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

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[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.

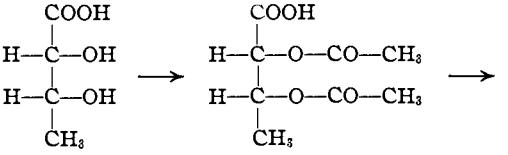
The aldehydes corresponding to the $C_4$-saccharinic acids are compounds still simpler than the aldotetroses for rearrangement studies and the preparation of some of these has been undertaken to provide more material for such studies. The synthesis of the *dl*-α,β-diacetoxy-isobutyric aldehyde was reported 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.




*dl-Erythro*-α,β-dihydroxybutyric acid — *dl-Erythro*-α,β-diacetoxybutyric acid

(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.

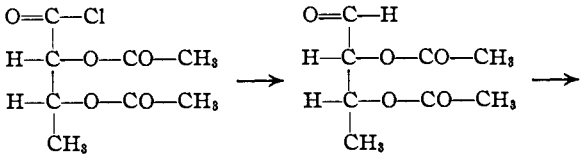
(2) Glattfeld and Mochel, THIS JOURNAL, **60**, 1011 (1938).

(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).

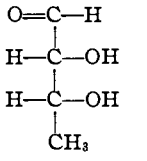
(6) Rosenmund, *Ber.*, **51**, 585, 594 (1918); Fröschl and Danoff, *J. prakt. Chem.*, **144**, 217 (1936); Cook and Major, THIS JOURNAL, **58**, 2410 (1936).



*dl-Erythro*-α,β-diacetoxybutyryl chloride



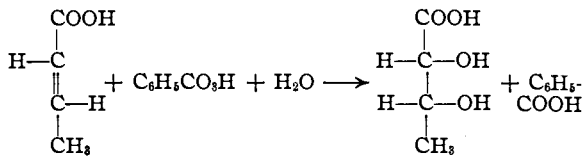
*dl-Erythro*-α,β-diacetoxybutyric aldehyde



*dl-Erythro*-α,β-dihydroxybutyric aldehyde

## Experimental Part

**Preparation of the *dl-erythro*-α,β-Acid.**—The procedure used by Braun[5b] was modified somewhat. A freshly-prepared chloroform solution which contained one mole of perbenzoic acid in 1 liter of chloroform was placed in a black 4-liter glass-stoppered bottle. The perbenzoic acid was prepared after the manner of Brooks and Brooks.[7] Two liters of distilled water and 86 g. (1 mole) of solid crotonic acid (m. p. 72°) were added, and the mixture thoroughly shaken. The reduction of the per-acid was extremely slow and a period of three months was required before a sample of the chloroform layer gave a negative test with potassium iodide–starch solution. The reaction takes place in the chloroform layer and it is advantageous to shake the mixture every second day in order to remove the *dl-erythro*-α,β-acid soon after it is formed.



Crotonic acid Perbenzoic acid *dl-erythro*-α,β-acid

The two layers were separated and the chloroform layer extracted three times with 500 cc. of distilled water. The aqueous extracts were combined and concentrated under reduced pressure at 50° to a volume of 400 cc. The solution was extracted with several 25-cc. portions of chloroform in order to remove the crotonic and benzoic acids which were partly crystalline. The water was then completely removed by further vacuum distillation at 50°.

The crude *dl-erythro*-α,β-acid remained in the flask as a slightly-colored viscous sirup. This was dissolved in 1 part of boiling anhydrous ethyl acetate and the coloring matter removed with charcoal. The filtered solution was cooled to 0° and colorless crystals formed as soon as the sides of the flask were scratched. These were removed by filtration, washed with 100 cc. of cold ethyl acetate, and dried in a vacuum desiccator over phosphorus pentoxide. The yield was 97 g. or 80% of the theoretical; m. p. 80.5–81.0°. The acid as thus prepared is somewhat hygroscopic.

One gram of the *dl-erythro*-α,β-acid was recrystallized several times from anhydrous ethyl acetate but the melting point did not rise above 81.5°. When the melting point tube was sealed, however, a melting point of 82.5° was obtained.

*Anal.* Calcd. for $C_4H_8O_4$: neut. equiv., 120. Found: n. e., 121.1, 120.9.

**The Phenylhydrazine Salt.**—Ten grams of the *dl-erythro*-α,β-acid was dissolved in 20 cc. of 90% ethyl alcohol and 15 g. of fresh, vacuum-distilled phenylhydrazine added to the solution. The reaction mixture was maintained for two hours at 70°, and then cooled to 0°. Crystallization began after a few minutes and continued for twelve hours. The solution was filtered, the crystals washed with ether, and dried on a plate. The yield was 14.3 g. Five grams of the impure compound was recrystallized from 10 cc. of anhydrous ethyl alcohol. The crystals were separated, washed with ether and dried; yield 3.5 g. A second recrystallization yielded 2.3 g. of colorless crystals which were dried to constant weight over phosphorus pentoxide; m. p. 105.5° with decomposition.

*Anal.* Calcd. for $C_{10}H_{16}O_4N_2$: N, 12.28. Found: N, 12.56, 12.53.

Woodruff[3] considered this product to be the phenylhydrazide with 1 molecule of water of crystallization, and reports the melting point as 103°. That the product was really the phenylhydrazine salt is shown not only by the analysis but also by its behavior. On standing the compound slowly decomposed. It was very soluble in water, less soluble in ethyl alcohol, and almost insoluble in ether. It reduced Fehling's solution at room temperature and reacted instantaneously with a neutral silver nitrate solution, forming finely-divided gray metallic silver.

**The Phenylhydrazide.**—Twelve grams of the *dl-erythro*-α,β-acid was dissolved in 40 cc. of absolute ethyl alcohol. Fifteen grams of fresh, vacuum-distilled phenylhydrazine was added. The reaction mixture was refluxed for five hours and at the end of this time 25 cc. of alcohol was removed by distillation. The mixture was then cooled to 0° and seeded with a crystal of the pure phenylhydrazine salt. After sixteen hours the crystals which had formed were removed by suction filtration and washed with ether; yield 3.2 g. This compound melted at 105.5° with decomposition and proved to be the phenylhydrazine salt.

All filtrates were combined and the alcohol and ether removed by evaporation under reduced pressure. The residue, a dark brown sirup, was dissolved in 25 cc. of boiling ethyl acetate and the solution cooled to 0°. Crystallization started when the sides of the flask were scratched. The crystals were separated and washed with 5 cc. of cold ethyl acetate; yield 4.7 g. Two successive recrystallizations from ethyl acetate yielded 3.4 g. of colorless crystals which melted at 123.5° after drying over phosphorus pentoxide in a desiccator. Analysis showed this product to be the true phenylhydrazide.

*Anal.* Calcd. for $C_{10}H_{14}O_3N_2$: N, 13.3. Found: N, 13.52, 13.47.

The phenylhydrazide was also prepared by maintaining 2 g. of the phenylhydrazine salt at 100° under 2 mm. pressure for two hours.[8] The cooled melt was dissolved in 4 cc. of boiling ethyl acetate and the crystals which were

(7) Brooks and Brooks, THIS JOURNAL, **55**, 4309 (1933).

(8) Primack, Master's Thesis, The University of Chicago, 1934.

THE ESTERS OF *dl-erythro*-α,β-DIHYDROXYBUTYRIC ACID

| Ester | Yield, % | B. p., °C. | Sapon. equiv. Calcd. | Found | Formula | Calcd., % C | H | Found, % C | H |
|---|---|---|---|---|---|---|---|---|---|
| Methyl | 72 | 109 | 134 | 134 | $C_6H_{10}O_4$ | 44.77 | 7.46 | 44.72 | 7.53 |
| Ethyl | 79 | 113 | 148 | 148 | $C_6H_{12}O_4$ | 48.65 | 8.10 | 48.45 | 8.03 |
| *n*-Propyl | 79 | 117 | 162 | 162 | $C_7H_{14}O_4$ | 51.85 | 8.64 | 51.90 | 8.56 |
| *n*-Butyl | 86 | 127 | 176 | 176 | $C_8H_{16}O_4$ | 54.54 | 9.09 | 54.71 | 9.27 |
| *n*-Amyl | 84 | 139 | 190 | 190 | $C_9H_{18}O_4$ | 56.84 | 9.47 | 57.14 | 9.68 |

obtained upon cooling to 0° were purified as described above; yield 0.4 g.; m. p. 123.5°.

The phenylhydrazide was soluble in warm, but not cold, water and ethyl alcohol and was slightly soluble in ether. It reduced warm Fehling's solution only slowly and reacted very slowly with a neutral silver nitrate solution. A cold concentrated sulfuric acid solution of the phenylhydrazide turned a deep red upon the addition of one drop of a dilute ferric chloride solution (Bulow's[9] reaction for phenylhydrazides of hydroxy acids).

**The Esters.**—The methyl, ethyl, *n*-propyl, *n*-butyl, and *n*-amyl esters of the *dl-erythro*-α,β-acid were prepared by the procedure used by Mochel.[2] Two hundred and fifty cc. of the proper anhydrous alcohol was placed in a 500-cc. round-bottomed flask. Hydrogen chloride which had been dried with sulfuric acid was passed into the alcohol until the increase in weight was 3% of the weight of the alcohol used. Twenty grams of the acid was added and the solution refluxed for eight hours after which it was transferred to a 500-cc. Claisen flask. The excess alcohol and water and a large part of the hydrogen chloride were first removed by distillation under 10 mm. pressure and the residue then completely distilled and collected in a 100-cc. Claisen flask. Silver oxide was added to the distillate until the chloride ion was completely precipitated. The mixture was warmed to 100° and then allowed to cool and stand at room temperature for twelve hours. It was then fractionated under reduced pressure.

The yields, boiling points under 10 mm. pressure, saponification equivalents, and the analyses for carbon and hydrogen, are recorded in the table.

The esters were all colorless, oily liquids possessing faint sweet odors. The methyl, ethyl and propyl esters were very soluble in water, the butyl ester only slightly so, and the amyl ester practically insoluble.

**Acetylation of the *dl-erythro*-α,β-Acid.**—Dry hydrogen chloride was passed into 34 g. (1/3 mole) of acetic anhydride contained in a 250-cc. round-bottomed flask until the weight increase was 3% of the weight of the acetic anhydride used. The solution was cooled to 0° and 10 g. (1/12 mole) of the acid added. The flask was then connected to a reflux condenser provided with a calcium chloride tube and immediately immersed in a water-bath at 20°. The acid dissolved quickly with the liberation of considerable heat. After solution of the acid the temperature of the water-bath was increased to 80° and so maintained for fifteen hours. The mixture was then transferred to a 100-cc. Claisen flask and the excess acetic anhydride removed under 4 mm. pressure. During this distillation the temperature was controlled by a water-bath, the temperature of which was raised slowly to a maximum of 80°. The crude diacetoxy acid remained as a colorless viscous liquid. It was dissolved in 30 cc. of warm distilled water, the solution filtered and the filtrate cooled to 0°. The colorless needles which separated proved to be the diacetoxy acid monohydrate. The evidence for this are the analytical figures given below and the fact that the *dl-erythro*-α,β-acid could be recovered when these crystals were refluxed with 0.1 *N* hydrochloric acid. The crystals were removed by filtration, recrystallized from distilled water and allowed to dry in the air overnight. The air-dry substance melted at 50°. The yield was 13.6 g.; 73% of the theoretical.

*Anal.* Calcd. for $C_8H_{12}O_6 \cdot H_2O$: sapon. equiv., 74.3; C, 43.24; H, 6.31; $H_2O$ of cryst., 8.1. Found: sapon. equiv., 74.6, 73.8; C, 43.40; H, 6.54; $H_2O$ of cryst., 8.3

The water of crystallization was removed easily from the diacetoxy acid monohydrate by heating the crystals to 60° in vacuum over phosphorus pentoxide for one hour. The residual diacetoxy acid is a colorless, odorless, viscous liquid which boils with decomposition at about 127° under 4 mm. pressure. When exposed to atmospheric conditions it readily adsorbs water, re-forming the crystalline monohydrate.

***dl-erythro*-α,β-Diacetoxybutyryl Chloride.**—Twenty-two and five-tenths grams (0.11 mole) of the anhydrous diacetoxy acid was dissolved in 26.2 g. (0.22 mole) of pure thionyl chloride. Hydrogen chloride and sulfur dioxide were evolved immediately. The reaction mixture was maintained at 50° for five hours, transferred to a 75-cc. Claisen flask and the excess thionyl chloride removed at 50° under 20 mm. pressure. The pressure was then reduced to 3 mm. and the temperature of the bath slowly raised to 110°. The acid chloride distilled smoothly at 79°. The yield was 23.9 g.; 97% of the theoretical.

*Anal.* Calcd. for $C_8H_{11}O_5Cl$: sapon. equiv., 55.6; C, 43.14; H, 4.94; Cl, 15.95. Found: sapon. equiv., 55.9, 55.6; C, 43.16; H, 5.18; Cl, 15.82, 15.73.

The acid chloride was a colorless, mobile liquid with a sharp odor. It fumed in moist air and reacted readily with water to give the diacetoxy acid monohydrate. When protected against moisture the acid chloride was perfectly stable.

***dl-erythro*-α,β-Diacetoxybutyric Aldehyde.**—To a solution of 44.5 g. of the acid chloride in 125 cc. of anhydrous xylene, 4 g. of 5% palladinized barium sulfate[10] was added. The mixture was heated to 150° under reflux by means of an oil-bath and hydrogen passed in at the rate of two bubbles per second. The reduction was complete within four hours as evidenced by the failure to form ammonium chloride fumes when the escaping gases were brought into contact with ammonia. After the solution had cooled the catalyst was removed by filtration and the colorless filtrate was subjected to vacuum distillation

(9) Bulow, *Ann.*, **236**, 194 (1886)

(10) Gattermann and Wieland, "Laboratory Methods of Organic Chemistry," 22nd edition, The Macmillan Co., New York, N. Y., 1932, pp. 369-370.

(water pump). A colorless mobile liquid remained after the xylene had distilled. The pressure was then reduced to 4 mm. and the temperature of the bath slowly raised to 105°. The diacetoxy aldehyde distilled smoothly at 87°. The yield was 32.8 g.; 87.3% of the theoretical.

*Anal.* Calcd. for $C_8H_{12}O_5$: $CH_3CO$, 45.74; C, 51.06; H, 6.38. Found: $CH_3CO$, 45.66; C, 51.07; H, 6.41.

The diacetoxy aldehyde was a colorless mobile liquid with an almond-like odor. It readily reduced Benedict's and Fehling's solutions. It was easily oxidized by silver oxide, by bromine, and by oxygen in the presence of palladinized barium sulfate but attempts to recover the original diacetoxy acid from such solutions were not successful.

**Hydrolysis of the Diacetoxy Aldehyde.**—Twenty-nine grams of the diacetoxy aldehyde was dissolved in 200 cc. of 0.1 *N* hydrochloric acid and the solution maintained at 80° for six hours. At the end of this time the solution was slightly yellow in color. The coloring matter was removed with charcoal and the filtrate subjected to vacuum distillation at 30° (water pump). The solution remained colorless until a volume of approximately 35 cc. was attained, when a slight color developed and greatly intensified as the distillation progressed. When all of the water had been removed an excess of anhydrous sodium carbonate was added to remove the last traces of acid. The aldehyde sirup was extracted with 70 cc. of anhydrous methyl alcohol and the extract decolorized with charcoal. The methyl alcohol was then removed by vacuum distillation at 25°. Color again appeared when the volume reached approximately 30 cc. and deepened as the distillation progressed. When all of the methyl alcohol had been removed a viscous brown sirup remained which did not crystallize. The residue weighed 14.2 g., an 88.5% yield calculated as pure aldehyde. This residue readily reduced Benedict's and Fehling's solutions.

An attempt was made to purify a sample of the aldehyde sirup by vacuum distillation but violent decomposition took place when a temperature of 50° was reached. All attempts to crystallize the aldehyde from solvents proved unsuccessful.

**The Osazone of *dl-erythro*-α,β-Dihydroxybutyric Aldehyde.**—Three grams of the aldehyde sirup was dissolved in 9 cc. of distilled water and a solution of 9 g. of freshly-distilled phenylhydrazine in 9 cc. of glacial acetic acid added. The mixture was allowed to stand in the dark for twenty-four hours. At the end of this time a mass of yellow crystals had formed. These were removed by suction filtration. After three recrystallizations from anhydrous benzene the compound was a canary yellow crystalline powder which melted at 173°. The purified compound weighed 1.2 g., a 14.8% yield calculated from the aldehyde.

*Anal.* Calcd. for $C_{16}H_{18}ON_4$: N, 19.86. Found: N, 19.79, 19.77.

This osazone was prepared by Wohl and Frank[11] by the action of phenylhydrazine on "methylglycerinaldehyde" which they obtained by the oxidation of crotonaldehyde acetal. They report a melting point of 171.5°. The production of what seems to be the same osazone from our aldehyde is evidence for the *erythro* configuration of the "methylglycerinaldehyde" of Wohl and Frank.

## Summary

1. Braun's procedure for the preparation of *dl-erythro*-α,β-dihydroxybutyric acid by the oxidation of solid crotonic acid by means of perbenzoic acid has been improved. Details of the modified procedure are given.

2. The phenylhydrazine salt and the phenylhydrazide of *dl-erythro*-α,β-dihydroxybutyric acid were prepared and studied. The phenylhydrazide was obtained by two different methods.

3. The methyl, ethyl, *n*-propyl, *n*-butyl and *n*-amyl esters of *dl-erythro*-α,β-dihydroxybutyric acid were prepared.

4. *dl-erythro*-α,β-Diacetoxybutyric acid and its monohydrate were prepared.

5. *dl-erythro*-α,β-Diacetoxybutyryl chloride was obtained by the action of pure thionyl chloride on the corresponding acid. The yield was almost quantitative.

6. Reduction of the diacetoxy acid chloride with pure hydrogen in the presence of palladinized barium sulfate gave *dl-erythro*-α,β-diacetoxybutyric aldehyde in good yield.

7. Hydrolysis of the diacetoxy aldehyde gave *dl-erythro*-α,β-dihydroxybutyric aldehyde, which was obtained as a brown sirup.

CHICAGO, ILL. RECEIVED APRIL 14, 1938

(11) Wohl and Frank, *Ber.*, **35**, 1908 (1902).