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The Preparation of Alpha Brompropionic Acid in the Presence of Various Catalysts

Walter V. Sharp

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THE PREPARATION OF ALPHA BROMPROPIONIC
ACID IN THE PRESENCE OF VARIOUS
CATALYSTS

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A Thesis Submitted to the Graduate Division of
the University of North Dakota in
Partial Fulfillment of the
Requirements for the
Degree
of
Master of Science

by

Walter V. ^{elmer} Sharp

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July , 1934

This thesis, presented by Walter V. Sharp, in partial fulfillment for the degree of Master of Science, is hereby approved by the Committee on Instruction in charge of his work.

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CHAPTER I

INTRODUCTION

Before beginning a discussion of the various methods of preparing the alpha halogen acids by direct halogenation in the presence of various catalysts, it will perhaps be in order to say a word concerning the importance of this group of compounds as a whole.

The alpha halogen substituted acids are used in the synthesis of the hydroxy acids, a number of which are of commercial importance, and of interest to the biochemist as they occur in plants and animals. Lactic acid, for example, is one of the most common. It plays an important role in the chemical changes accompanying muscular activity. It is also used in the dye industry and its ethyl ester is an important solvent. Beta hydroxybutyric is of definite biochemical interest because of its presence in the urine of those suffering from diabetes. Citric acid is another of considerable interest because its salts are used in some pharmaceutical preparations; the acid itself being used for preparation of beverages. Others, such as glycollic, malic and tartaric are perhaps of comparable importance.

The hydroxy acids are also of interest in synthetic organic chemistry because of the fact that they, in general, react like both alcohols and acids and therefore serve as an avenue for a wide variety of syntheses. As acids they form salts with bases

and esters with alcohols. As alcohols they form esters with acids. They may even form cyclic double esters with themselves, the one molecule acting as an acid and the other as an alcohol.

The alpha halogen substituted acids are also used in the syntheses of alpha amino acids, and this class of compounds is of importance in biochemistry because they are the units of structure in proteins.

Another recently suggested use for the high molecular weight alpha halogenated acids is in the manufacture of the soaps of these acids with a view toward using them in dentists' mouth washes. The theory here being, that in addition to the germicidal property of the soap itself, the presence of a halogen atom would increase its effectiveness, since halogens have germicidal properties. These halogenated acids themselves are known to have a marked physiological action. As an example, trichloroacetic acid is used in medicine as a corrosive agent for removing the outer tissues in the treatment of corns and warts.

The direct bromination of aliphatic acids is also used by organic chemists in determining structure. Since it is the hydrogen atom in the alpha position to the carboxyl group that is always replaced by the halogen, and if there is no alpha hydrogen atom no substitution takes place as in the case of trimethylacetic acid giving no brominated acid even when treated with bromine at 100°-135°.¹ This reaction serves then as a means of detecting the presence of an alpha hydrogen atom in aliphatic acids. The

¹Chem. Rev. 7, 180 (1930) or Ber. 23, 1594 (1890)

elimination of carbon dioxide from the chain by oxidation of hydroxy acids serves as a possible convenient means of degrading an acid step by step.

It is common knowledge among organic chemists that the lower members, at least, of the alpha brom- or chlor- aliphatic acids can be directly prepared from the acid and the halogen most effectively in the presence of a catalyst. However, a review of the literature reveals that little work has been done in determining the best methods of preparing this class of compounds from the standpoint of the best catalysts and conditions of treatment, nor is there complete agreement concerning the part that each of the separate catalysts plays in accelerating the reaction. In fact, practically all of the work that has been done previously along this line has had for its purpose the determination of the mechanism of the reactions with various catalysts through measurements of speeds of reactions with varying concentrations, and little reference is made in the available literature concerning specific methods of preparation.

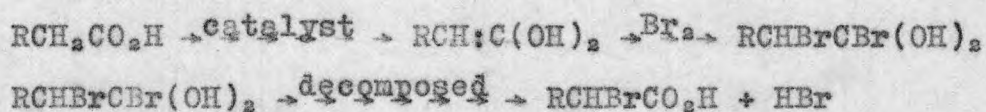
Before stating the problem of this investigation, the author intends to present a brief review of the different interpretations of alpha halogen substitution in aliphatic acids that prevail in the chemical literature, and to indicate the extent of the work done in determining the best catalysts and best conditions of treatment.

Hell and Mühlhauser¹ interpreted the accelerating effect of

¹J. Chem. Soc. 127, 1167-82 (1925) or Ber. 12, 729 (1879)

HBr on direct bromination of acetic acid on the hypothesis that bromination was preceded by the formation of a red additive compound previously isolated by Hell¹, to which he ascribed the formula, $C_2H_4O_2Br_2 \cdot HBr$. They regarded the observation that an initial period of very low velocity followed by a rapid disappearance of the halogen as being direct confirmation of this hypothesis.

A new view was advanced by Lapworth² after he had discovered that hydrogen chloride exhibited a similar catalytic effect on the bromination. He thought that the bromination with HCl or HBr as catalysts involved a relatively slow catalyzed change to the enol form of the acid, followed by a rapid bromination at the point of unsaturation, and this to be followed by loss of hydrogen bromide. He postulated a series of reactions, thus:



He also explained the catalytic effect of small quantities of red phosphorus in a similar way, as will be pointed out later.

Lapworth³ obtained a good yield of monobromacetic acid by saturating 99% acetic acid with dry hydrogen chloride and heating for nine hours on the water bath.

Shaw⁴ could not confirm this result but did get good results by using 99.6% acetic acid, taking precautions to exclude all moisture, and heating on the water bath for thirty-five hours.

¹Ber. 11, 244 (1878)

²J. Chem. Soc. 85, 41 (1904)

³Loc. cit.

⁴J. Chem. Soc. 123, 2233-40 (1923)

Another suggestion is made by Watson¹ to explain the catalytic action of the halogen acids wherein the halogen acid is in equilibrium with the aliphatic acid, thus:



The RCOX or acyl halide would then act as the catalyst. He points out that while the existence of such an equilibrium has never been demonstrated, it is suggested by the fact that this catalytic action of the halogen acids is specific and is not shared by acids in general. He considers this fact as evidence against the enolic theory advanced by Lapworth². In addition, he confirms Lapworth's observation that a small amount of water appreciably reduces the catalytic effect of the halogen acid. He points out that the water would displace the above equilibrium to the left and thus destroy the acyl halide and its catalytic effect.

The catalytic effect of small quantities of phosphorus or sulphur on bromination of aliphatic acids has been interpreted by Hell³, Volhard⁴, and Zelinsky⁵ on the basis that the aliphatic acid was completely converted into the acid bromide, followed by bromination of the latter. However, Ward⁶ points out that this theory does not hold where the amount of phosphorus is insufficient for any large conversion into the acid bromide. He then interprets the catalytic effect of phosphorus on the basis of Lapworth's⁷ suggestion that phosphorus acts on the halogen to form

¹Loc. cit.

²Loc. cit.

³Ber. 14, 891 (1881)

⁴Annalen 242, 141 (1888)

⁵Ber. 20, 2026 (1887)

⁶J. Chem. Soc. 121, 1161-82 (1922)

⁷Loc. cit.

phosphorus tribromide. The phosphorus tribromide acting on the acid or a trace of moisture forms HBr to bring about the enol transformation and the bromination then proceeds along the lines suggested by Lapworth¹ and Aschann². However, in a later article Ward states, "The theory demands the existence of carboxylic acids in a form that is neither observed nor indicated in other reactions."³ Watson⁴ also points out that although evidence points to the preliminary formation of an enolide in the case of ketones and ketonic acids the reactions of the carbonyl group in carboxylic acids differ in many respects from the reactions of the same group in ketones and that it is a case of forcing an analogy to assume an enolide is formed of the acid. Furthermore, he explains that some of the physical properties of carboxylic acids do not give values that would be anticipated if the usual type of carbonyl group were present.

Ward⁵ found that he could obtain his best yields of monobrom-acetic acid by using 20g. of acetic acid, .4g. of red phosphorus and 58g. of bromine and heating at 100°-105° for one hour. He also obtained good yields of alpha brombutyric acid by a similar method.

Hentschel⁶ observed a remarkable accelerating effect on the chlorination of acetic acid by the presence of a small quantity of acetic anhydride and postulated a pair of alternating reactions:

¹Loc. cit.

²Ber. 45, 1913 (1912)

³J. Chem. Soc. 123, 2212 (1923)

⁴Chem. Rev. 7, 181 (1930)

⁵J. Chem. Soc. 121, 1161-82 (1922)

⁶Ber. 17, 1286 (1884)



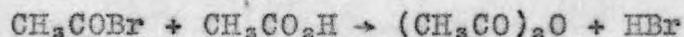
Shaw¹ also noticed the powerful accelerating effect of acetic anhydride on the bromination of acetic acid and its homologues and suggested that the reaction may take place either

- (a) through the preliminary enolization of the acid, or
- (b) through a series of changes involving acetic anhydride, similar to those postulated by Hentschel, the latter course being by far the more rapid.

He asserts that this view is substantiated by the experimental observation that HCl reduces the velocity of the reaction when acetic anhydride is the catalyst, which is as it should be if the above interpretation were correct. On the contrary, HCl should increase the velocity, if the enolic theory were correct.

Shaw² found the use of a trace of acetic anhydride as the catalyst in the bromination of acetic acid and its homologues to be the best method. Quantitative yields were obtained, although he found it difficult to remove the traces of bromoacetic acid and bromoacetyl bromide when he worked with homologues of acetic acid.

The catalytic action of acetyl bromide and chloride have also been a subject of controversy. Shaw³ believes that their action is through the acetic anhydride which may be formed thus:



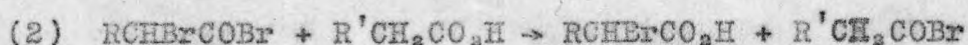
¹J. Chem. Soc. 123, 2233-40 (1923)

²Ibid.

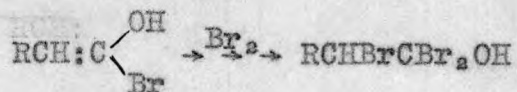
³Ibid.

The acetic anhydride then enolizes and is brominated as suggested before. He supports this in one instance when he points out that according to this view the velocity of the reaction between equivalent quantities of acetic acid and bromine in the presence of acetic anhydride should be proportional to the concentration of the latter and that this was found experimentally to be the case.

On the other hand, Watson' says, "The catalytic action of acid bromide can not be interpreted by postulating the intermediate formation of the acid anhydride, for an initial period of low velocity is observed when the anhydride is introduced but not when the acid bromide is there initially." He then postulates a series of reactions to show that the acid bromide itself enters into the reaction, thus:



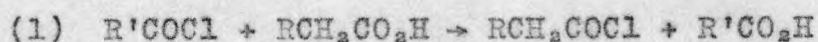
or, he suggests that perhaps the acid bromide enolizes more readily than the acid itself, thus:



In order to obtain evidence of the accelerating influence of acetyl bromide several experiments were performed in which acetyl bromide was introduced as such in varying amounts. It was found that if the acetyl bromide was in excess of the water present it exhibited a powerful influence, but if it was not in excess of the water the reaction proceeded as if HBr alone had been used.

'Loc. cit.

Watson¹ finds that acid chlorides exhibit an accelerating effect but not to such an extent as the bromides. The action here he interpreted by the following reactions:



According to the above scheme the velocity ultimately attained would depend upon the proportion of the acid bromide or the brominated acid bromide present in the equilibrium, and this he found to be in agreement with his results.

Auwers and Bernhardt² in making a study of the structure of the alpha halogen acids treated varying proportions of acetic, propionic, butyric and other acids with varying proportions of bromine in the presence of varying small amounts of red phosphorus at the temperature of the water bath. They converted the reaction product directly into the ethyl ester by treating it with absolute alcohol. However, their purpose was not to determine optimum conditions for maximum yields and no values were given for yields obtained.

Brückner³ determined that the velocity of chlorination of acetic acid in the presence of iodine, phosphorus or sulphur increased with the amount of the catalyst but not in direct proportion. He found that iodine gave the best results of the three used separately, but obtained best results with a mixture of three catalysts, iodine, phosphorus pentachloride and phos-

¹Loc. cit.

²Ber. 24, 2217-21 (1891)

³Z. angew. Chem. 41, 226-9 (1928)

phorus.

Magidson, Zilberg and Brazhenskii¹ could not confirm these results but obtained best results with sulphur, used in large quantities, as a catalyzer. Their sulphur was activated. Their product was pure and the yield was forty-seven percent of the theoretical after nine hours treatment in an improved apparatus.

Shilov² confirms and extends the work of Brückner³ and adds that when acetic acid is treated with chlorine in the presence of a mixture of iodine, phosphorus and phosphorus pentachloride, a yield of monochloroacetic acid equal to seventy-five to ninety percent is obtained. However, he finds phosphorus pentachloride unnecessary. By the addition of monochloroacetic acid the action is speeded up and the action is, therefore, shown to be auto-catalytic. He also finds that a small quantity of sulphuric acid increases this latter action.

Lyubarskii⁴ obtains similar results when he treats carefully frozen out acetic acid, mixed with one part iodine, two parts red phosphorus and four percent phosphorus pentachloride, with chlorine passed into the bottom of the reaction mixture.

It is evident then that no study has been made of the preparation of these alpha halogen acids from the standpoint of determining the optimum temperature treatment; nor is there complete agreement concerning the comparative values of the various catalyts.

¹C.A. 22, 4105 (1928). J. Chem. Ind. (Moscow) 5, 528-9 (1928)
²C.A. 24, 827 (1930). J. Chem. Ind. (Russia) 6, 538-40 (1929)
³Loc. cit.
⁴C.A. 24, 827^{7,8} (1930). Zhur. Prikladnoi Khim, 2, 621-7 (1929)

The problem of this investigation is to study the bromination of propionic acid with various catalysts and to determine which of the catalysts and what conditions of temperature treatment afford the best method of preparation of alpha brompropionic acid.

Only the more important catalysts that have been used by earlier investigators are employed in this study. Those used are red phosphorus, acetyl bromide, acetic anhydride, sulphur and iodine.

The method in brief is: to use molecular proportions of propionic acid and bromine and treat them in the presence of constant small amounts of the separate catalysts over varying temperature intervals at constant time intervals, and to determine the yields by fractional distillation of the reaction product.

No attempt will be made to measure the speed of the various reactions as was done by Watson and Shaw.

A more detailed description of the method will be presented in each chapter that follows.

CHAPTER II
BROMINATION OF PROPIONIC
ACID IN THE PRESENCE OF ACETYL BROMIDE

Since the apparatus used throughout this investigation was rather simple it is believed unnecessary to present more than a brief description of its set-up. The main apparatus consisted of a half-liter, round-bottomed flask fitted by means of a stopper to a reflux (water jacket) condenser, to the top of which was fitted through a stopper a small dropping funnel and a delivery tube which led to a separatory funnel whose lower end just dipped under the surface of a concentrated sodium hydroxide solution.¹ The reaction flask was set in an oil bath heated by an open gas flame. The temperature was gauged by a thermometer whose bulb dipped into the oil to the level of the reaction mixture in the flask.

The bromine², previously dried under concentrated sulphuric acid, was measured from a glass stoppered burette directly into the dropping funnel which was then closed at the top to prevent the escape of bromine fumes. The propionic acid³ was transferred

¹ This arrangement served to dispose of evolved gases such as bromine and hydrogen bromide which, if allowed to escape, would be very irritating to the operator's eyes and nasal passages.

² The bromine used for all the values shown in Table I was a Baker Chemical Company product, U. S. P., and for succeeding work, a C. P. product.

³ The propionic acid and acetyl bromide used were E. K. Co. products with boiling points of 140° - 142° and 41° respectively.

from the stock bottle to the reaction flask by means of a pipette and measured to the nearest .1 cc. The acetyl bromide was also transferred by means of a 1 cc. graduated pipette to the reaction flask.

The propionic acid and acetyl bromide were then heated to the desired reaction temperature. The bromine was then added through the condenser to the mixture of catalyst and acid from the dropping funnel by slow dropping, requiring an average of 50-60 minutes for complete addition.

Cold water was kept circulating through the reflux condenser to facilitate the return of reacting chemicals to the reaction flask.

In all cases 20 g. (20.3 cc.) propionic acid and 43 g. (13.8 cc.) of bromine were used, these being molecular proportions. The varying factors were the weights of acetyl bromide and the temperature treatment. The time of treatment was kept constant at two hours. The temperature was kept within a five degree range during the two hour treatment which began at the instant the bromine was started from the dropping funnel and ending, usually, about one hour after all of the bromine had been added.

Two sets of this apparatus were set up and run in duplicate simultaneously, thus affording a means of check on the accuracy of results.

The reaction products were immediately fractionally distilled first, from a 125 cc. common distilling flask, and second, from a 25 cc. distilling flask and cut into two main fractions which were collected, weighed and saved for analysis. These two frac-

tions which were collected and weighed in each case were collected over the following uncorrected boiling point ranges: 150°-195° and 195°-202°. The first of these fractions should contain most of the unchanged propionic acid and all of the alpha brompropionyl bromide that might remain since their boiling points are 140.7° and 155°, respectively. The last fraction should contain practically all of the alpha brom- acid and very little else since the corrected boiling point of the pure acid is 203°¹ and, since in nearly all cases all of the product had completely passed over below this temperature. Therefore, the author believes he is justified in calling the weights of this last fraction the yield of the alpha brompropionic acid. However, it may be entirely possible that the first fraction also contains some of the alpha brom- acid in view of the fact that it was found impractical to use a highly efficient fractionating column for so small an amount of distillate. The technique of carrying out the fractional distillation was as nearly uniform throughout as was possible to have it and for this reason the yields should be comparable, if not quantitative.²

Since no specific reference was found in the literature that would serve as a guide for the amount of acetyl bromide that was needed to induce rapid bromination it was decided to first perform a number of experiments in an effort to find an amount that would serve satisfactorily as a constant for varying temperature

¹International Critical Tables - Vol. I.

²The data for work done in 1933 was obtained by three fractional distillations but it was decided to reduce this to two in 1934 to save time. Only 1934 data are included in the graphs.

treatments.

In the first set of trials .5 g. of acetyl bromide was used and the temperature was varied over a considerable range. Reference to Table I, page 16, will show these results in a condensed form. It will be seen that .5 g. of this catalyst is entirely insufficient for bromination, at least for a two hour treatment at the lower temperatures but that a measureable yield is obtained at the temperature of 130°-135°.

Next, a pair of experiments were run using three times the former weight of the catalyst but at the temperature corresponding to the best yields found before. The mean value of the yields obtained here seemed to indicate a proportional increase.

A number of runs were then made using five times the original weight of the catalyst. Further reference to Table I, page 16, will show that the yield was again appreciably increased but not in proportion to the increase of catalyst. Since this observation would indicate an approach to the optimum amount of catalyst, it was decided, when work was resumed in 1934, to further increase the proportion of catalyst and, at the same time, make the amount equivalent to the amount of acetic anhydride which was used in other experiments in order that it might be possible to make comparisons with yields obtained with this catalyst. Consequently, 3.02 g. of acetyl bromide was chosen as the weight of the catalyst for the next trials. Here the yields will be seen to be not appreciably affected by the increase in weight at nearly corresponding temperatures.

Temperature treatment was the varying factor in all of the

TABLE I. YIELDS OF BROMINATED ACID FROM PROPIONIC ACID AND BROMINE IN THE PRESENCE OF ACETYL BROMIDE

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
95-100	.5	0.0	0.0	
95-100	.5	0.0	0.0	0.0
110-115	.5	0.0	0.0	
110-115	.5	0.0	0.0	0.0
120-125	.5	4.0	9.7	
120-125	.5	0.0	0.0	4.8
125-130	.5	5.6	13.6	
125-130	.5	0.0	0.0	6.8
130-135	.5	20.7	50.0	
130-135	.5	0.0	0.0	25.0
130-135	.5	7.6	18.3	
130-135	.5	6.1	14.7	16.5(a)
130-135	1.5	15.6	37.7	
130-135	1.5	20.0	48.3	43.0
130-135	2.5	22.8	55.0	
130-135	2.5	23.1	55.7	55.4
130-135	2.5	24.6	59.4	
130-135	2.5	26.0	62.8	61.1(b)
135-140	3.02	25.5	61.6	
135-140	3.02	24.2	58.5	60.1

(a) Values in this column up to this point are based on the first distillation of the reaction product instead of on the third fractionation, as in the following cases.

(b) These two values were the first obtained by the use of bromine dried under concentrated sulphuric acid.

succeeding trials where acetyl bromide was the catalyst. Reference to Table II, page 18, which gives the yields of the brominated acid, will show that as the temperature increases yields of the brominated acid also increase up to a certain limit and then fall off appreciably. It is also shown by Fig. 1, page 19, that the temperature is practically a linear function of the yield.

The falling off at the higher temperature may possibly have been due to the escape of more bromine or propionic acid from the top of the reflux condenser, since these temperatures were considerably above the boiling point of the propionic acid.

Referring back to the experiments wherein only .5 g. of acetyl bromide was used as the catalyst, a very interesting observation was made during the course of the experiments where no yields of the brominated acid were obtained. During the distillation of the reaction product a red crystalline compound appeared in the condenser which disappeared again by apparently decomposing after the condenser was changed to an air condenser and the vapors coming over at about 100° had raised the temperature in the condenser quite high. This red compound was not collected and no melting point was determined.

A red crystalline compound was originally described by Steiner¹ and later by Ward² in working with acetic acid, and to which Hell³ ascribed the formula $(C_2H_4O_2 \cdot Br_2)HBr$. While it is hardly possible that this compound described above could be the same as

¹ Ber. 7, 184 (1874)

² J. Chem. Soc. 121, 1161-65 (1922)

³ Ber. 11, 1244 (1878)

TABLE II. YIELDS OF BROMINATED ACID FROM PROPIONIC ACID AND BROMINE IN THE PRESENCE OF ACETYL BROMIDE

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
55-60	3.02	4.4	10.6	
55-60	3.02	5.4	13.0	11.8
75-80	3.02	9.7	23.4	
75-80	3.02	10.8	26.0	24.7
95-100	3.02	17.8	43.0	
95-100	3.02	17.3	41.8	42.4
110-115	3.02	21.5	51.9	
110-115	3.02	20.9	50.5	51.2
125-130	3.02	24.2	58.4	
125-130	3.02	24.2	58.4	58.4
135-140	3.02	25.5	61.6	
135-140	3.02	24.2	58.4	60.0
145-150	3.02	26.0	62.8	
145-150	3.02	25.8	62.5	62.6
155-160	3.02	25.5	61.6	
155-160	3.02	24.0	58.0	59.8

Mean Percentage Yield

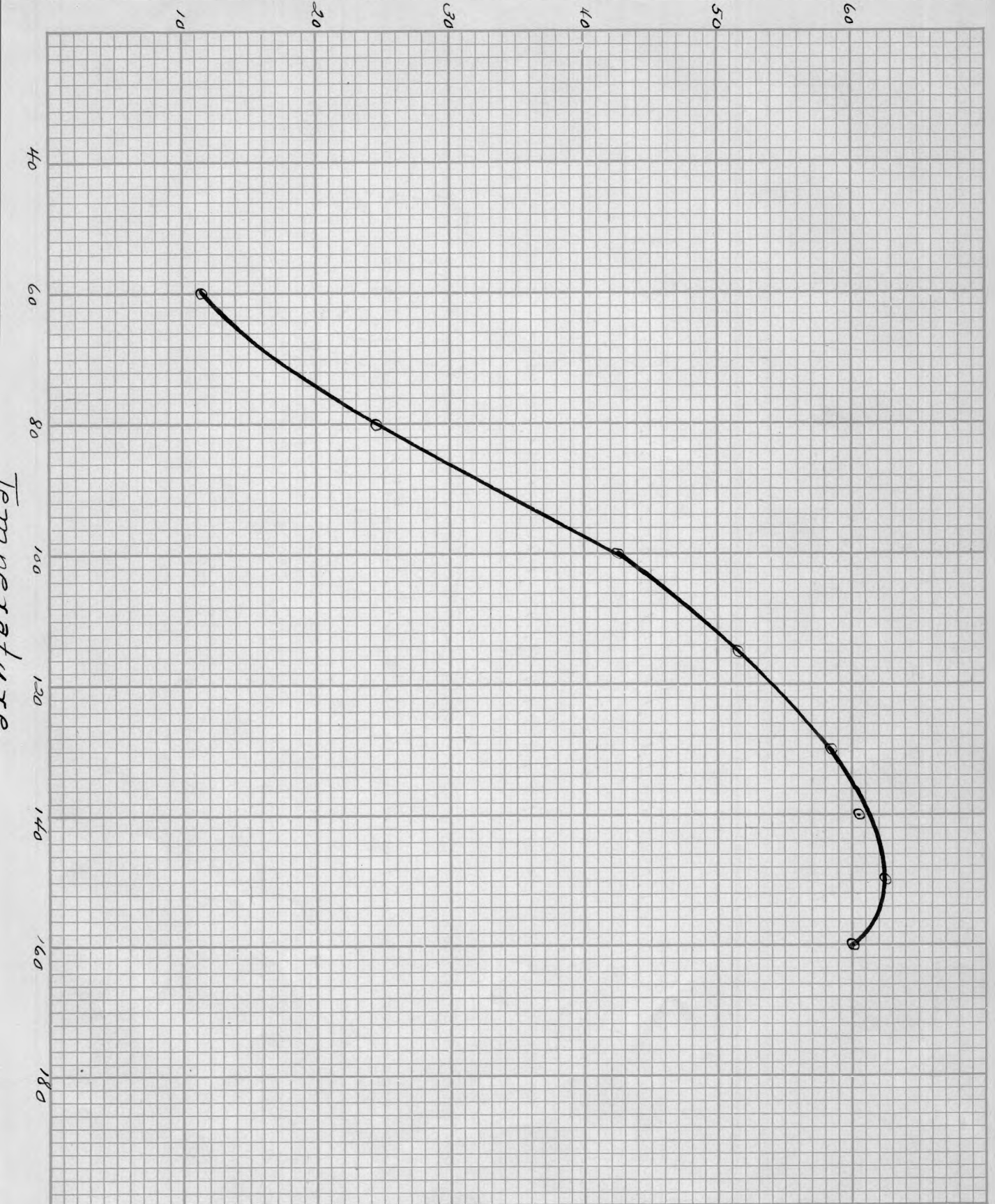


Fig. 1.

that described by these men, it is possible that it is homologous. Ward¹ further points out that if his acetic acid were originally dried by chemical means this compound decomposed into bromoacetic acid and hydrogen bromide at 90°, but if dried otherwise it decomposed losing bromine at 60°.

Since these red crystals appeared to decompose evolving bromine it would indicate, assuming Ward's² observation to be correct, that the acid or the bromine used was not perfectly dry.

Watson³ has also pointed out that if the acetyl bromide used as a catalyst is not in excess of the water present there is practically no catalytic effect observed. It is noted by reference to Table I, page 16, that better yields were obtained where bromine was dried under sulphuric acid. In view of this observation, it is possible that the low yields of brominated acid where the lesser weights of catalyst were used can be accounted for by the presence of water in excess of the catalyst which would hydrolyze it to the acid and thus destroy its catalytic effect. It would appear that in the cases of the greater weights of the acetyl bromide, such as 2.5 g. and 3.02 g., there is a sufficient amount to be in excess of the water and to serve as an efficient catalyst. It is an interesting fact that during the trials wherein a considerable amount of the red crystalline compound appeared that the bromine remained in great excess after the two hour period, and that there was no yield of brominated acid obtained.

¹ Loc. cit.

² Ibid.

³ J. Chem. Soc. 127, 2067-82 (1925)

It was observed during the course of the trials, where bromination of the acid did occur, as shown by the higher yields, that there was evolution of HBr from the commencement of the reaction period and this persisted for a few minutes after all of the bromine had been added. This evolution of HBr then stopped, but during the first stages of distillation white fumes, judged to be HBr, were given off profusely.

Whether the bromination of the propionic acid proceeds through the intermediate action of the anhydride¹, or through the acid bromide² itself it would be certain that a loss of HBr would necessarily reduce the bromine content of the reaction mixture, and thus reduce the yields of alpha brom- acid where molecular proportions are used. This would account, in part at least, for the lower yields reported in this investigation than are reported by other investigators where an excess of the halogen was used.

The percent of error, caused by loss in transfer of the liquids from one vessel to another would also be relatively high where such small amounts of chemicals were used.

¹J. Chem. Soc. 123, 2233-40 (1923)

²J. Chem. Soc. 127, 2067-82 (1925). Chem. Rev. 7, 178 (1930)

CHAPTER III
BROMINATION OF PROPIONIC
ACID IN THE PRESENCE OF ACETIC ANHYDRIDE

In the experimental investigation of the bromination of propionic acid in the presence of acetic anhydride the method was the same as for the preparations using acetyl bromide except for the difference in the nature and weight of the catalyst.

The same apparatus was employed as was described in Chapter II and the manipulation was duplicated as nearly as possible. The amounts of propionic acid (20 g.) and bromine (43 g.) were the same. The fractions were collected over the same boiling point ranges.

A weight of acetic anhydride (2.5 g.) was used equivalent to the 3.02 g. of acetyl bromide that was used in the experiments where the acid bromide was the catalyst.

Although in all cases the reaction proceeded quietly and was apparently complete in the course of a few minutes after all of the bromine had been added, the heating was continued for the full two hour period in order that the time factor could not possibly be interpreted as a variable having a profound influence on yields. As in the case of experiments with the acid bromide as the catalyst, the reaction product was distilled as soon as possible after the reaction period was completed so that the reaction

time would not be distorted by irregular intervals between the regular heat treatment and the distillation process.

Data are presented in Table III, page 24, that show the results of bromination that were obtained by three fractionations. Since they would then not be comparable with those in Table IV, page 24, which were obtained by only two fractionations, they were not plotted in Fig. 2, page 25.

It will be seen by reference to Table IV, page 24, that at the temperature of the room no bromination takes place during the two hour period, but that as the temperature treatment is raised the yields increase also. Reference to Fig. 2, page 25, will show this relationship more vividly.

It is interesting to note that the curves for the two catalysts are approximately of the same type, varying in yield values only slightly for corresponding temperature values up to 115° . However, the acetic anhydride curve almost flattens between 120° and 155° while the acid bromide curve shown in Fig. 1, page 19, reaches its peak at 150° and shows a maximum yield value higher than the maximum for the acetic anhydride.

It appears from this curve that the optimum temperature for bromination of propionic acid in the presence of acetic anhydride is within the range of 130° - 150° . Also, the indications are that for equivalent concentrations lower yields are obtained with this catalyst than with acetyl bromide.

TABLE III. YIELDS OF BROMINATED ACID FROM PROPIONIC ACID AND BROMINE IN THE PRESENCE OF ACETIC ANHYDRIDE

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
95-100	2.5	20.8	50.2	
95-100	2.5	21.4	51.7	50.9
110-115	2.5	18.1	43.7	
110-115	2.5	17.6	42.5	43.1
120-125	2.5	20.9	50.5	
120-125	2.5	23.5	56.8	53.8
125-130	2.5	25.5	61.4	
125-130	2.5	23.3	56.4	58.9
130-135	2.5	22.3	54.0	
130-135	2.5	20.0	48.4	51.2

TABLE IV. YIELDS OF BROMINATED ACID FROM PROPIONIC ACID AND BROMINE IN THE PRESENCE OF ACETIC ANHYDRIDE

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
25-30	2.5	0.0	0.0	
25-30	2.5	0.0	0.0	0.0
60-65	2.5	5.9	14.3	
60-65	2.5	5.4	13.1	13.7
95-100	2.5	18.1	43.7	
95-100	2.5	18.0	43.5	43.6
110-115	2.5	23.2	56.0	
110-115	2.5	22.9	55.2	55.6
130-135	2.5	24.5	59.2	
130-135	2.5	22.4	54.2	56.7
140-145	2.5	23.5	56.8	
140-145	2.5	23.2	56.0	56.4
150-155	2.5	23.0	55.6	
150-155	2.5	23.2	56.0	55.8

Mean Percentage Yield

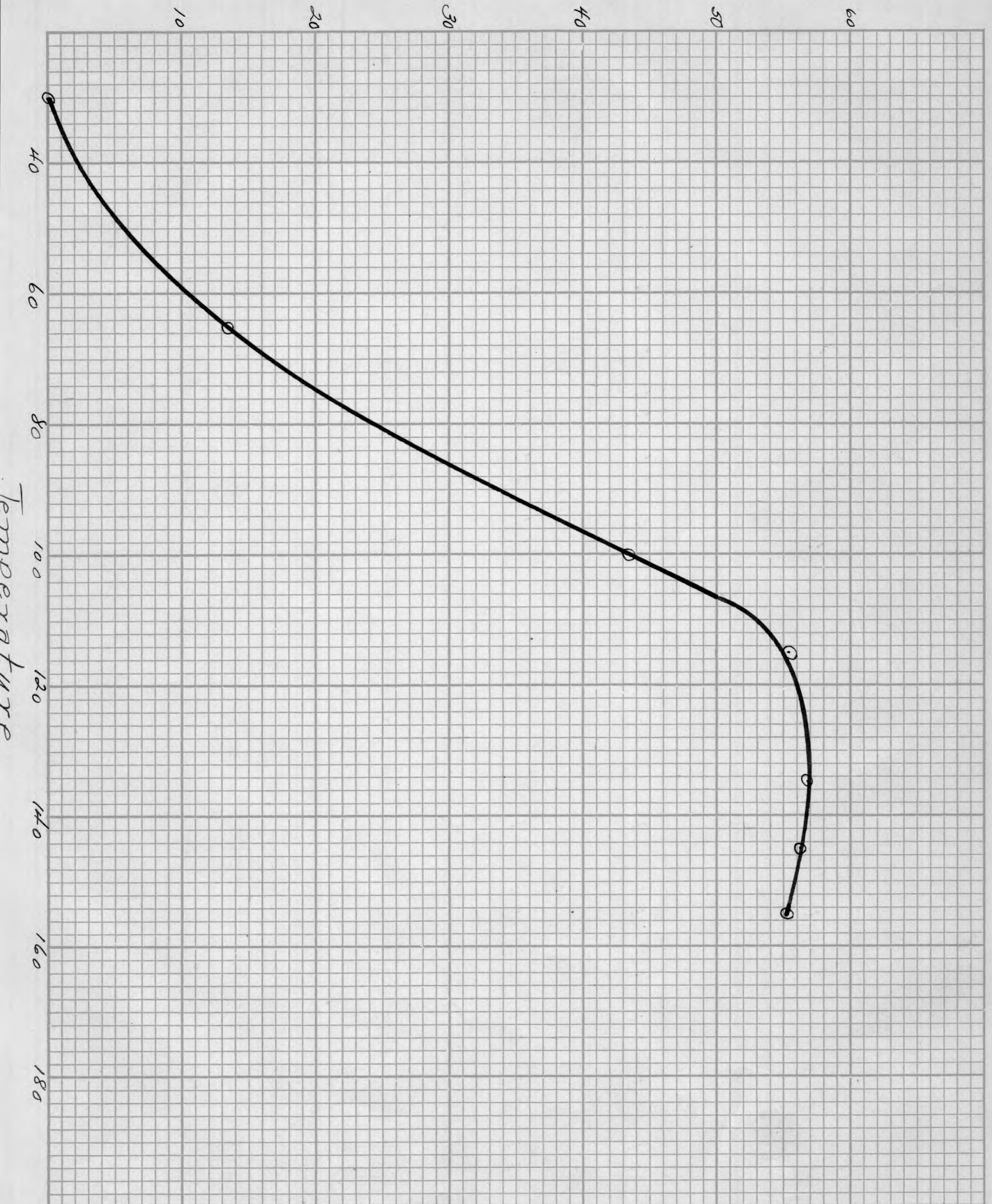


Fig. 2.

CHAPTER IV
BROMINATION OF PROPIONIC
ACID IN THE PRESENCE OF RED PHOSPHORUS

The method employed in the preparation of alpha brompropionic acid in the presence of red phosphorus duplicates, in the main, the method used wherein acetyl bromide and acetic anhydride were the catalysts and need not be described in detail here. Only important differences will be pointed out.

The first experiments with red phosphorus as the catalyst were of an exploratory nature, using two different weights of the catalyst, namely, .6 g. and .4 g.

Since it was apparent that the use of .6 g. of the catalyst did not result in better yields than the use of .4 g., it was decided to employ the lesser amount in the further investigations where the weight of the catalyst was to remain constant and the temperature treatments caused to vary over a wide range. However, the data shown in Table V, page 27, is only that obtained wherein yields were calculated only after a third fractional distillation. This data would not be suitable for comparison with that calculated from two fractionations. Consequently, this data is not plotted on Fig. 3, page 29.

It will be seen by reference to Table VI, page 28, and to Fig. 3, page 29, that the yield values do not lend themselves to

TABLE V. YIELDS OF BROMINATED ACID FROM PROPIONIC ACID AND BROMINE IN THE PRESENCE OF RED PHOSPHORUS

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
95-100	.6	18.4	44.5	
95-100	.6	17.2	41.7	43.1
110-115	.6	15.3	37.0	
110-115	.6	17.5	42.3	39.7
125-130	.6	16.2	39.2	
125-130	.6	22.0	53.0	46.1
95-100	.4	18.5	44.7	
95-100	.4	18.0	43.6	44.1

TABLE VI. YIELDS OF BROMINATED ACID FROM PROPIONIC ACID AND BROMINE IN THE PRESENCE OF RED PHOSPHORUS

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
25-30	.4	0.0	0.0	
25-30	.4	3.3	8.0	4.0
45-50	.4	3.1	7.5	
45-50	.4	5.5	13.3	10.4
65-70	.4	5.1	12.1	
65-70	.4	9.8	23.7	17.9
75-80	.4	14.0	33.8	
75-80	.4	12.6	30.4	32.1
85-90	.4	21.6	52.2	
85-90	.4	18.2	44.0	48.1
120-125	.4	21.2	51.2	
120-125	.4	21.0	50.7	50.9
135-140	.4	18.9	45.7	
135-140	.4	20.4	48.3	47.0
145-150	.4	23.9	58.0	
145-150	.4	23.0	55.6	56.8
155-160	.4	20.1	48.6	
155-160	.4	20.6	49.7	49.1

Mean Percentage Yield

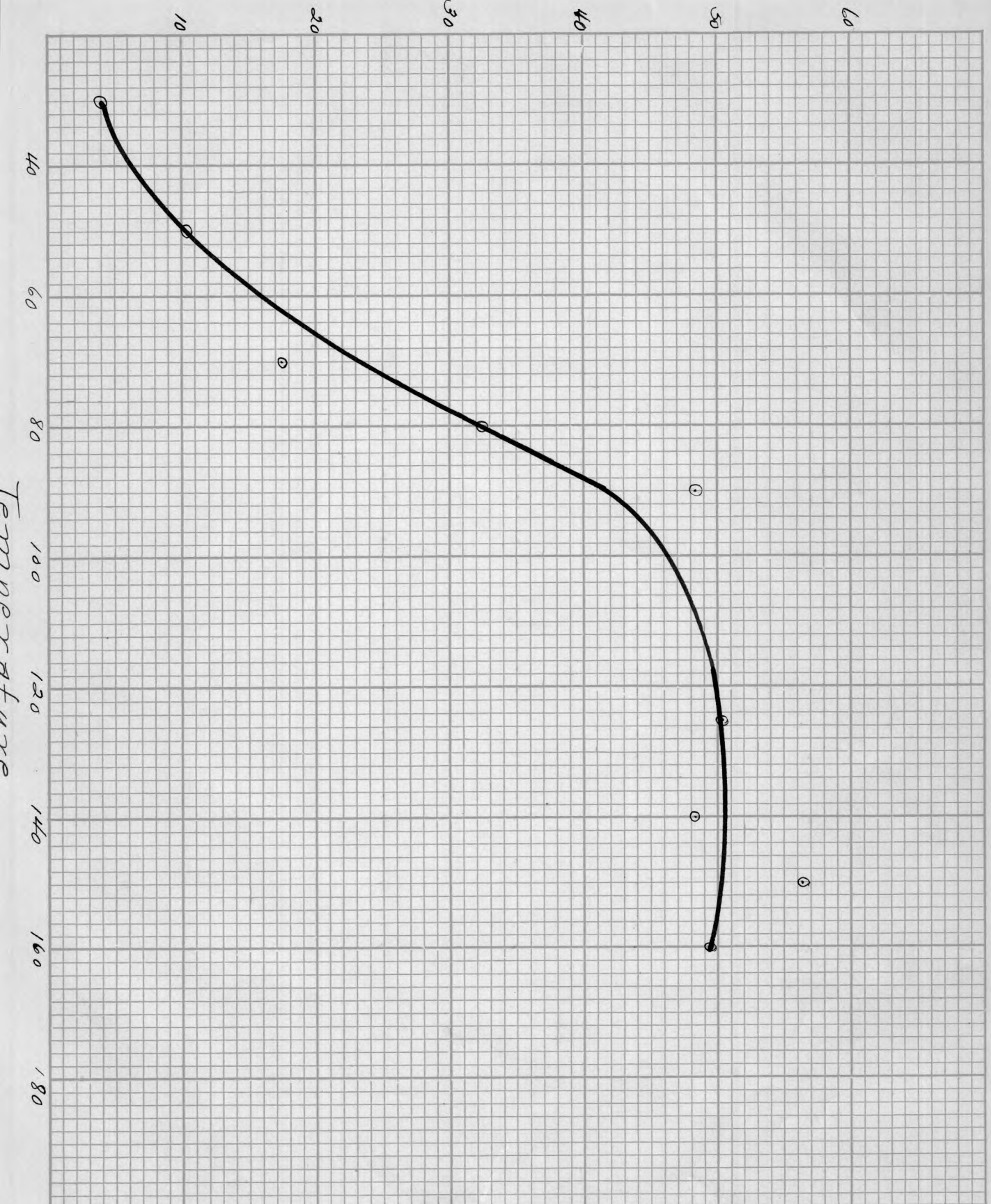


Fig. 3.

as rational a curve as was found to be the case with the other two catalysts investigated. Individual values do not fall on such a smooth curve. This would indicate greater experimental error, or that some unavoidable factor was exerting a great influence.

It is well known that in the case of catalysis in a heterogeneous system a slight difference of physical state can produce remarkable differences in the catalytic effect. If it were definitely known that here there is a case of surface catalysis, as is stated by Brückner¹ in his discussion of the action of red phosphorus, these variations would receive a possible explanation, for even though some precaution was taken to keep the phosphorus uniform it is entirely possible that considerable differences in the physical condition of the different samples could have existed.

However, in view of the fact that the phosphorus was probably converted into the tribromide early in the reaction period, which would then be evenly dispersed throughout the reaction mixture, it does not seem likely that variations from the normal curve could be accounted for in this way.

Brückner's² observation that most of the phosphorus remained unchanged at the end of the reaction could not be confirmed, but rather, the observation was made that only rarely was there any solid left in the reaction flask after the two hour treatment.

It was observed that during the course of all the reactions

¹Z. angew. Chem. 41, 226-9 (1928)

²Ibid.

wherein considerable bromination did occur that hydrogen bromide was evolved at approximately the same rate as in corresponding reactions wherein acetyl bromide and acetic anhydride were the catalysts.

The plotted data for these trials shown in Fig. 3, page 29, show a curve very similar to the curves for the acid bromide and the anhydride. Maximum yield values are lower, however, as would be expected since the weight of phosphorus used was not equivalent to that of the acid bromide or the anhydride.

It will be noted by reference to Fig. 3, page 29, that the optimum temperature for bromination in the presence of red phosphorus lies within the range of 125°-150°.

At this point it seems appropriate to make mention of the results of analyses of samples of the brominated acid prepared during the summer of 1933¹. The analysis for halogens was made by the method of Sepanow² as given in Kamm³. The results may be summarized as follows:

Catalyst	Fraction	Mean Percentage on Basis of Bromine
CH ₃ COBr	195°-202°	47.97
	150°-195°	23.39
(CH ₃ CO) ₂ O	195°-202°	46.96
	150°-195°	26.25
Phosphorus (red)	195°-202°	48.74
	150°-195°	30.22
Theoretical	195°-202°	52.23

Assuming that the analyses are correct, these data appear

¹ These analyses were made by Chas. Wagner, a student during the regular school year of 1933-1934.

² Ber. 39, 4056 (1906)

³ Kamm, O. Qualitative Organic Analysis, 2nd. Ed. pp. 199-200 (1932)

to indicate four points of interest, namely:

1. That the contents of the last fractions were kept fairly constant throughout the investigation thus far.
2. That the brominated acid content of the last fraction has been near the theoretical.
3. That there is a considerable amount of either the brominated acid or brompropionyl bromide in the 150°-195° fraction, either of which would tend to reduce the yield of the desired acid.
4. That the method of analysis is not as accurate as the Carius bomb-tube method for halogens.

However, even though the third possibility mentioned above be true, the effect on the conclusions of this investigation would be negligible so long as the losses have been kept constant.

CHAPTER V
BROMINATION OF PROPIONIC
ACID IN THE PRESENCE OF SULPHUR

In the preparation of alpha brompropionic acid using sulphur as the catalyst for the bromination the method and technique were essentially the same as in the preceding investigation and, therefore, need not be reviewed in detail here. Only differences will be mentioned.

The sulphur¹ used was weighed and added to the reaction flask containing the propionic acid.

The first set of trials, the results of which are shown in Table VII, page 34, were exploratory to determine the optimum weight of sulphur to use in the experiments where the varying factor was to be the temperature treatment. These results indicated that one gram of sulphur was approximately the correct amount and further experiments were then conducted with that amount.

The remainder of the work with sulphur consisted of an investigation of the effect upon yields when temperature treatments were varied over wide limits. Table VIII, page 35, and Fig. 4, page 36, show the data for these preparations. It will be noted by reference to this plotted data that again the same type of curve is produced and that the maximum yield values are reached at about the same temperature treatment range.

¹ A Baker Chemical Co. product labeled, Precipitated, C. P.

TABLE VII. YIELDS OF BROMINATED ACID FROM PROPIONIC
ACID AND BROMINE IN THE PRESENCE OF SULPHUR

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
125-130	1.0	18.1	43.8	
125-130	1.0	17.2	41.6	42.7
125-130	2.0	14.5	35.0	
125-130	2.0	16.5	39.9	37.5
125-130	.5	15.8	38.2	
125-130	.5	--	--	Rejected
125-130	1.5	16.6	40.1	
125-130	1.5	16.1	38.9	39.5

TABLE VIII. YIELDS OF BROMINATED ACID FROM PROPIONIC
ACID AND BROMINE IN THE PRESENCE OF SULPHUR

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
65-70	1.0	2.8	6.7	
65-70	1.0	2.4	5.8	6.3
95-100	1.0	7.4	17.9	
95-100	1.0	7.2	17.4	17.7
110-115	1.0	8.5	20.5	
110-115	1.0	7.7	18.6	19.6
120-125	1.0	16.2	39.0	
120-125	1.0	13.5	32.4	35.7
125-130	1.0	18.1	43.8	
125-130	1.0	17.2	41.6	
125-130	1.0	19.4	46.8	
125-130	1.0	17.7	42.8	43.7
130-135	1.0	16.2	39.2	
130-135	1.0	14.9	36.0	37.6
135-140	1.0	20.9	50.5	
135-140	1.0	20.5	49.5	
135-140	1.0	18.9	45.7	
135-140	1.0	17.4	42.2	47.0
140-145	1.0	17.3	41.8	
140-145	1.0	18.4	44.5	43.2
145-150	1.0	12.9	31.2	
145-150	1.0	12.7	30.7	
145-150	1.0	17.9	43.3	
145-150	1.0	15.2	36.9	35.5
150-155	1.0	16.3	39.4	
150-155	1.0	17.3	41.8	40.6
160-165	1.0	18.3	44.3	
160-165	1.0	18.3	44.3	44.3

Mean Percentage Yield

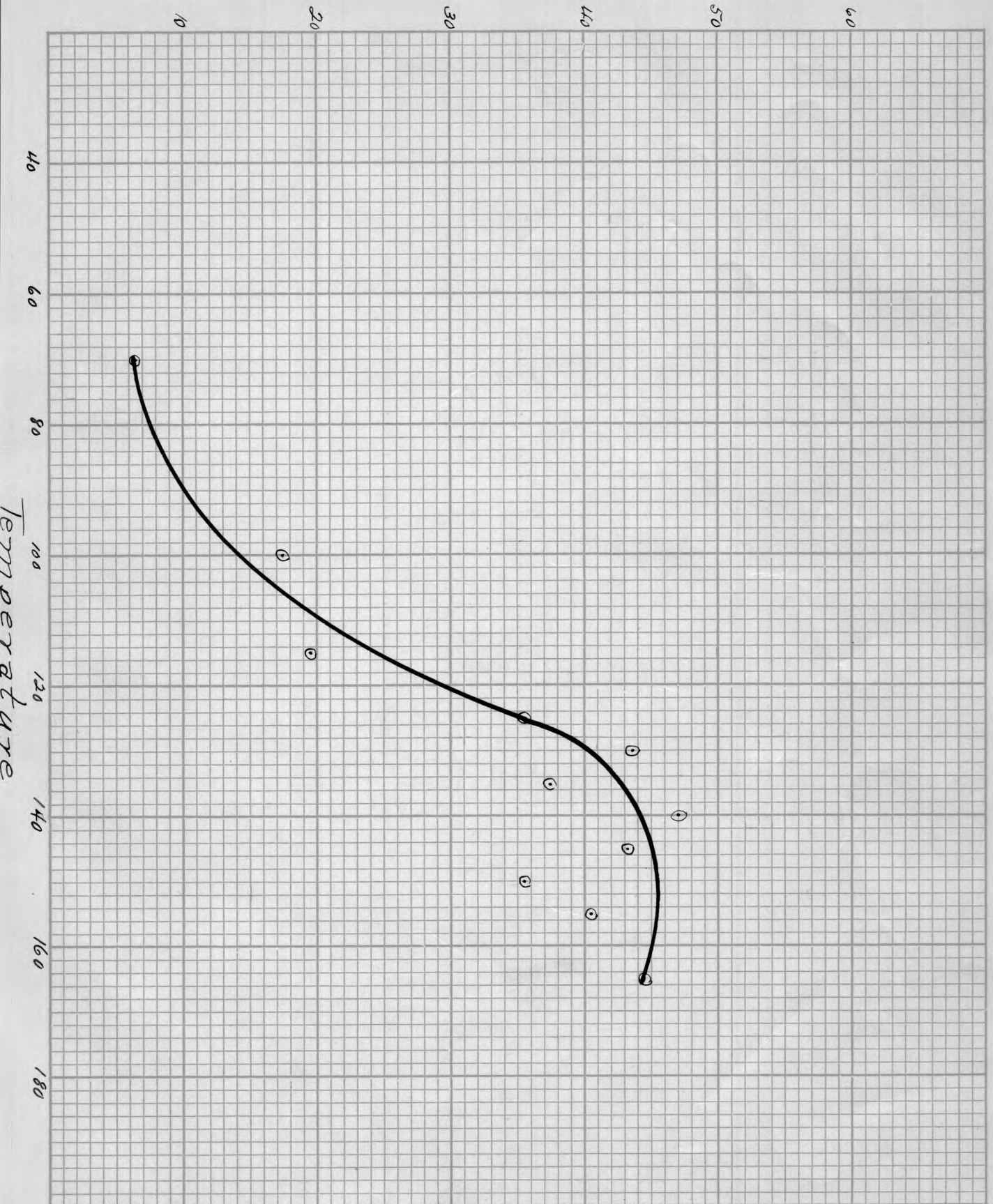


Fig. 4.

It is also noticeable that these data do not fall exactly upon a smooth curve, as was also found in the case of data obtained with phosphorus as the catalyst. Possibly, the same factor caused the irrational results in both cases.

It is important to note in the comparison of these curves that although sulphur was used in a much greater equivalent amount the yields obtained at corresponding temperature treatments were lower for sulphur in all cases.

It appears that results with sulphur more closely resemble those with phosphorus than those with the other two catalysts, which may be accounted for by the fact that with phosphorus and sulphur we are dealing with catalysts that are solids. At least, they may act in part as such. However, an investigation of the mechanism of these reactions is beyond the scope of this paper and this suggestion is offered only as a possible lead for anyone who might further pursue this study in the future.

It was noticed that, in general, the reactions employing sulphur did not proceed as smoothly as in the cases of reactions where the other catalysts were used. This was judged from the greater tendency for HBr to be evolved spasmodically.

CHAPTER VI
BROMINATION OF PROPIONIC
ACID IN THE PRESENCE OF IODINE

Here again the method used in the attempt to brominate propionic acid in the presence of iodine follows the same procedure as has been described in previous chapters.

The first weight (1.64 g.) of iodine crystals used was equivalent to the weight of the phosphorus that was used in the greater number of experiments with that catalyst. Then, since no yield of the alpha brom- acid was obtained, the temperature treatments and amounts of iodine were alternately varied in a number of trials. Reference to Table IX, page 39, shows the extent of these attempts.

Next, a pair of trials were run using .4 g. of red phosphorus and 1.64 g. of iodine with the same weights of propionic acid (20 g.) and bromine (43 g.) as were used before in an attempt to determine whether the iodine would catalyze in the presence of phosphorus.

A small increase in the yield here, over corresponding yields where the same weight of phosphorus was used alone, would indicate that the iodine had catalyzed the bromination were it not for an observation that discredits this view. Upon distillation of the final product it was found that iodine vapors persisted throughout, even into the last fraction after two fractional

TABLE IX. YIELDS OF BROMINATED ACID FROM PROPIONIC
ACID AND BROMINE IN THE PRESENCE OF IODINE AND
IN THE PRESENCE OF PHOSPHORUS AND IODINE

Temperature intervals	Grams of catalyst	Grams yield	Percentage yield	Mean percentage yield
95-100	4.0	0.0	0.0	
95-100	4.0	0.0	0.0	0.0
125-130	1.64	0.0	0.0	
125-130	1.64	0.0	0.0	0.0
140-145	1.64	0.0	0.0	
140-145	1.64	0.0	0.0	0.0
140-145	3.28	0.0	0.0	
140-145	3.28	0.0	0.0	0.0
150-155	4.0	0.0	0.0	
150-155	4.0	0.0	0.0	0.0
120-125	.4P + 1.64I	20.9	50.6	
120-125	.4P + 1.64I	22.6	54.5	52.6

distillations, to the extent of coloring the product a distinct reddish-violet.

This observation would show that, at least, part of the final product was iodine and that comparisons would be untenable.

This observation is a confirmation of Magidson's¹ observation during his investigation of the catalytic chlorination of acetic acid in the presence of iodine in which he states that his monochloroacetic acid could hardly be freed from contamination of iodine after repeated fractionations. He also reports, in the same reference, having used Brückner's² compounded catalyst consisting of PCl_5 , P and I in three different experiments and found that the mixed catalyst was unsatisfactory. That is, Brückner³ reports complete chlorination in two to three hours while Magidson⁴ reports that twenty to twenty-three hours were necessary to obtain a 50%-60% yield.

In view of the failure to obtain catalysis in this investigation and of the controversy discussed above, it appears that the value of iodine in the halogenation of these acids is still an unsettled question and open for further research.

¹J. Chem. Ind. 5, 528-9 (1928). C. A. 22, 4105³ (1928)

²Z. angew. Chem. 41, 226-9 (1928)

³Ibid.

⁴Loc. cit.

CHAPTER VII

SUMMARY

The effect of temperature on the catalytic bromination of propionic acid in the presence of small quantities of acetyl bromide, acetic anhydride, red phosphorus, sulphur and iodine has been investigated.

Mean values for yields of alpha brompropionic acid plotted against the corresponding temperatures gave similar types of curves for the above mentioned catalysts showing the effects of temperature to be analogous.

Optimum temperature ranges for treatment of propionic acid and bromine in the presence of the various catalysts were found to be as follows:

Acetyl bromide-----	150°-160°
Acetic anhydride-----	130°-150°
Phosphorus (red)-----	125°-150°
Sulphur-----	130°-150°
Iodine-----	Not determined.

Comparison of the efficiency of the five catalysts on the basis of maximum yields ranks them as follows:

Catalyst	Maximum Percentage Yield
Acetyl bromide-----	62.6
Phosphorus (red)-----	56.8
Acetic anhydride-----	56.7
Sulphur-----	47.0
Iodine-----	00.0

Comparison of the efficiency of the five catalysts on the basis of smoothness of bromination ranks them as follows:

Acetyl bromide-----	First
Acetic anhydride-----	Second
Phosphorus (red)-----	Third
Sulphur-----	Fourth
Iodine-----	Fifth