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

Lead Tetraacetate Oxidations in the Sugar Group. XI.[1] The Oxidation of Sucrose and Preparation of Glycerol and Glycol[2]

BY ROBERT C. HOCKETT[3] AND MORRIS ZIEF[3]

In 1942 Fleury and Courtois[4] described the oxidation of sucrose by periodic acid in aqueous solution. The primary product II was isolated after further hypobromite oxidation, in the form of the strontium salt III. In the present communication the oxidation of sucrose by lead tetraacetate in acetic acid and pyridine is reported. Under the standard conditions of Hockett, Dienes and Ramsden[5] the rate of oxidation curve for sucrose in dry acetic acid shows that, as with periodic acid, oxidation occurs without appreciable cleavage of the glycosidic links. This is illustrated in Fig. 1 by curve IV which approximately equals the graphical addition of the curves for methyl α-D-glucopyranoside and methyl α-D-fructofuranoside. The fructose component of sucrose would be more accurately represented by methyl β-D-fructofuranoside, but this difference is of no consequence for present purposes since configurational inversion at carbon one of glycosides does not significantly alter their oxidation rates.[6] If cleavage did occur substantially before oxidation a curve somewhat like VIII which has been produced by combining the oxidation curves of free glucose and free fructose, would be expected. The rate of oxidation of sucrose in pyridine at 0° (Curve V) is more rapid than in acetic acid at 25° but follows a similar course.

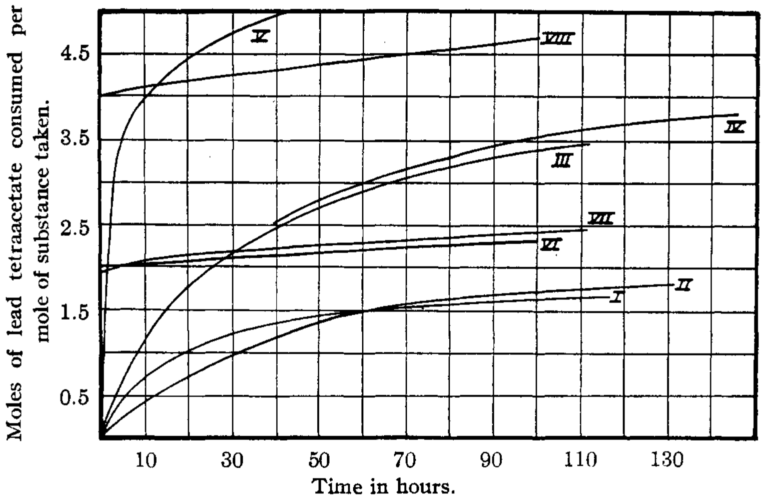

Fig. 1.—I, Methyl α-D-fructofuranoside; II, methyl α-D-glucopyranoside; III, graphical addition of I and II; IV, sucrose; V, sucrose in pyridine at 0°; VI, fructose; VII, glucose; VIII, graphical addition of VI and VII.

The oxidation of sucrose cannot be carried out satisfactorily in aqueous solutions since hydrolysis of the lead tetraacetate precedes the oxidation of sucrose in that medium. In this respect sucrose differs from glucose, xylose, mannitol or glycerol which are oxidized readily in water according to the procedure of Baer, Grosheintz and Fischer.[7]

The oxidation of sucrose in pyridine by lead tetraacetate in a molar ratio of one to three yielded a colorless, amorphous powder (II) showing $[\alpha]^{26.6}\text{D} + 7.4^\circ$ (*c*, 3.37, H_2O) which reduced Fehling and Schiff reagents and contained 3.8 aldehyde groups per mole according to a Kline and Acree[8] titration. Oxidation of this substance by strontium hypobromite produced a strontium salt III showing $[\alpha]^{22}\text{D} + 23^\circ$ (*c*, 2, H_2O) and containing 30.9% strontium, properties practically identical with those recorded for the compound isolated from the periodic acid oxidation by Fleury and Courtois.[4]

Compound II seemed to be an interesting intermediate for the preparation of glycerol and ethylene glycol according to the procedure described by Jayme and Sätre[9] for xylan. In this method, II is reduced with Raney nickel to IV which upon hydrolysis would be expected to yield two moles of glycerol, one mole of dihydroxyacetone and one mole of glycolaldehyde. Hydrogenation of this hydrolysis mixture should produce three moles of glycerol and one mole of ethylene glycol from each mole of sucrose. In a study of the production of polyhydric alcohols by the hydrogenolysis of sucrose, Lenth and DuPuis[10] showed in previous investigations that more complex mixtures consisting of propylene glycol, glycerol and polyhydric alcohols of higher molecular weight were produced.

When the product from the oxidation of sucrose in water with a three to one molar ratio of periodic

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(3) Present addresses: Robert C. Hockett, Sugar Research Foundation, 52 Wall Street, New York, N. Y.; Morris Zief, Sugar Research Foundation, Eastern Regional Research Laboratory, Wyndmoor, Pa.

(4) Fleury and Courtois, *Compt. rend.*, **214**, 366 (1942); **216**, 65 (1943).

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

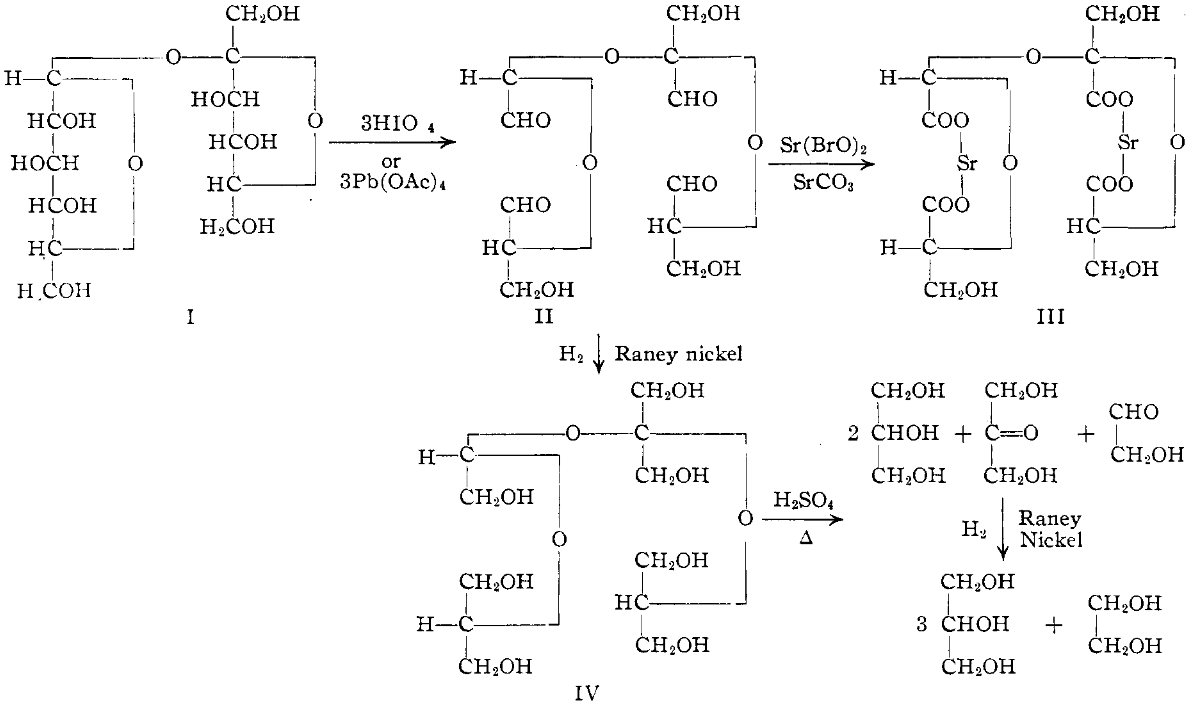
(6) Hockett and McClenahan, *ibid.*, **61**, 1667 (1939).

(7) Baer, Grosheintz and Fischer, *ibid.*, **61**, 2607 (1939).

(8) Kline and Acree, *Bur. Standards J. Research*, **5**, 1063 (1930).

(9) Jayme and Sätre, *Ber.*, **77**, 242 (1944); **77**, 248 (1944).

(10) Lenth and DuPuis, *Ind. Eng. Chem.*, **37**, 152 (1945).



acid to sucrose was hydrogenated, hydrolyzed and then hydrogenated again for eighteen hours at 140° and 2700 pounds pressure in the presence of Raney nickel, a viscous liquid product was formed, which possessed n^{20}_D 1.4619, corresponding to a 74.26% mixture of glycerol and ethylene glycol. The yields were 45 and 66%, respectively. After fractional distillation at 3 mm. the first fraction yielded ethylene glycol which was identified as the crystalline dibenzoate, while the last fraction (155 to 165°) yielded crystalline glycerol tribenzoate.

When sucrose was oxidized in pyridine with lead tetraacetate and the product similarly hydrogenated, hydrolyzed and hydrogenated, an oil was isolated showing n^{20}_D 1.4700. Glycerol tribenzoate was isolated after benzoylation. The yield of glycerol was 25%.

Experimental

Rate of Oxidation Determinations.—The rate determinations for all curves except V in Fig. 1 were carried out under the conditions described by Hockett, Dienes and Ramsden.[5]

Preparation of Tetraaldehyde II.—Sucrose (2 g., 0.006 mole), lead tetraacetate (8 g., 0.018 mole) and 100 cc. of pyridine were put on the shaking machine for three hours at 28°. Upon completion of shaking, a sample of the solution when acidified with concentrated hydrochloric acid showed no oxidizing activity with starch–iodide paper. The solution was filtered and concentrated *in vacuo* at 40°. The residue was dissolved in 200 cc. of water and gassed with hydrogen sulfide. After the lead sulfide was filtered off, the filtrate was concentrated *in vacuo* to a sirupy residue. Absolute ethyl alcohol (25 cc.) was added and the solution was concentrated again. Sulfur-free toluene was added to the semi-solid residue and the mixture was evaporated *in vacuo* to remove traces of acetic acid. After three more concentrations with toluene 1.2 g. of a flaky, amorphous, colorless material was obtained. This product was very soluble in water, slightly soluble in 95% ethyl alcohol, insoluble in acetone, chloroform and ethyl acetate; $[\alpha]^{26.6}_D$ +7.4° (*c*, 3.37, H_2O). The substance softened and melted between 90–115°; no sharp melting point was observed. A Kline and Acree[8] titration showed 3.8 aldehyde groups.

Preparation of Strontium Salt III.—After the concentration with toluene as described, the residue was diluted with 400 cc. of water, filtered and treated with 20 g. of strontium carbonate and 3.6 cc. of bromine. The reaction mixture was shaken occasionally and put away in the dark for twenty hours. Excess bromine was removed by aeration, the strontium carbonate was filtered off and the bromide ions were precipitated by shaking for five hours with 20 g. of silver carbonate. Silver ions were precipitated as the sulfide with hydrogen sulfide, and excess hydrogen sulfide was removed by aeration. The solution was made slightly alkaline with strontium hydroxide and concentrated to 30 cc. The strontium salt was precipitated by adding 95% ethyl alcohol to the first sign of permanent turbidity. After twenty-four hours in the refrigerator, an amorphous, colorless material was collected and dried *in vacuo*, $[\alpha]^{22}_D$ +23° (*c*, 2, H_2O). Fleury and Curtois[4] reported $[\alpha]^{20}_D$ "about +24°."

Anal. Calcd. for $C_{11}H_{12}O_{14}Sr_2$: Sr, 32.22. Found: Sr, 30.90.

Formation of Glycerol and Ethylene Glycol Following Oxidation of Sucrose. (a) Periodic Acid.—At 0°, 10 g. (0.0438 mole) of paraperiodic acid was added to 5 g. (0.0146 mole) of sucrose in 100 cc. of water, the reaction mixture was allowed to reach 25° within three hours, and was allowed to stand twenty-four hours longer at this temperature. The solution was exactly neutralized at 0° with 1 *N* sodium hydroxide, 5.5 g. of barium chloride dihydrate was added, and the mixture was filtered one hour later. Raney nickel (5 g.) was added to the strongly reducing filtrate (Fehling test) and the mixture was hydrogenated for eighteen hours at 140° under a pressure of 2700 pounds. After the removal of the Raney nickel by filtration, the filtrate did not reduce Fehling solution and did not form a precipitate with 2,4-dinitrophenylhydrazine in 2 *N* hydrochloric acid. The filtrate was treated with 3.4 cc. of concentrated sulfuric acid, the barium sulfate was filtered and the filtrate was heated under reflux at 100° for three and one-half hours. After neutralization of the cooled solution with barium carbonate and removal of the excess barium carbonate and barium sulfate, the filtered solution strongly reduced Fehling solution. The solution was hydrogenated again at 140° over Raney nickel for fifteen hours under a pressure of 2600 pounds. The Raney nickel was separated and the non-reducing filtrate was concentrated *in vacuo* at 40°. The residue was extracted four times with boiling acetone and the combined extracts were dried over anhydrous calcium sulfate. After removal of the acetone and drying *in vacuo*, 2.4 g. of a sirupy product was obtained; n^{20}_{D} 1.4619. From the refractive index curve of known mixtures of glycerol and ethylene glycol prepared by Jayme and Sätre[9] this value approximately corresponds to a 74% (1.8 g.) glycerol–26% (0.6 g.) ethylene glycol. Based on 5 g. of sucrose the over-all yield of glycerol was thus 45%, and the yield of ethylene glycol was 66%. The product was distilled in a semimicro fractionation apparatus consisting of a glass spiral column supported on an aluminum block, a heated jacket and a receiver of the rotating type described by Shrader and Ritzer.[11] At 3 mm. five fractions were collected from 80 to 165°. The main fraction distilled at 155–165°. The refractive indices at 20° of fractions 1 and 5, respectively, were 1.4326 and 1.4725. Fraction 1 gave a colorless solid upon shaking with benzoyl chloride and dilute sodium hydroxide in a typical Schotten–Baumann reaction. Recrystallization from alcohol yielded ethylene glycol dibenzoate, melting at 72–73°. A mixed melting point with a known product showed no depression. Fraction 5 under the same treatment yielded crystalline glycerol tribenzoate melting at 74–75°. A mixed melting point with a known sample also exhibited no depression.

(b) **Lead Tetraacetate.**—Five grams (0.0146 mole) of sucrose was suspended in 50 cc. of pyridine in a one-liter three-necked flask cooled to 0°. Twenty-two grams (0.049 mole) of lead tetraacetate in 650 cc. of pyridine was added slowly with motor stirring. Within four hours the original dark solution became clear. The solution was filtered and concentrated *in vacuo* at 40°. The concentrate was treated with 200 cc. of water containing 3.5 cc. of concd. sulfuric acid and the lead sulfate formed was separated with the aid of a centrifuge. The filtrate was neutralized with barium carbonate, filtered and concentrated *in vacuo* to a flaky solid. The solid was dissolved in 200 cc. of water and was concentrated to 65 cc., filtered twice through kieselguhr and treated with 10% sulfuric acid until no more barium sulfate precipitated. The filtered solution gave a strong Fehling test and a precipitate with 2,4-dinitrophenylhydrazine. The solution was neutralized with solid sodium bicarbonate and was then hydrogenated over fresh Raney nickel (4 g.) for twenty-two hours at 140° under a pressure of 2400 pounds. After removal of the Raney nickel, the filtrate did not reduce Fehling solution and gave no precipitate with 2,4-dinitrophenylhydrazine. The filtrate was then mixed with 3 cc. of concd. sulfuric acid carefully in the cold and was boiled under reflux for three and one-half hours. The solution was neutralized with barium carbonate and filtered. The filtrate showed strong reducing properties with Fehling solution and gave an immediate precipitate with 2,4-dinitrophenylhydrazine. The solution was hydrogenated over Raney nickel again as described. After removal of the catalyst, the filtrate was non-reducing to Fehling solution. The greenish solution was concentrated *in vacuo* at 40°, the residue was extracted with absolute ethyl alcohol three times, the combined extracts were dried over anhydrous calcium sulfate, filtered and concentrated. The residue was extracted with absolute ethyl alcohol, the extracts were filtered and concentrated *in vacuo* at 2 mm. to a colorless sirupy residue; n^{20}_{D} 1.4700; yield 1.0 g. Glycerol tribenzoate melting at 74–75° was isolated after benzoylation by the Schotten–Baumann reaction. Ethylene glycol was not identified. The yield of glycerol was about 25%.

Summary

The rate-of-oxidation curve of sucrose by lead tetraacetate in dry acetic acid shows that oxidation occurs without appreciable cleavage of the glycosidic link. The oxidation of sucrose in pyridine yielded a colorless, amorphous powder with the properties of a tetraaldehyde. Oxidation of this substance by strontium hypobromite produced the strontium salt. The preparation of glycerol and ethylene glycol from the primary oxidation product of oxidation of sucrose by periodic acid or lead tetraacetate has been described.

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[11] Shrader and Ritzer, *Ind. Eng. Chem., Anal. Ed.*, **11**, 54 (1939).

[Contribution from the Department of Chemistry, University of Rochester]

Curariform Activity and Chemical Structure. VI. Syntheses in the β- and γ-Carboline Series[1,2]

By V. Boekelheide and C. Ainsworth[3]

In view of the suggestions that several of the calabash curare alkaloids probably contain the carboline nucleus[4,5] and since a model compound derived from 3-indolylmethylamine has been found to have fairly high curariform activity,[6] we have prepared a number of quaternary salts of 1,2,3,4-tetrahydro-β-carboline and 1,2,3,4-tetrahydro-γ-carboline for physiological testing.

For the synthesis of 2-methyl-1,2,3,4-tetrahydro-γ-carboline (I), the Fischer indole synthesis was employed using phenylhydrazine hydrochloride and N-methyl-4-piperidone hydrochloride in a modification of the method of Cook and Reed.[7] This was then converted to the corresponding salts, II and III, in the usual manner.

Since bromination of C-curarine-I chloride has been found to greatly intensify its activity,[8] the corresponding 8-bromo compounds (IV, V and VI) were prepared by utilizing the same reaction with *p*-bromophenylhydrazine instead of phenylhydrazine.

[1] Aided by a grant from the National Foundation for Infantile Paralysis.

[2] For paper V of this series, see Boekelheide and Rothchild, This Journal, **71**, 879 (1949).

[3] Present address, Department of Chemistry, University of Colorado, Boulder, Colorado.

[4] Schmid and Karrer, *Helv. Chim. Acta*, **30**, 1162 (1947).

[5] Wieland, Witkop, and Bähr, *Ann.*, **558**, 144 (1947).

[6] Craig and Tarbell, This Journal, **71**, 462 (1949).

[7] Cook and Reed, *J. Chem. Soc.*, 399 (1945).

[8] Wieland, Pistor and Bähr, *Ann.*, **547**, 140 (1941).