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**Preliminary communication**

# Synthesis of monodeoxyfluorinated, mucin-type oligosaccharide fragments*

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In previous publications in this series[2,3], we discussed the use of low-molecular-weight oligosaccharides in the study of various glycosyltransferases. Therein, we employed *N*-acetyl-2′-*O*-methyllactosamine as a specific acceptor for the (1→3)-α-L-fucosyltransferase of human serum, exemplifying the utility of this type of compound[4]. As a further contribution to these studies, we wish to report the preparation of some selectively fluorinated oligosaccharides.

The removal, by fluorination, of an hydroxyl group at a potential site of glycosylation in an oligosaccharide, which normally could act as an acceptor for two different glycosyltransferases, would be expected to limit the action of the appropriate sugar nucleotide to only one glycosyl group. Alternately, such a compound may act as an inhibitor for the particular glycosyltransferase that would have transferred a glycosyl group to the position now occupied by the fluorine atom. Moreover, the similarities in bond length and polarization between the C–F and C–OH groups[5] make this approach particularly attractive. We describe herein the synthesis of some monodeoxyfluorinated, mucin-type fragments, the parent compounds of which were previously described[6–8]. In all of these syntheses, the appropriately protected 4,6-diol was treated with diethylaminosulfur trifluoride ($Et_2NSF_3$) to afford a corresponding derivative bearing a fluorine atom.

In a typical experiment, a solution of benzyl 2-acetamido-2-deoxy-3-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-α-D-galactopyranoside[6] (**1**; 0.78 mmol) in dry Diglyme (6 mL) was added, in small portions, to a cold (−20°, bath) and stirred solution of $Et_2NSF_3$ (3.12 mmol) in Diglyme (6 mL), and stirring was continued for 20 min at −20°. The mixture was allowed to gradually warm to room

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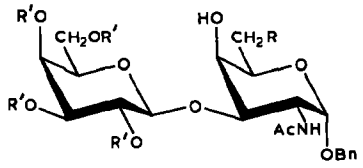

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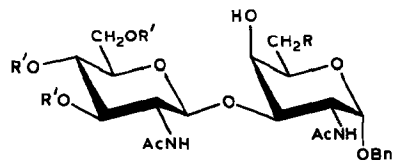
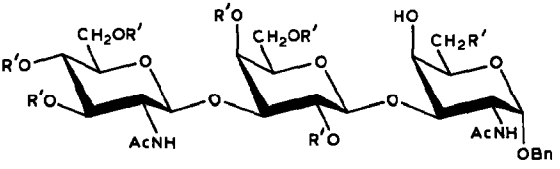
2 R = F, R′ = Ac
3 R = F, R′ = H



4 R = OH, R′ = Ac
5 R = F, R′ = Ac
6 R = F, R′ = H



7 R = OH, R′ = Ac
8 R = F, R′ = Ac
9 R = F, R′ = H

temperature, and stirring was continued for an additional 1.5 h. After being processed in the usual manner[9], the crude product was purified by column chromatography (8:1 chloroform–methanol) to afford, in 60% yield, **2**, m.p. 181–183°, $[\alpha]_D^{25}$ +71° (chloroform); $^{19}$F-n.m.r. ($CDCl_3$): $\phi$ −224.8 (sext., $J$ 48.7 and 14.7 Hz); $^1$H-n.m.r. ($CDCl_3$): $\delta$ 7.20 (m, 5 H, arom.) and 2.20–1.80 (s, 15 H, 4 OAc and NAc). *O*-Deacetylation of **2** in 2:1:1 (v/v) methanol–triethylamine–water furnished, in 85% yield, amorphous benzyl 2-acetamido-2,6-dideoxy-6-fluoro-3-*O*-β-D-galactopyranosyl-α-D-galactopyranoside (**3**), $[\alpha]_D^{25}$ +71.5° (dimethyl sulfoxide); $^{19}$F-n.m.r.: $\phi$ −227.2 ($J$ 47.4 and 16.2 Hz); in the $^{13}$C-n.m.r. spectrum ($Me_2SO$-$d_6$), the signal for C-6 was shifted downfield ($\delta$ 85.18) by comparison to that ($\delta$ 60.54) of the parent disaccharide[6], as would be expected by fluorination[10]. The signal for C′-6 ($\delta$ 60.61) however, remained close to that ($\delta$ 60.34) of its counterpart in the spectrum of the parent disaccharide.

On similar reaction with $Et_2NSF_3$, benzyl 2-acetamido-3-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-2-deoxy-α-D-galactopyranoside[7] (**4**), afforded, after column-chromatographic purification (2:1 chloroform–acetone), amorphous disaccharide **5** in 36% yield, $[\alpha]_D^{25}$ +71° (chloroform); $^1$H-n.m.r. ($CDCl_3$): $\delta$ 7.30 (m, 5 H, arom.) and 2.10–1.80 (s, 15 H, 3 OAc and 2 NAc). *O*-Deacetylation of **5** in methanol containing a catalytic amount of sodium methoxide gave crystalline benzyl 2-acetamido-3-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-2,6-dideoxy-6-fluoro-α-D-galactopyranoside (**6**; 75%), m.p. >300°, $[\alpha]_D^{25}$ +85° (dimethyl sulfoxide); $^{19}$F-n.m.r.: $\phi$ −233.5 ($J$ 47.8 and 26.2 Hz).

A similar reaction of $Et_2NSF_3$ with trisaccharide[8] **7**, followed by purification of the product by preparative t.l.c. (1:1 chloroform–acetone), afforded in 52% yield crystalline **8**, m.p. 259–261° (acetone–ether), $[\alpha]_D^{25}$ +73° (chloroform); $^1$H-n.m.r. ($CDCl_3$): $\delta$ 7.30 (m, 5 H, arom.), and 2.20–1.80 (s, 24 H, 6 OAc and 2 NAc). *O*-Deacetylation of **8** with methanol–triethylamine–water gave the desired compound **9** in 78% yield, m.p. >300°, $[\alpha]_D^{25}$ +79° (dimethyl sulfoxide); $^{19}$F-n.m.r.: $\phi$ −233.8 ($J$ 47.8 and 25.9 Hz).

All compounds reported gave satisfactory data for elemental analyses. The $^{19}$F-n.m.r. spectra for compounds **3**, **6**, and **9** were recorded for solutions in di($^2$H)methyl sulfoxide and trichlorofluoromethane was used as the internal standard for all $^{19}$F-n.m.r.-spectra.

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