These analyses indicate that this product is diiodoacetic acid, but our substance is white and melts at 95–96°, whereas the diiodoacetic acid, according to Angeli,[1] is yellow and melts at 110°. The explanation of these discrepancies must be left to future work. Our product is soluble in water, giving an acid reaction, and decomposing carbonates. It is also soluble in alcohol, ether, or benzene; practically insoluble in cold naphtha, soluble in hot, from which it is deposited in rosets of white needles. On exposure to the air it turns pink, and gives a test for free iodine. With lead acetate it gives a white precipitate, which can be crystallized from hot water.

The compound insoluble in naphtha, when crystallized from glacial acetic acid, gave white plates contaminated with a small quantity of white prisms, but the latter were removed by warming gently with water, after which the plates were crystallized several times from glacial acetic acid.

Subst. 0.2492; AgI, 0.4449; Calc. for C_2HI_5: I, 96.23; found: I, 96.49.

The substance therefore seems to be pentaiodoethane, but it is unfortunate that we did not have time to prepare enough for another analysis. It forms white plates melting at 182–184° (uncor.) and is soluble in alcohol, glacial acetic acid, or benzene, and insoluble in naphtha.

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[CONTRIBUTION FROM THE OTHO S. A. SPRAGUE MEMORIAL INSTITUTE, LABORATORY OF CLINICAL RESEARCH, RUSH MEDICAL COLLEGE.]

THE SYNTHETIC PREPARATION OF *dl*-GLYCERIC ALDEHYDE.

BY EDGAR J. WITZEMANN.

Received July 14, 1914.

The synthetic preparation of *dl*-glyceric aldehyde was accomplished by Wohl at least fifteen years ago.[2] Several workers have repeated the synthesis on a small scale since that time. In those instances in which crystalline glyceric aldehyde was obtained it was by the use of seed crystals obtained from Wohl. Others have been satisfied to work with the uncrystallized syrup. For some chemical work, such as that of Schmitz[3] on the mechanism of acrose formation, such syrups would be fairly satisfactory, but for certain biochemical as well as chemical work the pure crystalline compound is necessary, in order that the experimental results shall be sharply significant. As a part of the program of work on the metabolism of sugars, which is being followed in this laboratory, it became necessary to prepare a quantity of pure crystalline glyceric aldehyde for biochemical experiments. In the course of this work certain improvements were made in the method of preparation, especially in the manip-

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[1] *Ber.*, **26**, 596 (1893).

[2] Wohl, *Ber.*, **31**, 1797, 2394 (1898); Wohl and Neuberg, *Ber.*, **33**, 3095 (1900).

[3] *Ber.*, **46**, 2327 (1913).

ulations of the highly sensitive glyceric aldehyde itself, which now make the isolation of the crystalline compound very certain and relatively easy. Glyceric aldehyde, as prepared by the use of these modifications, is much more easily crystallized than any known hexose including galactose. In fact it has not been possible to prevent its spontaneous crystallization if care was used in the preparation of the syrup.

The actual work of preparation was done in the Kent Chemical Laboratory of the University of Chicago, through the kindness of Dr. J. U. Nef, and I hereby wish to thank him for this and for his helpful interest during the course of the work.

The method used by Wohl in the synthesis of glyceric aldehyde was followed carefully except that it was modified in some important details of manipulation. Briefly summarized, this method is as follows: acrolein is dropped fairly slowly into twice its weight of absolute alcohol previously saturated at 0° with dry hydrochloric acid gas.

$$CH_2 : CHCHO + HCl + 2C_2H_5OH \longrightarrow CH_2ClCH_2CH(OC_2H_5)_2 + H_2O.$$

The β-chloropropionicaldehyde diethylacetal forms a separate lower layer which is separated, neutralized, etc., and finally treated with powdered sifted potassium hydroxide in order to convert it into acrolein diethylacetal.

$$CH_2ClCH_2CH(OC_2H_5)_2 + KOH \longrightarrow CH_2 : CHCH(OC_2H_5)_2 + KCl + H_2O.$$

The acrolein acetal is oxidized with potassium permanganate to glyceric aldehyde diethylacetal.

$$3CH_2 : CHCH(OC_2H_5)_2 + 4H_2O + 2KMnO_4 \longrightarrow 3CH_2OHCHOHCH(OC_2H_5)_2 + 2KOH + 2MnO_2.$$

The glyceric aldehyde acetal in turn is hydrolyzed by 0.1 *N* sulfuric acid in the cold, and from this, finally, the true dimeric crystalline *dl*-glyceric aldehyde is obtained.

$$CH_2OHCHOHCH(OC_2H_5)_2 + H_2O \longrightarrow CH_2OHCHOHCHO + 2C_2H_5OH.$$

In the preparation of β-chloropropionicaldehyde diethylacetal, it was found best to add the acrolein[1] from a dropping funnel which passed through a cork fitted in the flask containing the absolute alcohol saturated with hydrochloric acid. A small slit cut in the side of the stopper allowed the air to escape as fast as it was displaced by the acrolein. A glass capillary tube in a cork was set into the top of the separatory funnel to prevent the acrolein vapors from passing out too freely. The reaction mixture was constantly agitated in an ice bath during the addition of the acrolein.

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[1] The acrolein used was obtained by the methods described in THIS JOURNAL, **36**, 1766 (1914).

If the acrolein was kept cooled in an ice bath and only added to the separatory funnel in relatively small amounts, this work could be done in the open room without causing any inconvenience or perceptible odor of acrolein.[1] The β-chloropropionicaldehyde acetal separates in part during the addition of acrolein. After standing an hour or so in the ice bath with occasional agitation, the lower layer was separated off. This was treated gradually with an excess of sodium bicarbonate according to the original suggestion of Wohl. The method of neutralizing the free hydrochloric acid with precipitated calcium carbonate[2] was not used. The voluminous precipitate of sodium chloride was filtered off under strong suction, pressed with a porcelain pestle and finally washed with a little absolute alcohol. The filtrate was washed several times with cold water, after which the β-chloropropionicaldehyde acetal was dried with potassium carbonate. In this condition it can be left over night. It is never advisable to keep the β-chloropropionic aldehyde acetal for long intervals. If it becomes necessary to keep it for a time it is not advisable to have it stand over moist potassium carbonate.

The crude β-chloropropionicaldehyde acetal thus obtained was always fractionally distilled *in vacuo*. The product distilling below 56° at 8 mm. pressure had a very powerful odor, probably due to β-chloropropionic aldehyde, which may arise either from the addition of hydrogen chloride to acrolein, which was not subsequently converted into the acetal, or it may arise from hydrolysis of the acetal. This fraction always gave an additional amount of the high boiling fraction on redistilling. The main fraction, distilling from 56–66° at 8 mm. was used at once for the preparation of acrolein acetal. The residue, on distillation, was a golden yellow liquid somewhat less viscous than glycerol. A portion of this residue was distilled *in vacuo*. Distillation took place all the way from 66° to 140° at 16 mm. (but most distilled at 120–40°). The first runnings were composed of β-chloropropionicaldehyde diethylacetal. On fractionating again a slightly yellow, nearly colorless, fraction, boiling at 127–40° at 10 mm., and having a mild odor resembling acrolein acetal was obtained. On attempting to remove this liquid with chromic acid cleaning mixture, a very large amount of acetaldehyde was evolved, showing that this distillate was composed in part of acetals. It was not further investigated.

Since no suitable copper still, such as was used by Wohl in the treatment

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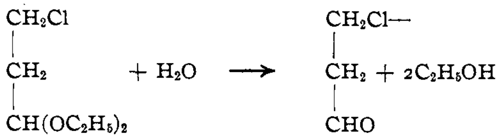
[1] This operation is very conveniently done in cold weather. The absolute alcohol saturated with HCl may be made up in quantity and kept for a long time by placing it in a strong bottle fitted with a rubber stopper. The bottle is set in a deep pan on the base of a strong ring stand and a ring is clamped down very firmly on the stopper. The whole is placed out of doors. If the temperature is above 0° the pan is filled with ice water a short time before removing the amount desired, otherwise not. In hot weather it is very troublesome to keep this solution.

[2] Wohl and Emmerich, *Ber.*, **33**, 2760 (1900).

of β-chloropropionicaldehyde acetal with potassium hydroxide was available, a 250 cc. round-bottomed flask was used. Fifty grams of β-chloropropionicaldehyde acetal were placed in the flask and 100 g. of powdered potassium hydroxide (passed through a 60-mesh sieve) were added a few grams at a time. Meanwhile, the contents of the flask were continually mixed by shaking. The flask was cooled in ice water from time to time. In this way a homogenous, cream-colored mixture was obtained. The flask was then fitted with a cork containing a three-ball Glinsky distilling tube. The latter was connected with a short Liebig condenser. The flask was then immersed in a paraffin bath up to the level of the mixture inside. When the bath reached 210–20° an active reaction took place and acrolein diethylacetal began to pass over at once. When the reaction proceeds quite normally, there was no difficulty in keeping the thermometer in the top of the Glinsky at or below 120°. The distilate was nearly always composed of two layers, the lower one of which was made up of a few drops of water. After removing the water with potassium carbonate the product was fractionated, using the Glinsky tube. Three portions of 50 g. thus gave an average of 80 g. of acrolein diethylacetal, distilling between 120–128° (95% of it between 123–5°). This is 68% of that theoretically possible. There was always about 5–10 g. of ethyl alcohol formed by the saponification of one of the acetals. Likewise, a few grams of acrolein acetal may be recovered by digesting the flasks with water. It was invariably noticed, on dissolving the potassium hydroxide residue, that there was a considerable amount of an insoluble substance floating in the solution of potassium hydroxide. The nature of this product was not determined. About 15% of the material used remained as a residue on fractionating the crude acrolein acetal. This sometimes gave satisfactory results on distilling again with powdered potassium hydroxide.

The formation of acrolein acetal from β-chloropropionicaldehyde acetal takes place with surprising ease and regularity when the powdered potassium hydroxide has the right qualities. If, however, a grade of potassium hydroxide is used which contains too much water, or if the grinding of the potassium hydroxide is done on a damp day, the results are regularly poor. It is very easy to determine, during the distillation, whether the results are going to be good. If the powdered potassium hydroxide melts before the acrolein acetal begins to distil over (105–20°), or if the distillation temperature remains at 78° (b. p. of alcohol), or if the distillate has an overpowering odor, (worse than acrolein) the reaction is not proceding normally. Usually all three of these signs occur together. Sometimes, however, only the latter (that is the overpowering odor) is present to a slight extent. This is usually a warning that the yield will be a bit low and that more care should be taken to keep the potassium hydroxide dry.

The explanation of this undesirable result is not difficult. The reaction may be written thus:



$$\begin{array}{l} CH_2Cl \\ | \\ CH_2 \\ | \\ CH(OC_2H_5)_2 \end{array} + H_2O \longrightarrow \begin{array}{l} CH_2Cl- \\ | \\ CH_2 \\ | \\ CHO \end{array} + 2C_2H_5OH$$

It is probable that only the β-chloropropionicaldehyde (the compound with the powerful odor) formed by the action of water vapor on the vapor of the acetal passes over into the distillate. The β-chloropropionicaldehyde formed by the action of water within the liquid mixture is no doubt polymerized instantly. This is shown by the fact that a white insoluble polymer appears in the distillation mass which increases in quantity as the reaction proceeds. Wohl and Emmerich[1] had similar trouble in hy*drolyzing β-chloropropionicaldehyde* acetal *with aqueous potassium* hydroxide in order to obtain β-hydroxypropionicaldehyde acetal.

After having gained sufficient experience with the technique, it was found possible to prepare, in about three weeks, enough acrolein (about 1600 g. from about 6000 g. of glycerol) and to convert this by successive stages into 735 g. of acrolein diethylacetal.

The oxidation of acrolein diethylacetal to glyceric aldehyde diethylacetal presents no difficulties, except that of getting a large yield. Wohl and Neuberg[2] succeeded in getting a maximum yield of about 40%. In my own experiments it was possible to get a maximum yield of 54%, not counting the unchanged acrolein acetal recovered, or an average of 52–53% for a series of oxidations. 540 cc. of water were placed in a three liter flask and 50 g. of acrolein acetal were added. To this 1100 cc. of an aqueous solution, containing 60 g. of potassium permanganate (*i. e.*, nearly saturated at room temperature), were added from a dropping funnel at the rate of 100 cc. in five minutes. Throughout the addition, the mixture was vigorously agitated in an ice bath. The reaction mixture was then allowed to stand for 2 hours in the ice bath. Usually the entire contents of the flask set into a stiff jelly (*i. e.*, of hydrated manganese dioxide hydrogel) in 15 to 30 minutes. This gel was so stiff that frequently the flask could be turned upside down without disturbing the gel. Gradually, if left undisturbed, this gel showed "condensation water" or syneresis and also deep fractures. After standing two hours it was placed on the steam bath. This hastens the further coagulation of the colloid, so that when the mixture has become fairly warm it may be thrown upon a large (8 inch) Buchner suction filter. By pressing the precipitate with a spatula the manganese dioxide may be sucked quite dry. It is then washed with about

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[1] *Ber.*, 33, 2760 (1900).

[2] *Ibid.*, 33, 3095 (1900).

150 cc. of water. The warm filtrate (about 1800 cc.), which smells strongly of acrolein acetal, is treated with 900 g. of commercial potassium carbonate and the solution cooled at once. It is not necessary to add about 1800 g. of potassium carbonate as stated by Wohl. The mixture is now transferred to a large separatory funnel; the upper layer (glyceric aldehyde acetal) is drawn off and the aqueous solution extracted 4 or 5 times with ether. On mixing the ether extract with the crude acetal first drawn off, solution at first results; on addition of more ether, however, a considerable amount of glyceric aldehyde acetal separates out as a lower layer. This was discarded as water at first, but later its true nature was discovered. Experiments with pure glyceric aldehyde acetal and ether failed to show any such miscibility break in this binary system, so that the miscibility break observed here must be due to some third component, probably the water dissolved in the ether. At least it was found that the glyceric aldehyde acetal was taken up into solution again instantly as soon as potassium carbonate was added in order to dry the solution. After distilling off the ether, the crude glycericaldehyde acetal was distilled *in vacuo*. It boiled at 120–1° at 8 mm. pressure.

From 60 g. of acrolein acetal 39 to 40 g. of glyceric aldehyde acetal were nearly always obtained, and about 3 g. of unchanged acrolein acetal were recovered. From 835 g. of acrolein acetal 512 g. of pure glycericaldehyde acetal were obtained. Altogether, 1465 g. of acrolein acetal were worked up in this way.

dl-Glyceric Aldehyde.

In the preceding pages I have given some additional observations and details concerning the preliminary stages in the synthesis *dl*-glyceric aldehyde from acrolein and glycerol, but significant and important improvements were also made in the manipulation of the free glyceric aldehyde itself. Wohl apparently had considerable difficulty in crystallizing his glyceric aldehyde, and states that it required weeks to get the first crystals. Schmitz[1] found that very small concentrations of alkali condense glyceric aldehyde into a definite mixture of 2-keto-hexoses. Nef's long studies with the sugars[2] have shown how sensitive even the hexoses are to the action of inorganic bases and salts. In glyceric aldehyde all these properties would be even more marked. In view of these considerations, Nef suggested the use of small amounts of acetic acid to overcome the undesirable effects of any traces of alkali. The results obtained in the crystallization of glyceric aldehyde as a result of this suggestion are so remarkable in comparison with anything described in chemical literature that they will be described in some detail.

The glyceric aldehyde acetal was dissolved in 10 times its weight of

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[1] *Ber.*, 46, 2327 (1913).

[2] *Ann.*, **357**, 214–312 (1907); **376**, 1–119 (1910); **403**, 204–383 (1914).

0.1 *N* sulfuric acid and allowed to stand at room temperature for a few days, or better for a whole week. To this was added 6.3 g. of glacial acetic acid per 100 cc. The solution was then warmed and slightly more than the calculated quantity of barium hydroxide (about 0.3 *N*) was added a little at a time.[1]

The solution was filtered after standing for some time to remove as much of the barium sulfate as possible (*i. e.*, all but at most a slight turbidity). Test portions were placed in test tubes and a small amount of the 0.1 *N* sulfuric acid was added to one of them. Both were warmed somewhat and the turbidities were compared. The solution was adjusted by the addition of small amounts of sulfuric acid until it showed only a very slight positive test for barium as shown by the formation of a slight turbidity on adding a little 0.1 *N* sulfuric acid to a test portion.

This solution was then filtered through a hard filter containing a pinch of animal charcoal and the water was then removed from the clear, colorless, filtrate by distillation at 20 mm. pressure. The syrup remaining was dissolved in the minimal amount of warm absolute alcohol and an equal volume of ether added (*i. e.*, until a turbidity begins to appear). On standing for 25 hours the last traces of inorganic matter were separated out and the clear filtrate then gave, on customary distillation at reduced pressure, a transparent syrup; this syrup was now transferred to a beaker and placed in a vacuum desiccator over night. The next morning the syrup showed a white opalescence. Before night the syrup had become white and opaque. A little ethyl alcohol was now stirred into the mass from time to time until the mass ceased to be sticky any longer. Thirty grams of glyceric aldehyde acetal treated in this way gave, in three days, 10 g. of a crystalline powder nearly insoluble in cold ethyl alcohol, with which it was freely washed on a filter. The glyceric aldehyde thus obtained melts 132° without further purification. This was the only experiment in which the passage of glyceric aldehyde through the colloidal state, was so clearly noticed. In all subsequent experiments more dilute syrups were used for crystallization in order to obtain larger crystals.

After a few more batches of glyceric aldehyde had been worked up in this way and inocculated with particles of the above crystals, it became evident that the yield in crystalline glyceric aldehyde was considerably less than the amount theoretically possible from the acetal used. This may have been due to unhydrolyzed acetal or to some condensation of rearrangement product of the glyceric aldehyde itself. The following procedure was therefore adopted:

The acetal was hydrolyzed for a week at room temperature just as

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[1] The method used by Wohl at this point was to simply neutralize the sulfuric by adding an excess of barium hydroxide and then to remove the excess of barium hydroxide at once by passing a stream of carbon dioxide through the solution.

before, except that it was twice warmed for about 2 hrs. to about 35° during the hydrolysis. Before adding the barium hydroxide, 0.5 g. of glacial acetic acid was added per 100 cc., of the solution. The end adjustment of the trace of barium acetate was made as before. The final removal of the last portions of barium sulfate was accomplished by filtering through a hard filter containing a pinch of animal charcoal, which had been washed thoroughly with hydrochloric acid and then with water till free from acid. The solution was now concentrated *in vacuo* to a thick syrup free from water. This was dissolved in absolute alcohol. When prepared in this way it is impossible to prevent spontaneous crystallization of alcohol solutions of the glyceric aldehyde. This solution is treated with ether, filtered and concentrated *in vacuo* at once. If it is to be transferred from the distilling flask it must be done quickly, because in twenty minutes after the removal of the water bath crystallization is well advanced. In fact, in a few cases, crystallization began while the flask was being heated. In twenty-four to forty-eight hours crystallization is complete.

When crystallization is complete the flask usually contains a thick, porous cake of crystals covered with a layer of limpid mother liquor a few millimeters thick. The cake is broken up and thrown on a suction filter. The flask and crystals are repeatedly washed with absolute alcohol after which the crystals are spread out on a porous plate and allowed to dry. After standing in the air one day the melting point was found to be 142°. The highest melting point previously observed (138°) was obtained by Wohl and Neuberg[1] after recrystallizing their product from 40% methyl alcohol and drying *in vacuo* over phosphorus pentoxide. A specimen kept in a vacuum desiccator over concentrated sulfuric acid for three days melted at the same temperature, thus showing that this sugar is not hygroscopic. The glyceric aldehyde syrup is quite sweet. Wohl states that the crystals are less sweet than the syrup. This is true. In fact, there is no perceptible taste whatever when crystals are placed on the tongue and allowed to dissolve there.

The mother liquor was concentrated *in vacuo* and allowed to crystallize again.

The behavior of *dl*-glyceric aldehyde in crystallization is very interesting. As was shown above, much better results in crystallization are obtained when inorganic compounds present in the small amount of bone-black used are kept out of the solution. Just what the effect of these salts ($Ca_2P_2O_7$, $CaCO_3$, etc.) is, has not as yet been determined experimentally. Furthermore, success in crystallization depends in part on the complete removal of water from the syrup. If the water has been completely removed and the syrup taken up in alcohol, the crystalline dimeric form (since this is almost insoluble in alcohol) begins to separate out at once.

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[1] *Ber.*, 33, 3095 (1900).

The addition of ether to the alcohol solution does not interfere with crystallization. In fact, considerable crystalline glyceric aldehyde was obtained from this mixed solvent. But even with the technique described, the results obtained in crystallization are somewhat variable, as will be seen from the results given below. Moreover, no experimental explanation has yet been found for the fact that usually only 75% of the glyceric aldehyde theoretically possible could be crystallized out of any given batch.

In some test experiments the following results were obtained: Ninety grams of the acetal gave, on the first crystallization, 28.5 g. of glyceric aldehyde crystals. On concentrating the mother liquor and washings *in vacuo* a second crop of 8.2 g. was obtained. The washings from the second crop gave 11.0 g. of gum which no longer crystallized on diluting with alcohol. Therefore, 75% of the 49.3 g. of glyceric aldehyde theoretically possible were obtained in the crystalline form.

In another experiment, 27 g. of crystalline glyceric aldehyde out of the 41.7 g. theoretically possible were obtained from the first crystallization, *i. e.*, 64.7%. A second crop of 4.7 g., and a third crop of 3. 7 g. was obtained, making a total of 84.8% recovered as crystals.

Altogether, enough material was worked up to have given 400 g. of crystalline glyceric aldehyde, assuming that 95% of it could be crystallized. As a matter of fact, only a little over 250 g. was obtained altogether.

CHICAGO, ILL.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF WASHINGTON UNIVERSITY.]

A FURTHER STUDY OF THE PREPARATION AND PROPERTIES OF THE AMMONIUM SALTS OF ORGANIC ACIDS.

FOURTH COMMUNICATION.[1]

BY LEROY MCMASTER.

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In continuation of the investigation of the preparation and properties of the neutral ammonium salts of organic acids, I still find that the salts were always prepared by neutralizing an aqueous solution of the organic acid with ammonia water or ammonium carbonate, and the solution allowed to evaporate. As a result, the acid salts, instead of the neutral salts, were generally obtained, due to the hydrolytic action of water upon them. The properties given are thus the properties of the acid salts. In some cases no record at all can be found of the preparation of any ammonium salt of the organic acid. Many of the salts also contained water of crystallization.

In attempting to prepare some neutral di-ammonium salts by the above

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[1] For previous papers on this subject see: *Am. Chem. J.*, **49**, 84–87 (1913); *Chem. News*, **108**, 136–137 (1913); *Am. Chem. J.*, **49**, 294–301 (1913); *Chem. News*, **108**, 182–183, 193–194 (1913); THIS JOURNAL, **36**, 742–747 (1914).