Stereoselective synthesis of α-*O*-fucosylated serine, threonine, tyrosine and saccharides

Hari Babu Mereyala,* Srinivas Reddy Gurrala and Rajendrakumar Reddy Gadikota

Organic Division III, Indian Institute of Chemical Technology, Hyderabad 500 007, India

Stereoselective fucosylation of Boc-Ser/Thr/Tyr-OMe 2–4 and several saccharide alcohols 5–7 by coupling with 2-pyridyl tri-*O*-benzyl-1-thio-β-L-fucosyl donor 1b under iodomethane activation procedure results in the formation of α-linked fucosylated amino acid methyl ester building blocks 8–10 and α-linked fucosyl saccharides 11–13, respectively.

Introduction

A large number of proteins found in nature are N- and/or O-glycosylated, and the structural diversity of the oligosaccharides and the variety of linkages between sugar and protein moieties is enormous.[1,2] Glycosylation of a protein is known to influence the properties of the protein in many ways.[2] Glycosylation provides protection against proteolysis, influences uptake of serum proteins of the liver, effects intramolecular transport of enzymes to lysosomes, determines human blood groups and regulates leukocyte trafficking to sites of inflammation.[3,4] Tumour cells show aberrant glycosylation of glycosphingolipids and glycoproteins.[5] A novel type of O-glycosylation where Xyl-Glc and Xyl-Xyl-Glc have been found attached to serine residues has been reported by several authors investigating the N-terminal Epidermal Growth Factor (EGF).[6] More recently, L-fucose has been found α-glycosidically linked to serine or threonine residues within the peptide motif Cys-X-X-Gly-Gly-Thr/Ser-Cys.[6] Harris *et al.* have identified the tetrasaccharide $NeuAc_{\alpha}(2\rightarrow6)Gal\beta(1\rightarrow4)GlcNAc\beta(1\rightarrow3)Fuc\alpha$ 1→O-linked to serine 61 of Human Factor IX.[7] Furthermore, L-fucose is known to be an important residue of branched oligosaccharides in glycoconjugates that bind to selectins.[8] These interesting biological properties have led to the synthesis of fucosylated peptides[9] and saccharides[10] by both enzymic[11] and chemical methods[12] by organic chemists in order to facilitate study of the biological functions of peptides which are not glycosylated in nature. Synthetic fucosylated glycopeptides might be potential mimetics of selectin-binding oligosaccharides. Chemical synthesis of building blocks required for glycopeptide[9,12] and fucosyl saccharide synthesis[10] has been achieved by use of fluoro, chloro, bromo, acetoxy, acetamidate and alkylthio fucosyl donors.[9,10] Proven success[13,14] in recent years in the development of the iodomethane activation procedure of 2-pyridylthio glycosides for the stereoselective synthesis of α-linked saccharides has prompted us to look into its applicability for the synthesis of α-fucosylated amino acids and saccharides.

Results and discussion

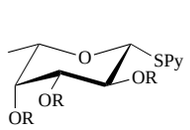
2,3,4-Tri-*O*-acetyl-α-L-fucopyranosyl bromide[15] was treated with 2-mercaptopyridine and K_2CO_3 in acetone–toluene (3:2) at room temperature for 4 h to obtain 2-pyridyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside **1a** as a crystalline compound in 79% yield, mp 120–122 °C; $[\alpha]_D$ −36.0 (*c* 1.0, $CHCl_3$).† Formation of compound **1a** was evident from the ^1H NMR spectrum by the appearance of the anomeric proton signal at δ 5.8 (d, $J_{1,2}$ 10 Hz) and aromatic protons (4 H) between δ 6.90–8.50. Compound **1a** on further reaction with a catalytic amount of sodium methoxide in methanol for 6 h at room temp. resulted in the formation of 2-pyridyl 1-thio-β-L-fucopyranoside (**l**; R = H) which was allowed to react with NaH–benzyl bromide (BnBr)–dimethylformamide (DMF) at 0 °C for 3 h to obtain 2-pyridyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside **1b** as a crystalline solid, mp 134–136 °C, in 76% yield. Fucosylation of *N*-Boc-serine methyl ester **2**‡ was carried out by reaction with compound **1b** in the presence of iodomethane as activator in dichloromethane at 50 °C for 62 h to afford, in high stereocontrol, the α-linked *N*-Boc-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-L-serine methyl ester **8** in 79% yield, as a syrup, $[\alpha]_D$ −31 (*c* 1.0, $CHCl_3$). The presence of an α-glycosidic linkage in compound **8** was confirmed by the small coupling constant $J_{1',2'}$ 3.8 Hz in the ^1H NMR spectrum and from the appearance of C-1′ at δ_C 94.53 in the ^{13}C NMR spectrum. Likewise, *N*-Boc-threonine methyl ester **3** and *N*-Boc-tyrosine methyl ester **4** were treated with compound **1b** to obtain *N*-Boc-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-L-threonine methyl ester **9** and *N*-Boc-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopranosyl)-L-tyrosine methyl ester **10**, respectively, in good yields (73–76%) and which were characterised by their respective ^1H and ^{13}C NMR spectra.

Coupling of the glycosyl acceptors 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside **5**, 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **6** and benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranose **7** with the 2-pyridylthio donor **1b** in dichloromethane containing iodomethane at 50 °C for 48–64 h gave their respective α-linked disaccharides 1,2:3,4-di-*O*-isopropylidene-6-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-α-D-galactopyranose **11** as a crystalline solid, mp 115–116 °C (lit.,[10] 116–117 °C), $[\alpha]_D$ −118 (*c* 2.0, CH_2Cl_2) {lit.,[10] $[\alpha]_D$ −117 (*c* 2.0, CH_2Cl_2)}, 1,2:5,6-di-*O*-isopropylidene-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-α-D-glucofuranose **12** as a syrup, characterised by comparison of the spectral data with those reported in the literature,[10] and benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-α-D-glucopyranoside **13** as a crystalline compound (mp 183 °C), characterised from the ^1H NMR spectral data: appearance of 1′-H signal at δ 5.21 as a doublet with a small coupling $J_{1',2'}$ of 3.5 Hz, and from the ^{13}C NMR spectrum: appearance of C-1,1′ signals at δ_C 97.2 and 99.4.

In conclusion, yet another highly stereoselective α-fucosylation of amino acid esters and several sugar alcohols has been achieved by iodomethane activation of perbenzylated 2-pyridyl thio-L-fucosyl donors.

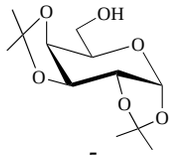
† Units for $[\alpha]_D$-values are 10^{-1} deg cm^2 g^{-1}.

‡ Boc = *tert*-butoxycarbonyl.

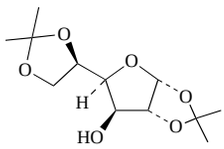


1a R = Ac
1b R = Bn

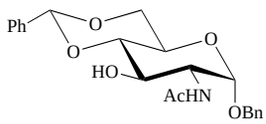
2 Boc-Ser-OMe
3 Boc-Thr-OMe
4 Boc-Tyr-OMe



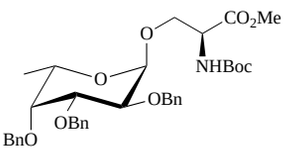
5



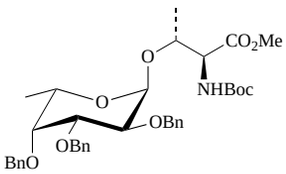
6



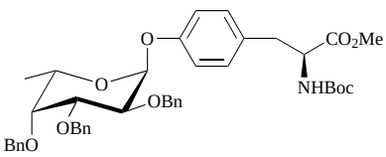
7



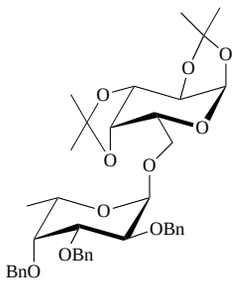
8



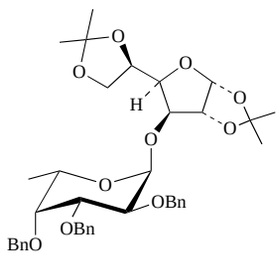
9



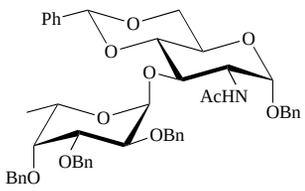
10



11



12



13

Experimental

^{1}H NMR spectra were measured with a Varian Gemini (200 and 400 MHz) spectrometer, with tetramethylsilane as internal standard for solutions in deuteriochloroform. *J*-Values are given in Hz. ^{13}C NMR spectra were taken with a Varian Gemini (50 MHz) spectrometer with $CDCl_3$ as internal standard (δ_C 77.0) for solutions in deuteriochloroform. Optical rotations were measured with a JASCO DIP-370 instrument. Organic solutions were dried over anhydrous Na_2SO_4 and concentrated below 40 °C *in vacuo*.

2-Pyridyl 2,3,4-tri-*O*-acetyl-1-thio-β-L-fucopyranoside 1a

To a solution of 2-mercaptopyridine (0.6 g, 5.4 mmol) in dry acetone (15 cm^3) was added anhydrous K_2CO_3 (0.75 g, 5.4 mmol) and the mixture was stirred at room temperature for 30 min. α-Acetobromofucose[15] (1.6 g, 4.5 mmol) as a solution in dry toluene (10 cm^3) was added to the above reaction mixture and the mixture was stirred for 4 h at room temp. The reaction mixture was diluted with toluene (20 cm^3) and filtered, and the organic phase was washed successively with water and saturated aq. $NaHCO_3$, dried (anhydrous Na_2SO_4), and concentrated to a residue, which was recrystallised from dichloromethane–hexane to obtain the title compound **1a** (1.3 g, 79%) as needles, mp 120–122 °C (Found: C, 52.32; H, 5.48. $C_{17}H_{21}NO_7S$ requires C, 53.26; H, 5.52%); $[\alpha]_D$ −36.0 (*c* 1.0, $CHCl_3$); δ_H(200 MHz; $CDCl_3$) 1.20 (3 H, d, *J* 6.3, 6-H$_3$), 2.0, 2.1 and 2.2 (9 H, 3 s, OAc), 3.95 (1 H, m, 5-H), 5.10–5.40 (3 H, m, 2-, 3- and 4-H), 5.80 (1 H, d, *J* 10, 1-H) and 6.90–8.50 (4 H, m, ArH).

2-Pyridyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside 1b

Compound **1a** (1.3 g, 3.3 mmol) was deacetylated by reaction with cat. NaOMe–MeOH at room temp. for 6 h, the product was neutralised with carbon dioxide, and the solvent was removed to obtain 2-pyridyl 1-thio-α-L-fucopyranoside (0.8 g, 92.6%), which was dried at 60 °C for 3 h, dissolved in DMF (3 cm^3), and sodium hydride (0.33 g, 14 mmol) was added followed by benzyl bromide (1.36 cm^3, 11.2 mmol) at 0 °C and the mixture was stirred for 3 h. When TLC indicated completion of the reaction, excess of NaH was decomposed by addition of methanol (1 cm^3), and the mixture was diluted with water (100 cm^3) and extracted into dichloromethane (2 × 50 cm^3). The organic phase was washed with water, dried, and concentrated to yield a syrup, which was purified by filtration on a bed of silica gel [60–120 mesh; hexane–ethyl acetate (7:1)] to obtain the *title compound* **1b** (1.2 g, 76%) as yellow needles, mp 134–136 °C (Found: C, 72.79; H, 6.21. $C_{32}H_{33}NO_4S$ requires C, 72.84; H, 6.30%); $[\alpha]_D$ −15 (*c* 1.0, $CHCl_3$); δ_H(200 MHz; $CDCl_3$) 1.25 (3 H, d, *J* 6.3, 6-H$_3$), 3.55–5.15 (10 H, m, 2–5-H, 3 × OC*H*$_2$Ph), 5.39 (1 H, d, *J* 10.0, 1-H) and 6.90–8.50 (19 H, m, ArH).

***N*-Boc-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-L-serine methyl ester 8**

A mixture of compound **1b** (0.2 g, 0.38 mmol), *N*-(*tert*-butoxycarbonyl)-L-serine methyl ester **2** (0.08 g, 0.38 mmol) and powdered 4 Å molecular sieves (20 mg) in dry dichloromethane (5 cm^3) containing 5% iodomethane was heated to 50 °C for 62 h. Reaction was monitored by TLC and when complete the reaction mixture was filtered on Celite, the filter was washed with ethyl acetate (15 cm^3) and the combined filtrate and washings were concentrated to obtain a residue, which was chromatographed [SiO_2; hexane–ethyl acetate (9:1)] to obtain the *title compound* **8** (0.19 g, 79%) as a syrup (Found: C, 67.92; H, 7.04. $C_{36}H_{45}NO_9$ requires C, 68.01; H, 7.14%); $[\alpha]_D$ −31 (*c* 1.0, $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.05 (3 H, d, *J* 6.4, 6′-H$_3$), 1.45 (9 H, s, CMe$_3$), 3.45–4.80 (12 H, m, 2-H, 3-H$_2$, 2′–5′-H and 2.5 × OC*H*$_2$Ph), 3.69 (3 H, s, OCH$_3$), 4.82 (1 H, d, $J_{1',2'}$ 3.8, 1′-H), 4.87 (1 H, d, J_{gem} 11.6, OC*H*$_2$Ph), 5.81 (1 H, d, *J* 9.0, NH) and 7.20–7.45 (15 H, m, ArH); δ_C(50 MHz; $CDCl_3$) 16.52 (C-6′), 28.35 (C*Me*$_3$), 52.14 (OCH$_3$), 54.95 (C-2), 68.90 (C-3), 72.30, 72.98, 73.80 and 74.82 (C-5′, 3 × O*C*H$_2$Ph), 76.02 (C-2′), 77.45 (C-3′), 79.10 (C-4′), 94.53 (C-1′), 127.3–138.52 (aromatic), 156.34 (C=O, carbamate) and 171.85 (C=O, ester).

***N*-Boc-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-L-threonine methyl ester 9**

A mixture of compound **1b** (0.3 g, 0.57 mmol), *N*-(*tert*-butoxycarbonyl)-L-threonine methyl ester **3** (0.12 g, 0.57 mmol) and powdered 4 Å molecular sieves (15 mg) in dry dichloromethane (10 cm^3) containing 5% iodomethane was heated to 50 °C for 60 h. When TLC indicated completion of the reaction, the mixture was filtered on Celite, the filter was washed with ethyl acetate (15 cm^3) and the combined filtrate and washings were concentrated to obtain a residue, which was chromatographed [SiO_2; hexane–ethyl acetate (9:1)] to obtain the *title compound* **9** (0.18 g, 73%) as a syrup (Found: C, 68.29; H, 7.17. $C_{37}H_{47}NO_9$ requires C, 68.39; H, 7.29%); $[\alpha]_D$ −42 (*c* 1.0, $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.05 (3 H, d, *J* 6.3, 6′-H$_3$), 1.19 (3 H, d, *J* 6.7, 4-CH$_3$), 1.46 (9 H, s, CMe$_3$), 3.40–4.80 (11 H, m, 2-

and 3-H, 2′–5′-H and 2.5 × OCH_2Ph), 3.19 (3 H, s, OCH_3), 4.81 (1 H, d, $J_{1',2'}$ 3.8, 1′-H), 4.85 (1 H, d, J_{gem} 12.0, OCH_2Ph), 5.35 (1 H, d, *J* 9.6, NH) and 7.2–7.45 (15 H, m, ArH); δ_C(50 MHz; $CDCl_3$) 15.83 (C-4), 16.58 (C-6′), 28.32 (CMe_3), 52.11 (OCH_3), 58.32 (C-2), 66.70 (C-3), 72.11 (C-5′), 74.76, 73.20, 72.97 (3 × OCH_2Ph), 76.0 (C-2′), 77.43 (C-3′), 78.90 (C-4′), 94.84 (C-1′), 127.4–138.52 (arom.), 156.36 (C=O, carbamate) and 171.54 (C=O, ester).

N-Boc-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-L-tyrosine methyl ester 10

A mixture of compound **1b** (0.2 g, 0.38 mmol), *N*-(*tert*-butoxycarbonyl)-L-tyrosine methyl ester **4** (0.1 g, 0.38 mmol) and powdered 4 Å molecular sieves (15 mg) in dry dichloromethane (5 cm^3) containing 5% iodomethane was heated to 50 °C for 78 h. When TLC indicated completion of the reaction, the mixture was filtered on Celite, the filter was washed with ethyl acetate (15 cm^3), the combined filtrate and washings were concentrated to obtain a residue, which was chromatographed [SiO_2; hexane–ethyl acetate (9:1)] to obtain the *title compound* **10** (0.2 g, 76%) as a crystalline solid, mp 106–107 °C (Found: C, 71.02; H, 6.77. $C_{42}H_{49}NO_9$ requires C, 71.16; H, 6.82%); $[\alpha]_D$ −44 (*c* 1.0, $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.05 (3 H, d, *J* 6.7, 6′-H_3), 1.41 (9 H, s, CMe_3), 3.02 (2 H, m, 3-H_2), 3.71 (3 H, s, OCH_3), 3.94–5.01 (12 H, m, NH, 2-H, 2′–5′-H and 3 × OCH_2Ph), 5.39 (1 H, d, *J* 3.6, 1′-H) and 6.97–7.41 (19 H, m, ArH); δ_C(50 MHz; $CDCl_3$) 16.54 (C-6′), 28.23 (*C*Me_3), 37.49 (C-3), 52.13 (OMe), 67.16 (C-2), 73.26, 74.90, 76.08, 77.62 and 79.18 (C-2′–5′, 3 × OCH_2Ph), 96.40 (C-1′), 116.92 (C-6, -8), 127.4–138.8 (aromatic), 156.36 (C=O, carbamate) and 172.30 (C=O, ester).

1,2:3,4-Di-*O*-isopropylidene-6-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-α-D-galactopyranose 11

A mixture of compound **1b** (0.3 g, 0.57 mmol), 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose **5** (0.15 g, 0.57 mmol) and powdered 4 Å molecular sieves (20 mg) in dry dichloromethane (15 cm^3) containing 5% iodomethane was heated to 50 °C for 48 h. Reaction was monitored by TLC and when complete the reaction mixture was filtered on Celite, the filter was washed with ethyl acetate (15 cm^3), and the combined filtrate and washings were concentrated to obtain a residue, which was chromatographed [SiO_2; hexane–ethyl acetate (4:1)] to obtain the title disaccharide **11** (0.3 g, 77%) as a crystalline solid, mp 115–116 °C (lit.,[10] 116–117 °C) (Found: C, 69.08; H, 7.05. $C_{39}H_{48}O_{10}$ requires C, 69.21; H, 7.15%); $[\alpha]_D$ −118 (*c* 2.0, CH_2Cl_2) [lit.,[10] −117 (*c* 2.0, CH_2Cl_2)]; δ_H(400 MHz; $CDCl_3$) 1.15 (3 H, d, *J* 6.5, 6′-H_3), 1.29, 1.32, 1.42 and 1.5 (12 H, 4 s, 2 × $OCMe_2$), 3.5–5.0 (17 H, m, 2–5-H, 6-H_2, 1′–5′-H and 3 × OCH_2Ph), 5.51 (1 H, d, *J* 5.0, 1-H) and 7.2–7.45 (15 H, m, ArH); δ_C(50 MHz; $CDCl_3$) 16.6 (C-6′), 24.4, 24.8, 25.9 and 26.0 (4 × CH_3), 65.2, 66.3, 70.4, 70.7, 72.7, 73.1, 74.6, 76.2, 76.3 and 79.2 (C-2–6, C-2′–5′, 3 × O*C*H_2Ph), 96.1 (C-1′), 97.2 (C-1), 108.3 and 108.9 (2 × O*C*Me_2) and 127.0–138.0 (aromatic).

1,2:5,6-Di-*O*-iospropylidene-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-α-D-glucofuranose 12

A mixture of compound **1b** (0.25 g, 0.47 mmol), 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose **6** (0.13 g, 0.47 mmol) and powdered 4 Å molecular sieves (20 mg) in dry dichloromethane (15 cm^3) containing 5% iodomethane was heated to 50 °C for 48 h. Reaction was monitored by TLC and when complete the reaction mixture was filtered on Celite, the filter was washed with ethyl acetate (10 cm^3), and the combined filtrate and washings were concentrated to obtain a residue, which was chromatographed [SiO_2; hexane–ethyl acetate (5:1)] to obtain the title disaccharide **12** (0.27 g, 85%) as a syrup (Found: C, 69.12; H, 7.04. Calc. for $C_{39}H_{48}O_{10}$: C, 69.21; H, 7.15%); $[\alpha]_D$ −102 (*c* 2.0, $CHCl_3$) [lit.,[10] −98 (*c* 2.0, $CHCl_3$)]; δ_H(400 MHz; $CDCl_3$) 1.10 (3 H, d, *J* 6.0, 6′-H_3), 1.22, 1.25, 1.36 and 1.46 (12 H, 4 s, 2 × $OCMe_2$), 3.5–5.0 (17 H, m, 2–5-H, 6-H_2, 1′–5′-H and 3 × OCH_2Ph), 5.80 (1 H, d, *J* 4.6, 1-H) and 7.2–7.45 (15 H, m, ArH); δ_C(50 MHz; $CDCl_3$) 16.8 (C-6′), 25.6, 26.5, 26.8 and 27.0 (4 × CH_3), 67.2, 68.1, 72.4, 73.3, 74.0, 75.1, 76.7, 78.1, 79.5, 81.4 and 82.5 (C-2–6, C-2′–5′, 3 × O*C*H_2Ph), 96.2 (C-1′), 105.6 (C-1), 109.3 and 112.1 (2 × O*C*Me_2) and 127–139 (aromatic).

Benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-α-D-glucopyranoside 13

A mixture of compound **1b** (0.155 g, 0.29 mmol), benzyl 2-acetamido-4,6-*O*-benzylidene-2-deoxy-α-D-glucopyranoside **7** (0.118 g, 0.29 mmol) and powdered 4 Å molecular sieves (10 mg) in dry dichloromethane (10 cm^3) containing 5% iodomethane was heated to 50 °C for 60 h. Reaction was monitored by TLC and when complete the reaction mixture was filtered on Celite, the filter was washed with ethyl acetate (10 cm^3), and the combined washings and filtrate concentrated to obtain a residue, which was chromatographed [SiO_2; hexane–ethyl acetate (3:1)] to obtain the *title disaccharide* **13** (0.18 g, 76%) as a crystalline solid, mp 183–184 °C (Found: C, 73.45; H, 6.62. $C_{49}H_{53}NO_9$ requires C, 73.56; H, 6.67%); $[\alpha]_D$ −30.6 (*c* 1.0, $CHCl_3$); δ_H(400 MHz; $CDCl_3$) 1.07 (3 H, d, *J* 3.67, 6′-H_3), 1.25 [3 H, br s, N=C(OH)CH_3], 3.62–5.0 (18 H, m, 2–5-H, 6-H_2, 2′–5′-H and 4 × OCH_2Ph), 5.19 and 5.21 (2 H, 2 d, *J* 3.12 and 3.57, 1- and 1′-H), 5.59 (1 H, s, O_2C*H*Ph) and 7.2–7.45 (25 H, m, ArH); δ_C(50 MHz; $CDCl_3$) 16.7 (C-6′), 22.4 [N=C(OH)*C*H_3], 54.0, 63.2, 67.6, 68.8, 70.0, 73.1, 74.5, 74.9, 75.8, 77.5, 78.1 and 82.0 (C-2–6, C-2′–5′ and 4 × OCH_2Ph), 97.2 and 99.4 (C-1, -1′), 100.0 (O_2*C*HPh), 125–138 (aromatic) and 170.3 (C=O).

Acknowledgements

S. R. G. and R. R. G. thank University Grants Commission, New Delhi for financial support in the form of a Junior Research Fellowship.

References

1 A. Varki, *Glycobiology*, 1993, **3**, 97.
2 H. Lis and N. Shoron, *Eur. J. Biochem.*, 1993, **218**, 1.
3 J. Kihlberg, J. Ahman, B. Walse, T. Darkenberg, A. Nilsson, C. Soderberg-Ahlm, B. Bengtsson and H. Olsson, *J. Med. Chem.*, 1995, **38**, 161.
4 M. F. Powell, T. Stewart, Jr., L. Otvos, L. Urge, F. C. A. Gaeta, A. Sette, T. Arrhenius, D. Thomson, K. Soda and S. M. Colon, *Pharm. Res.*, 1993, **10**, 1268.
5 S. Hakomori, *Cancer Cells*, 1991, **3**, 461.
6 A. M. Buko, E. J. Kentzer, A. Petros, G. Menon, E. R. P. Zuiderweg and V. K. Sarin, *Proc. Natl. Acad. Sci. USA*, 1991, **88**, 3992; R. J. Harris, C. K. Leonard, A. W. Guzzetta and M. W. Spellman, *Biochemistry*, 1991, **30**, 2311; S. Bjoern, D. C. Foster, L. Thim, F. C. Wiberg, M. Christensen, Y. Komiyama, A. H. Pedersen and W. Kisiel, *J. Biol. Chem.*, 1991, **266**, 11 051; R. J. Harris, V. T. Ling and M. W. Spellman, *J. Biol. Chem.*, 1992, **267**, 5102; H. Nishimura, T. Takao, S. Hase, Y. Shimonishi and S. Iwanaga, *J. Biol. Chem.*, 1992, **267**, 17 520.
7 R. J. Harris, H. Van Halbeck, J. Glushka, L. J. Basa, V. T. Ling, K. J. Smith and M. W. Spellman, *Biochemistry*, 1993, **32**, 6539.
8 C. T. Yuen, A. M. Lawson, W. Chai, M. Larken, M. S. Stoll, A. C. Stuart, F. X. Sullivon, T. J. Ahern and T. Feizi, *Biochemistry*, 1992, **31**, 9126.
9 H. Hietter, M. Schultz and H. Kunz, *Synlett*, 1995, 1219; S. Peters, T. L. Lowary, D. Hindsgaul, M. Meldal and K. Bock, *J. Chem. Soc., Perkin Trans. 1*, 1995, 3017.
10 R. U. Lemieux, K. B. Hendrike, R. V. Stick and K. James, *J. Am. Chem. Soc.*, 1975, **97**, 4056; R. U. Lemieux and H. Driguez, *J. Am. Chem. Soc.*, 1975, **97**, 4063; 4069; J.-R. Pougny, J.-C. Jacfuinet, M. N. D. Duschet, M.-L. Milat and P. Sinay, *J. Am. Chem. Soc.*, 1977, **99**, 6762; S. Sato, Y. Ito, T. Nokada, Y. Nakahara and T. Ogawa, *Carbohydr. Res.*, 1987, **167**, 197; R. R. Schmidt, *Tetrahedron Lett.*, 1991, **32**, 3353; L. Lay, F. Nicotra, L. Panza, G. Russo and E. Adobati, *Helv. Chim. Acta*, 1994, **77**, 509; L. Lay, L. Panza, G. Russo, D. Colombo, F. Ronchetti, E. Adobati and S. Canevari, *Helv. Chim. Acta*, 1995, **78**, 533.
11 C.-H. Wong, D. P. Dumas, Y. Chikawa, K. Koseki, S. J. Danishefsky, B. W. Weston and J. B. Lowe, *J. Am. Chem. Soc.*, 1992, **114**, 7321; H. Kondo, Y. Ichikawa and C.-H. Wong, *J. Am. Chem.*

Soc., 1992, **114**, 8748; J. Eberling, P. Braun, D. Kowalezyk, M. Schultz and H. Kunz, *J. Org. Chem.*, 1996, **61**, 2638.
12 M. Dejter-Juszynski and H. M. Flowers, *Carbohydr. Res.*, 1973, **28**, 61; G. O. Aspinall, D. W. Gammon, R. K. Stood, D. Chattergee, B. Pivivore and P. J. Brennan, *Carbohydr. Res.*, 1992, **237**, 57; H. Kunz and J. Marz, *Synlett*, 1992, 589; 591; A. Lubinean, J. L. Gallic and R. Lemoine, *J. Chem. Soc.*, *Chem. Commun.*, 1993, 1419; H. M. Zuurmond, G. H. Veeneman, G. A. Vander Marl and J. H. Van Boom, *Carbohydr. Res.*, 1993, **241**, 153; A. Lubinean, J. L. Gallic and R. Lemoine, *Bioorg. Med. Chem.*, 1994, **2**, 1143; M. Elofsson, B. Walse and J. Kihlberg, *Tetrahedron*, 1995, **51**, 5043; M. Elofsson, S. Roy, L. A. Salvador and J. Kihlberg, *Tetrahedron Lett.*, 1996, **37**, 7645.
13 B. Klaus and S. Troels, *J. Chem. Soc.*, *Perkin Trans. 1*, 1991, 1181; B. Klaus, S. Troels and R. Susanne, *J. Carbohydr. Chem.*, 1991, **10**, 969; G. V. M. Sharma and R. K. Palakodety, *Carbohydr. Res.*, 1993, **243**, 393.
14 H. B. Mereyala and G. V. Reddy, *Tetrahedron Lett.*, 1989, **30**, 4283; H. B. Mereyala, D. Ravi and V. R. Kulkarni, *Tetrahedron Lett.*, 1989, **30**, 4287; H. B. Mereyala and D. Ravi, *Tetrahedron Lett.*, 1991, **32**, 7317; H. B. Mereyala, and G. V. Reddy, *Tetrahedron*, 1991, **47**, 9721; H. B. Mereyala, V. R. Kulkarni, D. Ravi, G. V. M. Sharma, B. V. Rao and G. V. Reddy, *Tetrahedron*, 1992, **48**, 545; H. B. Mereyala and S. Guntha, *J. Chem. Soc.*, *Perkin Trans. 1*, 1993, 841; *J. Chem. Soc.*, *Chem. Commun.*, 1993, 62; H. B. Mereyala and B. R. Gaddam, *Proc. Indian Acad. Sci.*, *Chem. Sci.*, 1994, **106**, 1225; H. B. Mereyala and S. Guntha, *Tetrahedron*, 1995, **51**, 1741.
15 M. Dejter-Juszynski and H. M. Flowers, *Carbohydr. Res.*, 1971, **18**, 219.

Paper 7/04310D
Received 18*th June* 1997
Accepted 8*th July* 1997