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-methylenediglycolate. After several recrystallizations from mixtures of water and ethanol, crystals of doubtful purity containing 30.8% of strontium were isolated; specific rotation, +7.0° 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 $[M]_D \times 10^{-2} = -19.1°$. The specific rotation of L′-oxy-D-methylenediglycolic 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. RECEIVED FEBRUARY 26, 1940

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

The Ring Structure of D-Altrosan[1]

BY NELSON K. RICHTMYER AND C. S. HUDSON

A few years ago we reported[2] that "crystalline D-altrose is converted by hot hydrochloric acid from $[\alpha]^{20}_{D}$ +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 Griffith[3] 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 epiglucosamine" of Fischer, Bergmann and Schotte[4]; this substance, 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 later[7] 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

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[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).

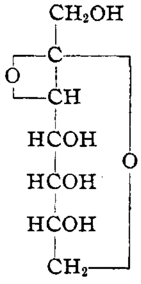
[5] K. Freudenberg, Burkhart and Braun, *ibid.*, **59**, 715 (1926).

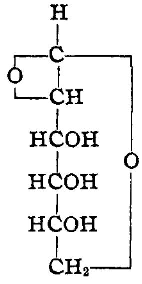
[6] Levene and Meyer, *J. Biol. Chem.*, **55**, 224 (1923).

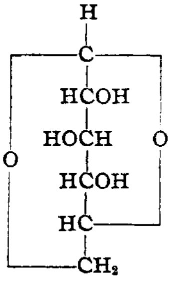
[7] Robertson and Dunlop, *J. Chem. Soc.*, 474 (1938).

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

unusual combination of an ethylene oxide and a septanoid ring (I).


Sedoheptulosan
I

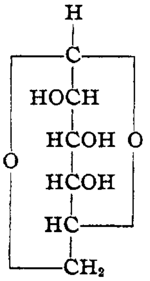

D-Altrosan (?)
II

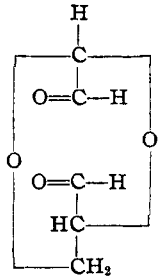

Levoglucosan
III

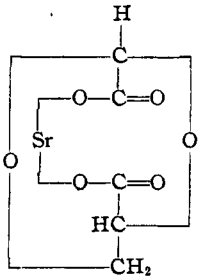
Because of the identical configurations of the asymmetric carbon atoms in sedoheptulose and D-altrose, and because of the ease with which these two sugars undergo anhydride formation in the presence of acids, it did not seem unreasonable to suggest that a similar structure II might be written for D-altrosan rather than a $<1,5>$ $<1,6>$ ring system like that which had been established previously for levoglucosan (III). It was emphasized, however, that formula II for D-altrosan rested solely upon the apparent analogy to sedoheptulosan (I), and that additional experimental data would be necessary to answer the question.

In a recent Communication[9] we announced the successful crystallization, after three years, of a sample of D-altrosan which had been prepared by removing the D-altrose component from the altrose–altrosan equilibrium mixture by oxidation with bromine water. With the additional crystalline material now available we are continuing our study of D-altrosan, and are reporting at this time a proof of its ring structure. To this end we have utilized the periodic acid method of oxidation developed by Jackson and Hudson,[10] especially as described in the preceding article.[11]

The oxidation of D-altrosan with periodic acid or with sodium metaperiodate has been shown to consume two equivalents of oxidizing agent, and to liberate one equivalent of formic acid. The resulting aldehyde upon further oxidation with bromine water produced a dibasic acid, readily isolated as a crystalline strontium salt of the composition $C_5H_4O_6Sr\cdot 5H_2O$. Of the many ring combinations possible for D-altrosan, $C_6H_{10}O_5$, only two could fulfill the requirements of reacting with two moles of periodic acid, with the elimination of one carbon atom as formic acid, and the subsequent formation of a dibasic acid containing the other five carbon atoms. These two possibilities are the $<1,2>$ $<1,6>$ formula II already suggested, and the $<1,5>$ $<1,6>$ formula IV analogous to that of levoglucosan (III).


D-Altrosan
IV


Dialdehyde
V


Strontium salt
VI

The actual decision between formulas II and IV for D-altrosan was relatively simple after the pioneer work reported in the preceding paper. Thus the rotation[12] $-14.7°$ for the dialdehyde V in the periodic acid solutions was in close agreement with the value recorded for L′-oxy-D-methylene-diglycolic aldehyde obtained from levoglucosan under comparable conditions. The crystalline strontium salt VI was found to agree in its rotation in water, its rotation in acid, in the conversion of the pentahydrate to the monohydrate (which is the stable form in air at room temperature), in its solubility in water, and by a determination of mixed solubilities,[13] with strontium L′-oxy-D-methylene-diglycolate from levoglucosan.

Since a compound with structure IV would be expected to produce the same dialdehyde V and the same strontium salt VI as are obtained from levoglucosan (III), whereas a compound with structure II could not, and since the proof of structure of the strontium salt from levoglucosan is in complete harmony with the structure III established previously for that compound, therefore D-altrosan must have the same ring system as levoglucosan, and accordingly may be designated[14] D-altrosan $\alpha<1,5>\beta<1,6>$.

Experimental

D-Altrosan.—The reactions by which lactose is converted to D-altrosan have been described previously.[2,9] Briefly,

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[9] Richtmyer and Hudson, THIS JOURNAL, **61**, 214 (1939).

[10] Jackson and Hudson, *ibid.*, **59**, 994 (1937).

[11] Jackson and Hudson, *ibid.*, **62**, 958 (1940).

[12] Throughout the article the rotations are specific rotations at 20° for sodium light; *c* designates concentration in grams per 100 cc. of solution.

[13] Montgomery and Hudson, THIS JOURNAL, **52**, 2105 (1930).

[14] The name altrosan (or altrose anhydride), rather than anhydroaltrose, is used to indicate anhydride formation involving the glycosidic hydroxyl group. This system of nomenclature is in accord with the proposal of M. Bergmann (*Ber.*, **58**, 2647, 2650 (1925); see also F. Micheel, "Chemie der Zucker und Polysaccharide," Akademische Verlagsgesellschaft m. b. H., Leipzig, 1939, p. 151).

lactose octaacetate was chlorinated and rearranged to acetochloroneolactose by the action of aluminum chloride and phosphorus pentachloride. The acetochloroneolactose[15] was hydrolyzed by six hours' boiling with water to hydrochloric and acetic acids, galactose and altrose; at the same time about 60% of the altrose was converted to altrosan. The acids were removed in the usual manner, the galactose by fermentation, the altrose by oxidation with bromine water and subsequent separation as calcium altronate, and the remaining altrosan was crystallized. From 1132 g. of acetochloroneolactose was obtained 75 g. of crystalline D-altrosan,[16] and from the mother liquors by acetylation was obtained 51 g. of crystalline 2,3,4-triacetyl-D-altrosan and 14 g. of altrose α-pentaacetate.[17]

Oxidation of D-Altrosan with Sodium Metaperiodate.—To 0.6173 g. of altrosan in 25 cc. of water was added 20 cc. of 0.419 *M* aqueous sodium periodate (2.2 equivalents of $NaIO_4$), and the solution left at 20° for forty-five hours. The volume was adjusted with water exactly to 50 cc. The specific rotation, calculated as the dialdehyde V, was −14.4° as compared with the value −14.7° obtained by Jackson and Hudson[11] for the dialdehyde formed in the same way from levoglucosan. The titration of an aliquot for excess periodate indicated the consumption of 1.97 equivalents of oxidizing agent. Titration of another aliquot with aqueous sodium hydroxide, using methyl red as indicator, showed the formation of 0.97 equivalent of acid, presumably formic acid.

Oxidation of D-Altrosan with Periodic Acid.—Since a preliminary experiment indicated that the reaction of altrosan with periodic acid proceeded almost instantaneously at 20°, with considerable evolution of heat, subsequent oxidations were carried out at a lower temperature. Thus, to 5.469 g. of D-altrosan, dissolved in 75 cc. of water and cooled in an ice-bath, were added six 25-cc. portions of 0.495 *M* aqueous periodic acid (2.2 equivalents of HIO_4) at ten-minute intervals. The solution was left overnight at 20°, and its volume adjusted to 250 cc. with water. The specific rotation, calculated as the dialdehyde V, was −14.5°, and in a second experiment −14.9°; these values are in good agreement with the rotation of −15.0° obtained by Jackson and Hudson from their similar oxidation of levoglucosan. The titration of an aliquot for excess periodic acid revealed that 1.96 equivalents of oxidizing agent had been consumed.

Isolation of the Dialdehyde V and Oxidation to the Strontium Salt VI.—The solutions from the oxidation of altrosan with periodic acid were combined, neutralized to phenolphthalein with strontium hydroxide, filtered, and the filtrate concentrated *in vacuo* to a small volume in the presence of 1 g. of strontium carbonate. The solution was filtered into a smaller flask and concentrated *in vacuo* practically to dryness. The dialdehyde was extracted readily with absolute methyl alcohol, and was left behind as a colorless sirup upon removal of the alcohol *in vacuo*. A concentrated aqueous solution of this sirup was estimated, from its rotation, to contain 4.95 g. of the dialdehyde, derived from 7.35 g. of D-altrosan.

For oxidation, the solution of dialdehyde was diluted with water to 1900 cc., and 145 g. of strontium carbonate and 7 cc. of bromine added. The mixture was shaken frequently during the first hour, then left fourteen hours more at room temperature (25°). Excess bromine, insoluble strontium salts and strontium bromide were removed by aeration, filtration and treatment with silver carbonate, respectively. The filtrate was freed from dissolved silver with hydrogen sulfide, and the solution concentrated *in vacuo*. The strontium salt which crystallized spontaneously during the distillation weighed 5.8 g. Twice recrystallized from water, and air-dried for two days, it had the composition of a pentahydrate.

Anal. Calcd. for $C_5H_4O_6Sr{\cdot}5H_2O$: Sr, 25.94; H_2O, 26.67. Found: Sr, 25.94; H_2O, 25.91.

Identification of the Strontium Salt as Strontium L'-Oxy-D-methylene-diglycolate VI.—Inasmuch as the strontium salt derived from levoglucosan was found at first by Jackson and Hudson to crystallize apparently as a trihydrate, and the strontium salt from D-altrosan had crystallized as a pentahydrate, a careful comparison of the two substances was made. The pentahydrate rotated +28.1° in water, equivalent to +38.3° calculated as the anhydrous strontium salt (*c*, 0.45), as compared with +37.5° reported by Jackson and Hudson for their anhydrous strontium salt (*c*, 0.45). Dissolved in an excess of aqueous hydrochloric acid, the pentahydrate showed a rotation of +7.9° calculated as the free organic acid (*c*, 1.3), as compared with the rotation +8.0° for the L'-oxy-D-methylene-diglycolic acid (*c*, 1.5) liberated by Jackson and Hudson from their anhydrous strontium salt.

Further comparison was made directly between the strontium salt from D-altrosan and the strontium salt from levoglucosan prepared by the same procedure. Thus, the latter salt also was obtained as a pentahydrate by the concentration of its aqueous solution *in vacuo* with the bath temperature about 40°. This salt was filtered, washed with cold water, and a portion of it placed on a watch glass in a room kept at 20° ± 1°. Overnight the strontium salt lost its adsorbed moisture, then remained constant in weight for two days. A sample removed at that time showed it to be a pentahydrate.

Anal. Calcd. for $C_5H_4O_6Sr{\cdot}5H_2O$: Sr, 25.94. Found: Sr, 25.92.

The remainder of this portion kept at 20° soon began to lose weight, slowly at first and then more rapidly as shown in Fig. 1, until a total of 3.85 molecular equivalents of water had been lost in thirty days. From another sample at 30°, the loss of water was complete in four days, and the final stage of the strontium salt monohydrate was reached.

Anal. Calcd. for $C_5H_4O_6Sr{\cdot}H_2O$: Sr, 32.98. Found: Sr, 32.79 (salt from levoglucosan), 32.82 (salt from D-altrosan, air-dried at 30° for twenty-four days).

The concluding proof of identity of the strontium salts from levoglucosan and D-altrosan was obtained through a study of their solubilities. In 5 cc. of aqueous solution,

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[15] It is unnecessary to isolate the acetochloroneolactose except in preliminary experiments designed to ensure favorable yields. Instead, the mixture of acetochloro derivatives may be used, and the lactose component removed by the regular hydrolysis and fermentation operations.

[16] The rotation in water (*c*, 2.5) of a carefully purified sample of D-altrosan has been determined as −213.0 ± 0.6°, or slightly lower than the −215° reported in our preliminary Communication.

[17] These compounds and some of their transformation products will be described in a future publication.

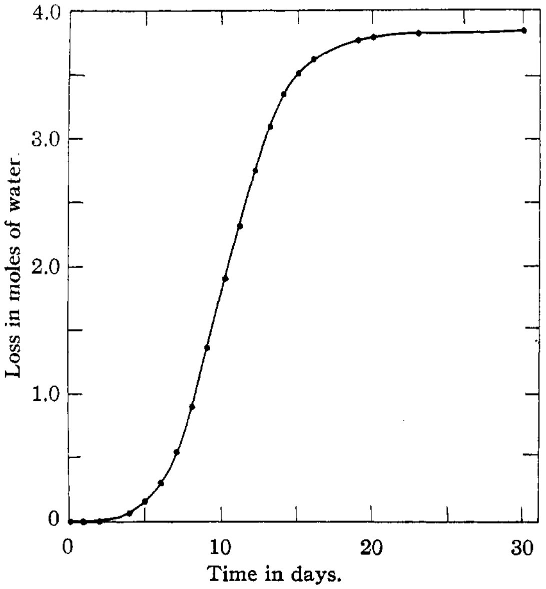

Fig. 1.—Conversion of strontium salt pentahydrate to monohydrate in air at 20°.

saturated by shaking five days at 20° with an excess of the solid strontium salt from levoglucosan, there was contained 40.6 mg. of the strontium salt monohydrate. In 5 cc. of a similar solution from D-altrosan there was 40.2 mg. To a portion of the solution saturated with the salt from levoglucosan then was added solid strontium salt from D-altrosan, and the mixture shaken five days at 20°; the filtered solution contained 40.2 mg. of the monohydrate in 5 cc. A similar value for the solubility, 40.6 mg. in 5 cc., was reached from supersaturation, by shaking the strontium salt from levoglucosan first at 30° (44.8 mg. soluble in 5 cc.), and then at 20°.

One of the authors (N. K. R.) desires to thank the Chemical Foundation of New York for a Research Associateship, and the American Academy of Arts and Sciences for a grant from the Cyrus M. Warren Fund. The authors also express their indebtedness to Dr. W. T. Haskins for carrying out the microanalyses, and to Dr. A. E. Knauf for the sample of levoglucosan which was oxidized.

Summary

The oxidation of D-altrosan with periodic acid, followed by bromine water and strontium carbonate, to the same strontium L'-oxy-D-methylenediglycolate which is obtained from levoglucosan, has shown that D-altrosan possesses the same ring system as levoglucosan, and accordingly is to be designated D-altrosan $\alpha<1,5>\beta<1,6>$.

WASHINGTON, D. C. RECEIVED FEBRUARY 26, 1940

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketene Acetals. IV. Polymers of Ketene Diethylacetal[1]

BY PAUL R. JOHNSON,[2] HARRY M. BARNES[3] AND S. M. MCELVAIN

One of the first chemical properties of ketene acetal to be noticed was its readiness to polymerize. The polymer appeared as a thin, white deposit on the interior of the flasks and condensers in which ketene acetal had been distilled and also as a semi-solid gum which settled out of distilled samples of ketene acetal after a few days of standing. It soon was noted that distillation apparatus that had been cleaned with the ordinary chromic acid–sulfuric acid mixture before the distillation of ketene acetal acquired an excessive amount of the polymer on the inner glass surfaces. If, however, the interior of the apparatus were washed with an aqueous alkali solution after the use of the acid cleaning solution, and then rinsed and dried in the usual manner, the amount of polymer formed during the distillation of ketene acetal was scarcely noticeable. Similarly, dusting the interior of the containers in which ketene acetal was kept with sodium or potassium *t*-butoxide practically eliminated the polymerization of the acetal on standing.

Although acidified glass surfaces cause some polymerization of ketene acetal, this catalyst is not efficient enough to allow for the preparation of the polymer in quantity. In the first paper of this series[4] it was reported that heat caused polymerization of the acetal. It is now believed that the polymerization then noted was due to the acidity of the inner surface of the container in which the acetal was heated, since later experiments have shown that ketene acetal may be heated at 190–240° for six hours in *new* Pyrex tubes without any perceptible polymerization. Also, a sample of ketene acetal sealed in a new soft-glass container and kept in diffuse sunlight has remained clear and mobile after three years.

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(1) The third paper of this series is Magnani and McElvain, THIS JOURNAL, **60**, 2210 (1938). This work was supported in part by the Wisconsin Alumni Research Foundation.

(2) du Pont Post-doctorate Research Assistant, 1938–1940.

(3) Wisconsin Alumni Research Foundation Scholar, 1935–1936, Research Assistant, 1937–1938.

(4) Beyerstedt and McElvain, THIS JOURNAL, **58**, 529 (1936).