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STUDIES IN ESTERIFICATION, I. VICTOR MEYER'S ESTERIFICATION LAW.

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Sec. I. Introductory.

The Esterification Law, discovered by Victor Meyer in 1894 and experimentally established by himself and others, is widely known. It is usually stated in the following form:¹ "If in a substituted benzoic acid both of the hydrogen atoms next to the carboxyl group are replaced by radicles, the resulting acid cannot be esterified by means of alcohol and acid." The radicles thus far studied include the halogens, the nitro-, amino-, methyl, carboxyl, and hydroxyl groups.

Several important exceptions to the Esterification Law are known. Not to speak of the influence of hydroxyl groups, which interfere with the formation of esters only to a moderate extent, we will mention the case of tetrachloro-ortho-phthalic acid.² According to the Esterification Law, this acid should give no ester. Chlorine atoms and carboxyl groups are supposed to exert an especially powerful hindering influence on esterification. Yet the monoethyl ester of this acid is readily formed by the action of alcohol and hydrochloric acid.

Notwithstanding such occasional exceptions, the Victor Meyer Law has been used in two or three cases, as an empirical rule, for solving problems of constitution and for isolating diortho-substituted from other acids.

If, however, the Esterification Law and its kindred rules had no other than the purely empirical aspect, their scientific value would be very small indeed, for diortho-substituted aromatic acids are but seldom met with in laboratory practice. The great importance of such rules lies, not so much in their immediate practical utility as in the light which, if correctly interpreted, they throw upon the connection between the structure of substances and their chemical behavior, and in the new power thus acquired by the atomic theory. Victor Meyer realized this from the beginning and early offered a hypothesis which, in the opinion of the majority of chemists, furnishes a satisfactory interpretation of the Esterification Law. We are referring to the well-known steric hindrance hypothesis, in accordance with which the carboxyl group cannot react with alcohols because it is shut in between the neighboring groups, and

¹ See, for instance, Scholtz, *Der Einfluss der Raumerfüllung der Atomgruppen auf den Verlauf chemischer Reaktionen* (Ahrens' Sammlung, Stuttgart, 1899), p. 12.

² Graebe, *Ann.*, **238**, 327 (1887); Victor Meyer, *Ber.*, **28**, 182 (1895). See also Graebe's work, *Ber.*, **33**, 2019 (1900), and Marckwald and McKenzie, *Ber.*, **34**, 486 (1901).

is (consequently) the less capable of reacting the larger those groups. The same mechanical conception explained to Victor Meyer the fact that the esters of diortho-substituted acids could be readily obtained by the action of alkyl halides on the corresponding silver salts: the large silver atom forces the two ortho-groups apart and renders the carboxyl readily accessible to the action of halogen compounds. This last idea is not altogether free from the possibility of objection, but we will not insist.

In the hope of producing experimental evidence in support of the steric hindrance hypothesis, Victor Meyer directed Kellas¹ to undertake a thorough investigation of the influence on the carboxyl of one single group in the orthoposition: if the steric hindrance hypothesis is correct, the velocity of esterification ought to be diminished in proportion to the magnitude of the substituting group. As a matter of fact, Kellas found (apparently) that a bromine atom retarded esterification to a greater degree than a chlorine atom, and an iodine atom to a greater degree than a bromine atom: the "heavier" the substituting atom or group, the greater its retarding influence on esterification. An inconsistency is presented by the nitro group, which, with its weight of only 46, exerts a greater retarding influence than bromine weighing 80 and even than iodine weighing 127.

Perhaps Nernst's estimate of hypotheses that lead to inconsistencies is not inapplicable to this case: "*Letztere [Gesetzmässigkeiten] werden dem Experimente zugänglich und der Erfolg beweist zwar durchaus nicht die Richtigkeit, wohl aber die Brauchbarkeit der Hypothese, während ein Misserfolg neben ihrer Unzweckmässigkeit auch die Unrichtigkeit der Vorstellungen, von denen wir ausgehen, überzeugend dartut.*"²

Even before the publication of Kellas's observations, Wegscheider³ had pointed out that the assumption of a state of tension produced by the substituting groups would furnish as easy a mechanical explanation of the phenomena described by the Esterification Law as the diametrically opposite hypothesis of steric hindrance. Then Bredig⁴ wrote: "*Einer solchen vieldeutigen Unbestimmtheit ihrer mechanistischen Hypothesen gegenüber, bleibt den organischen Chemikern nichts anderes übrig, als endlich die landläufigen Begriffe einer 'schwer' oder 'leicht' verlaufenden Reaktion mit den exakteren Begriffen der chemischen Statik resp. Dynamik zu vertauschen und mit diesen zu messen und zu rechnen.*"

¹ Victor Meyer, *Z. physik. Chem.*, **24**, 219 (1897); Kellas, *Ibid.*, 221. See also van Loon and Victor Meyer, *Ber.*, **29**, 839 (1896); Goldschmidt, *Ibid.*, **28**, 3218 (1895); Petersen, *Z. physik. Chem.*, **16**, 385 (1895).

² Nernst, *Theoretische Chemie*, Ed. 5 (Stuttgart, 1907), p. 3.

³ *Ber.*, **28**, 2535 (1895).

⁴ *Z. physik. Chemie*, **21**, 154 (1896); see also Wegscheider, *Ibid.*, 302.

Sec. 2. On the Possibility of Esterifying All Di-ortho-substituted Acids.

Bredig's idea, that the phenomena summed up by the Esterification Law could not be adequately interpreted until they had been described in the precise terms of chemical dynamics, has not hitherto been followed up. The esterification refused to take place and so a dynamic study of it remained impossible.

Attempts to force the reaction to occur have been made from time to time, but have failed. In 1897, Wegscheider¹ attempted to esterify 1,2,4,6-tribromo-benzoic acid as follows: 2 grams of the acid were heated for four and one-quarter hours on the water bath with 25 cubic centimeters of methyl alcohol and 1.75 cubic centimeters of concentrated sulphuric acid, and then the mixture was allowed to stand for twenty hours longer at the ordinary temperature. No ester was formed. Then a more drastic method was tried: 2 grams of the acid were heated for four hours with 20 cubic centimeters of methyl alcohol and no less than 20 cubic centimeters of concentrated sulphuric acid, and the mixture was left at the ordinary temperature for thirteen and one-half hours longer. This time 12% of the acid had been esterified. But if no more ester could be obtained in the presence of such an enormous excess of concentrated sulphuric acid, the problem of studying the dynamics of the esterification must have appeared inapproachable.

The work reported in the present communication is based on the discovery (made by one of us some years ago), that di-ortho-substituted acids can be esterified with great readiness by simply heating them at higher temperatures with ethyl alcohol. Not even a catalytic agent is necessary.

Following are a few experiments substantiating this statement:

(1) Half a gram of pure 1,2,4,6-tribromo-benzoic acid was heated in a sealed tube with 10 grams of absolute alcohol for 100 hours at 216°. On cooling, the alcohol was distilled off, the residue taken up with ether, the ethereal solution carefully washed with aqueous sodium carbonate and dried. The ether was distilled off and the residue weighed. The amount found was 0.54 gram, representing 100 per cent. of ester. A bromine determination gave 61.32 per cent. Br. Calculated for $C_6H_2Br_3COOC_2H_5$, 61.99 per cent. The ester, a white crystalline substance sparingly soluble in cold alcohol, melted at 86°.

(2) 0.4800 gram of 1,2,4,6-trichloro-benzoic acid was heated in a sealed tube with 1.7711 grams of absolute alcohol for 97 hours at 183°. Titration with standard sodium hydroxide showed that 73 per cent. of the acid had been esterified.

(3) 0.5030 gram of α -nitro-phthalic-monoethyl ester was heated with 1.5442 grams of absolute alcohol for 63 hours at 183°. Titration with standard sodium hydroxide showed that 91.5 per cent. of the acid had been esterified.

(4) Half a gram of pure mellitic acid was heated with 2.0 grams of absolute alcohol for 96 hours at 183°. As a result, 60.5 per cent. of the acid were transformed into the hexa-ethyl ester.

(5) Turning to a refractory acid of the aliphatic series, we heated 0.8120 gram

¹ *Monatsh. für Chemie*, 18, 643 (1897).

of trimethyl-acetic acid with 1.4083 grams of absolute alcohol for 63 hours at 183°: 89 per cent. of the acid were esterified.

Even at the temperature of boiling alcohol and working in open vessels we were able to esterify the 1,2,4,6-tribromo-benzoic acid by prolonged heating.

These facts make it plain that the acids which according to Victor Meyer's Law are unesterifiable by alcohol and hydrochloric acid, or esterifiable "to a very small extent," can really be esterified *ad libitum*.

Sec. 3. Experimental Method.

The possibility of esterifying the refractory acids established, we undertook a determination of their velocity constants at the temperature of boiling aniline.

Esterification is usually studied as an irreversible reaction of the first order, the alcohol being employed in very large excess. When such a study is carried out for the purpose of testing the law of mass action, nothing can be said against this. The magnitude of the constant, however, obtained in any given case depends upon the relative number of molecules of alcohol employed. Algebraically, if

$$\frac{dx}{dt} = k_1(a-x)(b-x),$$

and b is made so large that $(b-x)$ remains practically constant, say k_2 , during the reaction, the equation becomes

$$\frac{dx}{dt} = k_1 k_2 (a-x) = k(a-x).$$

But the constant k depends upon the magnitude of k_2 . If the problem is, to find the velocity constant in the true sense of the term, *i. e.*, a constant independent of the active masses of the reacting substances, then either the number of alcohol molecules must be taken into account, or else, preferably, esterification should be studied in its natural form, *i. e.*, as a reversible reaction of the second order. We doubt whether the accepted esterification constants are strictly comparable in all cases.

Again, usually some mineral acid is employed as a catalytic agent. This not only conceals the true value of the velocity constant, but in some cases profoundly influences the nature of the results. Thus, according to the researches of Lichty,¹ the velocity of esterification in the absence of foreign catalytic agents increases with the strength of the acid. On the other hand, Sudborough and Lloyd,² who used hydrochloric acid, found that the strong chloro-acetic acids esterified much less rapidly than the weak acetic acid itself. Catalysis, in the form of auto-catalysis, is of course unavoidable: but as the kinetic constants of a reaction

¹ *Am. Chem. J.*, **17**, 27 (1895); **18**, 590 (1896).

² *Trans. Chem. Soc.*, **75**, 467 (1899).

should express nothing but the influence of the nature of the reacting substances on the velocity of reaction, surely *foreign* catalytic agents must be excluded.

In accordance with these principles, our method of procedure is as follows. Tubes of fine Jena glass (7 millimeters internal diameter, with a wall 1 millimeter thick) are cut into pieces about 12 centimeters long, sealed at one end, and weighed on the balance of precision. About half a gram of solid acid is introduced into each tube by means of a long narrow-stemmed funnel, and the tubes are weighed again. A weighed glass rod about four centimeters long and of somewhat smaller diameter than the bore, is introduced into the tube, and the latter is drawn out into a fairly wide thick-walled capillary slightly above the upper end of the rod. Absolute ethyl alcohol, carefully dried, is then introduced into the tube by means of a funnel with a narrow capillary stem reaching down to the glass rod. When the level of alcohol has attained about 90 per cent. of the height of the tube, the funnel is withdrawn, the tube carefully sealed at the contracted part, and the sealed tube weighed together with the part removed. In this manner the quantities of acid and alcohol in the tube are ascertained within one-tenth of a milligram. The tube is now securely tied with fine copper wire to a long thin metal rod, lowered into the vapor of aniline boiling in a metal thermostat, and the time noted. Preliminary experiments showed that tubes so prepared are nearly filled with liquid at 183° , the gaseous phase being thus practically negligible.

The introduction of the glass rod was found necessary for the following reason. Most of the acids studied could not be dissolved in moderate quantities of alcohol. It was, therefore, impossible to introduce the reacting mixture through the capillary funnel in the form of a solution immediately before sealing the tube. On the other hand, after introducing the solid acid it would not have been possible to narrow the tube without either charring the acid or leaving too large a space above it.

After the required interval of time, the tube is removed from the thermostat and plunged for a first cooling into a water bath at 60° for five seconds, and then into cold water. The time required for the reduction of the temperature from 183° to about 20° was in all cases much less than one minute, usually about half a minute. In none of the cases studied, have we observed a separation of the liquid in the tube into two layers as long as the tube remained warm. On cooling, the height of the liquid in the tube is carefully marked, for the purpose of a subsequent estimation of the volume. The tube is now opened, its contents carefully rinsed into a beaker with a moderate quantity of alcohol to which a few drops of phenolphthalein and enough sodium hydroxide has been added to produce a faint pink coloration. Water, similarly treated,

is next added to the alcoholic solution almost to the beginning of precipitation. The solution thus obtained is carefully titrated with pure $N/17$ NaOH.¹ In every case, for purposes of control, a similar solution of the pure acid was prepared and titrated with the same sodium hydroxide.

The tube in which the esterification has taken place, with the glass rod in it, is now filled to its mark with water from a burette. This is repeated several times and the mean of the burette readings is taken. Special experiments showed that eleven-tenths of the volume thus found, represent approximately the volume occupied by the reacting mixture at the temperature of boiling aniline.

Sec. 4. The Law of Mass Action.

Owing to the practical impossibility of introducing into our tubes always the same relative amounts of the solid acids and of alcohol, it was necessary to employ the law of mass action in one of its most general forms. As far as we know, the law has never hitherto been applied to the kinetics of a reversible reaction of the second order in a liquid, with not only the time, but also the initial active masses of the reacting substances varying from experiment to experiment. The results given in this communication show, among other things, that in spite of the high concentrations involved, the law of mass action holds good under such conditions as well as when the experimental conditions are less complex.

We write the differential equation of mass action as follows:

$$\frac{dx}{vdt} = k \frac{(a-x)(b-x)}{v^2} - k' \frac{x^2}{v^2}$$

Division of dx by v refers the velocity constants to unit volume and renders their numerical values in different cases, involving different volumes, comparable. Many a misinterpretation in the literature of chemical dynamics is due, we believe, to the volume of reacting mixtures not being properly taken into account, and the employment of the above form of the law of mass action in kinetic studies generally, cannot be too strongly recommended.

We get immediately:

$$\frac{dx}{dt} = \frac{k}{v} (a-x)(b-x) - \frac{k'}{v} x^2,$$

and by integration, remembering that $\frac{k'}{k} = K'$ (the reciprocal of the equilibrium constant) and that $x = 0$ when $t = 0$,

$$k = \frac{2.3026v}{t\sqrt{(a-b)^2 + 4abK'}} \log_{10} \frac{2ab - x(a+b) - \sqrt{(a-b)^2 + 4abK'}}{2ab - x(a+b) + \sqrt{(a-b)^2 + 4abK'}}$$

¹ In one case barium hydroxide was used, but the end-point was less distinct than with sodium hydroxide.

To test the above form of the law of mass action, and also for the purpose of comparing our own constants with that for ethyl alcohol and acetic acid at ordinary temperatures, we applied our equation to the results obtained by Berthelot and Péan de St. Gilles¹ for 1 mol of ethyl alcohol with 1, 2, and 2.9 mols of acetic acid. By determining the specific gravities of such mixtures at 20°, we found the following volumes v required by the equation :

$$\begin{aligned} \text{for } b \text{ (alcohol)} = 1 \text{ mol, and } a \text{ (acid)} = 1 \text{ mol} \dots\dots\dots v_1 &= 0.114 \\ \text{for } b = 1 \text{ and } a = 2 \dots\dots\dots v_2 &= 0.171 \\ \text{for } b = 1 \text{ and } a = 2.9 \dots\dots\dots v_{2.9} &= 0.222 \end{aligned}$$

Remembering that $K = 4.0$, and therefore $K' = 0.25$, the velocity constants k_1 , k_2 , and $k_{2.9}$, for the three series, are readily computed. For $a = b = 1$, the above expression for k becomes

$$k_1 = \frac{2.3026 v}{t} \log_{10} \frac{2 - x}{2 - 3x},$$

and equally simple expressions are obtained for k_2 and $k_{2.9}$. The numerical results for the three series are given in Table I:

TABLE I.

t (days).	($a=1$), x (obs.).	k_1 .	($a=2$), x (obs.).	k_2 .	($a=2.9$), x (obs.).	$k_{2.9}$.
10	0.087	(0.00099)	0.078	(0.00071)	0.089	(0.00071)
19	0.121	0.00076	0.134	0.00067	0.150	0.00067
41	0.200	0.00064	0.246	0.00063	0.242	0.00054
64	0.250	0.00055	0.314	0.00055	0.300	0.00045
103	0.345	0.00054	0.450	0.00058	0.507	0.00059
137	0.421	0.00058	0.537	0.00059	0.634	0.00064
167	0.474	0.00060	0.618	0.00065	0.691	0.00066
190	0.496	0.00059	0.640	0.00062	0.749	0.00071

Leaving the earliest stage of the reaction out of account, the mean values of the velocity constants for the three series are as follows:

$$\begin{aligned} k_1 &= 0.00061 \\ k_2 &= 0.00061 \\ k_{2.9} &= 0.00061 \end{aligned}$$

That the values of the constants within each series should vary as they do, is not surprising, if one bears in mind that the experiments lasted over seven months, during which the reacting mixtures were abandoned at the "ordinary temperature" of the laboratory. Table I demonstrates the correctness of the mass law equation proposed above.

In order to ascertain the influence of the position of substituted groups upon the velocity of esterification, it was necessary in the first place to exclude differences of composition, and so we decided to study the esterification of three tribromo-benzoic acids, namely, with the bromine atoms in the positions 2,4,6, 2,3,5, and 3,4,5, respectively. Further,

¹ *Ann. chim. phys.* [3], **66**, 94 (1862).

in order to determine what influence bromine atoms may have on the reaction velocity as compared with hydrogen atoms, we studied the esterification of ordinary benzoic acid. Finally, and what is most important of all, in order to test the steric hindrance hypothesis, we studied the esterification velocity of 1,2,4,6-trichloro-benzoic acid. A second communication, published under the name of one of us (W. L. P.), reports the results of further work in this direction and deals with the monoethyl ester of α -nitro-phthalic acid and with acetic, propionic, isobutyric, trimethyl-acetic, monochloro-acetic, dichloro-acetic, and trichloro-acetic acids.

Sec. 5. Tribromo-benzoic Acid 1,2,4-6.

This acid was prepared in considerable quantities by a method similar to that used by Sudborough,¹ Wegscheider,² and others. Ordinary tribromo-aniline is finely powdered, diazotized with hydrochloric acid and sodium nitrite, the solid residue filtered off, and the filtrate treated according to Sandmeyer. After heating the reaction mixture for about eight hours, until the evolution of cyanogen gas has ceased and the solid separating out has settled, the solid is filtered out, dried, and thoroughly extracted with ether. We find that the crude nitrile remaining after evaporating the ether is best purified by dissolving in a moderate quantity of 80 per cent. alcohol and boiling with bone-black. On cooling the filtrate, the nitrile separates out in pure enough condition for further transformation into acid. The nitrile may be saponified by heating with an excess of concentrated hydrochloric acid at 200° to 220°. The reaction, however, refuses to take place unless the hydrochloric acid is very strong. On the other hand, the concentrated hydrochloric acid attacks the tubes at the high temperature of the reaction and these frequently blow out. We have found that strong aqueous hydrobromic acid saponifies the nitrile as well as hydrochloric acid and yields a considerable quantity of organic acid in every case. We are indebted to Professor Marston Taylor Bogert, of Columbia University, for suggesting the use of hydrobromic acid, which has saved us much trouble.

The melting point of our 1,2,4,6-tribromo-benzoic acid is 186°. The following table gives the results of the kinetic study.

TABLE II.

<i>t.</i>	<i>v.</i>	<i>a.</i>	<i>b.</i>	<i>x.</i>	<i>K.</i>	<i>k.</i>
0.833	0.00100	0.001763	0.009914	0.000741	(0.06)	0.091
1.038	0.000817	0.001619	0.008849	0.000904	(0.14)	0.088
1.245	0.000957	0.001892	0.009432	0.001018	(0.14)	0.076
1.459	0.000726	0.001267	0.006587	0.000786	(0.20)	0.098
1.667	0.001343	0.007153	0.001043	0.44	...
2.542	0.001686	0.01036	0.001408	0.40	...
3.000	0.002286	0.008889	0.001577	0.43	...

¹ *Ber.*, 27, 512 (1894).

² *Monatsh. Chem.*, 18, 652 (1897).

In this table, and the tables given further below,

t denotes time in days;

v denotes volume in liters;

a denotes the amount of acid in gram-molecules;

b denotes the amount of alcohol similarly expressed;

x denotes the amount of ester, similarly expressed, formed in the time t .

The data obtained in each of the experiments were introduced into the ordinary static equation of mass action:

$$\frac{x^2}{(a-x)(b-x)} = K.$$

When several consecutive experiments, at considerable intervals of time, gave about the same value of K , the reaction was considered as having attained equilibrium, and that value of K was taken as the equilibrium constant. Its reciprocal, K' , was used in computing the velocity constant by the equation given in the preceding section.

Table II yields the following average values of the constants:

$$\left\{ \begin{array}{l} K = 0.42, \\ k = 0.088. \end{array} \right.$$

Sec. 6. Tribromo-benzoic Acid, 1,3,4,5.

This acid was prepared according to Sudborough's directions.¹ It melted at 235° . One gram of the acid corresponds theoretically to 47.55 cc. of our sodium hydroxide solution. The amount actually required was 47.75 cc.

The esterification was carried out exactly as in the case of the tribromo-benzoic acid 1,2,4,6. The results are given in Table III.

TABLE III.

t .	v .	a .	b .	x .	K .	k .
0.0641	0.00103	0.001399	0.01305	0.000663	(0.05)	0.86
0.1291	0.00133	0.001290	0.01541	0.000866	(0.12)	0.86
0.1428	0.00103	0.001415	0.01147	0.000937	(0.17)	1.01
0.1523	0.00100	0.001385	0.01046	0.000943	(0.21)	0.89
0.1771	...	0.001486	0.01117	0.001111	0.33	..
0.2382	...	0.001479	0.01490	0.001130	0.27	..
0.4097	...	0.001382	0.02204	0.001160	0.29	..

The average value of the constants are thus:

$$\left\{ \begin{array}{l} K = 0.30, \\ k = 0.90. \end{array} \right.$$

Sec. 7. Tribromo-benzoic Acid, 1,2,3,5.

Preparation.—This acid has never been obtained before. We prepared it without difficulty from anthranilic acid by the following method. Ten grams of anthranilic acid are dissolved in about 200 cc. acetic acid and brominated by the gradual addition of a solution of 8 cc. of bromine

¹ *Ber.*, 27, 514 (1894).

in concentrated aqueous potassium bromide. A precipitate of a dibromo-amino-benzoic acid is formed. This precipitate is washed with water, dissolved in sodium carbonate, the solution filtered, and the filtrate re-precipitated with hydrochloric acid. The further steps in this preparation are similar to those employed by Sudborough in the preparation of tribromo-benzoic acid 1,3,4,5. Five grams of the dried precipitate last obtained are dissolved in the minimum of sodium hydroxide, 4 grams of sodium nitrite added, and the solution dropped into concentrated sulphuric acid cooled with ice and vigorously stirred (this is important!). A mixture is now prepared of 10 grams of concentrated sulphuric acid, 20 grams of copper filings, 30 grams of potassium bromide, 10 grams of copper sulphate, and 80 grams of water, and this is boiled in a flask under a reflux condenser to complete decolorization. The diazotized sulphuric acid solution is now added drop by drop, with frequent shaking, to the copper solution and boiled for 15 minutes. On cooling, the precipitate is filtered out and extracted with 95 per cent. alcohol (the dibromo-amino-benzoic acid is insoluble in cold alcohol). The alcoholic solution is precipitated with water and the acid purified by recrystallization from dilute alcohol. The resulting acid is a crystalline yellow substance, soluble in alcohol and ether, insoluble in water, and melting at 193.5° . A bromine determination gave 66.53 per cent. Br.; theory, 66.84 per cent. One gram of the acid corresponds, theoretically, to 47.55 cc. of our sodium hydroxide solution. The amount actually required was 47.75 cc.

Constitution.—To establish the constitution of our tribromo acid, the amino group was eliminated in the brominated anthranilic acid by diazotizing and heating the diazotized solution with alkaline sodium stannite. The solution was acidified with sulphuric acid and extracted with ether. On evaporating the ether and recrystallizing the residue from absolute alcohol, a compound was obtained which melted at 214.5° to 215.5° . The melting points of the dibromo-benzoic acids are given in Beilstein as follows:

- 1,2,3-dibromo-benzoic acid melts at 147° .
- 1,2,4-dibromo-benzoic acid melts at 166.5° or 169° .
- 1,2,5-dibromo-benzoic acid melts at 153° .
- 1,2,6-dibromo-benzoic acid melts at 136° - 137° .
- 1,3,4-dibromo-benzoic acid melts at 232° - 233° .
- 1,3,5-dibromo-benzoic acid melts at 213° - 214° .

The list points clearly to our brominated amino acid being 2-amino-3,5-dibromo-benzoic acid. This conclusion is strengthened by the fact that our brominated amino-benzoic acid melted at 225° , which is identical with the melting point of Hübner's 3,5-dibromo-2-amino-benzoic acid.¹ Hübner prepared his acid by starting with 1,3,5-dinitro-benzoic

¹ *Ann.*, 222, 175 (1884).

acid, changing it to 1,3,5-dibromo-benzoic acid (melting point 213° – 214°), nitrating this, and reducing the nitroxyl to an amino group. Elimination of the two bromine atoms in the resulting acid led to ortho-amino-benzoic acid. Another amino-dibromo-acid, melting at the same temperature as ours (225°), was obtained in Hübner's laboratory by Edgar F. Smith.¹ This acid, however, was derived from 1,3,4-dibromo-benzoic acid (melting point 232° – 234°), while our amino-dibromo-acid yielded, as stated, a dibromo-acid which melted at practically the same temperature as Hübner's dibromo-benzoic acid 1,3,5. These facts demonstrate the constitution of the new tribromo-benzoic acid conclusively. The value of the esterification constant found for the new acid is in harmony with its constitution.

Esterification.—The results of the esterification study are given in Table IV.

TABLE IV.

<i>t.</i>	<i>v.</i>	<i>a.</i>	<i>b.</i>	<i>x.</i>	<i>K.</i>	<i>k.</i>
0.0833	0.000949	0.001359	0.01213	0.000400	(0.014)	0.38
0.1153	0.000860	0.001276	0.01046	0.000442	(0.025)	0.34
0.1278	0.000851	0.001287	0.01106	0.000525	(0.034)	0.39
0.1791	0.001457	0.01004	0.000840	0.120	..
0.4056	0.001545	0.01421	0.000971	0.120	..

The averages of the static and kinetic constants in this case are obviously:

$$\begin{cases} K = 0.12, \\ k = 0.37. \end{cases}$$

Sec. 8. Benzoic Acid.

Having measured the influence of constitution upon the rate of esterification, we considered it important, as stated, to establish the effect of the bromine atoms as such by studying the esterification velocity of unsubstituted benzoic acid under the same conditions under which we had studied the brominated acids. The results are given in Table V.

TABLE V.

<i>t.</i>	<i>v.</i>	<i>a.</i>	<i>b.</i>	<i>x.</i>	<i>K.</i>	<i>k.</i>
0.0833	0.001340	0.004505	0.01362	0.001627	(0.077)	0.61
0.0979	0.001400	0.004477	0.01404	0.001766	(0.094)	0.60
0.1387	0.001237	0.004453	0.01287	0.002135	(0.18)	0.62
0.1530	0.001116	0.004293	0.01068	0.002106	(0.24)	0.69
0.2260	0.001606	0.005069	0.01657	0.002959	(0.31)	0.64
0.3750	0.004346	0.02055	0.003079	0.43	..
0.4380	0.004711	0.02011	0.003154	0.38	..

For benzoic acid and ethyl alcohol at 183° the mean values of the constants are thus:

$$\begin{cases} K = 0.40, \\ k = 0.63. \end{cases}$$

¹ *Ann.*, **222**, 189 (1884).

Sec. 9. Trichloro-benzoic Acid, 1,2,4,6.

This acid was prepared according to the directions of Victor Meyer,¹ except that the saponification of the trichloro-benzonitrile was effected by means of strong hydrobromic instead of hydrochloric acid. Our acid melted at 160°, which is identical with the melting point given by Victor Meyer. A chlorine determination gave 47.29 per cent. Cl; theory, 47.19 per cent. The results of the esterification study are given in Table VI.

TABLE VI.

<i>t.</i>	<i>v.</i>	<i>a.</i>	<i>h.</i>	<i>x.</i>	<i>K.</i>	<i>k.</i>
0.833	0.000941	0.001467	0.01140	0.000380	(0.012)	0.032
1.042	0.001106	0.001349	0.01462	0.000405	(0.012)	0.027
1.25	0.001364	0.001536	0.01865	0.000527	(0.015)	0.034
1.473	0.001000	0.001349	0.01320	0.000588	(0.036)	0.026
1.875	0.000825	0.001257	0.01056	0.000591	(0.033)	0.034
3.432	0.001244	0.01214	0.000760	0.105	...
4.523	0.001162	0.01608	0.000781	0.105	...

The mean values of the static and kinetic constants in this case are:

$$\begin{cases} K = 0.105, \\ k = 0.031. \end{cases}$$

Sec. 10. Summary and Conclusions.

The following table reproduces the several constants given in the preceding sections:

TABLE VII.

Acid.	Equilibrium constant <i>K.</i>	Velocity constant <i>k.</i>
Acetic.....	4.0	0.00061 (room temp.)
Trichloro-benzoic 1,2,4,6.....	0.105	0.031
Tribromo-benzoic 1,2,4,6.....	0.42	0.088
Tribromo-benzoic 1,2,3,5.....	0.12	0.37
Tribromo-benzoic 1,3,4,5.....	0.30	0.90
Benzoic.....	0.40	0.63

In the first place, the table reveals nothing singular about the equilibrium constants of diortho-substituted acids. Thus, the constant for 1,2,4,6-tribromo-benzoic acid, far from being zero, has about the same value as that for benzoic acid itself, and is much greater than the corresponding constants for the other two tribromo-acids. The Victor Meyer Law, as usually formulated, conveys the idea that diortho-substituted aromatic acids cannot, under ordinary conditions, be esterified at all, or can only be esterified to a slight extent. Our first column of constants shows clearly that this idea is false. Diortho-substituted acids can be esterified, by heating with alcohol, to a greater extent than many an acid constituted otherwise, and by employing a large excess of alcohol it is possible to render the esterification practically quantitative (just as in the case of other acids).

¹ *Ber.*, 27, 351 (1894).

The velocity constant of the 1,2,4,6-tribromo-benzoic acid is about one-fourth that of the 1,2,3,5-acid and only about one-tenth that of the 1,3,4,5-acid. The three constants in question express numerically the nature of the phenomena observed by Victor Meyer and explain the practical possibility of isolating diortho-substituted from other acids by esterification. On the other hand, 0.088, the velocity constant of 1,2,4,6-tribromo-benzoic acid at 183°, is about one hundred and fifty times as great as 0.00061, the velocity constant of acetic acid at ordinary temperatures. Yet no one would declare that acetic acid cannot be esterified at ordinary temperatures and invent stereochemical hindrance hypotheses explaining why this should be so.

The steric hindrance hypothesis is invalidated by the fact that the velocity constant of the diortho-substituted trichloro-benzoic acid, instead of being greater, is much smaller than that of the corresponding tribromo-acid. True, the velocity constants yielded by our esterification experiments cry for theoretical explanation (as do the velocity constants of chemical reactions in general). It is clear, however, that the alluring steric hindrance hypothesis of Victor Meyer fails to furnish such an explanation.

In conclusion, the subjects dealt with in this communication may be summarized as follows:

1. It is shown that diortho-substituted aromatic acids, which are generally assumed to be unesterifiable, can be esterified *quantitatively*, at higher temperatures or even (by prolonged warming) at the temperature of the water bath. The Esterification Law assumes the following form: *Aromatic acids with one or both positions next to the carboxyl occupied by substituting groups, combine with alcohols more slowly, though to no less extent, than acids otherwise constituted.*

2. The law of mass action is put in a form which permits of keeping account of the volume of reacting mixtures and will eliminate many a misinterpretation in chemical kinetics.

3. Finally, we give the results of a careful dynamic study of an important set of aromatic acids. The set includes the 1,2,3,5-tribromo-benzoic acid, which has not been obtained before, and whose constitution is here demonstrated. Our dynamic study proves that Victor Meyer's hypothesis of steric hindrance is untenable and thus, for the present, reduces the Esterification Law to the rank of an empirical rule of no theoretical and limited practical value.¹

CLARK UNIVERSITY,
WORCESTER, MASS., JUNE, 1908.

¹ In the following communication the practical applications of the Esterification Law are extended to mono-ortho-substituted acids, which are of course much more commonly met with in laboratory practice than the diortho-acids. Further work concerning the steric hindrance hypothesis is in progress in these Laboratories and will be published in due time.