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Synthesis of some Branched Trisaccharides using Photolabile o-Nitrobenzylidene Acetals as Temporary Protecting Groups

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Summary Methyl 2-O- $(\beta$ -D-glucopyranosyl)-3-O- $(\beta$ -D-glucopyranosyl)- α -L-fucopyranoside (4), methyl 2-O- $(\beta$ -D-galactopyranosyl)-3-O- $(\beta$ -D-galactopyranosyl)- α -L-fucopyranoside (5), and methyl 3-O- $(\beta$ -D-glucopyranosyl)-4-O- $(\beta$ -D-glucopyranosyl)- α -L-rhamnopyranoside (9) have been synthesised using o-nitrobenzylidene acetals as photosensitive temporary protecting groups.

BRANCHED oligosaccharides are currently of interest because of their importance as the antigenic determinants in microbial and blood-group polysaccharides.^{1,2} Synthesis of these compounds requires that the sugar at the branch point be constructed from an aglycone blocked with temporary and permanent protecting groups³ which permit sequential glycosylation at a preselected hydroxy-group. Several approaches have been made⁴ to solve this problem and in this communication⁵ we show, with model compounds, that the *o*-nitrobenzylidene group, which we studied earlier,⁶ serves this purpose well.

Glucosylation⁷ of methyl 3,4-O-o-nitrobenzylidene- α -L-fucopyranoside⁸ with acetobromoglucose in a mixture of benzene and nitromethane containing mercury(II) cyanide gave the disaccharide (1)[†] in 80% yield with a β -(1 \rightarrow 2) link as determined from the $J_{1,2}$ value in the ¹H n.m.r. spectrum of the deblocked methyl glycoside of the disaccharide. U.v. irradiation of (1) in methanol followed by mild oxidation with trifluoroperacetic acid in dichloromethane at 0 °C as described earlier⁶ gave, in 95% yield, the partially protected disaccharide (2) with a free hydroxygroup at C(3) and an o-nitrobenzoyl residue at O(4) as indicated by the lowfield resonance for H(4) at δ 5·3, dd, $J_{4,3}$ 3·0 and $J_{4,5}$ 1·0 Hz.

The disaccharide (2) could be glucosylated without prior recourse to chromatography, and upon condensation with acetobromoglucose it gave, in 75% yield, a 7:1 mixture of $\beta\beta$ - and $\alpha\beta$ -linked trisaccharides which was fractionated chromatographically to give the pure $\beta\beta$ -linked compound (3), m.p. 92—94 °C, $[\alpha]_{\rm p}^{23}$ -12°. The ¹H n.m.r. spectrum clearly showed resonances for the Ac, OMe, CMe and HCOCOAr hydrogens and the ¹³C n.m.r. spectrum exhibited three clean signals for the anomeric carbons.

Deacylation gave the methyl glycoside (4) of the branched trisaccharide, m.p. 143—145 °C, $[\alpha]_{23}^{23}$ —57·1°, the anomeric protons of which resonated at δ (D₂O) 5·08, 4·75, and 4·72 ($J_{1,2}$ 2·4, 7·9, and 7·3 Hz respectively), and the protons of the OMe and CMe residues resonated respectively at 3·54(s) and 1·40(d, J 6·3 Hz). The ¹³C n.m.r. spectrum corroborated these results, with the anomeric carbons resonating at δ (D₂O) 101·4, 100·4, and 98·3 p.p.m. and the carbons of the O- and C-methyl groups at 55·8 and 16·1 p.p.m. respectively.







 β -D-Glcp-(1-4) $\rightarrow \alpha$ -L-Rhap-1Me β -D-Glcp-(1-3) $\rightarrow \alpha$ -L-Rhap-1Me

(9)

 $G = Tetra-O-acetyl-\beta-D-glucopyranosyl Ar = o-O_2NC_8H_4$

(8) R = G

A similar series of transformations with acetobromogalactose and methyl 3,4-O-o-nitrobenzylidene- α -L-fucoside yielded the trisaccharide (5), m.p. 157–159 °C, $[\alpha]_{29}^{29}$ -58·2° (MeOH), $\delta_{\rm H}$ (D₂O 400 MHz) 4·73, 4·76, and 5·16 ($J_{1.2}$ 7·3, 7·5, and 3·0 Hz respectively) for the anomeric protons, 3·61(s, OMe), and 1·47 (d, J 6·5 Hz, CMe); $\delta_{\rm C}$ 102·1, 101·1, and 98·6 p.p.m. for the anomeric carbons, 55·3(OMe), and 16·1(CMe) p.p.m.

Trisaccharides with branching at rhamnose can also be prepared by this approach. Thus, condensing methyl 2,3-O-o-nitrobenzylidene- α -L-rhamnopyranoside⁸ with aceto-

 $[\]uparrow$ All new compounds gave satisfactory elemental analyses. Unless stated otherwise optical rotations are for chloroform solution and 1 H n.m.r. spectra were measured at 200 MHz in CDCl₃.

bromoglucose afforded in 85% yield the disaccharide (6) with the β -configuration as shown by the $J_{1,2}$ value of 7.5 Hz in the ¹H n.m.r. spectrum of the partially deblocked disaccharide. Irradiation of (6) in methanol containing 4%acetic acid followed by oxidation gave, after chromatography, the disaccharide (7) (60%), m.p. 185 °C, $[\alpha]_D^{23}$ -49.9°, δ 5.32 (q, $J_{2.1}$ 1.3 and $J_{2.3}$ 3.5 Hz), characteristic of a nitrobenzoyl group at O(2) of the rhamnose ring.

Glucosylation of the equatorial 3-hydroxy-group of (7) with acetobromoglucose gave, after chromatography, the trisaccharide (8) in 70% yield, m.p. 85-87 °C, [a]²⁴_D - 28.7° from which the deblocked trisaccharide methyl glycoside (9) was readily obtained in 95% yield, $\delta_{\rm H}$ (D₂O) 1.57 (d, J 5.7 Hz, CMe), 3.49(s, OMe), 4.89, 4.91, and 5.03 (3d, $J_{1.2}$ 7.3, 1.9, and 7.8 Hz, respectively, for the three anomeric protons); δ_c 17.8, 55.6, 101.3, 103.4, and 104.4 p.p.m.

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