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THE SCALE OF INFLUENCE OF SUBSTITUENTS IN PARAFFINE MONOBASIC ACIDS AND THE CORRELATION OF IONIZATION WITH STRUCTURE.

III. THE DIVALENT OXYGEN ATOM IN THE ε-POSITION.[1]

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Received December 17, 1917.

I. Historical Part.

This investigation is the continuation of the work of one of us upon the study of the effect of the nature and the position of one atom upon the tendency of another atom within the same molecule to enter into chemical reaction. The reaction chosen was the ionization of organic acids because of the comparative simplicity of the theoretical and laboratory treatment of this process. Incidentally, this also affords a means of correlating ionization with the structure of organic acids. On the synthetic side, a study of the factors which control the yields at each step of the process was made.

Van't Hoff[2] was the first to point out that in general the ionization constant of an acid depends on the nature, number and position of the substituents. He observed that the influence of a substituent usually decreased with an increasing number of atoms intervening between it and the acidic hydrogen. Exceptions which are difficult to explain have been found. Irregularities have been observed especially in the unsat-

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[1] The experimental part of this paper was presented at the Urbana meeting of the American Chemical Society, 1916. From a thesis, submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy at the University of Illinois.

[2] "Lectures on Theoretical and Physical Chemistry," Part III, pp. 113–143.

urated aliphatic and in aromatic acids and in acids substituted with certain groups as the anilino group C_6H_5NH—. Furthermore, there are radicals of feeble polarity which increase the degree of ionization when substituted into some acids and decrease it when substituted into others. Many attempted explanations have been offered but they lack the desired generality. These will not be discussed here, since consideration is to be given primarily to the measurement of these forces rather than to their causes. Michael[1] has stated that "If we number a certain atom in any 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 number 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." More recently, Derick[2] contended that for strongly negative atoms and radicals, substituted into monobasic paraffine acids, the order should be 1–2–3–4–5–6–7–8–9–10–11,[3] for the reaction of ionization.

In the complete study of this problem it must first be decided if a single scale of influence is applicable to all chemical reactions. This does not seem probable in the light of the above discussion and no decision can be made until accurate quantitative data are available for each reaction in question. A review of Michael's scale of influence shows that positions 4 and 8 are anomalous. Unfortunately no acids with a negative atom in position 4 can be prepared in a pure state and accurately measured, since such acids as Cl.COOH, Br.COOH, etc., are unknown. However, it is possible to measure the influence of a negative atom in position 8(δ) for the reaction ionization. A further study of the literature shows that no measurements of the ionization of acids with the negative atom in positions beyond the (δ) are known. Hence in order to test the relative magnitude of 8 and 9 in Michael's scale, acids with negative atoms in these positions must be prepared and measured. The experimental part of this investigation deals with the preparation and measurement of the ionization constant of ϵ-oxoheptanoic acid (δ-acetovalerianic acid), in which the oxygen atom is in Michael's position 9(ϵ).

Before accurate conclusions can be formed it is necessary to determine the true method of measuring the influence of one atom upon another for the reaction under consideration. It will be shown in a later section that the ionization constant is not an exact measure of this influence for the reaction ionization, although it may serve for estimating the relative order of a scale of influence in many cases.

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[1] *J. prakt. Chem.*, 168, 231 (1899); *Ber.*, 39, 2139 (1906); THIS JOURNAL, 32, 999 (1910).

[2] *Ibid.*, 33, 1182 (1911).

[3] NOTE.—This is using Michael's nomenclature numbering the carboxylic hydrogen atom 1, contrary to the accepted Geneva method for organic acids.

Ostwald[1] was the pioneer in the other phase of the problem. The ionization constant of the substituted acid divided by that for the unsubstituted acid, he called the factor for the substituent in a given position. Bethman,[2] Holleman,[3] and Wegscheider[4] continued the study, using this factor. By its use it was found possible to calculate approximately the ionization constants of several poly-substituted acids, especially in the aromatic series.

In 1911 Derick[5] proposed the use of the expression $\frac{\log k_0}{\log k_n} - 1$, where k_n is the ionization constant of the substituted acid and k_0 the constant for the corresponding unsubstituted acid, as a more general and useful expression. Many calculations were made definitely, establishing his claim.

II. A Comparison of the Ostwald and Derick Factors.

In 1912 Wegscheider[6] compared the use of the Ostwald factor with Derick's place factor in considerable detail, but with some misleading conclusions. He stated:

> "Ein Nachteil des Derickschen Ansatzes ist jedenfalls, dass er rechnerisch viel unbequemer ist als der Ostwaldsche. Er könnte daher nur dann mit dem Ostwaldschen erfolgreich in Wettbewerb treten, wenn er sonstige Vorzüge hätte. Als solche könnten in Betracht kommen: 1, Eine bessere theoretische Begründung; 2, das Auftreten einfacherer Zahl einbeziehungen zwischen den Factoren; 3, die genuarere Darstellung der Dissoziationkonstanten in jeden Fällen, wo sich die beiden Ansätze unterscheiden."

In the first place it is evident that merely for the purpose of correlation the question of a theoretical basis does not necessarily enter. Any formula which expresses the relationships most accurately and generally in a convenient form will be best. After discussing his first point rather vaguely, Wegscheider says:

> "Dem gegenüber gibt das Ostwaldsche Factorengesetz, wie aus Gleichung (4)[7] ersichtlich ist, eine einfache und durchsightige Beziehung zwischen Konstitution und RT ln k'."

Wegschieder's use of the logarithm of the Ostwald factor concedes the very point of Derick's contention, namely, that the logarithm of the ionization constant is a more fundamental function for this purpose. The reason for this will be seen in the following discussion. It should be kept in mind, however, that the logarithmic function of the ionization constant had not been used in this connection, previous to its use by

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[1] *Z. phys. Chem.*, **3**, 170, 369–422 (1889).

[2] *Ibid.*, **5**, 385–422 (1890).

[3] *Rec. des Tran. Chim.*, **20**, 360–364 (1901).

[4] *Monatsh.*, **16**, 153–158 (1895); **23**, 287–316 (1902); **26**, 1265 (1905),

[5] THIS JOURNAL, **33**, 1152–1189 (1911); **34**, 74–82 (1912).

[6] *Z. Elektrochem.*, **18**, 277–281 (1912).

[7] $\text{Log } k' = \log k \log a \log b$ . . . .

Derick. Wegscheider suggested its use here, but in another form, only, after its value had been recognized by Derick.

In discussing the second and third points raised by Wegscheider, the two uses of a correlation of ionization and structure should be kept clearly in mind. The first use is the calculation of the ionization constant from the structure, Wegscheider's third point, which will be discussed presently. The second use is the determination of the position of a substituent in an acid from a knowledge of its ionization constant. In this connection Derick[1] has previously shown that the place factors for the α, β, γ and δ positions for a strongly negative substituent stand roughly in the ratio of 1, 1/3, 1/9, 1/27, respectively. This regularity he called the *rule of thirds.* From this it is evident that it is possible to determine the position of the substituent in a negatively substituted monobasic paraffine acid from its ionization constant. This involves Wegscheider's second point. In discussing this he has made an unfortunate use of Derick's place factor. He claimed that if the rule of thirds holds, the factor for a given position divided by that for the next succeeding one should give 3 in each case. This is misleading at first thought, since it is evident that it is only necessary for the result to be nearer to 3 than to 9 or to 1, in order to determine the position of the substituent. Only in one case given would there be any question as to the position of the substituent. This was obtained by dividing the γ-place factor by the δ-place factor for iodine.

The rule of thirds is the most striking advantage of the Derick place factors α, β, γ and δ over the corresponding Ostwald factors a, b, c and d. No such regular and simple relationship between the Ostwald factors is obvious. The numerical values of both the Ostwald and Derick factors are given in Table I. The relationships are best seen in Table II, in which the α-place factor is taken as unity in each case and the place factors for the same substituent in the succeeding positions are expressed in fractions of the α-factor. The Ostwald factors are treated in a similar manner.

While it is true that it can be shown, as Wegscheider has done, that the Ostwald factors a, b, c and d should obey an approximate rule of cube roots, it should be observed that it had not been noted until Derick stated his rule of thirds. In reality, Wegscheider expressed the Ostwald factors in terms of Derick's factors and found the cube root rule. Practically, a cube root rule would be much more difficult to use in making calculations.

This phase of the correlation of ionization and structure, namely, the determination of structure, shows unquestionably that Derick has advanced this problem by the use of the logarithm of the ionization constant.

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[1] THIS JOURNAL, 33, 1181–1185 (1911).

TABLE I.—NUMERICAL VALUES OF FACTORS.

Substituent. Acid substituted.	Ostwald factor. $\frac{k_n}{k_o}$.				Derick's place factor $\frac{\log k_o}{\log k_n} - 1$.				$\frac{\text{Place influence}}{RT} = \log k_n - \log k_o$.			
	a.	*b.*	*c.*	*d.*	*α.*	*β.*	*γ.*	*δ.*	$\frac{I_{\alpha s}-I_{\alpha H}}{RT}$.	$\frac{I_{\beta s}-I_{\beta H}}{RT}$.	$\frac{I_{\gamma s}-I_{\gamma H}}{RT}$.	$\frac{I_{\delta s}-I_{\delta H}}{RT}$.
Chlorine												
Acetic..........	79	..	..	..	0.67	..	..	..	1.90	..	..	..
Propionic.......	110	6.5	..	..	0.72	0.195	..	..	2.04	0.81	..	..
Butyric.........	94	5.9	1.98	..	0.69	0.191	0.065	..	1.97	0.77	0.298	..
Valerianic.......	..	..	..	1.26	..	..	..	0.0224	..	..	..	0.100
Average......	94	6.2	1.98	1.26	0.69	0.193	0.065	0.0224	1.97	0.79	0.298	0.100
Bromine												
Acetic..........	71	..	..	..	0.64	..	..	..	1.85	..	..	..
Propionic.......	80	7.0	..	..	0.64	0.212	..	..	1.91	0.85	..	..
Butyric.........	67	..	1.75	..	0.62	..	0.0520	..	1.84	..	0.243	..
Valerianic.......	..	..	..	1.18	..	..	..	0.0153	..	..	..	0.073
Average......	72	7.0	1.75	1.18	0.63	0.212	0.0520	0.0153	1.86	0.85	0.243	0.073
Iodine												
Acetic..........	38	..	..	..	0.50	..	..	..	1.58	..	..	..
Propionic.......	..	6.5	..	..	..	0.199	..	..	..	0.81	..	..
Butyric.........	..	..	1.52	..	..	..	0.0392	..	..	..	0.182	..
Valerianic.......	..	..	..	1.05	..	..	..	0.0050	..	..	..	0.0239
Average......	38	6.5	1.52	1.05	0.50	0.199	0.0392	0.0050	1.58	0.81	0.182	0.0239
Hydroxyl												
Acetic..........	8.1	..	..	..	0.238	..	..	..	0.91	..	..	..
Propionic.......	10.3	2.33	..	..	0.262	0.081	..	..	1.01	0.37	..	..
Butyric.........	..	..	1.27	..	..	..	0.0223	..	..	..	0.105	..
Isobutyric......	7.4	..	..	..	0.218	..	..	..	0.87	..	..	..
Valerianic.......	..	..	1.25	..	..	..	0.0206	..	..	..	0.097	..
Average......	8.6	2.33	1.26	..	0.242	0.081	0.0214	..	0.93	0.37	0.101	..

TABLE II.—RATIOS TO THE ALPHA VALUES.

	Ostwald factors.				Derick place factors.			
Substituent.	$\frac{a}{a}$.	$\frac{b}{a}$.	$\frac{c}{a}$.	$\frac{d}{a}$.	$\frac{\alpha}{\alpha}$.	$\frac{\beta}{\alpha}$.	$\frac{\gamma}{\alpha}$.	$\frac{\delta}{\alpha}$.
Chlorine......	1	0.066	0.0213	0.0134	1	0.279	0.094	0.0324
Bromine......	1	0.097	0.0243	0.0164	1	0.336	0.082	0.0243
Iodine........	1	0.171	0.0400	0.0278	1	0.398	0.078	0.0100
Hydroxyl.....	1	0.271	0.1460	..	1	0.334	0.088	..

	Place influences.			
	$\frac{I_{\alpha S}-I_{\alpha H}}{I_{\alpha S}-I_{\alpha H}}$.	$\frac{I_{\beta S}-I_{\beta H}}{I_{\alpha S}-I_{\alpha H}}$.	$\frac{I_{\gamma S}-I_{\gamma H}}{I_{\alpha S}-I_{\alpha H}}$.	$\frac{I_{\delta S}-I_{\delta H}}{I_{\alpha S}-I_{\alpha H}}$.
Chlorine........	1	0.401	0.151	0.0507
Bromine........	1	0.455	0.131	0.0392
Iodine..........	1	0.513	0.115	0.0151
Hydroxyl.......	1	0.398	0.109	..

In connection with the third point Derick[1] has shown that, since the place factors for a given substituent follow the rule of third, it is necessary to know only the alpha factor for this substituent and the ionization constant of the corresponding unsubstituted acid in order to be able to calculate the ionization constant of an acid with this substituent in any position of a paraffine monobasic acid. He[2] has also shown that it is possible to calculate the ionization constants of several poly-substituted paraffine monobasic acids by the use of his rule of thirds.

In the aromatic series Derick[3] has found that no constant ratio exists between the ortho, meta and para place factors for substituents in the mono-substituted benzoic acids. He has shown, however, that with the aid of the place factors it is possible to calculate the approximate ionization constants of, as well as the structure of, many poly-substituted benzoic acids.

Obviously, the problem of correlating the ionization and structure of negatively substituted organic acids has been advanced by the use of the logarithm of the ionization constant.

III. The Ionization Constants of Certain Organic Acids Recalculated Using Modern Conductance Units.

The ionization data used in compiling the above tables are expressed in international ohms. The values for the equivalent conductances of the hydrogen and sodium ions at zero concentration (infinite dilution) are 34.7 and 51.5, respectively, at 25°. This has necessitated the recalculation of most of the data given by the original investigators.

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[1] THIS JOURNAL, 33, 1185–1189 (1911).

[2] *Ibid.*, 33, 1187–1189 (1911).

[3] *Ibid.*, 34, 74–82 (1912).

TABLE III.—IONIZATION CONSTANTS OF ORGANIC ACIDS.

Acid.	Ref.	$k \times 10^4$.
Acetic	1	0.185
Propionic	2	0.132
Butyric	2	0.149
Isobutyric	2	0.141
Valerianic	2	0.159
Chloroacetic	2	14.7
Bromoacetic	2	13.2
Iodoacetic	3	7.0
Hydroxyacetic	2	1.50
Phenylacetic	2	0.554
α-Chloropropionic	4	14.6
β-Chloropropionic	4	0.859
α-Bromopropionic	3	10.6
β-Bromopropionic	3	0.93
β-Iodopropionic	2	0.86
α-Hydroxypropionic	2	1.36
β-Hydroxypropionic	2	0.307
α-Phenylpropionic	2	0.422
β-Phenylpropionic	2	0.224
α-Chlorobutyric	4	14.0
β-Chlorobutyric	4	0.885
γ-Chlorobutyric	4	0.296
α-Bromobutyric	3	10.2
γ-Bromobutyric	4	0.261
γ-Iodobutyric	4	0.226
γ-Hydroxybutyric	5	0.190
α-Hydroxyisobutyric	2	1.05
δ-Chlorovalerianic	4	0.200
δ-Bromovalerianic	4	0.188
δ-Iodovalerianic	4	0.168
γ-Hydroxyvalerianic	5	0.199

IV. The Theoretical Basis for the Measurement of the Influence of a Substituent upon the Reaction Ionization, the *Place Influence.*

It follows from thermodynamics that if an acid passes from unit concentration of un-ionized molecules to unit concentration of its ions, the combined effect of all the atoms in the molecule upon the tendency of the reaction to occur is expressed by the equation

$$A = RT \ln k,$$

in which k is the ionization constant. If a substituent is introduced into this acid, the effect of all the atoms upon the reaction is readily seen to be

$$A - I_H + I_s = RT \ln k_1,$$

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[1] J. Kendall, *J. Chem. Soc.*, **101**, 1283 (1912).

[2] W. Ostwald, *Z. phys. Chem.*, **3**, 170–199 (1889).

[3] P. Walden, *Ibid.*, **10**, 638–664 (1892).

[4] K. Drucker, *Ibid.*, **52**, 643 (1905).

[5] P. Henry, *Ibid.*, **10**, 120 (1892).

where k_1 is the ionization constant of the substituted acid, I_H the influence of the replaced hydrogen atom and I_s the influence of the substituent upon the reaction. By combining the two equations we have

$$I_s - I_H = RT\ (\ln k_1 - \ln k).$$

In order to solve this equation for I_s it is evidently necessary to know the value of I_H or it must be proven to be negligibly small. At present there is not sufficient data obtainable for calculating the influence of the hydrogen atom. In this study $I_s - I_H$ has been called the *place influence* and $(I_s - I_H)/RT$ the *relative place influence* of a substituent under consideration. Obviously, it is necessary to know only the ionization constants of the substituted and corresponding unsubstituted acids, for a given substituent in different positions of an acid, in order to be able to calculate the relative place influences. That is, if we wish to compare the relative values of the place influences, RT is the same in each case and cancels out in the ratio, so we have, for example,

$$\frac{I_{\beta Cl} - I_{\beta H}}{I_{\alpha Cl} - I_{\alpha H}} = \frac{\log k_{\beta Cl} - \log k_o}{\log k_{\alpha Cl} - \log k_o}.$$

These relative values are given in Table I. The place influence for a given substituent is seen to have approximately the same value for the same position in each acid, and to follow, roughly, the rule of thirds for the α, β, γ and δ positions. This is best seen in Table II, where the α-place influence is taken as unity in each case.

V. The Relative ϵ-Place Influence of an Atom of Oxygen, Substituted into Monobasic Paraffine Acids, upon the Reaction Ionization.

As previously stated, the primary object of this investigation was to determine the relative ϵ-influence of an atom of oxygen upon the reaction ionization when substituted into paraffine monobasic acids. In the preceding section it was shown that the ionization constants of the substituted and the corresponding unsubstituted acids must be known in order to calculate this value. In the following sections the ionization constant of δ-acetovalerianic acid is shown to be 1.926×10^{-5}. From the considerations given in Section VIII, the value 1.4×10^{-5} was chosen as the approximate ionization constant of normal heptanoic acid. From these values the approximate relative oxygen ϵ-place influence, $I_{\epsilon O} - I_{\epsilon 2(H)}/RT$, for the reaction under consideration, is found to be 0.14.

Unfortunately, the uncertainty concerning the correct value for the ionization constant of heptanoic acid destroys the accuracy desired in the value for this place influence. This is seen most clearly when the criterion "calculated" Λ_o is applied to the measurements of heptanoic acid by Franke and Drucker. See Section VIII.

VI. Synthesis of δ-Acetovalerianic Acid and Its Intermediate Compounds, and a Study of the Factors Which Control the Yields at Each Stop of the Process.

The following method has not been previously used for making δ-acetovalerianic acid. Trimethylene glycol was converted into trimethylene bromide and from the latter γ-bromobutyronitrile was prepared. This was condensed with acetoacetic ester to give δ-cyano-α-acetovalerianic ethyl ester which was hydrolyzed to δ-acetovalerianic acid. These reactions afford a striking support of the use of the factors controlling yields as applied by the senior author and his students.

1. Trimethylene Glycol.—The literature shows that this substance has usually been prepared from trimethylene bromide, and it has long been known that it can be obtained from glycerine by the action of bacteria. Certain by-products on the American market, such as "Blizzard, Anti-Freeze," consist mainly of this substance. "Blizzard" was used as the source of the trimethylene glycol in this investigation and was obtained pure in an 80–90% yield by fractional distillation.

2. Trimethylene Bromide.—Trimethylene bromide has previously been prepared by the action of hydrobromic acid upon allyl bromide and upon trimethylene glycol under various conditions, usually in a sealed tube. The disadvantages of these methods are obvious, especially for the preparation of large quantities of the substance.

Excellent yields of trimethylene bromide were obtained, in this work, from the action of aqueous hydrobromic acid on trimethylene glycol without the inconveniences of the sealed tube method. The following equilibria will be established:

$$HOCH_2.CH_2.CH_2OH + HBr \rightleftarrows HOCH_2.CH_2.CH_2Br + H_2O$$

$$HOCH_2.CH_2.CH_2Br + HBr \rightleftarrows BrCH_2.CH_2.CH_2Br + H_2O$$

From a consideration of these equilibria it is predicted that the greater the concentration of the hydrobromic acid the better should be the yield of trimethylene bromide. This is forcefully substantiated in the following two experiments:

The Norris Method.—The technique of the Norris method[1] for making halides from alcohols was first used. 235 g. of trimethylene glycol and 1060 cc. of constant boiling aqueous hydrobromic acid were refluxed together for six hours. These amounts are equivalent to one mole of glycol to three moles of hydrogen bromide. Since the glycol is not very volatile with steam the mixture was distilled in order to remove the water and the bromide first, causing the residue to become concentrated with the glycol and hydrobromic acid, thus displacing the equilibria to favor the yield of the trimethylene bromide. The latter practically all came over

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[1] Norris, "Experimental Organic Chemistry," 1915, p. 100.

with the first 700 cc. of distillate, forming a clear, oily, bottom layer. The last 350 cc. was practically pure 48% aqueous hydrobromic acid.

The oily layer was separated and distilled. Since it boiled over a considerable range of temperature it was proven to be impure. Consideration of the above equilibria predicts it to contain some γ-bromopropyl alcohol and trimethylene glycol. In order to remove these, the product was washed twice with 100 cc. of sulfuric acid (sp. gr. 1.84), twice with an equal volume of water, once with a dilute carbonate solution, and finally, once again with an equal volume of water. During the washing with sulfuric acid it was necessary to keep the mixture cool and to rotate cautiously in order to prevent emulsification. The product was dried over $CaCl_2$ and was found to distil constant at 165°. The yield was 330 g. or 53% of the theoretical.

Method II.—The second method gave much better results. The principle involved was to reflux one mole of trimethylene glycol with enough constant boiling aqueous hydrobromic acid to furnish three moles of hydrogen bromide, as before, and then two moles more of gaseous hydrogen bromide were added and the refluxing was continued.

400 g. of trimethylene glycol and 1800 cc. of 48% aqueous hydrobromic acid were placed in a 4-liter flask and refluxed on a sand bath 3–4 hrs., when 850–900 g. of gaseous hydrogen bromide were introduced.

The hydrogen bromide was generated by dropping bromine upon a mixture of red phosphorus, water and sand, and purified by passing over moist red phosphorus spread over glass wool in U-tubes. A convenient charge was found to be 1600 g. of sand, 300 cc. of water, 200 g. of red phosphorus, and 1200 g. of bromine. With this apparatus it required but 2–3 hours to generate the amount of hydrogen bromide desired in this case.

The mixture was gradually brought to boiling and refluxed again for two hours in order to establish the equilibria. Upon cooling, the bromide completely separated from the solution. This was isolated and washed with water, sulfuric acid and carbonate solution as in the preceding experiment. The product, after drying with $CaCl_2$, distilled constant at 165°. The yield was 870 g. or 82% theoretical, as compared to 53% by the preceding method.

An amount of 48% hydrobromic acid, equivalent to the amount used, is regained by distilling the aqueous layer.

3. **γ-Bromobutyronitrile.**—*Gabriel's Method.*—Gabriel[1] prepared this substance from trimethylene bromide and potassium cyanide in the usual solvent, a mixture of ethyl alcohol and water. Obviously the main reactions are

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[1] *Ber.*, **22**, 3336 (1889).

$$BrCH_2.CH_2.CH_2Br + KCN \longrightarrow BrCH_2.CH_2.CH_2CN + KBr$$
$$BrCH_2.CH_2.CH_2CN + KCN \longrightarrow NC.CH_2.CH_2.CH_2CN + KBr$$

The yield of the γ-bromobutyronitrile was only 19%, and but 40% of the trimethylene bromide used was accounted for in the products of the reaction. This method was repeated in the present investigation with but little better results, as shown in Table V.

The poor yield may be due to the presence of water. Since the aqueous solution becomes alkaline by the hydrolysis of potassium cyanide, a large number of hydrolytic products would be expected. At the end of the reaction, the aqueous layer was actually found to turn congo-red paper blue, proving the presence of a strong acid. Some of the types of these hydrolytic reactions which might occur are shown by the following equations:

$$BrCH_2.CH_2.CH_2Br + H_2O \rightleftarrows BrCH_2.CH_2.CH_2OH + HBr$$
$$BrCH_2.CH_2.CH_2CN + H_2O \rightleftarrows BrCH_2.CH_2.CH_2CO.NH_2$$
$$BrCH_2.CH_2.CH_2CO.NH_2 + H_2O \rightleftarrows BrCH_2.CH_2.CH_2COOH + NH_3$$
$$NC.CH_2CH_2.CH_2CN + H_2O \rightleftarrows NC.CH_2.CH_2CH_2CO.NH_2$$
$$NC.CH_2.CH_2.CH_2CO.NH_2 + H_2O \rightleftarrows NC.CH_2.CH_2.CH_2COOH + NH_3$$
$$NC.CH_2.CH_2.CH_2COOH + H_2O \rightleftarrows H_2N.OC.CH_2.CH_2.CH_2.COOH$$
$$H_2N.OC.CH_2.CH_2.CH_2COOH + H_2O \rightleftarrows HOOC.CH_2.CH_2.CH_2.COOH + NH_3$$

Method II.—In the light of above considerations it is obvious that an anhydrous solvent might be preferable. Since methyl alcohol dissolves 5% of potassium cyanide at 0° it was chosen as the solvent for this reaction. Another important factor to be considered is the relative proportions of trimethylene bromide and potassium cyanide. An excess of the bromide should favor the yield of γ-bromobutyronitrile and decrease the yield of the trimethylene cyanide. Table V confirms this and shows the advantage of the use of anhydrous methyl alcohol as the solvent.

TABLE V.—ACTION OF POTASSIUM CYANIDE UPON TRIMETHYLENE BROMIDE.

Method.		G. material used.			G. products.		
		Solvent.	Potassium cyanide.	Trimethylene bromide.	Trimethylene bromide, 70–72°, 20 mm.[1]	γ-Bromobutyronitrile, 100–102°, 20 mm.[1]	Trimethylene cyanide, 148–153^6, 20 mm.[1]
I	*a*	C_2H_5OH 95%, 450	60	200	20	27	10
	b	H_2O, 120	65	202	15	39	14
II	*a*	CH_3OH 1000	65	200	32	44	20
	b	CH_3OH 1000	65	404	175	70	4

In both cases under Method II the materials were mixed together and refluxed on the steam bath 7–8 hours. The potassium bromide was fil-

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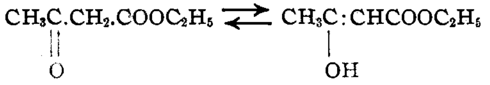
[1] The temperature readings in this table are not corrected.

tered off and the alcohol was distilled from the mixture. The residue was separated into its components by fractional distillation under reduced pressure.

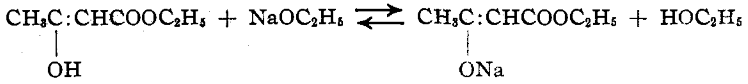
The methyl alcohol was that of Eimer and Amend freshly refluxed over and distilled from an excess of good lime. The trimethylene bromide was prepared as described in the preceding section. Eimer and Amend's 98–100% potassium cyanide was used.

Discussion of Table V.—The first horizontal column, Method I*a*, gives the results obtained by Gabriel. Method I*b* shows the results of the repetition of his method in this laboratory. A comparison of this with Method II*a* discloses, to some extent, the hydrolytic effect of the water present. Although the yield of γ-bromobutyronitrile is not appreciably greater with the use of methylalcohol, twice the amount of trimethylene bromide is recovered and half as much again trimethylene cyanide is obtained. The most striking advantage is shown by the use of an excess of trimethylene bromide in Method II*b*. When one mole each of trimethylene bromide and KCN were used in Method II*a*, only 44 g. of γ-bromobutyronitrile while 20 g. of trimethylene cyanide were obtained also. The use of two moles of trimethylene bromide to one of potassium cyanide gave 70 g. of γ-bromobutyronitrile and only 4 g. of trimethylene cyanide. The excess of trimethylene bromide is easily recovered in the distillation.

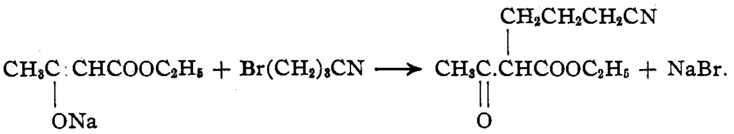
4. **δ-Cyano-α-acetovalerianic Ethyl Ester.**—This substance is not described in the literature. For the present purpose it was prepared by the action of γ-bromobutyronitrile on the sodium salt of acetoacetic ethyl ester with absolute ethyl alcohol used as the solvent. The principal reactions predicted are



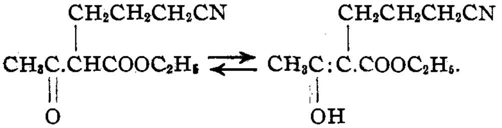
$$\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{CH_3C}}.\mathrm{CH_2.COOC_2H_5} \rightleftarrows \underset{\underset{\displaystyle \mathrm{OH}}{|}}{\mathrm{CH_3C}}\mathrm{:CHCOOC_2H_5} \qquad (1)$$



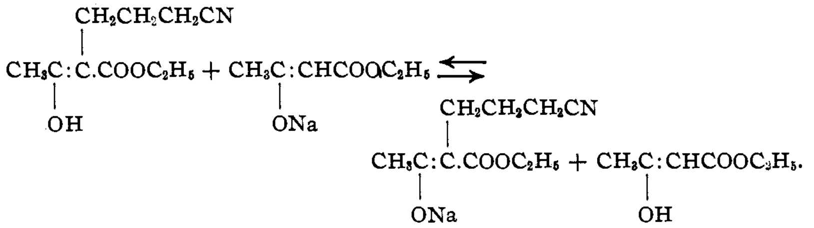
$$\underset{\underset{\displaystyle \mathrm{OH}}{|}}{\mathrm{CH_3C}}\mathrm{:CHCOOC_2H_5} + \mathrm{NaOC_2H_5} \rightleftarrows \underset{\underset{\displaystyle \mathrm{ONa}}{|}}{\mathrm{CH_3C}}\mathrm{:CHCOOC_2H_5} + \mathrm{HOC_2H_5} \qquad (2)$$



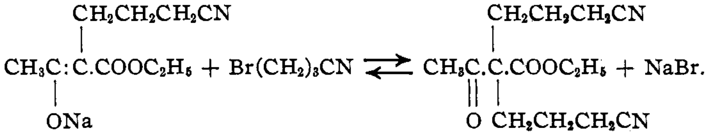
$$\underset{\underset{\displaystyle \mathrm{ONa}}{|}}{\mathrm{CH_3C}}\mathrm{:CHCOOC_2H_5} + \mathrm{Br(CH_2)_3CN} \longrightarrow \underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{CH_3C}}.\overset{\overset{\displaystyle \mathrm{CH_2CH_2CH_2CN}}{|}}{\mathrm{C}}\mathrm{HCOOC_2H_5} + \mathrm{NaBr}. \qquad (3)$$



$$\underset{\underset{\displaystyle \mathrm{O}}{\|}}{\mathrm{CH_3C}}.\overset{\overset{\displaystyle \mathrm{CH_2CH_2CH_2CN}}{|}}{\mathrm{C}}\mathrm{HCOOC_2H_5} \rightleftarrows \underset{\underset{\displaystyle \mathrm{OH}}{|}}{\mathrm{CH_3C}}\mathrm{:}\overset{\overset{\displaystyle \mathrm{CH_2CH_2CH_2CN}}{|}}{\mathrm{C}}\mathrm{.COOC_2H_5}. \qquad (4)$$



$$\underset{\displaystyle OH}{CH_3C}:\overset{\displaystyle CH_2CH_2CH_2CN}{C}.COOC_2H_5 + \underset{\displaystyle ONa}{CH_3C}:CHCOOC_2H_5 \rightleftarrows \underset{\displaystyle ONa}{CH_3C}:\overset{\displaystyle CH_2CH_2CH_2CN}{C}.COOC_2H_5 + \underset{\displaystyle OH}{CH_3C}:CHCOOC_2H_5. \quad (5)$$



$$\underset{\displaystyle ONa}{CH_3C}:\overset{\displaystyle CH_2CH_2CH_2CN}{C}.COOC_2H_5 + Br(CH_2)_3CN \rightleftarrows \underset{\displaystyle O}{\overset{\|}{CH_3C}}.\underset{\displaystyle CH_2CH_2CH_2CN}{\overset{\displaystyle CH_2CH_2CH_2CN}{C}}.COOC_2H_5 + NaBr. \quad (6)$$

From a consideration of these equations it was predicted that some 1,7-dicyano-4-aceto-4-carboxethyl heptane would be formed by Equations 5 and 6 at the expense of the desired product, δ-cyano-α-acetovalerianic ethyl ester by Equation 3 and, consequently, some acetoacetic ester would remain unchanged. Everyone who has made the acetoacetic ester condensation will recall that even when the calculated quantity of the ester is used some of it is usually regained from the products of the reaction. It follows that an excess of acetoacetic ester should displace equilibrium 5 to the left and thus decrease the yield of the undesired product. These predictions were decidedly substantiated in the two following experiments:[1]

The γ-bromobutyronitrile used in both cases was that prepared as described in the preceding section. The acetoacetic ester was made in the summer preparation work conducted at the University of Illinois. The alcohol was made absolute by twice refluxing the 95% product over an excess of good lime for several hours and distillation from the steam bath.

In both cases the procedure for making the condensation was identical. The only variable was the amount of acetoacetic ester used. The alcoholic solution of the sodium salt of acetoacetic ester was prepared in the usual manner. During the addition of acetoacetic ester to the sodium alcoholate, precautions were taken to keep the solution cool. The halide was added and the mixture was refluxed on the steam bath 7 hours. At the end of this time the sodium bromide was filtered off and the alcohol was distilled from the product. The residue was distilled under diminished pressure. The quantitative results are given in the following table:

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[1] It is further interesting to note that in every tautomeric condensation some of the initial tautomer may be recovered due to equilibria of type 5, and the resulting formation of an equivalent amount of the di-alkyl compound simultaneously with the mono-alkyl compound.

TABLE VI.—REACTIONS BETWEEN ACETOACETIC ESTER AND γ-BROMOBUTYRONITRILE.

	G. material used.				G. products.		
Experiment No.	Alcohol.	Sodium.	γ-Bromobutyronitrile.	Acetoacetic ester.	Acetoacetic ester, 80–82°,[1] 20 mm.	δ-Cyano-δ-acetovalerianic ethyl ester, 153–155°,[1] 3 mm.	1,7-Dicyano-4-aceto-4-carboxethyl heptane, 200–205°,[1] 3 mm.
I	80	8.5	55	48	5	45 (66%)	9
II	80	8.5	55	72	24	60 (82%)	1

It will be observed that equivalent quantities of materials were used in Expt. I while 1.5 equivalents of acetoacetic ester were used in Expt. II. It is seen that the production of the undesired product is almost entirely eliminated in the latter case. The advantage of a thorough consideration of mass action is obvious.

That Fraction II, Table VI, is δ-cyano-α-acetovalerianic ester is proven by its method of synthesis and its hydrolysis to δ-acetovalerianic acid as described in a following section. Because of superheating it was found difficult to determine accurately the boiling point of this substance under diminished pressure. It is approximately 154° under 2 mm. Under ordinary pressure it decomposes before the boiling point is reached. The odor of the product obtained was unpleasant but this may have been due to a trace of impurities. It is a colorless, viscous liquid soluble in most organic solvents.

5. 1,7-Dicyano-4-aceto-4-carboxethyl Heptane. Di(γ-cyanopropyl)-acetoacetic Ethyl Ester.—That Fraction III, Table VII, in the preceding section, is 1,7-dicyano-4-aceto-4-carboxethyl heptane has been established by the following considerations: In the first place the synthesis predicts its formation. The redistillation of this fraction gave a product boiling at approximately 200° under 5 mm. pressure. The distillate was a viscous and slightly yellowish liquid which crystallized very slowly. The solid was washed with ether and sucked dry on the filter. The product was colorless, possessed a pleasant, nutty color and melted sharply at 76.5°. A nitrogen determination was made by the Dumas method.

Calc. for $C_{14}H_{20}O_3N_2$: N, 10.6%. Found: N, 9.1%, 9.5%.

These are not good checks but a consideration of the possible products makes it very probable that it is the substance named above. The structure of this substance is further confirmed by hydrolysis. 1.3 g. were refluxed with constant boiling aqueous hydrochloric acid 6–7 hours. A gas was evolved, which with lime-water gave a precipitate effervescing when treated with dilute acid. This indicates the loss of a carboxethyl group from the initial substance. The acid liquors were made alkaline with sodium carbonate, extracted with benzene and then with ether in order to remove any unchanged nitrile. After acidification with hydro-

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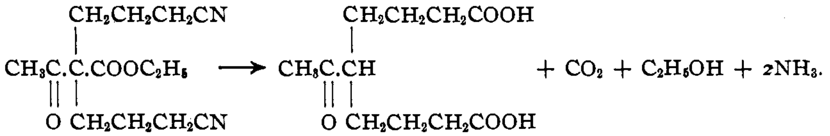
[1] As in Table V these temperatures are not corrected.

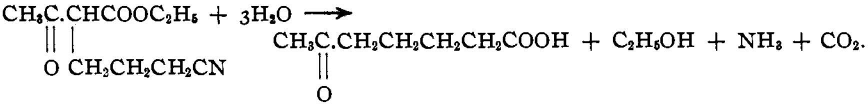
chloric acid the solution was extracted three times with ether and dried with anhydrous sodium sulfate. The evaporation of the ether left a small amount of a viscous liquid which could not be made to crystallize. This was placed in an evacuated desiccator over soda lime for several days. With dilute acid 1,7-dicyano-4-aceto-4-carboxethyl heptane should give δ-acetoazelaic acid, a substance which is not described in the literature, but its neutrality equivalent is 115.05. The product obtained possessed an equivalent of 115.5. The reaction equation is



$$\underset{\underset{\text{O}}{\|}}{\text{CH}_3\text{C}}.\overset{\overset{\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}}{|}}{\underset{\underset{\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}}{|}}{\text{C}}}.\text{COOC}_2\text{H}_5 \longrightarrow \underset{\underset{\text{O}}{\|}}{\text{CH}_3\text{C}}.\overset{\overset{\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}}{|}}{\underset{\underset{\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH}}{|}}{\text{CH}}} + \text{CO}_2 + \text{C}_2\text{H}_5\text{OH} + 2\text{NH}_3.$$

1,7-Dicyano-4-aceto-4-carboxethyl heptane is colorless and has a pleasant, nutty odor. It boils at approximately 200° under 5 mm. pressure, bath 290°; melting point, 73.5°. It is very sparingly soluble in alcohol, ether, carbon disulfide, chloroform, petroleum ether and water, but appreciably soluble in benzene.

6. δ-Acetovalerianic Acid and Its Sodium Salt.—δ-Cyano-α-acetovalerianic ester hydrolyzes almost quantitatively to δ-acetovalerianic acid with the constant boiling hydrochloric acid mixture.



$$\underset{\underset{\text{O}}{\|}}{\text{CH}_3\text{C}}.\underset{\underset{\text{CH}_2\text{CH}_2\text{CH}_2\text{CN}}{|}}{\text{CH}}\text{COOC}_2\text{H}_5 + 3\text{H}_2\text{O} \longrightarrow \underset{\underset{\text{O}}{\|}}{\text{CH}_3\text{C}}.\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COOH} + \text{C}_2\text{H}_5\text{OH} + \text{NH}_3 + \text{CO}_2.$$

The best results were obtained by using the ratio of about 20 g. of ester to 100 cc. of 20% hydrochloric acid. Although the ester dissolved in less than thirty minutes when the mixture was boiled, the solution was refluxed several hours longer. After cooling it was neutralized with sodium carbonate and was extracted with ether until a portion left no residue when dried with sodium sulfate and the ether was evaporated. It was next made distinctly acid to congo-red by the addition of hydrochloric acid and was repeatedly extracted with ether. This required 10–15 extractions of 25–30 cc. each. This number can be greatly reduced by salting out with ammonium sulfate. The ether solution was dried with sodium sulfate, the ether was evaporated and the residue was distilled under low pressure.

It was desired to obtain this acid in a state of absolute purity for conductivity measurements. Toward this end it was first distilled under different pressures. A fraction which boiled constant at 135° under about one mm. pressure was collected. This distilled at 181–182° under 25 mm.

This portion was next converted into the sodium salt. Instead of making it in the usual manner of precipitation from an alcoholic solution with sodium hydroxide, an equivalent amount of metallic sodium dissolved in absolute alcohol was employed. The advantages considered were the absence of water and the greater ease of solution of the sodium. 1.8 g. of sodium were dissolved in 200 cc. of absolute alcohol. To the hot solution 11.5 g. of the acid were gradually added. A small amount of insoluble material was filtered off. Upon cooling, the entire solution solidified to a mass of the consistency of a cake of moist soap. This product was sucked as dry as possible on a Büchner filter, using a hardened filter paper and washed three times with absolute ether. The filtrate was concentrated and treated in the same manner, this precipitate being added to the other. This process was repeated with two more portions of alcohol of about the same volume. The salt was dried in an electric oven at 90–100° for 4 hours, pulverized in an agate mortar and placed in a $CaCl_2$ evacuated desiccator overnight. The product was white and fluffy. The amount of sodium was determined by the sulfate method.

Calc. for $C_7H_{11}O_3Na$: Na, 13.85%. Found: Na, 13.85%, 13.84%.

The conductivity data of this salt will be found in a following section.

In order to recover the pure acid, 15 g. of this salt were dissolved in 50 cc. of water and 10 cc. of hydrochloric acid (sp. gr. 1.19, 37%) diluted with an equal volume of water, were added while the whole was kept cool. This solution was extracted twelve times with 20 cc. of alcohol-free ether and dried over sodium sulfate for several hours. After the evaporation of the ether and the reduction of the pressure at the beginning of the distillation a few drops of water came over. This suggests the formation of a hydrate. During the second distillation a fraction boiling at 160° under 13 mm., bath 235°, was collected. This was cooled in an evacuated $CaCl_2$ desiccator and pulverized in an agate mortar. Its neutrality equivalent was obtained by titration with standard barium hydroxide solution.

Calc. for $CH_3CO.(CH_2)_4COOH$: 144.1. Found: 143.8, 143.7.

The acid purified in the above manner melts sharply at 36.5°. Here again, because of the tendency to superheat, it was difficult to determine accurately the boiling points under reduced pressure. They were found to be approximately 135° at 1 mm. pressure, bath 195°, and 181° at 25 mm., bath 245°. The ionization constant is 1.926×10^{-5}. The data for the determination of this are given in the following sections.

Other investigators have reported the preparation of δ-acetovalerianic acid, but not by the above method. In all cases the product was of questionable purity. W. H. Perkin[1] reported its melting point at 40–42°. The yield was not stated. The acid could not be obtained, in more than a trace, by his method in the present case. In one investigation Wal-

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[1] *J. Chem. Soc.*, **57**, 230 (1890).

lach[1] states that he obtained this acid with a melting point of about 50°. By another method this investigator[2] obtained the same product with a melting point at 38–40°. Wallach thought that tautomerism or hydration might be interfering. Blaise and Koehler[3] gave its melting point at 31–32°. Thus it is seen that the melting points reported range from 31 to 50° as compared to the one at 36.5°, sharply, obtained in this investigation.

VII. Electrical Conductivity Measurements.

1. **Method and Apparatus.**—The method and apparatus used were those described by Derick and Kamm,[4] with the exception that a cell with platinized electrodes was used for measuring the conductivity of the acid. Its constant was 0.06233. A cell of about the same size with unplatinized electrodes and with a constant of the value 0.06776 was employed for the salt. A cell of about twice the size but of the same type with a constant 0.02952 was used for determining the conductance of the water.

2. **Preparation of Solutions and Procedure of the Measurements.**—The conductivity water was prepared as described by Derick and Kamm.[4] The solutions were prepared on the basis of one equivalent to 1000 g. of solution. Because of the extreme dilution this should cause no appreciable error.

For each concentration 300–400 g. of solution were prepared. They were weighed on a large balance to an accuracy of a few hundredths of one per cent. Both acid and salt were weighed in an ordinary weighing tube. Care was taken to allow the balance to come to equilibrium before the final weights were taken. Since the acid is somewhat hygroscopic, it was never poured from the weighing tube into a wet flask and it was exposed to the air as briefly as possible.

3. **Symbols Used for Conductivity Data.**—The symbols used for the conductivity data have the following meanings:

C = Moles of solute per 1000 g. of solution.
L = Specific conductance in reciprocal ohms.
Λ = Equivalent conductance at a given concentration.
Λ_0 = equivalent conductance at infinite dilution.
k = Ionization constant calculated from the Ostwald dilution law,

$$k = \frac{C\Lambda^2}{\Lambda_0(\Lambda_0 - \Lambda)}.$$

These same symbols with the subscript c means that they have been corrected for the conductance of the water by the subtraction of the

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[1] *Ann.*, **329**, 377 (1903).

[2] *Ibid.*, **359**, 309 (1908).

[3] *Compt. rend.*, **148**, 490 (1909).

[4] THIS JOURNAL, **39**, 392 (1917).

total specific conductance of the water from the specific conductance of the solution of the electrolyte.

All data is given at the temperature of 25° ± 0.01°.

4. Conductance and Ionization Constant of δ-Acetovalerianic Acid.—The acid used was that prepared in a very high degree of purity as described in Section VI - 6. The value for the specific conductance of the water is 0.60×10^{-6}.

TABLE VII.

δ-Acetovalerianic Acid. Temperature, 25.00 ± 0.01°.

C.	$L . 10^{-4}$.	$L_c . 10^{-4}$.	Λ.	Λ_c.	$k . 10^{-5}$.	$k_c . 10^{-5}$.
0.02	2.298	2.292	11.49	11.46	1.926	1.917
0.01	1.614	1.608	16.14	16.08	1.924	1.910
0.0075	1.393	1.387	18.58	18.49	1.927	1.907
0.005	1.131	1.125	22.62	22.50	1.926	1.904
0.0025	0.7900	0.7840	31.60	31.36	1.928	1.898
0.001	0.4872	0.4812	48.72	48.12	1.928	1.877

By the Ostwald[1] and the salt method, the data given in the next section give the value 376 for Λ_0 of this acid. The values 51.2 and 347.2 were used for the equivalent conductances of the sodium and hydrogen ions, respectively, at infinite dilution.

It will be observed that the values for the ionization constant, calculated from the uncorrected conductances, check each other to an accuracy of 0.1%, while those calculated from the corrected conductances gradually decrease in value with increasing dilution. It is generally agreed, however, that the total specific conductance of the water should not be subtracted from the specific conductance of the solution as has been done in this case. The application of "calculated" Λ_0 (Section VII-6) shows that the correction should not have been made in this manner. Kendal[2] has recently summarized the investigations made in this field and has shown that the *true* correction is insignificant, for acids stronger than acetic, if the water conductance is due to carbon dioxide only. The care which was taken in preparing the conductivity water and the solutions in the present case makes it highly probable that the only impurity was carbon dioxide. "Calculated" Λ_0 is shown to confirm this probability.

The conclusion is drawn from these considerations that the ionization constant of δ-acetovalerianic acid is $1.926 \pm 0.002 \times 10^{-5}$ at 25°.

5. Conductance Measurements on the Sodium Salt of δ-Acetovalerianic Acid.—The salt used was that prepared in a high degree of purity as previously described (Section VI-6). The specific conductance of the water was 0.926×10^{-6}.

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[1] Lundén's "Affinitätmessungen an schwachen Säuren und Basen," *Sammlung Chemischer und tech. Vortrage,* 14, 9 (1909).

[2] THIS JOURNAL, 39, 7 (1917).

TABLE VIII.

Sodium Salt of δ-Acetovalerianic Acid. Temperature, 25.00 ± 0.01°.

C.	L_c.	Λ_c.	$1/\Lambda_c$.	$(C\Lambda_c)^{0.45}$.	$\sqrt[3]{C}$.
0.01	0.0007155	71.55	0.01397	0.8601	0.2154
0.0075	0.0005433	72.44	0.01380	0.7599	0.1957
0.005	0.0003673	73.46	0.01361	0.6312	0.1710
0.0025	0.0001776	75.06	0.01332	0.4710	0.1357
0.001	0.00007645	76.45	0.01308	0.3144	0.1000
0.00075	0.00005774	76.98	0.01299	0.2771	0.09085
0.0005	0.00003896	77.92	0.01283	0.2322	0.07937
0.00025	0.00001955	78.20	0.01278	0.1703	0.06999
0.0001	0.000007929	79.29	0.01261	0.1134	0.04642

The value 80 was obtained for Λ_0 of the salt by two different methods of plotting the conductance data. One was the usual method of plotting $(C\Lambda_c)^{0.45}$ against $1/\Lambda_c$; in the other case $\sqrt[3]{C}$ was plotted against Λ_c.[1] The above value for Λ_0 was obtained by extrapolating a straight line through the points in each case. The necessary data is given in Table VIII.

6. The Application of "Calculated" Λ_0 to the Conductance Data of δ-Acetovalerianic Acid.—The criterion "calculated" Λ_0[2] has been applied to the conductance data of this acid corrected and uncorrected for the conductance of the water and recorded in Table IX. The uncorrected conductances (Λ, Table VII) were employed in making the calculations in Col. I; the corrected conductances (Λ_c, Table VII) in Col. II.

TABLE IX.—δ-ACETOVALERIANIC ACID.

Concentration.	I. "Calc." Λ_0.	II. "Calc." $\Lambda_{0\,(c)}$.
0.02 and 0.01	369	308
0.0075	383	307
0.005	370	319
0.0025	381	323
0.001	379	321
0.01 and 0.0075	413	305
0.005	370	321
0.0025	385	327
0.001	381	323
0.0075 and 0.005	350	331
0.0025	381	331
0.001	379	324
0.005 and 0.0025	397	331
0.001	383	323
0.0025 and 0.001	377	319

The values of "calculated" $\Lambda_{0\,(c)}$ are seen to be much lower than the value 376 obtained by the salt method. This shows the presence of a

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[1] Kohlrausch und Holborn, "Leitvermögen der Elektrolyte," p. 107.

[2] Derick, THIS JOURNAL, 36, 268 (1914).

constant error, produced by subtracting the total conductance of the water from that of the solution of the acid. This is to be expected if the conductance of the water is due to the presence of carbon dioxide only.

On the other hand, the values of "calc." Λ_0 are seen to be much closer to but slightly higher than 376. This indicates that a small constant error is involved somewhere. It is probably due to the slight conductance of carbon dioxide. However, the agreement is quite satisfactory considering the extreme sensitivity of the criterion. In order to appreciate this statement one should review the values of "calculated" Λ_0 applied by Derick[1] to the measurements on acetic by Ostwald, Jones, Van't Hoff and Kendall, where the deviations are much greater. The sensitivity of this criterion is also brought out in the application to Franke's and to Drucker's measurements of normal heptanoic acid (Section VIII).

The conclusion drawn from these considerations is that the conductance of the water is due to carbon dioxide and, consequently, no correction should be applied to the conductance of the acid for the desired accuracy of 0.1% in the ionization constant.

VIII. The Ionization Constant of, and the Application of "Calculated" Λ_0 to the Conductance Data of, Normal-Heptanoic Acid.

Different values for the conductances and the ionization constant of normal heptanoic acid have been found by Franke[2] and Drucker.[3] In order to obtain more accurate values, it was necessary to correct the conductances at the concentrations given by Franke to reciprocal ohms. His value of Λ_0 for the acid, corrected to reciprocal ohms and to the values 51.2 and 347.2 for the equivalent conductances of the sodium and hydrogen ions, respectively, at infinite dilution, was found to be 377. It was only necessary to correct Drucker's value for Λ_0 of the acid for the conductances of the sodium and hydrogen ions. 377 was obtained in this case also. The corrected conductances and ionization constants of both investigators are given in Table X.

TABLE X.—NORMAL HEPTANOIC ACID.

Franke.			Drucker.		
v.	$\Lambda_{(?)}$.	$k_{(?)}\cdot 10^{-5}$.	C.	Λ_C.	$k_C\cdot 10^{-5}$.
128	15.02	1.29	0.01103	13.17	1.40
256	21.00	1.28	0.005515	18.13	1.34
512	29.41	1.29	0.002760	26.00	1.40
1024	40.56	1.27	0.001380	36.30	1.41

It was not stated whether or not the conductance data of Franke was corrected for the conductance of the water,

The application of "calculated" Λ_0 to both sets of measurements are given in Table XI.

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[1] THIS JOURNAL, 36, 268 (1914).

[2] *Z. phys. Chem.*, 16, 463–92 (1895).

[3] *Ibid.*, 52, 641–704 (1905).

TABLE XI.—APPLICATION OF CALCULATED Λ_0.

Franke.		Drucker.	
Concentrations.	"Calc." Λ_0 (?).	Concentrations.	"Calc." Λ_0 (*c*).
128 and 256	280	0.01103 and 0.005515	108
512	362	0.002760	531
1024	304	0.001380	480
256 and 512	456	0.005515 and 0.002760	—251
1024	311	0.001380	—5812
512 and 1024	257	0.002760 and 0.001380	434

The presence of constant errors is disclosed in the measurements by Franke. From a consideration of the equations

$$\frac{dk}{k} = \frac{2\Lambda_0 - \Lambda}{\Lambda_0 - \Lambda}\left(\frac{d\Lambda}{\Lambda}\right) \quad \text{and} \quad \frac{d\Lambda_0}{\Lambda_0} = a\,\frac{d\Lambda}{\Lambda} + b\,\frac{d\Lambda_1}{\Lambda^1},^{1}$$

it follows that if "calculated" Λ_0 is uniformly less than the value determined by the salt method, the value of the ionization constant found, will be less than the correct one, and *vice versa*. Obviously, Franke's value for the ionization constant of normal heptanoic acid is too small. The measurements of Drucker are seen to lack precision and the ionization constant is probably a little large. Therefore, 1.4×10^{-5} is chosen as the approximate ionization constant of this acid.

IX. Summary.

1. Wegscheider's criticism of Derick's *place factor* and *rule of thirds* has been shown to be misleading. His suggestion for the use of the logarithm of the Ostwald factor concedes the very point of Derick's contention and demonstrates his error in stating that Derick and his students have not advanced the problem of the correlation of ionization and structure.

2. The ionization constants of several organic acids have been recalculated from conductances corrected to reciprocal ohms and for the recently determined conductances of the sodium and hydrogen ions.

3. The theoretical basis for the measurement of the *place influence* of substituents upon the ionization of organic acids has been developed.

4. The relative ϵ-place influence of the divalent oxygen atom, upon the ionization of paraffin monobasic acids, has been found to be approximately 0.14.

5. A convenient and efficient method for making pure trimethylene bromide on a large laboratory scale has been presented. A modified Norris method increases the yield 30%. 82% of the trimethylene glycol is converted into this bromide. The advantage of applying the collision method of study and mass action is demonstrated.

6. The use of methyl alcohol as a solvent, instead of the customary mixture of ethyl alcohol and water, for making γ-bromobutyronitrile

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[1] Derick, THIS JOURNAL, 36, 2270–2271 (1914).

from trimethylene bromide and potassium cyanide has been shown to be advantageous. This alcohol is suggested as a general solvent for making nitriles especially where there is danger of hydrolysis. Here again the yields are increased by the application of the collision method of study and mass action to the chemical equilibria involved.

7. It has been found that when γ-bromobutyronitrile is treated with one equivalent of aceto acetic ester two products result: one, γ-cyano-α-acetovalerianic ethyl ester, a combination of one molecule of each; the other, 1 : 7-dicyano-4-aceto-4-carboxethyl heptane, composed of one molecule of the ester and two of the nitrile. When 1.5 equivalents of aceto-acetic ester were used the latter was suppressed to one-ninth of the amount produced when one equivalent was used. This result was predicted from a consideration of the principle of mass action.

8. Two new substances, δ-cyano-α-acetovalerianic ethyl ester and 1,7-dicyano-4-aceto-4-carboxethyl heptane have been prepared and characterized.

9. δ-Acetovalerianic acid has been prepared in a pure state and in large quantities for the first time. Its ionization constant is $1.926 \pm 0.002 \times 10^{-5}$. The application of "calculated" Λ_0 proves this value to be accurate. Its correct capillary melting point is 36.5°.

10. The electrolytic conductance of the sodium salt of δ-acetovalerianic acid has been determined for a series of concentrations and the extrapolated Λ_0 value found to be 80.

11. The application of "calculated" Λ_0 to the existing conductance data of normal heptanoic acid shows that it is very inaccurate.

URBANA, ILL

[CONTRIBUTION FROM THE LABORATORIES OF THE INLAND REVENUE DEPARTMENT.]

THE MANGANESE CONTENT OF THE ASH OF CERTAIN DRUGS.

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Received December 18, 1917.

Although the significance of the presence of manganese in plants and its relation to plant metabolism is not yet clear, the quantity of manganese observed to be present in the barks of certain laxative drugs and in other portions of plants used for similar purposes, was considered by the authors to be worthy of general mention.

Hafner and Krist[1] have pointed out in a qualitative way that a large number of drug plants contain manganese. They were able to obtain positive tests for manganese on 164 drugs listed in the Austrian Pharmacopeia, and were led to this investigation by the occurrence of a greenish color in the ash of many drugs. This color is formed when the ash is

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[1] *Z. Osterr. Apoth. Ver.*, **45**, 387–399 (1907).