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SYNTHESIS OF D-*manno*-3-HEPTULOSE, D-*ido*-3-HEPTULOSE, AND SOME ALDOHEPTOSES VIA ISOPROPYLIDENE DERIVATIVES OF HEPTITOLS*

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ABSTRACT

D-*manno*-3-Heptulose (**5**) was synthesized by dimethyl sulfoxide–phosphorus pentaoxide oxidation of 1,2:3,4:6,7-tri-*O*-isopropylidene-D-*glycero*-D-*manno*-heptitol (**3**, prepared from volemitol), followed by hydrolysis. D-*ido*-3-Heptulose (**8**) was synthesized similarly by oxidation of 1,2:4,5:6,7-tri-*O*-isopropylidene-D-*glycero*-L-*galacto*-heptitol (**7**, prepared from D-*glycero*-L-*galacto*-heptitol, **6**). Another tri-*O*-isopropylidene derivative (**11**), having a free primary hydroxyl group, was produced in larger amount than **7**, and **11** yielded D-*glycero*-L-*galacto*-heptose (**14**). Compound **8** was also synthesized by way of 1,2:4,5:6,7-tri-*O*-isopropylidene-D-*glycero*-L-*gulo*-heptitol (**15**). The production of **15** from D-*glycero*-L-*gulo*-heptitol (**13**) was accompanied by a larger amount of 2,3:4,5:6,7-tri-*O*-isopropylidene-D-*glycero*-D-*ido*-heptitol (**17**) which, upon oxidation followed by hydrolysis, yielded D-*glycero*-D-*ido*-heptose (**18**). One of the two tri-*O*-isopropylidene derivatives obtained by acetonation of perseitol, 2,3:4,5:6,7-tri-*O*-isopropylidene-D-*glycero*-D-*galacto*-heptitol (**19**), yielded D-*glycero*-D-*galacto*-heptose (**20**).

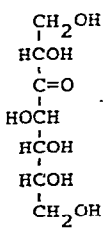
INTRODUCTION

The synthesis of DL- and D-*gluco*-3-heptulose (**1**) by acetonation of heptitols, followed by oxidation of the resultant tri-*O*-isopropylidene derivatives with dimethyl sulfoxide–phosphorus pentaoxide and subsequent hydrolysis, was reported previously[1]. The results show the formation, upon acetonation of five-membered *O*-isopropylidene rings, between the *threo*-disposed[2] hydroxyl groups and between the vicinal diols at both ends of heptitol chain. We have now tried to apply this method to the synthesis of other 3-heptuloses.

It is to be expected that the acetonation of volemitol (**2**) at the *threo*-glycol group will lead to the production of 1,2:3,4:6,7-tri-*O*-isopropylidene-D-*glycero*-D-

*Part X of the Series "Coriose and Related Compounds". For Part IX, see T. Okuda and M. Hayashi, *Phytochemistry*, 16 (1977) 600–601.

manno-heptitol (**3**) in preference to 1,2:4,5:6,7-tri-*O*-isopropylidene-D-*glycero*-D-*manno*-heptitol (**4**). Oxidation of **3**, followed by hydrolysis, should yield D-*manno*-3-heptulose[3] (**5**). Acetonation of D-*glycero*-L-*galacto*-heptitol (**6**) is also expected to give 1,2:4,5:6,7-tri-*O*-isopropylidene-L-*galacto*-heptitol (**7**), which would yield D-*ido*-3-heptulose (**8**) in preference to 1,2:3,4:6,7-tri-*O*-isopropylidene-D-*glycero*-L-*galacto*-heptitol (**9**).



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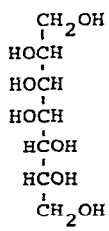

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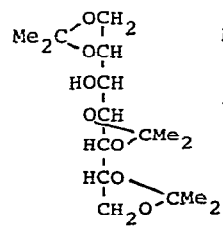

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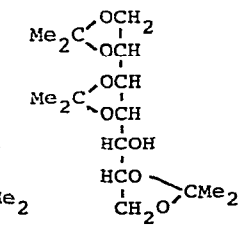

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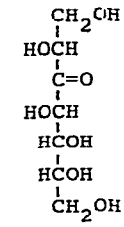

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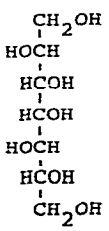

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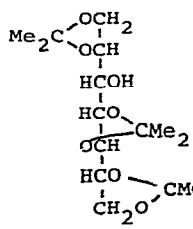

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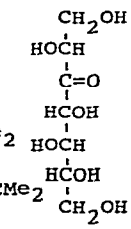

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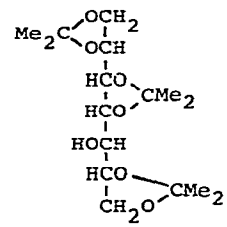

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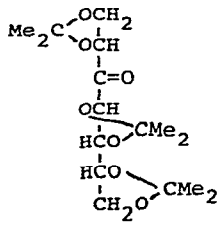

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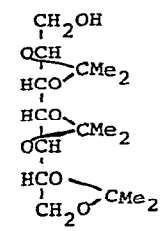

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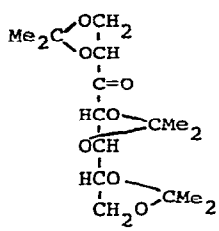

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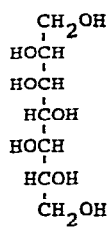

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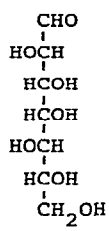

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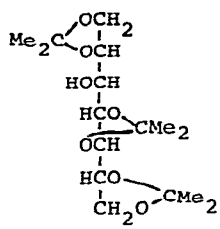

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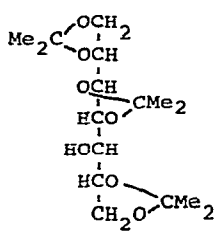

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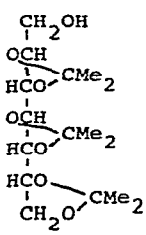

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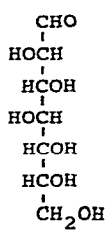

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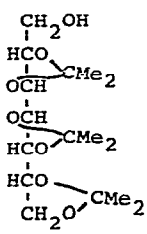

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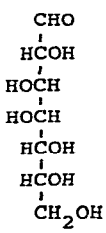

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RESULTS AND DISCUSSION

Acetonation of volemitol (prepared by the Kiliani synthesis from D-mannose followed by borohydride reduction of one of the two resultant heptonolactones, namely, D-*glycero*-D-*talo*-heptonolactone) yielded a syrupy mixture from which the main product (**3**), shown to be a tri-*O*-isopropylidene derivative by its p.m.r. spectrum, was isolated by column chromatography. Oxidation of **3** with dimethyl sulfoxide–phosphorus pentaoxide afforded a syrupy ketone **10**, presumed to have the carbonyl group at C-5 of the D-*glycero*-D-*manno*-heptitol precursor; this assignment is based on the p.m.r. spectrum, which exhibits a quartet for the proton at C-6, coupled with the methylene protons, and also on the generally observed preferential formation of isopropylidene acetals at *threo*-glycol groups. This assumption was proved by hydrolysis of **10** to give crystalline **5**, identical with a specimen synthesized through aldol condensation of 2,4-*O*-ethylidene-D-erythrose[3a].

For synthesis of D-*ido*-3-heptulose (**8**) from D-*glycero*-L-*galacto*-heptitol (**6**), compound **6** was prepared by the Kiliani synthesis from D-galactose, with subsequent borohydride reduction of one of the two resultant heptonolactones, D-*glycero*-L-*gluco*-heptonolactone. Acetonation of **6** gave a two-component mixture, separated by column chromatography to give a component of higher mobility (**7**, m.p. 75–76°), and one of lower mobility (**11**, m.p. 72–73°). The former isopropylidene acetal was shown to have a free secondary hydroxyl group, and the latter, obtained in higher yield than the former, was shown to have a free primary hydroxyl group; their p.m.r. spectra exhibited a deuterium-exchangeable proton as a broad doublet and a broad triplet, respectively. Oxidation of **7** with dimethyl sulfoxide–phosphorus pentaoxide yielded a syrupy ketone (**12**), which is presumed to have the carbonyl group at C-3, based on the analogy with **10** for adjacent protons in the p.m.r. spectrum. Acid hydrolysis of **12** yielded a syrupy sugar **8**, which showed a greyish-brown, single spot on a paper chromatogram, whose color closely matched that given by other 3-heptuloses. The elemental analysis was appropriate for D-*ido*-3-heptulose, and g.l.c. of the *O*-trimethylsilyl derivative exhibited four peaks, whose pattern was similar to that given by D-*gluco*-3-heptulose[1]. G.l.c.–mass spectrometry showed on M − 15 (*m/e* 627) ion-peak for each component, and the characteristic fragmentation of each tautomer[4]. Oxidation of **8** with oxygen in 2M potassium hydroxide, effected as for the oxidation of coriose[5], and borohydride reduction of the resultant syrupy lactone, yielded xylitol. Borohydride reduction of **8** yielded a mixture, g.l.c. of which (as the trimethylsilyl derivative) showed two peaks, corresponding to **6** and D-*glycero*-L-*gulo*-heptitol (**13**). Fractional crystallization of this mixture gave crystals of **6** and **13**, which were identified by comparison with an authentic specimen. These results indicate the syrupy heptulose synthesized to be D-*ido*-3-heptulose (**8**).

The production of the tri-*O*-isopropylidene derivative **11**, having a primary alcohol group, in higher yield than **7**, is presumed to be due to facile formation of an isopropylidene acetal at the *threo*-glycol group adjacent to a primary alcohol, and this derivative is presumed to have been formed by rearrangement of an isopro-

pylidene group from the 1,2 to the 2,3 position. This assumption is supported by the observed increase of **11**, accompanied by decrease of **7**, upon prolonged acetonation. Oxidation of **11** by dimethyl sulfoxide, followed by hydrolysis, yielded a syrupy aldoheptose considered to be D-*glycero*-L-*galacto*-heptose (**14**), based on the formation of **6** upon borohydride reduction and on the properties of its phenylosazone.

An alternative synthesis of **8** from D-*glycero*-L-*gulo*-heptitol (**13**), prepared by the Kiliani synthesis from D-glucose and borohydride reduction of the resultant D-*glycero*-D-*ido*-heptonolactone, was also performed. Between the two tri-*O*-isopropylidene derivatives, 1,2:4,5:6,7-tri-*O*-isopropylidene-D-*glycero*-L-*gulo*-heptitol (**15**) and 1,2:3,4:6,7-tri-*O*-isopropylidene-D-*glycero*-L-*gulo*-heptitol (**16**), having a secondary hydroxyl group, compound **15** is presumed to be formed in preference to **16**, as **16** may be transformed into another tri-*O*-isopropylidene derivative **17** having a primary alcohol, by analogy to the acetonation of **6**, because of the presence of a *threo*-glycol group at C-5–C-6. Acetonation of **13** gave a two-component mixture from which the component of higher mobility (**15**) and that of lower mobility (**17**) were isolated by column chromatography. The presence of a secondary hydroxyl group in **15** and a primary hydroxyl group in **17** was evident from their p.m.r. spectra; deuterium-exchangeable protons gave rise to a broad doublet in the former and a broad triplet in the latter. Oxidation of **15** with dimethyl sulfoxide–phosphorus pentaoxide gave a syrupy ketone identified as **12**, and the heptulose obtained by hydrolysis of this ketone was identified as D-*ido*-3-heptulose (synthesized from **6**).

The tri-*O*-isopropylidene derivative **17**, having a primary hydroxyl group, produced in higher yield than **15**, was oxidized with dimethyl sulfoxide–phosphorus pentaoxide and the oxidation product was hydrolyzed to yield D-*glycero*-D-*ido*-heptose (**18**), whose phenylosazone was identical with that from D-*glycero*-D-*gulo*-heptose. The tri-*O*-isopropylidene derivative **16** was not isolated from the mixture obtained after acetonation for 24 h.

Based on the foregoing observations of the formation of isopropylidene acetals from heptitols, formation of a tri-*O*-isopropylidene derivative having a primary hydroxyl group is also anticipated in the acetonation of perseitol. The major tri-*O*-isopropylidene derivative, of low mobility on t.l.c., formed together with the faster-migrating 1,2:4,5:6,7-*O*-isopropylidene-D-*glycero*-D-*galacto*-heptitol[1], has been shown to be 2,3:4,5:6,7-D-*glycero*-D-*galacto*-heptitol (**19**), as oxidation with dimethyl sulfoxide followed by hydrolysis yielded D-*glycero*-D-*galacto*-heptose (**20**), whose structure was confirmed by phenylosazone formation and borohydride reduction.

EXPERIMENTAL

General methods. — Thin-layer chromatography (t.l.c.) was performed on Wakogel B-10, developing with solvent *A* (8:2 benzene–acetone), unless mentioned otherwise, and detection was effected with conc. sulfuric acid. Paper chromatography (p.c.) was conducted by the ascending method with solvent *B* (6:4:3 1-butanol–pyridine–water), solvent *C* (40:10:5:15 1-butanol–ethanol–acetic acid–water), or

solvent *D* (5:1 phenol–water). Heptuloses were detected with 1:30:240 orcinol–trichloroacetic acid–1-butanol (saturated with water). Preparative p.c. was performed on filter paper (40 cm × 40 cm × 0.7 mm). Column chromatography was carried out on Wakogel C-200, with development by benzene (initial) → 3% acetone in benzene, unless mentioned otherwise. Solutions were dried with magnesium sulfate and solvents were evaporated *in vacuo* below 40°. Trimethylsilyl derivatives were prepared with 1:2:10 chlorotrimethylsilane–hexamethyldisilazane–pyridine. G.l.c. was effected with a Shimadzu 5A gas chromatograph equipped with a flame-ionization detector and a glass column (2 m × 3 mm i.d.) packed with 3% OV-17 or 1.5% OV-1 on 80–100 mesh Chromosorb W treated with hexamethyldisilazane. R_{Glc} is the retention time relative to that of per(trimethylsilyl)ated α-D-glucose.

1,2:3,4:6,7-Tri-O-*isopropylidene*-D-glycero-D-manno-*heptitol* (**3**). — A mixture of volemitol (1.6 g), dry acetone (200 ml), anhydrous cupric sulfate (2.0 g), and conc. sulfuric acid (1 ml) was stirred for 18 h at room temperature, and filtered. The filtrate and acetone washings from the solid were stirred with anhydrous potassium carbonate, and the mixture was filtered. The filtrate was evaporated to a pale-brown syrup (1.93 g), t.l.c. of which showed a main spot accompanied by three small spots of lower mobility. The main product (1.07 g) was isolated by column chromatography; it had $[\alpha]_D^{20}$ −11.3° (*c* 4.3, chloroform); $\nu_{max}^{CHCl_3}$ 3450 cm^{-1} (OH); n.m.r. ($CDCl_3$): δ 1.30–1.38 (6 Me), 3.60–4.35 (m, 9 H, H-1–H-7), and 2.86 (m, 1 H, OH, D exchangeable); *m/e* 317 (M − 15).

Anal. Calc. for $C_{16}H_{28}O_7$: C, 57.81; H, 8.49. Found: C, 57.55; H, 8.51.

1,2:4,5:6,7-Tri-O-*isopropylidene*-D-manno-*3-heptulose* (**10**). — To an ice-cooled solution of **3** (1.0 g) in dry dimethyl sulfoxide (50 ml), phosphorus pentaoxide (1.0 g) was added with stirring. After the phosphorus pentaoxide had dissolved at room temperature, the solution was kept for 1 h at 50–60°. The solution was then poured into ice–water, and extracted with dichloromethane. The dichloromethane solution was washed with aqueous sodium hydrogencarbonate, and water, dried, and evaporated to a syrup (870 mg); $[\alpha]_D^{20}$ −9.1° (*c* 2.0, chloroform); $\nu_{max}^{CHCl_3}$ 1730 cm^{-1} (C=O); n.m.r. ($CDCl_3$): δ 4.90 (q, *J* 6.0 Hz, 1 H, H-2), 4.56 (d, *J* 6.0 Hz, 1 H, H-4), 4.36–3.90 (m, 6 H, H-1,5,6,7), and 1.33–1.46 (6 Me); *m/e* 315 (M − 15).

Anal. Calc. for $C_{16}H_{26}O_7$: C, 57.81; H, 7.93. Found: C, 57.93; H, 8.00.

D-manno-*3-Heptulose* (**5**). — To a solution of **10** (700 mg) in acetone (1 ml), was added 1% sulfuric acid (20 ml), and the mixture was kept for 5 h at 50°. The solution was neutralized with aqueous barium hydroxide, and the precipitate was removed by centrifugation. The supernatant liquor was evaporated to a syrup (267 mg), which was purified by preparative p.c., developing with solvent *B* by the ascending method. After drying the paper, the area showing on guide strips a greyish-brown color with the orcinol reagent was cut into small pieces, dried *in vacuo* for 3 days, and extracted with 1:1 ethanol–water. The solution was evaporated to give a syrup (179 mg) showing a single spot on p.c. (R_F 0.34, solvent *B*) by the orcinol reagent and also by the potassium metaperiodate–benzidine reagent[6]. This syrup

(110 mg) was treated with ethanol (2 ml). After a week, the crystals deposited were filtered off and recrystallized from ethanol to give colorless crystals (56 mg), m.p. 79–81°, $[\alpha]_D^{20}$ −38.2° (*c* 4, water), identified as D-*manno*-3-heptulose by i.r. spectra and mixed m.p.

Anal. Calc. for $C_7H_{14}O_7 \cdot H_2O$: C, 36.84; H, 7.07. Found: C, 36.58; H, 7.19.

1,2:4,5:6,7-Tri-O-*isopropylidene*-D-glycero-L-galacto-*heptitol* (**7**) *and 2,3:4,5:6,7-tri*-O-*isopropylidene*-D-glycero-L-galacto-*heptitol* (**11**). — A mixture of D-*glycero*-L-*galacto*-heptitol (5.0 g), anhydrous cupric sulfate (5.0 g), conc. sulfuric acid (0.5 ml), and dry acetone (200 ml) was stirred for 28 h at room temperature, and then filtered. The residue was washed with dry acetone (30 ml), and the combined washings and filtrate were stirred with anhydrous potassium carbonate (10 g) for 3 h, and filtered. The filtrate was evaporated to a syrup (5.8 g) that showed two spots in t.l.c. This syrup was chromatographed on a column of silica gel (5 cm × 50 cm) to isolate the component of higher mobility (**7**) and that of lower mobility (**11**); these were recrystallized from hexane to give **7** (239 mg) and **11** (4.20 g) as colorless needles.

Compound **7** had m.p. 75–75.5°, $[\alpha]_D^{18}$ −10.2° (*c* 2.16, chloroform); $\nu_{max}^{CHCl_3}$ 3440 cm^{-1} (OH); *m/e* 317 (M−15); n.m.r. ($CDCl_3$): δ 1.38 (s, 3 Me), 1.43 (s, 3 Me), 2.57 (broad d, D exchangeable), and 3.33–4.45 (m, 9 H).

Anal. Calc. for $C_{16}H_{28}O_7$: C, 57.81; H, 8.49. Found: C, 57.52; H, 8.63.

Compound **11** had m.p. 72–73°, $[\alpha]_D^{18}$ −10.9° (*c* 1.28, chloroform); $\nu_{max}^{CHCl_3}$ 3450 cm^{-1} (OH); *m/e* 217 (M−15); n.m.r. ($CDCl_3$): δ 1.39 (s, 4 Me), 1.42 (s, 2 Me), 2.30 (broad t, D exchangeable), and 3.5–4.4 (m, 9 H).

Anal. Calc. for $C_{16}H_{28}O_7$: C, 57.81; H, 8.49. Found: C, 57.76; H, 8.61.

During acetonation of D-*glycero*-L-*galacto*-heptitol for three days, t.l.c. of the mixture after reaction for 12 h showed an appreciable amount of **7**, although the amount was smaller than that of **11**, and the total yield of the isopropylidene derivatives had not reached the maximum by then. After 24 h, t.l.c. showed a smaller ratio of **7** in the mixture. After three days, t.l.c. showed the mixture to be composed mostly of **11**, accompanied by a trace of **7**.

1,2:4,5:6,7-Tri-O-*isopropylidene*-D-ido-*3-heptulose* (**12**) *from* **7**. — To an ice-cooled solution of **7** (238 mg) in dry dimethyl sulfoxide (10 ml), was added phosphorus pentaoxide (200 mg) with stirring. After dissolution of the phosphorus pentaoxide at room temperature, the mixture was stirred for 5 h at 40–60°, and then poured into ice–water. The product was extracted with dichloromethane (100 ml). The extract was washed with aqueous sodium hydrogencarbonate and then with water, and dried. Evaporation of the solvent yielded a pale-brown syrup that was passed through a column of silica gel (20 g) to give a purified syrup (**12**, 179 mg); $[\alpha]_D^{20}$ +20.0° (*c* 0.8, chloroform); *m/e* 315 (M−15); n.m.r. ($CDCl_3$): δ 4.92 (dd, J_1 8, J_2 6 Hz, H-2), 4.56 (d, *J* 7 Hz, H-4), 4.37–3.88 (m, 6 H, H-1,5,6,7), and 1.45–1.38 (6 Me).

Anal. Calc. for $C_{16}H_{26}O_7$: C, 58.17; H, 7.93. Found: C, 58.00; H, 8.01.

D-ido-*3-Heptulose* (**8**). — To a solution of **12** (70 mg) in dry acetone (1 ml) was added 2% sulfuric acid (10 ml), and the mixture was warmed for 5 h at 55°, whereupon

the mixture showed no mobile spot in t.l.c. The solution was neutralized with saturate aqueous barium hydroxide under ice-cooling, the precipitate was removed b centrifugation, and the supernatant was evaporated to a syrup (114.7 mg) that wa purified by preparative p.c. (solvent *B*), extracting the paper with water. The syrup extract was taken up in methanol, and evaporation of the methanol yielded a syru (71 mg) that showed a greyish-brown, single spot on p.c. developed with thre different solvents: *B* (R_F 0.36), *C* (R_F 0.22), and *D* (R_F 0.41); $[\alpha]_D^{24}$ −41.0° (*c* 0.7 water). G.l.c. of the trimethylsilyl derivative showed peaks having R_{Glc} (3% OV-17 180°) 1.47, 1.58, 2.04, and 2.44.

Anal. Calc. for $C_7H_{14}O_7 \cdot H_2O$: C, 36.84; H, 7.07. Found: C, 36.49; H, 7.21.

Reduction of D-ido-*3-heptulose with sodium borohydride.* — Sodium borohydrid (11.9 mg) was added to an aqueous solution of D-*ido*-3-heptulose (53 mg) under ice cooling, and the resultant solution was refrigerated overnight. The solution was the passed through a column of Amberlite IR-120 (H^+, 5 ml) resin. The combine eluates were evaporated to a syrup that was dissolved in methanol (3 ml) and seede with D-*glycero*-L-*galacto*-heptitol (**6**). The crystals deposited were filtered off an recrystallized from methanol to give colorless crystals, m.p. 140–142° (9 mg identified as **6** by mixed m.p. and i.r. spectra.

Anal. Calc. for $C_7H_{16}O_7$: C, 39.62; H, 7.60. Found: C, 39.54; H, 7.48.

The mother liquors from **6** were concentrated to 2 ml and seeded with D *glycero*-L-*gulo*-heptitol (**13**). Crystals deposited after refrigeration for 2 days wer recrystallized from methanol to give colorless crystals (2 mg), identified as **13** b mixed m.p., i.r. spectra, and by g.l.c. of the *O*-trimethylsilyl derivative.

Anal. Calc. for $C_7H_{16}O_7$: C, 39.62; H, 7.60. Found: C, 39.27; H, 7.58.

Oxidative degradation of D-ido-*3-heptulose in alkali.* — Oxygen (~12 ml) wa passed through an ice-cooled solution of D-*ido*-3-heptulose (35 mg) in 2M potassiur hydroxide (5 ml) with stirring. The resulting solution was passed through a column c Amberlite IR-120 resin (H^+, 15 ml), and the eluate plus aqueous washings (100 ml were evaporated. The residue was dissolved in methanol, the solution was evaporatec and this procedure was repeated 5 times to give a syrup (26 mg). Sodium borohydrid (5 mg) was added to an ice-cooled solution of this syrup (20 mg) in water (2 ml), an after being kept overnight, the solution was passed through a column of IR-120 resi (H^+, 5 ml). The eluate and aqueous washings (50 ml) were evaporated. The residu was taken up in methanol (5 ml), the solution was evaporated, and this procedur was repeated 3 times. The residue was then dissolved in methanol (0.5 ml), fror which solution crystals (13.4 mg) were deposited upon keeping; these were identifie as xylitol by g.l.c. of the *O*-trimethylsilyl derivative, by i.r. spectra, and by mixed m.p

D-glycero-L-galacto-*Heptose* (**14**) *from* **11**. — To an ice-cooled solution of **1** (59 mg) in dimethyl sulfoxide (5 ml), phosphorus pentaoxide (20 mg) was slowl added with stirring, and then the mixture was stirred for 6 h at 60–70°. The mixtur was then poured into ice–water and extracted with chloroform. The chloroforr solution was washed successively with water, saturated aqueous sodium hydrogen carbonate, and water, and dried. The filtrate was evaporated *in vacuo* to a syru

(38 mg), which was passed through a column of silica gel to give a purified syrup (21 mg) that showed a single spot on t.l.c. This syrup was dissolved in methanol (1 ml), and the solution was warmed with 1% sulfuric acid (5 ml) for 5 h at 50°. The resultant solution was neutralized with aqueous barium hydroxide, and the precipitate was removed by centrifugation and subsequent filtration through Celite. The filtrate was evaporated, the resultant syrup was taken up in methanol, and the solution was refrigerated. The crystals deposited (6.0 mg) were filtered off and recrystallized from methanol to give **14**; m.p. 185–186°, $[\alpha]_D^{23}$ −67.7° (*c* 0.15, water).

Anal. Calc. for $C_7H_{14}O_7$: C, 40.00; H, 6.72. Found: C, 39.68; H, 6.81.

Sodium borohydride (4 mg) was added to an ice-cooled solution of **14** (23 mg) in water (2 ml), and the solution was kept overnight. Acetic acid was added to bring the pH of the solution 6.0, and the solution was then treated with IR-120 (H^+) resin, and evaporated. The residue was taken up in methanol and the solution was evaporated; this procedure was repeated 4 times. The resultant syrup was dissolved in 9:1 methanol–water and, after being kept, the crystals deposited were filtered off. Recrystallization from the same solvent-mixture afforded colorless crystals (8 mg) that were identified as perseitol by mixed m.p. and by g.l.c. of the *O*-trimethylsilyl derivative.

Heptose **14** yielded a phenylosazone that was recrystallized from aqueous ethanol to give crystals, m.p. 196–199° (dec.).

Anal. Calc. for $C_{19}H_{24}N_4O_5 \cdot 0.5H_2O$: C, 57.42; H, 6.34; N, 14.10. Found: C, 57.13; H, 6.45; N, 13.88.

This osazone was identified by m.p. with the phenylosazone from D-*glycero*-L-*galacto*-heptose[7], and showed m.p. depression on admixture with the phenylosazone from D-*glycero*-L-*gluco*-heptose[8]; the latter should have been produced had the three isopropylidene groups in **11** been formed at the 1,2:3,4:5,6-positions of D-*glycero*-L-*galacto*-heptitol.

1,2:4,5:6,7-Tri-O-*isopropylidene*-D-glycero-L-gulo-*heptitol* (**15**) *and 2,3:4,5:6,7-tri*-O-*isopropylidene*-D-glycero-L-gulo-*heptitol* (**17**). — A mixture of D-*glycero*-L-*gulo*-heptitol (2.85 g), anhydrous cupric sulfate (2.0 g), conc. sulfuric acid (1.0 ml), and dry acetone (200 ml) was stirred for 24 h at room temperature, and filtered. The filtrate was neutralized by stirring with anhydrous potassium carbonate, filtered, and the filtrate was evaporated to give a pale-brown syrup (3.3 g) that showed two spots on t.l.c. These two components were isolated by chromatography on silica gel (120 g) to give syrups of the faster-moving component (**15**, 0.77 g) and the slower moving component (**17**, 2.41 g).

Compound **15** had $[\alpha]_D^{20}$ −7.4° (*c* 2.0, chloroform); $\nu_{max}^{CHCl_3}$ 3450 cm^{-1} (OH); *m/e* 317 (M−15); n.m.r. ($CDCl_3$): δ 4.17–3.39 (m, 9 H, H-1–7), 1.86 (d, *J* 9.5 Hz, OH), 1.34 (s, 4 Me), and 1.27 (s, 2 Me).

Anal. Calc. for $C_{16}H_{28}O_7$: C, 57.81; H, 8.49. Found: C, 57.17; H, 8.35.

Compound **17** had $[\alpha]_D^{20}$ −3.0° (*c* 2.5, chloroform); $\nu_{max}^{CHCl_3}$ 3450 cm^{-1} (OH); *m/e* 317 (M−15); n.m.r. ($CDCl_3$): δ 4.30–3.38 (m, 9 H, H-1–7), 1.44 (broad t, *J* 6 Hz, OH), and 1.36–1.28 (6 Me).

Anal. Calc. for $C_{16}H_{28}O_7$: C, 57.81; H, 8.49. Found: C, 57.63; H, 8.56.

Oxidation of **15** *with dimethyl sulfoxide–phosphorus pentaoxide.* — To an ice-cooled solution of **15** (670 mg) in dry dimethyl sulfoxide (10 ml), was added phosphorus pentaoxide (0.5 g) with stirring. The mixture was stirred for 12 h at room temperature, and then poured into ice–water. After stirring for 20 min, the product was extracted with dichloromethane (100 ml). The dichloromethane solution was washed with aqueous sodium hydrogencarbonate and water, and dried. Evaporation of the solvent yielded a pale-brown syrup (331 mg) that was passed through a column of silica gel (20 g) to give a purified syrup (235 mg) identified as **12** by i.r., n.m.r., and mass spectra; $[\alpha]_D^{20}$ +19.3° (*c* 2.0, chloroform).

Anal. Calc. for $C_{16}H_{26}O_7$: C, 58.17; H, 7.93. Found: C, 58.33; H, 7.55.

Phenylosazone of D-glycero-D-ido-*heptose* (**18**) *from 2,3:4,5:6,7-tri-*O*-isopropylidene-*D-glycero-D-ido-*heptitol* (**17**). — Phosphorus pentaoxide (3 g) was slowly added to an ice-cooled solution of **17** (3.0 g) in dimethyl sulfoxide (30 ml) with stirring, and then the temperature was raised to 60–80°. After complete consumption of **17** had been observed on t.l.c., the mixture was poured into ice–water, and extracted with chloroform. The chloroform solution was washed with aqueous sodium hydrogencarbonate and water, and dried. The solution was evaporated, and the residual syrup (2.48 g) was passed through a column of silica gel (80 g) to give a purified syrup. To this syrup (115 mg) was added 1% sulfuric acid (10 ml), and the mixture was warmed for 4 h at 55°. The mixture was then neutralized with saturated aqueous barium hydroxide, and the precipitate was removed by centrifugation. The supernatant liquor was evaporated to give the syrupy heptose **18** (20 mg); p.c.: R_F 0.28 (solvent *B*). G.l.c. of the trimethylsilyl derivative showed R_{Glc} 1.95 and 2.61 (OV-17, 190°), 2.18 and 3.22 (OV-1, 180°). Heptose **18** yielded a phenylosazone, m.p. 197–198°, that was identified by i.r. spectra and mixed m.p., as the phenylosazone obtained from D-*glycero*-D-*gulo*-heptose.

D-glycero-D-galacto-*Heptose* (**20**) *from 2,3:4,5:6,7-tri-*O*-isopropylidene-*D-glycero-D-galacto-*heptitol* (**19**). — The major component (**19**, R_F 0.3 in t.l.c. developed with 24:1 chloroform–methanol; $[\alpha]_D^{20}$ −6.6° (*c* 5.3, chloroform) of the syrupy mixture of tri-*O*-isopropylidene derivatives obtained by acetonation of perseitol, reported in a previous paper[1] (2.5 g), was dissolved in dimethyl sulfoxide (25 ml), and under ice-cooling, phosphorus pentaoxide (2.5 g) was slowly added with stirring. The mixture was warmed for 2 h at 60–80°, whereupon t.l.c. of the mixture showed a spot of almost identical R_F value as **19**, but the product was distinguished from **19** by g.l.c. of the trimethylsilyl ethers. The mixture was then poured into ice–water, and extracted with chloroform. The chloroform solution was washed with aqueous sodium hydrogencarbonate and water, and dried. The solution was evaporated to a syrup (1.55 g) that was purified by chromatography on a column of silica gel. G.l.c. showed R_{Glc} 1.03 (3% of OV-17, 190°) (R_{Glc} of **19**: 2.16).

The oxidation product (300 mg) was added to 1% sulfuric acid (10 ml), and the mixture was warmed for 4 h at 55°. The mixture was neutralized with saturated, aqueous barium hydroxide, the precipitate removed by centrifugation, and the

supernatant liquor was evaporated to a syrup. This syrup was dissolved in 9:1 methanol–water, from which crystals were deposited on keeping, and were recrystallized from the same solvent-mixture to give colorless crystals of **20**, m.p. 131–133° (60 mg); p.c.: R_F 0.26 (solvent *B*), R_F 0.20 (solvent *C*); g.l.c. of the per(trimethylsilyl) derivative: R_{Glc} 2.34 and 3.54 (1.5% OV-1, 180°); 2.08 and 2.89 (3% OV-17, 200°); g.l.c.–m.s.: *m/e* 642 (M^+) and *m/e* 627 ($M-15$) for both of the two g.l.c. peaks.

Anal. Calc. for $C_7H_{14}O_7$: C, 40.00; H, 6.72. Found: C, 39.68; H, 6.81.

Sodium borohydride (2 mg) was added to a stirred solution of **20** (15 mg) in water (3 ml) under ice-cooling. After keeping overnight, acetic acid was added to bring pH of the solution to 6.0, and the solution was then treated with IR-120 (H^+) resin. The residue, after evaporation, was dissolved in methanol. The solution was evaporated and this procedure was repeated 4 times, to give a syrup that crystallized from 9:1 methanol–water. Recrystallization from the same solvent-mixture gave colorless crystals identified as perseitol by mixed m.p. and g.l.c. of the trimethylsilyl derivative.

Heptose **20** yielded a phenylosazone that was recrystallized from ethanol to give yeliow crystals, m.p. 198–200°, which were identified by mixed m.p. and i.r. spectra as the osazone from D-*manno*-2-heptulose.

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