mmoles) of *p*-toluenesulfonic acid, 98 mg. (0.25 mmoles) of X, and 1.0 ml. of acetic anhydride was stirred at ambient temperature for 10 min., solution taking place in 1 min.; when processed as described for V, a syrup was obtained on evaporation of the chloroform that was crystallized with difficulty from *N,N*-dimethylformamide–water–ethanol; yield 62.5 mg. (58%), m.p. 156–159°, uniform on t.l.c. Recrystallization from aqueous ethanol gave white needles: m.p. 157–159°; $[\alpha]^{24}D$ +43 ± 2°; ν_{max} 3400 (NH), 1730 (ester C=O), 1660, 1520 (amide I and II), 1130, 1110, 1070 (ether C–O–C), 760, 722, 696 cm.$^{-1}$ (C_6H_5); τ 6.86 (OCH_3), 7.89 (*O*-acetyl), 8.33 (*C*-methyl).

Anal. Calcd. for $C_{24}H_{27}NO_7$: C, 65.3; H, 6.16; N, 3.17. Found: C, 65.4; H, 6.39; N, 3.12.

Deacetylation with excess methanolic sodium methoxide at room temperature for 20 hr. gave X, identified by mixture melting point and comparative infrared spectra.

Preparation and Some Reactions of Mono-*O*-ethylidene Derivatives of D-Galactose, Methyl α- and β-D-Galactopyranosides, and of D-Threose

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Received August 23, 1965

Mono-*O*-ethylidene derivatives of D-galactose and of methyl α- and β-D-galactopyranosides have been prepared and shown by methylation studies to be 4,6-*O*-ethylidene derivatives. Reduction of 4,6-*O*-ethylidene-D-galactose (1) gave crystalline 4,6-*O*-ethylidene-D-galactitol and condensation of 1 with acetone–zinc chloride afforded crystalline 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose. Oxidation of 1 with sodium metaperiodate gave 2,4-*O*-ethylidene-D-threose, which crystallized as a dimer.

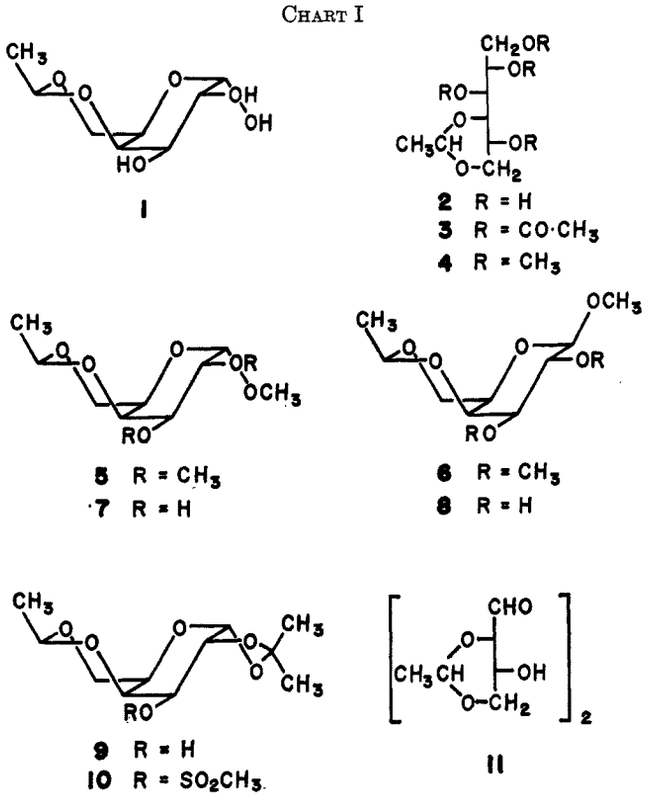
The preparation of crystalline 4,6-*O*-ethylidene-D-galactose (1) was reported several years ago[2] and this paper describes some reactions of this compound and also the preparation of 4,6-*O*-ethylidene derivatives of methyl α- and β-D-galactopyranosides.

Other workers have described 4,6-*O*-benzylidene-D-galactose[3] and the 4,6-*O*-benzylidene derivatives of methyl α-[4] and β-D-galactopyranosides[5] and of benzyl β-D-galactopyranoside.[6] The 4,6-*O*-ethylidene derivatives of glucose,[7] methyl α-[8] and β-D-glucopyranosides[7,9] and of methyl α-D-mannopyranoside[10] have also been reported.

Yields of 1 obtained from different commercial samples of D-galactose by treatment with paraldehyde–sulfuric acid under identical conditions were found to vary greatly. Experiments with samples of meshed D-galactose indicated that in addition to time, temperature, and acid concentration, particle size was a factor in the condensation. Satisfactory results were obtained by following trial condensations on paper chromatograms or by thin layer chromatography in acetone or 1-propanol.

Periodate oxidation of 1 resulted in the uptake of 2 equiv. of oxidant and the formation of 2 equiv. of formic acid. No formaldehyde was liberated by periodate oxidation at pH 8. These results indicate that the acetal group spans C-4 and C-6 of D-galactopyranose or C-5 and C-6 of D-galactofuranose. Reduction of 1 with borohydride or with hydrogen and Raney nickel gave a crystalline *O*-ethylidenegalactitol which, on periodate oxidation, consumed 2 equiv. of periodate and liberated 1 equiv. of formic acid and 1 equiv. of formaldehyde. These results eliminate the unlikely furanose structure for 1 and prove that the reduction product is 4,6-*O*-ethylidene-D-galactitol (2) (1,3-*O*-ethylidene-L-galactitol). The tetraacetate 3 and the tetramethyl ether 4 of 2 (see Chart I) were obtained crystalline.

CHART I



Methylation of 1 by the procedure of Kuhn, *et al.*,[11,12] gave two main products which were fractionated by chromatography on silica gel and shown to be the α (5) and β (6) anomers of methyl 4,6-*O*-ethylidene-2,3-

(1) This work was initiated while the author was working under the guidance of Professor J. K. N. Jones at Queen's University, Kingston, Ontario.

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(3) E. G. Gros and V. Deulofeu, *Chem. Ind.* (London), 1502 (1962).

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(6) B. Helferich and A. Porck, *Ann.*, **586**, 239 (1954).

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(8) (a) J. Honeyman and J. W. W. Morgan, *J. Chem. Soc.*, 3660 (1955); (b) J. Honeyman and T. C. Stening, *ibid.*, 3316 (1957).

(9) (a) J. Dewar and G. Fort, *ibid.*, 492 (1944); (b) D. O'Meara and D. M. Shepherd, *ibid.*, 4232 (1955).

(10) J. Honeyman and J. W. W. Morgan, *ibid.*, 744 (1954).

(11) R. Kuhn, H. Trischmann, and I. Löw, *Angew. Chem.*, **67**, 32 (1955).

(12) Earlier attempts to methylate 1 using methyl sulfate and sodium hydroxide or silver oxide and methyl iodide alone gave complex mixtures of products (t.l.c. in ethyl acetate) owing presumably to the lability of the *O*-ethylidene group.

di-*O*-methyl-D-galactopyranoside. Treatment of **5** with a mixture of fuming nitric acid and chloroform at 0°[9a] effected simultaneous removal of the ethylidene group and nitration, and crystalline methyl 2,3-di-*O*-methyl-4,6-di-*O*-nitro-α-D-galactoside was obtained with properties in good agreement with those previously reported.[4b]

Acidic hydrolysis of **5** was readily effected in two stages and the intermediate methyl 2,3-di-*O*-methyl-α-D-galactopyranoside was obtained by distillation as a colorless, chromatographically pure syrup. Complete hydrolysis afforded 2,3-di-*O*-methyl-D-galactose which was characterized as the *N*-phenylglycosylamine. Thin layer chromatography indicated that at least two isomers of this derivative are formed and this may explain the different properties reported by other workers.[4,13] The isomer obtained in this work corresponded to that described by Bell and Greville.[4b] Thin layer chromatography indicated that an equilibration occurred at the melting point and also that the mutarotation corresponded to the formation of an equilibrium mixture.

Treatment of methyl α-D-galactopyranoside with 1,1-dimethoxyethane and sulfuric acid[9b] gave a crystalline mono-*O*-ethylidene derivative in good yield. This was shown to be methyl 4,6-*O*-ethylidene-α-D-galactopyranoside (**7**) since methylation gave **5**. Methyl β-D-galactopyranoside also gave a 4,6-*O*-ethylidene derivative (**8**) which has so far not crystallized. Its structure was proved by methylation which gave **6** in 80% yield.

The condensation of **1** with acetone–zinc chloride[14] was examined by thin layer chromatography and it was found that two products were formed. These were separated by fractionation on a column of silica gel and the minor component was identified as 1,2:3,4-di-*O*-isopropylidene-D-galactose by conversion to the crystalline 6-*O*-tosyl derivative. The main product of the reaction crystallized and was shown to be 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose (**9**) by conversion to the 3-*O*-tosyl ester described previously.[2,15] The 3-*O*-mesyl derivative (**10**) of **9** was also obtained crystalline.

Periodate oxidation of **1** by the method described by Schaffer[16] for the preparation of 2,4-*O*-ethylidene-D-erythrose gave crystalline 2,4-*O*-ethylidene-D-threose (**11**) in 35% yield. A chloroform solution of **11** showed no carbonyl absorption in the infrared spectrum, and a molecular weight determination in chloroform indicated that **11** was dimeric, as was found for 2,4-*O*-ethylidene-D-erythrose.[16] In aqueous solution, vapor pressure osmometry indicated that **11** was monomeric.

Catalytic hydrogenation of **11** gave crystalline 1,3-*O*-ethylidene-D-threitol.

Experimental Section[17]

4,6-*O*-Ethylidene-D-galactose (1).—To a suspension of D-galactose (>100 mesh, 100 g.) in paraldehyde (Eastman, aldehyde-free, 400 ml.) was added concentrated sulfuric acid (1 ml.) and the mixture was shaken mechanically for 24 hr. Ammonium hydroxide (3 ml.) was then added and the mixture was filtered. The residue, which was washed with ethanol and air dried, was almost pure **1** (69 g.) and one recrystallization from methanol gave the compound previously described.[2]

Oxidation of **1** with 0.03 *M* sodium metaperiodate gave the following results (periodate reduced and acid liberated in moles per mole of **1**, respectively): 1.6 and 1.5 (8 min.), 1.9 and 1.7 (38 min.), 1.9 and 1.8 (108 min.), 1.9 and 1.9 (150 min., constant value). No formaldehyde was produced.

Reduction of 4,6-*O*-Ethylidene-D-galactose. A. With Sodium Borohydride.—A solution of **1** (5.0 g.) in water (20 ml.) was added during 5 min. to a stirred solution of sodium borohydride (0.5 g.) in water (10 ml.) at 0°. The solution was nonreducing after 2 hr. Sodium ions were removed by passage down a column of Amberlite IR 120 (H^+) resin, and the acidic effluent was concentrated and evaporated several times from methanol. Paper chromatograms revealed the presence of small amounts of galactitol, indicating that the work-up procedure had caused some hydrolysis of the *O*-ethylidene group. The product crystallized readily from methanol: yield 4.5 g., m.p. 135–147°. Two recrystallizations from methanol gave chromatographically pure 4,6-*O*-ethylidene-D-galactitol (**2**), m.p. 146–151°, $[\alpha]^{25}D$ −2.6° (*c* 5.0, water).

Anal. Calcd. for $C_8H_{16}O_6$: C, 46.15; H, 7.74. Found: C, 46.12; H, 7.72.

B. By Hydrogenation.—Ethanol (100 ml.) was added to a solution of **1** (5.0 g.) in water (5 ml.). A slurry of Raney nickel (*ca.* 3 g.) in ethanol was added and the suspension was hydrogenated in a Parr apparatus at room temperature and 30 p.s.i. for 24 hr. Paper chromatograms indicated complete hydrogenation. Raney nickel was removed by filtration and the filtrate was concentrated to a syrup which crystallized from methanol: yield 4.8 g., m.p. 138–143°. Recrystallization from methanol afforded pure **2**, m.p. 146–151°.

Oxidation of **2** with 0.03 *M* sodium metaperiodate resulted in a rapid uptake of 2.0 moles of periodate and the formation of 0.97 moles of formic acid/mole of **2**. One equivalent of formaldehyde was produced.

1,2,3,5-Tetra-*O*-acetyl-4,6-*O*-ethylidene-D-galactitol (3).—Acetylation of **2** with pyridine and acetic anhydride gave the crystalline tetraacetate **3**, and recrystallization from ethanol afforded pure material, m.p. 114–115°, $[\alpha]^{25}D$ −60° (*c* 2.0, ethanol).

Anal. Calcd. for $C_{16}H_{24}O_{10}$: C, 51.06; H, 6.43. Found: C, 51.13; H, 6.46.

4,6-*O*-Ethylidene-1,2,3,5-tetra-*O*-methyl-D-galactitol (4).—A solution of **2** (2 g.) in redistilled *N*,*N*-dimethylformamide (25 ml.) was stirred magnetically and cooled to 0° in a foil-covered flask. Methyl iodide (10 ml.) and silver oxide (10 g.) were added and stirring was continued for 24 hr. T.l.c. (ether) indicated complete methylation and also that lesser amounts of other compounds (probably resulting from migration of the *O*-ethylidene group) were formed at 0° than when the methylation was carried out at room temperature. The mixture was filtered, the residue was washed with dimethylformamide, and the combined filtrates were concentrated to a syrup. This was chromatographed on a column of silica gel (100 g.) with ether as eluent. Fractions containing the product were combined and concentrated, and the resulting syrup was crystallized from *n*-hexane: yield 1.5 g. (59%), m.p. 39–40°, $[\alpha]^{25}D$ −16° (*c* 2.0, ethanol).

(13) E. Pacsu and S. M. Trister, *J. Am. Chem. Soc.*, **62**, 2301 (1940).

(14) Treatment of **1** with acetone–phosphoric anhydride gave a complex mixture of products (shown by t.l.c. and v.p.c.) and this reaction was not further investigated.

(15) J. G. Buchanan and K. J. Miller, *Chem. Ind.* (London), 625 (1958).

(16) R. Schaffer, *J. Am. Chem. Soc.*, **81**, 2838 (1959).

(17) Solutions were concentrated under reduced pressure. Melting points were determined with a Thomas–Hoover capillary melting point apparatus and optical rotations were measured with an ETL-NPL automatic polarimeter (The Bendix Corporation, Cincinnati, Ohio). Molecular weights were determined in the solvents specified with a vapor pressure osmometer (Mechrolab, Inc., Mountain View, Calif.). Paper chromatography was carried out on Whatman No. 1 filter paper in the solvent system 1-butanol–pyridine–water (10:3:3), and the chromatograms were sprayed with *p*-anisidine hydrochloride solution [L. Hough, J. K. N. Jones, and W. H. Wadman, *J. Chem. Soc.*, 1702 (1950)] or with silver nitrate and alkali [W. E. Trevelyan, D. P. Procter, and J. S. Harrison, *Nature*, **166**, 444 (1950)]. Ascending thin layer chromatography (t.l.c.) was performed on 0.25-mm. layers of silica gel G according to Stahl (distributed by Brinkmann Instruments, Inc., Great Neck, N. Y.), and the plates were sprayed successively with a 1% solution of α-naphthol in ethanol and with 10% sulfuric acid and were then heated. Silica gel, grade 950, 60–200 mesh, from the Davison Co., Baltimore 3, Md., was used without pretreatment for column chromatography. Vapor phase chromatography (v.p.c.) was carried out using a Wilkins Aerograph Model A-700 (Autoprep) with helium as the carrier gas. N.m.r. spectra were recorded with a Varian Model A-60 spectrometer equipped with an integrator, and τ values are quoted relative to tetramethylsilane as the internal reference. Microanalyses were performed by Mr. C. DiPietro and the n.m.r. spectra were recorded by Mr. F. H. Bissett.

Anal. Calcd. for $C_{12}H_{24}O_6$: C, 54.53; H, 9.15. Found: C, 54.44; H, 9.21.

Methylation of 4,6-*O*-Ethylidene-D-galactose.[11,12]—To a solution of **1** (6.9 g.) in redistilled *N,N*-dimethylformamide (100 ml.) were added methyl iodide (20 ml.) and silver oxide (25 g.), and the mixture was shaken mechanically at room temperature in a foil-covered flask for 24 hr. T.l.c. (ethyl acetate) indicated complete methylation and only traces of rearrangement products. The mixture was filtered, the residue was washed with dimethylformamide, and the combined filtrates were concentrated to a syrup. This was fractionated on a column of silica gel (400 g.) with ethyl acetate as eluent. The two components of the mixture were difficult to separate by t.l.c. in any solvent tried, but a partial fractionation was achieved on the column and three fractions were collected. **Fraction A** (1.95 g.), the slightly faster moving component, crystallized, and recrystallization from ether–hexane afforded flakes, m.p. 80–81°, $[\alpha]^{25}D$ +9.0° (*c* 1.1, chloroform) [*Anal.* Calcd. for $C_{11}H_{20}O_6$: C, 53.21; H, 8.12; mol. wt., 248. Found: C, 53.20; H, 8.09; mol. wt., 251 (chloroform).]. Its n.m.r. spectrum in deuteriochloroform showed a doublet for H-1 at τ 5.80 ($J_{1,2} \sim 7$ c.p.s.) and was consistent with the structure methyl 4,6-*O*-ethylidene-2,3-di-*O*-methyl-β-D-galactoside (**6**). **Fraction B** (3.35 g.) was a mixture of both components and was not further examined. **Fraction C** (2.21 g.), the slower moving component, crystallized and was recrystallized from ether–heptane. The prisms had m.p. 115–116°, $[\alpha]^{25}D$ +235° (*c* 1.3, chloroform) [*Anal.* Calcd. for $C_{11}H_{20}O_6$: C, 53.21; H, 8.12; mol. wt., 248. Found: C, 53.46; H, 8.11; mol. wt., 250 (chloroform).]. The n.m.r. spectrum of this product in deuteriochloroform showed a doublet for H-1 at τ 5.03 ($J_{1,2} \sim 3$ c.p.s.) and was consistent with the structure methyl 4,6-*O*-ethylidene-2,3-di-*O*-methyl-α-D-galactoside (**5**).

A solution of **5** (0.5 g.) in chloroform (10 ml.) was cooled to 0° and treated with a cold mixture of fuming nitric acid (15 ml.) and chloroform (15 ml.). The mixture was kept at 0° for 15 min. with intermittent shaking and was then poured onto ice. The chloroform layer was separated, washed with sodium bicarbonate solution, and dried (Na_2SO_4). Concentration afforded a syrup which crystallized from ethanol: yield 0.30 g. (48%), m.p. 93.5–95°, $[\alpha]^{25}D$ +111° (*c* 0.6, chloroform), in good agreement with the values reported for methyl 2,3-di-*O*-methyl-4,6-di-*O*-nitro-α-D-galactoside.[4b]

Anal. Calcd. for $C_9H_{16}N_2O_{10}$: C, 34.62; H, 5.17; N, 8.97. Found: C, 34.79; H, 5.31; N, 8.89.

Hydrolysis of Methyl 4,6-*O*-Ethylidene-2,3-di-*O*-methyl-α-D-galactoside (**5**).—A solution of **5** (3.0 g.) in 0.02 *N* hydrochloric acid (50 ml.) was heated at 80° in a stream of nitrogen. The reaction was followed by t.l.c. (acetone or methyl acetate) and selective removal of the *O*-ethylidene group was complete after 8 hr. The solution was neutralized by passage down a column of Dowex 3 (OH^-) resin, and the effluent was concentrated to a syrup which was distilled at 0.1 mm. The distillate, presumably methyl 2,3-di-*O*-methyl-α-D-galactopyranoside, a colorless, viscous syrup, was homogeneous by t.l.c. but has so far failed to crystallize: yield 2.1 g. (79%), $[\alpha]^{25}D$ +154° (*c* 2.2, chloroform).

To hydrolyze this glycoside to the dimethylated sugar, a portion of the syrup (1.5 g.) was dissolved in 2 *N* hydrochloric acid (25 ml.), and the solution was boiled under reflux. T.l.c. (acetone) indicated that hydrolysis was complete in less than 2 hr. The solution was cooled, neutralized by passage down a column of Dowex 3 (OH^-) resin, and concentrated to a syrup which was purified by chromatography on silica gel (100 g.) with acetone as eluent: yield 1.3 g.

A portion of the sugar (0.5 g.) and redistilled aniline (0.5 ml.) were taken up in ethanol (5 ml.) and the solution was boiled under reflux for 8 hr. T.l.c. (methyl ethyl ketone) indicated the formation of two *N*-phenylglycosylamines of 2,3-di-*O*-methyl-D-galactose in approximately equal amounts. These could not be separated by chromatography on a column of silica gel (probably owing to a slow equilibration of the two forms), but one of the isomers (the slower moving) crystallized from acetone. It had m.p. 133–143°, raised to 139–145° by two recrystallizations from the same solvent, $[\alpha]^{25}D$ −50.3° (8 min.) → +12.4° (11 hr., constant, *c* 1.0, ethanol).[4b] T.l.c. (methyl ethyl ketone) indicated that this mutarotation corresponded to the formation of an equilibrium mixture of *N*-phenylglycosylamines.

Anal. Calcd. for $C_{14}H_{21}NO_5$: C, 59.35; H, 7.47; N, 4.94. Found: C, 59.14; H, 7.58; N, 4.81.

Condensation of Methyl α-D-Galactopyranoside with Acetaldehyde.—To a magnetically stirred suspension of methyl α-D-galactopyranoside (48.5 g., 0.25 mole) in 1,1-dimethoxyethane (200 ml.) was added concentrated sulfuric acid (2 ml.). The mixture was homogeneous after *ca.* 10 min., and t.l.c. (methyl ethyl ketone) indicated complete reaction after 1 hr. Solid potassium carbonate was added and the suspension was stirred until neutral. The mixture was filtered and the filtrate was concentrated to a syrup which was fractionated on a column of silica gel (1 kg.) with methyl ethyl ketone as eluent. The major component of the mixture crystallized and recrystallization from acetone–hexane gave 35 g. (64%) of a mono-*O*-ethylidene derivative of methyl α-D-galactopyranoside with m.p. 117–118°, $[\alpha]^{25}D$ +177° (*c* 2.0, ethanol).

Anal. Calcd. for $C_9H_{16}O_6$: C, 49.08; H, 7.32. Found: C, 49.17; H, 7.30.

To a solution of the methyl *O*-ethylidene-α-D-galactopyranoside (0.44 g., 2 mmoles) in redistilled dimethylformamide (8 ml.) were added methyl iodide (2 ml.) and silver oxide (1 g.), and the mixture was stirred magnetically at room temperature in a foil-covered flask. T.l.c. (methyl ethyl ketone) indicated complete methylation after 24 hr. and the mixture was filtered. The residues were washed with dimethylformamide and the filtrate and washings were concentrated to remove most of the dimethylformamide. The yellow concentrate was chromatographed on a column of silica gel (40 g.) with ethyl acetate as eluent. The product (0.43 g., 87%) crystallized and was recrystallized from ether–heptane to give prisms, m.p. 115–116°, undepressed by admixture with **5**. The infrared and n.m.r. spectra of this compound were identical with those of **5**, and the methyl *O*-ethylidene-α-D-galactoside is therefore methyl 4,6-*O*-ethylidene-α-D-galactopyranoside (**7**).

Condensation of Methyl β-D-Galactopyranoside with Acetaldehyde.—Methyl β-D-galactopyranoside (4.85 g.) was treated with 1,1-dimethoxyethane (20 ml.) and concentrated sulfuric acid (0.2 ml.) as described for the α anomer. The product was chromatographed on silica gel (250 g.) with methyl acetate as eluent, and a colorless syrup (4.8 g.) was obtained which was homogeneous by t.l.c. in several solvents.

A portion (0.44 g.) of the syrup was methylated as described for the α anomer, and after chromatography on silica gel, the product (0.40 g., 80%) crystallized. After recrystallization from ether–hexane, the crystals had m.p. 80–81°, not depressed by admixture with **6**. The infrared and n.m.r. spectra of this compound were identical with those of **6**, and the syrupy *O*-ethylidenegalactoside is therefore methyl 4,6-*O*-ethylidene-β-D-galactopyranoside (**8**).

Condensation of 4,6-*O*-Ethylidene-D-galactose with Acetone.—A suspension of **1** (20 g.) in acetone (500 ml.) was treated with granular zinc chloride (60 g.) as previously described except that the product was isolated from aqueous solution by continuous extraction with chloroform. Concentration of the dried (Na_2SO_4) extracts afforded a syrup (10.6 g.) and t.l.c. (ether or ethyl acetate) indicated that this contained two main components and trace amounts of other compounds. The syrup was fractionated on silica gel (900 g.) with ether as eluent. Minor components were discarded and the two main products were collected. **Fraction A** (3.2 g.) was shown to be 1,2:3,4-di-*O*-isopropylidene-D-galactose by conversion to the crystalline 6-*O*-tolyl-*p*-sulfonate. **Fraction B** (6.0 g.), the slower moving component, crystallized after several months and recrystallization from hexane gave needles with m.p. 72–74°, $[\alpha]^{25}D$ +58° (*c* 2.0, ethanol).

Anal. Calcd. for $C_{11}H_{18}O_6$: C, 53.65; H, 7.37. Found: C, 53.53; H, 7.36.

Treatment of this crystalline component with tosyl chloride in pyridine gave the crystalline 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-3-*O*-tosyl-D-galactose described previously,[2,14] and fraction B is therefore 4,6-*O*-ethylidene-1,2-*O*-isopropylidene-D-galactose (**9**).

Treatment of **9** with mesyl chloride in pyridine gave the crystalline 3-*O*-mesyl derivative **10** in 80% yield. After recrystallization from ethanol, it had m.p. 97–99°, $[\alpha]^{25}D$ +109° (*c* 1.0, ethanol).

Anal. Calcd. for $C_{12}H_{20}O_8S$: C, 44.43; H, 6.22; S, 9.88. Found: C, 44.21; H, 6.35; S, 10.09.

Preparation of 2,4-*O*-Ethylidene-D-threose (**11**).—A solution of **1** (10.3 g., 0.05 mole) in water (50 ml.) was added dropwise during 1 hr. to a stirred solution of sodium metaperiodate (23.5 g., 0.11 mole) in water (175 ml.). The solution was kept at 20–25° by external cooling and at pH 6 by addition of 2 *N* sodium

hydroxide from a Beckman automatic titrator (Model K). After an additional 3 hr. at room temperature, the solution was adjusted to pH 7.5 and lyophilized. The residue was extracted with hot ethyl acetate and the extracts were concentrated and cooled. The crystalline product was collected on a sinter and dried: yield 3.2 g. (44%), m.p. 163–165° (after recrystallization from ethanol), $[\alpha]^{25}D$ −5.2° (*c* 2.0 in chloroform).

Anal. Calcd. for $C_6H_{10}O_4$: C, 49.31; H, 6.90; mol. wt., 146. Found: C, 49.33; H, 7.00; mol. wt., 154 (water), 300 (chloroform).

Reduction of 2,4-O-Ethylidene-D-threose.—To a solution of 11 (0.14 g.) in 90% ethanol (10 ml.) was added Raney nickel (1–2 g.), and the suspension was hydrogenated at room temperature and 100 p.s.i. for 7 hr. T.l.c. (acetone) indicated complete reduction, Raney nickel was removed by filtration, and the filtrate was concentrated to a syrup which crystallized spontaneously. Recrystallization from ether gave prisms of 1,3-O-ethylidene-D-threitol, m.p. 78–80°, $[\alpha]^{25}D$ −17.6° (c 2.5, chloroform).

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.65; H, 8.15. Found: C, 48.82; H, 8.25.

Some Derivatives of 2,4-*O*-Ethylidene-D-erythrose and Erythritol[1]

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Received November 24, 1964

Alkaline conditions during the oxidation of 4,6-O-ethylidene-D-glucose have been found to facilitate aldol condensation of the 2,4-O-ethylidene-D-erythrose formed. Nitrogenous derivatives of 2,4-O-ethylidene-D-erythrose have been prepared and their structures have been studied. 1-Amino-1-deoxy-D-erythritol has been prepared as the crystalline *p*-toluenesulfonic acid salt.

For purposes of further synthesis, we were interested in preparing 1-aminobutane-2,3,4-triol. 1-Aminopolyols can be prepared by reduction of carbohydrate nitrogenous derivatives.[2] Reduction of a tetrose hydrazone can lead to the desired compound.

In an attempt to prepare the phenylhydrazone of a tetrose, 2,4-O-ethylidene-D-erythrose (II) was prepared from 4,6-O-ethylidene-D-glucopyranose (I) by oxidation with sodium metaperiodate according to Barker and MacDonald[3] or Rappoport and Hassid.[4] The crude tetrose derivative was extracted from the dried reaction mixture with ethyl acetate and treated with phenylhydrazine. Yields of the crystalline hydrazone ranged from 50% to zero. Later we observed that, when the above-mentioned procedures for the preparation of 2,4-O-ethylidene-D-erythrose (II) were followed, very frequently needle-shaped crystals formed in the ethyl acetate extract of the dried reaction mixture. The crystals melted at 210–215°, had a specific rotation of +50°, could be crystallized from ethyl acetate and petroleum ether (b.p. 40–60°), and reduced Fehling's solution when heated. In the infrared absorption spectrum, two bands for hydroxyl groups but none for a carbonyl group were revealed. The compound could be detected on the chromatogram with anilinium phthalate (but not with ammoniacal silver nitrate) or by t.l.c. (R_f 0.50). Elementary analysis of the crystals corresponded to $(C_6H_{10}O_4)_n$ and molecular weight determination showed that it could be a 2,4-O-ethylidene-D-erythrose dimer (mol. wt. 334, calcd. 292). The crystals were further characterized as a 2,4-O-ethylidene-D-erythrose derivative by the isolation, after acid hydrolysis, of the calculated amount of acetaldehyde 2,4-dinitrophenylhydrazone, and a 2,4-O-ethylidene-D-erythrose dimer structure was erroneously suggested for the compound by the authors.[5]

Prior to this, two 2,4-O-ethylidene-D-erythrose dimers have been described, one[6] of m.p. 149–150° ($[\alpha]^{22}D$ −40° initial; diacetate m.p. 171.5–172°; R_f of dimer by t.l.c. 0.59, see Experimental Section), and one[7] of m.p. 110–111° ($[\alpha]^{25}D$ −14° initial). Easy dimerization of erythrose and suitably substituted erythrose derivatives has been suggested by other authors.[8–10] The compound of m.p. 210–215°, reported above, yielded an acetate (m.p. 211–212°) and a benzoate (m.p. 182–183°). Elementary analysis of the esters corresponded, however, to a triester of $(C_6H_{10}O_4)_2$. A di-O-ethylidene branched octose, 1,3:5,7-di-O-ethylidene-3-C-formyl-D-*glycero*-D-*talo*-heptitol-3[1],6-pyranose (III), m.p. 228–229°, prepared[6] from dimeric 2,4-O-ethylidene-D-erythrose and whose structure has been proven by Schaffer,[6] has three esterifiable hydroxyl groups. The two compounds had the same optical rotation but differed in the reported melting point. The di-O-ethylideneoctose III, prepared according to the procedure of Schaffer, melted at 210–215° on a Fisher-Johns apparatus and showed no depression of melting point when mixed with the supposed dimer. Both compounds, however, separately and mixed, melted with prior softening at 227–228° in a liquid bath. This demonstrated that the alkaline conditions of the oxidation of 4,6-O-ethylidene-D-glucose, described by Rappoport and Hassid,[4] facilitated aldol condensation of the 2,4-O-ethylidene-D-erythrose (II) formed, and that the triacetate and tribenzoate obtained had structures IV and V, respectively (see Chart I).

To avoid dimerization or aldol condensation of 2,4-O-ethylidene-D-erythrose, the oxidation of the parent compound (I) was performed under acidic conditions. The reaction mixture was neutralized with barium carbonate and filtered. The filtrate was treated with benzylamine to form the crystalline 2,4-O-ethylidene-D-erythrose benzylamine Schiff base (VI) in 90% yield. The crystalline phenylhydrazone (VII) and 2,5-di-

(1) Part of this publication is taken from a thesis submitted by I. Z. to the Faculty of Science, The Hebrew University, in partial fulfillment of the requirements for the degree of M.Sc.

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