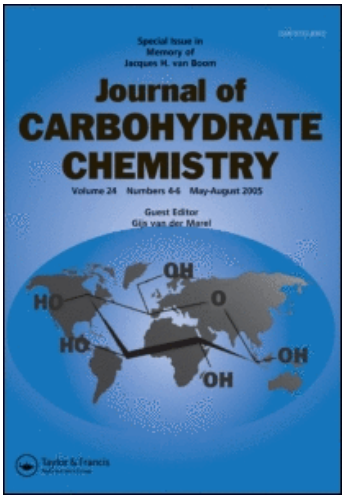

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Synthesis of *p*-Trifluoroacetamidophenyl 3-*O*-[2-Acetamido-2-Deoxy-3-*O*-(α-*L*-Fucopyranosyl)-β-*D*-Glucopyranosyl]-β-*D*-Galactopyranoside and of *p*-Trifluoracetamidophenyl 3-*O*-[2-Acetamido-2-Deoxy-3-*O*(α-*L*-Fucopyranosyl)-4-*O*(β-*D*-Galactopyranosyl)-β-*D*-Glucopyranosyl]-β-*D*-Galactopyranoside, a Trisaccharide and a Tetrasaccharide Fragment of the Le^X Tumor-Associated Antigen

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SYNTHESES OF *p*-TRIFLUOROACETAMIDOPHENYL 3-*O*-[2-ACETAMIDO-2-DEOXY-3-*O*-(α-L-FUCOPYRANOSYL)-β-D-GLUCOPYRANOSYL]-β-D-GALACTOPYRANOSIDE AND OF *p*-TRIFLUOROACETAMIDOPHENYL 3-*O*-[2-ACETAMIDO-2-DEOXY-3-*O*-(α-L-FUCOPYRANOSYL)-4-*O*-(β-D-GALACTOPYRANOSYL)-β-D-GLUCOPYRANOSYL]-β-D-GALACTOPYRANOSIDE, A TRISACCHARIDE AND A TETRASACCHARIDE FRAGMENT OF THE Le^x TUMOUR-ASSOCIATED ANTIGEN

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ABSTRACT

p-Trifluoroacetamidophenyl 3-*O*-[2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside and *p*-trifluoroacetamidophenyl 3-*O*-[2-acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside, which are trisaccharide and tetrasaccharide fragments respectively of the Le^x tumour-associated antigen (**1**), were synthesized, using mainly thioglycosides as glycosyl donors and dimethyl(methylthio)sulfonium triflate ("DMTST")[1] as promoter.

INTRODUCTION

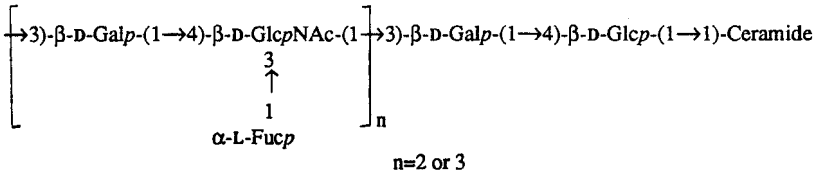
The Le^x tumour-associated glycosphingolipid accumulate in human colonic and liver adenocarcinoma and is virtually absent in normal colonic mucosa and normal liver tissue.[2] Previously, Ogawa *et al.*[3] and Norberg *et al.*[4,5] have reported on the synthesis of partial structures of the Le^x antigen. In this communication we report syntheses of a trisaccharide and a tetrasaccharide fragment of the Le^x tumour-associated antigen carrying a trifluoroacetamidophenyl group at their reducing ends suitable for making artificial antigens by coupling to a protein.

RESULTS AND DISCUSSION

The original concept for the synthesis of the tetrasaccharide **3** was to couple the glycosyl donor ethyl 6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl)-1-thio-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside[6,7] with the glycosyl acceptor *p*-nitrophenyl 4-*O*-acetyl-2,6-di-*O*-benzyl-β-D-galactopyranoside (**7**) in CH_2Cl_2 using methyl triflate or DMTST as promoter. This reaction, however, led to a recovery of the glycosyl acceptor and a fair yield of glycal formation from the glycosyl donor and only a poor yield (< 15%) of the tetrasaccharide. The same reaction as above but using *p*-nitrophenyl 2,6-di-*O*-benzyl-β-D-galactopyranoside (**6**) as glycosyl acceptor gave an even poorer yield.

To produce the trisaccharide **2**, *p*-nitrophenyl 3,4-*O*-isopropylidene-β-D-galactopyranoside (**4**)[8] was dibenzylated in 45% yield using benzyl bromide and sodium hydride in *N*,*N*-dimethylformamide, followed by hydrolysis of the 3,4-isopropylidene of **5** in aqueous acetic acid producing **6** in 95% yield. Compound **6** was treated with trimethyl orthoacetate and *p*-toluenesulfonic acid to give the 3,4-orthoacetate which was regioselectively hydrolysed using aqueous trifluoroacetic acid[9] affording the glycosyl acceptor *p*-nitrophenyl 4-*O*-acetyl-2,6-di-*O*-benzyl-β-D-galactopyranoside (**7**) in 95% yield from **5**. The appearance of the *O*-acetyl group on O-4 and not on O-3 of **7** was demonstrated by assigning its ^1H NMR spectrum employing a selective decoupling experiment and thereby finding the chemical shift of H-4 1.53 ppm downfield from that of H-3. The glycosyl donor ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside **3** and **7** were condensed under promotion by DMTST affording the fully protected trisaccharide **9** in 76% yield. Trisaccharide **9** was subsequently treated with hydrazine hydrate and with acetic anhydride and pyridine to afford **10** in 67% yield. Treatment of **10** with aluminium amalgam and trifluoroacetic acid and pyridine converted the nitro group in **10** to a *p*-trifluoroacetamido group affording **11** in 64% yield. Finally, **11** was treated with sodium methoxide in methanol followed by hydrogen and 10% palladium on charcoal affording the trisaccharide **2** in 91% yield.

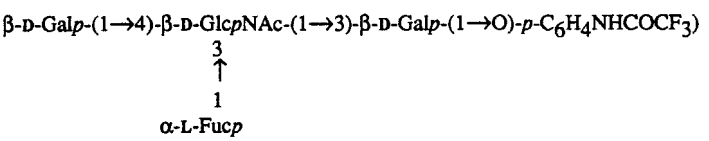
In order to produce the tetrasaccharide **3**, the 4,6-benzylidene compound **9** was reductively opened[10], using aluminiumn trichloride and the trimethylamine-borane complex to give the glycosyl acceptor **14** in 96% yield. This was condensed with 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl bromide using silver triflate as promoter affording **16** in 69% yield. The sequence from **16** to the target tetrasaccharide **3** (**16** → **17** → **18** → **19** → **3**) followed the same reaction scheme as that described above for the sequence **9** → **10** → **11** → **12** → **2** and afforded essentially similar yields. Attempts to use 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl bromide as the glycosyl donor afforded only 17% of fully protected tetrasaccharide.



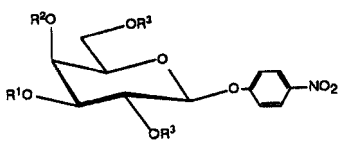
1

α-L-Fuc*p*-(1→3)-β-D-Glc*p*NAc-(1→3)-β-D-Gal*p*-(1→O)-*p*-$C_6H_4NHCOCF_3$)

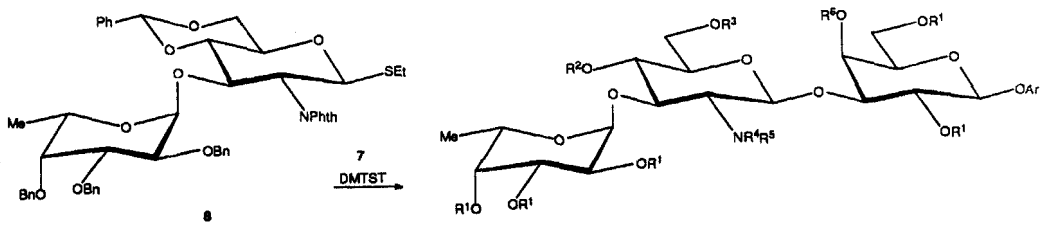
2



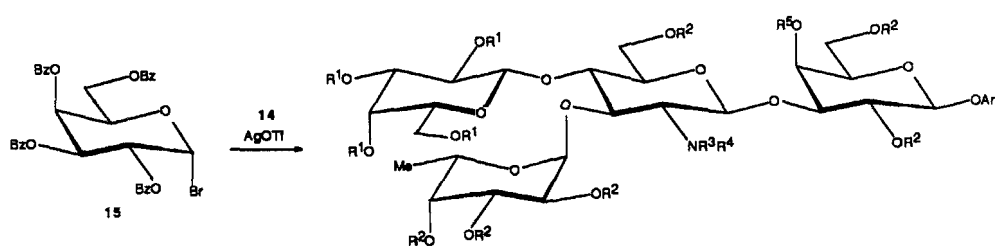
3



	R^1	R^2	R^3
4	$(CH_3)_2C$		H
5	$(CH_3)_2C$		Bn
6	H	H	Bn
7	H	Ac	Bn



	R^1	R^2	R^3	R^4	R^5	R^6	Ar
9	Bn	PhCH		Phth		Ac	$PhNO_2$
10	Bn	PhCH		H	Ac	Ac	$PhNO_2$
11	Bn	PhCH		H	Ac	Ac	$PhNHCOCF_3$
12	Bn	PhCH		H	Ac	H	$PhNHCOCF_3$
2	H	H	H	H	Ac	H	$PhNHCOCF_3$
14	Bn	H	Bn	Phth		Ac	$PhNO_2$



	R^1	R^2	R^3	R^4	R^5	Ar
16	Bz	Bn	Phth		Ac	$PhNO_2$
17	Ac	Bn	H	Ac	Ac	$PhNO_2$
18	Ac	Bn	H	Ac	Ac	$PhNHCOCF_3$
19	H	Bn	H	Ac	H	$PhNHCOCF_3$
3	H	H	H	Ac	H	$PhNHCOCF_3$

EXPERIMENTAL

General methods. - Melting points are corrected. Concentrations were performed at reduced pressure at < 40 °C (bath). Optical rotations were recorded with a Perkin-Elmer 241 polarimeter. NMR spectra were recorded using a JEOL FX-100 or a JEOL GSX-270 spectrometer. Chemical shifts are given in ppm downfield from those of internal Me_4Si ($CDCl_3$ solutions) or internal dioxane (67.4 ppm) (D_2O solutions). NMR spectra for all new compounds accorded with the postulated structures. TLC was performed on silica gel F_{254} (Merck) with detection by uv light and/or charring with sulfuric acid. Column chromatography was performed on silica gel 60 (0.04-0.063 mm, Merck). Elemental analyses were performed by Mikro Kemi AB (Uppsala, Sweden). Satisfactory elemental analyses were not obtained for syrupy or amorphous products, but they were shown to be pure by chromatography and NMR spectroscopy.

***p*-Nitrophenyl 2,6-Di-*O*-benzyl-β-D-galactopyranoside (6).** A solution of *p*-nitrophenyl 3,4-*O*-isopropylidene-β-D-galactopyranoside (**4**)[8] (1.44 g, 4.2 mmol) in *N,N*-dimethyl formamide (25 mL) containing benzyl bromide (1.3 mL, 10.9 mmol) was added to sodium hydride (0.63 g, 14.4 mmol) at 0 °C under nitrogen. After 2 h at 0 °C, methanol (2 mL) was added and the reaction mixture was partitioned between toluene and water. The organic layer was washed with water, dried over sodium sulfate, filtered, and concentrated. Silica gel column chromatography (toluene-ethyl acetate, 3:1) of the residue afforded syrupy *p-nitrophenyl 2,6-di-*O*-benzyl-3,4-*O*-isopropylidene-β-D-galactopyranoside* **5** (1.0 g, 45%), $[\alpha]_{578}^{22}$ -16° (*c* 0.6, chloroform). ^{13}C NMR (25 MHz, $CDCl_3$): δ 26.2, 27.6 (2 CH_3), 69.4-79.0 (C-2 - C-6, $PhCH_2$), 100.0 (C-1), 110.5 [$C(CH_3)_2$], 116.6 (C*-2, C*-6), 125.6 (C*-3, C*-5), 127.5-138.0 (2 Ph), 142.7 (C*-4), 161.9 (C*-1). Compound **5** (1.0 g, 1.9 mmol) was treated 1 h with 90% aqueous acetic acid at 100 °C. The solution was concentrated and the product was crystallised from isooctane to yield **6** (0.90 g, 97%), mp 132 °C, $[\alpha]_{578}^{22}$ -32° (*c* 0.6, chloroform). ^{13}C NMR (25 MHz, CDCl3): δ 68.8-78.8 (C-2 - C-6, $PhCH_2$), 100.9 (C-1), 116.6 (C*-2, C*-6), 125.7 (C*-2, C*-5), 127.7-138.0 (2 Ph), 142.5 (C*-4), 161.3 (C*-1).

Anal. Calcd for $C_{26}H_{27}NO_8$: C, 64.9, H, 5.6, N, 2.9. Found: C, 64.9, H, 5.6, N, 3.0.

***p*-Nitrophenyl 4-*O*-Acetyl-2,6-di-*O*-benzyl-3-*O*-[2-acetamido-4,6-benzylidene-2-deoxy-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside (10).** A mixture of **6** (1.37 g, 2.8 mmol), trimethyl orthoacetate (700 μL, 5.6 mmol), and *p*-toluenesulfonic acid (30 mg, cat.) in nitromethane was stirred for 10 min at room temperature and then concentrated. The residue was dissolved in nitromethane and 90% aqueous trifluoroacetic acid (0.35 mL) was added. After 10 min the mixture was concentrated. The residue was dissolved in dichloromethane and the solution was washed with satura-

ted aqueous sodium hydrogencarbonate, dried over sodium sulfate, filtered, and concentrated. The residue, after purification by silica gel column chromatography (toluene-ethyl acetate, 1:1), afforded syrupy p-*nitrophenyl 4-O-acetyl-2,6-di-O-benzyl-β-D-galactopyranoside* (**7**) (1.46 g, 98%), $[\alpha]_{578}^{22}$ -58° (*c* 0.3, chloroform). ^{13}C NMR (25 MHz, $CDCl_3$): δ 20.8 (CH_3), 68.4-79.0 (C-2 - C-6, $PhCH_2$), 100.8 (C-1), 116.5 (C*-2, C*-6), 125.8 (C*-3, C*-5), 127.8-137.9 (2 Ph), 143.0 (C*-4), 161.7 (C*-1), 170.8 (C=O). DMTST[1] (0.5 M) in dichloromethane (8 mL) was added to a stirred solution of **7** (873 mg, 1.7 mmol) and ethyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranoside (**8**)[6] (1.48 g, 1.7 mmol) in dichloromethane (65 mL) containing 4Å molecular sieves at 0 °C. The temperature was raised to that of the room, and after 1 h triethylamine (1.5 mL) was added. The reaction mixture was filtered through Celite, the filtrate was partitioned between dichloromethane and saturated aqueous sodium hydrogencarbonate. The organic layer was concentrated and purified by silica gel column chromatography (toluene-ethyl acetate, 9:1) to yield syrupy p-*nitrophenyl 4-O-acetyl-2,6-di-O-benzyl-3-O-[4,6-benzylidene-2-deoxy-2-phthalimido-3-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside* (**9**) (1.67 g, 76%), $[\alpha]_{578}^{22}$ -11° (*c* 0.6, chloroform). ^{13}C NMR (67.5 MHz, $CDCl_3$): δ 16.4 (C''-6), 20.8 (OAc), 56.0 (C'-2), 66.2-81.9 (C-2 - C-6, benzyl), 99.1, 99.5 and 100.3 (C-1, C'-1 and C''-1), 101.1 (PhCH), 116.0 (C*-2, C*-6), 125.6 (C*-3, C*-5), 123.1-138.9 (aromatic), 142.7 (C*-4), 161.6 (C*-1), 167.8, 168.1 (Phth), 170.0 (OAc).

Hydrazine hydrate (2 mL) was added to a stirred solution of **9** (166 mg, 0.12 mol) in 90% aqueous ethanol and the solution was then refluxed for 16 h, cooled and concentrated. The residue was dissolved in acetic anhydride (15 mL) and pyridine (35 mL), the solution was kept at 100 °C for 1 h, and then concentrated. Silica gel column chromatography (toluene-ethyl acetate, 2:1) of the residue gave **10** (104 mg, 67%), mp 97 °C (from ethyl acetate-isooctane) $[\alpha]_{578}^{22}$ 69° (*c* 0.5, chloroform). ^{13}C NMR (25 MHz, $CDCl_3$): δ 16.3 (C''-6), 20.9 (OAc), 23.1 (NHAc), 58.0 (C'-2), 66.2-80.4 (C-2 - C-6, benzyl), 98.2, 100.6, 101.1, 101.6 (C-1, C'-1, C''-1, PhCH), 116.6 (C*-2, C*-6), 125.7 (C*-3, C*-5), 126.2-138.6 (aromatic), 142.8 (C*-4), 161.7 (C*-1), 170.2, 170.4 (OAc, NAc).

Anal. Calcd for $C_{70}H_{74}N_2O_{18}$: C, 68.3, H, 6.1, N, 2.3. Found: C, 68.0, H, 6.1, N, 2.2.

***p*-Trifluoroacetamidophenyl 3-*O*-[2-Acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside (2).** A solution of **10** (52 mg, 0.042 mmol) in tetrahydrofuran (4.5 mL) and water (0.5 mL) was treated with aluminium amalgam at room temperature for 2 h. When TLC (toluene-ethyl acetate, 1:1) indicated complete reaction, the mixture was filtered through Celite and concentrated. A solution of the residue in dichloromethane (20 mL) and pyridine (5 mL) was treated with trifluoroacetic anhydride (40

μL, 0.28 mmol). After 3 h at room temperature, the reaction mixture was partitioned between dichloromethane and saturated aqueous sodium hydrogencarbonate, the organic layer was concentrated and the residue purified by silica gel column chromatography (toluene-ethyl acetate, 1:1) to give p-*trifluoroacetamidophenyl 4-O-acetyl-2,6-di-O-benzyl-3-O-[2-acetamido-4,6-O-benzylidene-2-deoxy-3-O-(2,3,4-tri-O-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside* (**11**) (35 mg, 64%). ^{13}C NMR (25 MHz, $CDCl_3$): δ 16.3 (C''-6), 20.9 (OAc), 23.1 (NAc), 57.8 (C'-2), 66.2-78.6 (aromatic), 98.1, 101.1, 101.6, 101.6 (C-1, C'-1, C''-1, PhCH), 117.4-138.6 (aromatic), 155.1 (trifluoroacetamido), 170.1 (OAc). Sodium methoxide in methanol was added to a stirred solution of **11** (35 mg, 0.027 mmol) in dichloromethane (6 mL) and methanol (4 mL) at room temperature. After 3 h acetic acid was added and the solution concentrated. Toluene was twice distilled from the residue, which was hydrogenated over 10% palladium on charcoal at 400 kPa in ethyl acetate-ethanol-water (12:3:2) for 16 h. The reaction mixture was filtered and concentrated and the residue purified on a Bio-Gel P-2 column (water). Lyophilization afforded **2** (17 mg, 91%) as an amorphous powder, $[\alpha]_{578}^{22}$ -79° (*c* 0.2, water). ^{13}C NMR (25 MHz, D_2O): δ 16.0 (C''-6), 23.1 (NAc), 56.3 (C'-2), 100.7, 101.8, 103.4 (C-1, C' -1, C''-1), 118.0, 125.0 (aromatic), 156.0 ($COCF_3$), 175.8 (NAc).

p-**Nitrophenyl 4-*O*-Acetyl-2,6-di-*O*-benzyl-3-*O*-[6-*O*-benzyl-2-deoxy-2-phthalimido-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside (14).** Aluminium trichloride (200 mg, 1.5 mmol) was added at room temperature to a solution of **9** (392 mg, 0.30 mmol) and trimethylamine-borane complex (100 mg, 1.4 mmol) in tetrahydrofuran (5 mL). The mixture was heated to 60 °C and stirred until TLC (toluene-ethyl acetate, 4:1, R_f 0.41), indicated complete reaction. The mixture was cooled to room temperature and partitioned between M aqueous sulfuric acid and toluene. The organic layer was washed with aqueous sodium hydrogencarbonate and water, concentrated and purified by silica gel column chromatography (solvent as for TLC, above) to afford **14** (377 mg, 96%), mp 67° (from ethanol), $[\alpha]_{578}^{22}$ +14° (*c* 0.2, chloroform). ^{13}C NMR (25 MHz, $CDCl_3$): δ 16.4 (C''-6), 20.8 (OAc), 55.0 (C'-2), 99.0, 100.4, 100.6 (C-1, C'-1, C''-1), 116.5 (C*-2, C*-6), 125.7 (C*-3, C*-5), 122.9-138.7 (2 Ph), 142.6 (C*-4), 161.7 (C*-1), 168.1, 168.7 (Phth), 170.1 (OAc).

Anal. Calcd. for $C_{76}H_{76}N_2O_{19}$: C, 69.1, H, 5.8, N, 2.1. Found: C, 68.8, H, 5.7, N, 2.1.

p-**Nitrophenyl 4-*O*-Acetyl-2,6-di-*O*-benzyl-3-*O*-[6-*O*-benzyl-2-deoxy-2-phthalimido-4-*O*-(2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl)-3-*O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside (16).** A solution of silver triflate (440 mg, 1.7 mmol) and *s*-collidine (150 μL) in dichloromethane (3 mL) and toluene

(2 mL) was added dropwise at -20 °C to a stirred solution of **14** (665 mg, 0.5 mmol) and 2,3,4,6-tetra-*O*-benzoyl-β-D-galactopyranosyl bromide (700 mg, 1.1 mmol) in toluene containing ground molecular sieves under nitrogen (4Å). When TLC (toluene-ethyl acetate, 6:1) indicated complete reaction, 10% aqueous sodium thiosulfate (5 mL) and toluene (15 mL) were added. The mixture was filtered through Celite. The organic layer was separated and washed with water, concentrated and the residue was purified by silica gel column chromatography (toluene-ethyl acetate, 6:1) to afford **16** (660 mg, 69%), $[\alpha]_{578}^{22}$ -1° (*c* 0.4, chloroform), mp 103 °C (from chloroform-methanol). ^{13}C NMR (25 MHz, $CDCl_3$): δ 16.9 (C''-6), 20.8 (OAc), 56.4 (C'-2), 61.4 (C''-6), 96.8, 98.8, 99.8, 100.6 (C-1, C'-1, C''-1, C'''-1), 116.5 (C*-2, C*-6), 125.5 (C*-3, C*-5), 123.3-139.0 (aromatic), 142.7 (C*-4), 161.6 (C*-1), 164.8, 165.3, 165.8, 165.8 (4 OBz), 167.8, 168.2 (Phth), 170.4 (OAc).

Anal. Calcd for $C_{110}H_{102}N_2O_{28}$: C, 69.5, H, 5.4, N, 1.5. Found: C, 68.9, H, 5.3, N, 1.3.

***p*-Trifluoroacetamidophenyl 3-*O*-[2-Acetamido-2-deoxy-3-*O*-(α-L-fucopyranosyl)-4-*O*-(β-D-galactopyranosyl)-β-D-glucopyranosyl]-β-D-galactopyranoside (3).** Hydrazine hydrate (5 mL) was added to a stirred solution of **16** (602 mg, 0.3 mmol) in 90% aqueous ethanol (70 mL) and refluxed for 16 h. The solution was cooled and concentrated and the residue was acetylated using acetic anhydride (15 mL) and pyridine (35 mL) at 100 °C for 1 h. The solution was cooled and concentrated. Silica gel column chromatography (toluene-ethyl acetate, 1:1) of the residue gave p-*nitrophenyl 4*-O-*acetyl-2,6-di*-O-*benzyl-3*-O-*[2-acetamido-6*-O-*benzyl-2-deoxy-3*-O-*(2,3,4-tri*-O-*benzyl*-α-L-*fucopyranosyl)-4*-O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl)*-β-D-*glucopyranosyl]*-β-D-*galactopyranoside* (**17**) (357 mg, 62%) mp 96 °C (from ethyl acetate-hexane), $[\alpha]_{578}^{22}$ -34° (*c* 0.6, chloroform). ^{13}C NMR (25 MHz, $CDCl_3$): δ 16.8 (C''-6), 20.5, 20.6, 20.6, 20.7, 20.9 (5 x OAc), 57.8 (C-2), 97.1, 99.5, 99.5, 100.7 (C-1, C'-1, C''-1, C'''-1), 116.2 (C*-2, C*-6), 125.8 (C*-3, C*-4), 127.1-138.9 (aromatic), 142.8 (C*-4), 161.8 (C*-1), 169.0, 169.1, 169.8, 170.0, 170.5 (5 x Ac). A satisfactory elemental analysis could not be obtained, therefore the yield is not absolutely representative for the reaction. A solution of **17** (102 mg, 0.065 mmol) in tetrahydrofuran (9 mL) and water (1 mL) was treated as for the preparation of **11** to yield p-*trifluoroacetamidophenyl 4*-O-*acetyl-2,6-di-benzyl-3*-O-*[2-acetamido-6*-O-*benzyl-2-deoxy-4*-O-*(2,3,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl)-3-O-(2,3,4-tri-O-benzyl*-α-L-*fucopyranosyl)*-β-D-*glucopyranosyl]*-β-D-*galactopyranoside* (**18**) (66 mg, 63%). ^{13}C NMR (25 MHz, $CDCl_3$): δ 16.9 (C''-6), 20.7, 20.8, 20.8, 20.9, 21.0 (5 x OAc), 23.1 (NAc), 57.7 (C'-2), 97.0, 99.6, 99.7, 101.7 (C-1, C'-1, C''-1, C'''-1), 117.5-139.0 (aromatic), 154.8 ($COCF_3$), 169.0, 170.6 (OAc, NAc). A solution of **18** (44 mg, 0.027 mmol) in dichloromethane (6 mL) and

methanol (4 mL) was treated as for the preparation of substance **2** affording **3** (18 mg, 87%), as an amorphous powder, $[\alpha]_{578}^{22}$ -53° (*c* 0.25, water). ^{13}C NMR (25 MHz, D_2O): δ 16.1 (C''-6), 23.1 (NAc), 56.8 (C'-2), 99.4, 101.8, 102.6, 103.4 (C-1, C'-1, C''-1, C'''-1), 118.0-130.4 (aromatic), 156.1 ($COCF_3$), 175.6 (NAc).

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