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Note

Reaction of Meldrum's acid with D-mannose and L-arabinose

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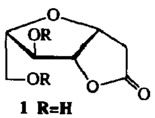
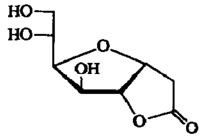
The reaction[1] of Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) with D-xylose, D-glucose, and D-galactose yields mainly 3,6-anhydro-2-deoxyaldono-1,4-lactones. We now report further examples of this reaction.

Thus, reaction of L-arabinose gave syrupy 3,6-anhydro-2-deoxy-L-*gluco*-heptono-1,4-lactone (**1**), which was characterised as its 5,7-diacetate **2**. The $J_{4,5}$ values (1.1 and 0.0 Hz, respectively) of **1** and **2** accord[2–4] with the *trans* arrangement of H-4,5 and confirm the proposed bicyclic structure.



1 R=H
2 R=OAc



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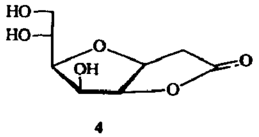

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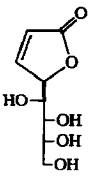

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Likewise, D-mannose gave the 3,6-anhydro-2-deoxy-D-*glycero*-D-*galacto*-octono-1,4-lactone (**4**), the $J_{4,5}$ value (4.0 Hz) of which accorded[3,5,6] with a *cis* arrangement of H-4,5. A second product isolated after this reaction was identified as the known[1] 3,6-anhydro-2-deoxy-D-*glycero*-D-*ido*-octono-1,4-lactone (**3**). Compound **3** could be formed by inversion of configuration at C-4 in the unsaturated lactone **5**, which is a probable intermediate in these reactions. This inversion has been observed with D-galactose[1] and D-mannose in the Wittig and Knoevenagel–Doebner reactions[7].

As the desired *C*-glycosyl derivatives of Meldrum's acid could not be obtained directly from unprotected sugars, the reaction was applied to 2,3,4,6-tetra-*O*-acetyl-D-glucose which gave **6**, the *β* configuration of which was indicated by the $J_{1,2}$ value (10.0 Hz). Compound **6** is a useful intermediate for the preparation of other *C*-D-glucosyl derivatives. Thus, hydrolysis in aqueous acetic acid gave a good yield of known[8] 4,5,6,7-tetra-*O*-acetyl-3,7-anhydro-2-deoxy-D-*glycero*-D-*gulo*-octonic acid (**7**).

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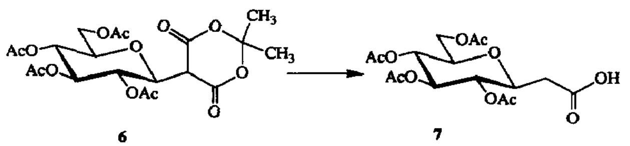

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EXPERIMENTAL

General. — Solutions were concentrated *in vacuo* at <40°. Melting points were determined with a Gallenkamp apparatus and are uncorrected. Optical rotations were measured at 18° with a Perkin–Elmer 141 polarimeter (10-cm cell). T.l.c. was performed on Silica Gel 60 F_{254} (Merck) with detection by u.v. light or charring with H_2SO_4. Flash-column chromatography was performed as described[9]. F.t.-i.r. spectra (KBr discs) were recorded with a Michelson 100 spectrometer. ^{1}H-N.m.r. spectra were recorded with a Bruker WP-80-SY (80.13 MHz) or Varian XL-200 (200 MHz) intrument, and ^{13}C-n.m.r. spectra with a Bruker WP-80-SY (20.15 MHz) spectrometer.

*3,6-Anhydro-2-deoxy-*L-gluco-*heptono-1,4-lactone* (**1**). — A solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (1.44 g, 10.0 mmol), L-arabinose (1.48 g, 10.0 mmol), and triethylamine (1.4 mL, 10.0 mmol) in *N,N*-dimethylformamide (5 mL) was heated for 7 days at 40–50°, then concentrated under diminished pressure. Column chromatography (6:1 $CHCl_3$–MeOH) of the residue gave **1** (0.8 g, 47%), isolated as a syrup, $[\alpha]_D$ + 10° (*c* 1, H_2O), R_F 0.65. N.m.r. data [$(CD_3)_2SO$]: ^{1}H, δ 5.66 (d, 1 H, $J_{5,OH}$ 4.8 Hz, HO-5), 4.85 (t, 1 H, $J_{7,OH}$ 5.2 Hz, HO-7), 4.76 (dd, 1 H, $J_{3,4}$ 4.4, $J_{4,5}$ 1.1 Hz, H-4), 4.69 (dd, 1 H, $J_{2a,3}$ 5.4, $J_{2b,3}$ 0.0 Hz, H-3), 4.02 (dd, 1 H, $J_{5,6}$ 4.6 Hz, H-5), 3.67 (td, 1 H, $J_{6,7a}$ = $J_{6,7b}$ = 5.5 Hz, H-6), 3.60–3.30 (m, 2 H, H-7a,7b), 2.85 (dd, 1 H, $J_{2a,2b}$ −18.2 Hz, H-2a), and 2.45 (d, 1 H, H-2b); ^{13}C, δ 35.8 (C-2), 61.2 (C-7), 75.4, 76.9, 87.1, 89.9 (C-3/6), 175.2 (C-1).

The 5,7-diacetate **2** (0.52 g, 71%) had m.p. 65–66° (from EtOH), $[\alpha]_D$ +86° (*c* 1, $CHCl_3$); ν_{max} 1788 and 1739 cm^{-1} (C=O). N.m.r. data ($CDCl_3$): ^{1}H, δ 5.21 (d, 1 H, $J_{4,5}$ 0.0, $J_{5,6}$ 3.9 Hz, H-5), 4.98–4.78 (m, 2 H, H-3, 4), 4.40–4.10 (m, 1 H, H-6), 4.38 (dd, 1 H, $J_{6,7a}$ 5.1, $J_{7a,7b}$ − 12.7 Hz, H-7a), 4.18 (dd, 1 H, $J_{6,7b}$ 4.1, H-7b), 2.74 (m, 2 H, H-2a,2b), 2.13, 2.08 (2 s, 6 H, 2 OAc); ^{13}C, δ 20.3 (2 $\mathit{C}H_3CO$), 35.8 (C-2), 63.1 (C-7), 77.7 (C-5), 78.2 (C-3), 83.2 (C-6), 86.9 (C-4), 169.4, 170.3 (2 $CH_3\mathit{C}O$), 173.8 (C-1).

Anal. Calc. for $C_{11}H_{14}O_7$: C, 51.16; H, 5.46. Found: C, 51.31; H, 5.44.

*3,6-Anhydro-2-deoxy-*D-glycero-D-ido-*octono-1,4-lactone* (**3**) *and 3,6-anhydro-2-deoxy-*D-glycero-D-galacto-*octono-1,4-lactone* (**4**). — Treatment of D-mannose (4.05 g, 22.5 mmol), as described for L-arabinose, gave, first, **3**[1] (1.8 g, 39%).

Eluted second was **4** (0.5 g, 11%), m.p. 166–167° (from EtOH), $[\alpha]_D$ + 136° (*c* 1, $CHCl_3$), R_F 0.32; ν_{max} 1785 and 1751 cm^{-1} (C=O). N.m.r. data [$(CD_3)_2SO$]: ^{1}H, δ 5.29 (d, 1 H, $J_{5,OH}$ 5.7 Hz, HO-5), 5.02 (d, 1 H, $J_{7,OH}$ 5.2 Hz, HO-7), 4.52 (t, 1 H, $J_{8,OH}$ 5.6 Hz, HO-8), 4.52 (dd, 1 H, $J_{3,4}$ 1.9, $J_{4,5}$ 4.0 Hz, H-4), 4.31 (dd, 1 H, $J_{2a,3}$ 4.01, $J_{2b,3}$ 0.0 Hz, H-3), 3.70–3.10 (m, 5 H, H-5/8), 2.87 (dd, 1 H, $J_{2a,2b}$ − 16.9 Hz, H-2a), 2.28 (d, 1 H, H-2b); ^{13}C, δ 37.8 (C-2), 61.0 (C-8), 66.8, 71.6, 72.9, 79.4, 81.6 (C-3/7), 175.6 (C-1).

Anal. Calc. for $C_8H_{12}O_6$: C, 47.06; H, 5.92. Found: C, 47.28; H, 5.93.

*2,2-Dimethyl-5-(2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranosyl)-1,3-dioxane-4,6-dione* (**6**). — A solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (0.74 g, 5.18 mmol), 2,3,4,6-tetra-*O*-acetyl-D-glucose (0.91 g, 2.59 mmol), and triethylamine (0.36 mL, 2.59 mmol) in acetonitrile (2 mL) was heated for 2 days at 40–50°, then concentrated under diminished pressure. Column chromatography (20:1 chloroform–methanol) of the residue gave **6** (0.72 g, 59%), m.p. 192–194° (from aq. 90% EtOH), $[\alpha]_D$ +12° (*c* 1, EtOH), R_F 0.20; ν_{max} 1746 and 1602 cm^{-1} (C = O). N.m.r. data [$(CD_3)_2SO$]: ^{1}H, δ 5.74 (t, 1 H, $J_{2,3}$ 9.5 Hz, H-2), 5.04 (t, 1 H, $J_{3,4}$ 9.5 Hz, H-3), 4.84 (t, 1 H, $J_{4,5}$ 9.5 Hz, H-4), 4.42 (d, 1 H, $J_{1,2}$ 10.0 Hz, H-1), 4.10 (dd, 1 H, $J_{5,6a}$ 5.04, $J_{6a,6b}$ − 11.8 Hz, H-6a), 3.87 (dd, 1 H, $J_{5,6b}$ 2.5, H-6b), 3.75–3.50 (m, 1 H, H-5), 1.99, 1.96, 1.88, 1.79 (4 s, 12 H, 4 OAc), 1.38 (s, 6 H, 2 CMe); ^{13}C, δ 20.1 (OAc), 25.5 (CH_3-2′), 62.7 (C-6), 70.3 (C-5′), 68.9, 69.3, 73.8, 75.0, 75.3 (C-1/5), 98.9 (C-2′), 146.7 (C-1′,3′), 168.2, 169.0, 169.4, 169.8 (4 OAc).

Anal. Calc. for $C_{20}H_{26}O_{13}\cdot H_2O$: C, 48.98; H, 5.34. Found: C, 48.70; H, 5.30.

*4,5,6,7-Tetra-*O*-acetyl-3,7-anhydro-2-deoxy-*D-glycero-D-gulo-*octonic acid* (**7**). — A solution of 2,2-dimethyl-1,3-dioxane-4,6-dione (0.65 g, 4.51 mmol), 2,3,4,6-tetra-*O*-acetyl-D-glucose (1.13 g, 3.24 mmol), and triethylamine (0.40 mL) in acetonitrile (4 mL) was treated as described in the preparation of **6**. After evaporation of the solvent, a solution of the residue in 10:1 acetic acid–water was heated for 2 h at 100°, then concentrated under diminished pressure, and the residue was treated with water. The residue was recrystallised from ethanol–water to give **7** (0.76 g, 60%), m.p. 99–100°, $[\alpha]_D$ − 2.4° (*c* 3.4, $CHCl_3$); lit.[8] m.p. 104.5–105.5°, $[\alpha]_D$ − 4.3° (*c* 1.95, $CHCl_3$). N.m.r. data ($CDCl_3$): ^{1}H, δ 5.40–3.50 (m, 5 H, H-3/7), 4.25 (dd, 1 H, $J_{7,8a}$ 4.6, $J_{8a,8b}$ − 11.5 Hz, H-8a), 4.05 (dd, 1 H, $J_{7,8b}$ 2.9 Hz, H-8b), 2.55 (m, 2 H, H-2a,2b), 2.07, 2.03, 2.02, 2.00 (4 s, 12 H, 4 OAc); ^{13}C, δ 20.5 (4 CH_3CO), 37.0 (C-2), 62.2 (C-8), 68.7, 71.7, 74.3, 74.4, 76.0 (C-3/7), 169.4, 169.6, 170.2, 170.6 (4 CH_3*C*O), 174.3 (C-1).

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