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Note

Unsaturated derivatives of 2,6-anhydro-D-*glycero*-L-*manno*- and D-*glycero*-D-*gulo*-heptonic acids*

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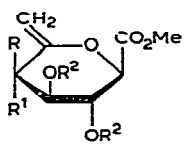
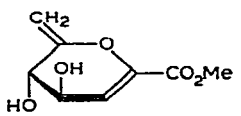
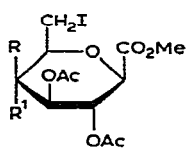
Unsaturated sugar derivatives are useful substrates in chemical[2] and biochemical reactions[3,4], and 2,6-anhydroheptonic acid derivatives have been studied as pyranosyl analogues[4–6]. Both these structural features are present in the unsaturated derivatives (**1–5**) of 2,6-anhydro-D-*glycero*-L-*manno*- and -D-*glycero*-D-*gulo*-heptonic acids, the syntheses of which we now report.



1 R = OAc, R^1 = H, R^2 = Ac
2 R = H, R^1 = OAc, R^2 = Ac
3 R = OH, R^1 = H, R^2 = H
4 R = H, R^1 = OH, R^2 = H



5



6 R = H, R^1 = OAc
7 R = OAc, R^1 = H

The starting materials were methyl 3,4,5-tri-*O*-acetyl-2,6-anhydro-7-*O*-toluene-*p*-sulphonyl-D-*glycero*-L-*manno*- and -D-*glycero*-D-*gulo*-heptonates[7], which, on treatment with sodium iodide in acetic anhydride, yielded the 7-iodides **6** and **7**. Reaction of **6** and **7** with silver fluoride in pyridine was surprisingly vigorous, and rapidly gave the unsaturated esters **1** and **2**. If the reaction was allowed to continue, additional products were formed, probably by further elimination. On deacetylation of **1** and **2**, small proportions of a side-product could be detected (t.l.c.), and column chromatography gave the main products **3** and **4**. One of the side-products crystallized and was methyl 2,6-anhydro-3,7-dideoxy-D-*threo*-hept-2,6-dienonate (**5**). The other side-product, which could be separated as a yellow oil, is probably the 5-epimer of **5**. The double bond between C-6 and C-7 in **1** and **2**, assisted by the ester group, facilitated the introduction of a second double bond between C-2 and C-3. The corresponding saturated compounds, namely methyl 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-L-

*Reactions of Enolic Sugar Derivatives: Part XII. For Part XI, see Ref. 1.

manno- and methyl 3,4,5,7-tetra-*O*-acetyl-2,6-anhydro-D-*glycero*-D-*gulo*-heptonates[7], are stable on catalytic deacetylation in methanolic sodium methoxide.

EXPERIMENTAL

General methods. — T.l.c. was carried out on silica gel F_{254} (Merck) with *A*, benzene–methanol (4:1) for compounds with free hydroxyl groups; and *B*, ether–light petroleum (b.p. 60–70°) (4:1) for fully protected compounds. Detection was effected by charring with conc. sulphuric acid at 150°. For column chromatography, Kieselgel 60 (Merck 0.063–0.2 mm) was used. G.l.c. was performed with glass columns containing Chromosorb G coated with silicone rubber (SE 52, 3%), nitrogen as carrier gas, and flame-ionization detection. I.r. and n.m.r. data were obtained with Perkin–Elmer Infracord Model 137 and Varian A-60 spectrometers, respectively. Melting points are uncorrected.

*Methyl 3,4,5-tri-*O*-acetyl-2,6-anhydro-7-deoxy-7-iodo*-D-glycero-D-gulo-*heptonate* (**6**). — A mixture of methyl 3,4,5-tri-*O*-acetyl-2,6-anhydro-7-*O*-toluene-*p*-sulphonyl-D-*glycero*-D-*gulo*-heptonate (15 g), NaI (5.25 g), and acetic anhydride (100 ml) was boiled under reflux for 20 min. The reaction was then interrupted because of excessive decomposition, although a large proportion of the starting material had not reacted (t.l.c., solvent *B*). The mixture was filtered and insoluble material was washed with acetone. The combined filtrates and washings were concentrated to give a dark-coloured syrup, a solution of which in chloroform (300 ml) was washed with water (300 ml), 0.1% aqueous sodium bisulphite (300 ml), and water (3 × 300 ml), and then dried (Na_2SO_4) and concentrated. The residue (13 g) was again treated with NaI (5 g) in acetic anhydride and worked-up as described above. The product was homogeneous in t.l.c., and recrystallization from methanol gave **6** (10.5 g, 78%), m.p. 166°, $[\alpha]_{578}^{23}$ +26° (*c* 1, chloroform), ν_{max}^{KBr} 1750 cm^{-1} (C=O). N.m.r. data ($CDCl_3$): δ 1.99, 2.01, and 2.06 (3 s, 9 H, 3 OAc); 3.10–3.55 (m, 2 H, CH_2); 3.77 (s, 3 H, OMe); 3.90–4.20 and 4.85–5.40 (2 m, 5 H, H-2,3,4,5,6).

Anal. Calc. For $C_{14}H_{19}IO_9$: C, 36.79; H, 4.18. Found: C, 36.89; H, 4.09.

*Methyl 3,4,5-tri-*O*-acetyl-2,6-anhydro-7-deoxy-7-iodo*-D-glycero-L-manno-*heptonate* (**7**). — A mixture of methyl 3,4,5-tri-*O*-acetyl-2,6-anhydro-7-*O*-toluene-*p*-sulphonyl-D-*glycero*-L-*manno*-heptonate (10 g), NaI (3.5 g), and acetic anhydride (65 ml) was boiled under reflux for 10 min, and then cooled and filtered. Insoluble material was washed with acetone, and the combined filtrate and washings were concentrated under reduced pressure. The residue was recrystallized from methanol to give **7** (8.0 g, 91%), m.p. 179°, $[\alpha]_{578}^{23}$ +2.5° (*c* 1, chloroform), ν_{max}^{KBr} 1750 cm^{-1} (C=O). N.m.r. data ($CDCl_3$): δ 1.99, 2.04, and 2.19 (3 s, 9 H, 3 OAc); 3.12–3.28 (m, 2 H, CH_2); 3.78 (s, 3 H, OMe); 3.88–4.10 (m, 2 H, H-5,6); 5.13–5.22 (m, 2 H, H-3,4); and 5.65 (q, 1 H, H-2).

Anal. Calc. for $C_{14}H_{19}IO_9$: C, 36.79; H, 4.18. Found: C, 36.65; H, 4.32.

*Methyl 3,4,5-tri-*O*-acetyl-2,6-anhydro-7-deoxy-*L-manno-*hept-6-enonate* (**1**). — A solution of **7** (10 g) in pyridine (60 ml) was shaken vigorously with anhydrous silver

fluoride (10 g) at room temperature for 5 min. The mixture was then diluted with ether (1 litre), and the solution was decanted, washed with 1% aqueous sodium thiosulphate (200 ml) and water (2 × 200 ml), dried ($MgSO_4$), and concentrated under diminished pressure to give **1** on crystallization from ether–light petroleum (60–70°) (4.5 g, 62%), m.p. 62°, $[\alpha]_{578}^{23}$ +5° (*c* 1, chloroform), ν_{max}^{KBr} 1730 (C=O) and 1650 cm^{-1} (C=C). N.m.r. data ($CDCl_3$): δ 2.03 and 2.12 (2 s, 6 H, 2 OAc), 2.12 (s, 3 H, OAc), 3.79 (s, 3 H, OMe), 4.26–4.37 and 5.00–5.78 (2 m, 4 H, H-2,3,4,5), 4.71 and 4.95 (2 d, 2 H, CH_2).

Anal. Calc. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49. Found: C, 50.84; H, 5.70.

*Methyl 3,4,5-tri-*O*-acetyl-2,6-anhydro-7-deoxy-*D-gulo-*hept-6-enonate* (**2**). — Compound **6** (10 g), when treated as described above for **7** but for 3 min only, gave **2** after crystallization from ether–light petroleum (60–70°) (5.0 g, 69%), m.p. 106°, $[\alpha]_{578}^{23}$ −4° (*c* 1, chloroform), ν_{max}^{KBr} 1750 (C=O) and 1660 cm^{-1} (C=C). N.m.r. data ($CDCl_3$): δ 2.01, 2.03, and 2.10 (3 s, 9 H, 3 OAc), 3.77 (s, 3 H, OMe); 4.08–4.38 and 5.00–5.58 (2 m, 4 H, H-2,3,4,5), 4.64 and 4.90 (2 t, 2 H, CH_2).

Anal. Calc. for $C_{14}H_{18}O_9$: C, 50.91; H, 5.49. Found: C, 50.95; H, 5.45.

*Methyl 2,6-anhydro-7-deoxy-*L-manno-*hept-6-enonate* (**3**). — Treatment of **1** (2 g) with 0.1M methanolic sodium methoxide (50 ml) gave two products (R_F 0.18 and 0.27, t.l.c., solvent *A*). Elution from a silica gel column with benzene–methanol (4:1) gave first the fraction having R_F 0.27; this was an oil (101 mg, 10%) that showed strong u.v. absorption on t.l.c. plates, and is probably the 5-epimer of **5**. The second fraction (R_F 0.18) was crystallized from chloroform and then from ether–methanol to give **3** (1.1 g, 70%), m.p. 120°, $[\alpha]_{578}^{23}$ −28° (*c* 1, pyridine); ν_{max}^{KBr} 3350 (OH), 1740 (C=O), and 1650 cm^{-1} (C=C). N.m.r. data (C_5D_5N): δ 3.72 (s, 3 H, OMe), 4.28–5.27 (m, 6 H, H-2,3,4,5, CH_2), and 6.67–7.14 (bs, 3 H, 3 OH).

Anal. Calc. for $C_8H_{12}O_6$: C, 47.06; H, 5.92; Found: C, 46.86; H, 5.73.

*Methyl 2,6-anhydro-7-deoxy-*D-gulo-*hept-6-enonate* (**4**) and *methyl 2,6-anhydro-3,7-dideoxy-*D-threo-*hept-2,6-dienonate* (**5**). — Treatment of **2** (2 g), as described above for **1**, and elution of the product from silica gel with benzene–methanol (4:1) yielded, first, **5** (144 mg, 13%), m.p. 79° (from ether, $[\alpha]_{578}^{23}$ −162° (*c* 1, pyridine); ν_{max}^{KBr} 3350 (OH), 1720 (C=O), and 1670 cm^{-1} (C=C). N.m.r. data ($CDCl_3$): δ 3.84 (s, 3 H, OMe), 4.08–4.45 (m, 2 H, H-4,5), 4.82 and 4.96 (2 m, 2 H, CH_2), and 6.09 (bd, 1 H, H-3).

Anal. Calc. for $C_8H_{10}O_5$: C, 51.61; H, 5.41. Found: C, 51.67; H, 5.51.

Eluted second was **4** which, after recrystallization from ether–methanol, gave material (1.175 g, 76%) having m.p. 105°, $[\alpha]_{578}^{23}$ −113.5° (*c* 1, pyridine); ν_{max}^{KBr} 3350 (OH), 1750 (C=O), and 1660 cm^{-1} (C=C). N.m.r. data (C_5D_5N): δ 3.78 (s, 3 H, OMe), 4.05–4.90 (m, 4 H, H-2,3,4,5), 5.10 and 5.43 (2 d, 2 H, $J_{7,7}$ 1.5 Hz, CH_2), and 7.77 (bs, 3 H, 3 OH).

Anal. Calc. for $C_8H_{12}O_6$: C, 47.06; H, 5.92. Found: C, 46.91; H, 5.85.

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