

Michael<sup>1</sup> 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  $\gamma$ - or  $\delta$ -carbon exerts a greater space or direct action upon the  $\alpha$ -carboxyl than when the same radicals are attached to the  $\beta$ ,  $\epsilon$ ,  $\zeta$ ,  $\eta$ , 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.

In Table I it was shown that a logarithmic function of  $K$  could be used as a measure of this direct influence of radicals as well as of their indirect influence. If this is true, the ionization constants of the  $\gamma$ - or  $\delta$ -halogen, hydroxyl or carboxyl substituted normal monobasic paraffin acids should be greater than that of the  $\beta$ -substituted isomeric acids. This must be true unless the excess of indirect influence of the  $\beta$ -position over that of the same substituent in the  $\gamma$ - and  $\delta$ -position is sufficiently great to compensate for the greater direct influence of the latter position which Michael assumes. In Table II will be found the factors of combined influence (direct or indirect) by which the conclusions drawn by Michael may be tested. The combined influence of the direct and indirect actions of halogen, hydroxyl and carboxyl radicals for  $\beta$ -,  $\gamma$ -, and  $\delta$ -positions (4, 5 and 6 in terms of nomenclature employed by Michael) are as follows:

$$\text{Chlorine } \beta : \gamma : \delta = 0.187 : 0.063 : 0.023$$

$$\text{Bromine } \beta : \gamma : \delta = 0.210 : 0.047 : 0.017$$

$$\text{Iodine } \beta : \gamma : \delta = 0.167 : 0.035 : 0.008$$

$$\text{Hydroxyl } \beta : \gamma : \delta = 0.073 : 0.018 : \dots$$

$$\text{Carboxyl } \beta : \gamma : \delta = 0.160 : 0.111 : 0.083$$

In no case, is the combined influence of the direct and indirect actions for these groups less in the  $\beta$ -position than in either the  $\gamma$ - or  $\delta$ -. This is opposite to the conclusions drawn by Michael. Obviously, we must look further for the reason of lactone and anhydride formations in the paraffin series.

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## APPLICATION OF POLARITY MEASURED IN TERMS OF A LOGARITHMIC FUNCTION OF THE IONIZATION CONSTANT.

### III. CORRELATION OF CHEMICAL STRUCTURE WITH IONIZATION.

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#### A. Determination of Structure from Ionization.

Many attempts have been made to use the ionization constant to determine the structure of organic compounds. Many interesting conclu-

<sup>1</sup> *J. prakt. Chem.*, [2] 60, 335 (1899).

sions have been drawn from isolated cases,<sup>1</sup> but no general connection between the chemical structure of organic electrolytes and their ionization has been found. It is the purpose of this paper to prove that such relationship exists, and that it is of the simplest possible nature for the negative substituted paraffin acids.

When the "scale of combined influence"<sup>2</sup> for a negative substituent upon a carboxyl group in position (1) is 2, 3, 4, 5, 6, 7, 8, 9, 10, etc., the position of the substituent may be predicted if the ionization constant of the substituted and unsubstituted acids together with that of any similar  $\alpha$ -substituted paraffin monocarboxylic acid is known. For example the "scale of combined influence" for chlorine in the monobasic paraffin acids upon the carboxyl group in position (1) is found from the following data:

	$K_a$	Log K.	Factor.
3 $\alpha$ -Chlorobutyric acid, $C_2H_5CHClCO_2H$ . . . . .	$1.39 \times 10^{-3}$	-2.857	0.6825
4 $\beta$ -Chlorobutyric acid, $CH_3CHClCH_2CO_2H$ . . . . .	$8.94 \times 10^{-5}$	-4.049	0.1873
5 $\gamma$ -Chlorobutyric acid, $CH_2Cl(CH_2)_2CO_2H$ . . . . .	$3.0 \times 10^{-5}$	-4.523	0.0627
6 $\delta$ -Chlorovalerianic acid, $CH_2Cl(CH_2)_3CO_2H$ . . . . .	$2.04 \times 10^{-5}$	-4.690	0.0229

From this it is evident that the scale for combined influence for chlorine in the monobasic paraffin acids upon the carboxyl groups in position (1) is:

$$\alpha : \beta : \gamma : \delta \text{ (or } 3 : 4 : 5 : 6) = 0.6825 : 0.1873 : 0.0627 : 0.0229$$

If we call the  $\alpha$ -factor one we have:

$$\alpha : \beta : \gamma : \delta, \text{ etc.} = 1 : 1/3 : 1/9 : 1/27, \text{ etc.}$$

In other words the effect of substituting chlorine in the  $\beta$ -position is about  $1/3$  of that in the  $\alpha$ -position, similarly that of the  $\gamma$ -position  $1/9$  and that of the  $\delta$ -position  $1/27$ . The fact that the  $\alpha$ -place factor for chlorine is slightly greater than three times the  $\beta$ -factor is due in part to the fact that  $\alpha$ -chlorobutyric is a fairly strong electrolyte and tends to deviate a little from the mass law by which the calculations were made. Or it may be due to inaccuracy in the determination of the constant. This fact, however, will not influence the accuracy with which structure may be determined, as will be seen later.

As shown in the article on the "Scale of Combined Influence of Substituents in Organic Compounds,"<sup>2</sup> the factors used above are determined as follows: The influence of all the atoms in the molecule upon the carboxyl group in position (1) is defined as proportional to  $1/\log K$ . It is assumed that this factor is made up additively of the factors of each atom in the molecule. The ratio of these combined influences for the

<sup>1</sup> W. Ostwald, *Z. physik. Chem.*, 3, 170 (1889), in the case of mono and dinitro caproic acids. Also H. Lunden, "Affinitätmessungen an schwachen Säuren und Basen," page 77.

<sup>2</sup> THIS JOURNAL, page 1167.

substituted acid to that of the unsubstituted acid is determined. To find the combined direct and indirect influences of the substituent for a given position, the combined influences of the rest of the atoms in the molecule are subtracted from the value of the ratio. The combined influence of the rest of the atoms in the molecule is taken equal to unity, thereby neglecting the value for the hydrogen atom replaced, which occurs additively and is a very small value. This result follows from the fact that in the above ratio the influence of all the atoms in the molecule of the unsubstituted acid is unity, since it occurs in the denominator. For example the  $\alpha$ -place factor for chlorine in  $\alpha$ -chlorobutyric acid is desired. The ionization constants of  $\alpha$ -chlorobutyric and butyric acids are  $1.39 \times 10^{-3}$  and  $1.56 \times 10^{-5}$ , respectively. The ratio of the combined influence of all the atoms in the  $\alpha$ -chlor acid to those in the unsubstituted butyric acid is

$$\alpha\text{-Chlorobutyric} : \text{Butyric} = 1/\log 1.39 \times 10^{-3} : 1/\log 1.56 \times 10^{-5} = \\ -4.807 / -2.857 = 1.6825/1.$$

The combined influences of the direct and indirect actions of chlorine in the  $\alpha$  (3) position upon the carboxyl group in position (1) is  $1.6825 - 1.0000 = 0.6825$ . In other words, the place factor for  $\alpha$ -chlorine is 0.6825. Finally the scale of combined influence for chlorine in the above series of chlor acids is:

$$\alpha : \beta : \gamma : \delta, \text{ etc. (or } 3 : 4 : 5 : 6, \text{ etc.)} = 0.6825 : 0.6825/3 : 0.6825/9 : \\ 0.6825/27, \text{ etc.}$$

The question immediately suggests itself, How general is this rule of thirds for the place factors? In the following table will be found the available data to test this rule.

From Table I, it is evident that the rule of thirds is generally applicable. It holds quite accurately for chlorine, bromine, iodine, hydroxyl and phenyl radicals. The fact that it does not hold for a molecule containing two carboxyl groups is to be expected, since the substitution of a second ionizing group must necessarily interfere with the above measure of the direct and indirect actions of substituents. Table I shows that the farther the two carboxyl groups are removed from each other the greater is the deviation, suggesting that both carboxyl groups are ionizing. The effect of the substituents would be thereby magnified. If each carboxyl group is affected the same amount, then the one-third rule should become a two-thirds rule. This is approximately true for glutaric, adipic, and succinic acids, since the place factor for the  $\beta$ -carboxyl group is 0.1594 and  $2/3$  of the same gives 0.1063, while the measured place factor for  $\gamma$ -carboxyl group is 0.1107 (glutaric acid). This fact in conjunction with the fact that beginning with succinic acid the half-esters of this homologous series give ionization constants just one-

half of the corresponding free acids, as discovered by J. Walker,<sup>1</sup> is very suggestive.

TABLE I.

Name.	Formula.	K <sub>a</sub> .	Log K <sub>a</sub>	Factor.
I. Chlorine:				
3 <sup>2</sup> or $\alpha$ -Chloroacetic acid . . .	CH <sub>2</sub> ClCO <sub>2</sub> H	1.55 10 <sup>-3</sup>	-2.80967	0.6830
3 $\alpha$ -Chloropropionic acid . . .	CH <sub>2</sub> CH(Cl)CO <sub>2</sub> H	1.47 10 <sup>-3</sup>	-2.83268	0.7083
4 $\beta$ -Chloropropionic acid . . .	CH <sub>2</sub> ClCH <sub>2</sub> CO <sub>2</sub> H	8.59 10 <sup>-5</sup>	-4.06601	0.1901
3 $\alpha$ -Chlorobutyric acid . . . .	C <sub>2</sub> H <sub>5</sub> CHClCO <sub>2</sub> H	1.39 10 <sup>-3</sup>	-2.85699	0.6826
4 $\beta$ -Chlorobutyric acid . . . .	CH <sub>2</sub> CHClCH <sub>2</sub> CO <sub>2</sub> H	8.94 10 <sup>-5</sup>	-4.04866	0.1873
5 $\gamma$ -Chlorobutyric acid . . . .	CH <sub>2</sub> Cl(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	3. 10 <sup>-5</sup>	-4.52288	0.0627
6 $\delta$ -Chlorovalerianic acid . . .	CH <sub>2</sub> Cl(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> H	2.04 10 <sup>-5</sup>	-4.69037	0.0230
II. Bromine:				
3 Bromoacetic acid . . . . .	CH <sub>2</sub> BrCO <sub>2</sub> H	1.38 10 <sup>-3</sup>	-2.86012	0.6539
3 $\alpha$ -Bromopropionic acid . . .	CH <sub>2</sub> CH.BrCO <sub>2</sub> H	1.08 10 <sup>-3</sup>	-2.96658	0.6312
4 $\beta$ -Bromopropionic acid . . .	CH <sub>2</sub> BrCH <sub>2</sub> CO <sub>2</sub> H	9.8 10 <sup>-5</sup>	-4.00877	0.2071
3 $\alpha$ -Bromobutyric acid . . . .	C <sub>2</sub> H <sub>5</sub> CHBrCO <sub>2</sub> H	1.06 10 <sup>-3</sup>	-2.97469	0.6159
5 $\gamma$ -Bromobutyric acid . . . .	CH <sub>2</sub> Br(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	2.6 10 <sup>-5</sup>	-4.58503	0.0484
6 $\delta$ -Bromovalerianic acid . . .	CH <sub>2</sub> Br(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> H	1.91 10 <sup>-5</sup>	-4.71897	0.0169
III. Iodine:				
3 Iodoacetic acid . . . . .	CH <sub>2</sub> ICO <sub>2</sub> H	7.5 10 <sup>-4</sup>	-3.12494	0.5138
4 $\beta$ -Iodopropionic acid . . . .	CH <sub>2</sub> I(CH <sub>2</sub> )CO <sub>2</sub> H	9. 10 <sup>-5</sup>	-4.04576	0.1961
5 $\gamma$ -Iodobutyric acid . . . . .	CH <sub>2</sub> I(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	2.3 10 <sup>-5</sup>	-4.63827	0.0363
6 $\delta$ -Iodovalerianic acid . . . .	CH <sub>2</sub> I(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> H	1.71 10 <sup>-5</sup>	-4.76700	0.0061
IV. Hydroxyl:				
3 Lactic acid . . . . .	CH <sub>2</sub> OHCO <sub>2</sub> H	1.5 10 <sup>-4</sup>	-3.82391	0.2371
3 Lactic acid . . . . .	CH <sub>2</sub> CH(OH)CO <sub>2</sub> H	1.38 10 <sup>-4</sup>	-3.86012	0.2536
4 $\beta$ -Hydroxypropionic acid . . .	CH <sub>2</sub> OHCH <sub>2</sub> CO <sub>2</sub> H	3.1 10 <sup>-5</sup>	-4.50864	0.0733
5 $\gamma$ -Hydroxybutyric acid . . . .	CH <sub>2</sub> OH(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	1.93 10 <sup>-5</sup>	-4.71444	0.0196
3 $\alpha$ -Hydroxyisobutyric acid . . .	(CH <sub>3</sub> ) <sub>2</sub> C(OH)CO <sub>2</sub> H	1.06 10 <sup>-4</sup>	-3.97469	0.2039
5 $\gamma$ -Hydroxyvalerianic acid . . .	CH <sub>2</sub> CHOH(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	2.0 10 <sup>-5</sup>	-4.69897	0.0214
V. Carboxyl:				
3 Malonic acid . . . . .	HO <sub>2</sub> C.CH <sub>2</sub> .CO <sub>2</sub> H	1.64 10 <sup>-3</sup>	-2.78516	0.6982
4 Succinic acid . . . . .	HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>2</sub> CO <sub>2</sub> H	6.7 10 <sup>-5</sup>	-4.17393	0.1594
5 Glutaric acid . . . . .	HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>3</sub> CO <sub>2</sub> H	4.7 10 <sup>-5</sup>	-4.32790	0.1107
6 Adipic acid . . . . .	HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>4</sub> CO <sub>2</sub> H	3.7 10 <sup>-5</sup>	-4.43180	0.0827
7 Pimelic acid . . . . .	HO <sub>2</sub> C(CH <sub>2</sub> ) <sub>5</sub> CO <sub>2</sub> H	3.2 10 <sup>-5</sup>	-4.49485	0.0761
VI. Oximido:				
3 $\alpha$ -Oximinodiacetic acid ( <i>syn</i> ) HON = CH.CO <sub>2</sub> H		9.95 10 <sup>-4</sup>	-3.00218	0.5756
3 $\alpha$ -Oximinobutyric acid ( <i>syn</i> ) HON = C.(C <sub>2</sub> H <sub>5</sub> )CO <sub>2</sub> H		8.3 10 <sup>-4</sup>	-3.08092	0.5602
VII. Phenyl:				
3 Phenylacetic acid . . . . .	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CO <sub>2</sub> H	5.6 10 <sup>-5</sup>	-4.25181	0.1126
3 $\alpha$ -Phenylpropionic acid . . . .	C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CO <sub>2</sub> H	4.3 10 <sup>-5</sup>	-4.36653	0.1082
4 $\beta$ -Phenylpropionic acid . . . .	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub> CO <sub>2</sub> H	2.3 10 <sup>-5</sup>	-4.63827	0.0434

A second important conclusion may be drawn from the table. The  $\alpha$ -factor is the same for a given substituent, independent of the acid from

<sup>1</sup> *J. Chem. Soc.*, 61, 605 (1892); 67, 147 (1895).

<sup>2</sup> Nomenclature used by Michael, *J. prakt. Chem.*, 60, 324 (1899).

which it is derived. For example, the  $\alpha$ -factors for chlorine as derived from acetic, propionic and butyric acids and their  $\alpha$ -chloro-derivatives are 0.6830, 0.7083, and 0.6826 respectively. If we add the influence of the other atoms in the molecule (equals 1) we have 1.6830, 1.7083, and 1.6826, respectively; that is, a difference of about two parts in one hundred and seventy as used in the calculations to follow. The data available show that the above fact holds for the negative substituents chlorine, bromine, hydroxyl, oximido and phenyl.

To determine the position of these radicals in the monobasic paraffin acids, we need only to know the  $\alpha$ -factor for the given radical (obtained from any  $\alpha$ -substituted monobasic paraffin acid and the corresponding unsubstituted acid) and the ionization constant of the substituted and corresponding unsubstituted acids. This will be illustrated as follows: Analysis and group tests or previous history show that an unknown substance is a bromopropionic acid. Its ionization constant is determined to be  $9.8 \times 10^{-5}$ , while that of the corresponding unsubstituted acid (propionic) is  $1.45 \times 10^{-5}$ . These two values give the place factor for the bromine in the unknown acid the value 0.2052. From Table I, the best  $\alpha$ -place factor is 0.6159. The ratio of the place factors for bromine in the unknown acid to that in the  $\alpha$ -brom acid is  $0.2052/0.6157 = 0.3332$ . Hence bromine is in the  $\beta$ -position in the unknown acid, according to the rule of thirds. From this illustration it is evident that the location of the negative substituent may be determined with certainty for the  $\alpha$ -,  $\beta$ -,  $\gamma$ - and  $\delta$ -positions even though the error in the ionization constants is relatively large, since if we use the  $\alpha$ -bromine place factors obtained from acetic and propionic acids, given in Table I, the above ratio gives the values 0.3137 and 0.3102. There can be no doubt that the bromine is in the  $\beta$ -position in the above acid, no matter which value is chosen for the  $\alpha$ -place factor. This method for the determination of structure will find much application in the cases where a new substituted paraffin acid is made which has not been previously characterized.

The calculation of the structure from these place factors will be extended to other than the derivatives of the paraffin acids and the  $\alpha$ -place factors for different negative radicals will be determined in the near future.

### B. Calculation of Ionization Constants from Structure.

In the calculation of structure from the place factors as determined above, it is evident that the fairly large errors in the ionization constant will not interfere with the accuracy by which the position of the substituent may be determined. In the determination of the position of the substituent, therefore, the rule of thirds need not hold with an accuracy greater than ten to twenty per cent. for the  $\alpha$ -,  $\beta$ -,  $\gamma$  or  $\delta$ -positions. In the calculation of ionization constants from structure, however, the rule of thirds must hold with an accuracy equal to that with which the

ionization constant may be determined, if it is to give accurate results.

The calculation of ionization constants will give a rigid test of this rule. From the knowledge of the value of the  $\alpha$ -place factor for a given negative substituent, the ionization constant of any saturated paraffin acid, substituted in any position by this given negative substituent, may be calculated, if we know the ionization constant of the corresponding unsubstituted acid. This will be illustrated by the following example. The ionization constant of  $\beta$ -bromopropionic acid is desired. The  $\alpha$ -place factor for bromine, calculated from  $\alpha$  bromobutyric acid, is found to be 0.6159. Since the ionization constant of  $\beta$ -bromopropionic acid is desired, applying the rule of thirds, the  $\beta$ -place factor for bromine is  $0.6159/3 = 0.2053$ . Adding to this value, the factor for the other atoms in the molecule, the result, 1.2053, gives the factor representing the combined influences of all the atoms in the molecule of  $\beta$ -bromopropionic acid. The ratio 1.2053/1 is the ratio between the influences of all the atoms in  $\beta$ -bromopropionic acid as compared to propionic acid. By definition these influences were obtained from

$$1/\log K (\text{bromopropionic}) : 1/\log K (\text{propionic}) = 1.2052 : 1.$$

$\log K$  (propionic acid) is known to be  $-4.83863$ . Hence  $1.2052/1 = -4.83863/X$  where  $X$  is the logarithm of the desired ionization constant of  $\beta$ -bromopropionic acid.  $X = -4.0154$  or  $-5.9845$ , which gives the numerical calculated value for  $K$  ( $\beta$ -bromopropionic acid)  $= 9.6 \times 10^{-5}$  while the measured value is  $K$  ( $\beta$ -bromopropionic acid)  $= 9.8 \times 10^{-5}$ . In the above calculation, the  $\alpha$ -factor for bromine, calculated from  $\alpha$ -bromobutyric acid was employed. To show with what accuracy the place factor must be known, the  $\alpha$ -place factors for bromine as determined from bromoacetic acid (0.6539) and  $\alpha$ -bromopropionic acid (0.6312) when used in the above calculations gives the calculated results  $1.04 \times 10^{-4}$  and  $1.00 \times 10^{-4}$ , respectively. The average for the place factors for  $\alpha$ -bromine, as determined from Table I, give the result  $1.00 \times 10^{-4}$ . A difference of four parts in sixty-one in the place factors make a difference of eight parts in ninety-six in the ionization constant. The average value of the  $\alpha$ -bromine place factor gives a result about 2 per cent. higher than the experimental value for  $\beta$ -bromopropionic acid, which is in error by that amount. From this single example it appears that the calculated result may fall within the limit of error of the experimental value. The fact that of the seven values necessary for the above calculations six were made by different observers makes the result of more value.

Table II gives the results of other calculations as compared with the experimental values. In the first column under the heading, ionization constant, is given the result using the average of all the  $\alpha$ -factors for a given negative substituent given in Table I. The second column, under the same head, gives the experimental values for the same acid and the

last column, the results calculated from the best value for the  $\alpha$ -factor for the given negative substituent.

TABLE II.

Name.	Ionization constants.		
	Calculated from average $\alpha$ -factor.	Measured.	Calculated from single $\alpha$ -factor.
$\gamma$ -Chlorobutyric acid	$3.5 \cdot 10^{-5}$	$3. \cdot 10^{-5}$	$3.4 \cdot 10^{-5}$
$\delta$ -Chlorovalerianic acid	$2.67 \cdot 10^{-5}$	$2.04 \cdot 10^{-5}$	$2.66 \cdot 10^{-5}$
$\beta$ -Bromopropionic acid	$1.0 \cdot 10^{-4}$	$9.8 \cdot 10^{-5}$	$9.7 \cdot 10^{-5}$
$\gamma$ -Bromobutyric acid	$3.2 \cdot 10^{-5}$	$2.6 \cdot 10^{-5}$	$3.1 \cdot 10^{-5}$
$\delta$ -Bromovalerianic acid	$2.04 \cdot 10^{-5}$	$1.91 \cdot 10^{-5}$	$2.03 \cdot 10^{-5}$
$\beta$ -Iodopropionic acid	$7.4 \cdot 10^{-5}$	$9. \cdot 10^{-5}$	.....
$\gamma$ -Iodobutyric acid	$2.8 \cdot 10^{-5}$	$2.3 \cdot 10^{-5}$	.....
$\delta$ -Iodovalerianic acid	$1.95 \cdot 10^{-5}$	$1.71 \cdot 10^{-5}$	.....
$\beta$ -Hydroxypropionic acid	$3.2 \cdot 10^{-5}$	$3.1 \cdot 10^{-5}$	$3.2 \cdot 10^{-5}$
$\gamma$ -Hydroxybutyric acid	$2.05 \cdot 10^{-5}$	$1.93 \cdot 10^{-5}$	$2.03 \cdot 10^{-5}$
$\gamma$ -Hydroxyvalerianic acid	$2.1 \cdot 10^{-5}$	$2.0 \cdot 10^{-5}$	$2.0 \cdot 10^{-5}$
$\beta$ -Phenylpropionic acid	$2.1 \cdot 10^{-5}$	$2.3 \cdot 10^{-5}$	$2.2 \cdot 10^{-5}$
$\gamma$ -Chlorobutyric acid	$3.0 \cdot 10^{-5}$	$3. \cdot 10^{-5}$	$3.0 \cdot 10^{-5}$
$\delta$ -Chlorovalerianic acid	$2.00 \cdot 10^{-5}$	$2.04 \cdot 10^{-5}$	$2.00 \cdot 10^{-5}$

Table II shows that the ionization constants of negative substituted paraffin monocarboxylic acids may be calculated with a fair degree of accuracy from the existing data. It must be borne in mind that the rule of thirds will not hold accurately for acids which do not obey the mass law. It is important to know, therefore, just how accurately the mass law holds for organic electrolytes. In the case of the chloro acids given in Table I a much better agreement between the calculated and experimental values (given in Table II) would be obtained if the value of the experimental  $\beta$ -chlorine factor is taken, rather than that of the  $\alpha$ -factor, to calculate the ionization constants of the  $\gamma$ - or  $\delta$ -chloro acids. The last two acids given in Table II were so calculated. Future experiments will be made to study this point in detail.

Finally, the question, as to whether this additive relation in the free energy of ionization will hold for more than one negative radical in the same molecule or for several different negative radicals, must be settled. For example, the rule of thirds will be applied to glyceric acid, in which there are present an  $\alpha$ - and a  $\beta$ -hydroxyl group, as follows:

$$\alpha\text{-Hydroxyl place factor from } \alpha\text{-hydroxypropionic acid} = 0.2536$$

$$\beta\text{-Hydroxyl place factor from } 0.2536/3 = 0.0843$$

$$\alpha + \beta\text{-place factors} = 0.3378$$

The factor representing the influence of all the atoms in the molecule of glyceric acid is  $1 + 0.3378 = 1.3378$ . The corresponding unsubstituted monobasic paraffin acid is propionic acid from which we have:

$$-4.83863/1.3378 = -3.61633 \text{ or } -4.38367 = 2.4 \times 10^{-5}$$

$$K \text{ (glyceric calculated)} = 2.4 \times 10^{-4}$$

$$K \text{ (glyceric measured)} = 2.0 \times 10^{-4}$$

If we use the  $\alpha$ -factor for the hydroxyl groups as determined from glycolic acid (0.2371), the calculated value for the ionization constant of glyceric acid is  $2.1 \times 10^{-4}$ .

Table III will give other examples testing this additive relation. The three columns under the heading ionization constants have the same meaning as under Table II.

TABLE III.

Name.	Substituent and its position.	Ionization constants.		
		Calculated from the average $\alpha$ -factor.	Measured.	Calculated.
Mesotartaric acid	$\alpha\text{OH}, \beta\text{OH}, \beta\text{COOH}$	$5.1 \times 10^{-4}$	$6.0 \times 10^{-4}$	$5.8 \times 10^{-4*}$
Chlorosuccinic acid	$\alpha\text{Cl}, \beta\text{COOH}$	$2.4 \times 10^{-3}$	$2.8 \times 10^{-3}$	$2.6 \times 10^{-3*}$
Bromosuccinic acid	$\alpha\text{Br}, \beta\text{COOH}$	$2.0 \times 10^{-3}$	$2.8 \times 10^{-3?}$	$2.1 \times 10^{-3*}$
Phenylsuccinic acid	$\alpha\text{C}_6\text{H}_5, \beta\text{COOH}$	$1.54 \times 10^{-4}$	$1.64 \times 10^{-4}$	$1.57 \times 10^{-4*}$
$\beta$ -Phenylglutaric acid	$\beta\text{C}_6\text{H}_5, \gamma\text{COOH}$	$6.5 \times 10^{-5}$	$7.7 \times 10^{-5}$	$6.5 \times 10^{-5}$
Tricarballic acid	$\beta\text{COOH}, \beta\text{COOH}$	$2.30 \times 10^{-5}$	$2.24 \times 10^{-5}$	.....
$\beta$ -Phenyl- $\gamma$ -acetobutyric acid	$(\beta\text{C}_6\text{H}_5), [\delta(\text{O} =)]$	$3.3 \times 10^{-5}$	$3.2 \times 10^{-5}$	$3.2 \times 10^{-5}$
Glyoxalic acid	$\alpha\text{OH}, \alpha\text{OH}$	$5.8 \times 10^{-4}$	$5. \times 10^{-4}$	$5.20 \times 10^{-4}$
Citric acid	$\alpha\text{OH}, \beta\text{COOH}, \beta\text{COOH}$	$8.0 \times 10^{-4}$	$8.2 \left. \begin{array}{l} \right\} \times 10^{-4} \\ 8.0 \end{array} \right\}$	.....

Table III shows that the additive relation of the place factors for different negative groups holds fairly well. It must be remembered that with more than one negative substituent, the factor representing the replaced hydrogen atoms, which is neglected in all the above calculations, may be large enough to influence, slightly, the accuracy of the calculations. The author suspects, however, that the error due to impurities in the reagents used to determine the ionization constants is far greater than that due to neglecting the additive factor for the hydrogen replaced. These calculations, again, show with what accuracy the rule of thirds will hold. In the case of the carboxyl group which does not obey this rule, the additive place factors for the carboxyl groups were calculated from the corresponding unsubstituted dibasic paraffin acids (see Table I, No. 5). This last fact shows that the free energy of ionization (proportional to the logarithm of K) of the paraffin acids is made up additively of the combined direct and indirect influences of each atom or radical in the molecule whether or not the acids obey the rule of thirds. Finally considering tricarballic and citric acids as derivatives of isobutyric acid rather than of butyric acid, a fine check between the experimental and calculated results is obtained as Table III shows. Hence this additive free energy relationship furnishes us with a means of determining

<sup>1</sup> Using the  $\alpha$ -place factor from  $\alpha$ -substituted propionic acids.



which carboxyl group in polybasic acids is ionizing. The experimental study of these place factors is now in progress and will be extended to other classes of compounds.

URBANA, ILL.

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[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WYOMING EXPERIMENT STATION.]

### CHEMICAL EXAMINATION OF WOODY ASTER.

BY L. CHAS. RAIFORD.

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During the past several years thousands<sup>1</sup> of sheep have died in Wyoming through what is supposed to have been the eating of poisonous plants on the ranges. For the last two or three seasons the losses have occurred, in many instances, in localities where the areas grazed were somewhat circumscribed, and in several of these places a certain plant that later came to be suspected as poisonous was found in enormous numbers. It is notable that the heaviest losses for the seasons of both 1908 and 1909 occurred in approximately the same localities, and that in nearly all of these places the suspected plant was abundant.

The facts stated above were secured through a preliminary investigation of the conditions that prevailed, during the seasons mentioned, by both botanist and veterinarian of this station; and, it may be added, the data collected tended to indicate a plant known as the woody aster as the possible source of the trouble. The idea that the losses were due to poisonous plants seemed to be favored indirectly by the inconclusive results of two veterinarians from the Bureau of Animal Industry, who studied the question during the seasons of 1907 and 1908, and who made careful search for animal parasites.<sup>2</sup> Still further support of the view at present entertained was secured from data<sup>3</sup> obtained by the veterinarian of this station during the season of 1910, when extracts prepared in this laboratory from the aster in question were fed to sheep kept under such conditions that the effect of the poison, if any, could be noted. Tests upon other experimental animals are now being conducted with these extracts, and the results so far obtained are in harmony with what has been recorded above.

The suspected plant belongs to the genus *Xylorrhiza*,<sup>4</sup> species of which have been collected in Wyoming, Colorado, and Utah.<sup>5</sup> These plants

<sup>1</sup> Tenth Annual Report of State Board of Sheep Commissioners, 7 (1908).

<sup>2</sup> The losses were at first attributed to the so-called "grub-in-the-head."

<sup>3</sup> *Wyoming Exp. Sta., Bull.* 88.

<sup>4</sup> Pammel, "Manual of Poisonous Plants," p. 138 (1910), designates this plant as the *Aster Parryi* Gray.

<sup>5</sup> According to the statements of herders, stock usually avoid this plant on the range, although analysis shows that it has a relatively high food value.