LACTIC ACID
and
ITS ANHYDRIDES

By

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Part I.

Method of Analysis and Equilibria Involved.

LACTIC ACID and ITS ANHYDRIDES.

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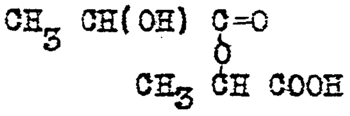
(I) Introduction.

Lactic acid as it appears upon the market is usually prepared by fermenting a solution of glucose made alkaline with milk of lime. Although the fermentation does not take place in a solution containing over two per-cent acid, a fifteen per-cent solution goes almost to completion in this way, as the excess of acid is precipitated as the calcium salt and separates. When fermentation is complete the solution is concentrated, the calcium lactate filtered off, and the free acid obtained by decomposition with sulphuric acid. The acid thus obtained is pure enough for most commercial purposes and is sold usually as 25 or 50% acid. Lactic acid of the U. S. and British pharmacopoeia is prepared by concentrating this acid to a sp. gr. of 1.2 after certain purifications. It is supposed to have an acid content of 75% in addition to 8% of anhydrides. The acid is usually sold on the basis of its free acid content as its chief uses are the reduction of chromium compounds used as mordants in dyeing and chrome tanning, and as a delimer in tanning where its value is due to its ability to keep calcium salts in solution and thus prevent harmful precipitation. Most dealers hold that the anhydrides are of no value for this purpose, however, T. A. Faust (vol. 10, 1915 Jour. Amer. Lea. Ass'n) shows that they are at least partially in error.

Lactic acid is a syrupy, almost colorless, bitter liquid miscible with water and alcohol in all proportions. On being heated in air it loses water and according to Thompson and Suzuki (vol. 13, 1918 Jour. Amer. Lea. Ass'n) is capable of forming three anhydrides, the first two only appearing in commercial acid.

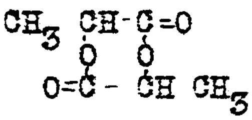
1.



$$\begin{array}{lll} CH_3 & CH(OH) & C{=}O \\ & & \;\,| \\ & & \;\,O \\ & & \;\,| \\ & CH_3 & CH\ COOH \end{array}$$

(anhydride)

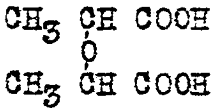
2.



$$\begin{array}{llll} & CH_3 & CH - & C{=}O \\ & & \;\;| & \;| \\ & & \;\;O & \;O \\ & & \;\;| & \;| \\ O{=} & C & - CH & CH_3 \end{array}$$

(lactide)

3.



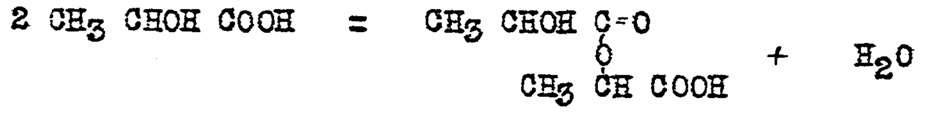
$$\begin{array}{ll} CH_3 & CH\ COOH \\ & \;| \\ & \;O \\ & \;| \\ CH_3 & CH\ COOH \end{array}$$

(di-lactic acid)

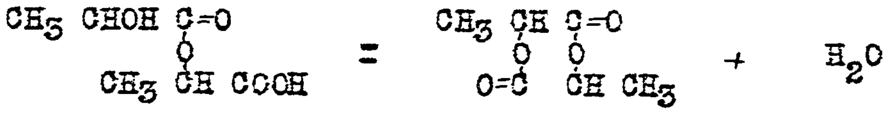
The literature contains many conflicting statements concerning these substances. Wislicenus (Ann. 164-181) says the anhydride is obtained by heating lactic acid to 130 C. in a current of dry air, and describes it as a light yellow, amorphous body only slightly soluble in water but very soluble in alcohol or ether. Monin (Abs. V 445) says the acid contains no anhydride which is only a laboratory product. Neither gives the experimental data upon which his statement is based. The lactide is usually described as a white crystalline body almost insoluble in water but fairly soluble in alcohol, ether, or acetone, however, one investigator refers to the brown, amorphous body above as lactide. Statements vary concerning the conditions under which these substances are formed from lactic acid. Pure (100%) lactic acid has been shown to remain unchanged and crystalline for months below 18 C. Partial conversion to anhydrides takes place when the acid is allowed to stand at a higher temperature. The commercial acid is said to form largely anhydride when heated at 130-140 C. which is subsequently converted to the lactide up to 200 C. where decomposition to form carbon dioxide and lactone sets in. Both anhydride and lactide are formed when commercial acid is allowed to stand over sulphuric acid at room temperature. In all cases partial anhydride formation occurs when lactic acid is concentrated by evaporation, and Wislicenus points out that lactide is formed while free acid is still present.

Hydrolysis of both anhydride and lactide with formation of lactic acid occurs when either substance is heated with water, or treated with alkali or acid. Besson says that the anhydrides are hydrolyzed by an excess of alkali in ten minutes, and thus are valuable as delimers.

All of the above statements seem to indicate that the reactions by which anhydride and lactide are formed are reversible, and that a condition of equilibrium exists between the three substances in solution. Wislicenus states that he believed this to be the case but attempted no experimental proof. The following equations probably express the equilibria involved.



$$2\ CH_3\ CHOH\ COOH \quad = \quad \begin{array}{r} CH_3\ CHOH\ \overset{}{C}{=}O \\ O\phantom{{=}O} \\ CH_3\ CH\ COOH \end{array} \quad + \quad H_2O \qquad (1)$$



$$\begin{array}{l} CH_3\,CHOH\,C{=}O \\ \qquad\quad\;\; O \\ \qquad CH_3\,CH\,COOH \end{array} = \begin{array}{l} CH_3\,CH\,C{=}O \\ \qquad\; O\quad O \\ O{=}C\quad CH\,CH_3 \end{array} + H_2O \qquad (2)$$

Preliminary experiments soon demonstrated the existence of a condition of equilibrium, for upon heating lactic acid of different concentrations in small sealed tubes at 140-160 C., the concentration of free acid (see below) came rapidly to a definite value which was unaltered by further heating, and the same value could be obtained from mixtures whose original composition varied considerably.

Attempts were then made to devise a method of analysis by which the concentration of the four constituents could be determined. This proved a very different problem.

The accepted method of analysis of commercial lactic acid (Allen Commercial Organic Analysis; Jour. Amer. Lea. Ass'n 10, (1915)) consists in (1) titrating a sample with 0.1 N. NaOH, using phenolphthalein as indicator; (2) adding an excess of standard alkali, and heating on a steam bath for fifteen minutes; (3) adding a slight excess of 0.1 N. sulphuric acid, and titrating the excess of acid. The first titration neutralizes the lactic acid present as such and also the free acid hydrogen of the anhydride (if present). The alkali used up in the second titration corresponds to hydrolysis of the anhydride salt and of lactide (if present). From these two titrations the amounts of all three constituents can not be obtained. Ordinarily the alkali consumed in the first titration is said to measure the "free acid", and lactic acid is sold on this basis. It is obvious that if the amounts of lactic acid, anhydride, and lactide in a given sample are represented by X, Y, and Z, respectively, and if (a) and (b) represent the 0.1 N. NaOH consumed in the first and second titrations respectively, we have the following relations. (1.0 cc of 0.1 N. NaOH is equivalent to .009 grs. lactic acid; .0162 grs. anhydride; .0072 grs. lactide (hydrolyzed)).

$$a = \frac{X}{.009} + \frac{Y}{.0162} \qquad (3)$$

$$b = \frac{Y}{.0162} + \frac{Z}{.0072} \qquad (4)$$

If we assume either Y or Z to be zero (as is usually done) or determine either X, Y, or Z separately (see below), these two equations suffice to permit the calculation of each constituent.

(II) Experimental.

The experiments described below represent efforts to determine by a separate method some one of the three constituents. After searching the literature no previous work on methods of ditinguishing between the anhydride and lactide was found to be available.

(a) Method of analysis.

(1) It was thought that probably by the use of different indicators two different end points might be determined corresponding to the free acid and anhydride, respectively, but it was found to be the same in all cases.

(2) Titrations were made at 25 C. making use of the electrical conductivity method. Curves drawn by plotting alkali concentrations against conductivity values showed only one break, corresponding to the end point obtained in (1).

(3) Nearly all salts of lactic acid are supposedly insoluble in ether. It was thought that probably the anhydride salt would be insoluble in certain ether-alcohol mixtures. Titrations were made with alcoholic sodium hydroxide in absolute alcohol solution and ether ranging from an equal amount to four times the amount of alcohol added. Although fairly concordant results were obtained the method was abandoned as impracticable, because instead of a crystalline precipitate a semi- solid mass, which could not be filtered off but had to be run off thru a separatory funnel, was found to separate from the solution.

(4) Lactic acid was found to be practically insoluble in chloroform while lactide was very soluble. It was attempted to extract the lactide from a water solution with chloroform. Results were variable and not reliable, probably due to the influence of the free acid present. This was found also to be the case even though the acid was neutralized first. Similar experiments with benzene and toluene proved unsuccessful for the same reason.

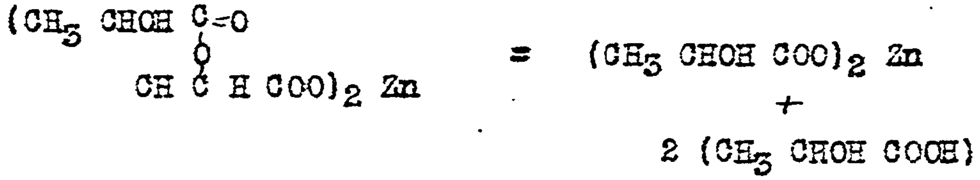
(5) Several salts of lactic acid are recorded as being insoluble in absolute alcohol at room temperature. The magnesium salt is one and it was attempted to precipitate the acid with magnesium acetate. The reaction was slow and

incomplete. After experimenting with the acetates and carbonates of several metals, it was found that zinc carbonate reacted readily with lactic acid in alcoholic solution, and apparently with the anhydride, forming insoluble salts, and leaving the lactide in solution. Evidence of the presence of the anhydride salt was given by the fact that an examination of the precipitate showed the presence of material using up alkali on hydrolysis. (The zinc present was first gotten rid of by the method given below.) This reaction was adapted to the quantitative determination as follows.

The sample for analysis was dissolved in absolute alcohol and a portion corresponding to about one gram of acid was at once titrated with 0.3 N. NaOH, using phenolphthalein as indicator, (titration "a"). An excess of alkali was then added, the solution was heated on the steam bath for fifteen minutes, and the excess alkali determined by titration with standard acid, (alkali used, titration "b"). It was found that it was not necessary to include step (3) given in the procedure above. A second portion of the alcoholic solution, equal to that above, was then treated with two grams of zinc carbonate, and was warmed, with stirring, until flocculent zinc lactate began to separate. (usually about five minutes) The precipitate was filtered off under suction, and washed with absolute alcohol. The filtrate was evapopated to about 10 cc and again filtered if further precipitation occured. 20 cc of water was added, and the solution washeated with an excess of standard alkali (to hydrolyze the lactide). Anexcess of standard acid was then added, together with a little potassium ferrocyanide, and the excess of acid determined by titration with standard alkali, (titration "c"). The following notes explain the procedure.

(1) Treatment of the alcoholic solution with zinc carbonate as indicated above gives a filtrate which is neutral (after the small amount of zinc in solution has been precipitated as ferrocyanide), showing that both the free acid and anhydride have been neutralized. Since the lactide is quite soluble in alcohol it must all be present in the filtrate, unless it has been hydrolyzed by the zinc carbonate. Such hydrolysis can hardly have occured to any appreciable extent, since duplicate determinations which had been heated for varying lengths of time gave closely agreeing results, which could hardly be expected if partial hydrolysis were occuring. Determinations allowed to stand at room temperature for 30 minutes also gave closely agreeing results, which would seem to indicate that hydrolysis was not occuring.

(2) A small amount of zinc remains in solution after the zinc carbonate treatment. Most of this separates later on evaporation of the solution. The zinc is apparently present as lactide, as it is found to be neutral and not to use up alkali on heating with an excess of sodium hydroxide and then titrating back with acid. It also separates almost completely on evaporation of the solution in the cold by a stream of dry air, without causing the remaining solution to become acid, as would be the case if it were the anhydride salt.



$$\begin{array}{l}(\mathrm{CH_3\ CHOH\ C{=}O}\\ \qquad\qquad\qquad\ \mathrm{O}\\ \qquad\qquad \mathrm{CH\ C\ H\ COO)_2\ Zn}\end{array} = \begin{array}{c}(\mathrm{CH_3\ CHOH\ COO})_2\ \mathrm{Zn}\\ +\\ 2\ (\mathrm{CH_3\ CHOH\ COOH})\end{array}$$

Thus, its presence does not introduce an error into the lactide determination. It is necessary, however, to remove it from solution,as it interferes with the end point, and the potassium ferrocyanide effects this result. The presence of this zinc has been somewhat difficult to account for. Zinc lactate is only slightly soluble in alcohol, yet in the experiment a fair amount of zinc lactate separates from the alcoholic solution on evaporation. The amount present increases steadily as the lactide content increases. The presence of this zinc at first threw some doubt on the accuracy of the experiment, as it was felt that it might perhaps be present as the salt of the anhydride, and that it was being hydrolyzed with the formation of zinc lactate, thus causing the precipitation during evaporation. In view of the fact that the filtrate did not show acidity and the following experiment, it seems certain that no appreciable amount of the anhydride salt is present in the filtrate.

Vrey concentrated mixtures, prepared by heating commercial acid in a current of dry air at 130 C., gave no precipitate when treated with zinc carbonate but a very large amount of zinc lactate was obtained on evaporating the solution. Even on adding relatively large amounts (0.5 gr. acid to 1.0 gr. mixture) of commercial acid to such solutions, the entire amount of zinc lactate formed was found to go into solution.

It seems possible that this is in colloidal suspension, and that it is peptized by the lactide, thus accounting for the increasingly large amounts held up as the percentage of lactide increases. In any case there seems every reason to believe that analysis of the alcholic filtrate measures the lactide fairly accurately, and thus combination of this value with the results of the two usual titrations, as described above, permits the calculation of the concentrations of all three constituents.

In some experiments mixtures of alchohol and chloroform (25%) were used as solvent instead of pure alcohol, but while less zinc appeared in the filtrate in this case, the results were not as easily duplicated as in the above method, although they gave approximately the same values. These results are given in table 2(a).

(b) Equilibrium Experiments.

A series of experiments were carried out to determine the composition of the equilibrium mixtures. To this end small glass tubes containing about five grams of acid were nearly filled, sealed, and heated for a number (9 to 25) of hours at 155 C. (Preliminary experiments by E. R. Hopkins had shown that temperature has very little effect upon the equilibrium.) These tubes were then cooled and broken, and their contents dissolved in absolute alcohol, the solution being then diluted with alcohol to a definite volume, and aliquot portions taken for analysis as indicated above. Results are given in Table I.

The original mixtures were made by mixing commercial acid, highly concentrated acid, pure lactide, and water in such proportions as to give a variety of concentrations, and to approach the equilibrium from both sides.

Experiments were also carried out in which acids of two concentrations were heated at 155 and 100 C. over a period of two weeks, portions being analyzed at intervals of one or two days. No appreciable change occured after the first day, so only a mean of the analyses are given. A slight decomposition took place in the tubes heated at 155 C. and some of them burst after several days heating. Results are given in Table 2(a).

(c) Dialysis Experiments.

For reasons to be discussed in the following section, the anhydride is thought to probably be present in colloidal suspension and experiments were attempted to prove this point. Parchment cups of materials of different porosity were made, partially filled with the mixtures, and placed in a bath of running water. Portions were pipetted off and analyzed at intervals. Mixtures of several concentrations were used, including a very concentrated one prepared by heating commercial acid to 130 C. If anhydride is present as a colloid, after sufficient time, disregarding hydrolysis, it alone should remain in the cup and titrations (a) and (b) should become equal. It was found that titration (b) finally became larger than (a) although both decreased rapidly. This will be discussed more fully below.

Table I.

Experimental Data.

No.	Titration (a) cc N/10 NaOH per gr.	Titration (b) cc N/10 NaOH per gr.	Titration (c) cc N/10 NaOH per gr.	per cent free lactic acid	per cent anhydride	per cent lactide	per cent water	Mols acid per 100 grs.	Mols anhydride per 100 grs.	Mols lactide per 100 grs.	Mols water per 100 grs.
1	74.34	10.39	6.14	63.14	6.88	4.43	25.55	0.7016	0.0424	0.0308	1.418
2	78.44	16.20	10.14	65.15	9.83	7.30	17.72	0.7240	0.0606	0.0507	0.485
3	75.44	10.85	7.63	65.05	5.20	5.50	24.25	0.7228	0.0321	0.0382	1.348
4	76.53	10.08	7.67	66.76	3.91	5.52	23.81	0.7418	0.0241	0.0383	1.323
5	75.14	9.36	7.48	65.98	3.05	5.39	25.58	0.7331	0.0188	0.03743	1.421
6	61.63	3.77	2.64	54.49	1.83	1.90	41.78	0.6054	0.0113	0.01319	2.321
7	79.19	24.04	21.97	69.47	3.35	15.83	11.35	0.7397	0.0206	0.110	0.6305
8	35.71	0.63	0.13	22.70	0.82	0.09	76.39	0.2522	0.0051	0.000625	4.244
9	----	----	----	62.13	2.46	3.16	32.25	0.6903	0.0152	0.02195	1.7918

Experimental Data.

Table 2(a).

No.	Titration (a) cc N/10 NaOH per gram.	Titration (b) cc N/10 NaOH per gram.	Titration (c) cc N/10 NaOH per gr.	per cent free acid.	per cent anhydride.	per cent lactide.	per cent water.	Mol fraction acid.	Mol fraction lactide.	Mol fraction water.	K_2 (lactide)	Temp. C.
1(a)	80.30	18.46	0	72.32	0	13.30	14.38	.474	.0545	.471	.0538	100 C.
1(b)	80.30	17.96	.84	71.57	1.36	12.33	14.74	.466	.0502	.478	.0528	155C.
2(a)	79.96	21.10	.43	71.63	.70	14.89	12.78	.494	.0341	.440	.0509	100 C.
2(b)	79.66	21.00	2.01	69.94	5.26	13.69	13.11	.480	.0588	.449	.0514	155 C.

Table 2(b).

No.	per cent acid	per cent anhydride	per cent lactide	per cent water	K_1 (anhydride)	K_2 (lactide)
1	63.71	5.55	3.92	26.82	.1017	.0535
2	62.64	7.82	3.64	25.90	.1432	.0488
3	66.04	6.54	6.50	20.92	.0870	.0635
4	65.69	6.64	18.85	8.82	.0474	.0424

(III) Treatment of Results.

Although the experimental data in Table I indicate clearly that a condition of equilibrium exists between lactic acid, its anhydrides, and water, a mathematical analysis of the conditions prevailing at equilibrium presents certain difficulties. In the first place the analytical results are not of the highest accuracy, at best, and in the second place in so concentrated a system some difficulty is to be expected in representing the activity of the components in terms of the composition of the mixture.

As the most likely assumption the activity was taken as proportional to the mol fraction, and equilibrium constants were then calculated from the data of Table I, expressing the relation between the acid, anhydride, and water, and between the acid, lactide, and water according to the equations:

$$K_1 = \frac{\text{mols anhydride x mols water}}{\text{mols}^2 \text{ acid}} \qquad (5)$$

$$K_2 = \frac{\text{mols lactide x mols}^2 \text{ water}}{\text{mols}^2 \text{ acid x total mols}} \qquad (6)$$

These results are given in the second and third columns of Table I.

The values for K_1 do not show any approach to constancy, and determinations which should be nearly duplicates exhibit an extremely wide variation. On the other hand the values for K_2 show a fair constancy and exhibit no definite trend. This suggests the possibility that the anhydride is not present in true solution, but as a colloid, and therefore not occuring in any definite amount. The properties assigned to the pure anhydride lend support to this idea. Thus, whereas lactic acid and the lactide are crystalline bodies of definite properties, the anhydride is described as a "gummy" amorphous material. If the anhydride is in colloidal suspension it should not affect the equilibrium between the components of the homogenous phase, and the data of Table I were therefore recalculated on this basis. The mol fractions of acid, lactide, and water were calculated, neglecting the anhydride present, and values for the equilibrium constant were calculated from them. The results, which are given in Table 3 as K_3, show a much greater constancy than those calculated on the assumption that the anhydride is present as a constituent of the equilibrium mixture. In order to show how closely the data agree with the equilibrium expression, the following calculations were made. Taking the mean value for K_3 as 0.0567 (the mean of the K_3 values in all the tables), we have

$$\frac{\text{mol frac. lactide x mol frac}^2\text{ water}}{\text{mol frac.}^2\text{ acid}} = 0.0567 \qquad (7)$$

and

$$\text{mol frac. lactide} + \text{mol frac. acid} + \text{mol frac. water} = 1.0 \qquad (8)$$

If we assume values for the mol fraction of water between 0.1 and 0.9, we can, by combining equations (7) and (8), calculate the mol fractions of acid and lactide, respectively. These results are plotted in figure III. Experimental values are

Table 3.

Equilibrium Constants.

			Mol Fractions neglecting anhydride.			
	K_1	K2	Acid	Lactide	Water	K_3
1	0.122	0.0573	0.3263	0.01433	0.6594	0.0585
2	0.114	0.0515	0.4114	0.02881	0.560	0.0554
3	0.083	0.0605	0.3426	0.01810	0.639	0.0613
4	0.0579	0.0573	0.3527	0.01823	0.639	0.0579
5	0.0498	0.0635	0.3347	0.01708	0.648	0.0642
6	0.0715	0.0656	0.2060	0.00419	0.790	0.0659
7	0.0219	0.0477	0.4998	0.07432	0.426	0.0559
8	0.338	0.0410	0.05604	0.000139	0.939	0.0410
9	0.0570	0.0588	0.2757	0.00877	0.715	0.0589

indicated by x's and their relation to the theoretical values will be discussed.

These results indicate quite clearly that as far as the free acid, the lactide, and water are concerned, a definite equilibrium exists between them at 155 C., which is expressed fairly accurately by equation (7) above. Data, given in Table 2(a), from later experiments on more concentrated mixtures show on an average a lower anhydride value and give a slightly lower K value. As indicated above, the values of K can hardly be expected to be constant over the whole range, and, although it shows a tendency to gradually decrease as concentration increases, it does not vary enough to cause a very appreciable difference in the results by taking as the true value a mean of all the values. Thus, the value 0.0567, as used in equation (7) above, was taken as the most probable value of K, and is well within the experimental error.

Data on experiments at 100 C. agree with those at 155 C. within the range of accuracy of experiment, so, although indicated as such in the table, they are plotted with the 155 C. values.

Table 4 gives data on a series of mixtures listed in order of increasing amount of lactide. The K values are calculated on the basis of titration (b) being used in the hydrolysis of lactide alone, assuming no anhydride present. The fact that the K values show a definite trend is of interest and will be discussed. Precentages of acid and lactide are plotted against total cc's (titrations (a) and (b)) of 0.1 N.

Table 4.

Experimental Data.

No.	Titration (a) cc N/10 NaOH per gr.	Titration (b) cc N/10 NaOH per gr.	Titrations (a)-(b) total cc N/10 NaOH per gr.	Per cent lactide	Per cent acid	K (no anhydride)	K_3 (neglecting anhydride)
1	25.70	..63	26.33	.45	23.15	.1902	.0410
2	45.61	1.57	47.18	1.14	41.08	.106	---
3	61.63	3.78	65.41	2.72	55.51	.0876	.0639
4	67.04	4.84	71.88	3.49	60.39	.0807	.0564
5	75.15	9.36	84.51	6.74	67.69	.0753	.0642
6	78.41	16.19	94.60	11.67	70.63	.0688	.0534
7	79.22	18.22	97.44	13.13	71.36	.0538	.0538
8	78.90	20.83	99.73	15.01	71.06	.0513	.0509
9	79.19	24.03	103.22	17.32	71.30	.0493	.0539
10	77.04	30.74	107.78	22.15	69.39	.0409	.0429
11	63.06	55.92	118.98	40.29	56.80	.0169	---

NaOH per gram of mixture. In preparing this table one or two mixtures that had apparently not reached equilibrium were not included.

For reference, the experimental results have been plotted in Figures I and II as percentages of free acid and lactide present at equilibrium with different waterconcentrations.

(IV) Discussion of Results.

As stated above these results indicate quite clearly that a definite equilibrium exists between free acid, lactide and water, and that it is not appreciably affected by temperature. On the whole the more concentrated mixtures give lactide values corresponding to a somewhat lower average K value than the dilute mixtures. The assumption that K should be constant over the whole range of concentrations may probably be in error, and K is actually lower at high concentrations than at low, as indicated by experimental results. Hydrolysis may be greater in the more concentrated mixtures and thus cause high acid values, however, this does not seem to play much part, as analyses in chloroform at room temperature show no great deviation from those in alcohol, although it should certainly be expected to be cut down if occuring. Probably a mean curve, holding more closely at lower and higher concentrations to theoretical curves plotted from means of the corresponding K values, would come~~s~~ nearer expressing the true values than the theoretical curve as drawn. This would certainly more nearly conform to experimental results.

It is interesting to note that commercial acid which has been standing for several months shows a K value very close to those above.

The behavior of the anhydride presents something of a puzzle, and several interesting things are to be noted from experiment.

(1) It is apparent from the data in Table I that the amountdoes not increase regularly as the water content decreases, and also that it may vary considerably with an identical water content.

(2) The amount in concentrated mixtures does not exceed and often is less than that in commercial acid.

(3) The amount at equilibrium must be largely determined by the previous history of the sample, however, the extent of its formation seems to be limited.

(4) Concentrated mixtures, prepared by heating commercial acid at 130 C. in a current of dry air, show only a small amount of anhydride, seldom over 4 or 5% and more often less.

The fact, that the amount of anhydride present does not follow any definite law but seems to be determined by the previous history of the sample, supports the assumption that it is present as a colloid. The experiments on concentrated mixtures were heated for a much longer period than the more dilute ones, thus probably accounting for the somewhat lower anhydride content. Mixtures heated at 100 C. show a slightly lower average anhydride content than those heated at 155 C. High temperature may cause such an increase, but, if so, it is not pronounced enough to say that this is the case. Above certain concentrations the anhydride seems to be unstable, for under no conditions was it possible to obtain a mixture containing more than a few per cent. The physical properties of the most concentrated mixtures studied seem to support this view. The anhydride is described as a gummy, semi-solid mass insoluble in water, so that, if it were present in any appreciable quantity, we would expect such a concentrated mixture to be almost solid. On the contrary, it was a fairly mobile solution even at room temperature and to a large extent soluble in cold water. This seems to indicate that the so called anhydride, obtained by heating lactic acid at 130 C. in a current of dry air, is rather aconcentrated solution of lactide in acid, and that increasing the temperature merely continues the same process of lactide formation instead of causing a conversion of anhydride to lactide, or that the anhydride is an unstable intermediate product. As pointed out above, Monin believed the former to be the case.

In spite of the above indications, dialysis experiments, attempting to prove the presence of a colloid, were unsuccessful. If a colloid were present, the mixture being dialyzed should become increasingly richer in colloid and the ratio of titration (a) to titration (b) should become unity. It was found that this ratio did decrease until it became unity, but, on continued hydrolysis, it proceeded steadily to a much smaller value until the solution became neutral. This indicates that the lactide diffuses much more slowly than the acid, a phenomenon to be expected, but it neither proves nor disproves the presence of a colloid. The process takes several days to go to completion, and it may be that hydrolysis of the anhydride occurs sufficiently rapidly to account for its disappearance even if it were present as acolloid. The actual concentration decreases fairly rapidly at first, and, as hydrolysis is found to be very slow in water solution, the experimental data again would indicate that the anhydride value is comparatively low in all cases.

It is a rather significant fact that the value of K decreases steadily as the lactide value (calculated on the basis of no anhydride) increases. Let us consider this in light of some of the things discussed above.

(1) As has been pointed out, such concentrated mixtures would hardly be expected to obey the mass law strictly over so wide a range, and if such is the case, it would be expected to cause a steady trend of the K values in one or another direction.

(2) A small, fairly constant amount of anhydride (and such seems to be the case) would have a similar effect. This is seen if we consider the mass law expression

$$K = \frac{\text{mols lactide x mols}^2 \text{ water}}{\text{mols}^2 \text{ acid x total mols}}$$

At low concentrations a small amount of anhydride would have very little effect on the water or acid values but would increase the lactide value (being small), comparatively, very considerably, and thus cause an increase in K. At high concentrations an equal amount of anhydride would have very little effect on the values of the lactide and acid, whereas, it would cause a comparatively large decrease in the water value and accordingly a decrease in the value of K.

(3) Suppose it is assumed, as was suggested above, that the anhydride salt splits into a molecule of lactate and a molecule of free acid which in turn passes into lactate in the first titration. This would not affect the lactide and water values but cause a constant increase in the acid value, which would, as the acid decreases, become comparatively larger. This means that the denominator is larger by a constant value, which thus has an increasingly greater effect on K as the mixture becomes more dilute. Accordingly, the downward trend of K should be in the opposite direction.

(4) If it is assumed that two molecules of the anhydride salt hydrolyze~~s~~ to two molecules of lactate and a molecule of lactide, the effect is opposite to that in (3) and explains the trend of K. However, such a change seems very unlikely.

Probably the best explanation of this gradual decrease in the value of K with the increase in concentration is that it is due to the combined effects of (1) and (2), likely augmented by an increase in the hydrolysis as the concentration of lactide increases. At any rate, the anhydride being small, acid and lactide values calculated on the basis of no anhydride being present are not greately in error with the experimental data, and probably are within one or two per cent of the actual values. For this reason the percentages of lactide and free acid, on this basis, have been plotted against total cc's 0.1 N. NaOH to neutralize one gram of material (figure IV). This should be useful in obtaining a close approximation to the equilibrium values by one titration. The data cover practically the whole range.

Summary.

(1) A method of analysis has been devised for determining all four constituents of mixtures of lactic acid, lactic anhydride, lactide, and water.

(2) This method has been applied to the analysis of mixtures of these constituents heated for some time at 155 and 100 C.

(3) The results indicate that a definite and calculable equilibrium condition exists between the lactic acid, lactide, and water.

(4) Temperature has been shown to have no appreciable effect upon the equilibrium.

(5) The anhydride is always present in relatively small amounts. There are indications that it is present in the colloidal state, however, attempts at experimental proof have been unsuccessful.

(6) Regularity in the variation of K, assuming no anhydride present, has been pointed out and possible reasons discussed.

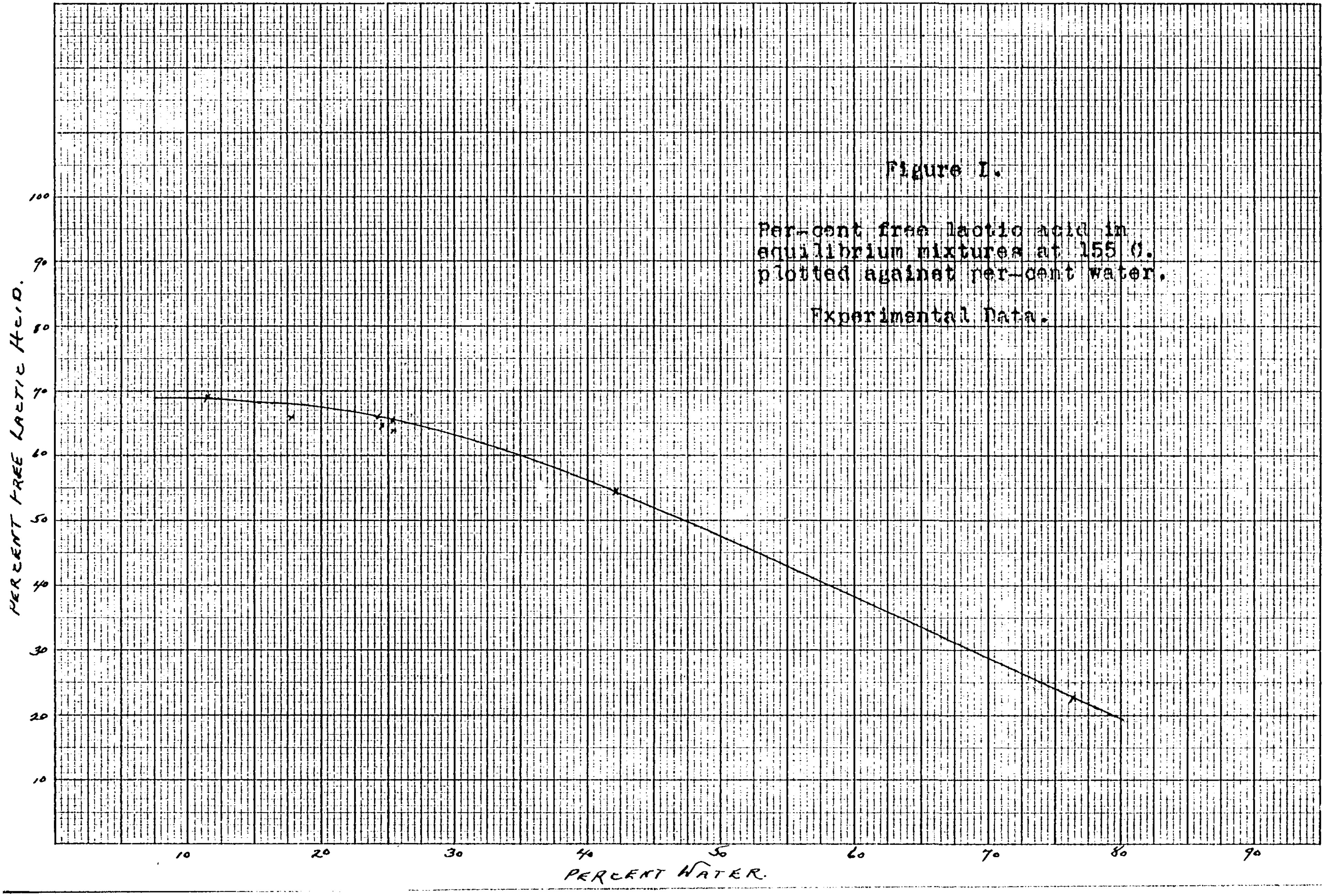


Figure I.

Per-cent free lactic acid in equilibrium mixtures at 155 C. plotted against per-cent water.

Experimental Data.

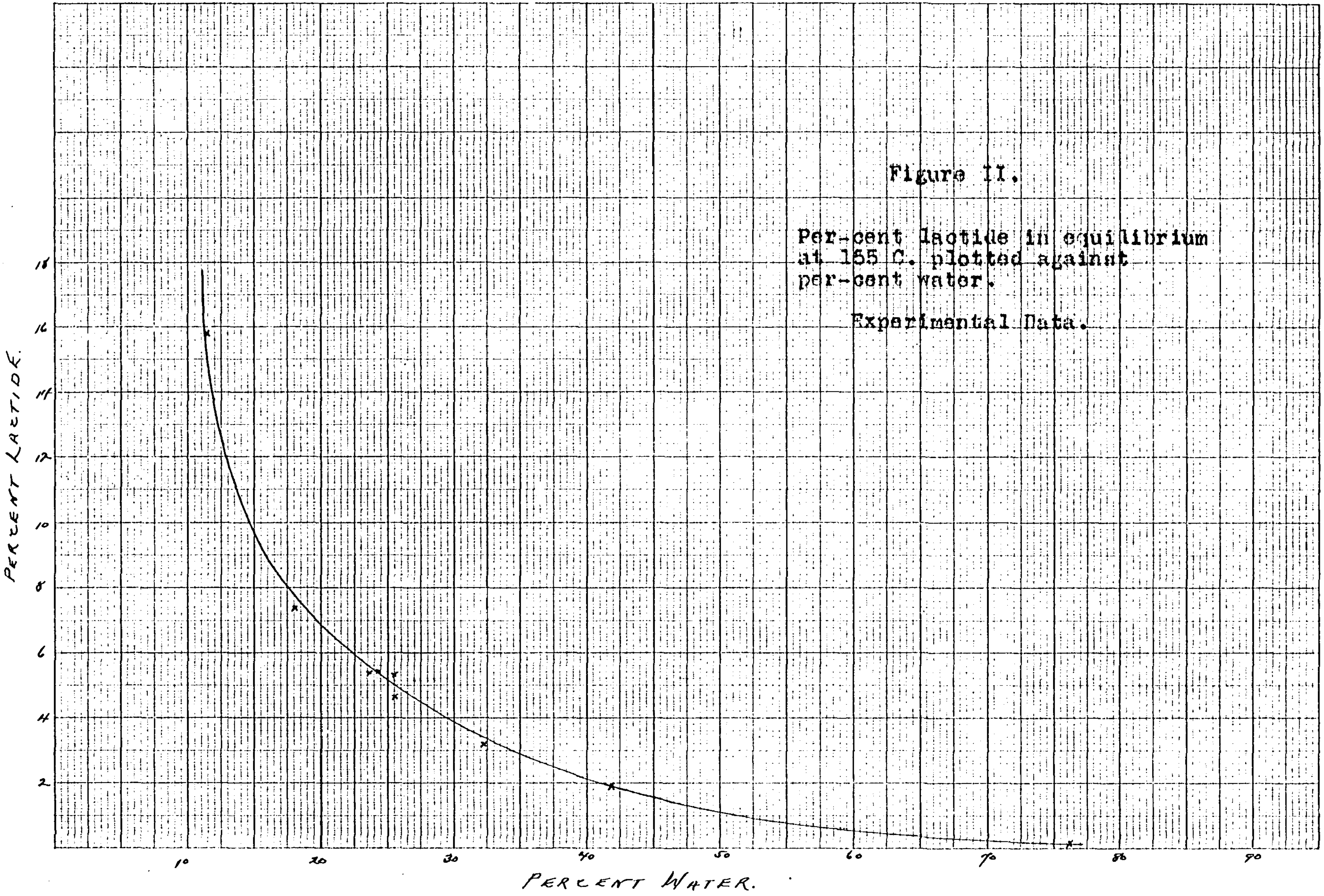


Figure II.

Per-cent lactide in equilibrium at 155 C. plotted against per-cent water.

Experimental Data.

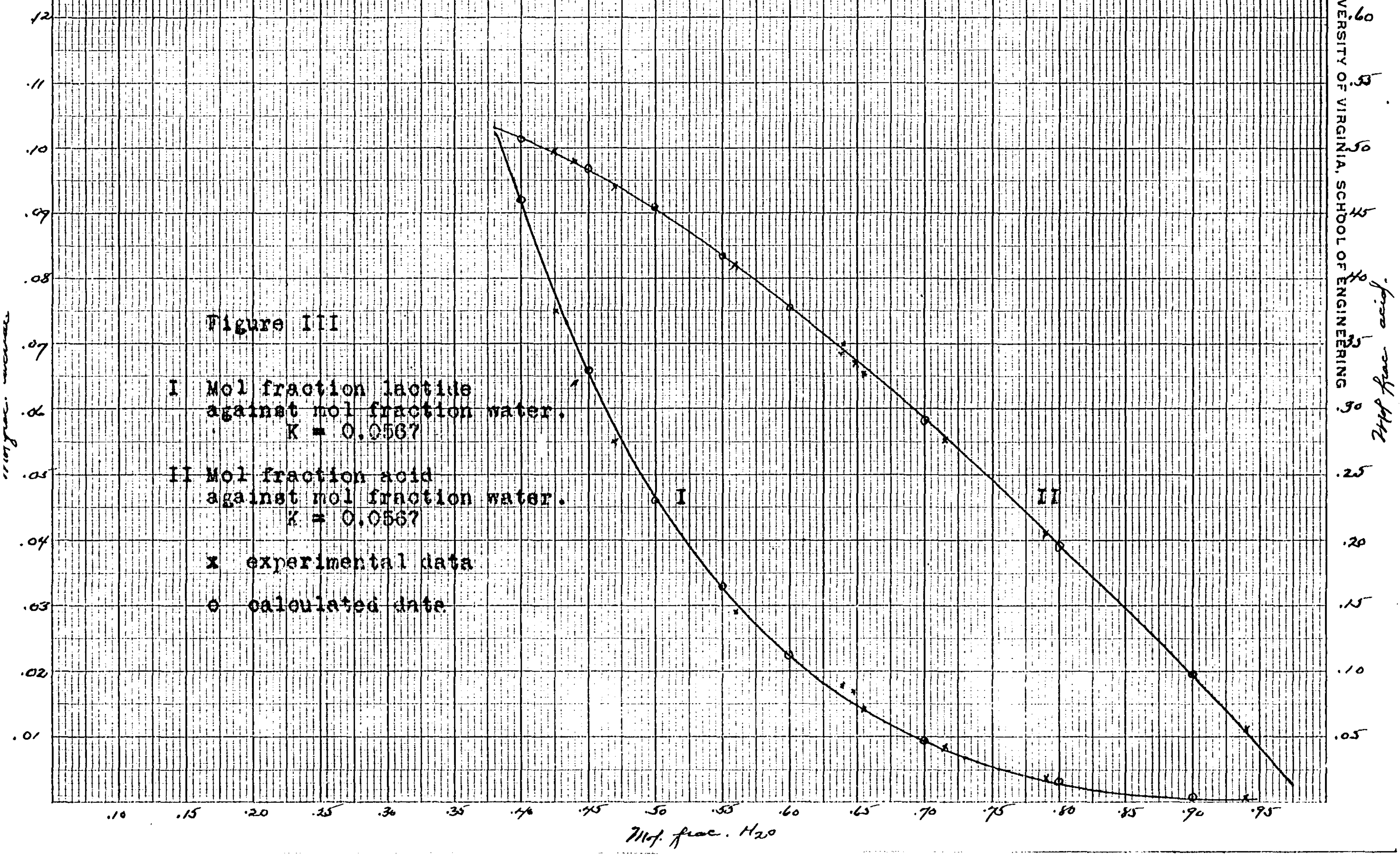


Figure III

I Mol fraction lactide
against mol fraction water.
K = 0.0567

II Mol fraction acid
against mol fraction water.
K = 0.0567

x experimental data

o calculated date

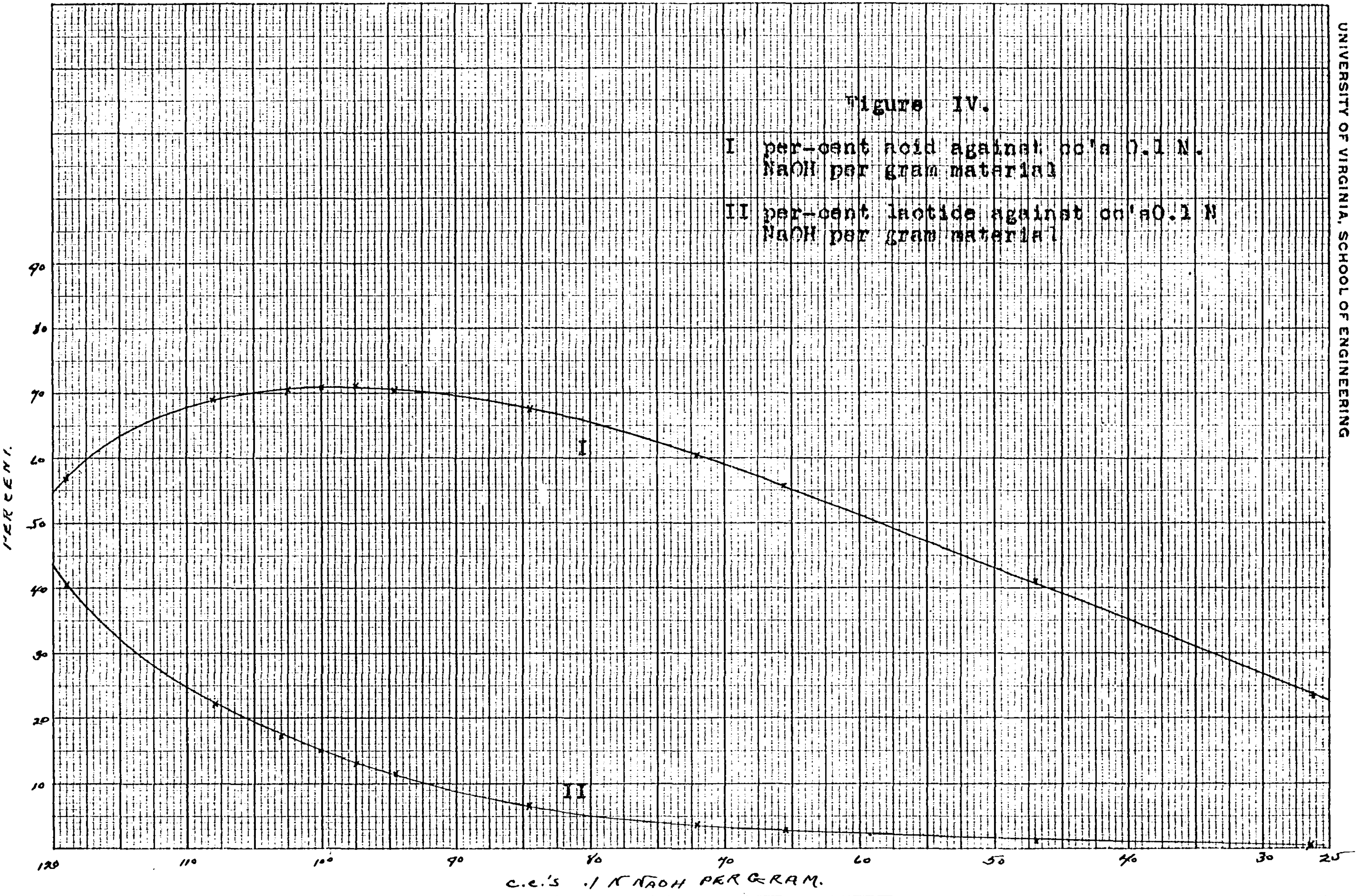


Figure IV.

I per-cent acid against cc's 0.1 N. NaOH per gram material

II per-cent lactide against cc's 0.1 N NaOH per gram material

Part II.

Rate of Lactide Formation and Distillation of Lactic Acid at Low Pressures.

(I) Introduction.

In the concentration and distillation of lactic acid it has long been recognized that lactide and anhydride formation represents a loss to the manufacturer, and various methods of preventing this loss have been patented from time to time, however, none proving entirely satisfactory. This failure has probably been largely due to a lack of knowledge of the exact mechanism and conditions of the formation of the anhydrides. In light of the data presented above certain principles seem reasonably clear.

(1) Lactide is formed from lactic acid by a reversible reaction which proceeds, at elevated temperatures, rather rapidly to a definite equilibrium represented by the equation

$$\frac{\text{mol frac. lactide} \times \text{mol frac.}^2 \text{ water}}{\text{mol frac.}^2 \text{ acid}} = K = 0.0567$$

K being little affected by temperature.

(2) If lactic acid is concentrated at temperatures sufficiently high for the rate of reaction to be fairly rapid, lactide will be formed as the water is removed. The amount of lactide in equilibrium increases very rapidly when the water content becomes low, but nothing is known as to the rate at which such a change takes place at various temperatures.

(3) The mechanism of the loss of lactic acid by anhydride formation is much less clear. In all cases the amount of anhydride present has been found to be small, never being over 5% and much less than this in highly concentrated solutions. Thus, in concentration or distillation, where we will be dealing with very concentrated solutions, the loss by anhydride formation can be neglected.

The purification of lactic acid involves usually two steps, concentration and distillation. It is impossible to make any intelligent suggestions as to avoiding loss of free acid in lactic acid purification by these processes, unless some data are available on (1) the vapor-pressure-composition curves, and (2) the rate of lactide formation at different temperatures. For this reason it was thought to be worth while to carry out some experiments on the distillation of lactic acid at low pressures and the rate of lactide formation at temperatures near those involved. Although the data are by no means complete, the time being too short for a very exhaust~~ed~~ive study, they show qualitatively what the changes are and permit certain fairly intelligent suggestions as to methods by which lactic acid can be purified.

(II) Experimental.

(a) Rates of reaction.

From one or two preliminary distillation experiments it was seen that, if purification was to be effected by distillation at a pressure of half a centimeter or less, the temperature would be between 90 and 100 C. This being the case, water was naturally chosen as the most suitable bath in which to carry out experiments on the rate of lactide formation, and, for this reason, most of the data is given at 100 C. One run was made in a bath of boiling toluene (110 C.) to see how great the effect of a ten degree increase in temperature would be on the rate. (The same mixture was also run at 100 C.)

A 25 cc erlenmeyer flask was fitted with a pressure top and about two-thirds filled with the acid mixture. This was immersed in a flask of water heated under reflux, and one gram samples pipetted off and analyzed at intervals as indicated. Analyses were made for acid and lactide according to the usual method, assuming no anhydride present. The data are given in Table I, and certain runs are expressed graphically as indicated in Figure I. In Figure II the rate of change of the percentage of acid of a concentrated solution at room temperature with time in days is shown. The solution was kept in a sealed brown bottle at room temperature, samples being drawn off and analyzed at intervals as shown in the table. As can be seen from Figure IV part I the mixture is still far above the equilibrium condition but proceeding rather rapidly toward it. This experiment shows the uselessness of concentrating lactic acid above 75 or 80%, if it is to be stored for any length of time. If the acid is to be kept in storage for six months or longer, the optimum concen-

Table I.

Rate of Reaction Data.

100 C.

Time	0	15mi	45mi	1hr 30mi	3hr 30mi	5hr 45mi
%acid	89.67 4.40 (lac)	87.85	84.59	80.00	75.30	72.51

110 C.

Time	0	15mi	45mi	1hr 45mi	3hr 45mi	5hr 45mi
%acid	90.28 3.93 (lac)	87.10	82.28	76.46	71.74	70.33

100 C.

Time	0	15mi	45mi	1hr 35mi	3hr 45mi	5hr 45mi
%acid	82.32 3.72 (lac)	81.33	79.81	77.25	73.93	72.89

100 C/

Time	0	15mi	45mi	1hr 45mi	3hr 45mi	5hr 45mi
%acid	74.41 3.46 (lac)	73.60	73.06	71.85	70.17	69.81

100 C.

Time	0	15mi	45mi	1hr 45mi	3hr 45mi	5hr 45mi
%acid	78.35 5.29 (lac)	77.83	76.47	74.91	73.12	72.17

100 C.

Time	0	15mi	45mi	1hr 45mi	3hr 45mi	6hr 50mi
%acid	92.20 5.77 (lac)	89.63	85.90	80.83	74.07	69.83

100 C.

Time	0	15mi	45mi	1hr 45mi	3hr 45mi	6hr 25mi
%acid	93.75 2.98 (lac)	91.57	87.70	82.13	75.20	70.18

Room Temperature.

Days	0	8	15	24	38	45	66	85
%acid	91.79	87.59	84.91	82.01	78.20	76.93	74.08	72.28

tration to avoid loss by lactide formation is about 80%, as seen from Figure IV part I. At this concentration the mixture contains 70% acid and 10% lactide. Above this concentration the acid content begins to slowly decrease and the lactide to rapidly increase.

Theoretically very little can be drawn from the data of Figure I. The reaction does not seem to be one of the first order, as the logarithms of the concentrations plotted against time do not give a straight line. However, the effect of the counter reaction was not taken into consideration, so this is not certain. Curves III and IV show that the rate is hardly doubled by a ten degree rise in temperature, as is usually approximately the case. But, the increase is over one half, so it is highly desirable to hold the temperature as low as possible in distillations. From curves I and II it does not seem that the rate of lactide formation is increased by a slightly greater initial lactide content. The curves are almost parallel over the whole range. Roughly speaking, for the approximate concentrations involved in distillation (98%), 10% of the acid is converted to lactide in two hours, so that, as will be seen later, this is about the time limit for a distillation.

(b) Distillation of lactic acid.

The rate of lactide formation is unappreciable at ordinary temperatures, but, as is seen from experiment, becomes quite appreciable around 100 C. For this reason, it is necessary that, if purification is to be effected by distillation, the distillation be carried out at as low a temperature as is possible. Thus, the experiments were carried out at pressures as low as it seemed reasonable to expect to maintain in practice.

Commercial acid was diluted to 25% with distilled water and heated under reflux until the equilibrium state was approximated (15 to20 hours), thus cutting the lactide content to a minimum. The weak acid solution was then distilled from a 500 cc flask of the Claisson type, the neck and side arm of which were insulated with a thick coat of magnesia, thru a condenser jacketed with ice water, and collected in a flask immersed in an ice bath. The distillation flask was heated by being immersed in an oil bath up to the magnesia coating. The vacuum was maintained by a water pump until the distillation temperature reached 50 C., the water pump then being replaced by a Cenco-Nelson vacuum pump. A closed mercury manometer, connected to the system between the receiver and pump by means of a T tube, was used to note the pressure. In experiment 4 the receiver was arranged so that fractions could be drawn off without allowing the pressure to rise, and a capillary tube was inserted in the distillation flask, so that samples could be drawn off by suction after allowing the pressuree to rise only a few centimeters. In the other experiments the system was brought to atmospheric pressure to change receivers and pipette samples from the residue.

The data of experiments #3 and #4 are complete enough

Distillation Data.

Temp.	Pressure	Weight of Dist.	% acid % lactide % water Dist.	Residue
		#1.		
----	----	409.7 grs.	----	25.43 .41 74.16
30 C.	16 mm	273.5	7.30 .14 92.56	----
40 C.	16 mm	8.8	water	72.56 1.58 25.86
60 C.	16 mm	25.5	v. s. acid	----
90 C.	16 mm	1.6	v. s. acid	92.66 3.75 3.59
120 C.	16 mm	47.9	88.83 2.81 8.36	51.32 47.27 1.41
150 C.	16 mm	15.0	75.36 14.71 9.93	27.34 70.81 1.84
		#2.		
----	----	415.5 grs.	----	25.00 .44 74.56
18 C.	14 mm	261.0	water	70.96 1.12 27.92
30 C.	6 mm	52.0	.43 acid	90.26 1.77 7.96
102 C.	6 mm	15.0	51.92 .34 47.74	93.74 4.39 1.87
93 C.	2 mm	74.0	96.64 1.79 1.57	55.19 42.04 2.77

Distillation Data.

		#3.	%acid %lactide %water	
Temp.	Pressure	Weight of Dist.	Dist.	Residue
---	---	418.0 grs.	---	24.66 .47 74.87
22 C.	14 mm	180.8	.99 acid	44.32 .73 54.95
30 C.	14 mm	42.5	.21 acid	55.75 .93 43.32
38 C.	14 mm	37.0	.27 acid	72.90 1.22 25.88
50 C.	14 mm	28.8	1.00 acid	94.52 1.86 3.62
to 110 C. (rapidly)	14 mm	2.7	8.49 .22 91.29	90.55 7.39 2.06 no anhydride
to 118	14 mm	10.5	82.61 1.64 15.75	82.88 14.87 2.25
118 C.	14 mm	33.2	89.76 3.29 6.95	60.63 38.13 1.24
to 160 C.	14 mm	24.6	76.77 20.01 3.22 no anhydride	23.13 76.77 .10

Distillation Data.

#4.

Temp.	Pressure	Weight of Dist.	%acid %lactide %water Dist.	Residue
---	---	417.0 grs.	---	25.73 .42 73.85
20 C.	14 mm	241.0	2.83 acid	---
30 C.	14 mm	53.0	.28 acid	85.16 2.06 12.78
35 C.	14 mm	15.0	.53 acid	---
90 C.	7 mm	1.0	.89 acid	89.20 7.64 3.16
97 C.	3 mm	22.5	94.05 1.59 4.36	79.36 18.58 2.06
97 C.	3 mm	15.5	94.20 2.41 3.39	66.43 31.94 1.63
97 C.	3 mm	26.2	91.75 3.95 4.30	49.71 49.24 1.05

#5.

Temp.	Pressure	Weight of Dist.	Dist.	Residue
---	---	416.0	---	24.73 acid
to 32 C.	15 mm	284.5	.18 acid	---
104 C.	5 mm	92.0	75.09 1.95 22.96	---
to 160 C.	5 mm	19.0	72.82 25.50 1.68	---

to permit a fairly complete graphical presentation of the vapor-pressure-composition changes. For experiment #4 the changes in composition for both distillate and residue with the temperature are plotted (figure III). The changes in the distillate of experiment #3 are similarly plotted in Figure IV. Altho the data on the residue are not complete, it can be seen that the curves would be similar to those in Figure III. During the first part of the distillation pure water distills over, the temperature remaining constant. (The acid in this part of the distillate is due to bumping.) When the water content has become very low, the temperature rises rapidly to the boiling point of lactic acid and almost pure acid distills over, the temperature remaining constant. When the ratio of acid to lactide has reached a value corresponding approximately to that for equilibrium condition (read from Figure IV part I), the temperature begins to rise and a distillate considerably richer in lactide distills over, the temperature gradually rising to 150 to 160 C. The percentage recovery will be discussed in the following section.

Bearing of the Results on Methods of Purification of Lactic Acid.

From the data above it can not be predicted what effect impurities will have on lactide formation in the distillation of crude lactic acid, as the experiments were carried out on material conforming to U. S. P. specifications. However, assuming that they will have none and neglecting the small amount of anhydride formed, there is reasonably good ground for certain speculations concerning possible methods of purification.

If the experimental data are indicative of what would take place on a commercial scale, the following should be true in a distillation.

Assuming that we start with a solution containing 75% water, that has been heated to bring the constituents to equilibrium, there will be about 24% acid and only 0.2 to 0.4% lactide present. If the pressure is now kept at 14 mm, the water will distill over between 20 and 50 C. with practically no formation of lactide. As seen from experiments #1 and #2, the residue, when water ceases to distill over, will contain about 93 to 94% acid and 4 to 5% lactide. If the pressure can now be lowered and held at 2 mm, 96% acid will distill over until the ratio of acid to lactide in the residue corresponds to that of the equilibrium condition (experiment #2). At this point approximately 80% of the acid will have distilled over. Above this temperature no lactide will be formed , but a mixture of lactide and acid will distill over until lactide alone remains in the residue, which will distill between 140 and 160 C.

Experiments #2 and #5 were run somewhat more rapidly than the others and more nearly indicate the possible recovery. In experiment #2 the recovery was 90% acid, the lactide not being distilled over. In experiment #5 the recovery was 85% acid and about 12% lactide, a small amount of lactide being lost due to condensation taking place in the flask and receiver.

If these distillates were now diluted to the point where they contain 70% of acid, that of experiment #2 would contain less than the amount of lactide required by the equilibrium and experiment #5 only very slightly more. Thus, if in practice the pressure can be maintained at 2 to 3 mm, it should be possible to purify lactic acid by an intermittent distillation process, obtaining a good recovery and an acid that has the composition of the commercial acid now on the market.

If a more concentrated acid were desired for immediate use, it might possibly be prepared as follows. By the process above an 80 to 85% yield of 95% acid can be obtained, leaving a residue of the composition corresponding to the equilibrium condition, namely, about 45% lactide. This residue is found to be still fairly mobile when cold, so could very easily be run off while hot. Thus, the distillation could be stopped at this point and the residue run off, diluted, hydrolyzed, and again distilled. A number of residues could be collected and run together, thus making the total loss very small.

Processes in which lactic acid is distilled with a current of inert gas under pressure have been patented. The use of steam at low pressures was thought of as another possibility, serving the double purpose of carrying the acid over and keeping the lactide content at a low value. It is seen from the experiments that the water content drops to a very low value before acid begins to distill over, and there is no intermediate period where the vapor pressure of the acid is appreciable as compared to that of the water, thus making it impossible to obtain a moderately concentrared acid at a lower temperature. Though the admission of a small amount of steam during the distillation might help the yield to a slight extent, it does not seem likely that it would enter into the reaction and prevent the formation of lactide.

It has been suggested that purification of lactic acid might best be accomplished by some means of vaporizing the acid rapidly, thus cutting down the time for lactide formation. It seems that it should be possible to distill off the water, as above, at 14 mm, and to then spray the acid onto a series of plates or into an atmosphere hot enough to immediately volatilize both acid and lactide, thus obtaining a distillate of approximately the same composition. There is one evident objection to this process. Any residue formed would be solid or more likely "gummy" and would be very difficult to remove from the still. For this reason a continuous distillation process does not seem to be very well adapted to the purification of lactic acid.

Of course, these are only speculations from a practical viewpoint and further experiments are necessary to determine their value as a commercial process. However, they do not seem to be taken entirely from the air.

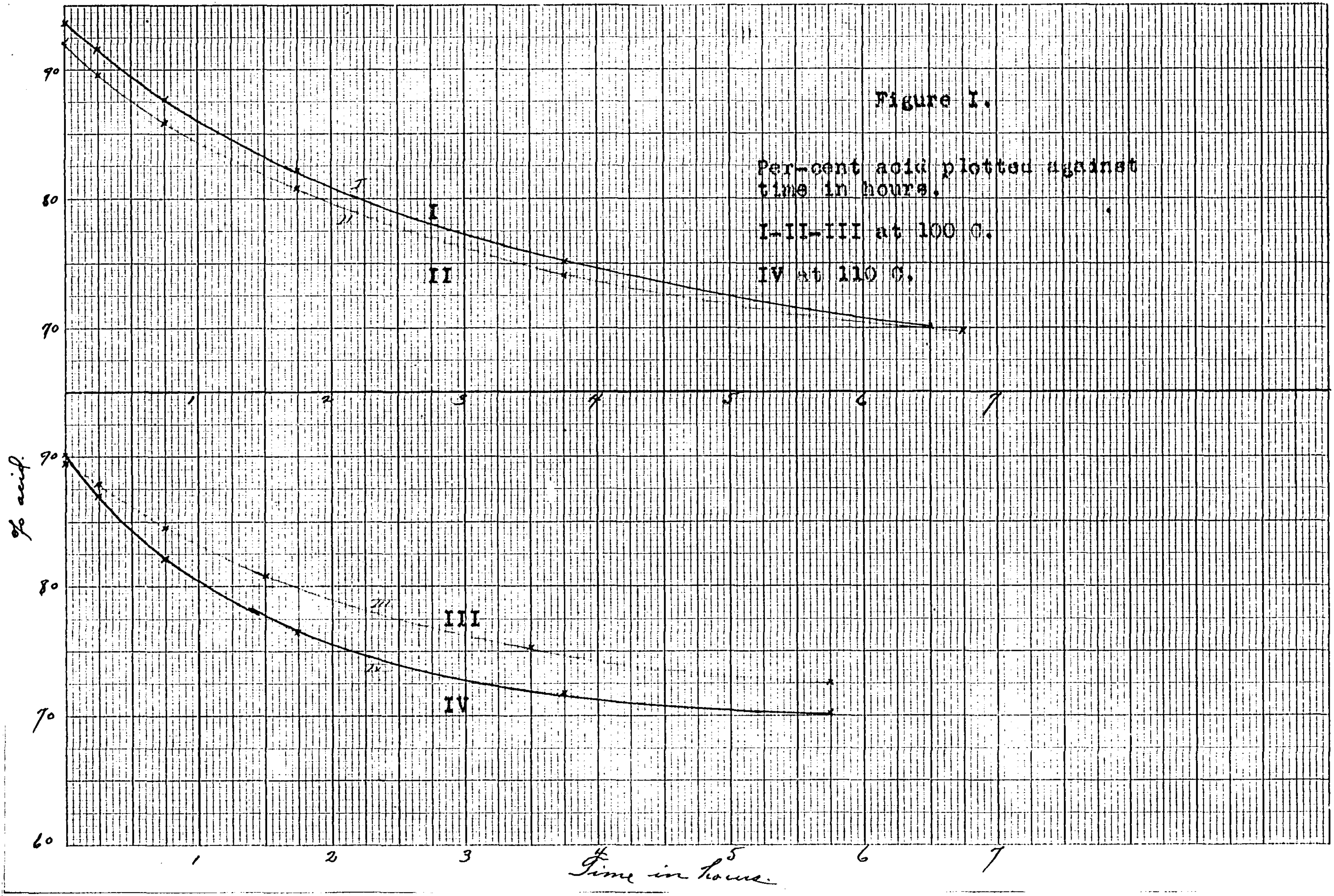


Figure I.

Per-cent acid plotted against time in hours.

I-II-III at 100 C.

IV at 110 C.

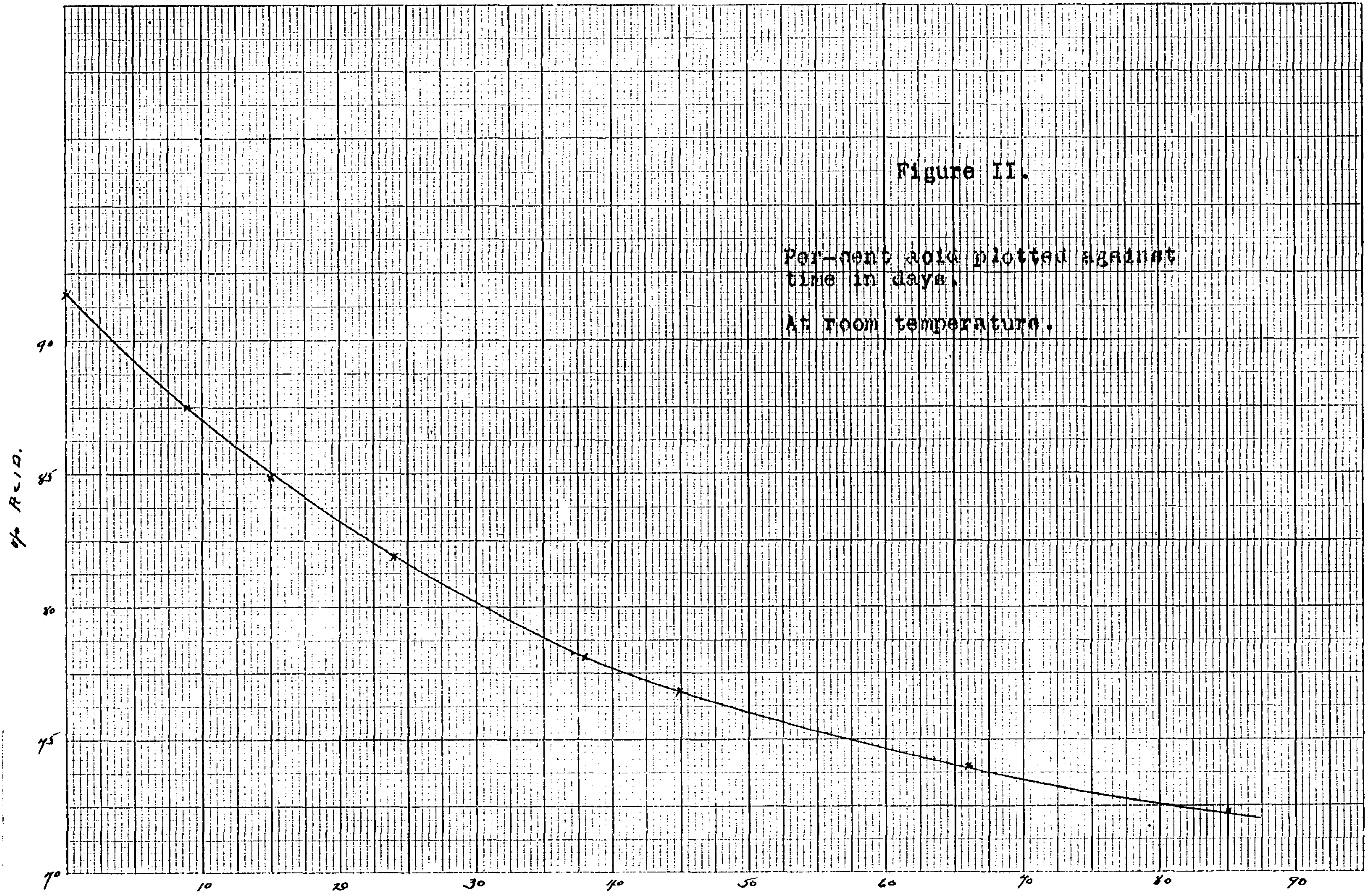


Figure II.

Per-cent acid plotted against time in days.

At room temperature.

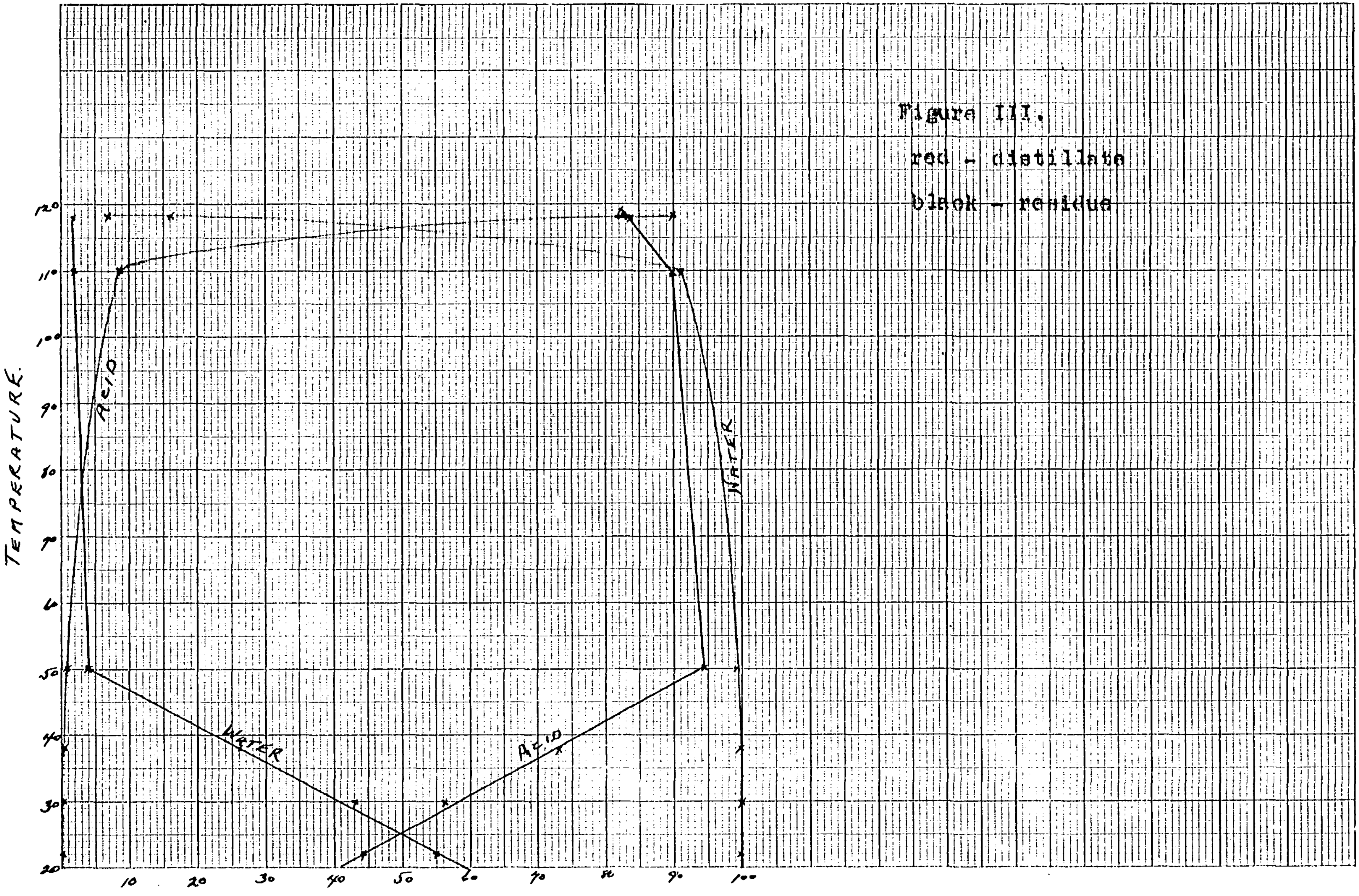


Figure III.
red - distillate
black - residue

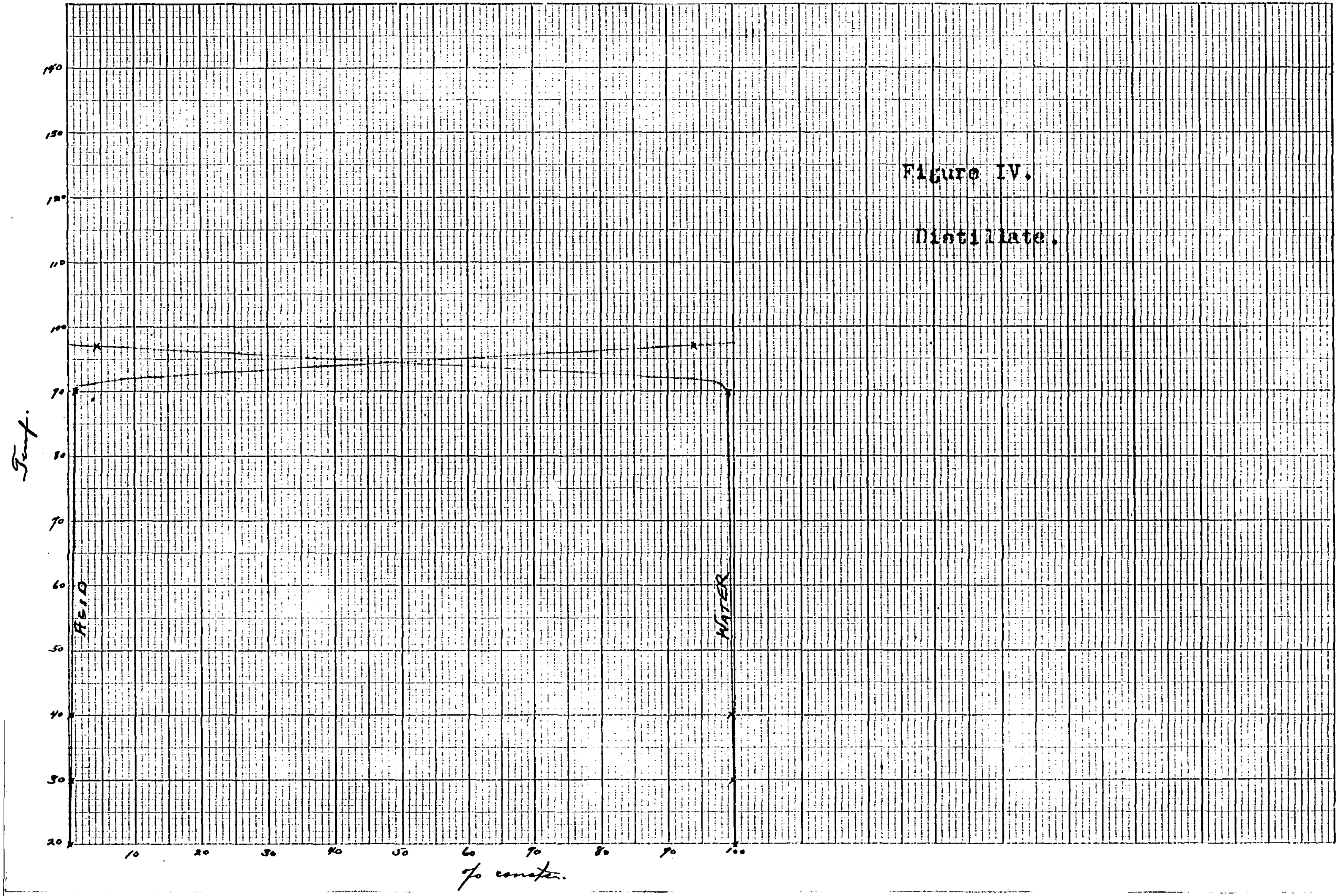


Figure IV.

Distillate.