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APPLICATION OF THE "SCALE OF COMBINED INFLUENCE" TO EXPLAIN THE IONIZATION CONSTANTS OF ORGANIC ACIDS AND A REPLY TO THE CRITICISM OF C. G. DERICK.

BY ARTHUR MICHAEL.

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In a paper published in 1899[1] the writer endeavored to show that a better insight into the chemical properties and relations of organic substances may be obtained from a consideration of the constituent atoms of the molecule than in the usual way of starting from larger parts, or groups. Attention was directed to a then almost forgotten hypothesis of van't Hoff,[2] that two atoms in a molecule act on each other either through direct union or through space, or indirectly, that is through intermediate atoms, and the extent of this mutual influence was expressed as follows: "if we number a certain atom in any fatty compound with a normal carbon chain by the figure 1, our present knowledge of the combined mutual influence between this atom and others in the molecule is expressed by the following 'scale of combined influence,' the numbers indicating the degree of removal and the extent of the influence decreasing in the order given: 2–3–5–6–4–7–(9–10–11)–8. It is to be strongly emphasized that the effect of an atom in the position 2 or 3 is *far greater* than that of any similar atom less closely connected, and, in the case of atoms farther removed, the influence must be largely direct, *i. e.*, spatial."[3] A considerable number of relations and reactions of organic substances were discussed from the new theoretical views presented in the above paper, among them the effect on the ionization constants of replacing

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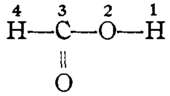
[1] *J. prakt. Chem.*, [2] **60**, 286, 409.

[2] *Ansichten über organ. Chem.*, **1**, 284; **2**, 252.

[3] THIS JOURNAL, **32**, 999; *J. prakt. Chem.*, **60**, 331.

hydrogen in acetic acid by alkyl. As C. G. Derickolwir a recent criticism of the "scale of combined influence," has gradually misrepresented my discussion of this subject[2] a brief reyiaril will be given. The acidity value of an organic acid is measured the its capacity to neutralize the energy of a metal at the position of the carboxyl hydrogen and, as the electrolytic dissociation constant represents the relative reactivity of this hydrogen towards water, it is obvious in applying a "scale of combined influence" to explain the change in the ionization constant caused by replacing an atom in the acid by another, that this hydrogen should be considered as number 1 in the scale.

Replacing in formic acid (0.0214)



$$\overset{4}{H}—\underset{\underset{O}{\|}}{\overset{3}{C}}—\overset{2}{O}—\overset{1}{H}$$

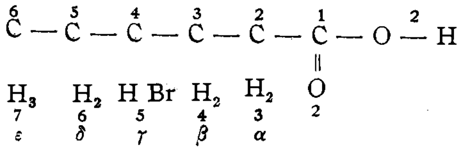
$\overset{4}{H}$ by $\overset{4\,5}{CH_3}$ brings a carbon in the relatively unimportant 4- and three hydrogens in the important 5-position towards the carboxyl hydrogen, which explains the very considerable decrease in the constant in passing from formic to acetic acid (0.0018). The change from acetic to propionic acid (0.00134) is much less, as in this case a hydrogen in the important position 5 is replaced by the negative carbon, whereby the positive influence of the three hydrogens introduced in the sixth position is neutralized to a considerable extent. Butyric from propionic acid means the replacement of a hydrogen by a carbon in the important sixth position, while the three introduced hydrogens enter into the less important seventh place. This relation is obviously quite different from that in the preceding examples, and it results in an increase of the constant from 0.00134 to 0.00145, that is, one carbon in an important position (6) may exert a greater influence than three hydrogens in a comparatively unimportant place (7). The influence of $\overset{6\,7}{CH_3}$ in comparison to that of $\overset{6}{H}$ is that of a very weak negative, not as in the previous cases, of a positive radical.[3] A similar change (0.00149 to 0.00161) occurs in passing from valeric to caproic acid, as here, too, a hydrogen is replaced by a carbon in a more important position (7) than the introduced hydrogens (8) occupy. The constants of the normal acids in the immediate higher series decrease, in agreement with the "scale of combined influence." According to Derick, "to understand Michael's scale of combined influence it is better to translate his nomenclature into that commonly employed by the organic chemist,"[4] and to show the relation he gives the following illustration with γ-bromcaproic acid:

[1] THIS JOURNAL, 33, 1167 (1911).

[2] *J. prakt. Chem.*, 60, 333.

[3] See *Ber.*, 39, 2142, footnote 2.

[4] THIS JOURNAL, 33, 1171.



$$\underset{\underset{\underset{\varepsilon}{7}}{H_3}}{\overset{6}{C}}-\underset{\underset{\underset{\delta}{6}}{H_2}}{\overset{5}{C}}-\underset{\underset{\underset{\gamma}{5}}{H\,Br}}{\overset{4}{C}}-\underset{\underset{\underset{\beta}{4}}{H_2}}{\overset{3}{C}}-\underset{\underset{\underset{\alpha}{3}}{H_2}}{\overset{2}{C}}-\underset{\underset{\underset{2}{O}}{\|}}{\overset{1}{C}}-O\overset{2}{-}H$$

Derick then states, "thus in the γ-position, the carbon is in position 4 and the bromine in position 5 with respect to the carbonyl carbon in position 1,"[1] and that, in his paper, "in Table II the first column gives Michael's nomenclature and the last column the factor corresponding to the combined influence of the direct and indirect actions of the given radical for the given position."[1] These statements of Derick are as inapplicable as they are inaccurate. A new nomenclature for designating substituting atoms or groups was neither used nor suggested in my paper; in fact throughout the customary use of Greek letters for this purpose was followed. It was to avoid confusion with this so universally adopted nomenclature that a numeral system to show the position of the atoms toward each other was adopted.[2]

Ostwald[3] showed that a great increase in the ionization constant of a normal fatty acid occurs by replacing α-hydrogen by halogen, then Lichty[4] proved that it is much less when halogen takes the β- and still more in the γ- and δ-positions and Wegscheider[5] calculated factors to show the relative changes in these relations. Derick,[6] *who does not mention the conclusions of Lichty and Wegscheider*, gives these relations in another form and uses them to test my "scale of combined influence." In doing this Derick starts from the carbon of the carboxyl group in position 1 and he, therefore, comes to the same conclusion regarding the influence of halogen that Lichty and Wegscheider had previously arrived at, *viz.*, that it decreases in the order $3 : 4 : 5 : 6$ or $\alpha : \beta : \gamma : \delta$. Derick concludes that the combined influence of halogen is therefore "proportional to the number of carbon atoms intervening"[6] and not, as it should be, according to the "scale of combined influence" in the order $3 : 5 : 6 : 4$.

As stated above one of the underlying principles of my views is that in such theoretical considerations we should consider the intramolecular relations of the atoms in the molecule, and not use groups as units and Derick would have avoided an obvious error in his reasoning if he had been better acquainted with the spirit of the paper. Although the presence

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[1] THIS JOURNAL, 33, 1172.

[2] As numerals are used in the Geneva nomenclature to designate the positions of atoms and groups towards carboxyl, it is to be hoped that the above correction of Derick's error will suffice to prevent this glaring mistake from passing into literature.

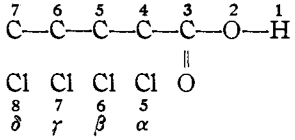
[3] *Z. physik. Chem.*, 3, 176, 178 (1889).

[4] *Ann.*, 319, 369 (1901).

[5] *Monatsh.*, 23, 287 (1902).

[6] THIS JOURNAL, 33, 1172 (1911).

of a carboxyl group denotes an acid, it does not follow from this relation that the influence which atoms outside of this group exert in determining the ionization constant is shown primary , or is in a direct relation, to their influence on the *carbon* of the carboxyl, as Derick has assumed in his speculations. In fact, the polarity of this carbon does not necessarily change proportionally to that of the carboxyl hydrogen, and, in certain cases, may not change even in the same direction.[1] Starting, as one should, with the carboxyl hydrogen in position 1, it will be readily seen with the following illustration



$$\begin{array}{ccccccccccccc}
7 & & 6 & & 5 & & 4 & & 3 & & 2 & & 1\\
\mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{O} & - & \mathrm{H}\\
 & & & & & & & & \| & & & & \\
\mathrm{Cl} & & \mathrm{Cl} & & \mathrm{Cl} & & \mathrm{Cl} & & \mathrm{O} & & & & \\
8 & & 7 & & 6 & & 5 & & & & & & \\
\delta & & \gamma & & \beta & & \alpha & & & & & &
\end{array}$$

that Lichty's and Wegscheider's conclusions are not opposed to my "scale of combined influence," as Derick states, but are in agreement with it. Furthermore, the scale of combined influence, which Derick has followed from the above data, is not only inapplicable to connect the structures with the ionization constants of organic acids, but would fail utterly if it were applied to explain organic reactions.

Derick also criticizes my statement that the "effect of any atom in the position 2 or 3 is *far greater* than that of any similar atom less closely connected, and, in the case of atoms farther removed, the influence must be largely direct, *i. e.*, spatial."[2] He states it is implied in my paper "that the spatial influence of groups is always less than the direct influence of a group in position 3 (α),"[3] and that "this is not necessarily true,"[3] since the ionization constant of malonic acid (1.63×10^{-3}) which has a carboxyl in position 3 (α) to the carbon of the other carboxyl is less than that of maleic acid (1.2×10^{-2}), where the second carboxyl is in position 4 (β). Here we have a similar error and misrepresentation as was shown in the above discussion of the halogen acids; the more remarkable for his quoting my statement in regard to the influence of *atoms* and then stating I imply that of *groups*. Again we have the application of a scale of combined influence used in connection with ionization constants and in reference to the position of a group towards the *carbon* of the carboxyl, which error in itself makes Derick's conclusions and criticism untenable and irrelevant. Moreover Derick has failed to grasp the problem which is more complicated than he assumes, since it involves the question of configuration, besides that of structure. Malonic (I) and

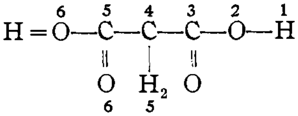
[1] For the same reason that the relative polarity of the carboxyl hydrogen may change with the position of the carbon and the hydrogens of an introduced methyl group.

[2] THIS JOURNAL, 32, 1000.

[3] *Ibid.*, 33, 1173.

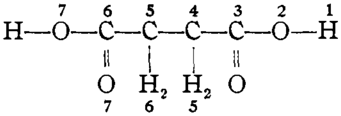
succinic (II) acids are represented according to the "scale of combined influence" as follows:

I.



$$\mathrm{H{=}\overset{6}{O}{-}\underset{\underset{6}{\overset{\|}{O}}}{\overset{5}{C}}{-}\underset{\underset{5}{\overset{|}{H_2}}}{\overset{4}{C}}{-}\underset{\overset{\|}{O}}{\overset{3}{C}}{-}\overset{2}{O}{-}\overset{1}{H}}$$

II.



$$\mathrm{H{-}\overset{7}{O}{-}\underset{\underset{7}{\overset{\|}{O}}}{\overset{6}{C}}{-}\underset{\underset{6}{\overset{|}{H_2}}}{\overset{5}{C}}{-}\underset{\underset{5}{\overset{|}{H_2}}}{\overset{4}{C}}{-}\underset{\overset{\|}{O}}{\overset{3}{C}}{-}\overset{2}{O}{-}\overset{1}{H}}$$

The removal of two oxygen atoms in the sixth to the less important seventh position, and the replacement of these oxygen by hydrogen and carbon atoms, causes a great decrease in the ionization constant (1.6×10^{-3} to 6.8×10^{-5}). Since the maleinoid form of an unsaturated acid has a greater constant than the fumaroid modification,[1] it is evident that, in comparing the constants of such acids with those of saturated acids, analogous configurations must be used. Thus, we may compare succinic with fumaric acid, as Bruni[2] has shown that these acids have analogous configurations, but we are not justified in comparing maleic acid with malonic or succinic acids, or to apply the "scale of combined influence" to explain the differences in the ionization constants, without taking the different spatial relations into consideration. There is nothing in the above data, which invalidates my statement regarding the influence of atoms in position 2 or 3 in the least and Derick's criticism is in no wise relevant.

The most astonishing of Derick's misrepresentations is in his criticism of the explanation I gave of the formation of lactones and anhydrides. It was stated in my paper,[3] that the "scale of combined influence" differs from one representing the distance separating the atoms in a normal, fatty compound from each other, and that the following scale agrees with our present knowledge of the latter relations:

1–2–5–6–4–3–7–9–10–11.

This scale of distance between the atoms was then applied to explain the formation of lactones and anhydrides. Hjelt,[4] who first considered the formation of lactones from a stereomeric point of view, believed that when CHBr is in the γ- and δ-position to COONa the lactone formation is due to the Br and NaO being spatially near to each other; Wislicenus,[5] because the halogen and metal are in spatial proximity. In my paper,[6] attention was called to the fact that the halogen and metal in such derivatives are in positions 7 and 8, and that they therefore cannot be spatially as near together as they are in salts of the α- and β-halogen acids, where

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[1] Ostwald, *Z. physik. Chem.*, **3**, 241; see Michael, *Am. Chem. J.*, **39**, 1; Michael and Bunge, *Ber.*, **41**, 2907.

[2] *Ueber feste Lösungen*, 47.

[3] *J. prakt. Chem.*, **60**, 335.

[4] *Ber.*, **15**, 630 (1882).

[5] *Räumliche Anordnung*, **68** (1888).

[6] *J. prakt. Chem.*, **60**, 336.

they stand in positions 5 and 6. Further, that halogen and metal in all such derivatives must show a more or less marked affinity for each other, but to form a lactone this affinity has to overcome a chemical hindrance, due to the tension in forming a ring. When this hindrance is small, as it is in the formation of a five- or six-membered ring, such derivatives are formed intramolecularly and with ease, otherwise the decomposition has a tendency to proceed in a different manner. Thus, heating a salt of an α-halogen acid, two molecules interact forming a lactide with a six-membered ring, and the salt of a β-acid breaks down to alkylene and carbon dioxide, owing to the tension in a four-membered ring lactone.

It is indeed difficult to understand how any one could misconstrue these views to the extent which Derick has done in the following statements: "Michael finds the best support of his 'scale of combined influence,' (1)-2-3-5-6-4-7-(9-10-11)-8, in lactone and anhydride formations. He attributes the cause of the same to the fact that halogen, hydroxyl or carboxyl attached to the γ- or δ-carbon exerts a greater space or direct action upon the α-carboxyl than when the same radicals are attached to the β, ε, ζ, η, etc., carbons. Therefore in his 'scale of combined influence' positions 5 and 6 are of greater influence than 4, 7 (9-10-11) and 8."[1] And this, after I had emphasized that the "scale of combined influence" should not be used to explain the lactone and anhydride formation and given the reasons why. Derick then states that the combined influence of halogen on the ionization constants is in the γ- or δ- less than it is in the β-position to the carboxyl, which is "opposit to the conclusions drawn by Michael."[1] Derick's criticism is evidently not only wholly supposititious, but his reasoning is wrong, even if I had made the statements he attributes to me, as the combined influence of halogen as deduced from ionization constants has not necessarily a direct connection with that of the halogen in relation to the carbon of the carboxyl group.

A "scale of combined influence" to explain the ionization constants of organic acids was first used by the writer and not by Derick, as the reader of his paper would certainly suppose.[2] *In the above remarks all of his*

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[1] THIS JOURNAL, 33, 1181.

[2] In other places in his papers Derick has stated generally known facts without referring to the authors and thereby leads the reader to the belief that he is making new contributions to the subject. For instance (THIS JOURNAL, 33, 1153) using water as the standard and deducing the relative positivity or negativity of atoms or radicals from the effect they exert on the hydrogen or hydroxyl ionization certainly can make no claim to originality. On the following page, Ostwald's relation between the free energy of ionization and the ionization constant is stated in a manner (see page 1155, lines 15 and 16 from top of page) that leads one to suppose it to be new. That the affinity of a reaction, not that of an acid as Derick states, may be calculated from the ionization is generally known (see Lunden, *Affinitätsmessungen, u. s. w.* 2). Derick (THIS JOURNAL, 33, 1181; 34, 74) claims to have shown that the free energy of ionization of negatively substituted, monobasic fatty acids is an additive resultant of each

objections have been shown to be based on misunderstandings and his criticism to be without relevance; further, that his scale is fundamentally wrong and that the conclusions he has drawn from its application have no real bearing on the subject.

The "scale of combined influence" when applied to explain the relations between structure and configuration of organic acids and their ionization constants offers a plausible explanation for quite a number of facts, which from other points of view appear anomalous. But, when we attempt to apply it systematically to all the observed data in this field we are inevitably led to the conclusion that there are unconsidered and unknown factors entering into the determination of the values. One of these factors is, besides the chemical nature and the position of the atom,[1] its content in free *chemical* energy. The enormous increase in the constant, when we pass from maleic to acetylenedicarboxylic acid, whose value is comparable with that of the strongest mineral acids,[2] certainly cannot be due alone to the removal of two hydrogens even though they are in the sixth position to the carboxyl hydrogens; but also, in a large measure, to the great increase in the free *chemical* energy of the unsaturated carbons, which are in the fifth position. Probably for the same reason, an increase in the ionization constants takes place in passing from $\Delta^{\alpha,\beta}$- to $\Delta^{\beta,\gamma}$-acids,[3] where, in the first group, the unsaturated carbons are in the fourth and fifth, while, in the second, they are in the fifth and sixth positions, towards the carboxyl hydrogens; and, that cyan- and thiocyanacetic acids possess larger ionization constants than chloracetic acid.

SALT SOLUTIONS AND THE LAW OF MASS ACTION.

BY F. H. MACDOUGALL.

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The fact that Ostwald's dilution formula does not hold for aqueous solutions of salts, strong acids and strong bases has been a disturbing feature in our theory of solutions and an incentive to further investiga-

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atom in the molecule, but any one acquainted with the literature on this subject knows that this conclusion is due to Ostwald, who also showed that in many cases there is a good agreement between the calculated and found values of ionization constants. This line of work was subsequently successfully pursued by Bethmann (*Z. physik. Chem.*, **5**, 385), Holleman and de Bruyn (*Rec. trav. chim.*, **20**, 360) and particularly by Wegscheider (*Monatsh.*, **23**, 287; **26**, 1265), whose papers Derick fails to mention. It is open to question whether the use of values representing the free energy of ionization, instead of those of ionization constants, is at present of much importance as what is now most urgent in this field is not a restatement of explanations in other terms, but a clearer insight into why so many facts elude a consistent theoretical treatment.

[1] Ostwald, *Z. physik. Chem.*, **3**, 415.

[2] Ostwald, *Ibid.*, **3**, 382.

[3] Fichter and Pfister, *Ann.*, **348**, 257 (1906).