residue was obtained which could not be crystallized. When an acetone solution of this material was treated with an ethereal solution of diazomethane no evolution of nitrogen took place.

Oxidation of *epi*-Neoergosteryl Acetate.—*epi*-Neoergosterol was prepared from neoergosterol according to the method of Windaus and Deppe.[8] Crystals were first obtained which melted at 171–172°. Further recrystallizations from an ether–acetone solution gave a product which melted sharply at 175–176°.

The acetate, m. p. 98°, prepared from 4.0 g. of *epi*-neoergosterol was dissolved in 240 cc. of glacial acetic acid. To this solution there was added drop by drop in the course of three hours a solution of 8 g. of chromic acid anhydride in 1 cc. of water and 30 cc. of glacial acetic acid. The solution was stirred mechanically and during the oxidation the temperature was kept at 60–65°. After the addition of the chromic acid the heating was continued for four more hours. The solution was then cooled and worked up in the usual manner. The ether residue which contained the neutral products of oxidation was dissolved in alcohol, and to it was added an aqueous alcoholic solution of 1.7 g. of semicarbazide hydrochloride and 1.7 g. of sodium acetate. The mixture was refluxed for two hours, and then worked up in the usual manner. The semicarbazone thus prepared melted at 255° with decomposition; yield 47 mg.

The above semicarbazone was taken up in alcohol and hydrolyzed in the usual manner with a small amount of sulfuric acid. Crystals of the free ketone were obtained which melted at 114–115°. Its absorption spectrum in alcohol was measured by Dr. T. J. Webb of the Research Laboratories of Merck and Company, Inc., Rahway, N. J. A portion of this ketone was reconverted into its semicarbazone. The compound so obtained again melted at 255° with decomposition. Analysis of the semicarbazone: Calcd. for $C_{19}H_{23}ON_3$: N, 13.58. Found: N, 13.64.

We wish to take this opportunity to express our thanks to the American Philosophical Society for a grant-in-aid for this work and to Dr. T. J. Webb, Research Laboratories, Merck and Company, Inc., Rahway, N. J., for the absorption spectrum curve published in this article.

Summary

Trianhydroouabain lactone monoacetate has been oxidized with chromic acid in acetic acid solution. No ketonic material could be isolated from the reaction products. Attempts to obtain either benzene-tetracarboxylic acid-(1,2,3,4) or methylbenzene-tetracarboxylic acid from the products of oxidation of the above lactone with concentrated nitric acid have been described. Certain observations on the structure of this lactone are made in the light of these results.

A study of the nature of the oxidation products of *epi*-neoergosteryl acetate with chromic acid in acetic acid has been made. A ketone in the form of its semicarbazone (m. p. 255° with decomposition) has been isolated. Hydrolysis of this compound gives a ketone which melts at 114–115°. Its absorption spectrum is recorded. A discussion of the significance of these experiments in connection with certain observations of Marker and his co-workers and of Windaus and Deppe is given.

PRINCETON, N. J. RECEIVED MARCH 24, 1938

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Transformation of Dihydroxyacetone Derivatives into Pyruvic Aldehyde Derivatives[1]

BY CHARLES LLEWELLYN BERNIER AND WM. LLOYD EVANS

The conversion of the ketotriose, dihydroxyacetone, into pyruvic aldehyde has long been known. Pinkus[2] distilled a mixture of the former compound with dilute sulfuric acid and obtained, in the distillate, pyruvic aldehyde which he identified as the phenylosazone. Neuberg and Rewald[3] obtained pyruvic aldehyde phenylosazone by treating dihydroxyacetone with phenylhydrazine in either dilute ammonium hydroxide or sodium carbonate solution. More recently it has been found that the extent of the conversion in potassium hydroxide solution is influenced by the concentration of the alkali and the temperature.[4]

The transformation of the ketotriose is paralleled by a similar reaction of the isomeric aldotriose, glyceric aldehyde, from which Wohl[5] obtained pyruvic aldehyde phenylosazone by reaction with phenylhydrazine in weakly alkaline solution. It has been shown[6] that the experi-

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[1] Abstracted from a thesis which was offered by Charles Llewellyn Bernier to the Graduate School of The Ohio State University in partial fulfilment of the requirements for the degree of Master of Science. This paper was presented at the Denver Meeting of The American Chemical Society, 1932.

[2] G. Pinkus, *Ber.*, **31**, 36 (1898).

[3] C. Neuberg and B. Rewald, *Biochem. Z.*, **71**, 144 (1915).

[4] W. L. Evans and W. R. Cornthwaite, THIS JOURNAL, **50**, 486 (1928).

[5] Wohl in V. Lippmann, "Chemie der Kohlenhydrate," 1891; *cf. Biochem. Z.*, **5**, 56 (1907).

[6] W. L. Evans and H. B. Hass, THIS JOURNAL, **48**, 2703 (1926)

mental conditions surrounding this transformation of dihydroxyacetone are paralleled by similar conditions for the conversion of *dl*-glyceric aldehyde into pyruvic aldehyde. That these two simple sugars should behave in the same way in potassium hydroxide solution is to be expected since they become tautomers in alkaline media. This was clearly demonstrated by Fischer, Taube and Baer,[7] who transformed crystalline glyceric aldehyde into dihydroxyacetone in boiling pyridine. In acid solution the conversion of *dl*-glyceric aldehyde into pyruvic aldehyde differs from that of dihydroxyacetone in that the first reaction takes place only in the presence of an amine.[8]

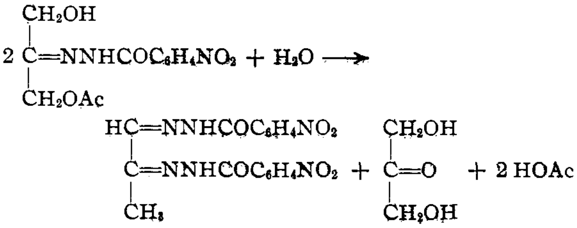
The authors have discovered that derivatives of dihydroxyacetone undergo transformation to derivatives of pyruvic aldehyde in various solvents and in the apparent absence of the solvent.

Dihydroxyacetonemonoacetate *m*-nitrobenzoylhydrazone, formed by the reaction of *m*-nitrobenzhydrazide with dihydroxyacetonemonoacetate, is transformed into pyruvic aldehyde *m*-nitrobenzoylosazone under various conditions. *This transformation of the hydrazone was first noticed when it was recrystallized from absolute ethanol.* The longer it was boiled in this solvent the more of the osazone was precipitated. Subsequently, it was found that the transformation occurred in other solvents even more readily. In order of increasing reaction rate the solvents were: 95% ethanol to which a few drops of acetic acid had been added, dilute acetic acid, and 16% phosphoric acid. The occurrence of this transformation in phosphoric acid solution is interesting in view of the fact that Fischer and Feldmann[9] have converted dihydroxyacetone itself into anhydrous pyruvic aldehyde through the use of phosphoric anhydride. A solid specimen of the hydrazone which had been crystallized three times from absolute ethanol and subsequently preserved in a glass bottle was found to have become transformed into the osazone in the course of three or four years. A sharp odor of acetic acid was perceived when the bottle was opened.

Dihydroxyacetonemonoacetate semicarbazone, prepared in a manner similar to that of the hydrazone above, was found to be easily transformed into pyruvic aldehyde disemicarbazone under conditions similar to those for the transformation of the hydrazone.[10]

Since pyruvic aldehyde *m*-nitrobenzoylosazone was found to be less soluble in water and seemed to be more stable to acid than the disemicarbazone, dihydroxyacetonemonoacetate *m*-nitrobenzoylhydrazone was the derivative selected for studying the transformation.

The reaction which occurs in the transformation possibly may be represented by the equation



$$2\ \begin{matrix}CH_2OH\\|\\C{=}NNHCOC_6H_4NO_2\\|\\CH_2OAc\end{matrix} + H_2O \longrightarrow \begin{matrix}HC{=}NNHCOC_6H_4NO_2\\|\\C{=}NNHCOC_6H_4NO_2\\|\\CH_3\end{matrix} + \begin{matrix}CH_2OH\\|\\C{=}O\\|\\CH_2OH\end{matrix} + 2\,HOAc$$

When the reaction is carried out in boiling 16% phosphoric acid, the derivatives are completely deacetylated and the acetic acid formed can be accounted for quantitatively by titrating the distillate from the boiling solution kept at constant volume.

To ascertain what happened to the dihydroxyacetone liberated in the reaction several experiments were devised. From these it was found that the dihydroxyacetone either remained unchanged or was converted into pyruvic aldehyde. When a mixture of the hydrazone with 16% phosphoric acid was distilled, some of the pyruvic aldehyde was found in the distillate and could be determined by forming its *m*-nitrobenzoylosazone. After one such distillation 27.06% of the dihydroxyacetone originally present (as hydrazone) in the distilling flask, was recovered as the osazone in the distillate and 40.33% was recovered from the distilling flask as precipitated osazone. When the hydrazone was refluxed with 16% phosphoric acid, 37.95% of the dihydroxyacetone precipitated as pyruvic aldehyde *m*-nitrobenzoylosazone. After filtering this derivative, an excess of *m*-nitrobenzhydrazide was added to the filtrate. Thus 48.32% more of the dihydroxyacetone was recovered as the osazone derivative. This accounts for 86.27% of the dihydroxyacetone originally present. To ascertain if much more than this percentage could be recovered, the hydrazone was refluxed in 16% phosphoric acid together with an excess of *m*-

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(7) H. O. L. Fischer, C. Taube and E. Baer, *Ber.*, **60**, 479 (1927).

(8) H. H. Strain and H. A. Spoehr, *J. Biol. Chem.*, **89**, 527 (1930).

(9) H. O. L. Fischer and L. Feldmann, *Ber.*, **62**, 854 (1929).

(10) *Cf.* Whitmore, "Organic Chemistry," D. Van Nostrand Company, New York, N. Y., 1937, p. 552.

nitrobenzhydrazide. The amount recovered was 92.80%. The decomposition of the osazone in the phosphoric acid and consequently its suitability as an analytical precipitate was tested by refluxing it with the acid and weighing the residue. A recovery of 98.80% was effected from a sample weighing 0.1 g. The hydrazone derivative which rearranged in a stoppered bottle weighed 7.7 g. The purified osazone transformation product from it weighed 5 g. This represents a return of 48.13% of the dihydroxyacetone originally present. Theoretically, 50% should have been obtained.

Experimental

Dihydroxyacetonemonoacetate.—Dihydroxyacetonemonoacetate was prepared by the method of Fischer, Baer and Feldmann.[11]

Dihydroxyacetonemonoacetate Semicarbazone.—Dihydroxyacetonemonoacetate semicarbazone was prepared by treating 5 g. of the dihydroxyacetonemonoacetate in 5 cc. of water with a solution of 4.22 g. of semicarbazide hydrochloride and 3.12 g. of anhydrous sodium acetate in 10 cc. of water and allowing the mixture to stand at 20° for twenty-four hours. The precipitate of the derivative weighing 3.85 g. was filtered off and recrystallized from 18 cc. of methanol per gram of crystals; m. p. 137.5 to 138°.

Anal. Calcd. for $C_6H_{11}N_3O_4$: N, 22.22; C, 38.07; H, 5.86; acetyl (using 0.1 *N* base), 5.29 cc. Found: N, 22.01; C, 37.96; H, 5.86; acetyl, 5.31 cc.

Pyruvic Aldehyde Disemicarbazone.—Pyruvic aldehyde disemicarbazone was prepared by heating a mixture of 2 g. of dihydroxyacetonemonoacetate in 14 cc. of water with 5.1 g. of semicarbazide hydrochloride and 3.73 g. of anhydrous sodium acetate to boiling and allowing the mixture to stand at room temperature for several days. The dried residue was recrystallized from 825 cc. of boiling water per gram; m. p. 266 to 267°, with decomposition.[12] A mixture of this derivative and an authentic sample of the disemicarbazone of pyruvic aldehyde prepared from dihydroxyacetone, melted at 265 to 267° with decomposition.

Anal. Calcd. for $C_5H_{10}N_6O_2$: N, 45.16; C, 32.24; H, 5.32. Found: N, 45.10; C, 32.51; H, 5.55.

Dihydroxyacetonemonoacetate *m*-Nitrobenzoylhydrazone.—Dihydroxyacetonemonoacetate *m*-nitrobenzoylhydrazone was prepared by refluxing a mixture of 3 g. of dihydroxyacetonemonoacetate with 4.1 g. of *m*-nitrobenzhydrazide dissolved in 65 cc. of absolute ethanol for ten minutes and allowing the reaction mixture to stand overnight. A yield of 4.38 g. of crystals was obtained. When recrystallized from 13 cc. of absolute ethanol per gram, the melting point was 130 to 131°. The melting of this compound was unusual. In the course of about a minute, the melt would change into a tan solid which gradually darkened as the temperature was raised and decomposed rapidly between 253 and 260°.

Anal. Calcd. for $C_{12}H_{13}N_3O_6$: N, 14.24; C, 48.79; H, 4.54; acetyl (using 0.1 *N* base), 3.39 cc. Found: N, 14.00; C, 48.55; H, 4.49; acetyl, 3.37 cc.

Pyruvic Aldehyde *m*-Nitrobenzoylosazone.—Pyruvic aldehyde *m*-nitrobenzoylosazone was prepared by boiling 3 g. of dihydroxyacetonemonoacetate with 8.2 g, of *m*-nitrobenzhydrazide in 125 cc. of absolute ethanol for eight to ten hours. The yield was 2.80 g. or 31% of theory. It was recrystallized from 40 cc. of nitrobenzene per gram; m. p. 280 to 281° with decomposition.[13] A mixture of this derivative and an authentic sample of pyruvic aldehyde *m*-nitrobenzoylosazone prepared from dihydroxyacetone melted at 278–282° with decomposition.

Anal. Calcd. for $C_{17}H_{14}N_6O_6$: N, 21.11; C, 51.34; H, 3.86. Found: N, 20.91; C, 51.04; H, 3.54.

The transformations of the hydrazone (see above) and the semicarbazone into their respective pyruvic aldehyde derivatives were discovered during their recrystallization. Because the transformation product, pyruvic aldehyde *m*-nitrobenzoylosazone, was found to be least soluble in various solvents and apparently most stable in them, dihydroxyacetonemonoacetate *m*-nitrobenzoylhydrazone was chosen for studying these transformations. To conserve the hydrazone, samples weighing 0.1 g. were used for each experiment. The precautions of analytical chemical procedures were used throughout.

(a) To 0.1 g. of the hydrazone was added 25 cc. of 16% orthophosphoric acid and the mixture refluxed. At first the hydrazone dissolved. In about ten minutes, the osazone began to precipitate. At the end of an hour the flask was cooled and the osazone filtered into a weighed crucible. The dried osazone weighed 0.0512 g., which represents 37.95% of the dihydroxyacetone originally present. The filtrate was transferred quantitatively back into the reaction flask and 0.1 g. of *m*-nitrobenzhydrazide was added to react with the remaining dihydroxyacetone or pyruvic aldehyde believed to be present. The mixture was heated for a short time and allowed to stand overnight. More of the osazone formed. This was filtered and dried. It weighed 0.0652 g., which represents 48.32% of the dihydroxyacetone present in the original 0.1 g. of derivative. Thus a total of 86.27% of the dihydroxyacetone was recovered as pyruvic aldehyde derivative.

(b) To a second 0.1 g. of the hydrazone contained in a distilling flask was added 25 cc. of 16% orthophosphoric acid. The mixture was then distilled and the distillate caught in a flask containing 25 cc. of 16% orthophosphoric acid and 0.1 g. of *m*-nitrobenzhydrazide. From time to time water was added to the distilling flask to make up for losses. After an hour of distillation, during which about 100 cc. was condensed, the flasks were cooled and the precipitates allowed to stand overnight. These precipitates were then filtered and weighed. The osazone formed in the distillate weighed 0.0365 g. and that formed in the distillation flask, 0.0544 g. The weights represent returns of dihydroxyacetone of 27.06 and 40.33%, respectively. Thus a total of 67.39% of dihydroxyacetone was recovered.

(c) To attempt a maximum recovery of the dihydroxyacetone as pyruvic aldehyde, 0.1 g. of the hydrazone was refluxed with a mixture of 25 cc. of 16% orthophosphoric acid and 0.1 g. of *m*-nitrobenzhydrazide. The osazone

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(11) H. O. L. Fischer, E. Baer, L. Feldmann, *Ber.*, **63**, 1732 (1930).

(12) C. Harries and H. Turk, *ibid.*, **38**, 1633 (1905).

(13) H. H. Strain and H. A. Spoehr, *J. Biol. Chem.*, **89**, 528 (1930).

recovered weighed 0.1252 g. and represents 92.80% of the dihydroxyacetone from the 0.1 g. of hydrazone.

(d) As a check on the adequacy of the osazone as an analytical precipitate, 0.1 g. of the recrystallized osazone was refluxed for thirty minutes with 25 cc. of 16% orthophosphoric acid, allowed to stand overnight, filtered and weighed. Of the 0.1 g. used, 0.0988 g. was recovered. This represents a recovery of 98.80%.

Summary

1. Two derivatives of dihydroxyacetonemonoacetate have been prepared, analyzed and characterized. They are these: (a) dihydroxyacetonemonoacetate semicarbazone and (b) dihydroxyacetonemonoacetate *m*-nitrobenzoylosazone.

2. The transformation of these two derivatives into pyruvic aldehyde disemicarbazone and pyruvic aldehyde *m*-nitrobenzoylosazone, respectively, has been discovered and studied.

Columbus, Ohio Received April 25, 1938

[Contribution from the Kent and George Herbert Jones Chemical Laboratories, The University of Chicago]

The Preparation of *dl-erythro*-α,β-Dihydroxybutyric Aldehyde[1]

By J. W. E. Glattfeld and W. G. Straitiff

As was stated in a recent article from this Laboratory the preparation of the eleven theoretically possible C_4-saccharinic acids has now been completed.[2] These acids have been synthesized and studied in order to provide the information necessary for their detection in, and separation from, reaction mixtures obtained when aldotetroses are treated with alkali under conditions favorable to saccharinic acid formation. The preparation of the *dl*-aldotetroses necessary for the proposed study of their saccharinic acid rearrangement, is now being carried forward actively.

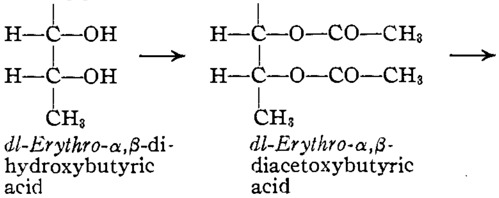
The aldehydes corresponding to the C_4-saccharinic acids are compounds still simpler than the aldotetroses for rearrangement studies and the preparation of some of these has been undertaken to provide more material for such studies. The synthesis of the *dl*-α,β-diacetoxy-isobutyric aldehyde was reported in a previous paper[2] and that of *dl-erythro*-α,β-dihydroxybutyric aldehyde is reported below.

The starting point of the work was one of the C_4-saccharinic acids first prepared in this Laboratory by Glattfeld and Woodruff[3] and called by them *dl*-1,2-dihydroxybutyric acid. This acid was later studied by Braun[4] who modified the name to *dl*-1,2-*erythro*-dihydroxybutyric acid in order to distinguish it from a closely-related acid of different stereochemical configuration which he called *dl-threo*-1,2-dihydroxybutyric acid. All of these names are open to objection and the acid under discussion will henceforth be called *dl-erythro*-α,β-dihydroxybutyric acid, a name which is in accordance with common usage. This name will be shortened in this paper to *dl-erythro*-α,β-acid to save space.

The reports on the *dl-erythro*-α,β-acid are very few, the two papers cited[3,4] and three others by Braun[5] constituting the entire literature. Consequently it was necessary to spend some time on the synthesis of the acid from crotonic acid. Braun's method was followed in general. The directions which finally proved most satisfactory are given in detail below.

Next a series of esters of the *dl-erythro*-α,β-acid was prepared. The reason for preparing these esters was that the original program included plans to reduce them to the aldehyde. Before this work could be carried out, however, a better scheme of reduction became available.[6] As the esters are new to the literature, the method of preparation and constants are recorded below.

The scheme of reduction which was finally successful consisted of the following steps.



$$\begin{array}{c} \text{COOH} \\ | \\ \text{H—C—OH} \\ | \\ \text{H—C—OH} \\ | \\ \text{CH}_3 \end{array} \longrightarrow \begin{array}{c} \text{COOH} \\ | \\ \text{H—C—O—CO—CH}_3 \\ | \\ \text{H—C—O—CO—CH}_3 \\ | \\ \text{CH}_3 \end{array} \longrightarrow$$

dl-Erythro-α,β-dihydroxybutyric acid

dl-Erythro-α,β-diacetoxybutyric acid

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[1] This article is condensed from a dissertation presented by W. G. Straitiff in partial fulfilment of the requirements for the degree of Doctor of Philosophy in the University of Chicago.

[2] Glattfeld and Mochel, This Journal, **60**, 1011 (1938).

[3] Glattfeld and Woodruff, *ibid.*, **49**, 2309 (1927).

[4] Géza Braun, *ibid.*, **51**, 228 (1929).

[5] Géza Braun, (a) *ibid.*, **52**, 3176 (1930); (b) *ibid.*, **52**, 3185 (1930); (c) *ibid.*, **54**, 1133 (1932).

[6] Rosenmund, *Ber.*, **51**, 585, 594 (1918); Fröschl and Danoff, *J. prakt. Chem.*, **144**, 217 (1936); Cook and Major, This Journal, **58**, 2410 (1936).