

In a larger run using a more concentrated solution the yield was poorer and more polymer was encountered. In another experiment the preliminary refluxing was omitted and the solution of the carbinol in acetic acid was shaken with catalyst and hydrogen in a vessel equipped with a sealed-in steam coil. No polymer was formed, but the yield of saturated hydrocarbon was lower.

The picrate crystallized from ethanol as reddish-orange needles, m. p. 128–128.5°, with slight previous sintering.

Anal. Calcd. for $C_{24}H_{17}O_7N_3$: N, 9.15. Found: N, 8.72.

Summary

9-Methyl-3,4-benzfluorene has been synthesized for comparison with the actively carcinogenic 10-methyl-1,2-benzanthracene.

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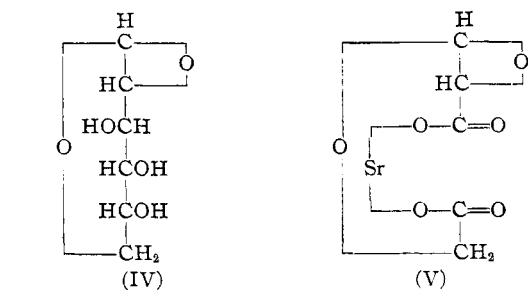
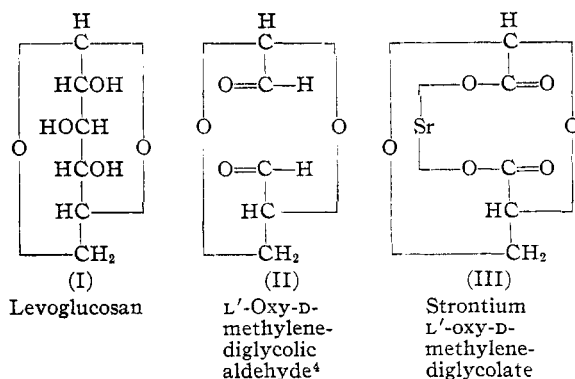
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[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Cleavage of the Carbon Chain of Levoglucosan by Oxidation with Periodic Acid¹

BY ERNEST L. JACKSON AND C. S. HUDSON¹

The structure of levoglucosan (I) has been established by methylation methods² and by its relationship to the structure of β -methylglucopyranoside.³ A compound having this structure should be oxidized by periodic acid to produce the dialdehyde (II).



The oxidation of levoglucosan with periodic acid or sodium metaperiodate yields a sirupy product which is doubtless L'-oxy-D-methylene-

diglycolic aldehyde (II). Oxidation of this product by bromine water kept neutral with strontium carbonate produces in good yield a crystalline strontium salt of a dibasic acid and, under the conditions employed, smaller amounts of strontium oxalate and strontium D-glycerate. The strontium salt of the dibasic acid was proved to be strontium L'-oxy-D-methylene-diglycolate (III) by oxidizing it with bromine water in the presence of strontium carbonate to produce strontium oxalate and strontium D-glycerate. The structure of the dialdehyde (II) follows from that of the strontium salt (III). The formation of strontium oxalate and strontium D-glycerate during the oxidation of the dialdehyde (II) to the strontium salt (III) with bromine water and strontium carbonate evidently is due to the oxidation of some strontium L'-oxy-D-methylene-diglycolate. These results prove levoglucosan to have structure (I); the beta configuration for carbon atom 1 is required by the accepted stereo configurations of the α - and β -forms of D-glucopyranose.⁵

Levoglucosan, upon oxidation by periodic acid or sodium metaperiodate, consumes two moles of the oxidant and produces one mole of formic acid.⁶ These figures agree with formula (I). The same data could fit a compound having structure (IV), but (IV) is excluded since the corresponding strontium salt (V) could not yield strontium D-glycerate by oxidation with bromine water and strontium carbonate.

L'-Oxy-D-methylene-diglycolic acid, which is a cyclic acetal having as its two components glyoxylic and D-glyceric acids, could not be hydrolyzed by hot 2.5 N hydrochloric acid. This

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented in part before the Division of Organic Chemistry, at the Boston meeting of the American Chemical Society, Sept. 11–15, 1939. (Not copyrighted.)

(2) Irvine and Oldham, *J. Chem. Soc.*, 119, 1744 (1921); Charlton, Haworth and Herbert, *ibid.*, 2855 (1931).

(3) Josephson, *Ber.*, 62, 313 (1929).

(4) The dialdehyde is named according to the plan previously adopted by Jackson and Hudson, *This Journal*, 59, 994 (1937).

(5) See F. Mischele, "Chemie der Zucker und Polysaccharide," Akademische Verlagsgesellschaft m. b. H., Leipzig, 1939, p. 153.

(6) Cf. Jackson and Hudson, *This Journal*, 61, 1580 (1939).

acetal, like the chloraloses⁷ and trichloroethylidene glycerol,⁸ is exceptional in its stability in the presence of acids.

These oxidation reactions can be employed in the study of the structure of other sugar anhydrides. Strontium L'-oxy-D-methylene-diglycolate serves as a reference compound for the determination of the ring structure of any aldohexose anhydride, the two rings of which are of the α -1,5 and the β -1,6 type. An application of this method to the study of the structure of D-altrosan is shown in the following article.⁹

Experimental

Oxidation of Levoglucosan with Periodic Acid.—To 25 ml. of 0.542 *M* aqueous periodic acid solution (2.1 molecular equivalents) was added a solution of 1.0432 g. of pure levoglucosan in water. The solution, diluted with water to 50 ml. at 20° and kept in a 20–21° room, showed $[M]_D \times 10^{-2}$: –98.2 (4.3 min.); –92.5 (7.6 min.); –84.4 (13.8 min.); –71.9 (27.1 min.); –60.5 (50.7 min.); –48.4 (90.3 min.); –40.3 (145 min.); –33.6 (236 min.); –28.9 (357 min.); –19.5, constant (24 hrs.). The specific rotation of L'-oxy-D-methylene-diglycolic aldehyde, calculated from the final $[M]_D$ value of the oxidation solution, is –15.0°. After twenty-four hours an analysis of 5 ml. of the solution showed an excess of 0.14 molecular equivalent of periodic acid, the consumption of the oxidant thus being 1.96 molecular equivalents.

For the preparation of strontium L'-oxy-D-methylene-diglycolate, the oxidation of 10.4 g. of levoglucosan with 500 ml. of 0.271 *M* aqueous periodic acid solution was carried out as described above. Upon completion of the reaction, the solution was neutralized cautiously to phenolphthalein with hot strontium hydroxide solution. L'-Oxy-D-methylene-diglycolic aldehyde was isolated as a colorless sirup by the procedure described in a previous paper⁴ for the methoxydiglycolic aldehydes from the methyl-pentopyranosides, with the exception that the solvent for extraction of L'-oxy-D-methylene-diglycolic aldehyde from the strontium salts was absolute methanol. To a solution of the dialdehyde in 2500 ml. of water were added 190 g. of strontium carbonate and 15 ml. of bromine. After the bromine had been dissolved, the mixture was kept in the dark at 25° for fifteen hours with frequent shaking during the first hour. Excess bromine was removed by aeration, and excess strontium carbonate was filtered off and washed with water. The solution, freed from bromine ions with silver carbonate and from excess silver with hydrogen sulfide, was concentrated *in vacuo* (bath, 50–55°) to 300 ml., filtered and the concentration continued to about 100 ml., when prismatic needles of strontium L'-oxy-D-methylene-diglycolate usually had started to separate. After the addition of 10–15% of ethanol, the mixture was left in the refrigerator to complete

crystallization; yield¹⁰ calculated as $C_6H_4O_6Sr$,¹¹ 7.2 g. (45%). The mother liquor contained strontium D-glycerate. The strontium L'-oxy-D-methylene-diglycolate, after one or two recrystallizations from water, was pure; it crystallizes from water at 20° or at refrigerator temperature as long prismatic needles of its pentahydrate; at 30° or above as small compact clusters of short needles of its monohydrate, which is less soluble in water than the pentahydrate. In preparing the solution of the strontium salt in water for crystallization, the less soluble monohydrate may be precipitated during the process of dissolving the pentahydrate, if a minimum amount of water and steam-bath temperature are employed. The procedure adopted, therefore, was to dissolve the strontium salt in a large excess of warm water, then concentrate the solution *in vacuo* (bath, 45–50°) to a relatively small volume and filter it quickly to remove any crystals that might be present. Thereafter, crystallization was allowed to proceed at a temperature selected to yield the desired hydrate of the strontium salt. For analysis and determination of the rotation of strontium L'-oxy-D-methylene-diglycolate, crystals of the pure pentahydrate were dried to constant weight at 100° *in vacuo*. The anhydrous strontium salt showed a specific rotation¹² of +37.5° in water (*c*, 0.45; *l*, 2). Upon exposure to the air at 20–25° the anhydrous salt soon showed an increase in weight in excess of the amount calculated for the water content of the monohydrate.

Anal. Calcd. for $C_6H_4O_6Sr$: C, 24.23; H, 1.63; Sr, 35.38. Found: C, 24.19, 23.99; H, 1.77, 1.49; Sr, 35.32, 35.16.

The monohydrate of strontium L'-oxy-D-methylene-diglycolate was prepared both by crystallization of the strontium salt from water, preferably at 45° which yields homogeneous crystals, and by efflorescence of the pentahydrate. Crystals of the pentahydrate, exposed to comparatively humid air at about 30°,¹³ showed no appreciable change in composition during ten to fifteen days, but thereafter effloresced in the course of several weeks to produce the monohydrate. The monohydrate is characterized by its pronounced stability at high temperature. It lost weight only slowly at 145–150° *in vacuo*, but at 175° *in vacuo* was converted to an anhydrous strontium salt. The specific rotation in water of samples of the monohydrate obtained under three different conditions were: (from water at 30°) +36.9° (*c*, 0.38; *l*, 4); (from water at 45°) +36.8° (*c*, 0.39; *l*, 4); (from efflorescence) +36.4° (*c*, 0.47; *l*, 4).

Anal. Calcd. for $C_6H_4O_6Sr \cdot H_2O$: H_2O , 6.78; C, 22.60; H, 2.28; Sr, 32.98. Found: (from water at 45°) H_2O ,

(10) The yield was only 25% in an experiment carried out under the same conditions, with the exception that the time for the oxidation of the dialdehyde was twenty-nine hours instead of fifteen hours.

(11) The water content of the crystals varies with the conditions of time, temperature and humidity under which they are dried. It was at first believed that the salt had crystallized as a trihydrate (*cf.* the accompanying article⁴), but a careful study has revealed with certainty only a mono and a pentahydrate.

(12) Except where otherwise stated, all rotations in this article are specific rotations at 20° for sodium light; *c* = g. per 100 ml. of solution; *l* = length in dm.

(13) Crystals of the pentahydrate, exposed to the air simultaneously at 20°, were stable as shown by the result of an analysis at the end of forty-five days. Calcd. for $C_6H_4O_6Sr \cdot 5H_2O$: H_2O , 26.67; Sr, 25.94. Found: H_2O , 26.71, 26.51; Sr, 25.80, 25.61.

(7) Hanriot and Richet, *Compt. rend.*, **117**, 734 (1893); Pictet and Reichel, *Helv. Chim. Acta*, **6**, 621 (1923); White and Hixon, *This Journal*, **55**, 2438 (1933).

(8) Hibbert, Morazain and Paquet, *Can. J. Research*, **2**, 131 (1930).

(9) Richtmyer and Hudson, *This Journal*, **62**, 961 (1940).

6.77, 6.85; C, 22.45, 22.64; H, 2.28, 2.43; Sr, 32.85, 32.81; (from water at 30°) Sr, 32.85, 32.72; (from water at 95–100°) Sr, 32.84; (from efflorescence) Sr, 32.79, 32.95.

Strontium D-glycerate, which is produced during the oxidation of L'-oxy-D-methylene-diglycolic aldehyde with bromine water and strontium carbonate, was isolated as well-formed octahedral prisms of the dihydrate¹⁴ by concentrating the filtrate from the crude strontium L'-oxy-D-methylene-diglycolate pentahydrate *in vacuo* to about 10 ml.; air-dried; yield of the crude dihydrate, 3 g. After purification by recrystallization from about three parts of water, the dihydrate melted at 136–137° (uncor.) and rotated +15.2° in water (*c*, 0.5; *l*, 2). The pure dihydrate is stable at 100° *in vacuo*, but at 125° *in vacuo* it loses approximately the weight calculated for two moles of combined water and becomes slightly colored. A specimen of calcium D-glycerate dihydrate, prepared from the strontium salt, rotated +15.5° in water (*c*, 0.6; *l*, 2) and melted at 142–143° (uncor.) alone or mixed with authentic calcium D-glycerate dihydrate.

Anal. Calcd. for $C_6H_{10}O_8Sr \cdot 2H_2O$: H_2O , 10.80; Sr, 26.26. Found: H_2O (dried at 125° *in vacuo*), 11.20, 11.30; Sr, 26.24, 26.08.

Oxalic acid was produced in the course of these oxidation reactions, as shown by the isolation of strontium oxalate from the excess strontium carbonate, which was recovered from the oxidation of L'-oxy-D-methylene-diglycolic aldehyde. A solution of the excess strontium carbonate in hydrochloric acid was boiled to expel carbon dioxide, cooled and neutralized with ammonium hydroxide solution. From the precipitate of strontium oxalate monohydrate (yield, 1.8 g.) was prepared oxalic acid dihydrate, which was characterized by usual methods.

L'-Oxy-D-methylene-diglycolic Acid.—The specific rotation of L'-oxy-D-methylene-diglycolic acid, obtained by liberating it from its pure anhydrous strontium salt in aqueous solution with an equivalent of hydrochloric acid, was +8.0° (*c*, 1.3; *l*, 2). The acid was isolated in crystalline condition, and was shown to be stable in hot aqueous solution. A solution of 2 g. of pure strontium L'-oxy-D-methylene-diglycolate in 80 ml. of hot water was cooled to 25°. After the addition of the calculated amount of *N* sulfuric acid solution and 90 ml. of absolute ethanol, the strontium sulfate was filtered off and the filtrate was concentrated *in vacuo* (bath, 50°) to a colorless sirup, which was made up to 50 ml. of solution in water. The rotation of this solution was unchanged by heating it in a stoppered flask on the steam-bath for five and one-half hours. The solution was then concentrated *in vacuo* to a sirup, which crystallized as needles during evacuation of the flask at room temperature to remove the last traces of solvent. The crystalline acid is readily soluble in acetone and in ether, but practically insoluble in petroleum ether. That the acid was unchanged by the heating of its aqueous solution and the subsequent operations was proved by neutralization of its solution in water with strontium hydroxide and isolation of strontium L'-oxy-D-methylene-diglycolate, which in the anhydrous condition rotated +37.5° in water (*c*, 0.4). Calcd. for $C_6H_8O_8Sr$:

Sr, 35.38. Found: Sr, 35.28. The acid was not hydrolyzed by hot 2.5 *N* hydrochloric acid solution. To a suspension of 0.3 g. of pure strontium L'-oxy-D-methylene-diglycolate in water was added sufficient 5 *N* hydrochloric acid to balance the strontium ions and make the concentration of the hydrochloric acid approximately 2.5 *N* after the solution had been diluted with water to 25 ml. The rotation of this solution was unchanged by heating it in a stoppered flask on the steam-bath for four hours.

L'-Oxy-D-methylene-diglycolic aldehyde, likewise, seemed resistant to acid hydrolysis. A solution of the dialdehyde, prepared from 2.67 g. of levoglucosan as previously described, in 100 ml. of 0.1 *N* hydrochloric acid showed only a minor change in rotation when it was heated on the steam-bath for seven hours; the rotation, measured in a 1-dm. tube, changed from $\alpha_D -0.31^\circ$ to $\alpha_D -0.24^\circ$; full hydrolysis to glyoxal and D-glyceraldehyde would be expected to cause reversal of the sign of rotation.

Strontium D-Glycerate and Strontium Oxalate from the Oxidation of Strontium L'-Oxy-D-methylene-diglycolate.—

Five grams of pure strontium L'-oxy-D-methylene-diglycolate, containing about 15% of combined water as indicated by its specific rotation of +31.9°, was dissolved in approximately 1500 ml. of water. After the addition of 90 g. of strontium carbonate and 7 ml. of bromine, the mixture was shaken until the bromine had dissolved and, thereafter, shaken occasionally while it was kept in the dark at room temperature. The rotation of the solution, measured in a 4-dm. tube, decreased during forty-two hours from $\alpha_D +0.39^\circ$ to $\alpha_D +0.05^\circ$. Excess bromine was then removed by aeration, and excess strontium carbonate was filtered off and washed with water. The excess strontium carbonate was dissolved in hydrochloric acid, the solution was boiled to expel carbon dioxide and neutralized with ammonium hydroxide, which precipitated 1 g. (about 30% yield) of strontium oxalate monohydrate. Oxalic acid dihydrate, prepared from the strontium oxalate, was characterized by customary methods. The filtrate from the excess strontium carbonate, after being freed from bromine ions with silver carbonate and from excess silver with hydrogen sulfide, was concentrated *in vacuo* to 75 ml., filtered and the concentration continued to about 10 ml. The solution, which was somewhat acid, was neutralized to litmus paper with strontium hydroxide solution and then concentrated to a thin sirup to which ethanol was added to turbidity. After being seeded with crystals of strontium D-glycerate dihydrate, the solution yielded at room temperature 0.7 g. of crystals rotating +9.9° in water. From the mother liquor was obtained, by concentration and dilution with ethanol, 0.4 g. of crystals rotating +7.3° in water. The first crop gave by two recrystallizations from water about 0.1 g. of prisms, which resembled crystals of strontium D-glycerate dihydrate; air-dried; m. p. 131–132° (uncor.); rotation, +14.3° in water. Calcd. for $C_6H_{10}O_8Sr \cdot 2H_2O$: Sr, 26.26. Found: Sr, 26.70, 27.01. After another recrystallization from a mixture of water and ethanol, the crystals melted at 134–135° (uncor.) and showed no depression when mixed with authentic strontium D-glycerate dihydrate.

There were indications that another substance, as yet unidentified, may be formed in this oxidation reaction.

(14) Cf. Frankland and Appleyard, *J. Chem. Soc.*, 68, 300 (1893).

The rotation of the crude product, which was a mixture not readily separable into its constituents with a small quantity of material, was considerably lower than that of both strontium D-glycerate and strontium L'-oxy-D-methylene-diglycolate. After several recrystallizations from mixtures of water and ethanol, crystals of doubtful purity containing 30.8% of strontium were isolated; specific rotation, $+7.0^\circ$ in water.

Oxidation of Levoglucosan with Sodium Metaperiodate.—A solution of 0.3488 g. of pure levoglucosan in water was mixed with 10 ml. of 0.453 *M* aqueous sodium metaperiodate solution (2.1 molecular equivalents). The solution, after being diluted with water to 25 ml. at 20° and kept in a 20° room for twenty hours, showed $[M]_D \times 10^{-2} = -19.1^\circ$. The specific rotation of L'-oxy-D-methylene-diglycolic aldehyde, calculated from the final $[M]_D$ value of the oxidation solution, is -14.7° ; this value is in good agreement with the specific rotation of -15.0° calculated from the end rotation of the periodic acid oxidation solution. After twenty hours an analysis of 5 ml. of the solution showed an excess of 0.11 molecular equivalent of sodium metaperiodate; the consumption of the oxidant was thus 1.99 molecular equivalents. The acidity of the reaction solution at the end of twenty hours corresponded to the production of 1.00 molecular equivalent of formic acid (5 ml., diluted with 300 ml. of water and neutralized to methyl red, required 4.30 ml. of 0.1 *N* sodium hydroxide; calcd. 4.30 ml.).

We express our thanks to Drs. A. E. Knauf and W. D. MacLay for a supply of levoglucosan and

to Dr. W. T. Haskins for carrying out the microanalyses.

Summary

Levoglucosan yields, by oxidation with periodic acid or sodium metaperiodate, L'-oxy-D-methylene-diglycolic aldehyde, which is oxidized by bromine water kept neutral with strontium carbonate to produce, under specified conditions, crystalline strontium L'-oxy-D-methylene-diglycolate in 45% yield and smaller amounts of strontium oxalate and strontium D-glycerate. The structure of strontium L'-oxy-D-methylene-diglycolate was proved by its oxidation with bromine water in the presence of strontium carbonate to produce strontium oxalate and strontium D-glycerate. These results show the levoglucosan molecule to have two rings, one of which is of the pyranoid and the other of the septanoid type. This confirmation of the generally accepted ring structure of levoglucosan demonstrates the applicability of these oxidation reactions to the structural study of the sugar anhydrides.

L'-Oxy-D-methylene-diglycolic acid, which could not be hydrolyzed by hot 2.5 *N* hydrochloric acid, is one of the few acetals possessing such stability.

WASHINGTON, D. C.

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[CONTRIBUTION FROM THE NATIONAL INSTITUTE OF HEALTH, U. S. PUBLIC HEALTH SERVICE]

The Ring Structure of D-Altrose¹

BY NELSON K. RICHTMYER AND C. S. HUDSON

A few years ago we reported² that "crystalline D-altrose is converted by hot hydrochloric acid from $[\alpha]_D^{20} +34$ to -98° ; this is accompanied by partial loss of reducing power presumably due to the formation of an anhydro-D-altrose to the extent of 57% at equilibrium." Independently, Robertson and Griffith³ found that the removal of the glycosidic methoxyl group from certain partially methylated α -methyl-altrosides by hydrolysis with 4–8% hydrochloric acid "leads to the production of an anhydro-derivative in equilibrium with a small amount of a reducing sugar." They cited also the case of the "methyl epiglucoamine" of Fischer, Bergmann and Schotte⁴; this sub-

stance, which is probably a 3-amino methylaltroside,⁵ undergoes acid hydrolysis with the formation of an anhydro compound from the liberated sugar and consequent loss of reducing power.⁶ Robertson and Griffith suggested that the anhydro-linkage in these compounds must involve position 4 or 6, since only these positions are available in the case of the 2,3-dimethylaltrose which forms an anhydride. The suggestion was confirmed later⁷ by the fact that 4,6-dimethyl- α -methylaltroside is hydrolyzed in normal fashion to a reducing sugar without anhydride formation.

Hudson,⁸ in 1938, presented conclusive evidence that sedoheptulosan, the anhydride which is formed spontaneously from sedoheptulose (D-altroheptulose) in acid solution, possesses the

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented in part before the Division of Organic Chemistry, at the Boston meeting of the American Chemical Society, Sept. 11–15, 1939. (Not copyrighted.)

(2) Richtmyer and Hudson, *THIS JOURNAL*, **57**, 1721 (1935).

(3) Robertson and Griffith, *J. Chem. Soc.*, 1196 (1935).

(4) Fischer, Bergmann and Schotte, *Ber.*, **53**, 541 (1920).

(5) K. Freudenberg, Burkhart and Braun, *ibid.*, **59**, 715 (1926).

(6) Levene and Meyer, *J. Biol. Chem.*, **55**, 224 (1923).

(7) Robertson and Dunlop, *J. Chem. Soc.*, 474 (1938).

(8) Hudson, *THIS JOURNAL*, **60**, 1241 (1938).