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Note

Synthesis of 6-deoxy-D-*altro*-heptose

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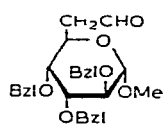
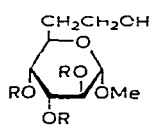
The cell-wall antigen of the Gram-positive bacterium *Eubacterium saburreum*, strain 49, is composed of D-*glycero*-D-*galacto*-heptose and a 6-deoxyheptose[1] The latter unit, which occurs as furanosidic end-groups, was tentatively identified as 6-deoxy-D-*altro*-heptose, and we now report a synthesis and comparison with the natural sugar .

6-Deoxy-D-*manno*-heptose[2] and 6-deoxy-D-*galacto*-heptose[3] have been prepared from the corresponding methyl 2,3 4-tri-*O*-benzyl-α-hexodialdo-1,5-pyranosides, *via* a Wittig reaction Attempts to prepare the *altro* derivative by the same method were not successful, probably because of the hindered position of the aldehyde group

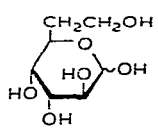
Methyl 2,3 4-tri-*O*-benzyl-α-D-altropyranoside was prepared by conventional methods (see Experimental), and its 6-tosylate was treated with tetrabutylammonium cyanide in *N*,*N*-dimethylformamide to give methyl 2,3,4-tri-*O*-benzyl-6-cyano-6-deoxy-α-D-altropyranoside (88%) Reduction of this product with diisopropylaluminium hydride[4], followed by mild acidic hydrolysis, produced methyl 2,3,4-tri-*O*-benzyl-6-deoxy-D-*altro*-heptodialdo-1 5-pyranoside (**1**) The poor yield (29%) of **1** was probably due to the hindered position of the cyano group in the precursor Reduction of **1** with borohydride and catalytic hydrogenation of the product (**2**) gave **3**, acidic hydrolysis of which yielded 6-deoxy-D-*altro*-heptose (**4**) The synthetic and natural sugars were indistinguishable in p c , and their alditol acetates were indistinguishable in g l c ^{1}H-N m r spectra of the sugars and the mass spectra of their alditol acetates were superimposable The synthetic sugar had $[\alpha]_D$ +20°, compared to $[\alpha]_{578}$ +40° for the natural sugar, the latter value is probably inaccurate because of the small amount of sugar available The previous, tentative identification of the



1



2 R = Bzl
3 R = H



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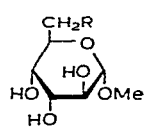

5 R = I
6 R = H

6-deoxyheptose from *Eubacterium sabureum* strain 49 as the D-*altro* derivative was therefore confirmed

Methyl 6-deoxy-α-D-altropyranoside was also prepared by a shorter route (suggested by Professor R U Lemieux) As has been demonstrated in the D-*gluco* and D-*galacto* series[5], methyl 6-deoxy-6-iodo-hexopyranosides, on photolysis in aqueous formaldehyde, give fair yields of 6-deoxyheptosides, in addition to the 6-deoxyhexosides which are the main products When methyl 6-deoxy-6-iodo-D-altropyranoside[6] (**5**) in aqueous formaldehyde was illuminated with a Hanovia lamp, it gave a mixture of methyl 6-deoxy-α-D-*altro*-heptopyranoside (**3**, 5%) and methyl 6-deoxy-α-D-altropyranoside (**6**, 9%)

EXPERIMENTAL

General methods were the same as those previously reported[7] ^{1}H-N m r spectra were recorded for all new compounds and were in agreement with postulated structures Only especially significant n m r data are presented The purity of syrupy new compounds, for which elemental analyses were not performed was carefully ascertained by t l c in solvent systems which gave R_F values of ~0 5, and the substances were rechromatographed until they were pure

Methyl 2,3,4-tri-O-benzyl-α-D-altropyranoside — The three reaction steps were carried out without purification of the main bulk of material Aliquots were removed after each of the first two steps, purified, and characterized The main bulk of material was purified after the third step

Chlorotriphenylmethane (10 g) was added to a stirred solution of methyl α-D-altropyranoside[8] (7 g) in dry pyridine (40 ml) at 0° The mixture was stirred at room temperature for 24 h, and then diluted with water and extracted with ethyl acetate The extract was dried (Na_2SO_4), filtered and concentrated to give methyl 6-*O*-trityl-α-D-altropyranoside m p 50–51° (from ethanol) $[\alpha]_D$ −42° (*c* 1, chloroform) A satisfactory analysis could not be obtained for this compound

A solution of the trityl derivative in *N*,*N*-dimethylformamide (50 ml) was added to a stirred mixture of sodium hydride (7 g) in *N*,*N*-dimethylformamide (50 ml) at 0°, and benzyl bromide (17 ml) was then added The mixture was stirred for ~30 min, methanol (50 ml) was then added during 30 min, and a solution of the mixture in diethyl ether was extracted with water, dried ($MgSO_4$) filtered, and concentrated to give methyl 2,3 4-tri-*O*-benzyl-6-*O*-trityl-α-D-altropyranoside, m p 154–156° (from ethanol), $[\alpha]_D$ +1° (*c* 1, chloroform) A satisfactory analysis could not be obtained for this compound

A mixture of the benzyl derivative in acetone (240 ml) containing 2M hydrochloric acid (18 ml) was boiled under reflux for 6 h, the acid was then neutralized (aqueous $NaHCO_3$), and the solution was extracted with chloroform The extract was washed with water, dried (Na_2SO_4), filtered, and concentrated Crystalline triphenylmethanol was removed, and the product in the filtrate was purified by

chromatography on silica gel (toluene–ethyl acetate, 1 1) to give the title compound as a syrup (7 9 g, 47%), $[\alpha]_D$ −77° (*c* 0 9, chloroform)

*Methyl 2,3,4-tri-O-benzyl-6-O-toluene-*p*-sulphonyl-α-*D*-altropyranoside* — Tosyl chloride (4 g) was added to a solution of the foregoing product (7 8 g) in dry pyridine (25 ml), and the mixture was stored at ~5° for 24 h Ice was then added and the product was extracted with chloroform The extract was dried (Na_2SO_4), filtered and concentrated, and the product (10 3 g) was recrystallized from diethyl ether to give the title compound, m p 84°, $[\alpha]_D$ +56° (*c* 1 1 chloroform)

Anal Calc for $C_{35}H_{38}O_8S$ C, 67 9 H, 6 19 Found C, 67 9 H 6 20

*Methyl 2,3,4-tri-*O*-benzyl-6-cyano-6-deoxy-α-*D*-altropyranoside* — Tetrabutylammonium cyanide* (10 g) was added to a solution of the foregoing product (9 4 g) in *N N*-dimethylformamide (25 ml) The mixture was stirred at 85° for 10 min and then dissolved in diethyl ether The ether solution was washed with water, dried (Na_2SO_4), decolourized with charcoal, filtered, and concentrated The resulting syrup (6 3 g) which was pure in t l c (toluene–ethyl acetate, 4 1), had $[\alpha]_D$ +85° (*c* 1 3 chloroform) ν_{max}^{KBr} 2260 cm^{-1} (weak, C≡N) The ^{1}H-n m r ($CDCl_3$) spectrum at 40° showed three peaks at δ 2 7–2 9 (2 H, H-6 and H-6′)

*Methyl 2 3,4-tri-*O*-benzyl-6-deoxy-α-*D*-altro-heptodialdo-1 5-pyranoside* (**1**) — 3 6M Diisobutylaluminium hydride in benzene (20 ml) was added at room temperature, under nitrogen with stirring to a solution of the foregoing nitrile (0 95 g) in dry toluene (20 ml) The mixture was stirred for 50 min at 55°, and then toluene (30 ml) was added The mixture was cooled to −40° 1 5M sulphuric acid (100 ml) was added during 15 min and the mixture was stirred for 1 h at room temperature The organic phase was then added to the top of a column of silica gel which was eluted with toluene–ethyl acetate (2 1) The appropriate fraction was dried (Na_2SO_4) and concentrated to yield syrupy **1** (0 28 g) $[\alpha]_D$ +71° (*c* 1 1, chloroform), ν_{max}^{KBr} 1730 cm^{-1} (strong CHO) The ^{1}H-n m r spectrum showed a triplet at δ 9 70 (1 H, CHO)

*Methyl 6-deoxy-α-*D*-altro-heptopyranoside* (**3**) — (*a*) Sodium borohydride (50 mg) was added to a solution of **1** (0 316 g) in methanol (15 ml) After 1 h at room temperature the solution was neutralized with Dowex-50 (H^+) resin filtered and concentrated Boric acid was removed from the residue by distillation of methanol therefrom The product **2** (0 264 g), which was used directly in the next step showed a multiplet at δ 1 9 (2 H, H-6 and H-6) in its ^{1}H-n m r spectrum

A solution of **2** (0 204 g) in ethanol (10 ml) was hydrogenated at room temperature and atmospheric pressure over 10% palladium-on-charcoal The mixture was filtered through Celite and concentrated to give syrupy **3** (0 109 g), $[\alpha]_D$ +105° (*c* 0 1, water) the tetra-acetate of which had m p 72–74° $[\alpha]_D$ +66° (*c* 1 4 chloroform)

Anal Calc for $C_{16}H_{24}O_{10}$ C, 51 1 H 6 42 Found C, 50 9 H 6 35

*10M Sodium hydroxide (1 ml) was added with stirring to a solution of tetrabutylammonium hydrogen sulphate (3 4 g 0 01 mol) in dichloromethane (10 ml) followed by sodium cyanide (0 49 g 0 01 mol) The mixture was stirred at room temperature for 30 min, filtered and concentrated to an oil which was dried by azeotropic vacuum distillation with toluene or with molecular sieves

(*b*) A solution of **5** (4 7 g) and sodium hydrogen carbonate (2 7 g) in 33% formaldehyde (400 ml) was irradiated at room temperature for 7 h with a medium-pressure 450-W Hanovia lamp (unfiltered) under nitrogen in a quartz apparatus The formaldehyde was removed by repeated concentrations with water to constant weight The product was added to the top of a column of silica gel which was eluted with ethyl acetate–methanol–water (85 10 5) to give methyl 6-deoxy-α-D-altropyranoside (420 mg) and **3** (225 mg), the tetra-acetate of which was identical with the product described in (*a*)

6-Deoxy-D-altro-*heptose* (**4**) — A solution of **3** (5 mg) in 0 5M sulphuric acid (5 ml) was kept at 100° overnight, neutralized with barium carbonate, filtered, and concentrated to give **4** as a syrup, $[\alpha]_D^{22}$ +20° (*c* 1, water)

Methyl 6-deoxy-6-iodo-α-D-altropyranoside (**5**) — A mixture of methyl α-D-altropyranoside[8] (3 g), *N*-iodosuccinimide (7 g), triphenylphosphine (8 1 g), and *N,N*-dimethylformamide (150 ml) was stirred at 50° for 2 h and worked up as previously described[9] to yield **5** (4 0 g), m p 108–110°, $[\alpha]_D$ +96° (*c* 1, chloroform) lit [6] m p 105–106°, $[\alpha]_D$ +91° (chloroform)

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