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Preliminary communication

Synthesis of a nonahexosyl unit of a complex type of glycan chain of a glycoprotein*

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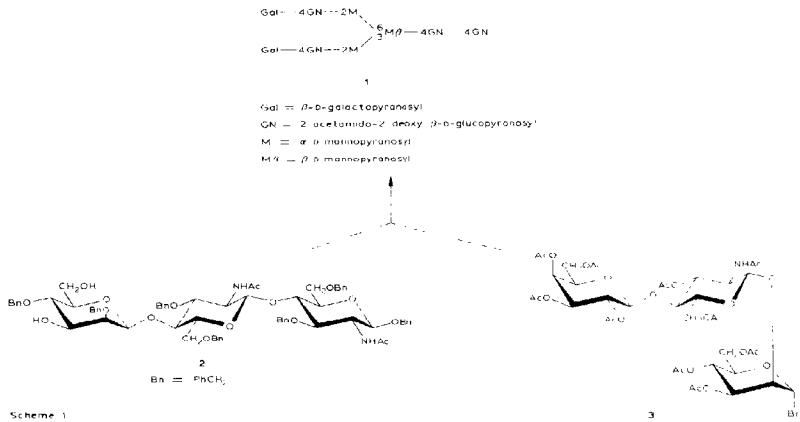
As part of a project on the synthesis[1] of a complex type of glycan of a glycoprotein[2], we had reported a synthesis of a hexasaccharide unit[3]. Recently, Paulsen and his co-workers[4] described an elegant synthesis of the octahexosyl unit of a complex type of glycan. We now report a synthesis of the nonahexosyl unit **1** with high regio- and stereocontrol (see Scheme 1).



Scheme 1

As the key intermediate, the trihexosyl acceptor **2**, is now available[1], we designed trihexosyl donor **3** as another key intermediate for the synthesis of **1**. Glycosidation of **4** (ref. 5) with the lactosaminyl donor **5** (ref. 6) in the presence of $AgOSO_2CF_3$–powdered

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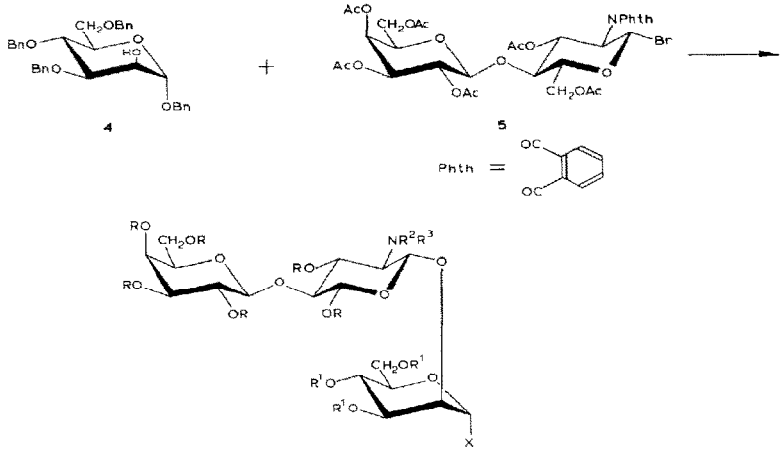
molecular sieves 4A in $Cl(CH_2)_2Cl$ afforded a 94% yield of **6**. $[\alpha]_D$ +4.2°***; R_F 0.39 in 2:1 toluene–EtOAc. Successive treatment of **6** with (*i*) a catalytic amount of sodium methoxide in methanol, (*ii*) reflux[7] in MeOH–$BuNH_2$ for 2 days, and (*iii*) Ac_2O–pyridine, afforded, *via* **7** and **8**, a 95% yield of **9**, $[\alpha]_D$ +6.5°; R_F 0.54 in 5:1 CH_2Cl_2–acetone. Catalytic hydrogenolysis of **9** in the presence of 10% Pd- C in AcOH at 80°, to give **10**, and acetylation of **10**, afforded an 84% yield of **11**, $[\alpha]_D$ −9.6°; R_F 0.41 in 3:1 CH_2Cl_2–acetone, δ_C: 100.98 (C-1c, $^1J_{CH}$ 161.1 Hz), 100.30 (C-1b, $^1J_{CH}$ 158.7 Hz), and 90.99 (C-1a, $^1J_{CH}$ 175.8 Hz). Treatment of **11** with HBr in AcOH–CH_2Cl_2 gave a quantitative yield of **3**; R_F 0.51 in 3:1 CH_2Cl_2–acetone; see Scheme 2.

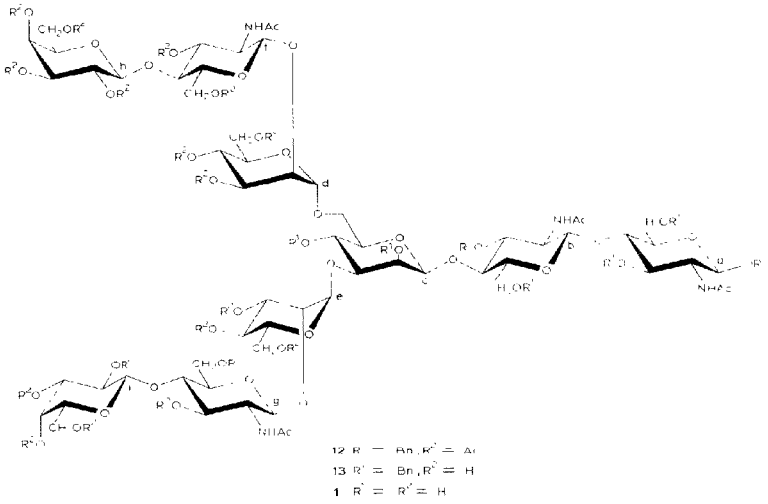


6 R = Ac, R^1 = Bn, R^2, R^3 = Phth, X = OBn
7 R = H, R^1 = Bn, R^2, R^3 = Phth, X = OBn
8 R = H, R^1 = Bn, R^2, R^3 = H_2, X = OBn
9 R = Ac, R^1 = Bn, R^2, R^3 = H, Ac, X = OBn
10 R = Ac, R^1 = H, R^2, R^3 = H, Ac, X = OH
11 R = R^1 = Ac, R^2, R^3 = H, Ac, X = OAc
3 R = R^1 = Ac, R^2, R^3 = H, Ac, X = Br

Scheme 2

Glycosidation of **2** with 6 molar equivalents of **3** in the presence of $AgOSO_2CF_3$–powdered molecular sieves 4A in 3:1 $Cl(CH_2)_2Cl$–toluene, and gel chromatography of the product on Toyopearl HW 40 in 1:1 $CHCl_3$–MeOH, afforded a 59% yield of the protected

***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.



12 R = Bn, R' = Ac
13 R = Bn, R' = H
1 R = R' = H

nonasaccharide **12**; R_F 0.13 in 2:1 CH_2Cl_2–acetone. Deacetylation of **12** with NaOMe–MeOH to give **13**, and hydrogenolysis of **13** with 10% Pd–C in AcOH at 80° afforded the target nonasaccharide **1**; $[\alpha]_D$ +1.8° (*c* 0.11, H_2O); R_F 0.54 in 10:1:1 MeOH–AcOH–H_2O. The stereochemistry at the two anomeric carbon atoms, C-1d and C-1e, introduced by the last glycosidation step was each assigned to be α-D by 400-MHz. ^{1}H-n.m.r. data of **1** (for a solution in D_2O at 60°); the spectrum contained two singlets, at δ 5.139 and 4.926, for H-1e and H-1d, respectively, in addition to a singlet for H-1c at δ 4.766, in good agreement with the data for both the natural[8] and synthetic[3,9] sample of similar structures. Other aspects of the ^{1}H-n.m.r. spectrum of **1** were also in good agreement with the target structure **1**, showing signals at δ 5.201 (d, *J* 3.0 Hz, for H-1aα), 4.713 (d, *J* 7.8 Hz, H-1aβ), 4.625 (d, *J* 8.0 Hz, H-1b), 4.592 (d, *J* 8.8 Hz, H-1f and H-1g), 4.478 (d, *J* 7.6 Hz, H-1h and H-1i), 4.263 (bs, H-2c), 4.200 (bs, H-2e), and 4.120 (bs, H-2d).

In conclusion, a regio- and stereo-controlled synthesis of the nonahexosyl unit **1** was achieved by employing the two key intermediates **2** and **3**.

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