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SYNTHESIS OF 1,2-O- AND 1,3-O-ETHYLENE-D-GLUCOFURANOSE

H.C. Srivastava, K.V. Ramalingam and A.S. Chaudhari
Ahmedabad Textile Industry's Research Association
Ahmedabad 9, India

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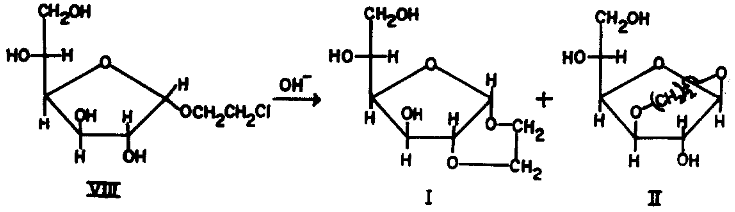
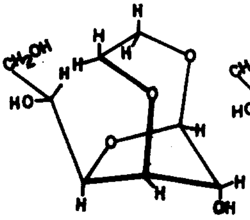
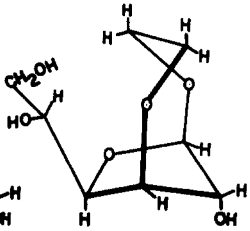
Höök and Lindberg(1) have recently synthesized 1,2-O-ethylene-α-D-glucofuranose <u>via</u> two routes: (1) by treatment of 2-O-hydroxyethyl-D-glucose with hydrogen chloride in N,N-dimethyl formamide, and (2) by intramolecular etherification of 2-chloroethyl α-D-glucofuranoside by alkali. 2-Chloroethyl α-D-glucofuranoside was itself prepared by reaction of D-glucose with 2-chloroethanol in the presence of a cation exchange resin followed by fractionation of the glycoside mixture on a silicic acid column. In this laboratory, we have isolated 1,2-O-ethylene-α-D-glucofuranose and 1,2-O-ethylene α- and β-D-glucopyranose from the hydrolyzate of a commercial sample of hydroxyethyl corn starch (D.S., 0.1).(2) This paper is concerned with the synthesis of 1,2-O-ethylene-α-D-glucofuranose (I) by a route somewhat different from that of Höök and Lindberg (<u>loc</u>. <u>cit</u>.) as well as that of 1,3-O-ethylene-β-D-glucofuranose (II), a hitherto unknown bicyclic compound.

D-Glucose diethyl dithioacetal(3) (III) was partially demercaptalated to ethyl 1-thio-α-D-glucofuranoside(4) (IV) which was then acetylated to afford ethyl tetra-O-acetyl-1-thio-α-D-glucofuranoside (V). The latter was converted to syrupy tetra-O-acetyl-D-glucofuranosyl bromide (VI) by the method of Weygand and co-workers.(5) VI (1.35 g.) was dissolved in dry benzene and to the resulting solution dry 2-chloroethanol (5 ml.) was added with stirring. Silver carbonate (2 g.) was added to the solution over a period of 20 min. and then the mixture was shaken for 20 hours. The reaction mixture was worked up in the usual way to afford a syrupy 2-chloroethyl tetra-O-acetyl-D-glucofuranoside (VII, 1.3 g.). Deacetylation of VII with sodium methoxide gave 2-chloroethyl-D-glucofuranoside (VIII, 0.59 g.) as a syrup, $[\alpha]_D$ -20° (water). Höök and Lindberg (<u>loc</u>. <u>cit</u>.) report a value of +82° for this compound which was essentially the α-anomer. Our preparation was, therefore, a mixture of α - and β -anomers, the latter predominating. VIII was dissolved in 50% aqueous ethanol (10 ml.) and after adding solid sodium hydroxide (400 mg.), the mixture was refluxed for 3 hours. Neutralization of the reaction mixture followed by filtration and evaporation afforded a moist solid (0.55 g.) which on recrystallization from ethanol gave I (150 mg.), m.p. and mixed m.p. 218-220°, $[\alpha]_D$ -56° (H_2O)(1,2), and which on acid hydrolysis gave 2-O-hydroxyethyl-D-glucose (IX).

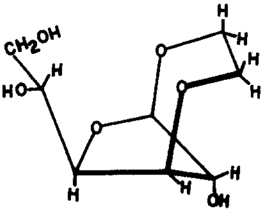




IIa



IIb



IIc

Paper chromatography of the syrup (350 mg.), left after removal of I, in butanol-pyridine-water (6:4:3) showed the presence of a major component (A), moving slightly slower than I in addition to small amounts of the latter compound. The mixture was resolved by a combination of paper and silica gel chromatography to afford pure A in the form of a syrup (150 mg.), $[\alpha]_D$ -40° (H_2O). A did not reduce Fehling solution nor was it detectable on paper by p-anisidine hydrochloride(6) or by silver nitrate reagent.(7) It could, however, be located on paper chromatogram by the periodate-benzidine reagent.(8) Upon acid hydrolysis, A gave 3-O-hydroxyethyl-D-glucose (X) which was identified by paper and thin layer chromatography, and by paper electrophoresis. Compound A on oxidation with sodium metaperiodate produced formaldehyde (chromotropic acid test) indicating thus that it had a furanoid structure. These facts prove that compound A is 1,3-O-ethylene-D-glucofuranose (II), the anomeric configuration being β - as the corresponding α-compound is not possible. The above results suggest that the β-anomer of VIII has cyclized under alkaline conditions to give II and not 1,2-O-ethylene-β-D-glucofuranose (XI), which would be relatively unstable due to the <u>trans</u> fusion of a six-membered ring to a five-membered ring in addition to a strong anomeric effect.(1) Inspection of molecular models reveals that II has a flexible seven membered ring and can exist in three different conformations IIa, IIb and IIc. Conformation IIc, which appears to have least intramolecular interactions, is expected to be the most stable. Although rare, bicyclic seven-membered ring compounds having oxygen as a hetero atom have been encountered earlier in hemialdals produced by periodate oxidation of methyl 4,6-O-alkylidene-D-hexopyranosides(9), and in methyl 4,6-O-ethylidene-2,3-O-oxidodiethylidene-α-D-glucoside.(10)

It is worthy of note that when 3-O-hydroxyethyl-D-glucose was treated with methanolic hydrogen chloride or with hydrogen chloride in dimethyl formamide, a mixture of several components was obtained as revealed by t.l.c. One of these was chromatographically indistinguishable from II. I was also produced in good yield from IX when the latter was treated with methanolic hydrogen chloride.(2)

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