

240 × 54 mm. (diam.) column of Magnesol-Celite (5:1 by wt.) by development with 2750 ml. of benzene-*i*-butyl alcohol (75:1 by vol.). Three zones were located on the extruded column. The material from the bottom zone on rechromatography in the same manner yielded a small amount (15 mg.) of β -maltose octaacetate (identified by melting point, 158–159°).

The sirup obtained from the zone located near the middle of the column was dissolved in 50 ml. of benzene and rechromatographed on a 215 mm. × 44 mm. (diam.) column of Magnesol-Celite (5:1 by wt.) by development with 1500 ml. of benzene-*i*-butyl alcohol (75:1 by vol.). Four zones were located on the extruded column. The zone nearest the bottom yielded an unidentified sirup which has resisted crystallization. The third zone from the column top yielded a sirup which crystallized from absolute ethanol and was identified as β -isomaltose octaacetate; yield 55 mg. (1.3% as isomaltose), m.p. 144–145° unchanged on admixture with an authentic specimen of like melting point; $[\alpha]_D^{25} + 97^\circ$ (*c* 1.1, chloroform). Wolfrom, Georges and Miller⁷ cite for β -isomaltose octaacetate: m.p. 143–144°; $[\alpha]_D^{25} + 97^\circ$ (*c* 2.7, chloroform). The eluent from the next higher zone was crystallized from absolute ethanol and was identified as β -maltotriose hendecaacetate; yield 62 mg., m.p. 134–135° unchanged on admixture with an authentic specimen of like melting point; $[\alpha]_D^{25} + 86^\circ$ (*c* 1.5, chloroform). Wolfrom and co-workers⁹ cite for β -maltotriose hendecaacetate: m.p. 134–136°, $[\alpha]_D^{25} + 86^\circ$ (*c* 1.5, chloroform).

Another hydrolysis investigated in the same manner but wherein the hydrolysis was carried to 75% completion yielded 2.2% (92 mg.) of isomaltose as the crystalline β -octaacetate.

Acid Hydrolysis of Amylose.—An amount of 5.0 g. of corn amylose, prepared from defatted corn starch according to the procedure of Schoch,²⁷ was hydrolyzed in 2% concentration in 0.050 *N* sulfuric acid at 100° for 9 hours (degree of hydrolysis *ca.* 80%). The resulting amorphous solid (3.8 g.) was subjected to hot acetylation with 25 ml. of acetic anhydride and 2.8 g. of fused sodium acetate.

The acetylated hydrolyzate (5.7 g.) was chromatographed in the above-described manner on Magnesol-Celite (5:1 by wt.) and the following compounds were isolated and identified: β -D-glucopyranose pentaacetate (2.03 g.), β -maltose

octaacetate (1.20 g.) and β -maltotriose hendecaacetate (0.59 g.). No isomaltose octaacetate was detectable. The remaining more highly adsorbed material (1.79 g.) on further resolution has yielded only sirups which have resisted crystallization.

Summary

1. The first order specific reaction constants for the hydrolysis of glycogen in 2% concentration in 0.05 *N* hydrochloric acid at 100° were found to be essentially constant throughout the range investigated (0 to 60% hydrolysis). Under these conditions the ratio of the rates of hydrolysis of maltose to isomaltose was found to be 4:1.

2. A statistical treatment of the random hydrolysis of glycogen was made whereby the yields of those oligosaccharides containing one α -1,6-glycosidic linkage may be calculated for any desired degree of hydrolysis. An analysis is presented for the case of isomaltose from glycogen which demonstrates that under the chosen hydrolytic conditions the maximum yield of isomaltose obtainable from the acid hydrolysis of glycogen is 6.8% and that this maximum will occur when 89% of the glycogen is hydrolyzed.

3. By utilizing chromatographic techniques, an acetylated hydrolyzate of glycogen was resolved into β -D-glucopyranose pentaacetate, β -maltose octaacetate, β -isomaltose octaacetate and β -maltotriose hendecaacetate, all isolated in crystalline condition.

4. An appropriate blank experiment with amylose indicated that the isomaltose was not formed by reversion; β -D-glucopyranose pentaacetate, β -maltose octaacetate and β -maltotriose hendecaacetate were the only crystalline products isolated from the acetylated hydrolyzate of this substance.

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(27) T. J. Schoch, *Cereal Chem.*, **18**, 121 (1941); *THIS JOURNAL*, **64**, 2957 (1942).

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

The Preparation of 4,6-Ethylidene-D-glucopyranose from Sucrose and its Hydrogenation to 4,6-Ethylidene-D-sorbitol¹

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Reports of only a few attempts to allow sucrose to react with carbonyl compounds can be found in the literature. Only one of these can be said to have been successful in the sense that crystalline substances were isolated. Ohle, Wolter and Wohinz³ allowed sucrose to react with acetone and obtained " β -diacetonefructose" and 1,2-isopropylidene-D-glucofuranose in the crystalline condition. Sutra⁴ allowed sucrose to react with a large excess of paraldehyde in the presence of sulfuric acid and obtained a sirup which he said apparently con-

tained diethylidenesucrose which was not isolated in a pure condition. Sorgato⁵ condensed sucrose with formaldehyde at 80–120° and obtained a solid polymerized material insoluble in water.

We have found that a crystalline reaction product is obtained from sucrose and a reasonable quantity of paraldehyde in the presence of the minimum catalytic concentration of sulfuric acid. This substance has been identified as 4,6-ethylidene-D-glucopyranose which was first obtained by Helferich and Appel⁶ as the reaction product of D-glucose and paraldehyde in the presence of sulfuric acid. We obtained it in about 60% yield based on the D-glucose content of sucrose, and have also improved its method of preparation from D-glucose. The crystalline product obtained from sucrose appears to be identical with that obtained

(1) The material in this paper is taken in part from a thesis submitted to the Department of Chemistry of the Massachusetts Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy by David V. Collins in June 1948. A preliminary report of some of this work was given at the 113th meeting of the American Chemical Society, Chicago, Ill., April, 1948.

(2) Sugar Research Foundation, 52 Wall Street, New York 5, N. Y.

(3) Ohle, Wolter and Wohinz, *Ber.*, **63**, 843 (1930).

(4) Sutra, *Bull. soc. chim.*, **9**, 794 (1942).

(5) Sorgato, *Ann. chim. applicata*, **33**, 113 (1943).

(6) Helferich and Appel, *Ber.*, **64**, 1841 (1939).

from D-glucose in both rotation and mixed melting point.

The course of the reaction between sucrose and acetaldehyde (from paraldehyde) may involve the initial formation of an ethylenesucrose, so far unisolated, and water. The water and the ethylenesucrose may then form 4,6-ethylidene-D-glucopyranose and D-fructose, or an unisolated ethylenefructose. The water necessary for this reaction may actually not be set free, and the actual mechanism may involve displacement reactions of an initially formed hemiacetal. Attempts made in this Laboratory to secure a crystalline ethylidene-D-fructose or an ethylidenesucrose have not been successful so far.

We have found that hydrogenation of 4,6-ethylidene-D-glucopyranose from either sucrose or D-glucose leads to the formation of the same crystalline 4,6-ethylidene-D-sorbitol. This substance has never been obtained from the reaction of D-sorbitol and paraldehyde, and none of the products obtained from this direct reaction is known to have a 4,6-acetal ring.⁷

Lead tetraacetate oxidation of 4,6-ethylidene-D-glucopyranose and of 4,6-ethylidene-D-sorbitol under the standard conditions of Hockett, Dienes and Ramsden⁸ produced similar curves in which the consumption of the theoretical quantity of two moles of lead tetraacetate per mole of sugar derivative took place (Fig. 1).

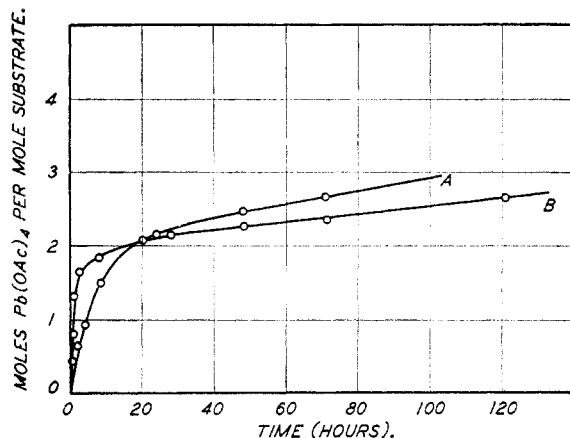


Fig. 1.—Moles of lead tetraacetate consumed under standard conditions per mole of 4,6-ethylidene-D-glucopyranose (Curve A) and 4,6-ethylidene-D-sorbitol (Curve B) plotted against time in hours.

Acknowledgment.—The authors wish to thank Dr. Franklin E. Morris and Mr. Juan C. Grau for repetition of some of the experimental work reported here.

Experimental Part⁹

4,6-Ethylidene-D-glucopyranose from D-Glucose.—One half-mole of D-glucose (either 90 g. of Merck Reagent Anhydrous Dextrose or 99 g. of Baker C.P. Dextrose Hydrate) was suspended in 0.5 to 0.66 mole of paraldehyde (66 to 88 ml. of U.S.P. paraldehyde supplied by the Niacet Chemi-

cals Division of U. S. Vanadium Corp.) containing 0.5 ml. of concentrated sulfuric acid. The crystalline slush was shaken mechanically in a one-liter erlenmeyer flask at room temperature (25 to 30°) for periods from 50 to 100 hours. The reaction was considered to be complete when a sample of the crystalline slush went completely into solution when heated to boiling with an equal volume of dioxane. If the reaction is allowed to proceed for too long a time, the product begins to go into solution again, evidently being converted into other products as yet unisolated. Differences in subdivision of the starting glucose, efficiency of shaking, and temperature make it difficult to state the time for maximum yield with accuracy.

At the end of the proper period of time 100 ml. of ethyl acetate was thoroughly mixed with the crystalline slush. After refrigeration for several hours the product was removed by suction filtration and washed with quantities of ethyl acetate and ether in a generally unsuccessful attempt to remove traces of acid still detectable by a pH-indicating paper. The yield of crude dry product (which charred when an attempt was made to determine the melting point) was generally 60–90 g. (60–90% but contained some unchanged D-glucose).

The crude material was recrystallized from hot absolute alcohol (4 to 7 ml. per gram solid) or hot dioxane (3 ml./g.). One ml. of strong aqueous ammonia was mixed with the entire sample of either solvent before the solid was added. As soon as the suspension of crude material in hot solvent had been made, the pH was determined with indicating paper and sufficient ammonia water added if necessary to bring the pH slightly above 7. Prolonged boiling of the crude acid-containing product with a solvent was found to lower the yield. The hot solution was treated with a filter-aid (generally a mixture of Florex and Celite) and then filtered. The recrystallized product was not collected until after at least twenty-four hours of thorough chilling, as crystallization of this substance appeared to be slow. Up to 80% of the weight of crude product could be recovered by recrystallization as a material m.p. 179–181°, $[\alpha]_D^{25} -2.4^\circ$ (final) (c, 2.5 g./100 ml. H₂O). The substance was recrystallized a second time before hydrogenation. Helferich and Appel⁶ reported m.p. 179–182°, $[\alpha]_D -2.36^\circ$ (final) after many recrystallizations from aqueous alcohol, with 33% recovery.

Among the other electrophilic substances that were found to catalyze the reaction between D-glucose and paraldehyde were zinc chloride (0.5 mole) and boron trifluoride (30% in ether, 10 cc.), but these catalysts gave the product in lower yield. Unsuccessful attempts were made to carry out the reaction in aqueous solution, but the use of glucose hydrate for glucose had little effect on the yield.

The purified product strongly reduced hot Fehling solution. A sample of 0.4899 g. (0.002375 mole) of 4,6-ethylidene-D-glucopyranose was dissolved in 25 ml. of 1 N H₂SO₄ and the hydrolysis of this approximately 0.1 M solution was followed polarimetrically at room temperature (24°). The results are plotted in Fig. 2. The specific rotation of the completely hydrolyzed solution was +49.7° calculated for D-glucose. The recorded value for equilibrium D-glucose

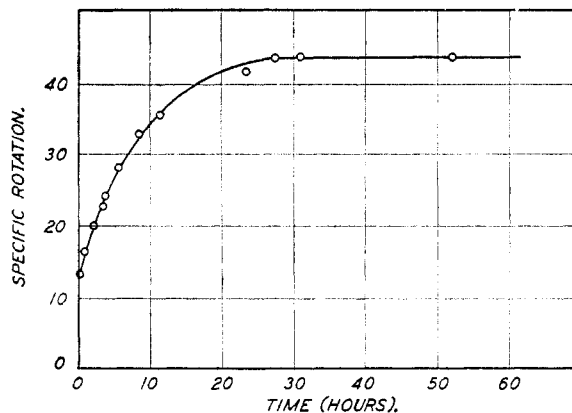


Fig. 2.—Specific rotation of a solution approximately 0.1 M in 4,6-ethylidene-D-glucopyranose and 0.1 N in H₂SO₄ plotted against time in hours at 24°.

(7) (a) Appel, *J. Chem. Soc.*, 425 (1935); (b) Shaefer, Thesis, M. I. T., 1943; (c) Vargha and Puskas, *Ber.*, **76B**, 859 (1943); (d) Sullivan, *THIS JOURNAL*, **67**, 837 (1945); (e) Wiggins, *J. Chem. Soc.*, 388 (1946).

(8) Hockett, Dienes and Ramsden, *THIS JOURNAL*, **65**, 1474 (1943).

(9) All melting points are corrected. The microanalyses were performed by Mr. S. M. Nagy and Mrs. Louise W. Spencer.

is $+52.7^\circ$. The consumption of lead tetraacetate by 4,6-ethylidene-D-glucose under standard conditions⁸ is shown in Fig. 1, Curve A.

4,6-Ethylidene-D-glucopyranose from Sucrose.—One mole of sucrose (342 g. of granulated sugar) was shaken with two moles of paraldehyde (260 ml. of U.S.P. paraldehyde supplied by the Niacet Chemicals Division, U. S. Vanadium Corp., Niagara Falls, N. Y.) containing 2 ml. of concentrated sulfuric acid. The mixture was placed in a one-liter glass stoppered erlenmeyer flask and shaken at room temperature. The time of shaking to secure a maximum yield depended upon the acid concentration, subdivision of the sucrose, efficiency of shaking and the temperature and was found to lie between 20 and 70 hours. It was also found that at least one mole of the paraldehyde used functions mainly as a reaction medium as it could be replaced with a mole (88 ml.) of dioxane. The dioxane tended to prevent sticking and made it possible to conduct the reaction by heating under reflux in a shorter time, but its use generally lowered the yields.

At the end of the reaction time, 400 ml. of ethyl acetate was mixed thoroughly with the reaction mixture which was then worked up as described in the preparation from D-glucose. The crude yield was generally 50 to 60% based on the D-glucose content of sucrose. The material melted in the range $150\text{--}160^\circ$. After two recrystallizations from alcohol, containing sufficient aqueous ammonia to render the solution alkaline, the product melted at $174\text{--}176^\circ$ uncor. The melting point of this product mixed with an equal amount of product secured from D-glucose (m.p. $172\text{--}175^\circ$) was $176\text{--}179^\circ$.

4,6-Ethylidene-D-sorbitol.—One hundred grams (0.485 mole) of twice recrystallized 4,6-ethylidene-D-glucopyranose (from either D-glucose or sucrose) was dissolved in 400 ml. of distilled water containing 1 ml. of concentrated ammonia water. Three grams of Raney nickel catalyst was added and the solution was shaken under hydrogen at 1000–1500 p.s.i. for 5 hours at 100° . At the end of the hydrogenation the mixture no longer reduced Fehling solution. The filtrate was vacuum concentrated to a sirup and dissolved in an equal volume of isobutyl alcohol. The solution deposited crystals overnight and, after refrigeration, the crystals were removed, washed with ether and dried *in vacuo* (95 g., 95%). After recrystallization from four parts of isobutyl alcohol the product from D-glucose melted at $98\text{--}99^\circ$ and showed $[\alpha]_D^{25} -44.4^\circ$ (*c*, 1.18, H_2O). The product from sucrose melted at $99\text{--}100^\circ$ and showed $[\alpha]_D^{25} -43.3^\circ$.

The consumption of lead tetraacetate by 4,6-ethylidene-D-sorbitol under standard conditions⁸ is shown in Fig. 1, Curve B.

Anal. (product from D-glucose) Calcd. for $\text{C}_8\text{H}_{16}\text{O}_6$: C, 46.15; H, 7.77. Found: C, 46.11; H, 7.76.

Samples of 4,6-ethylidene-D-sorbitol (0.667 g., 0.0032 mole) were dissolved in 25.0 ml. of 0.5 *N* H_2SO_4 (solution A, 0.128 *M*) and in 25.0 ml. of 1.0 *N* H_2SO_4 , respectively (solution B, 0.128 *M*). The specific rotation, calculated throughout the experiment for an ethylidene-D-sorbitol at 24° , is plotted against time in hours in Fig. 3. The rotational change represented was found to conform roughly to the first order law, and the approximate first order rate constant was calculated to be $5.3 \times 10^{-4} \text{ min.}^{-1}$ in 1.0 *N* acid. Since the final specific rotation, calculated as for D-sorbitol, was -3.44° compared with the recorded specific rotation of -2.01° , the reaction being followed polarimetrically was considered to be that of hydrolysis of 4,6-ethylidene-D-sorbitol to D-sorbitol without the formation of appreciable concentrations of rotationally significant intermediates.

It is interesting to compare the first order rate constant for the hydrolysis of 4,6-ethylidene-D-sorbitol with that for the ethyl acetal of acetaldehyde. The first order rate constant for the latter acetal has been found¹⁰ to lie between

50 and 56 per minute at 25° using natural logarithms and re-calculating to normal hydrochloric acid with the assumption that the constant is proportional to the normality of the acid. Thus this simple open-chain acetal hydrolyzes about 10^6 times as rapidly as the cyclic polyol acetal of acetaldehyde reported here. Unfortunately the rate constant of the corresponding unsubstituted cyclic acetal, 2-methyl-1,3-dioxane, has not yet been measured, so it is not certain to which structural feature this large difference in rate should be attributed.

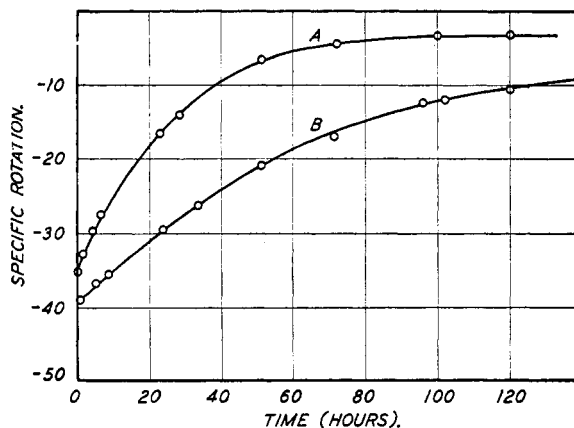


Fig. 3.—Specific rotation of a solution 0.128 *M* in 4,6-ethylidene-D-sorbitol and approximately 0.5 *N* (Curve A) and 1.0 *N* (Curve B) in sulfuric acid at 24° plotted against time in hours.

1,2,3,5-Tetrabenzoyl-4,6-ethylidene-D-sorbitol.—4,6-Ethylidene-D-sorbitol (5.0 g., 0.025 mole, from D-glucose) was dissolved in 12 g. (0.15 mole) of anhydrous pyridine and 14.0 g. (0.1 mole) of benzoyl chloride added slowly with shaking. After the reaction mixture had been allowed to remain 24 hours at room temperature, 100 ml. of water was stirred in. The insoluble sirup formed was washed several times with water and then dissolved in 50 ml. of hot ethanol. On cooling, the solution deposited white needles. After refrigeration, the crystals were removed, washed with alcohol and ether, and they then weighed 9.4 g. The material was recrystallized from absolute ethanol (8 ml./g.) and 8.7 g. (55% of the theoretical yield) of the substance, m.p. $152.6\text{--}153.4^\circ$, was removed. The specific rotation in chloroform (*c*, 1.81 g./100 ml.) was $[\alpha]_D^{25} -12.45^\circ$.

Anal. Calcd. for $\text{C}_{38}\text{H}_{32}\text{O}_{10}$: C, 69.30; H, 5.13. Found: C, 69.18; H, 5.24.

Summary

1. The crystalline product of the acid-catalyzed reaction of sucrose with paraldehyde has been identified as 4,6-ethylidene-D-glucopyranose.

2. Hydrogenation of 4,6-ethylidene-D-glucopyranose prepared either from sucrose or D-glucose gave crystalline 4,6-ethylidene-D-sorbitol. A crystalline tetrabenzoate of the latter substance has also been prepared.

3. The rates of hydrolysis of these substances in normal hydrochloric acid and of oxidation by lead tetraacetate under standard conditions have been measured.

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(10) (a) Skrabal and Schiffrer, *Z. physik. Chem.*, **99**, 290 (1921); (b) Skrabal and Mirtl, *ibid.*, **111**, 98 (1924); (c) Riesch and Kilpatrick, *J. Phys. Chem.*, **39**, 561 (1935).