

[CONTRIBUTION FROM THE SUGAR RESEARCH FOUNDATION LABORATORY, DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Structure of 2,4;3,5-Dimethylene-D-gluconic Acid¹

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This article confirms the finding of Mehlretter and his collaborators² that the oxidation of 2,4;3,5-dimethylene-D-gluconic acid with alkaline potassium permanganate yields the corresponding derivative of D-saccharic acid. The oxidation was carried out under substantially the same conditions as used by these authors and the crude product was isolated as a dimethyl ester with the same analysis and the same melting point of 156–157° (cor.) that they reported. The identification of this ester as dimethyl 2,4;3,5-dimethylene-D-glucosaccharate was confirmed by a mixed melting point determination with an authentic specimen. It was noted that the ester reduced boiling Fehling solution.

As the other authors pointed out, the positions of the methylene groups in the substituted gluconic acid must be identical with those in the saccharide acid derivative, which Haworth and Wiggins³ obtained by oxidizing the 2,4;3,5-dimethylenesorbitol definitely characterized by Hann, Wolfe and Hudson.⁴

We take this opportunity of recording a modification of Henneberg and Tollens⁵ preparation of 2,4;3,5-dimethylenegluconic acid, and also the preparation of di-*p*-bromophenacyl 2,4;3,5-dimethylenesaccharate, which appears to be a new derivative.

Experimental

2,4;3,5-Dimethylene-D-gluconic Acid.—Glucono- δ -lactone (17.8 g., 0.1 mole) was dissolved by shaking in 25 cc. of concentrated hydrochloric acid. Trioxane (9 g., 0.1 mole equivalent to 0.3 mole of formaldehyde) was added and the mixture was placed on a shaking machine for twenty-four hours; then it was diluted with water to 50 cc. and shaken for forty-eight hours longer. The colorless reaction product was collected on a Buchner funnel, dried and recrystallized from hot water in the form of beautiful needles melting at 217.4–219.4° (cor.); yield, 13 g. or 59% of the theoretical. The substance showed a specific rotation of +40.2° (*c*, 0.722; water) at 29.5°. When calcium gluconate was used as the starting material, the yields were poorer. When 25 cc. of 6 *N* hydrochloric acid was substituted for the concentrated acid, shaking

for two weeks yielded extremely small quantities of product.

Oxidation with Potassium Permanganate.—Dimethylene-D-gluconic acid (4.4 g., 0.02 mole) was suspended in 40 cc. of water. The acid was dissolved by adding 16 cc. of 10% sodium hydroxide. Cracked ice (150 g.) was added along with a few crystals of potassium permanganate. The pink color was discharged instantaneously. A total of 4.16 g. (0.026 mole) of potassium permanganate was added and the mixture was put on the shaking machine for twenty-one hours. After the manganese dioxide had been removed by filtration through kieselguhr and carbon black, the colorless alkaline filtrate was neutralized and made very slightly acid with hydrochloric acid, then concentrated to a volume of 20 cc. This stock solution did not form a precipitate with 2 *N* hydrochloric acid saturated with 2,4-dinitrophenylhydrazine. The solution decolorized bromine water and reduced Fehling solution upon heating.⁷

Di-*p*-bromophenacyl 2,4;3,5-dimethylenesaccharate.—One-fourth of the stock solution described above (5 cc. containing approximately 1 g. of product) was mixed with 12 cc. of 95% ethyl alcohol and 2 g. of *p*-bromophenacyl bromide and boiled under reflux for two and one-tenth hours.⁸ After one hour a precipitate began to settle out. More ethyl alcohol (4 cc.) was added and heating was continued, but the precipitate did not dissolve. The precipitate filtered off from the hot solution was readily soluble in chloroform but was recrystallized from chloroform and ethyl acetate; it showed melting point 199.8–200.8° (cor.).

Anal. Calcd. for $C_{24}H_{20}O_{10}Br_2$: Br, 25.5. Found: Br, 25.6, 25.8.

Dimethyl 2,4;3,5-dimethylenesaccharate.—One-half of the stock solution described above was concentrated *in vacuo* to dryness. The residue was heated in 175 cc. of boiling 2% methanolic hydrochloric acid under reflux for eight and one-half hours. The reaction mixture was treated with fresh silver carbonate to remove chloride, then the filtered solution was concentrated dry under diminished pressure. The colorless residue was recrystallized from hot water. When dried under reduced pressure, it melted at 156–157° (cor.). When mixed with methyl 2,4;3,5-dimethylenesaccharate prepared from 2,4;3,5-dimethylene-D-sorbitol, this sample showed no depression in melting point. The product reduced boiling Fehling solution.⁷

Anal. Calcd. for $C_{16}H_{14}O_8$: C, 45.8; H, 5.34. Found: C, 45.8, 46.0; H, 5.28, 5.27.

Summary

Oxidation of the dimethylene-D-gluconic acid of Henneberg and Tollens with potassium permanganate yields a dimethylenesaccharic acid which has been identified as the dimethyl and di-*p*-bromophenacyl esters. This fact indicates that the free hydroxyl group originally must occupy the terminal, primary position in dimethylene-D-gluconic acid. It has been shown that the diacetal is 2,4;3,5-dimethylene-D-gluconic acid.

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(7) Haworth, Jones, Stacey and Wiggins, *J. Chem. Soc.*, 64 (1944).

(8) Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, New York, N. Y., 2nd ed., p. 132.

(1) After the present work was completed, it was learned that Dr. C. L. Mehlretter, at the Northern Regional Research Laboratory, Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture, Peoria, Illinois, had determined the structure of this compound independently. By agreement with the Director of that Laboratory and with Dr. Mehlretter, this paper is published simultaneously with theirs. As shown by notebooks, the work of Mehlretter bears chronological priority.

(2) Mehlretter, Mellies, Rist and Hilbert, *THIS JOURNAL*, **69**, 2130 (1947).

(3) Haworth and Wiggins, *J. Chem. Soc.*, 58 (1944).

(4) Hann, Wolfe and Hudson, *THIS JOURNAL*, **66**, 1898 (1944).

(5) Henneberg and Tollens, *Ann.*, **292**, 31 (1896).

(6) All rotations cited in this paper refer to specific rotations of the D line of sodium. Concentrations are stated in grams of substance in 100 cc. of solution.