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Note

Synthesis of methyl 2-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranoside and two analogues thereof

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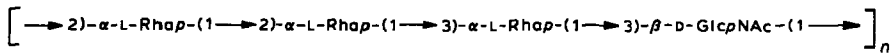
The O-antigenic polysaccharide of *Shigella flexneri* bacteria has the structure[1] **1**. Monoclonal antibodies have been prepared[2] that bind to the non-reducing terminal part of the O-antigen. In order to study the specificity of the antibodies more closely, synthetic oligosaccharides were needed and we now report the synthesis of methyl 2-*O*-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (**5**) by a route different to that previously reported[3]. This disaccharide is bound by the antibodies[2]. Also synthesised were the analogues methyl 2-*O*-α-L-lyxopyranosyl- (**6**) and 2-*O*-α-L-mannopyranosyl-α-L-rhamnopyranoside (**7**), in which Me-5′ of **5** is replaced by hydrogen and hydroxymethyl, respectively.

The key intermediate in the syntheses was methyl 3,4-di-*O*-benzoyl-α-L-



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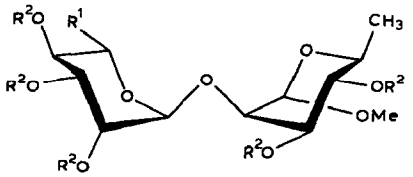

2 R^1 = Me, R^2 = Bz
3 R^1 = H, R^2 = Bz
4 R^1 = CH_2OBz, R^2 = Bz
5 R^1 = Me, R^2 = H
6 R^1 = H, R^2 = H
7 R^1 = CH_2OH, R^2 = H

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rhamnopyranoside[4], silver triflate-promoted glycosidation of which with the benzoylated glycosyl halides of L-rhamnose, L-lyxose, and L-mannose gave the methyl glycoside derivatives **2–4** in yields of 95, 85, and 74%, respectively. Treatment with methanolic sodium methoxide then gave high yields of the methyl glycosides **5–7**. The substitution patterns in **5–7** were demonstrated by methylation analysis[5], and the α configurations at C-1′ were evident from the $J_{C\text{-}1',H\text{-}1'}$ values[6].

EXPERIMENTAL

General methods. — These were as previously reported[7].

Methyl 3,4-di-O-benzoyl-2-O-(2,3,4-tri-O-benzoyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside (**2**). — A solution of 2,3,4-tri-*O*-benzoyl-α-L-rhamnopyranosyl bromide[8] (0.30 g) in toluene–nitromethane (4:1, 6 mL) was added dropwise to a stirred mixture of methyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranoside[4] (0.15 g) and silver triflate (0.15 g) in toluene–nitromethane (4:1, 4 mL) containing 4 Å molecular sieves at −30°. The mixture was then allowed to attain room temperature, filtered, and concentrated. Column chromatography (toluene–ethyl acetate, 30:1) of the residue gave **2** (0.31 g, 95%), $[\alpha]_D$ +153° (*c* 1.4, chloroform). ^{13}C-N.m.r. data ($CDCl_3$): δ17.7 (CH_3), 55.0 (OCH_3), 66.7, 67.5, 69.7, 70.5, 71.1, 71.8, 71.9, 76.6 (C-2,3,4,5, C-2′,3′,4′,5′), 99.4, 99.7 (C-1, C-1′), 164.9, 165.1, 165.4, 165.6, 165.7 (C=O).

Anal. Calc. for $C_{48}H_{44}O_{14}$: C, 68.2; H, 5.3. Found: C, 68.4; H, 5.2.

Methyl 3,4-di-O-benzoyl-2-O-(2,3,4-tri-O-benzoyl-α-L-lyxopyranosyl)-α-L-rhamnopyranoside (**3**). — This compound (0.74 g, 85%), prepared from methyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranoside[4] (0.34 g), 2,3,4-tri-*O*-benzoyl-α-L-lyxopyranosyl bromide[9] (0.68 g), and silver triflate (0.34 g) essentially as described for the preparation of **2**, had $[\alpha]_D$ +127° (*c* 1, chloroform). ^{13}C-N.m.r. data ($CDCl_3$): δ 17.7 (CH_3), 55.1 (OCH_3), 61.0, 66.8, 68.1, 69.1, 70.3, 71.2, 72.0, 76.4 (C-2,3,4,5, C-2′,3′,4′,5′), 99.7, 99.9 (C-1, C-1′), 165.1–165.8 (C=O).

Anal. Calc. for $C_{47}H_{42}O_{14}$: C, 67.9; H, 5.1. Found: C, 67.6; H, 5.1.

Methyl 3,4-di-O-benzoyl-2-O-(2,3,4-tri-O-benzoyl-α-L-mannopyranosyl)-α-L-rhamnopyranoside (**4**). — This compound (0.42 g, 74%), prepared from methyl 3,4-di-*O*-benzoyl-α-L-rhamnopyranoside[4] (0.39 g), 2,3,4,6-tetra-*O*-benzoyl-α-L-mannopyranosyl bromide[10] (0.78 g), and silver triflate (0.39 g) essentially as described for the preparation of **2**, had $[\alpha]_D$ −54° (*c* 0.9, chloroform). ^{13}C-N.m.r. data ($CDCl_3$): δ 17.7 (CH_3), 54.9 (OCH_3), 63.2, 66.8, 67.2, 69.8, 69.9, 70.3, 71.0, 72.0, 77.2 (C-2,3,4,5, C-2′,3′,4′,5′,6′), 99.5, 99.5 (C-1, C-1′), 164.9, 165.2, 165.5, 165.6, 165.7, 166.0 (C=O).

Anal. Calc. for $C_{55}H_{48}O_{16}$: C, 68.5; H, 5.0. Found: C, 68.7; H, 5.1.

Methyl 2-O-α-L-rhamnopyranosyl-α-L-rhamnopyranoside (**5**). — A solution of **2** (0.30 g) in methanolic 0.05M sodium methoxide was kept for 2 h at room temperature, then neutralised with Dowex 50 (H^+) resin, and concentrated. The residue was subjected to column chromatography (chloroform–methanol, 5:1). The

fractions containing **5** were concentrated, and a solution of the residue in water was applied to a column of Sephadex G-15 and eluted with water to give **5** (0.097 g, 84%), $[\alpha]_D$ −46° (*c* 1, water); lit.[3] $[\alpha]_D$ −92° (*c* 1.28, water). The reason for the large difference in $[\alpha]_D$ values is unclear. The ^{13}C-n.m.r. spectrum was essentially the same as that reported[3]. N.m.r. data (D_2O): ^{13}C, δ 17.5 (CH_3), 55.8 (OCH_3), 69.5 (C-5), 70.0 (C-5′), 70.9 (C-2′, C-3,3′), 72.9 (C-4′), 73.0 (C-4), 79.4 (C-2), 100.6 ($J_{C\text{-}1,H\text{-}1}$ 170 Hz, C-1), 103.1 ($J_{C\text{-}1',H\text{-}1'}$ 183 Hz, C-1′).

Anal. Calc. for $C_{13}H_{24}O_9 \cdot H_2O$: C, 45.6; H, 7.7. Found: C, 44.6; H, 7.3.

Compound **5** was methylated and the product hydrolysed to give a 6-deoxy-2,3,4-tri-*O*-methylhexose and a 6-deoxy-3,4-di-*O*-methylhexose, as demonstrated by g.l.c.–m.s. of the derived alditol acetates[5].

Methyl 2-O-α-L-lyxopyranosyl-α-L-rhamnopyranoside (**6**). — A solution of **3** (0.32 g) in methanolic 0.05M sodium methoxide was treated as described for the preparation of **5**, to give **6** (0.09 g, 83%), $[\alpha]_D$ −46° (*c* 1, water). N.m.r. data (D_2O): ^{13}C, δ 17.5 (CH_3), 55.7 (OCH_3), 63.8 (C-5′), 67.6 (C-4′), 69.4 (C-5), 70.6, 71.0, 71.3 (C-3,2′,3′), 73.1 (C-4), 79.4 (C-2), 100.4 ($J_{C\text{-}1,H\text{-}1}$ 170.9 Hz, C-1), 103.3 ($J_{C\text{-}1',H\text{-}1'}$ 170.9 Hz, C-1′); ^{1}H, δ 1.27 (d, 1 H, $J_{5,6}$ 6 Hz, H-6), 4.81 (d, 1 H, $J_{1,2}$ 1.5 Hz, H-1), 4.94 (d, 1 H, $J_{1,2}$ 2.9 Hz, H-1′).

Anal. Calc. for $C_{12}H_{22}O_9 \cdot H_2O$: C, 43.9; H, 7.4. Found: C, 44.4; H, 7.3.

Methylation analysis of **6**, as described above, gave a 2,3,4-tri-*O*-methylpentose and a 6-deoxy-3,4-di-*O*-methylhexose.

Methyl 2-O-α-L-mannopyranosyl-α-L-rhamnopyranoside (**7**). — A solution of **4** (0.27 g) in methanolic 0.05M sodium methoxide was treated as described for the preparation of **5**, to give **7** (0.093 g, 98%), $[\alpha]_D$ −54° (*c* 1, water). N.m.r. data (D_2O): ^{13}C, δ 17.6 (CH_3), 55.7 (OCH_3), 61.9 (C-6′), 67.7 (C-4′), 69.3 (C-5), 70.8, 70.9, 71.2 (C-3,2′,3′), 73.0 (C-4), 74.2 (C-5′), 79.3 (C-2), 100.3 ($J_{C\text{-}1,H\text{-}1}$ 170.9 Hz, C-1), 103.2 ($J_{C\text{-}1',H\text{-}1'}$ 170.9 Hz, C-1′); ^{1}H, δ 1.27 (d, 1 H, $J_{5,6}$ 6 Hz, H-6), 4.85 (d, 1 H, $J_{1,2}$ <1 Hz, H-1), 5.03 (d, 1 H, $J_{1,2}$ <1 Hz, H-1′).

Anal. Calc. for $C_{13}H_{24}O_{10} \cdot 0.5\,H_2O$: C, 44.7; H, 7.2. Found: C, 44.9; H, 7.5.

Methylation analysis of **7**, as described above, gave a 2,3,4,6-tetra-*O*-methylhexose and a 6-deoxy-3,4-di-*O*-methylhexose.

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