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Note

Synthesis of 2-O-methyl-D-rhamnose, a constituent of a bacterial lipopolysaccharide

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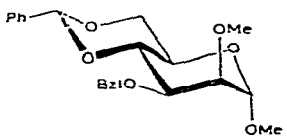
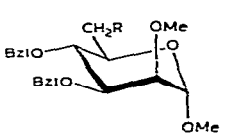
Recently, 2-*O*-methyl-D-rhamnose (6-deoxy-2-*O*-methyl-D-mannose) has been identified[1] in the hydrolysate of a lipopolysaccharide isolated from *Bacterium faecalis alcaligenes*, and a synthesis of this sugar is now described.

Treatment of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-*O*-methyl-α-D-mannopyranoside[2] (**1**) with $LiAlH_4$–$AlCl_3$ in ether–dichloromethane afforded methyl 3,4-di-*O*-benzyl-2-*O*-methyl-α-D-mannopyranoside (**2**, 67%). Reaction of the 6-tosylate (**3**) of **2** with $LiAlH_4$ in benzene–ether (1 : 1) gave 86% of methyl 3,4-di-*O*-benzyl-2-*O*-methyl-α-D-rhamnopyranoside (**4**). Prolonged reduction of **3** also removed one of the two benzyl groups and gave methyl 4-*O*-benzyl-2-*O*-methyl-α-D-rhamnopyranoside (**5**). The synthesis of L-**5** has been described[3].

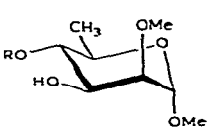
Hydrogenolysis of **4** over Pd/C afforded methyl 2-*O*-methyl-α-D-rhamnopyranoside (**6**), hydrolysis of which gave the title compound (**7**). The ^{13}C-n.m.r. spectra of **6** and **7** were indistinguishable from those[4,5] of the L enantiomers.



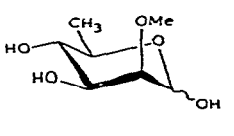
1



2 R = OH
3 R = OTs
4 R = H



5 R = Bzl
6 R = H



7

EXPERIMENTAL

Optical rotations were measured with a Perkin–Elmer 241 polarimeter. N.m.r. spectra (internal Me_4Si) were obtained by using Jeol MH-100 or Bruker WP-200 instruments. T.l.c. was performed on Kieselgel G (Merck).

*Methyl 3,4-di-*O*-benzyl-2-*O*-methyl-α-D-mannopyranoside* (**2**). — To a solution of **1**[2] (2.75 g) in 1 : 1 ether–dichloromethane (60 mL) was added $LiAlH_4$ (0.9 g) with stirring, and the mixture was slowly heated to the boiling point. To the hot solution was added $AlCl_3$ (2.75 g) in ether (20 mL) during 5 min, and the mixture

was boiled under reflux for a further 2 h; t.l.c. then indicated that all **1** had disappeared. The mixture was cooled, the excess of $LiAlH_4$ was decomposed by the addition of ethyl acetate (8 mL), and $Al(OH)_3$ was precipitated by the addition of water (12 mL). After dilution with ether (40 mL), the organic layer was separated and the residue was washed with ether. The organic phase was washed with water (3 × 20 mL), dried, and concentrated. The crude product (2.3 g) was eluted from Kieselgel G (120 g) with dichloromethane–acetone (85:15), to give syrupy **2** (1.85 g, 67.2%), $[\alpha]_D$ +56° (*c* 0.7, chloroform), R_F 0.49. ^{1}H-N.m.r. data ($CDCl_3$): δ 7.40–7.20 (m, 10 H, 2 Ph), 4.80 (q, 4 H, 2 CH_2-Ph), 4.71 (b, 1 H, H-1), 3.82 (dd, 1 H, $J_{2,3}$ 3.2, $J_{3,4}$ 8.9 Hz, H-3), 3.49 (s, 3 H, OMe), 3.34 (s, 3 H, OMe), and 2.30 (t, 1 H, HO-6).

Anal. Calc. for $C_{22}H_{28}O_6$: C, 68.02; H, 7.26. Found: C, 68.25; H, 7.32.

The syrupy 6-tosylate (**3**) of **2** had $[\alpha]_D$ +55.5° (*c* 0.6, chloroform), R_F 0.52 (hexane–ethyl acetate, 7:3). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.71 (d, 2 H), 7.40–7.20 (m, 12 H, aromatic protons), 4.66 (s, 1 H, H-1), 4.60 (s, 2 H, CH_2-Ph), 4.58 (q, 2 H, CH_2-Ph), 3.45 (s, 3 H, MeO-2), 3.28 (s, 3 H, MeO-1), and 2.36 (s, 3 H, tosyl Me).

Anal. Calc. for $C_{29}H_{34}O_8S$: C, 64.18; H, 6.31; S, 5.91. Found: C, 64.35; H, 6.26; S, 6.05.

*Methyl 3,4-di-*O*-benzyl-2-*O*-methyl-α-*D*-rhamnopyranoside* (**4**). — A solution of **3** (1.62 g) in 1:1 dry benzene–ether (60 mL) was boiled under reflux with $LiAlH_4$ (230 mg) for 30 min; the presence of two products in the ratio 9:1 could then be detected, but no **3**. After cooling, the excess of the reagent was decomposed with ethyl acetate (2 mL), and $Al(OH)_3$ was precipitated by addition of water (12 mL). The organic layer was decanted and the residue washed with ether (2 × 10 mL). The combined organic layer was washed with water (3 × 20 mL), dried (Na_2SO_4), and concentrated. The syrupy mixture was eluted from Kieselgel G (50 g) with hexane–ethyl acetate (7:3) to give, first, **4** (960 mg, 86.3%), $[\alpha]_D$ +54° (*c* 0.49, chloroform), R_F 0.59; lit.[5] for the L isomer, $[\alpha]_D$ −38° (chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.40–7.20 (m, 10 H, 2 Ph), 4.72 (q, 2 H, CH_2-Ph), 4.68 (s, 3 H, CH_2-Ph and H-1), 3.84 (dd, 1 H, $J_{2,3}$ 3, $J_{3,4}$ 9 Hz, H-3), 3.49 (s, 3 H, MeO-2), 3.30 (s, 3 H, MeO-1), and 1.30 (d, 3 H, $J_{5,6}$ 6.5 Hz, Me-5).

Anal. Calc. for $C_{22}H_{28}O_5$: C, 70.49; H, 7.58. Found: C, 71.10; H, 7.66.

Eluted second was methyl 4-*O*-benzyl-2-*O*-methyl-α-D-rhamnopyranoside (**5**; 90 mg, 10.7%), $[\alpha]_D$ +53° (*c* 0.84, chloroform), R_F 0.26; lit.[3] for the L isomer, $[\alpha]_D$ −56° (chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.40–7.20 (m, 5 H, Ph), 4.78 (q, 2 H, CH_2-Ph), 4.70 (b, 1 H, H-1), 3.86 (dd, 1 H, H-3), 3.48 (s, 3 H, MeO-2), and 3.34 (s, 3 H, MeO-1).

Anal. Calc. for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 64.05; H, 7.96.

*Methyl 2-*O*-methyl-α-*D*-rhamnopyranoside* (**6**). — A solution of **4** (900 mg) in ethanol (40 mL) and acetic acid (20 mL) was hydrogenolysed in the presence of 10% Pd/C (300 mg); the reaction was complete within 3 h. The mixture was filtered and concentrated, to give syrupy **6** (410 mg, 88.4%), $[\alpha]_D$ +43° (*c* 1.2, chloroform); lit.[4,5] for the L enantiomer, $[\alpha]_D$ −37° (chloroform), −49° (chloroform).

^{13}C-N.m.r. data ($CDCl_3$): δ C-1, 97.33; C-2, 80.24; C-3, 71.52; C-4, 73.82; C-5, 67.61; C-6, 17.47; MeO-1, 54.76; and MeO-2, 58.80.

2-O-Methyl-D-rhamnose (**7**). — A solution of **6** (300 mg) in M sulfuric acid (10 mL) was kept at 100° for 6 h, and then neutralised with barium carbonate, filtered, and concentrated. The residue was extracted with boiling ethanol (3 × 20 mL), and the combined extracts were concentrated, to yield chromatographically homogeneous, syrupy **7** (210 mg, 75.8%), $[\alpha]_D$ −28° (*c* 1.12, water); lit.[6,7] for the L enantiomer, $[\alpha]_D$ +24° m.p. 113–114°.

^{13}C-N.m.r. data (D_2O, internal DSS): α anomer, δ C-1, 93.52; C-2, 83.67; C-3, 72.60; C-4, 75.41; C-5, 70.99; C-6, 19.61; and OMe 61.51; β anomer, δ C-1, 96.71; C-2, 84.45; C-3, 76.03; C-4, 71.21; C-5, 74.97; C-6, 19.61; and OMe, 64.72.

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