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Preliminary communication

A new synthesis of D-*glycero*-D-*manno*-heptose

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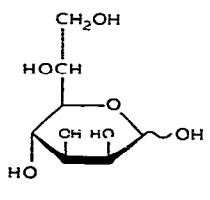
D-*glycero*-D-*manno*-Heptose (**1**) is a component of many bacterial polysaccharides[1] and two syntheses have been described[2,3] each starting from D-altrose. We now report a synthesis of **1** from furan and D-glyceraldehyde, based on the Achmatowicz approach[4].

Condensation (reflux, 8 h) of furan (40 mL) with 2,3-*O*-isopropylidene-D-glyceraldehyde (0.1 mol) in the presence of chloroacetic acid (0.06 mol) gave an 85:15 mixture (37%) of two diastereoisomers of 1-*C*-(2-furyl)-2,3-*O*-isopropylidene-D-glycerol (**2**), $[\alpha]_D^{22}$ +26° (*c* 2.4, chloroform). P.m.r. data ($CDCl_3$, internal Me_4Si): *inter alia*, δ 1.36, 1.45 (2 s, 6 H, CMe_2), 4.55 (d, 0.15 H, *J* 6.5 Hz, H-1 *threo*), 4.75 (d, 0.85 H, *J* 5.0 Hz, H-1 *erythro*), 6.34, and 7.40 (2 m, 3 H, furan protons). The *R* configuration at C-1 of the *erythro* isomer was deduced by degradation (by application in sequence of acetic anhydride–pyridine, 80% acetic acid at 60°, lead tetra-acetate, and lithium aluminium hydride) of **2**, to give partially racemised, known[5] 2-(D-*glycero*-1,2-dihydroxyethyl)furan, $[\alpha]_D^{20}$ +7.5° (*c* 1.8, chloroform); lit.[5] $[\alpha]_D^{22}$ +36.7° (chloroform).



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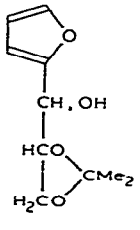

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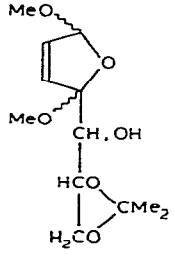

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The mixture of diastereoisomers was converted with bromine–methanol into 1-*C*-(2,5-dihydro-2,5-dimethoxy-2-furyl)-2,3-*O*-isopropylidene-D-glycerol (**3**, 92%), b.p. 105° (bath)/0.05 Torr. P.m.r. data: *inter alia*, δ 1.42, 1.48 (2 s, 6 H, CMe_2), 3.20, 3.26, 3.41, 3.56 (4 s, 6 H, OMe of *cis* and *trans* isomers), and 6.0–6.3 (m, 2 H, olefinic protons). Acid hydrolysis of **3** gave 2,3-dideoxy-6,7-*O*-isopropylidene-D-*erythro*-hept-2-enopyranos-

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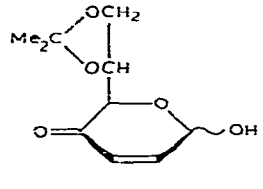
4-ulose (4, 70%), which was not purified but used immediately for the next step P.m.r. data: *inter alia*, δ 1.45, 1.51 (2 s, 6 H, CMe_2), 5.55, 5.71 (2 bs, H-1 of *cis* and *trans* isomers), 6.1–6.3 and 6.9–7.2 (2 m, 2 H, olefinic protons). The conversions 2→3→4 were performed using the general procedures previously described[4].

Treatment of 4 (4.3 mmol) with methyl iodide (17 mL) and silver oxide (1.8 g) at room temperature for 24 h gave a mixture (66%) of methyl 2,3-dideoxy-6,7-*O*-isopropylidene-α-D-*erythro*-hept-2-enopyranosid-4-ulose (5) and the β anomer (6); αβ-ratio, 2:3. Elution of the mixture from a column of silica gel (230–400 mesh, Merck) with hexane–ether–methanol (14:6:1) gave 5, $[\alpha]_D^{22}$ +23° (*c* 0.9, chloroform). P.m.r. data: δ 1.45, 1.51 (2 s, 6 H, CMe_2), 3.66 (s, 3 H, OMe), 4.08 (d, 2 H, H-7,7'), 4.6–4.9 (m, 2 H, H-5,6), 5.22 (d, 1 H, $J_{1,2}$ 3.2 Hz, H-1), 6.12 (d, 1 H, $J_{2,3}$ 10 Hz, H-3), and 6.92 (dd, 1 H, H-2).

Eluted second was 6, $[\alpha]_D^{22}$ −10° (*c* 2, chloroform). P.m.r. data: δ 1.45, 1.52 (2 s, 6 H, CMe_2), 3.62 (s, 3 H, OMe), 4.11 (m, 2 H, H-7,7'), 4.26 (d, 1 H, $J_{5,6}$ 5.5 Hz, H-5), 4.71 (m, 1 H, H-6), 5.30 (bs, 1 H, H-1), 6.17 (dd, 1 H, $J_{1,3}$ 1.4, $J_{2,3}$ 10 Hz, H-3), and 6.91 (dd, 1 H, $J_{1,2}$ 1.8 Hz, H-2).



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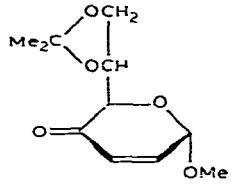

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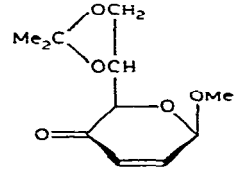

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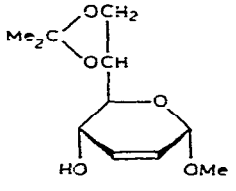

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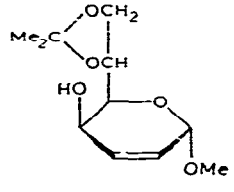

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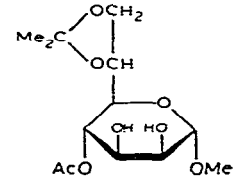

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Treatment of 5 with sodium borohydride in aqueous tetrahydrofuran at 0° for 1 h gave a mixture (60%) of methyl 2,3-dideoxy-6,7-*O*-isopropylidene-α-D-*ribo*- (7) and -*arabino*-hept-2-enopyranoside (8) in the ratio 5:1. Elution of the mixture from silica gel with hexane–ether–methanol (12:8:1) followed by acetylation gave the acetate of 7, $[\alpha]_D^{22}$ +107° (*c* 1.1, methanol). P.m.r. data: δ 1.40, 1.49 (2 s, 6 H, CMe_2), 2.11 (s, 3 H, OAc), 3.50 (s, 3 H, OMe), 3.3–4.4 (m, 4 H, H-5,6,7,7'), 4.95 (bs, 1 H, H-1), 5.45 (d, 1 H, $J_{4,5}$ 9 Hz, H-4), 5.7–6.0 (m, 2 H, H-2,3). The acetate of 8 had $[\alpha]_D^{22}$ −137° (*c* 1.8, methanol). P.m.r. data: δ 1.41, 1.47 (2 s, 6 H, CMe_2), 2.17 (s, 3 H, OAc), 3.56 (s, 3 H, OMe), 3.9–4.5 (m, 4 H, H-5,6,7,7'), 5.03 (d, 1 H, $J_{1,2}$ 2.5 Hz, H-1), 5.15 (dd, 1 H, $J_{3,4}$ 5, $J_{4,5}$ 2.3 Hz, H-4), 6.08 (dd, 1 H, $J_{2,3}$ 10 Hz, H-2), and 6.33 (dd, 1 H, H-3).

Treatment of **7** (1.7 mmol) with *N*-methylmorpholine *N*-oxide (2 mmol) and a catalytic amount of osmium tetraoxide in 1 : 1 *tert*-butyl alcohol–tetrahydrofuran (2.5 mL) at room temperature for 36 h gave methyl 4-*O*-acetyl-6,7-*O*-isopropylidene-α-D-*glycero*-D-*manno*-heptopyranoside (**9**, 72%), m.p. 89–89.5° (from hexane–ethyl acetate), $[\alpha]_D^{22}$ +52° (*c* 1, chloroform).

Zemplén deacetylation of **9** followed by hydrolysis with M HCl in aqueous 1,4-dioxane at 100° for 15 min gave syrupy D-*glycero*-D-*manno*-heptose (**1**), $[\alpha]_D^{22}$ +21.5° (*c* 3.2, methanol); lit.[3] $[\alpha]_D$ +21° (methanol). The diethyl dithioacetal had m.p. 158–159° (from ethanol), $[\alpha]_D^{17}$ +31.5° (*c* 1.1, water); lit.[2] m.p. 151–153°, $[\alpha]_D$ +31.1° (water); lit.[3] m.p. 155–156°, $[\alpha]_D^{25}$ +29.6° (water).

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