Note

The synthesis of methyl 4-deoxy-β-L-*threo*-hex-4-enopyranoside*

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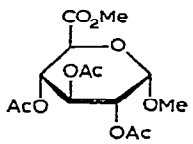
In connection with studies of the deamination of axial amines[1], it became necessary to synthesise the title compound. Hex-4-enopyranose derivatives are well known[2], glycosides of methyl 4-deoxy-β-L-*threo*-hex-4-enopyranuronate having been isolated from the methyl ester of pectic acid by enzymic hydrolysis[3]; the methyl glycoside **2** was subsequently synthesised[4]. The hex-4-enopyranose moiety has recently been reported to occur in the antibiotic sisomycin[5].



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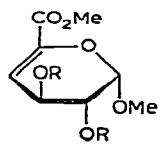
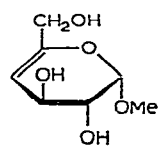


2 R=Ac
3 R=H



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Attempts to form a hex-4-enoside by base-catalysed elimination of methanesulphonic acid from methyl 2,3,6-tri-*O*-benzoyl-4-*O*-methanesulphonyl-α-D-galactopyranoside, and from the corresponding debenzoylated compound, and by elimination of water from methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside with thionyl chloride in pyridine were all unsuccessful. The successful synthetic route involved reduction of the known uronoside **3** with sodium borohydride. A similar reaction, involving reduction with lithium aluminium hydride, was used by Kiss[6] to prepare the 2,3-di-*O*-benzyl derivative of **4**.

The crystalline methyl ester of methyl α-D-galacturonoside was acetylated with sodium acetate in acetic anhydride to yield the crystalline triacetate (**1**). The facile elimination of acetic acid from such compounds (and of methanesulphonic acid from the corresponding 4-methanesulphonate) to yield the conjugated 4-enoside derivatives has been described[6,7]. The formation of the unsaturated uronoside **3** by treatment of the triacetate **1** with sodium methoxide has been referred to briefly[7], but no experimental details were given. Deacetylation competed with the elimination of the C-4 acetoxyl group. We have found that elimination of acetic acid proceeded cleanly at

*Dedicated to Professor M. Stacey, C.B.E., F.R.S., in honour of his 65th birthday.

room temperature when the triacetate **1** was treated with 1,5-diazabicyclo(5.4.0)-undec-5-ene (DBU)[8] in pyridine. The alkene **2** was obtained pure in 78% yield, and conventional base-catalysed deacetylation gave the diol **3**. Both **2** and **3** were obtained as syrups, and their spectra (see Experimental) were consistent with the assigned structures.

Reduction of the uronate **3** with sodium borohydride in methanol yielded methyl 4-deoxy-β-L-*threo*-hex-4-enopyranoside (**4**), which was separated from some unchanged **3** by preparative, paper chromatography. The syrupy product was chromatographically homogeneous, and its structure was confirmed by the i.r. and n.m.r. spectral data.

EXPERIMENTAL

General. — Melting points were measured on a Kofler hot-stage and are uncorrected. Optical rotations were measured on a Perkin–Elmer 141 polarimeter. Spectra were recorded on the following instruments: i.r., Perkin–Elmer 257; n.m.r., Varian HA-100 (with Me_4Si as internal reference; spin-decoupling was used when necessary to aid interpretation); mass spectra, A.E.I. MS-9 spectrometer. Thin-layer chromatography (t.l.c.) was performed on Kieselgel G (Merck) plates, with system (*A*) benzene–ether (1:1), or (*B*) benzene–methanol (7:3). Spots were located by spraying with 5% sulphuric acid in ethanol and heating the plates at 120° for 30 min. Paper chromatography was performed with system (*C*) 1-butanol–ethanol–water (4:1:5, organic phase), the paper being pre-equilibrated in solvent vapour before irrigation. Spots were located by spraying with 0.5% silver nitrate in moist acetone followed by 5% ethanolic sodium hydroxide. G.l.c. was carried out on an F and M 810 gas chromatograph, with columns of (*1*) 10% Carbowax 20M on Chromosorb W, and (*2*) silicone rubber SE 30 (10%) on silanised Chromosorb W at 180° (argon carrier).

Methyl (methyl 2,3,4-tri-O-acetyl-α-D-galactopyranosid)uronate (**1**). — Methyl (methyl α-D-galactopyranosid)uronate[10] (500 mg, 2.27 mmoles)was slowly dissolved in boiling acetic anhydride (3.5 ml) containing sodium acetate (250 mg, 3.28 mmoles) and refluxed for 5 min. The cooled solution was poured on to crushed ice (10 g), allowed to stand for 2 h, and then extracted with chloroform (3 × 15 ml). The organic phase was washed with saturated, aqueous sodium hydrogen carbonate (3 × 15 ml) and water (2 × 20 ml), dried ($MgSO_4$), and concentrated to a syrup which crystallised on standing. Recrystallisation from ether–pentane gave **1** (555 mg, 71%), m.p. 95–96°, $[\alpha]_D^{22}$ +160° (chloroform); ν_{max}^{KBr} 1740 cm^{-1} (C=O stretch). N.m.r. data (deutero-chloroform): τ 8.02, 7.94, 7.92 (singlets, 3 × 3H, Me acetyl), 6.57 (s, 3H, OMe), 6.26 (s, 3H, OMe), 5.40 (d, 1H, 1.5 Hz, H-5), 5.0–4.5 (m, 3H, H-1, H-2, H-3), and 4.24 (q, 1H, 3.5 and 1.5 Hz, H-4). The mass spectrum showed prominent peaks at *m/e* 317 (M−OMe), 289 ($M-C_2H_3O_2$), 229 (289*−HOAc), and 169 (229*−HOAc).

Anal. Calc. for $C_{14}H_{20}O_{10}$: C, 48.27; H, 5.79. Found: C, 48.16; H, 5.79.

*Metastable ions for these steps were observed.

Methyl (methyl 2,3-di-O-acetyl-4-deoxy-β-L-threo-hex-4-enopyranosid)uronate (**2**). — The triacetate **1** (485 mg, 1.4 mmoles) was dissolved in dry pyridine (8 ml) and DBU (0.6 ml, 3.55 mmoles) added. T.l.c. analysis showed that reaction was complete after 2 h at room temperature, and concentration of the golden solution under diminished pressure gave a syrup which was partitioned between ether (40 ml) and water (10 ml). The aqueous layer was washed with more ether (2 × 15 ml), and the combined and dried ($MgSO_4$) ether layers were concentrated to a syrup which was dried *in vacuo*. The product (311 mg, 78%) was homogeneous by t.l.c. (system *A*; the spot fluoresced under u.v. light) and had $[\alpha]_D^{22}$ +241° (chloroform); ν_{max}^{film} 1750 cm^{-1} (C=O stretch), 1660 cm^{-1} (C=C stretch). N.m.r. data (deuterochloroform): τ 7.93, 7.90 (singlets 2 × 3H, Me acetyl), 6.49 (s, 3H, OMe), 6.20 (s, 3H, OMe), 4.95–4.80 (m, 2H, H-1, H-2), 4.43 (m, 1H, H-3), 3.95 (d, 1H, 3 Hz, H-4). The mass spectrum displayed prominent peaks at *m/e* 229 ($M-C_2H_3O_2$), 228 (M − HOAc), 197 (M − OMe–HOAc), and 186 (M − HOAc–C_2H_2O); accurate mass measurement on peak 228 gave the formula $C_{10}H_{12}O_6$.

Anal. Calc. for $C_{12}H_{16}O_8$: C, 50.00; H, 5.59. Found: C, 50.49; H, 5.01.

Methyl (methyl 4-deoxy-β-L-threo-hex-4-enopyranosid)uronate (**3**). — The diacetate **2** (266 mg, 0.92 mmole) was dissolved in dry methanol (20 ml) containing sodium (8.2 mg), and the solution was allowed to stand for 2 h, after which time reaction was complete. Deionisation with Amberlite MB3 resin, followed by filtration and concentration to dryness, gave the syrupy uronate **3** (160 mg, 85%). The product was homogeneous by t.l.c. (system *B*, R_{MG} 2.0*) and by paper chromatography (system *C*, R_{MG} 2.2), and had $[\alpha]_D^{22}$ +207° (methanol); lit.[4] $[\alpha]_D^{20}$ +165.5° (methanol); ν_{max}^{film} 3400 (broad, O-H stretch), 1730 (C=O stretch), 1655 cm^{-1} (C=C stretch). N.m.r. data (pyridine-d_5, after D_2O exchange): τ 6.48 (s, 3H, OMe), 6.31 (s, 3H, OMe), 5.70 (q, 1H, 2.6, 7.7 Hz, H-2), 5.07 (q, 1H, 3.1, 7.7 Hz, H-3), 4.65 (d, 1H, 2.6 Hz, H-1), and 3.49 (d, 1H, 3.1 Hz, H-4).

Methyl 4-deoxy-β-L-threo-hex-4-enopyranoside (**4**). — Uronate **3** (63.4 mg, 0.31 mmole) was dissolved in methanol (4 ml) and sodium borohydride (112 mg) was added. After effervescence had subsided, the solution was refluxed for 2 h. Water (4 ml) was added to the cooled solution, which was then deionised with Amberlite MB3 resin. Concentration under diminished pressure gave a syrup, which was shown by paper chromatography (system *C*) to contain two compounds, one of which corresponded to starting material. Preparative, paper chromatography yielded methyl 4-deoxy-β-L-*threo*-hex-4-enopyranoside (**4**) (17.4 mg; 49%, based on amount of **3** consumed) and unchanged **3** (21.9 mg). The enoside **4** was a colourless syrup, $[\alpha]_D^{22}$ +192° (methanol), which was homogeneous by t.l.c. (system *B*, R_{MG} 1.4), paper chromatography (system *C*, R_{MG} 1.7), and g.l.c. of the TMS ether[9] on columns (*1*) and (*2*); ν_{max}^{film} 1680 cm^{-1} (C=C stretch). N.m.r. data (pyridine-d_5, after D_2O exchange): τ 6.49 (s, 3H, OMe), 5.65 (q, 1H, 2.6, 7.1 Hz, H-2), 5.62 (m, 2H, H-6, H-6'), 5.09 (m, 1H, H-3), 4.73 (d, 1H, 2.6 Hz, H-1), and 4.42 (m, 1H, H-4).

*R_{MG} = mobility relative to methyl α-D-glucopyranoside

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