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Preliminary communication

The synthesis of part of the repeating unit of a pneumococcal polysaccharide*

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The chemical synthesis of oligosaccharides constituting parts of the chemical structure of bacterial, capsular polysaccharides is of special importance for the immunological study of the relationships between structure and biological specificity, as their isolation in pure form and sufficient amount by acid hydrolysis is very difficult. We now report the synthesis of the trisaccharide methyl α-L-glycoside, **5** which represents the branching point of the immunogenic determinant of the *Streptococcus pneumoniae* type II antigenic polysaccharide[1]. As the intermediate trisaccharide **3** will be used for the synthesis of higher oligosaccharides, the protective groups were selected for convenient and selective removal, and for preparation on a rather large scale. Stereoselectivity of the condensation of methyl 4-*O*-acetyl-3-*O*-(2,3,4-tri-*O*-acetyl-α-L-rhamnopyranosyl)-α-L-rhamnopyranoside[2] (**1**) with 2,3,4,6-tetra-*O*-benzyl-α-D-glucopyranosyl chloride[3] (**2**) was achieved by applying a modification of a method suggested by Igarashi *et al.*[4,5] namely, use of a mixture of dimethyl ether and 1,2-dimethoxyethane as solvents (the proportion of the latter being kept as low as possible), and silver perchlorate as the catalyst. This route was selected because of its simplicity and the good yield of α-D-glucoside, 86% in the present case. The anomeric configuration of the compounds formed (**3** and **6**) was readily established on the basis of the optical rotation, which was positive for the α-D and negative for the β-D anomer, and the n.m.r. data, which, for the D-glucopyranosyl group, indicated a *cis* disposition for H-1 and H-2 of **5** ($J_{1,2} < 4$ Hz), and a *trans* orientation for H-1 and H-2 of **8**($J_{1,2}$ 6–9 Hz).

To a solution of **1** and silver perchlorate in ether and 1,2-dimethoxyethane was slowly added a solution of **2** in ether. The reaction was complete overnight, and t.l.c. in 2:1 (v/v) ether–hexane (two developments) showed two spots (R_F 0.47 and 0.52), corresponding, respectively, to **3**, syrup, $[\alpha]_D^{20}$ +24.4° (*c* 1.1, chloroform), and **6**, m.p. 49–50.5°, $[\alpha]_D^{20}$ −13.2° (*c* 1.3, chloroform) (overall yield 63%; ratio of **3** to **6**, 43:7).

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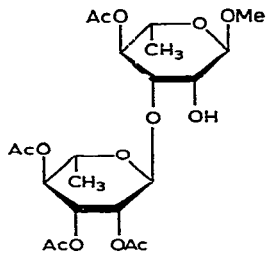

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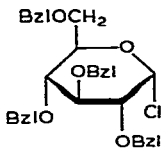

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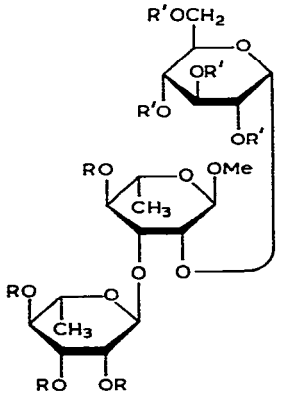
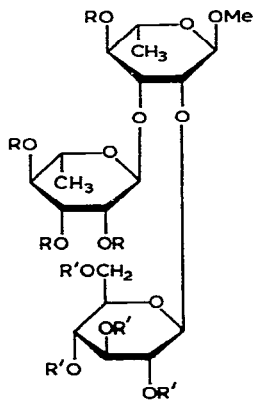


3 R = Ac, R' = Bzl
4 R = H, R' = Bzl
5 R = H, R' = H



6 R = Ac, R' = Bzl
7 R = H, R' = Bzl
8 R = H, R' = H

Treatment of **3** and **6** with 0.1M sodium methoxide in methanol respectively gave **4** and **7**, which were hydrogenolyzed in methanol in the presence of palladium-on-charcoal to give methyl *O*-α-D-glucopyranosyl-(1→2)-[*O*-α-L-rhamnopyranosyl-(1→3)]-α-L-rhamnopyranoside (**5**), m.p. 157–158.5°, $[\alpha]_D^{20}$ +15.3° (*c* 1.0, water); ^{1}H-n.m.r. at 270 MHz: δ 5.04 ($J_{1,2}$ 3.5 Hz, H-1); and methyl *O*-β-D-glucopyranosyl-(1→2)-[*O*- α-L-rhamnopyranosyl-(1→3)]-α-L-rhamnopyranoside (**8**), m.p. 156–158°, $[\alpha]_D^{20}$ –31° (*c* 0.9, water); ^{1}H-n.m.r. at 270 MHz: δ 4.58 ($J_{1,2}$ 7.8 Hz, H-1), in 87% and 83% yield, respectively. All of the compounds described gave n.m.r., i.r., and elemental analysis data in agreement with the structures proposed.

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