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Preliminary communication

Synthesis of a protected trihexosyl unit: a glycosyl acceptor corresponding to the core structure of the N-linked glycan of a glycoprotein*

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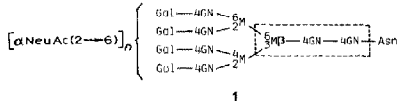
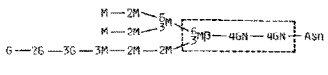
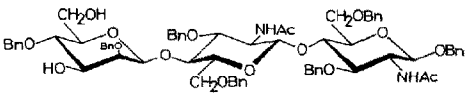
As part of a project on the synthesis of the glycans of such glycoproteins[2] as **1** and **2**, we describe here a synthesis of the trihexosyl glycosyl-acceptor **3**, which may be regarded as a common, synthetic intermediate for both **1** and **2**.



1



2



3

Bn = $PhCH_2$

(Tributylstannyl)ation[3] of **4**, $[\alpha]_D$ +40.3°, to **5**, and alkylation[4] of **5** with benzyl bromide for 2 days at 90° in the presence of tetrabutylammonium bromide[5] gave a 76% yield of the dibenzyl ether **6**, $[\alpha]_D$ +33.8°***. Acetylation of **6** to give **7**, $[\alpha]_D$ +64.4°, and deallylation of **7** with $PdCl_2$ in[6,7] aq. AcOH–AcONa for 2 h at 70°, afforded **8**,

*Synthetic Studies on Cell Surface Glycans, Part XXIV. For Part XXIII, see ref. 1.
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***Values of $[\alpha]_D$ were measured for $CHCl_3$ solutions at 25°, unless noted otherwise. Compounds with $[\alpha]_D$ recorded gave satisfactory data for elemental analyses.

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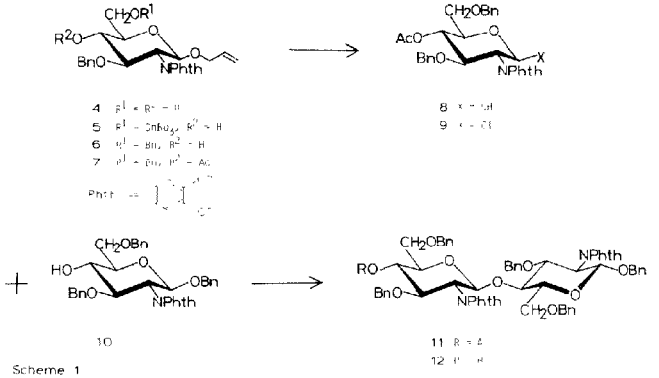
$[\alpha]_D$ +82.6° (R_F 0.35 in 2:1 toluene–EtOAc) in 83% yield from **6**. Treatment of **8** with $SOCl_2$ in the presence of a catalytic amount[8] of $HCONMe_2$ (DMF) in CH_2Cl_2 for 2 h at 20° gave a quantiative yield of **9**, R_F 0.58 in 5:1 toluene–EtOAc. Glycosidation[9] of **10** in the presence of $AgOSO_2CF_3$ and powdered molecular sieves 4A for 16 h at 20° afforded a 62% yield of the chitobiosyl derivative **11**, $[\alpha]_D$ +15.9°, R_F 0.50 in 5:1 toluene–EtOAc. Deacetylation of **11** in boiling HCl–H_2O–acetone[10] for 4 days under reflux gave an 82% yield of **12**, $[\alpha]_D$ −7.8°; R_F 0.50 in 3:1 toluene–EtOAc; δ_C: 96.88 (C-1a and C-1b, $^1J_{CH}$ 164.8 Hz).



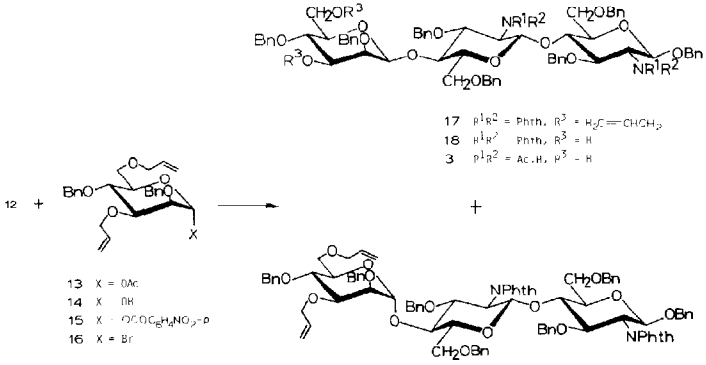
Scheme 1

Saponification of the acetate[7] **13** in 3:3:4:1 Et_3N–THF–MeOH–H_2O for 16 h at 20° gave hemiacetal **14** ($[\alpha]_D$ +31.0°, R_F 0.45 in 2:1 toluene–EtOAc) in 85% yield; this was acylated with *p*-nitrobenzoyl chloride to give an 82% yield of **15** ($[\alpha]_D$ +52.5°, R_F 0.52 in 10:1 toluene–EtOAc) together with a 17% yield of the β anomer of **15**, R_F 0.43. Treatment of **15** with HBr in CH_2Cl_2 for 20 min at 0° gave the unstable bromide **16**, R_F 0.64 in 10:1 toluene–EtOAc.

Glycosidation of the dihexosyl acceptor **12** with **16** in the presence of Ag silicate[11] and powdered molecular sieves 4A in CH_2Cl_2 afforded a 40% yield of the β anomer **17**; $[\alpha]_D$ −2.1°; R_F 0.47 in 5:1 toluene–EtOAc; δ_C: 97.03 (C-1a and C-1b, $^1J_{CH}$ 164.8 Hz), 101.47 (C-1c, $^1J_{CH}$ 156.3 Hz), and a 36% yield of the α anomer **19**; $[\alpha]_D$ +15.6°; R_F 0.53 in 5:1 toluene–EtOAc; δ_C: 96.74 (C-1a or C-1b, $^1J_{CH}$ 164.8 Hz), 97.13 (C-1a or C-1b, $^1J_{CH}$ 164.8 Hz), and 100.11 (C-1c, $^1J_{CH}$ 169.7 Hz).

Deallylation of **17** with $PdCl_2$ in aq AcOH–AcONa for 1 h at 70° afforded a 58% yield of diol **18** ($[\alpha]_D$ −4.5°, R_F 0.55 in 2:1 toluene–EtOAc) which was treated with (*1*) 1:1 $BuNH_2$–MeOH (ref. 12) for 8 days at 90°, (*2*) Ac_2O–pyridine, and (*3*) NaOMe–MeOH, to give a 90% yield of the target structure **3**, $[\alpha]_D$ −38.7°, R_F 0.47 in 3:1 CH_2Cl_2–acetone.

In conclusion, the properly protected, trihexosyl acceptor **3** was synthesized by employing regioselectively benzylated, monohexosyl synthons.



Scheme 2 19

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