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PREPARATION OF *meso*-ERYTHRITOL AND D-ERYTHRONIC LACTONE FROM PERIODATE-OXIDIZED STARCH

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The readily available 1,4-linked polyglucosans would appear to offer, *via* periodate oxidation, a convenient source for the preparation of erythritol, D-erythronic acid, and possibly, D-erythrose. However, little work has been reported along these lines. Jackson and Hudson, using native cornstarch and cotton, hydrolyzed the products of periodic acid oxidation, then oxidized with bromine water and isolated D-erythronic lactone in small yields. Some destruction of the polyaldehyde was believed to have occurred during hydrolysis (1). Jayme and Maris subjected periodate-oxidized cellulose to oxidation or reduction followed by hydrolysis, but isolated D-erythronic acid and *meso*-erythritol only in the form of derivatives (2). Recently, the advantageous procedure of reducing the polyaldehyde prior to hydrolysis has been perfected (3) and applied in analytical procedures (3, 4).

Described here are improved procedures by which both *meso*-erythritol and D-erythronic lactone have been obtained crystalline in good yields from periodate-oxidized starch. Heretofore, *meso*-erythritol has been obtained from natural sources (5, 6) or by synthesis (6) and D-erythronic lactone has been obtained only through complex synthetic procedures (7, 8).

In this investigation, sodium metaperiodate rather than periodic acid (1, 9) was employed as oxidant. Use of a mildly acid-modified potato starch gave significantly better yields than native potato starch. In this work, as in that of Jackson and Hudson (1, 9) starch in the granular state was oxidized by periodate. This simplified our operations and resulted in slightly higher yields than when starch in solution was employed. Use of the polyaldehyde in the highly hydrated state without drying avoided possible structural changes and facilitated subsequent treatment. For preparation of D-erythronic lactone, it was found advantageous to oxidize the polyaldehyde with bromine water in the presence of barium acetate buffer rather than without buffer (1). Subsequent hydrolysis of the resultant polyacid and removal of glyoxylic acid as the insoluble basic barium salt permitted direct isolation of D-erythronic lactone in 30% yield without recourse to an intermediate derivative (1, 2). However, isolation of the intermediate brucine D-erythronate in 53% yield indicated that the actual production of D-erythronic acid from starch was greater than the yield of the lactone (36% as obtained through the brucine salt) would indicate. Incomplete lactonization of the acid was suspected.

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Our observations showed that during reduction of the polyaldehyde by hydrogen and Raney nickel for production of *meso*-erythritol, considerable degradation in molecular size occurred.

EXPERIMENTAL

Materials and methods. A modified Lintner's solubilized potato starch was used which was prepared by treating commercial potato starch with 6% hydrochloric acid at 20° for 24 hours. The product was washed free of acid and air-dried at room temperature. The moisture content was determined and sample weights were calculated to the dry basis.

In this article, quantities of starch are expressed in terms of moles. For this purpose, the formula for starch is considered to be that of its monomeric unit, the anhydroglucopyranose unit (AGU).

Periodate determinations were made by the method of Fleury and Lange (10). Analyses for formic acid were made on reaction solutions, or on the combined filtrates and washings from oxidized granular starch, after reduction of excess periodate by ethylene glycol. The solutions were titrated directly with 0.05 *N* sodium hydroxide solution to a Methyl Red end point, or were distilled *in vacuo* under conditions for quantitative recovery of volatile acid, and the distillate was titrated. The volatile acid was proved to be formic by conversion to crystalline barium formate in 63% yield, and by comparison with a synthetic control.

Anal. Calc'd for $C_2H_2BaO_4$: Ba, 60.41; C, 10.55; H, 0.886.
Found for starch product: Ba, 60.24; C, 10.82; H, 1.33.
Found for synthetic control: Ba, 60.26; C, 10.65; H, 1.23.

Optical activity is reported in terms of specific rotation for sodium light. For reaction products which were not isolated, the weight of the product expected was calculated from the weight of the starting material.

Preparation and properties of periodate-oxidized starch. Granular starch was treated with 1.2 moles of sodium metaperiodate per mole AGU at 20° for 24 hours. The concentration of sodium metaperiodate in the reaction mixture was approximately 0.43 *molar*. The oxidized starch was removed by filtration and washed with water until free of iodate and periodate. Analysis of the filtrate and washings showed that 1.02 moles of periodate had been reduced and 0.034 mole of formic acid had been liberated per mole of anhydroglucopyranose unit in the starch.

The polyaldehyde product, having been dried only on a suction filter, was used immediately for further treatment. In this condition, the polyaldehyde retained approximately five times its weight of water.

The moist polyaldehyde from 0.05 mole of starch (8.1 g.) dissolved to a limpid, colorless solution when stirred in 400 ml. of water in a boiling water bath for 45 minutes. The solution, which showed $[\alpha]_D^{20}$ +8.9° (*c*, 1.6) and reduced Fehling solution strongly, was retained completely within a viscose membrane when dialyzed against distilled water for 24 hours.

Preparation of meso-erythritol. The product from periodate oxidation of 0.15 mole of starch (24.3 g.), suspended in 170 ml. of water, was reduced in the presence of 10 g. of Raney nickel catalyst, under 2,500 lbs. per sq. in. pressure of hydrogen, for 5 hours at 100°. The mixture was agitated gently. After removing the catalyst by filtration, a neutral, colorless, non-reducing, limpid solution was obtained which showed $[\alpha]_D^{20}$ +5.4°. This solution dialyzed completely through a viscose membrane. A portion of the solution developed no color when heated in 0.5 *N* sodium hydroxide solution for 8 hours at 100°. Hydrolysis in 1% sulfuric acid for 5 hours at 100° resulted in a colorless solution having the constant value, $[\alpha]_D^{20}$ +1.5°. If all expected reactions had been complete, this value would have been zero. The solution, made free of sulfuric acid by barium hydroxide, was concentrated until free of water, and the product was crystallized from absolute ethanol in well-formed octahedra. The crude crystalline product was obtained in 59% yield. After one recrystallization from absolute ethanol, the yield of the first crop obtained was 54%; m.p. 120° after slight fusion at 115°. An authentic sample melted identically. The product showed no rotation in water.

Anal. Calc'd for $C_4H_{10}O_4$: C, 39.31; H, 8.25.

Found: C, 39.76; H, 8.31.

Preparation of D-*erythronic lactone.* The granular product from periodate oxidation of 0.05 mole of starch (8.1 g.) was suspended in 400 ml. of water and dissolved by stirring at 100° for 45 minutes. To this solution, cooled in ice-water, was added a cold solution of 124 g. of barium acetate monohydrate (thrice the calculated amount) in 200 ml. of water made neutral to litmus by addition of 40 ml. of 5% acetic acid. Immediately, 10.5 ml. of bromine (twice the calculated amount) was added and a fine precipitate formed at once. The solution was stirred vigorously in the cold for half an hour and then allowed to stand at room temperature for one hour. The bromine was removed by aeration, the colorless mixture was cooled to 0° and the precipitate was removed by filtration and washed free of inorganic matter by ice-water. Analyses showed a 92% recovery of carbon and a barium content 54% of that expected from complete conversion of aldehyde groups to carboxyl.

The precipitate was dissolved at 20° in 150 ml. of water containing 7.2 ml. of concentrated hydrochloric acid, and 2 ml. of bromine was added. After 24 hours, 150 ml. of water and 2 ml. of bromine were added and the solution was allowed to stand 6 days at 20°. Bromine was removed by aeration and the volume was made to 500 ml. for hydrolysis. The specific rotation was +5.4°. The solution was heated at 100° for 11 hours when the constant specific rotation, −25.2°, was reached. (A product comparable in all respects with this except that the starch was oxidized in solution by approximately 0.11 *molar* sodium metaperiodate for 48 hours and the excess periodate and the iodate removed by barium chloride, required 20 hours hydrolysis to reach constant rotation.) Development of a little color during hydrolysis indicated the presence of some aldehydic groups. Inorganic ions were removed and the solution was concentrated to 200 ml. The total acidity (free plus lactone) was 0.114 equivalent.

Glyoxylic acid was removed from this solution as the insoluble basic barium salt by adding a large excess of barium hydroxide to the cold hydrolysate. Dilution of the reaction mixture was avoided as much as possible by adding the barium hydroxide in hot, concentrated solution to the cold hydrolysate. The basic barium salt which precipitates is believed to undergo some decomposition to glycolic and oxalic acids (11). The weight of salt precipitated was 5.50 g. After removal of barium ions from the filtrate and concentration to 200 ml., the total acidity was found to be 0.044 equivalent. This solution showed slight reducing power to Fehling solution.

1. By direct extraction. One half of the solution was concentrated *in vacuo* to a sirup and then the flask and contents were held at 70–75° for 2 hours under a vacuum and then were kept in a drying oven for an hour. A waxy mass of crystals formed on cooling. This was extracted with ethyl acetate. On standing, first at room temperature and then at 4°, needles characteristic of D-erythronic lactone formed in the solution; m.p. 101–102°; yield 30%. More crystalline material was obtained from the mother liquors, and by further heating of the sirup insoluble in ethyl acetate remaining in the flask.

2. From brucine D-*erythronate.* The other half of the solution containing erythronic acid and its lactone was treated with the calculated amount of brucine by heating on a steam-bath. Heating was continued for an hour after all the brucine was in solution. A trace of color was removed by carbon, the solution was concentrated to a small volume and 10 volumes of absolute ethanol were added. Clear, heavy prisms, characteristic of brucine D-erythronate formed; m.p. 214° (dec.); $[\alpha]_D^{20}$ −22.43° (*c*, 4.3, water). Accepted values: 212–215° and −23.5 to −25.5°, respectively (10, 11). Yield, 53%.

Anal. Calc'd for $C_{27}H_{34}N_2O_9$: OCH_3, 11.69. Found: OCH_3, 11.85.

When the polyaldehyde was oxidized by bromine water buffered with barium acetate for 20 hours, the yield of brucine erythronate was 49%. When native, granular starch was oxidized by periodate, the yield was 39% and m.p., 209–211°.

D-Erythronic lactone was obtained from the brucine salt essentially as described by Glattfeld (7). The lactone melted at 102–103° and showed $[\alpha]_D^{20}$ −73.3° (c, 1.2, water); accepted values 102–103° and −73.11°, respectively (1, 7, 8). Yield 69% of theory based on the brucine salt and 36% based on starch.

Anal. Calc'd for $C_4H_6O_4$: C, 40.66; H, 5.11.
Found: C, 40.75; H, 5.16.

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SUMMARY

meso-Erythritol and D-erythronic lactone have been prepared in yields of 54–59% and 30–36%, respectively, from periodate-oxidized potato starch.

Factors contributory to these good yields were the use of a mildly acid-modified potato starch, oxidation of the granular starch with sodium metaperiodate, and reduction or oxidation of the polyaldehyde without drying and prior to hydrolysis.

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NOTICE TO AUTHORS

On and after September 1, 1955, the Journal will accept *Notes*; the Journal will accept *Communications to the Editor* received on or after November 1, 1955 for publication in Volume 21. See revised Notice to Authors for details.

Effective with Volume 21, the Journal will use a double column format with a page size approximately 6½" by 9". Authors should consider this in connection with graph sizes, and table compositions.