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Note

The synthesis of 6,7-dideoxy-D-*gluco*-heptose and 6,7-dideoxy-L-*ido*-heptose

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The 6-deoxyaldohexoses are a well known class of simple sugars having at least ten specific members found in Nature[1], and several others prepared by strictly synthetic methods[2]. As has previously been shown[3], one route that generates both 6-deoxy-D-*gluco* and 6-deoxy-L-*ido* derivatives involves addition† of methylmagnesium iodide to the aldehydo sugar 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-*xylo*-pentodialdo-1,4-furanose. In a previous paper[4], we reported that the addition of ethylmagnesium bromide to this aldehyde gives a separable mixture of the 6,7-dideoxy homologs **1** and **4**. These two compounds served as the starting points for the previously unreported 6,7-dideoxy-L-*ido*-heptose (**3**) and 6,7-dideoxy-D-*gluco*-heptose (**6**).

Catalytic hydrogenolysis of the L-*ido* isomer **1** proceeded rapidly (3 h) with hydrogen at atmospheric pressure in the presence of freshly prepared palladium black, to give crystalline **2** (98%; m.p. 73–74°). Similarly, diastereoisomeric **4** was readily converted into the debenzylated alcohol **5** (95%; m.p. 97–99°). The n.m.r. spectra (60 MHz) of **2** and **5** were consistent with the structures given, but, as expected, were very much alike. Both spectra exhibited a triplet for the terminal C-7 methyl protons ($J_{6,7}$ 6.5 Hz), but lacked any signal due to protons on an aromatic ring. The principal difference between the two spectra was the increased complexity of the multiplet from the C-6 protons of **5** (δ ~1.72 p.p.m.) as compared to those of **2** (δ ~1.72 p.p.m.). Despite the similarity of these two compounds, they were readily distinguishable by t.l.c. (with ether), the D-*gluco* isomer moving slightly ahead (R_F 0.53) of the L-*ido* isomer (R_F 0.44).

The hydrolysis of the isopropylidene group in **2** and **5**, catalyzed by the acid form of a cation-exchange resin, was, in both instances, complete within 16 h. T.l.c. on microcrystalline cellulose showed that a single product was formed from each. The free dideoxy monosaccharides **3** and **6** were obtained as analytically pure syrups by lyophilization of their aqueous solutions; for **3**, $[\alpha]_D^{20}$ −26.6°, for **6**, $[\alpha]_D^{20}$ +32.0°.

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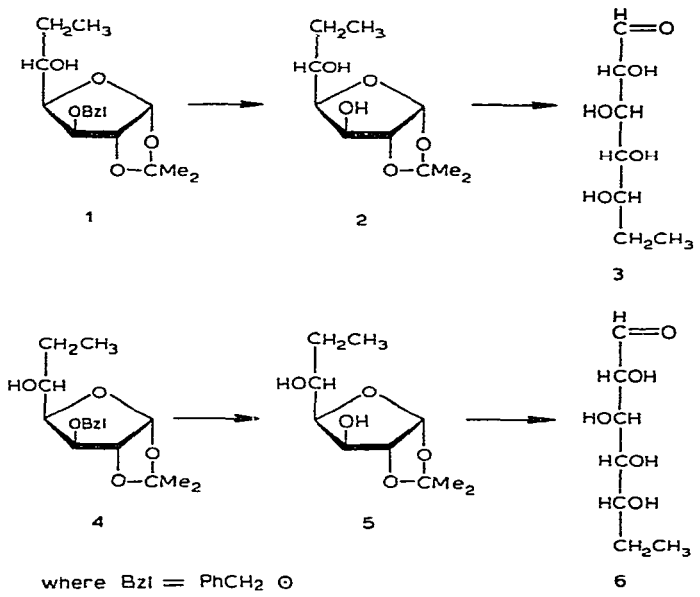
†This preparation was also described in ref. 4.



Although we observed a single product from each hydrolysis, it has been shown that such reactions can lead to a mixture of products. Wolfrom and Hanessian[5] reported that the acid-catalyzed hydrolysis of 6-deoxy-1,2-*O*-isopropylidene-β-L-idofuranose gives both 6-deoxy-L-idose and the isomeric 6-deoxy-L-sorbose. However, the reaction conditions that we employed were considerably milder than those they used.

EXPERIMENTAL

General methods. — Melting points were observed with a Fisher–Johns melting-point apparatus and are uncorrected. T.l.c. separations were conducted with microscope slides coated with Silica Gel GF-254 (E. Merck, Darmstadt) or plates precoated with microcrystalline cellulose (250-μm layer) (Analtech, Inc., Newark, Delaware). Components on plates of silica gel were visibilized by spraying with 20% sulfuric acid and heating. Reducing sugars were detected on plates of microcrystalline cellulose by spraying with ammoniacal silver nitrate[6] and heating at 100°. Compositions of chromatographic solvents are reported as volume to volume ratios. Optical rotations were measured with a Perkin–Elmer Model 141 Polarimeter at 20°, and i.r. spectra were recorded with a Perkin–Elmer 337 Grating Infrared Spectrophotometer. P.m.r. spectra were recorded with a Varian Model HA 60-IL n.m.r. spectrometer for solutions in chloroform-*d*, with tetramethylsilane as the internal standard.

6,7-Dideoxy-1,2-O-isopropylidene-β-L-ido heptofuranose (**2**) *by catalytic hydrogenolysis of* **1**. — A solution of compound **1** (0.49 g) in ethanol (20 ml) was vigorously agitated with ethanol-washed palladium black [freshly prepared from palladium chloride (0.50 g) Engelhard Industries, Inc., Newark, N.J.] in a hydrogen atmo-

sphere. T.l.c. with 7:1 benzene–ether showed that the conversion of **1** into **2** was complete after 3 h. The catalyst was removed by filtration, and the filtrate was evaporated *in vacuo* to give crystalline **2** as rosettes (0.34 g, 98 %). Analytically pure **2** was obtained by chromatographing the crude product on a column of silica gel (7 g) with 4:1 benzene–ether; m.p. 73–74°, $[\alpha]_D^{20}$ −14.4° (*c* 2.15, chloroform), ν_{max}^{KBr} 3550 and 3400 cm^{-1} (OH); n.m.r. signals at δ 1.03 (t, $J_{6,7}$ 6.5 Hz, H-7), 1.36 and 1.52 [each s, $(CH_3)_2C$], ~1.72 (m, partially under the 1.52 signal, H-6), 2.64 (broad signal, OH), 4.08 and 4.26 (unresolved two-proton and one-proton signals; H-3, H-4, and H-5), and 4.53 and 6.00 (each d, $J_{1,2}$ 3.5 Hz, H-2 and H-1).

Anal. Calc. for $C_{10}H_{18}O_5$ (218.3): C, 55.03; H, 8.31. Found: C, 55.13; H, 8.15.

*6,7-Dideoxy-1,2-*O*-isopropylidene-α-*D*-gluco-heptofuranose* (**5**) *by catalytic hydrogenolysis of* **4**. — Catalytic hydrogenolysis of **4** (0.26 g) in ethanol (20 ml) with hydrogen in the presence of palladium black, followed by the standard processing, gave crude, crystalline **5** (0.18 g, 95%). Chromatography of this material on a column of silica gel (7 g) with 4:1 benzene–ether gave analytically pure **5**, m.p. 97–99°, $[\alpha]_D^{20}$ −23.8° (*c* 0.63, chloroform), ν_{max}^{KBr} 3400 cm^{-1} (OH); n.m.r. signals at δ 1.07 (t, $J_{6,7}$ 6.5 Hz, H-7), 1.33 and 1.50 [each s, $(CH_3)_2C$], ~1.72 (m partially under the 1.50 signal, H-6), 4.02 and 4.35 (unresolved two-proton and one-proton signals; H-3, H-4, and H-5), and 4.53 and 5.98 (each d, $J_{1,2}$ 3.5 Hz, H-2 and H-1).

Anal. Calc. for $C_{10}H_{18}O_5$ (218.3): C, 55.03; H, 8.31. Found: C, 54.90; H, 8.26.

Chromatographic distinction between the isomers **2** *and* **5**. — T.l.c. of **2** and **5** (ether) on the same large plate (5 × 25 cm) of silica gel resulted in movement of the D-*gluco* isomer (**5**) slightly ahead (R_F 0.53) of the L-*ido* isomer **2** (R_F 0.44).

*6,7-Dideoxy-*L*-ido-heptose* (**3**) *by hydrolysis of* **2**. — A solution of **2** (0.11 g) in water (3 ml) was kept, without stirring, with AG 50W-X2 (H^+) (200–400 mesh) resin (3 ml, Bio-Rad Laboratories, Richmond, California) for 16 h at 45–50°. T.l.c. on silica gel with 1:1 benzene–ether then showed that the hydrolysis was complete, and t.l.c. on microcrystalline cellulose (ethyl acetate–pyridine–water, 2:1:2, upper phase[7]) indicated the presence of a single, reducing component (**3**), R_F 0.79. The resin was removed by filtration, and the filtrate was lyophilized to give colorless, gummy **3**, $[\alpha]_D^{20}$ −26.6° (*c* 0.87, water).

Anal. Calc. for $C_7H_{14}O_5$ (178.2): C, 47.19; H, 7.92. Found: C, 46.97; H, 8.00.

*6,-7-Dideoxy-*D*-gluco-heptose* (**6**) *by hydrolysis of* **5**. — Acid-catalyzed hydrolysis of compound **5** (0.094 g), as described for the preparation of **3**, yielded the colorless, homogeneous, noncrystalline, reducing heptose **6**; R_F 0.58 in t.l.c. on microcrystalline cellulose with ethyl acetate–pyridine–water (2:1:2, upper phase); $[\alpha]_D^{20}$ +32.0° (*c* 0.82, water).

Anal. Calc. for $C_7H_{14}O_5$ (178.2): C, 47.19; H, 7.92. Found: C, 47.27; H, 8.03.

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