the meta-substituted acids were situated on a similar curve, although x and a differed from series to series, e.g., for benzoic acids $x = 0.402$ and $a = 0.14$; for phenylacetic acids $x = 0.125$ and $a = 0.076$. The values of dipole moments employed were those for benzene solutions at a fixed temperature; more satisfactory values, relating to vapors, have since been forthcoming, but on replotting very similar results have been obtained (169).

Upon examination of the elementary possibility that K (for benzoic and phenylacetic acids) is itself very simply related to μ (for mono-substituted benzenes (71, 124)), it was found by the author (38, 46) that the points for the meta-substituted acids are collinear (although where methyl is the substituent the para-substituted acids are included; see below). In figure 4 the points for the phenylacetic acids are plotted; consideration of the methoxy compounds is now excluded, because doubt exists as to the "effective" moment of the methoxyl substituent, which is an inclined group. The relationship has been extended to the β-phenylpropionic series (still employing the dipole moments of mono-substituted benzenes), although it has been shown that with cinnamic acids the points are somewhat irregular; it is appreciated that in the latter series the existence of a double bond in the side chain considerably affects the polarity of the molecule, and thus a comparison with the substituted benzenes is rendered unsound.

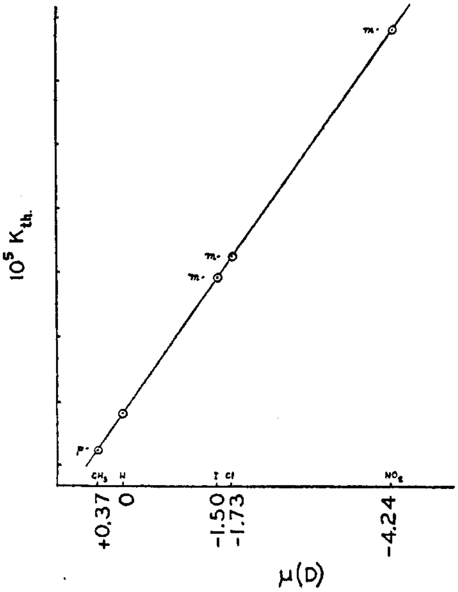


FIG. 4. Plot of μ (in Debye units) for mono-substituted benzenes against values of $10^5 K_{th.}$ for substituted phenylacetic acids.

It has already been mentioned that in the case of the methyl substituent the para-substituted acids, and not the meta-substituted acids, are included in these relationships. This indicates that in toluene the permanent electromeric displacements make a very substantial contribution to the measured moment, in contrast to halogeno- and nitro-benzenes, where apparently the moments are largely the outcome of the intrinsic electron-attractive capacities of the substituents (*cf.* 9). In other words, a considerable part of the polar effect of methyl, as measured in μ for toluene, is inoperative from the meta-position as, for example, in *m*-toluic and *m*-tolylacetic acids (169). In the phenylacetic acid series the points representing the halogeno-substituted acids are on the line (figure 4), showing that any abnormality due to the mesomeric influence has become comparatively insignificant. Again, it would be seen that the points for the *p*-halogeno acids fall well below the line, and that for the *p*-nitro acid, above the line; these divergences are due to the different extents to which electromeric displacements occur in the acids and substituted benzenes. Any connection which this linear relationship may have with the earlier equation proposed by Nathan and Watson is not obvious. It may be that the linear equation, within the narrow limits of its application (it has been applied in each case to acids the strengths of which vary by little more than an order of ten), is simply an approximation of a broader relationship. It certainly has the advantage of being exacting and simple to apply and, at the same time, involves no arbitrary constants.

A different type of correlation has been attempted by Hammett (81, 77), who connects the logarithms of the dissociation constants of acids (or bases) with the velocity constant data for reactions of compounds related in constitution to the acids (or bases), e.g., the strengths of benzoic acids are connected in this way with alcoholysis rates of benzoyl chlorides. In a number of such cases Hammett and other workers (29, 36, 36a, 144a, 88a, 26a) have demonstrated approximate linearity; moreover, similar results have been obtained when log K for two related series of acids or log k for two series of comparable reactions are plotted (80), although it appears that in aliphatic systems the scope of the relationship is limited. The success of these studies has led Hammett (79) to propose a simple formula to represent the influence of a meta- or para-substituent upon the velocity or equilibrium constant of a reaction in which the reacting group is in the side chain; after an analysis of data for a large number of reactions, a table of "reaction" and "substituent" constants was compiled (the effect of a substituent in any given reaction is the product of the appropriate constants).

The equation of Nathan and Watson, cited earlier, has been shown to apply just as well to velocity coefficient data as to dissociation constants (K is simply replaced by k) (132,133,58). In view of this Dippy and Watson (48) have combined the equations,

$$\log K = \log K_u - x(\mu + a\mu^2)$$

$$\log k = \log k_u - y(\mu + b\mu^2)$$

and show that a linear relationship between log K and log k is indicated only if $a = b$. Calculations show that there is no such equality in the coefficients of the μ^2 term, although they may be of the same order of magnitude. Thus Hammett's relationship is not an outcome of known expressions involving μ. Certain of the results discussed by Hammett and by Burkhardt (29) have been replotted by Dippy and Watson with the aid of more reliable dissociation constant data, but distinct divergences still occur; these are inevitable when strict proportionality does not exist between electromeric effects, and this applies especially to the para-substituted systems included in the relationship.

From time to time efforts have been made to estimate the effect upon dissociation constants brought about by removing the substituent along a chain. In 1902 Wegscheider (170) stated that K for a substituted acid was the product of K for the unsubstituted acid and a factor determined by the position of the substituent; he deduced a table of such factors. Again, Derick (37) claimed, as a result of his calculations, that the dissociation constants of α-, β-, γ-, and δ-substituted aliphatic acids were related to the dissociation constants of the unsubstituted acids by a "rule of thirds", although this applied only where powerful electron-attractive groups were involved.

The relationship of MacInnes (125) is particularly interesting; here the dissociation constants of hydroxy- and halogeno-aliphatic acids are connected with the distance of the substituent along the carbon chain. Straight lines were obtained on plotting log K against $1/d$, where d = 1, 2, 3, etc. for α-, β-, γ-(etc.)substitution, meaning that the data fit the equation

$$\log K = C + S\frac{1}{d}$$

(C and S are constants which depend on the nature of the substituent.) The assumption is made that the constant C is the logarithmic function of the dissociation constant of the hypothetical acid obtained by moving the substituent an infinite distance along a chain, although, as MacInnes points out, this K must not be identified with the K of an unsubstituted long-chain acid. It has been claimed that this formula also holds reasonably well for methyl-, hydroxy-, and halogeno-benzoic acids, if the relative distances (d) separating carboxyl and the substituent in the ortho-, meta-, and para-positions are taken to be 1, $\sqrt{3}$, and 2, respectively, i.e., the distances across a regular hexagon. The applicability of the formula has since been extended, although largely in connection with aliphatic amino compounds (54, 68, 152). Recently Greenstein (69) has given this relationship a more precise physical significance; he replaces d by l^2, where l is the distance, in Ångström units, between the dipole center of the group and the carboxyl center (assuming an extended chain); the molecular dimensions recorded by Pauling were employed in calculating l.

The success of the MacInnes relationship is certainly striking, as far as it applies to saturated aliphatic systems. Where the inductive effect of the substituent alone operates, it should follow, as a consequence of the definition of this effect, that the magnitude of the dissociation constant of an acid will be governed in a simple manner by the distance separating carboxyl and the substituent group. It is noteworthy, however, that in the benzoic acid series the MacInnes equation fails to hold good when the present trustworthy dissociation constants data are plotted; this is to be expected in a system where tautomeric effects operate (from the ortho- and para-positions) in addition to the inductive effects, and where steric influences may introduce complications. From figure 5 it is seen that serious irregularities occur with the hydroxy-, methoxy-, and fluorobenzoic acids, as well as with the nitrobenzoic acids (mentioned by MacInnes), and these cannot be corrected by making allowance for the suggested "puckering" of the ring.

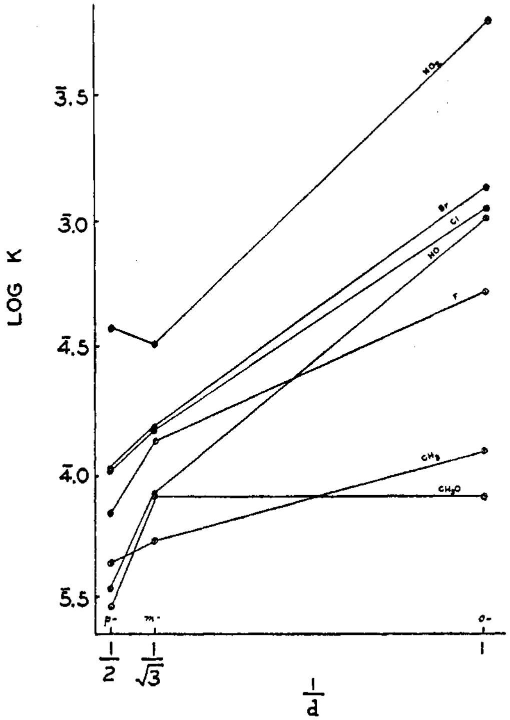


FIG. 5. Plot of $1/d$ against log K for various substituted benzoic acids

Very recently, Jenkins (102a) reëxamined the connection between acid strength and the distance separating carboxyl and the substituent group. He has succeeded in finding a linear relation between log K (for *o*-, *m*-, and *p*-isomers) and the electric intensity due to the substituent dipole (calculated from a knowledge of dipole moment and interatomic distances) in the case of nitro- and halogeno-benzoic acids. This relation has an important bearing on views expressed in regard to the ortho-effect in acids (discussed on page 186), although its applicability is bound to be limited.

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APPENDIX

The scope of this review is limited to monobasic acids. The dissociation constants assembled in the following tables have been determined by modern methods of procedure. Strengths of phenols and bases that are relevant to the discussion are included for the sake of completeness. Data are expressed as thermodynamic constants ($K_{th.}$) except those obtained by Hall and Sprinkle and W. C. Davies, who prefer to record their results for bases in terms of pK_H.

Several independent measurements of $K_{th.}$ have been made on certain of the acids, and agreement, on the whole, is good. The bulk of the data refer to aqueous solution, although in some investigations aqueous alcoholic solutions have been employed. The standard temperature throughout is 25°C., except where otherwise stated. Where several values of K are given for one acid, the first one is the one cited in the discussions of this paper.

I. ACIDS

(*1*) *Saturated aliphatic carboxylic acids*

ACID	VALUES OF 10^5K IN AQUEOUS SOLUTION	METHOD USED*	EXPERIMENTERS
Formic acid	17.12	E	Harned *et al.* (83, 84, 86)
Acetic acid	1.75_5	C	Dippy (41)
	cf. 1.754	E	Harned *et al.* (83, 84, 86)
	1.753	C	MacInnes and Shedlovsky (126)
	1.759	C	Ives, Linstead, and Riley (99)
	1.764	C	Jeffery, Vogel, and Lowry (102)
Propionic acid	1.33_5	E	Harned *et al.* (83, 84, 86)
	cf. 1.343	C	Belcher (12a)
n-Butyric acid	1.50	C	Dippy (41)
	cf. 1.515	E	Harned *et al.* (83, 84, 86)
	1.508	C	Belcher (12a)
Isobutyric acid	1.38	C	Dippy (41)
n-Valeric acid	1.38	C	
Isovaleric acid	1.67	C	
n-Hexoic acid	1.32	C	
n-Heptoic acid	1.28	C	
n-Octoic acid	1.27_5	C	
n-Nonoic acid	1.11	C	
Trimethylacetic acid	0.891	C	
Diethylacetic acid	1.77_5	C	
Chloroacetic acid	137.8	E	Wright (175)

* C = conductimetric method; E = Harned's cell method.

(2) *Unsaturated aliphatic carboxylic acids*

ACID	VALUES OF 10^5K IN AQUEOUS SOLUTION	METHOD USED*	EXPERIMENTERS
Acrylic acid	5.56	C	Dippy and Lewis (44)
	cf. 5.501	C	German, Jeffery, and Vogel (64)
trans-Crotonic acid	2.03	C	Ives, Linstead, and Riley (99)
	cf. 2.030	C	German, Jeffery, and Vogel (64)
	cf. 1.97_5	C	Saxton and Waters (151)
Vinylacetic acid	4.48	C	Ives, Linstead, and Riley (99)
	cf. 4.62	C	Dippy and Lewis (44)
Δ^{α}-*n*-Pentenoic acid	2.02	C	Ives, Linstead, and Riley (99)
Δ^{β}-*n*-Pentenoic acid	3.11	C	
Δ^{γ}-*n*-Pentenoic (allylacetic) acid	2.10	C	
	cf. 2.11_5	C	Dippy and Lewis (44)
β,β-Dimethylacrylic acid	0.76	C	Ives, Linstead, and Riley (99)
	cf. 0.7569	C	German, Jeffery, and Vogel (64)
Δ^{α}-*n*-Hexenoic acid	1.98	C	Ives, Linstead, and Riley (99)
Δ^{β}-*n*-Hexenoic acid	3.05	C	
Δ^{γ}-*n*-Hexenoic acid	1.91	C	
Δ^{δ}-*n*-Hexenoic acid	1.90	C	
γ-Methyl-Δ^{α}-pentenoic acid	1.99	C	
γ-Methyl-Δ^{β}-pentenoic acid	2.51	C	
trans-β-Methyl-Δ^{α}-pentenoic acid	0.74	C	
cis-β-Methyl-Δ^{α}-pentenoic acid	0.71	C	
δ-Methyl-Δ^{γ}-hexenoic acid	1.59	C	
Tetrolic acid	222.8	C	German, Jeffery, and Vogel (64)

* C = conductimetric method.

(3) *Aromatic carboxylic acids*

(*a*) *Values of 10^5K for acids of the benzoic acid series in aqueous solution*

10^5K for benzoic acid = 6.27[a]; *cf.* 6.527[b], 6.373[c], 6.295[d], 6.312[e]

POSITION OF SUBSTITUENT	CH_3	C_2H_5	*iso*-C_3H_7	*tert*-C_4H_9	C_6H_5	CH_3O	C_6H_5O	HO
o-	12.3_5[a]				34.7[a]	8.06[a] (8.2[f])	29.7[a]	105[f] (107[g])
m-	5.35[a]					8.17[a] (9.0[f])	11.2[a]	8.3[f] (8.71[g])
p-	4.24[a]	4.43_5[a]	4.43[a]	3.98[a]		3.38[a] (3.6[f])	3.00[a]	2.9[f] (3.31[g])

	F	Cl	Br	I	NO_2	
o-	54.1[a]	114[a] (119.7[g])	140[a]	137[a]	671[a]	10^5K for 2-methyl-6-nitrobenzoic acid = 1335[a]
m-	13.6_5[a]	14.8[a] (15.06[g])	15.4[a]	14.1[a]	32.1[a]	
p-	7.22[a]	10.5_5[a] (10.4[g])	10.7[a]		37.6[a]	

[a] Dippy and coworkers (51, 52, 43, 45, 8, 46); conductimetric method.
[b] Ives, Linstead, and Riley (99); conductimetric method.
[c] Vogel and Jeffery (163); conductimetric method.
[d] Saxton and Meier (150); conductimetric method.
[e] Brockman and Kilpatrick (27); conductimetric method.
[f] Branch and Yabroff (23); potentiometric method.
[g] Kuhn and Wassermann (114); potentiometric method.

(*b*) *Values of 10^5K for acids of the benzoic acid series in 50 per cent aqueous methyl alcohol solution*[a]

10^5K for benzoic acid = 0.513

POSITION OF SUBSTITUENT	F	Cl	Br	I
o-	6.61	7.08	7.08	6.6
m-	1.41	1.45	1.35	1.41
p-	0.832	1.00	0.933	1.00

[a] Kuhn and Wassermann (114); potentiometric method at 17–20°C.

(*c*) *Values of 10^5K for acids of the benzoic acid series in 25 per cent aqueous ethyl alcohol solution*[a]

10^5K for benzoic acid = 2.29

POSITION OF SUBSTITUENT	HO	CH_3O
o-	63.8	2.09
m-	2.43	2.87
p-	0.750	1.16

[a] Branch and Yabroff (23); potentiometric method.

(d) Values of 10^5K for acids of the phenylacetic acid series in aqueous solution

10^5K for phenylacetic acid = 4.88[a]; cf. 4.88[b]

POSITION OF SUBSTITUENT	CH_3	C_2H_5	*iso*-C_3H_7	*tert*-C_4H_9	CH_3O	F	Cl	Br	I	NO_2
o-							8.60[a]	8.84[a]	9.16[a]	9.90[a]
m-							7.24[a]		6.93[a]	10.8[a]
p-	4.27[a]	4.24[a]	4.06[a]	3.82_5[a]	4.36[a]	5.68[a]	6.45[a]	6.49[a]	6.64[a]	14.1[a]

ACID	10^5K
3,4-Dimethoxyphenylacetic acid	4.64[a]
Mandelic acid	38.8[c]
2,4-Dinitrophenylacetic acid	31.5[a]

[a] Dippy and coworkers (50, 51, 43, 45); conductimetric method.

[b] Jeffery and Vogel (101); conductimetric method.

[c] Banks and Davies (12); conductimetric method.

(e) Values of 10^5K for acids of the β-phenylpropionic acid series in aqueous solution[a]

10^5K for β-phenylpropionic acid = 2.19

POSITION OF SUBSTITUENT	CH_3	CH_3O	Cl	NO_2
o-	2.17	1.57	2.65	3.13_5
m-	2.10_5	2.22	2.60	
p-	2.07	2.04_5	2.47	3.36

[a] Dippy and coworkers (44, 46); conductimetric method.

(f) Values of 10^5K for acids of the cinnamic acid series in aqueous solution*[a]

10^5K for *trans*-cinnamic acid = 3.65; for *cis*-cinnamic acid = 13.2

POSITION OF SUBSTITUENT	CH_3	HO	CH_3O	Cl	NO_2
o-	3.16_5	2.44	3.45	5.83	7.07
m-	3.61_5	4.00_5	4.21	5.08_5	7.58
p-	2.73		2.89	3.86	8.99

[a] Dippy and coworkers (44, 45, 46); conductimetric method.

* All of the acids given in the table are *trans*-modifications.

(g) Values of 10^5K for some unclassified acids in aqueous solution[a]

ACID	10^5K
Diphenylacetic acid	11.5
γ-Phenylbutyric acid	1.75
Cinnamylideneacetic acid	3.75

[a] Dippy and coworkers (50, 44); conductimetric method.

(4) Phenylboric acids

(a) Values of $10^{10}K$ for monosubstituted phenylboric acids[*] in 25 per cent aqueous ethyl alcohol[a]

$10^{10}K$ for phenylboric acid = 1.97; 13.7†; 0.164‡

POSITION OF SUBSTITUENT	CH_3	C_6H_5	C_2H_5O	C_6H_5O	F	Cl	Br	NO_2
o-	0.261 (1.81†)	(0.00984‡)	0.910			14.0		5.6
m-	1.4	(0.185‡)	3.05		11.0	13.5	14.6	69
p-	1.0	(0.158‡)	0.068	0.116	3.66	6.30	7.26	98

OTHER BORIC ACIDS	$10^{10}K$
Boric acid	1.34 (6.53†)
Unclassified boric acids:	
β-Phenylethylboric acid	1.81 (1.0†)
n-Butylboric acid	0.0344 (0.182†)
Benzylboric acid	1.49 (7.55†)
α-Naphthylboric acid	0.888
β-Naphthylboric acid	2.6

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[a] Branch, Yabroff, *et al.* (178, 24, 179, 19); potentiometric method.

[*] $RB(OH)_2$ is, in effect, a monobasic acid, since K appears to be constant over a range of concentrations.

† In water.

‡ In 50 per cent aqueous ethyl alcohol.

(5) Phenols

(a) Values of $10^{10}K$ for monosubstituted phenols

$10^{10}K$ for phenol = 0.32[a]; 0.123[b]

POSITION OF SUBSTITUENT	F	Cl			Br	I
	a	a	b	c	a	a
o-	4.27	10.2	3.2	7.97	9.78	9.12
m-	1.51	4.90	1.95	3.30	4.37	3.89
p-	0.76	1.32	0.47	1.46	1.55	2.19

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[a] Bennett, Brooks, and Glasstone (14); 30 per cent aqueous ethyl alcohol solution; potentiometric method.

[b] Kuhn and Wassermann (114); 50 per cent aqueous methyl alcohol solution; temperature, 20°C.; potentiometric method.

[c] Branch, Yabroff, and Bettmann (24); 25 per cent aqueous ethyl alcohol solution; potentiometric method.

II. BASES

(*a*) *Values of 10^5K_B for methylamines in aqueous solution*[a]

BASE	10^5K_B
Methylamine	43.8
Dimethylamine	52.0
Trimethylamine	5.45
Ammonia	1.79

[a] Harned and Owen (85); Harned's alternative cell method.

(*b*) *Values of $10^{12}K_B$ for monosubstituted anilines in 30 per cent aqueous ethyl alcohol*[a]

$10^{12}K_B$ for aniline = 126

POSITION OF SUBSTITUENT	F	Cl	Br	I
o-	2.95 (9.20*)	1.35	1.00	0.36
m-	10.5 (25.7*)	8.51	7.94	7.59
p-	120 (441*)	28.8	21.9	15.1

[a] Bennett, Brooks, and Glasstone (14); potentiometric method.

* In aqueous solution.

(*c*) *Values of 10^5K_B for monosubstituted benzylamines in aqueous solution*[a]

10^5K_B for benzylamine = 2.35

POSITION OF SUBSTITUENT	CH_3	CH_3O	
o-	1.70	5.56	
m-	2.40	1.56	
p-	2.55	3.22	
	CH_3	C_2H_5	*iso*-C_3H_7
N-alkyl	3.80	4.75	4.18

[a] Carothers, Bickford, and Hurwitz (30); potentiometric method.

(*d*) *Values of 10^5K_B for other phenylamines in aqueous solution*[a]

AMINE	10^5K
β-Phenylethylamine	6.78
γ-Phenylbutylamine	24.8
δ-Phenylpropylamine	15.9
ε-Phenylamylamine	30.6
β-Phenylethylmethylamine	13.9

[a] Carothers, Bickford, and Hurwitz (30); potentiometric method.

In the last four tables (e, f, g, and h) given in the appendix, the results obtained by Hall and Sprinkle (75) and by Davies and coworkers (36, 36a) are presented. These authors give their results in terms of pK_H. These constants are more easily calculated and involve no assumption of the value of K_w. The values follow the same trend as the K_B data.

(e) Values of pK_H for amines of the aniline series[a] *in aqueous solution*

pK_H for aniline = 4.62

POSITION OF SUBSTITUENT	CH_3	CH_3O	C_2H_5O
o-	4.39	4.49	4.47
m-	4.69	4.20	4.17
p-	5.12	5.29	5.25

N-ALKYL DERIVATIVES	pK_H	N-ALKYL DERIVATIVES	pK_H
N-CH_3	4.85	N-CH_3, N-n-C_3H_7	5.64
N-C_2H_5	5.11	N,N-$(C_2H_5)_2$	6.56
N-n-C_3H_7	5.02	N-C_2H_5, N-n-C_3H_7	6.34
N,N-$(CH_3)_2$	5.06	N,N-$(n$-$C_3H_7)_2$	5.59
N-CH_3, N-C_2H_5	5.98		

[a] Hall and Sprinkle (75); potentiometric method.

(f) Values of pK_H for unclassified amines in aqueous solution[a]

AMINE	pK_H
Ammonia	9.27
Diphenylamine	0.85
Triphenylamine	0
Cyclohexylamine	10.61
α-Naphthylamine	3.92
β-Naphthylamine	4.11
2-Aminodiphenyl	3.78
4-Aminodiphenyl	4.27
Pyridine	5.21
Piperidine	11.13

[a] Hall and Sprinkle (75); potentiometric method.

(g) Values of pK_H for derivatives of dimethylaniline in 30 per cent aqueous ethyl alcohol at 20°C.[a]

pK_H for dimethylaniline = 4.76

POSITION OF SUBSTITUENT	CH_3	CH_3O	C_2H_5O
o-	5.42		
m-	4.86		
p-	5.29	5.53	5.59

[a] Davies and coworkers (36, 36a); potentiometric method.

(h) Values of pK_H for derivatives of dimethylaniline in 50 per cent aqueous ethyl alcohol at 20°C.[a]

pK_H for dimethylaniline = 4.21

POSITION OF SUBSTITUENT	CH_3	C_2H_5	C_3H_7	*iso*-C_3H_7	*n*-C_4H_9	*tert*-C_4H_9	CH_3O	F	Cl	Br	I	NO
o-	5.07						5.49					
p-	4.77	4.69	4.43	4.78	4.62	4.65	5.16	4.01	3.33	2.82	2.73	3.52

pK_H for diethylaniline = 5.85; for di-*n*-butylaniline = 4.84

[a] Davies and coworkers (36, 36a); potentiometric method.