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THE EFFECT OF THE POSITION OF SUBSTITUTION ON THE IONIZATION CONSTANTS OF SOME ORGANIC ACIDS

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Since the early work of Ostwald[1] a number of attempts have been made to obtain a definite relation between the ionization constant of a substituted fatty acid and the position, α, β, γ, ... of substitution in the carbon chain. Wegscheider,[2] for instance, has given a table of factors by which the constant of an unsubstituted acid may be multiplied to obtain the corresponding constant of a substituted acid. With chlorine substitution, for example, these factors are $\alpha = 90$, $\beta = 6.2$, $\gamma = 2.0$, $\delta = 1.3$. Such factors are, however, admittedly approximate and are entirely empirical. The subject has also been discussed in various papers by Flürscheim, Michael, Walker, Nelson and Falk, Derick, Simms, and Hixon and Johns.

The following simple relation, which has apparently been overlooked by the writers on the subject, holds for a large number of substituted acids. Briefly, if the logarithm of the ionization constant of each acid is plotted against $1/d$ in which $d = 1$ for the α position, 2 for the β position, etc., remarkably straight lines are obtained for a number of series of substituted acids. For instance, in Fig. 1, the data for the chlorine and hydroxyl substituted acids are plotted as described. The points under consideration are those marked α, β, γ and δ corresponding to the equivalent substituted acids; the other points will be discussed later. In this plot the data have been chosen for the longest chain acid for which measurements are available. These straight lines mean, of course, that the data fit an equation of the type

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

in which K_s is the ionization constant of the substituted acid and C and S are constants. A similar plot, with a slightly greater value for the slope S, is obtained if the data are used for the acids having the substituent

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[1] Ostwald, *Z. physik. Chem.*, **3**, 170, 241, 369 (1889).

[2] Wegscheider, *Monatsh.*, **23**, 287 (1902).

always on the last carbon atom of the chain. Such a series is, for instance, chloro-acetic acid, β-chloropropionic acid, γ-chlorobutyric acid, etc. The agreement is even better in this case than with the long chain series. It appears unlikely that the relation can be accidental. It must have a definite physical origin.

In this connection it is important to recall that if the mutual electric potentials of two charged spheres carrying charges of like sign are plotted as abscissas against the reciprocals of the distances between their centers a straight line is obtained. Thus a system consisting of two like-charged spheres will gain in mutual potential energy, E, by being brought near to each other, according to the relation

$$E = C' \frac{1}{d}$$

the energy E and the constant C' depending on the two charges and the dielectric constant of the space d separating them. It seems, therefore, that it may be more than an analogy that the free energy of ionization, $R\ T \log K$, is connected with the distance, d, between the carboxyl group and, for instance, a combined chlorine atom by the same function as the energy of a system of two electrical charges is affected by the distance between them.

At an infinite distance, however, the expression for the electrical energy becomes zero, whereas the ionization constant of a long chain acid with the substituent at infinity would have, from Equation 1, an ionization constant

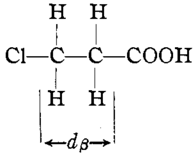
$$\log K_\infty = C$$

This is assuming, of course, that the tendencies observed in the change of ionization constants for the first members of the chain would continue without modification for very long chains, which may not be the case.

It might be expected, at first sight, that $\log K_\infty$ should be the ionization constant of such an unsubstituted long chain acid. The ionization constant of such an acid is nearly independent of the length of the chain, and varies irregularly between the narrow range 1.4×10^{-5} and 1.6×10^{-5}. The constant C, however, leads to a value of $\log K_\infty$ about 65% lower than this for chlorine substitution and about 43% lower for hydroxyl substitution. Though these constants are of the same order of magnitude as the ionization constant of the unsubstituted acid, it is evident that the latter does not fit into the equation or as a point in the plot.

On further consideration, however, it becomes clear that the unsubstituted acid is by no means a member of the series of substituted acids. The attachment of a chlorine or hydroxyl group to the chain can only take place by means of a vigorous chemical reaction or series of reactions, involving the removal of a hydrogen atom and its replacement by another atom or group. That this is attended by a lowering of the total energy of the molecule is shown by the fact that the heat of combustion of the substituted substance is lower than that of the unsubstituted material. It does not seem unreasonable to suppose, therefore, that the primary effect of the halogen or hydroxyl substitution into the molecule is a *lowering* of its free energy of ionization. The second effect is an *increase* of the ionization constant produced by bringing the negative substituent near to the carboxyl group. According to this point of view $C = \log K_\infty$ is the ionization constant of a hypothetical acid in which the chemical change of substitution has taken place, but in which the substituent is still at a long (theoretically infinite) distance from the carboxyl group. The term $S(1/d)$ is, accordingly, a measure of the potential energy involved in bringing the two negative groups near to each other. In any case, and whatever may prove to be the final interpretation of the physical meaning of the constant C, the effect of change of position of a substituent can, strictly, only be studied with isomeric compounds. Otherwise the results of changes of position of atoms or groups will be confused with the results of chemical reactions.

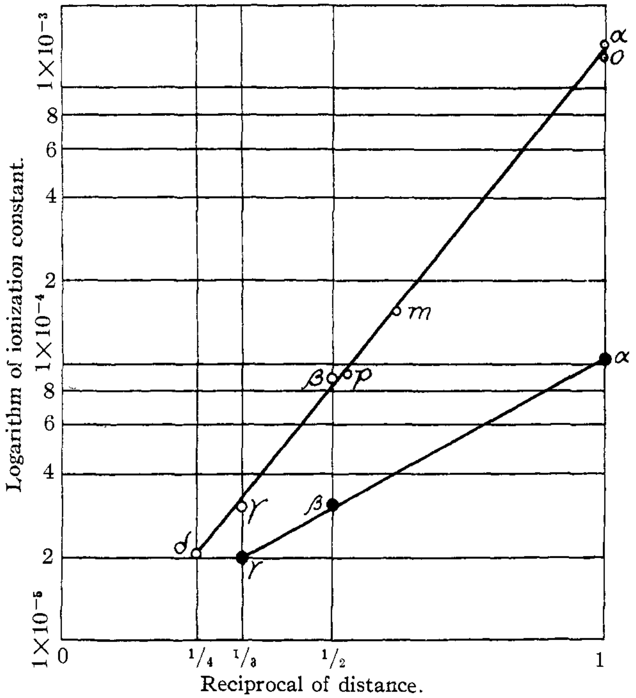
It is of interest to speculate as to the significance of the distance d in terms of atomic dimensions. It is my opinion that it refers to the distance between the polar bond joining the carboxyl to the carbon chain and the polar bond joining the other substituent to the chain, as, for instance, with β-chloropropionic acid



$$\mathrm{Cl{-}\overset{H}{\underset{H}{C}}{-}\overset{H}{\underset{H}{C}}{-}COOH}$$

The movement of a valence electron from a carbon atom to the outer shell of electrons of, for instance, a chlorine atom, probably takes place at such a bond. If the charges involved were situated in the center of the carboxyl carbon and chlorine atoms the series involving d would be $1/(1 + x)$, $1/(2 + x)$, $1/(3 + x)$ (x being the distance between the charges when the two groups are in contact) instead of 1, $^1/_2$, $^1/_3$, . . . as in Fig. 1. Using the available data on the sizes of atoms I have attempted to give values to x, without success. The best agreement with the data is obtained when $x = 0$. The length, d, appears therefore to be the distance between the polar bond joining the carboxyl group to the chain and the polar bond connecting the substituent to the chain, although, if the polar bond is a simple electric dipole, with a constant separation of the charges, the observed relations would not be expected.

Since the simple relation given in Equation 1 applies to the chlorine substituted aliphatic acids, it is important to discover whether the relation also applies to the aromatic series. In this connection it is important to note that *o*-chlorobenzoic acid and α-chlorobutyric acid have very nearly the same ionization constant. The two values are, respectively, 1.3×10^{-3} and 1.4×10^{-3}. It therefore seems reasonable to suppose that, as a close approximation, the polar bonds of the carboxyl group and of the chlorine atom are the same distance apart in the two molecules. Due to the angular relations imposed on the bonds by the ring structure, this can be nearly true for a flat ring, even though the substituent is on the second carbon atom from the carboxyl group in the ortho acid and on the first carbon atom in the α-substituted acid. With the "puckered" ring structure to be discussed below the bonds can approach still nearer each other. However, if we take the ratios of the *o*-, *m*- and *p*-distances as 1,2 and 3, respectively, we obtain a decided curvature on a plot similar to Fig. 1. More nearly straight lines, which are shown in Fig. 2, are obtained for the chlorine and methyl substituted benzoic acids, if the ratios of the distances across a regular hexagon, *through the intervening space for the meta and para position*, are used. With a regular hexagon, the ratios for the *o*-, *m*- and *p*-positions become $1 : \sqrt{3} : 2$. Though the plots in Fig. 2 are nearly straight lines, there is, nevertheless, a distinct bend upward in both.

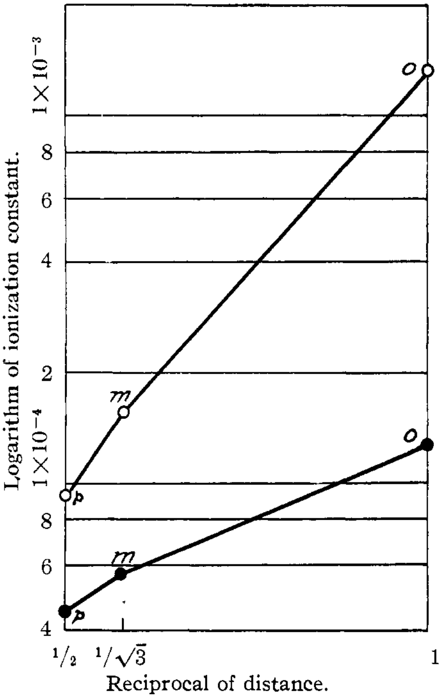


○ = Cl substitution; ● = OH substitution.

Fig. 1.—Chlorine and hydroxyl substituted acids.

A more probable structure for benzene seems to be, however, a "puckered" ring, that is to say, one in which the carbon atoms, and therefore the bonds to the hydrogen or other radicals, are in two parallel planes each containing three carbon atoms.[3] According to this conception the polar bonds would be at the corners of two equilateral triangles which are at a distance, we will call y, apart. The spacial arrangement is shown in Fig. 3. Considering the radius of a circle in which the triangles can be inscribed as unity the ratios of the *o*-, *m*- and *p*-distances are readily seen, in such a model, to be

$$d_o : d_m : d_p = \sqrt{1 + y^2} \; : \; \sqrt{3} \; : \; \sqrt{4 + y^2}$$



O = ClC_6H_4COOH; ● = $CH_3C_6H_4COOH$.

Fig. 2.

By assuming successive values for the distance y, a value 0.36 was found at which the curves in Fig. 2 become straight lines. This empirical procedure would be of little interest except that, dividing these newly computed ratios by $\sqrt{1 + y^2}$ (so that the ortho distance now equals unity) *the points for the three chlorobenzoic acids fall on the line containing the points for the long chain aliphatic chloro substituted acids*. The resulting points are marked *o*, *m* and *p* on Fig. 1. The equation

$$\log \{K \times 10^5\} = -0.30 + 2.44\,(1/d)$$

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[3] Attempts to explain the structure of benzene by positions of electrons led to the arrangement described. See, for instance, Huggins, This Journal, **44**, 1607 (1922), and **45**, 264 (1923); Lewis, "Valence and the Structure of Atoms and Molecules," Chemical Catalog Company, New York, 1923, p. 92; Morse, *Proc. Nat. Acad. Sci.*, **13**, 789 (1927). Hendricks and Bilicke, This Journal, **48**, 3007 (1926), and Dickinson and Bilicke, *ibid.*, **50**, 764 (1928), have arrived, by analysis of x-ray measurements, at a structure for benzene hexabromide having the bromine atoms in two parallel planes each containing three atoms, as in Fig. 3. Victor Henri, *Compt. rend.*, **174**, 809 (1922); *J. Phys. Radium*, **3**, 181–214 (1922), has arrived at the same conclusion as a result of his extensive measurements on absorption spectra. On the other hand, the workers in the field of electric moments of molecules favor a flat molecule for benzene (Smyth and Morgan, This Journal, **49**, 1030 (1927), and Williams, *ibid.*, **50**, 2350 (1928)), although the evidence seems inconclusive.

therefore, holds for both series of acids provided the distances *d* are computed as just described for the benzene substituted series. It is not impossible that the data are insufficiently accurate to decide between the two structures for the benzene ring, and the computations do not preclude the possibility of other structures. However, it is of interest to note that the data for these ionization constants at present in the literature favor the structure in which the carbon atoms are in two planes, provided, of course, that the underlying assumptions of this paper are accepted.

Most of the relatively few substituted benzoic acids that have been measured in the *o*-, *m*- and *p*-forms show at least fair agreement with the relations observed for the chlorine and methyl substituted acids. An exception, if the present data can be trusted, is the nitrobenzoic series. The hydroxyl acids agree reasonably well with the relation, but there is apparently no connection between the aromatic and aliphatic acids as is found for the chlorine series.

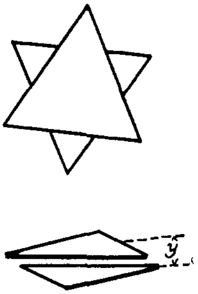

Fig. 3.

Turning our attention to the bromine and iodine substituted compounds, it has been found that the ortho and meta acids have, very closely, the same ionization constants as the corresponding chlorine compounds. This is shown in Fig. 4 in which the solid line, it will be observed, has the same ordinates and abscissas as in Fig. 1. (The data for the para-iodo and para-bromo acids have not yet been obtained.) With the aliphatic bromine and iodine compounds there seems to be a secondary effect producing systematic deviations from this line. Except for the α-substituted iodo acids, this effect is relatively small, and the solid line is the best that can be drawn through the points. A perceptible effect of the kind may possibly be seen in the slight deviations of the aliphatic chlorine compounds and it increases with the weight or complexity of the halogen atom. This effect may be due to the same cause that produces the other well-known systematic changes in carbon chains.

In these computations it has been assumed that the aliphatic carbon chains are straight, or, at least, that the distance *d* increases by regular increments as the substituent is moved out on the chain. This would be expected to be the case if the groups at each end strongly repel each other. If, however, a basic group such as NH_2 is substituted in the chain, this group and the carboxyl group can apparently attract each other, producing distorted molecules. Thus a basic group far out on a carbon chain may, by bending, get very near the carboxyl group, resulting in a lowering of the ionization constant and possibly inner salt formation. The ionization constants of amino substituted fatty acids are in fact found to be very small. On the other hand, the effects of substitution by basic groups in benzoic acid follow closely what would be expected from an undeformable benzene ring. The experimental data are particularly uncertain in this field and they are difficult to interpret since the acids are amphoteric and the ionization "constants" change rapidly with dilution. However, plots of the average "constants," as given by Scudder,[4] for amino- and N-methylaminobenzoic acids, give straight lines within the large experimental error when plotted as described above. It is found that the basic groups yield acids which *increase* with the distance of the sub-

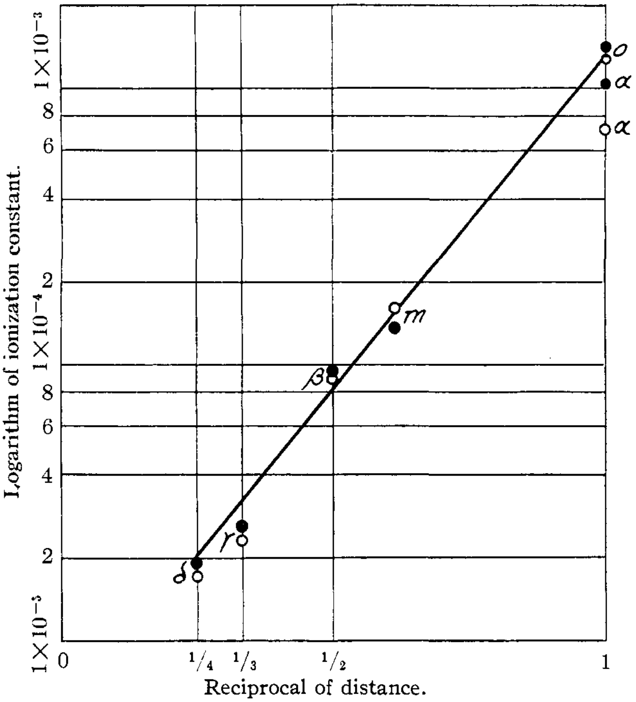

Fig. 4.—Bromine and iodine substituted acids.

stituted group from the carboxyl group. The CH_3NH-group, being probably more strongly basic than the NH_2-group, gives a weaker ortho acid and the effect of removal to the meta and para positions is greater than is the case with the amino group. Both of these effects would be expected from the theory as outlined above.

It is an interesting fact that the aliphatic and aromatic data fall on the same line when the structure of the aliphatic molecule is such that a straight carbon chain is to be expected. The necessary condition is a strong electronegative group on each end of the chain. With com-

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[4] Scudder, "Conductivity and Ionization Constants of Organic Acids," D. Van Nostrand Co., New York, 1914.

pounds containing a carboxyl and a basic group there is no relation yet evident between the behavior of the aliphatic and aromatic series. The data for the latter fit Equation 1 at least roughly, as has just been stated. The aliphatic compounds, however, have very small ionization constants, which would be expected if bending and a consequent close approach of the positive and negative groups should occur. This appears to be evidence that the benzene ring is a stable system, and that the aliphatic chains are comparatively flexible.

Through the kindness of Dr. E. W. Washburn and Dr. James Kendall I have had access, before publication, to the recomputations of ionization constants made by the latter for the International Critical Tables. In these recomputations the best value for the limiting conductance of the hydrogen ion was used, and the data were otherwise, as far as possible, brought to the same standards for necessary fundamental constants. The plots in this paper were prepared from these recomputed constants which, as a matter of fact, differ but little, on the scale of precision which concerns us here, from those found in the last edition of Landolt and Börnstein. The constants used are all at 25°.

No attempt has been made in this paper to recompute the constants to allow for interionic attraction and ionic activities, as the author has done in a previous paper.[5] In the first place, sufficiently accurate data are not available for the recomputation for any except the few acids dealt with in that paper. Also such computations have shown that the value of a constant found by the older method of computation, for more dilute solutions, is not very different, due to a compensation of two factors, from a corresponding value computed on the newer basis. The latter, however, holds over a far wider range of concentrations even for relatively strong acids. The small difference between the two methods of computation may be illustrated by the constants for *o*-chlorobenzoic acid. The older method gives 1.28×10^{-3} as a limiting value and the newer 1.23×10^{-3}, the difference hardly appearing on a plot of the scale of Fig. 1. Provision is, however, already being made to redetermine the conductances of solutions of the chlorine substituted acids in order to obtain constants based on the more modern conceptions.

Brief mention may be made of some of the conclusions reached by others in this field. Derick[6] has proposed a "rule of thirds," which may be stated as follows. If K_u and K_α, K_β, K_γ are the ionization constants of the unsubstituted acid and the α-, β- and γ-substituted acids, respectively, Derick finds that

$$\frac{(\log K_u)}{(\log K_\alpha)} - 1 : \frac{(\log K_u)}{(\log K_\beta)} - 1 : \frac{(\log K_u)}{(\log K_\gamma)} - 1 : \ldots\ldots = 1 : \frac{1}{3} : \frac{1}{9} \ldots\ldots$$

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[5] MacInnes, THIS JOURNAL, **48**, 2068 (1926).

[6] Derick, *ibid.*, **33**, 1152, 1167, 1181 (1911); **34**, 74 (1912).

approximately, for several series of substituents. It is difficult to find a physical basis for this observation, especially as the chemical effect of substitution and the effect of shifting the substituent are both included, as has been shown above, when the formula contains K_u. Hixon and Johns[7] have, in an interesting paper, shown that the logarithms of the ionization constants for a large series of substituents can be plotted on smooth curves and expressed as empirical equations, as functions of an arbitrary "electron combining capacity," and also that the effect of the distance along the chain at which substitution takes place can be dealt with according to empirical formulas of the same form.

Summary

The ionization constants K_s of chlorine and hydroxyl substituted aliphatic acids follow the formula

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

in which C and S are constants and $d = 1$ for the α-position, 2 for the β-position, etc. Theoretically this equation would follow if, in the first place, the substituting and carboxyl groups repel each other according to the inverse square of the distance between their polar bonds, and, secondly, the free energy of ionization is increased in proportion to the mutual potential energy of the two groups.

The ionization of the chlorine substituted benzoic acids follows the same formula accurately if the ortho distance is equal to the α-distance and a slightly "puckered ring" structure for the benzene nucleus is assumed.

The constants for bromine and iodine substituted aliphatic acids show small systematic deviations from the equation, although the corresponding aromatic compounds agree with it closely.

New York, N. Y.

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[7] Hixon and Johns, This Journal, **49**, 1786 (1927).