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Preliminary communication

Synthesis of specifically fluorinated methyl β-glycosides of (1→6)-β-D-galacto-oligosaccharides

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In connection with studies on the modes of binding of monoclonal antibodies that show anti-(1→6)-β-D-galactan specificity, a theory was proposed[1] suggesting that the process might involve hydrogen bonding. That theory was pursued further in an investigation[2] of the interactions of immunoglobulins with some methyl deoxyfluoro-β-D-galactopyranosides. Preliminary results of our studies[3] involving the recently synthesized[4] methyl 3-deoxy-3-fluoro-β-D-galactopyranoside indicated that the replacement of HO-3 in methyl β-D-galactopyranoside by a fluorine atom markedly affects the binding properties of the parent glycoside. In order to obtain ligands that might provide important information about these interactions, we have now undertaken the synthesis of methyl β-glycosides of β-D-(1→6)-galactobiose and of the corresponding D-galactotriose in which HO-3 of the nonreducing end-group is replaced by a fluorine atom.

Stepwise construction of the target oligosaccharides was achieved by using methyl 2,3,4-tri-*O*-acetyl-β-D-galactopyranoside (**1**), m.p. 125–126°, $[\alpha]_D$ +5.2°, as the initial nucleophile, and acetylated α-D-galactosyl bromides **2** and **3** as glycosylating agents*.

When treated** with 2,3,4-tri-*O*-acetyl-6-*O*-(chloroacetyl)-α-D-galactopyranosyl bromide[5] (**2**), compound **1** afforded the disaccharide derivative **4** a (colorless foam, $[\alpha]_D$ −8.1°) in 80% yield. Likewise, reaction of **1** with 2,4,6-tri-*O*-acetyl-3-deoxy-3-fluoro-α-D-galactopyranosyl bromide[4] (**3**) gave, in ~70% yield, the fluorinated disaccharide **5** (m.p. 181–181.5°, $[\alpha]_D$ −1°). Deacetylation of **5** with sodium methoxide in methanol produced the target compound **6** (m.p. 200–201°, $[\alpha]_D$ −18°) in theoretical yield.

The chloroacetyl group in **4** was removed with thiourea[6] in ethanol, to afford the disaccharide nucleophile **7** (colorless foam, $[\alpha]_D$ −3°) in 96% yield. Condensation

*All new compounds gave correct microanalyses; $[\alpha]_D$ values (c ~1) of the intermediates and of the deblocked methyl β-glycosides of oligosaccharides were respectively determined for their chloroform and aqueous solutions.

**Condensation reactions were conducted at room temperature in benzene, in the presence of mercuric cyanide and mercuric bromide, using 1.5–2 molar proportions of the glycosyl halides. Chromatography on columns of Silica Gel 60 gave both α- and β-linked products in the ratio of ~1:10, but only those having a β-linked, terminal galactosyl group are noted in the text. The configuration of the newly formed, inter-sugar linkage was determined by ^{13}C-n.m.r. spectroscopy.

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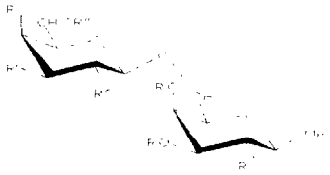

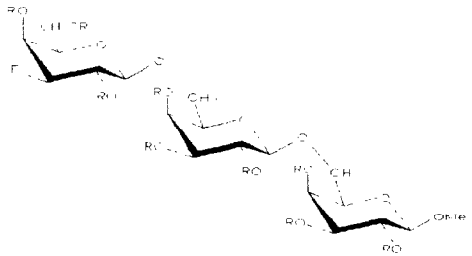

8 R = Ac
9 R = H

of 7 with **3** gave **8** (62%; colorless foam, $[\alpha]_D$ −80.3°), which was deacetylated, as described for the preparation of **6**, to give the fluorinated trisaccharide **9** (colorless foam, $[\alpha]_D$ −14°).

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