GLYCOLLIC ACID

A Thesis

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FOREWORD

To Dr. Hilton Ira Jones, to
whose untiring interest and un-
failing cooperation the writer
owes much, and under whose di-
rection and supervision this
work has been brought to its
completion, the following pages
are respectfully dedicated.

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INTRODUCTION

Among the most notable outgrowths of the recent war is the new impetus which it has furnished chemistry and the numerous industries which find the very fundamentals of their existence based upon that particular branch of science. Especially is this true as regards the field of organic chemistry, which, at the present time, is fast being accorded the degree of recognition it so well deserves. Previous to the outbreak of hostilities, America and the other great powers looked, with one accord, to Germany for their supply of rare organic chemicals and dyestuffs. Indeed, so prevalent was the idea that no one but the Teuton could produce these all important materials, that none but the most sporadic and abortive attempts were undertaken elsewhere, even in the laboratories of our own United States. However, with the advent of war and the consequent cessation of imports from Germany, the other powers became aware that were a famine to be averted, immediate measures toward the production of organic chemicals was a matter of paramount importance. The impetus thus furnished served to stimulate the chemists of this and other countries to the domestic production of chemical goods on a hitherto unprecedented scale. The remarkable efficiency shown by the American chemist in meeting this situation is now a matter of history.

Nor did these activities remain confined wholly to the industrial and commercial field. America was upon the threshold of an industrial renaissance, and the urgency of the situation demanded that every available source of energy be brought to bear upon it. It is not surprising, then, to find this phase of industrial activity mirrored in the life of many of our great educational institutions today. Chemists the country over have become imbued with the spirit of chemical research, and the response which has been elicited from our colleges and universities augurs well for America's future in the chemical world.

In direct connection with this thot is the material embodied in the following pages, and has to do with the study of glycollic acid and the methods heretofore used in its production. Attention has been given to possible improvements in these methods as well as means by which new ones could be devised. Glycollic acid has, heretofore, been a laboratory curiosity; due, principally, to numerous difficulties incident to its production in any but the smallest quantities. Consequently, its status has been one of purely theoretical interest; but like many other similar compounds, the production of which has been made desirable thru the extensive research now in progress, a demand has been created which makes the investigation of this problem a matter of practical import. It shall be the purpose of this paper, then, to deal with the chemistry and history of glycollic acid, to set forth briefly a resume of the literature concerning it, and lastly to give an account of the experimentation carried out by the writer.

In the preparation of glycollic acid, the first matter
to be taken into consideration was a compilation of the
methods hitherto used in its manufacture, and a study of
these methods from the standpoint of their desirability and
applicability. Obviously, as a perusal of the means of
preparation set down in the following pages will reveal,
many of these methods are of little more than passing
interest, owing to the small yield of glycollic acid
obtained, to the cumbersome nature of their mechanism,
and often to the fact that the materials employed are in
themselves rare or even unobtainable. Therefore, those
methods involving the use of common reagents, and giving
promise of adaptability and ready manipulation were selected,
and an effort made to put them on a comparative basis as to
ease of control, yield, etc. While the nature of some of
the processes investigated was such as to admit of little
variation in procedure, nevertheless the possibility of
introducing innovations and modifications, such as would
promise a betterment or simplification of these methods,
was considered at all times. In a few instances, such
means were employed and found to be of material assistance,
and will be touched upon as they come up in the account of
the experimental work concerning them.

In dealing with this subject, a study was made, not
only of glycollic acid itself, but of the nature of its
related compounds as well. Of especial interest is its
relation to many well-known organic substances which may be
readily synthesized from it; and while research into such
a field promises much, the fact that we are concerned
primarily with the production of glycollic acid itself
precludes the possibility of such study at this time. No
attempt will be made, therefore, to mention the individual
derivatives and related compounds with an intimate account
of their chemical structure and constants. However, they
will be considered briefly in a section devoted to a short
account of such derivatives.

Emphasis, then, in this research, has been laid upon
the production of glycollic acid alone to the exclusion of
such matters as would tend to detract from the importance
of the main issue; dealing first with the chemistry and
nature of glycollic acid from the theoretical standpoint,
the possible means by which its production is possible,
and, lastly, the practical application of such methods.

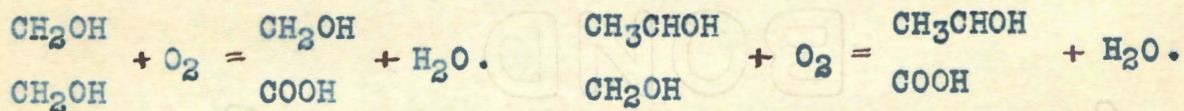———o———

THE CHEMISTRY OF GLYCOLLIC ACID

(a) Constitution of Glycollic Acid.

Glycollic acid, $CH_2(OH).COOH$, known also as hydroxy-acetic acid, is a member of the group of so-called alcohol or oxy-acids to which have been ascribed the general formula of $C_nH_{2n}.OH.COOH$. The chemical deportment of the acids of this series is singular in that they constantly exhibit two-fold characteristics. Since they contain the carboxyl (COOH) group, they are monobasic acids with all the attaching properties and transpositions of the latter, while the presence of the hydroxyl (OH) group within the molecule lends to it all the properties of the monohydric alcohols. As in dihydric compounds these alcohols are classed as primary, secondary, and tertiary, according as they contain, in addition to the COOH group, the group CH_2OH, characteristic of all primary alcohols; the radical CHOH, peculiar to all secondary alcohols; and the triple-bonded C.OH or tertiary group. This is demonstrated in the differing behavior of these bodies when subjected to oxidation. The manner in which the alcoholic hydroxyl group in an alcohol-acid acts upon the carboxyl group in the same molecule depends upon the position of the two groups in relation to each other. These acids are termed oxy- or hydroxy-fatty acids because of their derivation from the members of the fatty acid series, in which a hydrogen atom linked with the first carbon atom of the chain is considered as replaced by a hydroxyl group. Thus, glycollic acid, $CH_2.OH.COOH$, is the hydroxyl derivative of acetic acid, $CH_3.COOH$, in which the replacement of H in the methyl radical of the latter by OH is effected. Among the best known and most important representatives of this series are glycollic acid and the ordinary lactic acid of fermentation.

(b) Methods of Preparation.

There are a number of general methods which have been proposed whereby the formation of glycollic acid is possible. Briefly, these are as follows:

(1) By the careful oxidation of (a) di-primary, primary-secondary, and primary-tertiary glycols with dilute nitric acid or with a platinum sponge and air; and (b) the oxidation of oxyaldehydes. (a) is illustrated as follows:

$$\begin{matrix} CH_2OH \\ | \\ CH_2OH \end{matrix} + O_2 = \begin{matrix} CH_2OH \\ | \\ COOH \end{matrix} + H_2O. \qquad \begin{matrix} CH_3CHOH \\ | \\ CH_2OH \end{matrix} + O_2 = \begin{matrix} CH_3CHOH \\ | \\ COOH \end{matrix} + H_2O.$$

(Glycol to Glycollic Acid)   (a-propylene glycol to a-lactic
                                                  acid)

(2) By the action of nascent hydrogen (from sodium amalgam or from zinc and HCl) on aldehyde-acids, the ketonic-acids (such as pyroracemic acid, $CH_3.CO.COOH$), and the dicarboxylic acids, such as oxalic acid. Thus:

$$CH_3.CO.COOH + H_2 = CH_3.CH(OH).COOH.$$

$$COOH.COOH + 2 H_2 = CH_2.OH.COOH + H_2O.$$
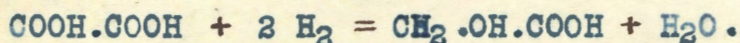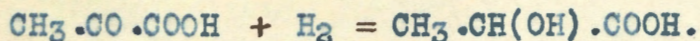
This reaction has often been used in the preparation of beta-, gamma-, and delta-oxy-acids from the corresponding ketone carboxylic esters.

(3) Some fatty acids have OH directly introduced, as by oxidation in alkaline solution with $KMnO_4$. This, however, applies only to acids containing the tertiary group, CH.

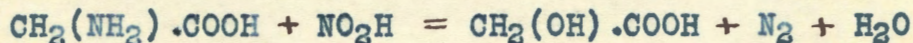(4) By heating an unsaturated fatty acid to 100° C. with aqueous KOH or NaOH.

(5) By the interaction of monohalogen fatty acids with Ag_2O, boiling alkali, or H_2O. Thus:

$$CH_2Cl.COOH + H_2O = CH_2(OH).COOH + HCl$$
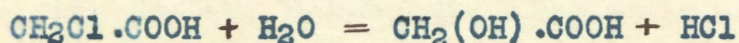
(Chloracetic acid to glycollic acid)

In this manner the a-oxy-acids are obtained from a-derivatives.

(6) By the action of HNO_2 on amido-acids:

$$CH_2(NH_2).COOH + NO_2H = CH_2(OH).COOH + N_2 + H_2O$$

(Glycocoll)   (Glycollic acid)

(7) By boiling diazo-fatty acids with with water or dilute acids.

(8) By treating a-ketone-alcohols (as butyroin and isovaleroin) with alkalies and air.

(9) Neucleus-synthetic methods: by allowing HNC or HCl to act on aldehydes and ketones. Oxycyanides, the nitriles, are first formed, after which HCl changes the CN group into COOH:

$$H.CHO + NCH = CH_2OH.CN$$
(formaldehyde to glycollic nitrile)

$$CH_2OH.CN + 2 H_2O + HCl = CH_2OH.COOH + NH_4Cl$$
(glycollic nitrile to glycollic acid)
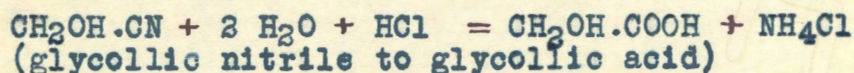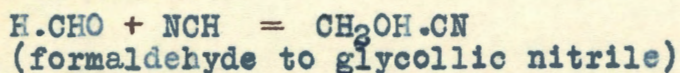
In preparing oxy-cyanides, the aldehyde or ketone is treated with pure HCN; another method is to add finely pulverized KCN to the ethereal solution of the ketone and follow this with the gradual addition of conc. HCl, which changes cyanides to acids. Amides of the acids are first formed in the cold, but on boiling with more dilute acid they are changed to acids. The change may be more quickly effected with a little dilute sulfuric acid.

(10)   Glycol chlorhydrins may also be used with KCN and acids. Thus, $CH_2OH.CH_2Cl$ gives $CH_2OH.CH_2.COOH$.

(11)   Synthesis of oxy-acids may be readily accomplished thru the action of zinc and alkyl iodides on diethyl oxalic ester (Frankland and Duppa method). This procedure is analogous to the formation of tertiary alcohols from formic esters, in which one and two alkyl groups may be introduced into one carboxyl group. Thus, by twice treating diethyl oxalic ester, $C_2H_5.OOC:COO.C_2H_5$, with zinc methyl, $Zn(CH_3)_2$, dimethyl oxalic ester, $(CH_3)_2C(OH).COO.C_2H_5$, is formed. This compound, better known as di-methyl oxyacetic ester, or the dimethyl derivative of glycollic acid, may be transformed into the latter thru treatment with HI.

(12)   From hippuric acid, $C_6H_5CONH.CH_2COOH$, either by treatment with HNO_2 and decomposition of the resulting benzoyl-glycollic acid by boiling with dilute H_2SO_4, or by treatment with the latter and decomposition of the resulting glycocoll with HNO_2. (1)

(13)   Tartronic acid, $COOH.CH(OH).COOH$, is heated to 180° C.; the residue, consisting of nearly pure glycolide, is dissolved in aqueous KOH. $AgNO_3$ is then added, and the precipitated silver glycollate decomposed by HCl. (2)

(14)   From glyoxal by the action of alkalies (Debus) and even of water. From glyoxal and water heated to 150° C., one-third being converted into glycollic acid. (3)

(15)   By boiling silver-brom-acetate with water. By boiling iodo-acetic acid with moist Ag_2O, or lead iodo-acetate with water (4). Likewise, by boiling chloracetic acid with alkalies, or by heating crystallized chloracetate of potassium or sodium (5).   By boiling chloracetonitrile with line-water (6).

(1) Socoloff and Strecker, A., 80, 18.
(2) Dessaignes, C.R., 38, 44.
(3) De Forcrand, C.R., 98, 295.
(4) Perkin and Duppa, P.M., (4), 18, 54.
(5) Kekule, A., 105, 286.
(6) Beckurts and Otto, Ber., 9, 1591.

(16) By allowing a solution of glycol (1 vol) in nitric acid (4 vols., S.G. 1.33) to stand for some time. (1)

(17) Together with other products from propylene glycol by oxidation with HNO_3, or with air and platinum black. (2)

(18) By placing in a tall cylinder layers of alcohol, water, and conc. HNO_3 one above another, and leaving the liquids to mix by diffusion, which they do in about a week. Glyoxal, glyoxalic and oxalic acids, aldehyde and acetic acid are formed at the same time. (3)

(19) Found in the mother liquor in the preparation of mercury fulminate. (4) (5)

(20) By the action of zinc and dilute H_2SO_4 on oxalic acid. (6) (7)

(21) By boiling an aqueous solution of oxalic acid 8 days with zinc. (8) (9)

(22) By the action of HNO_3 on acrolein. (10)

(23) When tartaric acid is warmed with conc. H_2SO_4 at 45° C. it gives off CO, CO_2, and SO_3, and the residue contains glycollic, pyruvic, tartaric, and racemic acids. These acids are separated by crystall- ization, first of their barium, then of their calcium salts. (This is described more fully under History). (11)

(24) From acetylene tetrachlorid and alcoholic KOH at 100° C. (12)

(25) From dichlorovinyl ethyl oxid and water at 130° C. (13)

(1)   Wurtz, C.R., 45, 306.
(2)   same as (1).
(3)   Debus, A, 100, 1.
(4)   Cloez, C.R., 34, 264.
(5)   Fahlberg, J. pr., (2) 7, 331.
(6)   Schulze, Z., 1862, 616, 682.
(7)   Church, C.J., 16, 301.
(8)   Crommydis, Bl., (2) 27, 3.
(9)   De Forcrand, Bl., (2) 39, 310.
(10) Claus, A. Suppl., 2, 119.
(11) Bouchardat, C.R., 89, 99.
(12) Berthelot, Z., 1869, 683.
(13) Guether and Brockhoff, J. pr., (2) 7, 114.

(26) Occurs among the products of the action of
HNO3 on glycerin.

(27) Together with gluconic and formic acids by
the action of red HgO and baryta-water on glycerin. (1)
Also from glycerin and Ag2O. (2)

(28) By heating cupric acetate (2 pts) with water
(5 pts) at 200° C. in a sealed tube, copper glycollate
and cuprous oxid being formed. (3)

(29) By oxidizing inulin with HNO3. (4)

(30) From glucose, levulose, or starch-sugar by
oxidation with Ag2O. Glycollic, oxalic, and carbonic
acids are formed. The theoretical yield of glycollic
acid with dextrose at ordinary temperatures is 41-47 %
of the theory; with levulose, 20-22 %; and with starch-
sugar, 35 %. (5)

(31) To a solution of 50 grams of chloracetic
acid in 500 c.c. water is added 120 grams BaCO3. Reflux
for 30 hours or until evolution of CO2 ceases. Agitate
frequently toward the last. Filter off the excess of
BaCO3, and precipitate the barium with the calculated
amount of H2SO4. Filter hot and wash the precipitate
several times with water. Filter again and concentrate
in vacuo. The resulting syrup is subjected to gentle
heat over a water-bath for two hours which serves to
expel most of the HCl present as an impurity. The
glycollic acid crystallizes from this upon standing.(6)

(32) By the oxidation of glycerol with Ag2O in
the presence of alkali. 10 grams of glycerol in 200 c.c.
of water, 6 grams of slaked lime, and the Ag2O from 60
grams of AgNO3 are placed together and heated at 60° C.
for 4 hours. Treat with CO2 to precipitate excess cal-
cium , and filter. Calcium glycollate is obtained upon
concentrating the filtrate. By redissolving this and
decomposing with oxalic acid, glycollic acid is
liberated. (7)

(1) Kiliani, Ber., 16, 2415.
(2) Cazeneuve, C.R., 89, 525.
(3) Kiliani, A., 305, 168.
(4) Kiliani, A., 305, 191-193. (J.C.S., 1881, 40, 251.
(5) Williams, J.A.C.S., 1917, 39, 109.
(6) Kiliani, Ber., 16, 2414-2416. (J.C.S., 1884, 46, 295.
(7) Herzfeld, A., 345, 27.

(33) By the electrolytic reduction of oxalic acid.
(Tafel and Friedrichs, Ber., (1904), 37, 3187; Centralblatt,
1905, II, 1699. Described in Cohen's "Practical Organic
Chemistry", 1913). A similar method is described in the
J.C.S., (1908), 94, 600, taken from the Deutsche Gold- und
Silber-Scheide Anstalt (D.R.-P., 194038).

(34) HCHO and HCN react to form glycollic nitrile,
CH$_2$(OH).CN. Evaporate and extract the nitrile with ether.
The nitrile is converted into glycollic acid with dilute
acid, such as HCl. (1)

(35) An aqueous solution of chloracetic acid, when
boiled with water for a few hours, gives glycollic and
hydrochloric acids. Distill in vacuo and concentrate to
a residue on the water bath. The resulting syrup contains
a trace of Cl which is practically all removed by again
evaporating with water. Glycollic acid crystallizes from
the syrup. (2)

(36) The mother liquors of fulminating mercury are
treated with H$_2$S and Ca(OH)$_2$ to separate the mercury from
the oxalic and glyoxalic acids present. By boiling,
calcium oxalate is formed, and the calcium glyoxalate is
decomposed giving calcium glycollate. Filter. Excess
lime is precipitated with with CO$_2$. Evaporate the filtrate
to a syrup. Calcium glycollate separates and is purified
by recrystallization. (3)

(37) To a solution of 500 grams of chloracetic
acid in 4 liters of water are added 560 grams powdered
marble. Reflux for three days. Three layers are formed,
two of which contain hydrous and anhydrous calcium
glycollate, respectively. These are decomposed with
oxalic acid, liberating glycollic acid. (4)

(1) Henry, C.R., 110, 759-760. (J.C.S., 1890, 58, 739.
(2) Fittig, Ber., IX, 1198. (J.C.S., 1877, 31-59.
(3) Fahlberg, J. pr. Chem., (2), VII, 329-346. (J.C.S.,
1874, 27, 142.
(4) Caseneuve, C.R., 89, 525. (J.C.S., 1880, 38, 32.

(c)   Isomerism of Glycollic Acid.

In considering the possible isomers of the oxy-acids, we find that glycollic acid is not isomeric with any other substance, altho it is to be expected that the higher members of the series, thru the increasing complexity of the molecule, would give rise to such compounds. As a matter of fact, propionic acid, $CH_3.CH_2.COOH$, the member next above glycollic acid, yields two oxy-acids; n-butyric acid yields three, and iso-butyric acid two such acids. However, in considering the structure of acetic acid, $CH_3.COOH$, of which glycollic acid, $CH_2.OH.COOH$, is the monohydroxyl derivative, it is at once apparent that only one such derivative is possible in this case. Glycollic acid is, then, a primary alcohol-acid, and is the only monohydroxy derivative of its corresponding fatty acid.

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(d)   Properties and Behavior of Glycollic Acid.

The properties of glycollic acid are represent-ative of those of all other oxy-fatty acids. Such acids, containing, of course, one hydroxyl group, are more readily soluble in water and less soluble in ether than the parent acids. They are less volatile and in general cannot be distilled without decomposition. Especially is this true of glycollic acid; for, when the aqueous solution is concentrated too closely, glycollic anhydride is formed. However, if evaporation is properly carried out, the acid characteristically remains as a brown syrup from which it may be crystallized. A careful search of the journals reveals the fact that glycollic acid is exceedingly difficult to obtain in the crystalline form, and the experience of the writer has been such as to amply confirm this fact. Indeed, when formed thru the hydrolysis of chloracetic acid with water, the hydrochloric acid produced is sufficient to altogether inhibit its crystallization. (l)   The acid differs morphologically depending upon the character of the medium from which it is crystallized, it separating from aqueous solution in stellated needles, and from alcohol or ether in plates. Both of these methods result in the production of a body which melts at $79-80°$ C., and is unalterable in the air. The difficulty met with in crystallization is ascribed to various impurities which are inevitably present in many of the methods used in its production, and to the fact that being closely related to the sugars, it partakes of their property of being exceptionally difficult to crystallize.

HOLZER, Ber., 16, 2954-2957

Glycollic acid, like the other alcohol-acids, acts as a monocarboxylic alcohol in yielding normal salts, esters, amides, and nitriles thru a change in the COOH group. Thus: $CH_2.OH.COOH$ ---- $CH_3.OH.COO.C_2H_5$ ---- $CH_2.OH.CO.NH_2$ ---- $CH_3.OH.CN$.

The remaining OH group behaves in a manner similar to that present in alcohols. The H may be replaced by alkali metals and alkyl groups, or acid radicals or a nitro group may be substituted for it by the action of chlorides of monobasic acid radicals and a mixture of concentrated nitric and sulfuric acids. The action of PCl_5, for example, is to replace the OH with Cl. In this manner glycollic acid is transformed into glycolyl chlorid (chloracetyl chlorid) :

$$CH_2.OH.COOH + 2\ PCl_5 = CH_2.Cl.CO.Cl + 2\ POCl_3 + 2\ HCl.$$
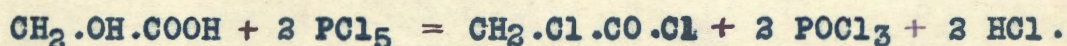
The above equation is representative of the fact that, instead of the acid chlorid being formed thru such treatment, the product obtained is the chlorid of the corresponding monochlor-fatty acid. Indeed, if such substances as the acid chlorides of any of the fatty acids exist, they have escaped the searchlight of ample and exhaustive experimentation. In the above case, the Cl combined with CO is very reactive with water and alcohols, giving free acids and their esters. The remaining Cl atom is more firmly united as in the case of ethyl chlorid, altho under suitable treatment it may be replaced by other radicals. Thus, three ethyl esters of glycollic acid are known: ethyl glycollic ester, $CH_2.OH.COO.C_2H_5$; ethyl glycollic acid, $CH_2.OC_2H_5.COOH$; and ethyl etho-glycollic ester, $CH_2.OC_2H_5.COOC_2H_5$. The alkyl group in combination with COO is readily attacked by alkalies with the formation of COOH.

Upon being heated with hydriodic acid, glycollic acid is reduced to its corresponding fatty acid, but upon oxidation aldehyde acids are obtained. In this manner glycollic acid may be oxidized to oxalic acid, glyoxalic acid being formed as an intermediate product. When heated with mineral acids or when exposed to SO_3 fumes glycollic acid undergoes a change into a cyclic double ester. This change is similar to that in which the higher a-oxy-acids undergo a transformation into lactides, and takes place thru the condensation of two molecules of the acid with the elimination of a molecule of water. This change may be as readily achieved by merely heating the acid, the product, which has already been referred to, being known as glycollic anhydride, or more properly as glycoglycollic acid. If, however, glycollic acid is strongly heated to a

high temperature, glycolide is formed. The structure of these compounds is best seen as represented below:

$$CH_2.OH.COO$$
$$|\qquad|$$
$$COO.OH.CH_2$$

$$CH_2.O.CO$$
$$|\qquad|$$
$$CO.O.CH_2$$
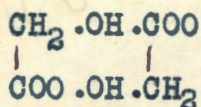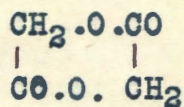
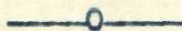(Glycoglycollic acid)   (Glycolide)

Glycollic acid is identified by the formation of its phenylhydrazine salt, which crystallizes slowly, but almost completely, from alcohol in hexagonal plates melting at 100-101° C. These, however, are unstable even at ordinary temperatures and decompose with evolution of gas.

Glycollic acid is formed, not only by the oxidation of l-arabinose, but from all aldo- and keto-pentoses and -hexoses.

When heated with acetic anhydride it forms acetyl-glycollic acid, which crystallizes in needles, readily soluble in water, and melting at 68-70° C. (1)

The following sensitive reactions aid in the ready identification of glycollic acid. (2) It has been found that glycollic acid, when heated with H_2SO_4, yields HCHO. 0.3 c.c. of a 2 % solution of the acid is warmed to 100° C. for two minutes with 2 c.c. H_2SO_4 (S.G. 1.84). Cool and add one drop of alcoholic guiacol or codeine solution. Codeine produces a yellow coloration changing to an intense violet, while guaiacol gives a violet changing to a brown upon dilution with alcohol, or to a green tint with p-cresol. In using the phenol, the mixture of glycollic acid, H_2SO_4, and phenol is slightly diluted with acetic acid and the whole warmed together.

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(e) Derivatives of Glycollic Acid.

While glycollic acid itself is little known, a study of the literature reveals the fact that it is very closely related to, and indeed may form the chemical basis of, many other organic compounds. However, since we are dealing primarily with the production of the acid itself, an exhaustive description of its many related compounds would be beside the question. Suffice it to say that other than the metallic salts which have been prepared,

(1) Nef., A., 1907, 357, 214-312. (J.C.S., 1908, 94, 5-8.
(2) Deniges, Bull. Soc. Chim., 1909, (IV) 5, 647-649. (J.C.S., 1909, 96, 627)

the ethers and ethereal compounds, sulfur compounds, amido compounds, carbamide compounds, and guanidine compounds are known. Among these aresuch well-known compounds as creatinine, creatine, sarcosine, betaine, muscarine, glycocoll, and hippuric acid.

Altho a minimum of importance has been attached to the derivatives of glycollic acid in the course of this research, a study of the methods of producing the acid has led, incidentally, to the preparation of a number of its metallic salts. Among those prepared are the copper, lead, barium, cobalt, nickel, calcium, manganese, and basic lead salts. All of these, with the exception of the last namedm were prepared by heating an aqueous solution of glycollic acid with the carbonate of the metal. The resulting metallic salt of glycollic acid was in each case filtered off and recrystallized from water. The basic lead salt was prepared by treating a solution of the acid with a freshly prepared solution of basic lead acetate. This salt, however, is difficult of purification owing to its relative insolubility in the ordinary menstruums. The others mentioned are reasonably soluble in water, especially the lead salt, thus permitting of their being readily obtained in the pure condition. In the production of the metallic derivatives of glycollic acid, it has been the experience of the writer that treatment with the metallic carbonate presents by far the simplest and best means of preparation. The following reaction amply demonstrates this type of reaction:

$$2 \; CH_2.OH.COOH + PbCO_3 = (CH_2.OH.COO)_2Pb + H_2CO_3$$
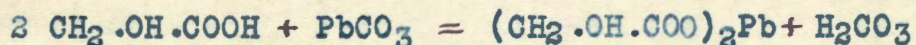
In this case, the only other substance produced is carbonic acid, which, owing to its instability, decomposes, as fast as formed, into water and carbon dioxide gas. In this manner the difficulties attendant upon the elimination of impurities which would tend to inhibit the reaction are completely avoided.

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HISTORY OF GLYCOLLIC ACID

Glycollic acid occurs in nature in unripe grapes,
but disappears during the process of ripening, doubtless
being transformed into tartaric acid. (1) It is also
found as the potassium salt in the grease of sheep's wool,
and in the green leaves of the Virginia creeper. (2)
Its presence in suint with pyrotartaric acid as the (3)
potassium salt has been demonstrated, and it is also
said to occur in the juice of the sugar cane. (4)

To Strecker belongs the credit for first isolating
glycollic acid, he having obtained it by the action of
nitrogen trioxide on glycocoll (amido-acetic acid), and
later, in collaboration with Socoloff, from hippuric acid
(benzoyl amido-acetic acid). (5) It is interesting to
note, however, that as early as 1806, Berzelius noticed
this substance in the acid residues obtained in the
preparation of ethyl nitrite by Black's method. He
supposed it to be malic acid, and Strecker, therefore,
is considered as the discoverer. The next step in the
history of glycollic acid was taken by Debus, who showed
that it is produced along with oxalic acid, its aldehyde,
acetic acid, and glyoxalic acid by the action of nitric
acid on alcohol. (6) It was next obtained by Wurtz in
the oxidation of ethylene alcohol. (7) (8) Kekule
found it could be obtained by heating aqueous potassium
chloracetate. (9) Lautemann (10) and Drechsel (11)
claimed to have improved upon Debus' method, when,
instead of exposing alcohol to gradual oxidation with
nitric acid, they employed the mother liquors obtained
in the manufacture of fulminating mercury. Cloez,
however, was the first to note that an acid occurs in
this liquid, and named it homolactinic acid. (12)
Dessaignes suggested that it was glycollic acid (13),
an idea which was later confirmed by Fahlberg. (14)

1 Erlenmeyer and Hoster, Jahresb., 1864, 359. ib. 1866, 373.
(2) Besanez, Ann. Chem. Pharm., clxi. 229.
(3) Buisine, C.R., 107, 789-791. (J.C.S., 1889, 56, 178).
(4) Shorey, J.A.C.S., 1899, 21, 45-50.
(5) Ann. Chem. Pharm., lxviii. 55; ib. lxxx, 34.
(6) Ib. c. 1.
(7) C.R., xliv. 1306. (8) Ann, Chem. Pharm., ciii. 367.
(9) Ib. cv. 286.
(10) Kolbe, Lehrb. Org. Chem., i. 678.
(11) Ann. Chem. Pharm., cxxvii. 150.
(12) Ib., lxxxiv. 282.
(13) Ib., lxxxix. 339.
(14) Journ. Prakt. Chem., vii. 329.

According to the latter, very little of the acid is present in the liquor at first, but that it is formed in large quantity when allowed to stand indefinitely at 35°. These fundamental discoveries mark the beginning of a more or less desultory research in this field, the results of which are seen under Methods of Preparation.

Of historical interest are some of the attempts made in England to produce and study the properties of glycollic acid (1), it being formed from glyoxalic acid by reduction with hydrogen. It was found that glycollic acid is converted into a mixture of oxalic and glycollic acids by the action of water, while metallic zinc acts upon it with the production of glycollate and glyoxalate of zinc. Glyoxalates containing more than one atom of metal were found to decompose at room temperature and form compounds of glycollic and oxalic acids. Glycollic acid is also described as the alcohol of oxalic acid, and glyoxalic acid as the aldehyde of both.

Schulze (2) obtained glycollic acid from oxalic acid and zinc in the presence of sulfuric acid. This gave glyoxalic acid, the zinc salt of which was boiled with an excess of $Ca(OH)_2$, producing calcium oxalate and glycollate. The solution was saturated with CO_2, boiled, and filtered, the filtrate containing calcium glycollate.

Attention has already been called to the pioneer investigations of Strecker and his collaborator, Socoloff. (3) An abstract of their work appears in the J.C.S., 1853, 5, 79. They found glycollic acid as a decomposition product of certain benzene derivatives, and the result was a study of its preparation from benzo-glycollic acid. This substance was boiled with water for several days, with the addition of small amounts of sulfuric acid at intervals, and the replacement of the evaporated water. The benzoic acid freed in this process was largely volatilized, and the rest removed by crystallization. The mother liquor was neutralized with $BaCO_3$, filtered, and evaporated to a syrup, from which a salt with the ascribed formula, $BaO.C_4H_3O_5$, was obtained. The formulae of the corresponding hydrous and anhydrous acids were given as $C_4H_4O_6$ and $C_4H_3O_5$, respectively; and while these substances obtained by them were undoubtedly glycollic acid, one is struck by the construction assigned to it as seen in the above formulae, especially in view of the fact that the empirical formula of anhydrous glycollic acid is $C_2H_3O_3$. The error in determining the structure of the acid was no doubt due to faults inherent in the laboratory technic of that time. And were it not that Strecker's work is considered as fundamental, such discrepancies would tend to seriously

(1) J.C.S., 1865, 18, 203.
(2) J.C.S., 1863, 16, 302.
(3) A., 80, 18.

invalidate it, leaving its value open to question. He
states here that the acid had never been obtained before,
and quotes Laurent (1) as assigning it the name glycollic
acid since glycocoll is its amide. He further describes
the isolation of the acid from the barium salt by de-
composition with sulfuric acid. The resulting glycollic
acid, however, refused to crystallize, altho the article
goes on to describe the properties of glycollic acid with
marked fidelity. It was found to possess a strong sour
taste, to be miscible with water, alcohol, and ether in
all proportions, and to closely resemble lactic acid in
its properties. It gave, however, with lead acetate and
ammonium hydrate, a flocculent precipitate, while lactic
acid did not. It is further stated that glycollic acid
gives no precipitate with any metallic salt, an assertion
which is obviously without foundation; and in this
connection it is interesting to note that the zinc salt
was prepared from zinc carbonate, and a description
given of the silver salt.

An attempt was also made to show the decomposition
of glycollic acid into formic acid and formaldehyde, the
following equation being given:

$$C_4H_4O_6 \quad = \quad C_2H_2O_4 + C_2H_2O_2$$
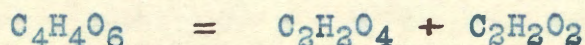
(Glycollic acid) (Formic acid) (Formaldehyde)

Again one is struck by the nature of the formulae
assigned to these compounds, since the correct structure
of formic acid is represented in the formula CH_2O_2, and
that of formaldehyde as CH_2O.

Another method of preparation was embodied in the
treatment of glycocoll with nitrous acid, nitrogen being
evolved in the reaction. The glycocoll was said to be
oxidised by nitric acid formed from the nitrous acid used.
The solution was evaporated, an impurity consisting of
oxalic acid removed, and the remainder extracted with ether.
The following equation was given as an illustration:

$$C_4H_5NO_4 + NO_3 = C_4H_4O_6 + HO + 2 N$$
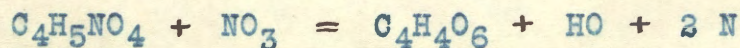
(Glycocoll)   (Glycollic acid)

The formation of benzo-glycollic acid from benzoic
acid and glycollic acid is similarly illustrated:

$$C_{14}H_6O_4 + C_4H_4O_6 = C_{18}H_8O_8 + 2 HO$$

(Benzoic) (Glycollic) (Benzo-glycollic)

Again are noted striking discrepancies in formulae,

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(1) Ann. Chem. Phys., (3) xxiii, 112.

nor is any explanation given as to what HO is. Nor is it clear why nitrous acid was used in the treatment of glyco-coll when it apparently underwent a change into nitric acid during the reaction.

Fahlberg (1) prepared glycollic acid from the mother liquors of fulminating mercury. The mercury was precipitated with H_2S and removed by filtration. The glyoxalic and oxalic acids were converted to their calcium salts with lime-water. Upon boiling, the glyoxalate is converted into glycollate. Filter, pass in CO_2 to precipitate excess lime, and evaporate the filtrate to a syrup from which calcium glycollate separates. It is stated that a concentrated solution gives rise to the anhydrous salt, while a dilute solution produces one with two molecules of water of crystallization. Upon re-crystallization, the latter changes over to the former. He describes the preparation of similar salts from the action of nitric acid on alcohol, and of hydrogen on oxalic acid. The glycollic acid was obtained from the calcium salt by decomposition of the latter with oxalic acid. The calcium oxalate was filtered off, and the filtrate treated with fresh lead carbonate. Pass in H_2S, filter, and evaporate to a syrup. The glycollic acid produced is described as quite non-volatile. Its preparation from chloracetic acid is also mentioned.

The article further describes the formation of glycollic anhydride by the action of heat or of SO_3 fumes upon glycollic acid, the preparation of the neutral and basic lead salts, and the copper and thallium salts; all of which are stated to be anhydrous.

Caseneuve (2) heated cupric acetate with water in a sealed tube at 200° C. for one hour, which gave rise to the formation of copper glycollate and cuprous oxid.

Bouchardat (3) treated tartaric acid with conc. sulfuric acid at 40-50°. The residue was dissolved in water and baryta-water added. Filter and evaporate. This gives barium tartrate and racemate. However, upon again sat-urating with baryta-water, filtering, and evaporating, a non-crystalline mass of barium glycollate and pyruvate is produced. The barium was removed with H_2SO_4, and the gly-collic and pyruvic acids liberated are converted into their calcium salts. This serves as a means of separation, since calcium glycollate crystallizes, while pyruvate does not. Tartaric acid is described as containing two formyl groups; which, when treated with conc. H_2SO_4, lose water and CO with the formation of glyoxal. This then assimilates water to form glycollic acid.

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(1) J. pr. Chem., (2) vii, 329-346. (J.C.S., 1874, 27, 142)
(2) C.R., 89, 525. (J.C.S., 1880, 38, 32.
(3) Ib. 89-101. (J.C.S. 1879, 36, 916)

EXPERIMENTAL

As has been stated, the first problem to be settled in this research was a selection of the known methods by which glycollic acid could be produced, excluding those of doubtful utility, and seeking to develop those of greatest promise. Obviously, such a method as the production of glycollic acid from hippuric acid, which is in itself a rare chemical, has no practical significance. On the other hand, however, a process such as the electrolytic reduction of oxalic acid by means of nascent hydrogen has much to recommend it for serious consideration; it being borne in mind that the substances entering into the reaction are common laboratory reagents, while the process itself is simple in principle and easily adapted to the usages of any laboratory. With this idea in mind, the following methods, or modifications of them which gave promise of favorable results, were selected:

1. The oxidation of ethyl alcohol with nitric acid.
2. The preparation of glycollic nitrile and its conversion into glycollic acid.
3. The electrolytic reduction of oxalic acid.
4. The investigation of sugar cane juice and filter-cake.
5. The hydrolysis of chloracetic acid with water.
6. The hydrolysis of chloracetic acid with KOH.
7. The hydrolysis of chloracetic acid with $BaCO_3$.

Among the first of these methods to be investigated was that of the oxidation of ethyl alcohol by means of dilute nitric acid. The technic of this process consists of placing in a tall cylinder layers of alcohol, water, and nitric acid one above another in equal volumes. Gradual diffusion takes place, about a week's time being required for the completion of the reaction. Glycollic acid, however, is not the only product formed; glyoxal, and oxalic, acetic, and glyoxalic acids being produced also. These latter may be considered as impurities, altho the glyoxal and glyoxalic acid may be in part transformed into glycollic acid by appropriate treatment. The method used was as follows: The mother liquor was boiled with an excess of lime-water, by which means portions of the glyoxal and glyoxalic acid were converted into glycollic acid. The excess of lime then operated to cause the precipitation of these products as calcium glycollate. The oxalic acid present was at the same time thrown down as calcium oxalate. The precipitate was then filtered off from the liquor and digested with boiling water. In this manner the soluble calcium glycollate was separated from the oxalate, the latter being insoluble in water. Upon filtration, a solution of calcium glycollate remained, which was further purified by re-crystallization. Glycollic acid was obtained by decom-

posing the aqueous solution of the calcium salt with oxalic acid, insoluble calcium oxalate being precipitated leaving glycollic acid in solution. Upon careful evapo- ration of its aqueous solution, the glycollic acid is obtained as a syrupy liquid. Difficulty was experienced in inducing it to crystallize, due to impurities present, and the product was later used in the preparation of a number of the metallic salts. The yield was small, and the method as a whole found to be very unsatisfactory. The chief difficulty is in the wide limits within which the process of oxidation may vary; in addition, the length of time required for this to take place is so great as to render it highly objectionable. The method has nothing of exactness about it, and owes its chief in- terest to the fact that glycollic acid does happen to be one of the many substances formed.

None of the literature relating to this process gave exact information as to the time necessary for the conversion of the alcohol into the largest possible amount of glycollic acid, nor was there any means suggested by which the acid could be liberated from the mother liquor. The method just described, wherein such separation was effected by treatment with lime-water, was worked out by the writer after a study of the relative properties of the products of oxidation, and the behavior of the calcium salts obtained. The meagerness of description and lack of detail in the literature regarding this method is characteristic of many of the processes described for the production of glycollic acid, and has constituted one of the greatest difficulties encountered by the writer in this research. Especially id this true of methods ab- stracted from German publications, not only because of the fact that an abstract is necessarily brief, but even more so because of the inherent closeness of the German scientist in describing the operation of a given process. Moreover, owing to the inaccessibility of many of the foreign journals referred to in the literature, it has been necessary to depend upon abstracts for the necessary data, upon much of which one must put his own interpretation.

2. Preparation of Glycollic Nitrile.

Perhaps one of the most interesting methods to come to the attention of the writer is that of the prepar- ation of glycollic nitrile and its subsequent hydrolysis into glycollic acid. Previous to finding an account of the preparation of the nitrile, the writer was struck by the possibility of such a reaction thru the study of the preparation of mandelic acid from benzaldehyde. (1) This

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(1) Gattermann, "Practical Methods of Organic Chemistry", pp. 307-311.

reaction is typical of those whereby the addition of hydro-
cyanic acid to an aldehyde takes place, since aliphatic as
well as aromatic aldehydes and ketones unite with hydro-
cyanic acid with the formation of a-oxy-acid nitriles. By
means of this reaction, the acid formed is that next above
the aldehyde used, because of the absorption of the cyanogen
radical and its subsequent saponification into COOH. Thus,
commencing with formaldehyde, the aldehyde of formic acid,
hydrocyanic acid is added quantitatively with the formation
of glycollic nitrile. The latter, upon saponification,
yields glycollic acid, the monohydroxyl derivative of
acetic acid. This method is standard in proceeding from
a given acid to the one next higher in the same series.
The following equation will illustrate the mechanism of
the reaction:

(a) $H_2C:O + HCN = H_2C.OH.CN$ (glycollic nitrile)

(b) $H_2C.OH.CN + 2 H_2O + HCl = CH_2.OH.COOH + NH_4Cl$
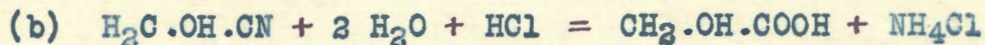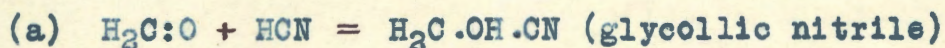
      Since the reaction takes place quantitatively,
molecular quantities of formaldehyde and hydrocyanic acid
are allowed to react. This was done as follows: 65 grams
of finely pulverized potassium cyanide were placed in a
250 c.c. Pyrex flask, which was fitted with a rubber cork,
dropping-funnel, and delivery tube. The latter was con-
ducted thru a rubber cork to the bottom of a second and
similar flask which contained 30 grams of formaldehyde in
the form of 85 c.c. of formalin solution. Owing to the
poor condition of the hoods, it was imperative that
another means be devised of disposing of any HCN not ab-
sorbed by the formaldehyde. This was accomplished by
connecting a delivery tube from the second flask to a
water suction-pump. In this manner, any noxious fumes
escaping would be conducted thru the pump and carried
away by the water in which hydrocyanic acid is extremely
soluble. It later developed that thru fluctuations in
the water pressure back suction frequently occurs, causing
the contents of the second flask to be drawn back into
the first, adding greatly to the dangers normally present
in this method. To obviate this, it is recommended that
a third flask be introduced in series between the other
two, thus acting as a receptacle for the contents of the
other flasks should the reaction proceed too violently in
either direction. After arranging the apparatus as
described, 98 grams of dilute sulfuric acid were then
added gradually thru the dropping-funnel, gentle suction
being applied at the same time. The sulfuric acid and
potassium cyanide react to form hydrocyanic acid gas and
potassium hydrogen sulfate, the former passing thru the
formalin solution where it is taken up by the aldehyde.
After the reaction has ceased, the contents of the second
flask are evaporated to small bulk and extracted with
ether. The glycollic nitrile obtained upon evaporation
of the ether appears as a colorless oily liquid with no
appreciable odor. This is then carefully evaporated in a

porcelain dish on the water-bath with four times its bulk
of concentrated HCl, crystals of glycollic acid separating.
These are filtered off and recrystallized from water. The
yield obtained the first time was very small, due to the
fact that the method was largely in the experimental stage.

Several later attempts to prepare glycollic acid
by this method were, singularly, failures. The chief
difficulty lay in the fluctuations of the water pressure,
causing back-suction and leading to other disturbances in
the flasks.. Moreover, the reaction between the sulfuric
acid and KCN is very violent, and even when controlled with
the utmost care is subject to occasional ebullitions of
gas violent enough to blow the corks out of the flasks, a
condition which is further augmented by the variations in
pressure due to back-suction. In the present research,
no less than three such accidents occurred in as many
consecutive attempts, and the method was finally discon-
tinued owing to the dangers necessarily incident to the
sudden freeing of quantities of hydrocyanic acid gas.

However, it is the opinion of the writer that
this method, despite its hazardous nature, has much to
recommend it. Much of the trouble experienced was due to
the water pressure, and it is certain that were this
method to be carried out in an adequately constructed
hood without the necessity of resorting to suction, the
reaction could be depended upon to proceed naturally
without the likelihood of any untoward developments.
The chief technical difficulty lies in the use of HCl
in the last step, this acid having a marked tendency to
inhibit the crystallization of glycollic acid. The
method, however, has the great advantage of giving
almost a quantitative yield from reagents which are
common in all laboratories.

3. The Electrolytic Reduction of Oxalic Acid.

One of the most promising methods investigated
is that of the electrolytic reduction of oxalic acid. To
gain a clear idea of the mechanism that takes place, it
it will be of advantage to refer to the following equation:

$$COOH.COOH + 2 H_2 = CH_2.OH.COOH + H_2O$$

(oxalic acid)   (glycollic acid)
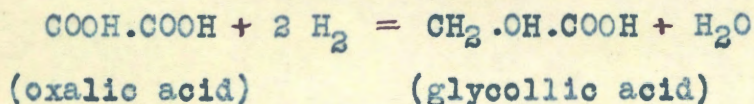
The technic of this process is found in Cohen's
"Practical Organic Chemistry", pp. 102-104. The method was
originally planned for the production of glyoxalic acid,
and was first used by Tafel and Friedrichs. (1) In this

(1) Ber., 1904, 37, 3187; Centralblatt, 1905, II 1699.

reaction the reduction of oxalic acid takes place thru the following intermediate reaction, first producing glyoxalic acid in accordance with the equation:

$$COOH.COOH + H_2 = CHO.COOH.H_2O.$$
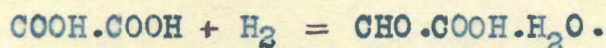
However, since glyoxalic acid, upon reduction with hydrogen, is converted into glycollic acid, it is obvious that this method may be readily utilized in the production of the latter compound, it being necessary only to make a slight variation in the procedure. This consists of doubling the number of ampere-hours as calculated to reduce a given quantity of oxalic acid to glyoxalic acid, and in allowing the temperature to rise above 10° C., below which only glyoxalic acid is formed. The normal temperature of this reaction is fairly constant, varying from 35° to 40° C. The problem of temperature regulation, then, becomes entirely automatic, 35° C. being the accepted optimum for glycollic acid.

The apparatus used consists of a glass jar, the size of which may vary according to the scale upon which it is desired to work the process. This acts as the cathode jar, the anode receptacle being a porous cup of 4 x 8 inches. The electrodes are lead plates, the cathode, in this instance, having a surface of 120 sq. m.m. A 220 volt direct current was used, it being conducted thru a set of carbon lamps connected in parallels to cut down the voltage and reduce current pressure to a minimum. In the apparatus used in the present research, the voltage was reduced to five, while the amperage remained constantly at eight.

In estimating the amount of current needed, several things must be taken into consideration. Cohen states that reduction requires theoretically 9 ampere-hours per 100 sq. cm. of cathode surface for the reduction of oxalic acid to glyoxalic acid. Doubling this for glycollic acid, 18 ampere-hours per 100 sq. cm. of cathode surface are needed. However, since the cathode used contained 120 sq. cm., but 15 ampere-hours are necessary. The above figures represent the current needed to reduce 20 grams of oxalic acid. In the reduction of larger amounts, the number of ampere-hours is increased proportionately. Thus, 100 grams would require 75 ampere-hours, but since the current registers 8 amperes, reduction would be complete in 10 hours. This implies the use of the full cathode surface.

In regard to the amount of reagents used, Cohen suggests 20 grams of finely powdered oxalic acid in 100 c.c. of 10 % sulfuric acid solution. This is placed in the cathode compartment, while the anode cell contains 10 % sulfuric acid solution alone. Before starting, it is advisable to reverse the current for a time to insure clean metallic surfaces on the electrodes.

With these figures as a basis, experimentation was conducted as follows: 100 grams of oxalic acid and 1000 c.c. of 10 % sulfuric acid were placed in the cathode jar, which in this case was a glass battery-jar of about two liters capacity. The current was then allowed to pass thru for the calculated period of time. The cathode liquor is then removed and treated with sufficient $BaCO_3$ to precipitate the sulfuric acid, a slight excess being added to dispose of any unchanged oxalic acid. The precipitate is removed with suction filter, the filtrate concentrated in vacuo, and then neutralized with calcium carbonate. By this means, calcium glycollate, which is readily soluble in water, is separated from any calcium glyoxalate should any be present. The latter is filtered off, leaving a solution of calcium glycollate from which the salt readily crystallizes. It is weighed, redissolved in water, and the amount of oxalic acid required to precipitate the calcium is added. The calcium oxalate thus formed is removed by filtration, and the filtrate carefully concentrated in vacuo to small bulk, and then with gentle heat over a carefully regulated water-bath. Upon such condensation glycollic acid appears as a syrup, sometimes brown in color from partial decomposition. If allowed to spontaneously evaporate it crystallizes from such solution.

The yields were not large, 40 grams being the most obtained at one time. This was due largely to fluctuations in the current and to the fact that the process was largely in the experimental stage. The yield is further kept down by the partial decomposition of the product thru the charring action of the sulfuric acid, a fact which serves to indicate the unstable nature of glycollic acid.

Due to the undesirability of such decomposition, and to the fact that 10 % sulfuric acid requires a large amount of barium carbonate to effect its precipitation, a modification of this part of the procedure seemed desirable. Theoretically, 360 grams of $BaCO_3$ are needed to precipitate the 100 c.c. of sulfuric acid (S.G. 1.84) used in the cathode liquid. Admitting the necessity of using a mineral acid to ionize the solution, the question then arises as to whether so large an amount of acid is necessary. With this in mind, numerous experiments were carried out using but 1 % of acid in the cathode solution. The results were all that were anticipated, the amount of ionization being entirely comparable to that gained thru the use of the larger amount of acid, while the yield was improved. The water, of course, undergoes electrolytic dissociation and furnishes the nascent hydrogen whereby reduction is effected. And while the sulfuric acid is likewise dissociated into its positive and negative constituents, it apparently is reformed in the process and never entirely exhausted, altho slight loss takes place thru the evolution of small quantities of SO_3.

The results attained thru the use of this method were
such as to render it very desirable. The chemicals needed,
consisting of barium and calcium carbonates, and oxalic and
sulfuric acids, are all common laboratory reagents easily
obtainable at low cost. The cost of the current is likewise
so cheap as to be almost negligible. A current of 8 amperes
for ten hours, multiplied by a voltage of five, gives a
total of 400 watt-hours or 0.4 kilowatt-hours. At a rate of
fifteen cents per kilowatt-hour, the low cost of the amount
of current needed is at once apparent. Therefore, from the
standpoint of economy and ease of operation, the foregoing
method is perhaps the best of those investigated.

4. The Investigation of Sugar Cane Juice and Filter-cake.

Another possible source of glycollic acid which was
investigated was that of its occurrence in, and extraction
from, sugar cane juice. That it is present in the juice of
the sugar cane is attested to by Shorey (1). He says: "On
adding a few drops of nitric acid to sugar cane juice
clarified by means of a slight excess of basic lead acetate,
a white crystalline precipitate forms, which is a mixture
of the lead salts of glycollic acid. The acid exists as
such in the cane and can be readily isolated by treating
the fresh cane juice with an excess of freshly precipitated
cupric hydroxid; the precipitate formed is thoroughly
washed with cold water, decomposed with hydrogen sulfide,
and the liquid freed from CuS by filtration. The resulting
acid filtrate is evaporated until crystals begin to form,
when on cooling, a solid mass of glycollic acid crystals
separate. The quantity thus obtained corresponds to 75-80
% of the total acidity of the juice". He further states
that "the occurrence of glycollic acid in cane juice is
held to account for (1) the occasional presence of formic
acid in the vapors from multiple-effect evaporators, since
it decomposes below 100°, yielding formic acid; (2) part,
at least, of the color of low-grade sugar products, as it
readily chars; (3) the frothing of boiled molasses on
standing, the gas to which this is due being evolved in
the decomposition of glycollic acid."

In the hope that cane juice would furnish a cheap
commercial method for the production of glycollic acid, a
quantity of cane juice and filter-cake were obtained from
the Louisiana Sugar Experiment Station. The former was
preserved by the addition of a small amount of formaldehyde
to prevent fermentation. The filter cake is the residue
obtained by precipitating the cane juice with lime, the
sample of juice submitted being the filtrate. Applying
the Shorey method, numerous experiments were made on the
sample of juice, but no trace of glycollic acid was found.

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(1)   J.A.C.S., 1899, 21, 45-50.

In hopes that it might have been precipitated out in the filter-cake, attention was turned to this substance, but with no better results. The negative results obtained provoked a further search of the literature in regard to crude sugar juices and their acid constituents, bringing to light the fact that in sorghum juice, which is almost exactly identical with cane juice, the following organic acids only are present: aconitic, citric, malic, oxalic, and tartaric. (1) While it is not unreasonable to suppose that glycollic acid is present in unripe cane juice, its occurrence in the ripe juice seems extremely doubtful. No mention is made by Mr. Shorey as to whether the juice employed by him was from ripe or unripe sugar cane, which serves to add further confusion to the matter. Admitting the presence of glycollic acid in the unripe juice, it seems not unlikely that during the process of ripening it is oxidized to oxalic acid, or possibly undergoes a transformation into tartaric acid, or both. The statement that 7 5-80 % of the acidity of cane juice is due to the presence of glycollic acid also seems doubtful in view of the fact that so many organic acids of a different nature are present. Efforts were made to secure fresh untreated cane juice, but to no purpose. No doubt a careful investigation of both ripe and unripe sugar cane would lead to interesting results, but as none was obtainable the matter was left as it is.

5. The Hydrolysis of Chloracetic Acid with Water.

The next method to be considered is that of the hydrolysis of chloracetic acid with water. The mechanism of the reaction seems simple enough at first glance, but its use entails many difficulties which are sufficient to render it undesirable. The technic used is:

35 grams of chloracetic acid were dissolved in 250 c.c. of water and refluxed for a number of hours. The literature is singularly non-committal regarding the number of hours necessary for the conversion of chloracetic acid into glycollic acid by this method. Experiments, then, were conducted with a view of ascertaining the length of time necessary to bring about this change. Periods ranging in length from 6 to 24 hours were tried, with the conclusion that from 6 to 8 hours refluxing is sufficient to bring about the desired change.

The next step is the concentration of the resulting solution to small bulk, it being presumed that the glycollic acid would crystallize out. The reaction takes place in accordance with the following equation:

$$CH_2Cl.COOH + HOH = CH_2.OH.COOH + HCl$$
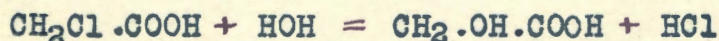
(1) Jour. Agr. Res., 1919, XVIII, 22.

Extreme difficulty was experienced in inducing crystallization, altho upon long standing crystalline compounds were obtained. These, however, failed to respond to tests confirmatory of glycollic acid. Melting points in all cases were irregular and did not correspond to that assigned to glycollic acid. The question then arises, what are the factors' entering into a reaction so seemingly elementary in operation as to give rise to results of so discordant a nature? In attempting an explanation, attention is first called to the fact that a molecule of hydrochloric acid is liberated in the interaction of the water with the halogen atom of the acid (chloracetic) used. It is almost needless to repeat that glycollic acid is extremely unstable under certain conditions, and is very easily decomposed or transformed into other compounds even when subjected to slight rises in temperature. Especially is this true in the presence of mineral acids, and it is entirely reasonable to assume that the glycollic acid, is, under the influence of the steadily increasing amount of hydrochloric acid liberated in the reaction and the effect of the heat applied during this period, further hydrolyzed into glycolide and possibly glyoxalic acid. In addition, the concentration of HCl, upon final evaporation of the solution, is very marked and quite effectively inhibits crystallization, while at the same time giving rise to further opportunities of decomposition. This is borne out by the experience of a number of investigators, Holzer (1), in particular, having had little or no success with this method. In view of this fact, the small amounts that have been produced by this method seem to have been due to conditions of a fortuitous nature, since the boiling of glycollic acid with water alone is sufficient to bring about marked changes in its structure. This is evident in consideration of the fact that glycollic acid melts at 79-80°, undergoing decomposition as the temperature rises above this point. There are then, two manifestly deleterious influences in operation at practically all stages of the process, either of which is quite capable of bringing about radical changes in the composition of the glycollic acid formed. With these statements in mind, and in the light of the uniformly unreliable results attending the use of this method, the hydrolysis of chloracetic acid with water is not recommended.

6. The Hydrolysis of Chloracetic Acid with KOH.

The hydrolysis of chloracetic acid with KOH is a method much similar in principle to that just described, excepting that instead of glycollic acid being the direct product of hydrolysis, its potassium salt is obtained. The

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(1) Ber., 1883, 16, 2954.

reaction takes place in accordance with the equation:

$$CH_2Cl.COOH + 2 KOH = CH_2.OH.COOK + KCl + H_2O$$
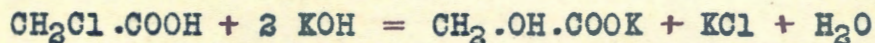
The amounts of the reacting substances were used in the proportion of one molecular part of chloracetic acid to two molecular parts of potassium hydroxid. The chloracetic acid (25 grams) was dissolved in about 250 c.c. of water. 30 grams of KOH were then added and the resulting solution refluxed for a number of hours. Here, the same difficulty was met with as in the preceding experiment, there being no data given in the literature regarding the time needed for refluxing. Consequently, experimentation was again resorted to as before to determine approximately the length of time during which such treatment should be carried on. Periods ranging in length from 4 to 24 hours were tried, with the result that 6 hours was found to be the optimum. Shorter periods than this are likely to result in incomplete hydrolysis, since the chlorin atom of the molecule is difficult of replacement. However, the process of refluxing, in this case, is free from the disadvantages noted in the case of hydrolysis with water, the glycollate formed being quite stable. Furthermore, the process has the advantage of not contrubuting to the liberation of acids or other substances which would tend to result in undesirable secondary reactions.

Upon completion of the hydrolysis, the best means of separating the glycollate is thru the formation of the copper salt. This is done by treating the liquor with copper sulfate solution until precipitation is complete. The difficultly soluble copper glycollate is filtered off from the liquor which contains the impurities in solution. It is then purified by recrystallization and decomposed with hydrogen sulfide. Upon filtering off the residue of copper sulfide, the filtrate contains relatively pure glycollic acid in solution. This is then evaporated to a syrup and allowed to crystallize. This method is capable of quite successful application, the main disadvantage being the cost of chloracetic acid.

While engaged upon this method, it was noted that the addition of solid KOH to an aqueous solution of chloracetic acid gave rise to a reaction of almost explosive violence, especially if the solution was warm. The KOH rapidly went into solution with the evolution of a tremendous amount of heat. This led to further experimentation regarding this phenomenon, with the discovery that solid KOH and crystalline chloracetic acid, when intimately mixed, fuse with extreme violence, the heat liberated being sufficient to reduce the mass to a black charred residue. It was found, however, that bybimmersion of the receptacle containing the two substances, the speed of the reaction could be effectively controlled and a white

crystalline mass obtained which was composed chiefly of potassium chlorid, potassium monochloracetate, and potassium glycollate. The speed of the reaction is greatly increased by the addition of a few drops of water. Time did not permit of an exhaustive investigation of this matter, but it seems certain that the production of potassium glycollate could, by proper temperature control, be produced in a few moments by this method. Much work was done onnit, and results were such as to make this seem more than likely.

In addition to the methods cited, another was devised by the writer in the hope that a still sharper separation of the glycollate from its impurities could be effected. The liquor obtained after refluxing was treated with freshly prepared basic acetate of lead solution until no further precipitate formed. Since basic lead glycollate is soluble in water only to the extent of one part in ten thousand, while the impurities formed are all readily soluble in that medium, it seemed that practically a complete separation could be effected in this manner. The plan was to suspend the basic lead glycollate in water and decompose it with hydrogen sulfide. In this manner it was thot that a solution of pure glycollic acid could be obtained. Following is the reaction:

$$PbO.(CH_2.OH.COO)_2Pb + 2\ H_2S = 2\ CH_2.OH.COOH + 2\ PbS + H_2O$$
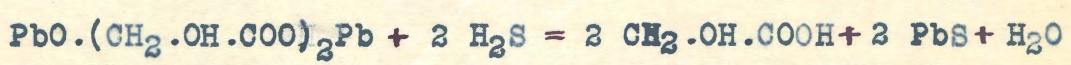
However, exhaustive experimentation led to no results which could be considered as encouraging. In each case, upon evaporation of the supposed solution of glycollic acid, the characteristic syrupy solution failed to appear. Instead, a beautiful white, needle-like body crystallized out before evaporation had proceeded far. Investigation showed this to be a complex lead salt, probably a mixture of the neutral and basic lead salts, as quantitative determinations showed a percentage of lead midway between that theoretically present in the two. Analyses of the initial precipitate of basic lead glycollate proved the identity of that body to begin with. What took place upon treatment with H_2S is a question, altho it is quite certain that the expected double decomposition did not take place completely, due probably to the complex nature and stability of the basic lead salts.

7. Hydrolysis of Chloracetic Acid with Barium Carbonate.

Another method from which it was hoped good results would be forthcoming is that of the hydrolysis of chloracetic acid with barium carbonate. This first results in the formation of the barium salt of chloracetic acid; which, upon refluxing, is converted into barium glycollate in

accordance with the following equation:

$$2\ CH_2Cl.COOH + BaCO_3 + 2\ H_2O = (CH_2OHCOO)_2Ba + 2\ HCl + H_2CO_3$$
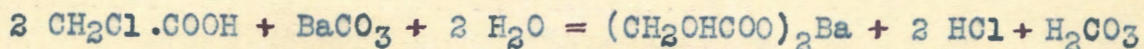
The method is as follows (1) : 50 grams of chlor-
acetic acid are dissolved in 500 c.c. of water. This is then
treated with 120 grams of $BaCO_3$ in a large flask and re-
fluxed for 30 hours or until evolution of carbon dioxid
ceases. The contents should be frequently agitated,
especially toward the last. The excess of $BaCO_3$ is filtered
off and the barium precipitated from solution with the
calculated amount of sulfuric acid. The barium sulfate
thus formed is removed by filtration and the filtrate con-
centrated in vacuo to a syrup. This is further concentrated
with gentle heat over a water-bath. The glycollic acid
precipitates from this upon standing.

Several objections were found to the use of this
method, chief of which is the formation of hydrochloric
acid during the procees of refluxing. It was found impossible
to obtain a solution of glycollic acid that did not contain
a large quantity of this objectionable impurity. It is
almost impossible, further, to expel it even thru a process
of slow and careful evaporation, due to the formation in
the solution of an acid of constant-boiling concentration.
Upon close evaporation the percentage of HCl is so great as
to altogether inhibit the crystallization of the glycollic
acid. In addition to this, there is the objection brought
out before relative to the decomposition inevitably
attending the presence of mineral acids. It is possible,
however, by diluting the solution with water numerous times
and again evaporating, to expel most of the acid, but this
method is so laborious and slow as to render it of little
practical value, the continued evaporation itself being
an objectionable feature. Moreover, the yield obtained
is small and contaminated with small amounts of various
decomposition products.

It was observed that refluxing for about 10 hours
is sufficient in this case, there being no further
evolution of CO_2 after that time. This part of the re-
action takes place with much foaming, making it necessary to
frequently agitate the contents of the flask. This could
as readily be carried on in an open vessel, from time to
time restoring the water lost thru evaporation, In either
case, more or less disintegration of the barium glycollate
takes place under the influence of the HCl liberated in the
reaction. This method, then, because of the many
objectionable features encountered, is not recommended.

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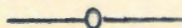
(1) J.A.C.S., 1917, 39, 109.

SUMMARY

1.   This research has led to a study of the known methods of producing glycollic acid, with the elimination of those which were deemed unsuitable, and the further study and manipulation of those which it was thot would lend themselves to ready development. Many methods were found to be of a purely theoretical or historical interest; others involved the use of rare chemicals; while others were discarded because of their obvious failure to embody a principle of operation capable of being brought to a high degree of development. No new methods were evolved.

2.   The electrolytic decomposition of oxalic acid with nascent hydrogen was found to offer the most promise of the methods investigated. The chemicals used are cheap and easily obtainable, the cost of current almost negligible, while the process itself is free of mechanical difficulties.

3.   The best method from the standpoint of simplicity is that of the conversion of glycollic nitrile to glycollic acid. Its disadvantage is the danger inherent in the type of chemicals used. There is great ease of manipulation, the entire process requiring little time for completion. The reagents used are cheap. A minor disadvantage is the use of hydrochloric acid.

4.   Another very practical method is that of the hydrolysis of chloracetic acid with KOH. This embodies simplicity of operation with marked freedom from technical difficulties arising from the presence of impurities.

5.   The oxidation of alcohol with nitric acid is not recommended.

6.   The methods depending upon the hydrolysis of chloracetic acid with water and barium carbonate, respectively, are not recommended for reasons already stated.

7.   No success was met with in attempts to obtain glycollic acid from cane juice or filter-cake.

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