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Chemical synthesis of sulfated oligosaccharides with a β -D-Gal-(1 \rightarrow 3)-[β -D-Gal-(1 \rightarrow 4)-(α -L-Fuc-(1 \rightarrow 3)- β -D-GlcNAc-(1 \rightarrow 6)]- α -D-GalNAc sequence

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Abstract

The syntheses of two sulfated pentasaccharides: β -D-Gal6SO₃Na-(1 \rightarrow 3)-[β -D-Gal-(1 \rightarrow 4)- α -L-Fuc-(1 \rightarrow 3)- β -D-Glc-NAc-(1 \rightarrow 6)]- α -D-GalNAc \rightarrow OMe (1) and β -D-Gal6SO₃Na-(1 \rightarrow 3)-[β -D-Gal-(1 \rightarrow 4)- α -L-Fuc-(1 \rightarrow 3)- β -D-Glc-NAc6SO₃Na-(1 \rightarrow 6)]- α -D-GalNAc \rightarrow OMe (2) by using Lewis^X trisaccharides 12 and 16 as glycosyl donors are described. Sulfated oligosaccharides 1–2 and intermediate compounds are fully characterized by 2D ¹H-¹H DQF-COSY and 2D ROESY experiments. © 2000 Elsevier Science Ltd. All rights reserved.

Keywords: Chemical synthesis; 2D DQF-COSY; 2D ROESY; Sulfated oligosaccharides; Crystallography

1. Introduction

Mammalian lectins mediate the early steps of recruitment of leukocytes from the bloodstream in a variety of normal and pathological situations [1-4]. In the last decade there has been a tremendous interest in the synthesis of high affinity molecules that target the selectin family of cell-surface proteins (L, P and E) because these molecules can become future drugs for treatment of various diseases such as chronic and acute inflammation. Since the natural selectin ligands (GlyCAM-1 and PSGL-1) carry sially Le^x or NeuAca- $(2 \rightarrow 3)$ -Gal β -(1 \rightarrow 3)-GalNAc oligosaccharide unit as part of core 2 O-linked structures, much effort has been made for the synthesis of sialylated and sulfated Lewis^x, and mimics of SLe^x [5,6]. Recently, Kiessling and co-workers [7] have examined the inhibition of L-selectin with various disulfated Le^x derivatives. We became interested in the synthesis of sialyl and sulfated core 2 analogs for the binding studies of these selectins because the role of core 2 analogs as inhibitors for these selectins has become evident [8]. Our interest in core 2 branched structures which contain sulfates has also stemmed from our study of sulfotransferase using the core 2 branched structures as acceptors [9]. We hereby report the synthesis of branched structures 1 and 2.

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2. Results and discussion

Synthesis of trisaccharide building blocks 12 and 16.—In order to synthesize two sulfated oligosaccharides 1 and 2,



key building blocks **12**, **16**, **21** and **27** were prepared starting from monosaccharide building blocks



according to Schemes 1–3. The HO-4 of diol **5** was regioselectively

glycosylated with donor 6 in the presence of silver triflate-tin chloride as catalyst [10] to give disaccharide 7 in good yield (73%). The stereochemical outcome of both the glycosylic and position connectivity of disaccharide 7 was well established through homonuclear correlation experiments (2D 1H-1H DQF-COSY: Fig. 1 and 2D ROESY: Fig. 2). The $(1 \rightarrow 4)$ -linkage of disaccharide 7 was indicated by the observation of a strong NOE cross peak between H-1^{II} and H-4^I in the 2D ROESY spectrum. A 1,2-trans glycoside of disaccharide 7 was confirmed by a larger coupling constant of ${}^{3}J_{1,2}$ (J 8.0 Hz). The strucdisaccharide 7 was further ture of characterized by X-ray diffraction analysis (Fig. 3).

Disaccharide 7 was fucosylated with methyl 2,3,4-tri-O-benzyl-1-thio- β -L-fucoside (3) in the presence of tetrabutylammonium bromide-copper bromide as catalyst [11], affording trisaccharide 8 in good yield (76%). The removal of benzyl groups from compound 8 was achieved in the presence of 10% palladium-on-carbon catalyst under a hydrogen atmosphere. Compound 9 was then treated with 1:1 acetic anhydride-pyridine in the presence



Scheme 1. Reagents and conditions. (a) 5:1 AgOTf-SnCl₂/CH₂Cl₂-toluene, 4 Å 10% MS, -15 to 0 °C, 12 h, 73%; (b) 3, CuBr₂-*n*-Bu₄NBr, 5:1 ClCH₂CH₂Cl-DMF, 4 Å MS, rt, 16-24 h, 91%; (c) 10% H₂/Pd-C, 1:1 CH₂Cl₂-CH₃OH, rt, 12 h, 96%; (d) 1:1 Ac₂O-pyridine, DMAP, rt, 12 h, 96%; (e) H₂SO₄-Ac₂O, rt, 12 h, 76%; (f) PhSH/CH₂Cl₂, BF₃·Et₂O, rt, N₂, 16 h, 67%.



Scheme 2. Reagents and conditions: (a) AgOTf-SnCl₂/5:1 CH₂Cl₂-toluene, 4 Å MS, -15 to 0 °C, 12 h, 75%; (b) 3, CuBr₂-n-Bu₄NBr, 5:1 ClCH₂CH₂Cl-DMF, 4 Å MS, rt, 16–24 h, 76%.



Fig. 1. 400 MHz 2D ¹H-¹H DQF-COSY spectrum of disaccharide 7 recorded in CDCl₃ at 303.0 K.



Fig. 2. 400 MHz 2D ROESY spectrum of disaccharide 7 recorded in CDCl₃ at 303.0 K.



Scheme 3. Reagents and conditions: (a) BnBr/KOH, 18-crown-6, THF, rt, 12 h, 86%; (b) 1 N HCl-1,4-dioxane, 4 h, 75%; (c) 1:1 pyridine–Ac₂O, 65–70 °C, 3 h, 76%; (d) Me₃SiBr/BiBr₃, CH₂Cl₂, rt, 12 h, 59%; (e) Hg(CN)₂–HgBr₂/ClCH₂CH₂Cl, 4 Å MS, rt, 12 h, 66%; (f) 60% HOAc, 60–65 °C, 1.5 h, 76%.

of a catalytic amount of DMAP, providing compound 10. The conversion of compound 10 into compound 11 was successfully performed by treatment of 10 with acetic anhydride [12] and a catalytic amount of concentrated sulfuric acid. Trisaccharide donor 12 was obtained by treatment of compound 11 with thiophenol in the presence of BF_3Et_2O [13] under a nitrogen atmosphere (Scheme 1). The structure of trisaccharide donor 12 was fully confirmed by a combination of 2D DQF-COSY and 2D ROESY experiments. For preparation of trisaccharide donor 16, a strategy of sequential glycosylation is employed. Use of three different leaving groups (fluorine, SMe and SPh) which exhibit different reactivities in different coupling reactions allows us to carry out the direct glycosylation of monosaccharide acceptor 13. The construction of trisaccharide donor 16 was outlined in Scheme 2. Regioselective glycosylation of diol 13 with donor 14 was performed in the presence of silver triflate-tin chloride as catalyst to afford disac-



Fig. 3. An ORTEP [22] diagram showing the molecular structure of disaccharide 7.



Scheme 4. Reagents and conditions: (a) NIS-TfOH (cat)/ CH₂Cl₂, 4 Å MS, -65 to -60 °C, 3-4 h, 44%; (b) 1:1 Ac₂O-pyridine, DMAP, rt, 12 h, 86%; (c) 1:5 NH₂NH₂·xH₂O-CH₃OH, 85–90 °C, 4 h, then, 1:1 Ac₂Opyridine, DMAP, rt, 12 h, 76%; (d) H₂, 10% Pd-C, CH₂Cl₂-CH₃OH, rt, 6–8 h, quantitative; (e) SO₃·pyridine-pyridine, 0-25 °C, 6 h, 79%; (f) 1 M, 1:1 CH₃ONa-CH₃OH (cat)/ CH₃OH-water, rt, 24 h, 36%.



Scheme 5. Reagents and conditions: (a) NIS–TfOH (cat)/ CH₂Cl₂, 4 Å MS, -75 to -70 °C, 1.5 h, 46%; (b)HN₂CSNH₂/2,6-lutidine, 60-65 °C, 18 h, 87%; (c) SO₃·pyridine–pyridine, 0-5 °C, 12 h, 79%; (d) DDQ/4:1 CH₂Cl₂–CH₃OH, rt, 20 h, 79%; (e) SO₃·pyridine–pyridine, 0-5 °C, 12 h, 78%; (f) H₂/10% Pd–C, 4:1 CH₂Cl₂–MeOH, rt, 10 h, 87%; (g) 1:5 NH₂NH₂·xH₂O–CH₃OH, 85–90 °C, 4-5h, then, 1:1 Ac₂O–pyridine, DMAP, rt, 12 h, 76%; (h) 1 M, CH₃ONa–CH₃OH (cat)/1:1 CH₃OH–water (1:1), rt, 12 h, 26%.

charide **15** in good yield (75%). Disaccharide **15** was further fucosylated with donor **3** to give trisaccharide **16** in excellent yield (76%).

The structure of trisaccharide **16** was established by 2D NMR experiments (2D DQF-COSY and 2D ROESY). The α -L-fucopyranoside of trisaccharide **16** was indicated by a small coupling constant of ${}^{3}J_{1,2}$ (J 3.3 Hz), which is a characteristic feature of a 1,2-*cis*- α -L-fucopyranoside.

Synthesis of disaccharide building block 21.—Disaccharide building block 27 was prepared according to documented protocol [14]. The construction of disaccharide acceptor 21 is illustrated in Scheme 3. Compound 17 was prepared according to literature procedures [15]. Monosaccharide 17 was treated with potassium hydroxide in the presence of a phase-transfer catalyst [16] (18-crown-6) in dry THF, followed by benzyl bromide, to afford compound 18 in excellent yield (86%). Compound 18 was treated with 1 N HCl in 1,4-dioxane at reflux, resulting in removal of the O-isopropylidene group from 18. The resulting 6-O-benzyl-D-galactose was further acetvlated with 1:1 acetic anhydride-pyridine at 65-70 °C to give 6-O-benzyl-1,2,3,4-tetra-O-acetyl-D-galactopyranose, which was then treated with bromotrimethylsilane in the presence of bismuth(III) bromide [17] to give donor 19. Disaccharide 21a was obtained by treatment of compound 20 with glycosyl donor 19 in the presence of mercury cyanide and mercury bromide as catalysts [18]. Compound 21a was treated with 60% acetic acid at 60-65 °C to give the desired disaccharide acceptor 21 in good yield (76%).

The construction of target sulfated oligosaccharides 1 and 2.—The target sulfated oligosaccharides 1 and 2 were constructed as shown in Schemes 4 and 5. On account of the much higher reactivity of the primary hydroxyl group in acceptors 21 and 27, totally regioselective glycosylation of the primary HO-6 of disaccharide acceptor 21 with trisaccharide donor 12 was achieved under controlled glycosylation conditions to give 22 as the only glycosylation product. The β -(1 \rightarrow 6)linkage of 22 was indicated by observation of strong NOE cross peaks between H-1^{III} of sugar residue III and H-6a^I, H-6b^I of sugar residue I by 2D ROESY spectroscopy. Compound 22 was acetylated with 1:1 acetic anhydride-pyridine in the presence of a catalytic

amount of DMAP to give compound 23. Compound 23 was then treated with 1:5 NH₂NH₂·H₂O-methanol at 85-90 °C, which resulted in the removal of the phthalimido group, followed with 1:1 acetic anhydridepyridine in the presence of a catalytic amount of DMAP at room temperature to afford compound 24. Compound 24 was treated with 10% palladium-on-carbon in a hydrogen atmosphere to give compound 25. Compound 26 was obtained by treatment of compound 25 with sulfur trioxide-pyridine complex in dry pyridine. O-Deacetylation of 26 was performed by treatment with 1 M sodium methoxide to give compound 1. The structure of compound 1 was well characterized by 2D ¹H⁻¹H DQF-COSY, 2D ROESY (Fig. 4), and ¹³C NMR spectroscopy and by FABMS. Similarly, the synthesis of target oligosaccharide 2 was carried out as outlined in Scheme 5. Regioselective glycosylation of HO-6 of diol 27 was achieved by treatment of diol 27 with trisaccharide donor 16 under controlled glycosylation conditions.

Compound 28 was obtained in reasonable yield (46%). The β -(1 \rightarrow 6)-linkage of compound 28 was indicated by observation of strong NOE cross peaks between H-1^{III} of sugar residue III and H-6a^I, H-6b^I of sugar residue I by 2D ROESY spectroscopy. The α-bromoacetyl group was removed by treatment of compound 28 with thiourea and 2.6lutidine at reflux in dichloromethane to give compound 29. Compound 29 was then treated with the sulfur trioxide-pyridine complex in dry pyridine to give compound 30. The next reaction was the selective removal of the 2naphthymethyl (NAP) protecting group from compound **30**. The NAP protecting group was recently introduced as a hydroxyl protecting group [19] and can be removed by DDO in the presence of benzyl groups [20]. Thus, compound 30 was carefully treated with DDQ, resulting in the removal of NAP protecting group. Compound 31 was then treated with the sulfur trioxide-pyridine complex in dry pyridine to give 32. Compound 32 was deprotected by the following procedure to give target oligosaccharide 2: (a) removal of benzyl



Fig. 4. 600 MHz 2D ROESY spectrum of pentasaccharide 1 recorded in D₂O at 303.0 K.

protecting groups; (b) removal of the phthalimido group, followed with acetic anhydride– pyridine and DMAP; (c) removal of acetyl and trimethylacetyl groups, which is shown in Scheme 5. Target oligosaccharide **2** was well characterized with 2D ¹H–¹H DQF-COSY, 2D ROESY, and ¹³C NMR spectroscopy and by FABMS.

In summary, we describe the convergent syntheses of two sulfated pentasaccharides 1 and 2 through a potentially general strategy of regio- and stereoselective glycosylation by the use of unprotected or partially protected acceptors.

3. Experimental

General procedures.-TLC was conducted on glass plates precoated with a 0.25-mm layer of Silica Gel 60 F-254 (Analtech, GHLF uniplates). The components were located either by exposure to UV light or by spraying with 10% H₂SO₄, and 0.2% *p*-anisaldehyde in EtOH soln. Solutions were concd under reduced pressure. The silica gel used for column chromatography was Baker Analyzed (60-200 mesh ASTM). Optical rotations were measured at 25 °C with a Perkin-Elmer 241 polarimeter. ¹H NMR spectra were recorded at 303.0 K with either a Bruker AM 400 (400 MHz) or AMX 600 (600 MHz) spectrometer. The values of δ (ppm) are given relative to the signal (δ 0) for internal Me₄Si for solns in CDCl₃, CD₂Cl₂, or CD₃OD. ¹³C NMR spectra were recorded at 303.0 K with a Bruker AM 400 (100.6 MHz) spectrometer using CDCl₃ (77.0 ppm), CD₂Cl₂ (54.15 ppm), CD₃OD (49.15 ppm), or acetone- d_6 (206.0 or 29.8 ppm) as reference. First-order chemical shifts and coupling constants (J/Hz) were obtained from one-dimensional spectra, and assignments of protons were based on 2D DQF ¹H⁻¹H COSY and 2D ROESY experiments. Two-dimensional double-quantum filtered phase sensitive ${}^{1}H-{}^{1}H$ correlated spectra (DQF ${}^{1}H-{}^{1}H$ COSY), rotating-frame nuclear Overhauser enhancement spectroscopy (ROESY) were recorded at 303.0 K using a Bruker AM 400 (400 MHz) spectrometer and a Bruker AMX 600 (600 MHz) spectrometer.

For ROESY experiments, the mixing time was set at 400 ms. All samples submitted for elemental analyses were dried under vacuum over P_2O_5 at rt. Elemental analyses were carried out by Robertson Laboratory, Madison, NJ. *p*-Toluenesulfonic acid monohydrate (*p*-TsOH·H₂O) was dried by co-evaporating with dry MeCN three times at 80 °C before use. Dichloromethane, MeCN, MeOH, benzene, and DMF were kept dry over 4 Å MS, pyridine was redistilled over KOH, and nitromethane was freshly distilled over P₂O₅.

Methyl (2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl) - $(1 \rightarrow 4)$ - 6 - O - benzyl - 2 - deoxy - 2phthalimido- β -D-glucopyranoside (7).—A soln of compound 5 (1.18 g, 3.38 mmol), compound 6 (2.37 g, 5.75 mmol), and SnCl₂ (1.13 g, 4.39 mmol) in dry 5:1 CH₂Cl₂-toluene (43 mL) containing 4 Å MS (8 g) was stirred at -15 °C for 2 h under a N₂ atmosphere. Silver triflate (832 mg, 4.39 mmol) was added, and the mixture was stirred overnight at -15 to 0 °C under a N₂ atmosphere, then neutralized with Et₃N. The solids were filtered off, and the organic layer was washed with satd NaHCO₃ soln, water, and dried (Na_2SO_4) . The organic solvent was evaporated under reduced pressure to give a crude mixture, which was then applied to a column of silica gel and eluted with 1:1 hexane-EtOAc to give pure compound 7 (1.84 g, 73%) as a white solid. $R_f 0.34$ (1:1 hexane–EtOAc); $[\alpha]_D + 8.8^\circ$ (c 0.5, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 7.84-7.82 (m, 2 H, ArH), 7.72-7.70 (m, 2 H, ArH), 7.41–7.32 (m, 5 H, ArH), 5.33–5.32 (d, 1 H, J 3.2 Hz, H-4^{II}), 5.21–5.16 (dd, 1 H, J 8.0, 10.4 Hz, H-2^{II}), 5.13–5.11 (d, 1 H, $J_{1, 2}$ 8.8 Hz, H-1^I), 4.95–4.92 (dd, 1 H, J 3.6, 10.2 Hz, H-3^{II}), 4.77–4.74 (d, 1 H, J_{gem} 12.4 Hz, OCH_APh, ABq), 4.55–5.52 (d, 1 H, J_{gem} 12.0 Hz, OCH_BPh, ABq), 4.50–4.48 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1^{II}), 4.42–4.37 (t, 1 H, H-3^I), 4.18– 4.13 (dd, 1 H, J 8.8 Hz, H-2^I), 4.06–4.04 (m, 2 H, H-6b^{II}, H-6a^{II}), 3.95 (d, 1 H, OH-3^I), 3.91–3.88 (t, 1 H, J 7.2, 6.4 Hz, H-5^{II}), 3.77– 3.69 (m, 3 H, H-5^I, H-4^I, H-6b^I), 3.65-3.62 (m, 1 H, H-6a^I), 3.44 (s, 3 H, OCH₃), 2.11 (s, 3 H, Ac), 2.00 (s, 3 H, Ac), 1.95, (s, 3 H, Ac), 1.91 (s, 3 H, Ac); ¹³C NMR (CDCl₃, 100.6 MHz): δ 170.46 (C=O), 170.06 (C=O), 169.92 (C=O), 169.15 (C=O), 138.18, 133.99,

Table	1					
X-ray	crystal	data	and	structure	refinement	for 7

Compound	Methyl (2,3,4,6-tetra-
	O-acetyl-β-D-galactopy-
	ranosyl)- $(1 \rightarrow 4)$ -6-O-
	benzyl-2-deoxy-2-phthalimido-
	β -D-glucopyranoside (7)
Color/shape	white/rectangular needle
Empirical formula	C. H. NO.
Formula weight	743 7
Temperature (°C)	22 + 3
Crystal system	monoclinic
Space group	
Unit cell dimensions	$I Z_1$
$a_{\alpha}(\mathbf{A})$	12 520 (2)
$a(\mathbf{A})$	12.329(3)
$D(\mathbf{A})$	14.703 (3)
$c(\mathbf{A})$	10.728 (3)
α (°)	90.0
β (°)	113.98 (2)
γ (°)	90.0
Volume (A ³)	1813.3(9)
Ζ	2 (two molecules per unit
_	cell)
$D_{\rm calcd} \ ({\rm g \ cm^{-3}})$	1.362
Absorption coefficient	0.915
(mm^{-1})	
Difftractometer	CAD-4
Radiation ($\lambda = 1.5418$ Å)	Cu K _a
<i>F</i> (000)	784
Crystal size (mm)	$0.15 \times 0.45 \times 0.25$
2θ Range for data	0–150
collection (°)	
Index ranges (°)	$-10 \le h \le 10, \ 0 \le k \le 17,$
	$-18 \le l \le 18$
Reflections collected	4099
Independent/observed	3892 (3820 with $I < 3\sigma$)
reflections	
Absorption correction	semiempirical from psi scans
Range of relative	0.99 and 0.90
transmission factors	
Refinement method	full-matrix least-squares on
Remembert metrica	F^2
Computing	shfi xs-96
Data/restraints/parameters	3820/0/643
$Goodness_of_fit on F^2$	1 120
Function minimized	$\sum [E^2 - (1/k) E^2]$
Final <i>P</i> indices	$\Delta [I_0 - (I/k) I_c]$ 0.0870 for all 3802
i mai A maices	reflections
	0.064 for 2186 [I > 4 - (D)]
Final artinotion coefficient	$101 \text{ 5100 } [I \ge 4\sigma(I)]$
Final extinction coefficient	0.15 and 0.15
hole (e $Å^{-3}$)	0.13 and -0.13

131.92, 128.55, 127.91, 127.86, 123.34, 101.54, 99.26, 82.06, 74.27, 73.74, 71.22, 70.81, 69.69, 68.80, 67.97, 66.90, 61.47, 56.75, 55.94, 20.72

(Ac), 20.56 (Ac), 20.50 (Ac), 20.33 (Ac); Anal Calcd for $C_{36}H_{41}NO_{16}$: C, 58.12; H, 5.56; N, 1.88. Found: C, 58.00; H, 5.59; N, 1.81.

X-ray crystallography.—Crystals of 7 were obtained by a slow evaporation of the compound dissolved in hexanes–EtOAc. The crystals were rectangular needles. A crystal of dimensions $0.15 \times 0.45 \times 0.25$ mm was used for the X-ray diffraction. The crystals belonged to a monoclinic system, space group $P2_1$. Table 1 gives the crystal data and structure refinement parameters.

Complete three-dimensional data were collected on an Enraf-Nonius CAD-4 computercontrolled diffractometer. A total of 4099 reflections ($2\theta_{max} = 150^\circ$) were collected by the $\omega/2\theta$ method, out of which 3820 were considered significant ($I \ge 3\sigma$). The crystal structure was solved by a routine and straightforward application of the SHELX-96 program on a Silicon Graphics R10,000 computer. The structure was refined using the SHELX-96 package [21] of programs. All hydrogen atoms were located on a difference Fourier map. Refinements were carried out with anisotropic thermal parameters for the nonhydrogen atoms and isotropic thermal parameters for the hydrogen atoms. The final reliability index (R-factor) was 0.0879 for all the observed 3892 reflections and 0.064 for 3186 reflections $(I \ge 4\sigma)$ with a goodness of fit parameter S =1.120. Table 2 gives the final positional parameters for the nonhydrogen atoms in the structure. The crystal structural investigation confirms the structure of compound 7. The disaccharide has the sugar residues, the galactopyranosyl and the glucopyranoside in the ${}^{4}C_{1}$ chair conformation. The ring-to-ring conformation can be described as $(\phi, \psi) = (159.7, \psi)$ -126.3). The conformation across the C-5–C-6 bond is trans-gauche for the galactopyranosyl ring and gauche-gauche for the glucopyranosyl ring. The crystal structure is stabilized by a network of O-H…O hydrogen bonds.

Methyl $(2,3,4,6-tetra-O-acetyl-\beta-D-galacto$ $pyranosyl)-(1 \rightarrow 4)-[(2,3,4-tri-O-benzyl-\alpha-L$ $fucopyranosyl)-(1 \rightarrow 3)]-6-O-benzyl-2-deoxy-2$ $phthalimido-\beta-D-glucopyranoside (8).—A soln$ of compound 7 (320 mg, 0.36 mmol), methyl $2,3,4-tri-O-benzyl-1-thio-<math>\beta$ -L-fucopyranoside Table 2Final fractional positional parameters for nonhydrogen atomswith estimated standard deviations given in parentheses for 7

Atom	X	у	Ζ	$U_{ m eq}~^{ m a}$
O-1	0.0784(3)	0.5082(3)	0.7758(4)	0.0480(8)
O-2	0.1769(3)	0.3972(2)	0.9223(4)	0.0487(9)
O-3	-0.0120(3)	0.7273(3)	0.8543(4)	0.0508(9)
O-4	0.0887(4)	0.8505(3)	0.9695(4)	0.0523(9)
O-5	-0.0927(4)	0.3807(3)	0.6207(4)	0.0587(10)
O-6	-0.0191(4)	0.2016(3)	0.6622(4)	0.0553(10)
O- 7	0.2190(4)	0.2272(3)	0.8293(5)	0.0595(11)
O-8	0.3041(5)	0.7413(5)	1.2883(5)	0.0765(15)
O-9	0.2848(4)	0.5702(3)	1.0130(5)	0.0598(10)
O-10	-0.1547(4)	0.5666(4)	0.8231(5)	0.0711(13)
O-11	-0.0860(5)	0.1083(3)	0.7786(7)	0.0686(13)
O-12	0.1886(5)	0.0781(3)	0.8058(7)	0.0840(20)
O-13	0.3417(4)	0.8014(4)	0.8940(5)	0.0714(13)
O-14	-0.0515(7)	0.3525(7)	0.4401(6)	0.1130(20)
O-15	0.3475(8)	0.3787(6)	1.1611(9)	0.1220(30)
O-16	0.2713(11)	0.3584(11)	1.3027(11)	0.1760(50)
N-1	0.2987(4)	0.7553(3)	1.0723(5)	0.0466(10)
C-1	0.0170(5)	0.2641(4)	0.7725(6)	0.0499(12)
C-2	0.0793(5)	0.5834(3)	0.8617(6)	0.0441(11)
C-3	0.1733(6)	0.3142(4)	0.9879(6)	0.0520(13)
C-4	0.1874(5)	0.7107(4)	1.0002(6)	0.0442(11)
C-5	0.0977(5)	0.7733(4)	0.9023(6)	0.0458(11)
C-6	0.0652(5)	0.4242(4)	0.8260(6)	0.0475(12)
C-7	0.1981(5)	0.6268(4)	0.9215(6)	0.0486(12)
C-8	0.1329(5)	0.2379(4)	0.8859(6)	0.0507(12)
C-9	-0.0132(5)	0.6506(4)	0.7745(6)	0.0503(12)
C-10	0.0228(5)	0.3563(4)	0.7127(6)	0.0491(12)
C-11	0.3474(6)	0.7676(4)	1.2134(6)	0.0547(14)
C-12	-0.0712(8)	0.1259(6)	0.6711(11)	0.0640(20)
C-13	0.0335(8)	0.9240(4)	0.8793(8)	0.0620(20)
C-14	0.5617(6)	0.8844(5)	1.1259(9)	0.0680(20)
C-15	-0.3636(6)	0.5634(4)	0.7549(8)	0.0610(20)
C-16	0.3661(5)	0.7984(4)	1.0152(6)	0.0516(13)
C-17	0.2945(7)	0.3002(5)	1.0978(9)	0.0720(20)
C-18	0.4672(5)	0.8372(4)	1.1276(7)	0.0553(14)
C-19	0.2375(6)	0.1436(5)	0.7931(8)	0.0670(20)
C-20	0.4576(5)	0.8172(4)	1.2462(7)	0.0561(14)
C-21	0.6384(7)	0.8890(7)	1.3696(10)	0.0830(20)
C-22	-0.2430(14)	0.3994(12)	0.4055(12)	0.1130(50)
C-23	-0.1078(10)	0.0681(7)	0.5539(10)	0.0870(30)
C-24	-0.1212(8)	0.3753(6)	0.4867(7)	0.0770(20)
C-25	-0.5262(8)	0.6569(7)	0.6200(10)	0.0850(20)
C-26	0.3151(11)	0.3873(11)	1.2405(14)	0.1330(60)
C-27	-0.5626(8)	0.6626(7)	0.7244(11)	0.0880(20)
C-28	-0.4034(8)	0.5695(6)	0.8603(9)	0.0760(20)
C-29	-0.4275(7)	0.6083(6)	0.6365(8)	0.0740(20)
C-30	-0.2567(6)	0.5123(6)	0.7767(10)	0.0750(20)
C-31	0.6463(7)	0.9103(6)	1.2502(10)	0.0760(20)
C-32	0.5421(6)	0.8417(6)	1.3724(8)	0.0740(20)
C-33	0.3241(14)	0.1464(10)	0.7335(20)	0.1250(70)
C-34	0.3829(11)	0.4979(7)	1.3227(10)	0.0890(20)
C-35	-0.5004(9)	0.6193(7)	0.8430(11)	0.0890(20)
C-36	-0.1354(6)	0.6116(5)	0.7199(7)	0.0604(15)

 $^{\rm a} U_{\rm eq}$ is defined as the trace of the orthogonalized U_{ij} tensor.

0.72 mmol) in dry 5:1 1.2mg, dichloroethane–DMF (15 mL) containing 4 Å MS (2 g) was stirred for 2 h at rt under a N_2 atmosphere. Copper bromide (161 mg, 0.72 mmol) was added, and the mixture was stirred overnight at rt. An additional portion of compound 3 (790 mg), CuBr₂ (101 mg) and n- Bu_4NBr (145 mg) were added, and the stirring was continued for a total of 24 h. The solids were filtered off, the organic layer was washed with satd NaHCO₃ soln, and water, and then it was dried (Na_2SO_4) and concd. The crude product was applied to a short column of silica gel and eluted with 2:1 hexane-EtOAc to give compound 8 (380 mg, 0.32 mmol, 91%) as a white solid. R_f 0.17 (2:1 hexane-EtOAc); $[\alpha]_{D}$ + 5.4° (*c* 0.7, CHCl₃); ¹H NMR (CDCl₃, 600 MHz): δ 7.67–7.66 (m, 2 H, ArH), 7.41–7.39 (m, 2 H, ArH), 7.26–7.01 (m, 20 H, ArH), 5.23–5.22 (d, J_{1.2} 3.2 Hz, H-4^{II}), 5.01–4.99 (m, 2 H, H-2^{II}, H-1^I, $J_{1,2}$ 8.4 Hz), 4.85–4.73 (m, 4 H, OCHPh, H-1^{III}, OCHPh, H- 3^{II}), 4.71–4.62 (m, 2 H, H- 1^{II}). H-3^I), 4.61–4.59 (dd, 2 H, OCH₂Ph), 4.58– 4.55 (d, 1 H, J_{gem} 12.0 Hz, OCHPh, ABq), 4.51-4.48 (d, 1 H, J_{gem} 12.0 Hz, OCHPh, ABq), 4.42–4.33 (m, 2 H, OCHPh, H-2^I), 4.26-4.23 (d, 1 H, J_{gem} 12.0 Hz, ABq), 4.15-4.09 (m, 2 H, H-4^I, H-6b^{II}), 4.00-3.94 (dd, 1 H, H-6a^{II}), 3.92–3.80 (m, 4 H, H-6a^I, H-3^{III}, H-6b^I, H-2^{III}), 3.61 (d, 1 H, J 3.2 Hz, H-4^{III}), 3.55-3.45 (m, 2 H, H-5^I, H-5^{II}), 3.28 (s, 3 H, OCH₃), 2.01 (s, 3 H, Ac), 2.00 (s, 3 H, Ac), 1.94 (s, 3 H, Ac), 1.84 (s, 3 H, Ac), 1.21–1.19 (d, 3 H, J 6.4 Hz, CH_{3}^{III}); ¹³C NMR (CDCl₃, 100.6 MHz): δ 170.56 (C=O), 170.36 (C=O), 170.09 (C=O), 169.84 (C=O), 168.79 (C=O), 139.93, 139.85, 138.89, 138.62, 134.93, 134.82, 129.28, 128.78, 128.66, 128.59, 128.51, 128.07, 127.83, 127.79, 124.19, 100.47, 99.95, 98.32, 80.42, 78.90, 75.97, 75.81, 75.34, 75.26, 74.18, 73.56, 73.16, 72.94, 71.69, 71.30, 69.58, 68.53, 67.63, 67.18, 61.21, 57.25, 56.97, 21.90 (Ac), 21.87 (Ac), 21.67 (Ac), 20.83 (Ac), 16.89 (CH₃); Anal Calcd for C₆₃H₆₈NO₂₀: C, 65.27; H, 5.91; N, 1.21. Found: C, 64.57; H, 5.94; N, 1.11.

(3, 338 mg, 0.72 mmol), and n-Bu₄NBr (232)

Phenyl (2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl)- (1 \rightarrow 4)- [(2,3,4-tri-O-acetyl- α -L- fucopyranosyl)- $(1 \rightarrow 3)$]-6-O-acetyl-2-deoxy-2*phthalimido-1-thio-\beta-D-glucopyranoside* (12). -A soln of compound **8** (310 mg, 0.32) mmol), and 10% Pd-C (320 mg) in a mixture of MeOH (5 mL) and CH₂Cl₂ (5 mL) was stirred overnight at rt under a H₂ atmosphere. The catalyst was filtered off, and the filtrate was concd under reduced pressure to give crude 9, which was then treated with 1:1 Ac_2O -pyridine (6 mL) in the presence of a catalytic amount of DMAP (3 mg) at rt overnight. The reaction mixture was then concd. The crude product was applied to a column of silica gel and eluted with 1:2 hexane-EtOAc to give pure compound 10 (250 mg, 0.21 mmol, 96%) in two steps. To a cold (0 °C) soln of compound 10 (320 mg, 0.33 mmol) in Ac₂O (3.6 mL), was added Ac₂O (3.6 mL) and concd H_2SO_4 (80 µL). The reaction mixture was stirred for 16-20 h at the same temperature, then neutralized with satd NaHCO₃ soln and concd to give a crude residue, which was extracted with CH₂Cl₂ (30 mL). The organic extract was washed with satd NaCl soln $(3 \times 100 \text{ mL})$, dried over anhyd Na_2SO_4 and concd to give a crude product. BF₃Et₂O (120 µL) was added to a soln of the crude product and thiophenol (0.3 mL) in dry CH_2Cl_2 (6 mL), and the mixture was stirred for 16 h at rt under a N₂ atmosphere, then neutralized with Et₃N and concd to a mixture, which was applied to a column of silica gel and eluted with 1:1 hexane-EtOAc to give pure compound 12 (260 mg, 67%) as an amorphous solid. $[\alpha]_{\rm D} = -38.8^{\circ}$ (c 0.5, CHCl₃); ¹H NMR (CDCl₃, 600 MHz): δ 7.75-7.00 (m 9 H, ArH), 5.55-5.40 (m, 2 H, H-1^I, $J_{1,2}$ 7.8 Hz, H-4^{II}, J 2.8 Hz), 5.40–5.30 (d, 1 H, J 3.2 Hz, H-4^{III}), 5.29–5.20 (m, 2 H, H-3^{III}, H-2^{II}), 5.19–5.15 (dd, 1 H, H-3^{II}), 5.15-5.10 (dd, 1 H, H-5^{III}), 4.95-4.90 (d, 1 H, J 3.1 Hz, H-1^{III}), 4.85–4.80 (dd, 1 H, H-2^{III}), 4.75–4.65 (m, 2 H, H-3^I, H-6b^I), 4.60–4.50 $(m, 2 H, H-1^{II}, H-6b^{II}), 4.40-4.30 (m, 2 H,$ H-2^I, H-6b^I), 4.20-4.19 (dd, 1 H, H-6a^I), 4.00-3.90 (m, 2 H, H-4^I, H-5^{II}), 3.80-3.70 (dd, 1 H, H-5^I), 2.30 (s, 3 H, Ac), 2.29 (s, 3 H, Ac), 2.27 (s, 3 H, Ac), 1.99 (s, 3 H, Ac), 1.20 (d, 3 H, J 6.4 Hz, CH₃^{III}); ¹³C NMR (CDCl₃, 100.6 MHz): δ 170.90 (C=O), 170.86 (C=O), 170.80 (C=O), 170.69 (C=O), 170.35 (C=O),

170.20 (C=O), 169.90 (C=O), 169.15 (C=O), 134.75, 133.0, 132, 129.00, 128.25, 124.00, 101.00, 95.50, 84.30, 77.30, 75.50, 72.55, 71.89, 71.45, 71.40, 69.00, 68.30, 67.88, 66.89, 64.50, 62.20, 61.00, 56.50, 21.60 (Ac), 21.20 (Ac), 20.98 (Ac), 20.88 (Ac), 20.84 (Ac), 20.81(Ac), 20.70 (2 Ac), 16.45 (CH₃); Anal Calcd for $C_{48}H_{55}NO_{23}S$: C, 55.10; H, 5.30; N, 1.34, S, 3.07. Found: C, 55.38; H, 5.29; N, 1.26, S, 2.94.

Phenyl (2,3,4-tri-O-acetyl-6-O-trimethylacetyl- β -D-galactopyranosyl)- $(1 \rightarrow 4)$ -2-deoxy-6-O-naphthymethyl-2-phthalimido-1-thio- β -Dglucopyranoside (15).—A soln of compound 13 (4.74 g, 8.73 mmol), compound 14 (6.83 g, 17.5 mmol), and SnCl₂ (4.97 g, 26.2 mmol) in dry 5:1 CH₂Cl₂-toluene (100 mL) containing 4 Å MS (25 g) was stirred at -15 °C for 1.5-2 h under a N₂ atmosphere. Silver triflate (6.73 g, 26.2 mmol) was added, and the reaction mixture was stirred overnight at -15 to 0 °C under a N₂ atmosphere, then neutralized with Et₃N. The solids were filtered off, the organic layer was washed with satd NaHCO₃ soln, water, and then dried (Na_2SO_4) . The solvent was evaporated under reduced pressure to give a crude mixture that was applied to a column of silica gel and eluted with 1:1 hexane-EtOAc to give pure 15 (5.97 g, 75%) as an amorphous solid. R_f 0.54 (1:1 hexane-EtOAc); $[\alpha]_{D}$ + 35.0° (c 0.5, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 7.86-7.80 (m, 6 H, ArH), 7.68-7.64 (m, 2 H, ArH), 7.52-7.40 (m, 5 H, ArH), 7.28–7.16 (m, 3 H, ArH), 5.65–5.63 (d, 1 H, $J_{1,2}$ 10.4 Hz, H-1^I), 5.32– 5.31 (d, 1 H, J 2.0 Hz, H-4^{II}), 5.20-5.16 (t, 1 H, J 10.0, 8.8 Hz, H-2^{II}), 4.94–4.90 (dd, 1 H, H- 3^{II}), 4.89–4.86 (d, 1 H, J 12.0 Hz, OCH_AC₁₀H₇, ABq), 4.72–4.69 (d, 1 H, J 12.0 Hz, $OCH_BC_{10}H_7$, ABq), 4.53–4.51 (d, 1 H, J 8.0 Hz), 4.47–4.42 (t, 1 H), 4.05–4.03 (m, 4 H), 3.87–3.71 (m, 4 H), 2.14–2.10 (s, 3 H, Ac), 1.96 (s, 3 H, Ac), 1.94 (s, 3 H, 2 Ac), 1.12 (s, 9 H, *t*-Bu); ¹³C NMR (CDCl₃, 100.6 MHz): δ 177.90 (C=O), 169.93 (C=O), 169.83 (C=O), 169.20 (C=O), 168.30 (C=O), 16.84 (C=O), 135.63, 134.14, 133.09, 132.64, 128.91, 128.39, 127.94, 127.81, 126.71, 126.34, 126.09, 125.95, 123.60, 123.28, 100.42, 83.57, 81.51, 78.30, 73.82, 71.43, 70.79, 70.78, 68.80, 67.99, 66.69, 61.82, 55.17, 38.67, 27.09 (3 CH₃), 20.63 (Ac),

20.52 (Ac), 20.33 (Ac); Anal Calcd for $C_{48}H_{51}NO_{15}S$: C, 63.08; H, 5.62; N, 1.53. Found: C, 62.90; H, 6.06; N, 1.98.

Phenvl (2,3,4-tri-O-acetyl-6-O-trimethylacetyl- β -D-galactopyranosyl)- $(1 \rightarrow 4)$ -[(2,3,4 $tri - O - benzyl - \alpha - L - fucopyranosyl) - (1 \rightarrow 3)] - 2$ deoxy-6-O-naphthymethyl-2-phthalimido-1*thio-\beta-D-glucopyranoside* (16).—A soln of compound 15 (5.2 g, 5.7 mmol), methyl 2,3,4tri-O-benzyl- β -L-fucopyranoside (3, 10.63 g, 22.8 mmol), and *n*-Bu₄NBr (7.36 g, 22.8 mmol) in dry 5:1 1,2-dichloroethane-DMF (30 mL) containing 4 A MS (25 g) was stirred for 2 h at rt under a N_2 atmosphere. Copper bromide (1.25 g, 5.6 mmol) was then added, and the mixture was stirred for 16-24 h at the same temperature. The solids were filtered off, the organic layer washed with satd NaHCO₃ soln, and water, dried (Na₂SO₄) and concd. The crude product was applied to a column of silica gel and eluted with 2:1 hexane-EtOAc to give compound 16 (87%) as a white solid. $R_f 0.17$ (2:1 hexane-EtOAc); $[\alpha]_D + 10.2^\circ$ (c 0.54, CHCl₃); ¹H NMR (CDCl₃, 600 MHz): δ 7.93–7.87 (m, 4 H, ArH), 7.70–7.60 (m, 3 H, ArH), 7.56–7.44 (m, 4 H, ArH), 7.40–7.36 (m, 3 H, ArH), 7.28–7.16 (m, 14 H, ArH), 6.98–6.92 (m, 3 H, ArH), 5.50–5.45 (d, 1 H, J 7.8 Hz, H-1^I), 5.24–5.18 (d, 1 H, J 2.8 Hz, H-4^{III}), 5.10-5.00 (dd, 1 H, H-2^{II}), 4.97-4.92 (d, 1 H, J_{gem} 11.6 Hz, OCHAr, ABq), 4.88-4.86 (dd, 1[°]H, J 3.6, 10.4 Hz, H-3^{II}), 4.82–4.80 (m, 2 H, OCHAr, H-1^{III}, $J_{1,2}$ 3.3 Hz), 4.80– 4.78 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1ⁱⁱ), 4.74–4.70 (m, 2 H, H-3^I, OCHAr, ABq), 4.68–4.60 (m, 2 H, H-5^{III}, J_{sem} 11.8 Hz, OCHAr, ABq), 4.40–4.32 (t, 1 H, J 10.4 Hz, H-2^I), 4.32–4.20 (dd, 4 H, 2 OCH₂Ar), 4.19–4.16 (t, 1 H, J 9.2 Hz, H-4^I), 4.14–4.00 (dd, 1 H, H-6b^{II}), 4.00–3.84 (m, 4 H, H-6a^{II}, H-6b^I, H-6a^I, H-3^{III}), 3.80 (dd, 1 H, H-2^{III}), 3.76-3.60 (m, 3 H, H-4^{III}, H-5^I, H-5^{II}), 1.94 (s, 3 H, Ac), 1.92 (s, 6 H, 2 Ac), 1.20 (d, 3 H, J 6.4 Hz, CH₃^{III}), 1.16 (s, 9 H, t-Bu); ¹³C NMR (CDCl₃, 100.6 MHz): δ 170.09 (C=O), 169.94 (C=O), 168.89 (C=O), 138.84, 138.35, 135.49, 134.42, 133.43, 133.25, 132.65, 131.89, 129.04, 128.70, 128.38, 128.34, 128.27, 128.19, 128.15, 128.09, 128.03, 127.99, 127.61, 127.42, 127.34, 127.17, 126.80, 126.49, 126.21, 126.01, 123.84, 99.77, 97.85, 84.53, 79.95, 79.77, 75.29, 74.75, 74.40, 73.88, 73.83,

73.19, 72.52, 71.20, 70.60, 69.20, 68.05, 66.90, 66.74, 60.30, 55.76, 20.80 (3 Ac), 20.67 (Ac), 16.89 (CH₃); Anal Calcd for $C_{75}H_{79}NO_{19}S$ · H_2O : C, 66.80; H, 5.90; N, 1.04, S, 2.38. Found: C, 66.33; H, 6.02; N, 0.70, S, 2.24.

2,3,4-Tri-O-acetyl-6-O-benzyl-α-D-galactopyranosyl bromide (19).—Compound 18 was obtained in quantitative yield by treatment of compound 17 with BnBr in the presence of powdered KOH and 18-crown-6 at rt for 4-5 h in dry THF. The removal of the O-isopropylidene group was achieved by treatment of compound 18 with 1 N HCl in refluxing 1,4-dioxane, and the product was acetylated with 1:1 pyridine-Ac₂O and followed by treatment of the acetylated compound with BiBr₃ as described in the literature [17]. After purification by silica gel chromatography (2:1 hexane-EtOAc), compound 19 was obtained in 59% yield. R_f 0.45 (2:1 hexane-EtOAc); ¹H NMR (CDCl₃, 400 MHz): δ 7.42–7.26 (m, 5) H, ArH), 6.76–6.72 (d, 1 H, H-1), 5.58–5.52 (d, 1 H, J 2.8 Hz, H-4), 5.44–5.36 (dd, 1 H, H-2), 5.10-5.00 (dd, 1 H, H-3), 4.56-4.50 (d, 1 H, J 12.6 Hz, OCHPh, ABq), 4.50–4.40 (d, 1 H, OCHPh), 3.50-3.40 (m, 3 H, H-6a, H-6b), 2.05 (s, 3 H, Ac), 2.03 (s, 3 H, Ac), 1.99 (s, 3 H, Ac); ¹³C NMR (CDCl₃, 100.6 MHz): δ 170.30 (C=O), 170.10 (C=O), 169.59 (C=O), 137.44, 128.73, 128.21, 108.51, 73.86, 72.65, 70.46, 69.31, 67.29, 67.05, 20.90 (Ac), 20.81 (Ac), 20.77 (Ac).

Methyl 2 - acetamido - 2 - deoxy - 4,6 - O - (pmethoxybenzylidene) - α - D - galactopyranoside (20).—*p*-Toluenesulfonic acid monohydrate (769 mg) was added to a soln of methyl 2-acetamido-2-deoxy- α -D-galactopyranoside (3.35 g, 14.3 mol) and α,α -dimethoxy(pmethyloxy)toluene (3.90 g, 21.39 mmol) in dry MeCN (105 mL). The mixture was stirred overnight at rt and quenched with Et₃N, and concd under reduced pressure to give a crude product, which was then applied to a column of silica gel and eluted with 30:1 CH₂Cl₂-MeOH to give pure compound 20 (4.40 g, 87%) as a white solid. R_f 0.39 (1:1 hexane-EtOAc); ¹H NMR (CDCl₃, 400 MHz): δ 7.46-7.43 (d, 2 H, J 8.4 Hz, ArH), 6.91-6.89 (d, 2 H, J 8.0 Hz, ArH), 5.74–5.72 (d, 1 H, J 8.0 Hz, NHAc), 5.53 (s, 1 H, PhCHO₂), 4.844.83 (d, 1 H, J 2.8 Hz, H-1), 4.48–4.43 (m, 1 H), 4.28–4.19 (m, 3 H), 4.07–4.04 (d, 1 H), 3.81 (s, 3 H, OCH₃), 3.64 (s, 1 H), 3.40 (s, 3 H, OCH₃), 1.98 (s, 3 H, Ac);); ¹³C NMR (CDCl₃, 100.6 MHz): δ 160.91 (C=O), 130.34, 127.93, 113.87, 101.49, 99.67, 76.92, 69.54, 69.35, 63.05, 55.69, 55.56, 50.66, 23.67 (Ac).

Methyl $(2,3,4-tri-O-acetyl-6-O-benzyl-\beta-$ D - galactopyanosyl) - $(1 \rightarrow 3)$ - 2 - acetamido - 2 $deoxy-\alpha$ -D-galactopyranoside (21).—To a mixture of compound 20 (2.20 g, 6.23 mmol), powered Hg(CN)₂ (7.6 g) and HgBr₂ (760 mg) in dry CH₂Cl₂ (60 mL) containing 4 Å MS (20 g) was added 2,3,4-tri-O-acetyl-6-O-benzyl-a-D-galactopyranosyl bromide 19 (4.27 g, 9.30 mmol), and the mixture was stirred overnight at rt. The reaction mixture was diluted with benzene and washed with satd aq NaHCO₃, 10% KI soln, and water. The organic layer was dried with Na₂SO₄ and concd. The crude residue was applied to a column of silica gel and eluted with 20:1 CH₂Cl₂-MeOH to give compound 21a (2.3 g, 51%) as an amorphous solid. ¹H NMR (CDCl₃, 400 MHz): δ 7.48– 7.42 (d, 2 H, J 8.7 Hz, ArH), 7.40-7.28 (d, 5 H, ArH), 6.96-6.88 (d, 2 H, J 8.6 Hz, ArH), 5.70-5.60 (d, 1 H, J 7.8 Hz, NHAc), 5.47 (s, 1 H, PhCHO₂), 5.42–5.40 (d, 1 H, J 4.4 Hz, H-4^{II}), 5.20–5.10 (dd, 1 H, H-2^{II}), 5.05–4.95 (dd, 1 H, H-3^{II}), 4.80–4.70 (d, 1 H, J 4.0 Hz, H-1^I), 4.70–4.60 (d, 1 H, J_{1.2} 8.0 Hz, H-1^{II}), 4.56–4.44 (dd, 2 H, OCH₂Ph, AB), 4.30–4.20 (d, 1 H), 4.20–4.10 (dd, 1 H), 4.00–3.85 (m, 3 H), 3.85–3.75 (m, 4 H, OCH₃), 3.65–3.55 (dd, 1 H), 3.55–3.50 (m, 2 H), 3.42 (s, 3 H, OCH₃), 2.08 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.95 (s, 3 H, Ac), 1.94 (s, 3 H, Ac); ¹³C NMR (CDCl₃, 100.6 MHz): *δ* 171.12 (C=O), 171.10 (C=O), 170.40 (C=O), 161.50 (C=O), 131.80, 129.50, 128.83, 128.80, 128.40, 114.50, 103.18, 101.72, 101.51, 76.71, 76.46, 74.44, 73.27, 72.22, 70.06, 69.82, 69.02, 68.60, 63.85, 56.22, 48.99, 24.17 (NAc), 21.39 (Ac), 21.33 (Ac), 21.13 (Ac); Anal Calcd for C₃₆H₄₅NO₁₅: C, 59.07; H, 6.20; N, 1.92. Found: C, 58.97; H, 6.19; N, 1.61.

Compound **21a** was treated with 60% HOAc at 60–65 °C for 1.5 h and purified by silica gel column to give pure compound **21** (76%) as an amorphous solid. R_f 0.47 (20:1 CH₂Cl₂–MeOH); [α]_D + 5.7° (c, 0.1, CHCl₃); ¹H NMR (CDCl₃, 400 MHz): δ 7.60–7.20 (m,

5 H, ArH), 5.60–5.52 (m, 1 H, J 8.6 Hz, NHAc), 5.44-5.40 (d, 1 H, J 3.0 Hz), 5.20-5.12 (dd, 1 H), 5.04–4.96 (dd, 1 H), 4.80–4.72 (d, 1 H, J 3.2 Hz, H-1^I), 4.60–4.56 (d, 1 H, J 7.8 Hz, H-1^{II}), 4.54–4.48 (d, 1 H, J_{gem} 12.6 Hz, OCHPh, ABq), 4.48-4.40 (d, 1 H, J_{gem} 12.4 Hz, OCHPh, ABq), 4.10 (s, 1 H), 4.00-3.80 (m, 3 H), 3.80–3.70 (m, 4 H), 3.60–3.45 (m, 3 H), 3.44 (s, 3 H, OCH₃), 2.08 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 1.99 (s, 3 H, Ac), 1.98 (s, 3 H, Ac); ¹³C NMR (CDCl₃, 100.6 MHz): δ 170.50 (C=O), 170.30 (C=O), 169.70 (C=O), 128.75, 128.25, 128.00, 101.75, 99.30, 74.10, 72.85, 71.00, 69.83 (2 C), 69.21, 68.20, 67.85, 63.00, 55.21, 48.00, 23.60 (NAc), 20.90 (Ac), 20.83 (Ac), 20.75 (Ac); Anal Calcd for $C_{28}H_{39}NO_{14}$: C, 54.81; H, 6.41; N, 2.28. Found: C, 54.28; H, 6.19; N, 1.98.

Methyl $[(2,3,4,6-tetra-O-acetyl-\beta-D-galac$ topyranosyl)- $(1 \rightarrow 4)$ - $[(2,3,4-tri-O-acetyl-\alpha-L$ fucopyranosyl)- $(1 \rightarrow 3)$]-6-O-acetyl-2-deoxy-2phthalimido - β - D - glucopyranosyl) - $(1 \rightarrow 6)$ - $[(2,3,4-tri-O-acetyl-6-O-benzyl-\beta-D-galacto$ pyranosyl]- $(1 \rightarrow 3)$ -2-acetamido-4-O-acetyl-2deoxy-a-D-galactopyranoside (23).—A soln of trisaccharide donor 12 (264 mg, 0.21 mmol), disaccharide acceptor 21 (233 mg, 0.19 mmol), and N-iodosuccinimide (NIS, 126 mg, 0.62 mmol) in dry CH₂Cl₂ (12 mL) containing 4 Å MS (8 g) was stirred for 2 h at -65 to -60 °C under a N₂ atmosphere. Trifluoromethanesulfonic acid (TfOH) (20 µL) in dry CH_2Cl_2 (2 mL) was then added dropwise, and the mixture was stirred for 2 h at the same temperature. The mixture was then neutralized with satd aq NaHCO₃ soln. The solids were filtered off, the organic layer was washed with satd NaHCO₃ soln, 10% Na₂S₂O₃, and water, and then it was dried (Na_2SO_4) and concd. The crude mixture was applied to a column of silica gel and eluted with 30:1 CH_2Cl_2 -MeOH to give pure compound 22 (200 mg, 41%) as a glassy white solid. Compound 22 was further acetylated with 1:1 pyridine $-Ac_2O$ (10 mL) in the presence of a catalytic amount of DMAP (5 mg). The soln was concd and the crude product was purified by silica gel column chromatography (30:1 CH_2Cl_2 –MeOH) to give compound 23 in quantitative yield as an amorphous solid. R_f 0.46 (30:1 CH₂Cl₂-MeOH); ¹H NMR

(CDCl₃, 600 MHz): δ 7.88–7.68 (m, 4 H, ArH), 7.40-7.24 (m, 5 H, ArH), 5.53-5.50 (d, 1 H, J 9.2 Hz, NHAc), 5.47-5.46 (d, 1 H, J 3.2 Hz, H-4^{II}), 5.38–5.37 (d, 1 H, J 2.8 Hz, H-4^{IV}), 5.34-5.33 (d, 1 H, J 2.0 Hz, H-4^V), 5.17-5.08 (m, 3 H, H-4^I, H-3^V, H-2^{II}), 5.05-4.88 (m, 6 H, H-2^{IV}, H-1^{III}, H-3^{II}, H-5^V, H-1^V, H-3^{IV}), 4.81–4.75 (dd, 1 H, J 4.0, 11.0 Hz, H-2^v), 4.72–4.60 (m, 2 H, H-3^{III}, H-6b^{III}), 4.57-4.40 (m, 5 H, OCHPh, ABq, H-1^{II}, H-1^{IV}, H-6b^{II}, OCHPh, ABq), 4.32–4.16 (m, 5 H, H-1^I, H-6a^{II}, H-2^I, H-2^{III}, H-6a^{III}), 3.97-3.86 (m, 2 H, H-4^{III}, H-5^{II}), 3.84-4.71 (m, 4 H, H-6b^I, H-3^I, H-5^I, H-5^{IV}), 3.63-3.60 (dd, 1 H, H-5^{III}), 3.56–3.48 (dd, 1 H, H-6b^{IV}), 3.46– 3.40 (dd, 1 H, H-6a^{IV}), 3.28-3.18 (dd, 1 H, H-6a^I), 2.89 (s, 3 H, OCH₃), 2.18 (s, 3 H, Ac), 2.17 (s, 9 H, 3 Ac), 2.10 (s, 3 H, Ac), 2.09 (s, 3 H, Ac), 2.05 (s, 6 H, 2 Ac), 2.03 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.97 (s, 3 H, Ac), 1.90 (s, 3 H, Ac), 1.89 (s, 3 H, Ac), 1.21 (d, 3 H, J 6.4 Hz, CH₃^V); ¹³C NMR (CDCl₃, 100.6 MHz): δ 170.82 (C=O), 170.73 (C=O), 170.68 (C=O), 170.59 (C=O), 170.37 (C=O), 170.33 (C=O), 170.30 (C=O), 170.23 (C=O), 170.11 (C=O), 169.84 (C=O), 169.68 (C=O), 169.64 (C=O), 169.07 (C=O), 134.47, 128.66, 128.09, 127.99, 100.84, 100.80, 98.77, 98.29, 95.28, 75.36, 73.81, 73.76, 73.36, 72.85, 72.52, 71.54, 71.24, 71.06, 70.17, 69.92, 69.09, 68.51, 68.23, 67.99, 67.75, 67.50, 66.81, 64.41, 61.72, 60.87, 56.33, 54.70, 48.96, 31.02 (Ac), 23.46 (Ac), 20.96 (Ac), 20.92 (Ac), 20.87 (Ac), 20.80 (Ac), 20.76 (Ac), 20.64 (Ac), 15.99 (CH₃); Anal Calcd for $C_{72}H_{90}N_2O_{38}$: C, 54.34; H, 5.70; N, 1.76. Found: C, 54.49; H, 5.81; N, 1.64.

Methyl (2,3,4,6-tetra-O-acetyl-β-D-galacto $pyranosyl) - (1 \rightarrow 4) - [(2,3,4 - tri - O - acetyl - \alpha - L$ fucopyranosyl) - $(1 \rightarrow 3)$] - 2 - acetamido - 6 - O $acetyl - 2 - deoxy - \beta - D - glucopyranosyl) - (1 \rightarrow 6)$ -[(2,3,4-tri-O-acetyl-6-O-benzyl-β-D-galactopyranosyl)- $(1 \rightarrow 3)$]-2-acetamido-4-O-acetyl-2deoxy- α -D-galactopyranoside (24).—Compound 23 (80 mg, 0.05 mmol) in a mixture of MeOH (5 mL) and $NH_2NH_2 \cdot H_2O$ (1 mL) was stirred for 4-5 h at 80-85 °C. The reaction mixture was concd under reduced pressure to give a crude mixture, which was co-evaporated with toluene and acetylated with 1:1 Ac_2O -pyridine (2 mL) with a catalytic amount of DMAP at rt overnight. The acety-

lated mixture was concd and passed through a short column of silica gel and eluted with 30:1 CH_2Cl_2 -MeOH to give compound 24 (65 mg, 86%) as an amorphous solid. $[\alpha]_{\rm D} = -16.6^{\circ} (c$ 0.2, CHCl₃); ¹H NMR (CDCl₃, 600 MHz): δ 7.40-7.25 (m, 5 H, ArH), 6.00-5.90 (d, 1 H, J 8.3 Hz, NHAc), 5.80-5.78 (d, 1 H, J 8.4 Hz, NHAc), 5.43–5.37 (m, 4 H, H-1^{III}, H-1^V, H-4^{II}, H-4^{IV}), 5.26–5.24 (d, 1 H, J 2.8 Hz, H-4^I), 5.22-5.18 (dd, 1 H, J 3.2, 11.2 Hz), 5.12-4.95 $(m, 5 H, H-2^{IV}, H-2^{II}, H-2^{V}, H-3^{IV}, H-3^{II}),$ 4.95–4.88 (dd, 1 H, H-5^V), 4.74–4.73 (d, 1 H, $J_{1,2}$ 3.6 Hz, H-1^I), 4.59–4.42 (m, 7 H, H-1^{II}, $H-6b^{IV}$, OCH_APh , $H-6b^{III}$, $H-1^{IV}$, $H-2^{I}$, OCH_BPh), 4.32–4.29 (dd, 1 H, H-6a^{III}), 4.14– 4.10 (dd, 1 H, H-6a^I), 4.00–3.99 (dd, 1 H, $H-3^{I}$), 3.97–3.93 (m, 1 H, $H-5^{I}$), 3.87 (t, 1 H, $H-5^{III}$), 3.82–3.79 (m, 4 H, $H-5^{II}$, $H-6b^{I}$), 3.60-3.50 (m, 2 H, H-6b^{II}, H-5^{IV}), 3.50-3.40 (m, 2 H, H-6a^{II}, H-6a^I), 3.39 (s, 3 H, OCH₃), 2.19 (s, 3 H, Ac), 2.18 (s, 3 H, Ac), 2.15 (s, 3 H, Ac), 2.09 (s, 3 H, Ac), 2.08 (s, 3 H, Ac), 2.07 (s, 3 H, Ac), 2.06 (s, 3 H, Ac), 1.98 (s, 3 H, Ac), 1.97 (s, 3 H, Ac), 1.95 (s, 3 H, Ac), 1.94 (s, 3 H, Ac), 1.69 (s, 6 H, 2 Ac), 1.24-1.20 (d, 3 H, J 6.4 Hz, CH_3^V); ¹³C NMR (CDCl₃, 100.6 MHz): δ 171.85 (C=O), 171.20 (C=O), 171.15 (C=O), 170.90 (C=O), 170.80 (C=O), 170.60 (C=O), 170.49 (C=O), 170.43 (C=O), 170.40 (C=O), 170.35 (C=O), 170.20 (C=O), 170.15 (C=O), 170.10 (C=O), 169.40 (C=O), 137.52, 128.83, 128.33, 128.25, 100.75 (2 C), 100.50, 98.90, 95.50, 74.85, 73.89, 73.25, 72.60, 72.20, 71.60, 71.40, 71.30, 71.20, 69.90, 69.25, 69.00, 68.60, 68.45, 68.25, 67.90, 67.60, 66.98, 64.50, 62.25, 61.00, 55.80, 49.85, 23.57 (NAc), 23.40 (NAc), 21.16 (Ac), 21.06 (Ac), 21.02 (2 Ac), 20.98 (Ac), 20.94 (Ac), 20.86 (2 Ac), 20.82 (2 Ac), 20.76 (Ac), 20.72 (Ac), 16.20 (CH₃); Anal Calcd for $C_{66}H_{90}N_2O_{37}$: C, 52.73; H, 6.03; N, 1.86. Found: C, 53.16; H, 5.30; N, 1.56.

Methyl (2,3,4,6-tetra-O-acetyl- β -D-galactopyranosyl)- $(1 \rightarrow 4)$ - $[(2,3,4-tri-O-acetyl-<math>\alpha$ -Lfucopyranosyl)- $(1 \rightarrow 3)]$ - 2- acetamido - 6- Oacetyl-2-deoxy- β -D-glucopyranosyl)- $(1 \rightarrow 6)$ - $[(2,3,4-tri-O-acetyl-6-O-sulfo-<math>\beta$ -D-galactopyranosyl)- $(1 \rightarrow 3)]$ -2-acetamido-4-O-acetyl-2-deoxy- α -D-galactopyranoside sodium salt (26).— A soln of compound 24 (25 mg, 0.017 mmol) and 10% Pd-C (25 mg) in 1:4 MeOH– CH_2Cl_2 (3 mL) was stirred for 2.5 h at rt under a H_2 atmosphere. The solids were filtered off, and the organic layer was concd. The crude residue was treated for 6-9 h at 0-25 °C with the SO₃·pyridine complex (10 mg) in pyridine (2 mL), then quenched with MeOH and treated with Amberlite IR 120 (Na⁺) cation-exchange resin in MeOH at rt for 1.5 h. The filtrate was concd and purified by a short column of silica gel eluted with 10:1 CH_2Cl_2 -MeOH to give pure compound 26 (25 mg, 97% in two steps) as an amorphous solid. ¹H NMR (CD₃OD, 600 MHz): δ 5.48– 5.40 (m, 3 H), 5.40-5.30 (m, 2 H), 5.28-5.20 (dd, 1 H), 5.16-4.4.92 (m, 5 H), 4.75-4.70 (d, 1 H), 4.70–4.60 (m, 3 H), 4.48–4.32 (m, 2 H), 4.32–4.28 (m, 2 H), 4.24–4.04 (m, 4 H), 4.04– 3.92 (m, 3 H), 3.92–3.60 (m, 6 H), 3.52–3.44 (m, 1 H), 3.38 (s, 3 H, OCH₃), 2.17 (s, 3 H, Ac), 2.16 (s, 3 H, Ac), 2.15 (s, 3 H, Ac), 2.14 (s, 3 H, Ac), 2.09 (s, 6 H, 2 Ac), 2.08 (2s, 6 H, 2 Ac), 2.04 (s, 3 H, Ac), 2.00 (s, 3 H, Ac), 1.96 (2s, 6 H, 2 Ac), 1.93 (s, 3 H, Ac), 1.90 (s, 3 H, Ac), 1.20 (d, 3 H, J 6.4 Hz, CH₃); ¹³C NMR (CD₃OD, 100.6 MHz): δ 173.38 (C=O), 173.21 (C=O), 172.57 (C=O), 172.55 (C=O), 172.33 (C=O), 172.23 (C=O), 172.11 (C=O), 171.60 (C=O), 171.16 (C=O), 103.03, 102.36, 101.79, 100.14, 96.99, 76.66, 75.48, 74.43, 74.15, 73.01, 72.60, 72.42, 72.32, 72.26, 72.02, 70.60, 70.52, 70.34, 69.82, 69.63, 69.38, 68.81, 68.70, 66.07, 65.45, 63.56, 62.52, 56.87, 56.14, 55.69, 23.65 (NAc), 23.22 (NAc), 21.47 (Ac), 21.35 (Ac), 21.30 (Ac), 21.21 (Ac), 21.17 (Ac), 21.07 (Ac), 20.99 (Ac), 20.96 (Ac), 20.93 (Ac), 16.70 (CH_3) .

Methyl (β - D - galactopyranosyl) - (1 \rightarrow 4)-[(α -L-fucopyranosyl)-(1 \rightarrow 3)]-(2-acetamido-2deoxy- β -D-glucopyranosyl)-(1 \rightarrow 6)-[(6-O-sulfo- β -D-galactopyranosyl)-(1 \rightarrow 3)]-2-acetamido-2deoxy- α -D-galactopyranoside sodium salt (1). —Sodium methoxide (80 µL of a 1 M soln) was added to a soln of compound **26** (25 mg, 0.017 mmol) in 1:1 MeOH–water (3 mL). The reaction mixture was stirred for 24 h at rt and concd. The crude product was applied to a short column of silica gel and eluted with 3:1:1 n-C₃H₇OH–HOAc–water to give pure compound **1** (8 mg, 48%) as an amorphous solid. R_f 0.26 (3:1:1 n-C₃H₇OH–HOAc–water); ¹H NMR (D₂O, 600 MHz): δ 5.16–5.08 (d, 1 H,

 $J_{1,2}$ 3.0 Hz, H-1^V), 4.88–4.78 (dd, 1 H, H-5^V), 4.78-4.60 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1^I), 4.60-4.52 (d, 1 H, $J_{1.2}$ 8.8 Hz, H-1^{II}), 4.52–4.46 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{IV}), 4.46–4.44 (d, 1 H, $J_{1,2}$ 7.6 Hz, H-1^{II}), 4.36-4.28 (dd, 1 H, H-2^I), 4.28-4.24 (d, J 2.8 Hz, H-4^I), 4.22-4.18 (d, 2 H), 4.14-3.84 (m, 11 H, H-5^I, H-4^{III}, H-4^{II}, H-2^{III}, H-4^{IV}, H-3^{III}), 3.84-3.46 (m, 12 H, H-4^V, H-6a^I, H-3^{IV}, H-3^{II}, H-5^{III}, H-2^{IV}, H-2^{II}), 3.36 (s, 3 H, OCH₃), 2.13 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.20 (d, 3 H, J 6.4 Hz, CH₃^V); ¹³C NMR (D₂O, 100.6 MHz): δ 173.50 (C=O), 173.20 (C=O), 103.40, 100.45, 100.22, 97.45, 97.20, 76.48, 74.45, 73.90, 73.83, 72.80, 71.55, 71.53, 71.50, 70.98, 70.00, 69.53 (2 C), 68.54, 68.52, 67.90, 67.40, 67.30, 66.75, 66.25, 65.63, 60.50, 58.90, 54.98, 54.00, 47.50, 21.25 (Ac), 21.00 (Ac), 14.25 (CH₃^V); FABMS (m/z) (positive ion mode): Calcd for C₃₅H₅₉N₂NaO₂₈S: 1012; found: 1034.0 $[M^+ + Na]$, 1012 $[M^+]$.

(2,3,4-tri-O-acetyl-6-O-trimethyl-Methyl acetyl- β -D-galactopyranosyl)- $(1 \rightarrow 4)$ -[(2,3,4 $tri - O - benzyl - \alpha - L - fucopyranosyl) - (1 \rightarrow 3)] - 2$ deoxy-6-O-naphthylmethyl-2-phthalimido- β -Dglucopyranosyl)- $(1 \rightarrow 6)$ -[(2,3,4-tri-O-benzoyl- β - D - galactopyranosyl) - $(1 \rightarrow 3)$] - 2 - acetamido -2-deoxy- α -D-galactopyranoside (29).—A soln of trisaccharide donor 16 (722 mg, 0.54 mmol), disaccharide acceptor 27 (460 mg, 0.50 mmol), and N-iodosuccinimide (NIS, 365 mg, 0.62 mmol) in dry CH₂Cl₂ (12 mL) containing 4 Å MS (10 g) was stirred for 2 h at -65 to -70 °C under a N₂ atmosphere. Trifluoromethanesulfonic acid (TfOH) (60 µL) in dry CH₂Cl₂ (2 mL) was then added dropwise, and the mixture was stirred for 2 h at the same temperature. The mixture was neutralized with satd aq NaHCO₃. The solids were filtered off, and the organic layer was washed with satd NaHCO₃ soln, 10% Na₂S₂O₃, and water. The organic extract was dried (Na_2SO_4) and concd under reduced pressure. The crude mixture was applied to a column of silica gel and eluted with 1:1 hexane-EtOAc to give pure compound 28 (490 mg, 46%) as an amorphous solid. Compound 28 (490 mg, 0.23 mmol), 2,6-lutidine (10 μ L) and thiourea (52 mg) in 1:1 EtOH- CH_2Cl_2 (30 mL) were stirred overnight at 60-65 °C. The reaction mixture was then concd to give a crude product, which was applied to a column of to give pure compound 29 (390 mg, 84%) as an amorphous solid. R_f 0.47 (1:3 hexane — EtOAc); $[\alpha]_{D}$ + 70.8° (c 0.6, CHCl₃); ¹H NMR (CDCl₃, 600 MHz): δ 8.10-7.82 (m, 10 H, ArH), 7.80–7.77 (m, 3 H, ArH), 7.60–7.50 (m, 2 H, ArH), 7.50-7.30 (m, 10 H, ArH), 7.30-7.10 (m, 15 H, ArH), 7.00-6.90 (m, 1 H, ArH), 5.75–5.15 (m, 2 H, H-4^{II}, H-2^{II}), 5.60– 5.50 (dd, 1 H), 5.30-5.20 (d, 1 H), 5.15-5.05 (m, 2 H, H-4^v, H-1^{III}, $J_{1,2}$ 8.6 Hz), 5.01–4.98 (dd, 1 H, H-2^{IV}), 4.96-4.92 (d, 2 H, J_{gem} 12.6 Hz, 2 OCHAr), 4.90–4.84 (d, 1 H, J_{1.2} 7.8 Hz, H-1^{II}), 4.84–4.75 (m, 3 H, OCHAr, H-1^I, H- 3^{IV}), 4.75-4.64 (m, 3 H, $H-1^{IV}$, $H-3^{III}$, OCHAr), 4.64–4.60 (m, 2 H, H-5^V), 4.60– 4.52 (d, 2 H, J_{gem} 12.4 Hz, 2 OCHPh), 4.40-4.32 (m, 2 H, H-2^{III}), 4.32–4.24 (dd, 2 H, OCH₂Ph), 4.20–4.12 (t, 1 H, H-4^{III}), 4.12– 4.04 (m, 2 H), 4.04–3.96 (t, 1 H, H-5^{II}), 3.92–3.84 (m, 2 H, H-3^I), 3.84–3.76 (m, 1 H), 3.76-3.69 (dd, 1 H, H-2^I), 3.69-3.48 (m, 7 H, H-5^{III}), 3.12-3.04 (t, 1 H), 2.90-2.84 (t, 1 H), 2.84 (s, 3 H, OCH₃), 1.92 (s, 3 H, Ac), 1.84 (s, 3 H, Ac), 1.80 (s, 3 H, Ac), 1.79 (s, 3 H, Ac), 1.20 (d, 3 H, J 6.4 Hz, CH_3^V), 1.12 (s, 9 H, *t*-Bu); ¹³C NMR (CDCl₃, 100.6 MHz): δ 177.85 (C=O), 170.20 (C=O), 170.00 (C=O), 169.90 (C=O), 168.90 (C=O), 166.85 (C=O), 165.78 (C=O), 165.00 (C=O), 138.85, 138.45, 135.10, 134.23, 134.00, 133.60, 133.48, 133.41, 133.25, 130.27, 130.00, 129.86, 128.89, 128.76, 128.47, 128.40, 128.30, 128.24, 128.18, 128.16, 120.05, 127.82, 127.60, 127.36, 127.25, 126.60, 126.30, 126.04, 123.60, 102.30, 99.86, 99.00, 98.50, 97.80, 80.00, 79.86, 75.66, 75.45, 75.20, 75.00, 74.50, 74.20, 73.21, 72.55, 71.89, 71.40, 70.50, 70.34, 69.30, 69.20, 68.80, 68.50, 68.00, 67.78, 67.00, 66.70, 61.00, 60.30, 56.50, 54.80, 48.00, 38.85, 27.50, 22.50 (Ac), 20.58 (3 Ac), 16.85 (CH₃); Anal Calcd for $C_{105}H_{110}N_2O_{33}$: C, 65.60; H, 5.65; N, 1.43. Found: C, 65.35; H, 5.81; N, 1.64.

Methyl (2,3,4-tri-O-acetyl-6-O-trimethylacetyl- β -D-galactopyranosyl)- $(1 \rightarrow 4)$ -[(2,3,4) $tri - O - benzyl - \alpha - L - fucopyranosyl) - (1 \rightarrow 3)] - 2$ deoxy-6-O-naphthylmethyl-2-phthalimido- β -Dglucopyranosyl)- $(1 \rightarrow 6)$ -[(2,3,4-tri-O-benzoyl-6-O-sulfo- β -D-galactopyranosyl)- $(1 \rightarrow 3)$]-2acetamido - 2 - deoxy - α - D - galactopyranoside sodium salt (30).—Sulfur trioxide-pyridine

(35 mg, 0.23 mmol) was added to a cold (ice bath) soln of compound 29 (300 mg, 0.15 mmol) in dry pyridine (2 mL). The mixture was stirred for 18-24 h at the same temperature then guenched with MeOH and treated in MeOH with Amberlite IR 120 (Na⁺) cationexchange resin. The filtrate was concd to give a crude residue, which was applied to a short column of silica gel and eluted with 30:1 CH_2Cl_2 -MeOH to give pure compound 30 (260 mg, 82%) as an amorphous solid. $[\alpha]_{D}$ + 38° (c 0.2, CHCl₃); ¹H NMR (CD₃OD, 600 MHz): δ 8.15–7.86 (m, 10 H, ArH), 7.90–7.78 (m, 2 H, ArH), 7.60-7.50 (m, 3 H, ArH), 7.50-7.40 (m, 10 H, ArH), 7.30-7.15 (m, 14 H, ArH), 7.00-6.90 (m, 2 H, ArH), 5.33-5.26 (m, 2 H, H- 4^{II} , H- 2^{II}), 5.70–5.55 (dd, 1 H), 5.25-5.20 (d, 1 H), 5.15-5.08 (m, 2 H, H-4^{IV}) H-1^{III} , $J_{1,2}$ 8.6 Hz), 5.05–4.98 (dd, 1 H, H-2^{IV}), 4.96–4.94 (d, 1 H, J_{gem} 12.6 Hz, OCHAr), 4.90–4.84 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{II}), 4.84– 4.77 (m, 4 H, 2 OCHAr, H-1^I, H-3^{IV}), 4.76-4.68 (m, 3 H, H-1^{IV}, H-3^{III}, OCHAr), 4.64–4.60 (m, 2 H, H-5^v), 4.60–4.52 (d, 2 H, J_{gem} 12.4 Hz, 2 OCHPh), 4.48-4.32 (m, 2 H, H-2^{III}), 4.32–4.24 (dd, 2 H, OCH₂Ph), 4.20– 4.12 (t, 1 H, H- 4^{V}), 4.12–4.04 (m, 2 H), 4.04-3.96 (t, 1 H), 3.92-3.84 (m, 2 H, H-3^I), 3.84-3.76 (m, 1 H), 3.76-3.69 (dd, 1 H, H-2^I), 3.69-3.48 (m, 7 H, H-5^{III}), 3.12-3.04 (m, 1 H), 2.90–2.84 (m, 1 H), 2.84 (s, 3 H, OCH₃), 1.92 (s, 3 H, Ac), 1.88 (s, 3 H, Ac), 1.87 (s, 3 H, Ac), 1.80 (s, 3 H, Ac), 1.21 (d, 3 H, J 6.4 Hz, CH_3^V), 1.12 (s, 9 H, *t*-Bu); ¹³C NMR (CDCl₃, 100.6 MHz): δ 177.86 (C=O), 170.26 (C=O), 170.05 (C=O), 169.98 (C=O), 168.93 (C=O), 166.88 (C=O), 165.79 (C=O), 165.00 (C=O), 138.95, 138.45, 135.10, 134.23, 134.08, 133.60, 133.48, 133.41, 133.26, 130.27, 130.05, 129.85, 128.86, 128.76, 128.37, 128.30, 128.28, 128.24, 128.15, 128.11, 120.05, 127.88, 127.65, 127.36, 127.35, 126.80, 126.37, 126.24, 123.60, 102.30, 99.86, 99.00, 98.50, 97.80, 80.00, 79.86, 75.66, 75.45, 75.20, 75.08, 74.50, 74.20, 73.21, 72.55, 71.89, 71.46, 70.55, 70.34, 69.34, 69.20, 68.85, 68.50, 68.00, 67.86, 67.80, 66.70, 61.06, 60.30, 56.50, 54.20, 48.25, 38.85, 27.50, 22.60 (Ac), 20.59 (3 Ac), 16.45 (CH₃).

Methyl (2,3,4-tri-O-acetyl-6-O-trimethylacetyl- β -D-galactopyranosyl)- $(1 \rightarrow 4)$ -[(2,3,4 $tri - O - benzyl - \alpha - L - fucopyranosyl) - (1 \rightarrow 3)] - 2$ - deoxy-2-phthalimido-6-O-sulfo- β -D-glucopyranosyl) - $(1 \rightarrow 6)$ - [(2,3,4 - tri - O - benzoyl - 6 - O - b $sulfo - \beta - D - galactopyranosyl) - (1 \rightarrow 3) - 2 - aceta$ mido-2-deoxy- α -D-galactopyranoside disodium salt (32).—To a soln of compound 30 (235 mg, 0.12 mmol) in 4:1:trace CH₂Cl₂-MeOHwater (10 mL) was added DDQ (40 mg). After stirring for 3.5 h at rt, an additional portion of DDQ (20 mg) was added, and the mixture was stirred at the same temperature for a total of 16 h. The mixture was concd under reduced pressure to give a crude residue, which was dissolved in CH₂Cl₂ (100 mL) and washed with satd NaHCO₃ soln $(3 \times 100 \text{ mL})$. The organic extract was dried over Na₂SO₄ and concd. The crude product was applied to a column of silica gel and eluted with 20:1 CH_2Cl_2 -MeOH to give pure compound 31 (120 mg, yield: 51%) as an amorphous solid. Compound 31 was treated with SO₃·pyridine for 12 h in dry pyridine at 0-5 °C, then purified by a short column of silica gel that was eluted with 15:1 CH₂Cl₂-MeOH to give pure compound 32 (79%) as an amorphous solid. $[\alpha]_D$ + 59° (c 0.5, CHCl₃); ¹H NMR (D₂O, 600 MHz): δ 8.10–7.82 (m, 10 H, ArH), 7.80-7.77 (m, 3 H, ArH), 7.70-7.59 (m, 2 H, ArH), 7.56-7.30 (m, 6 H, ArH), 7.30-7.15 (m, 12 H, ArH), 7.00-6.90 (m, 1 H, ArH), 5.70–5.65 (m, 2 H, H-4^{II}, H-2^{II}), 5.60– 5.50 (dd, 1 H, H-3^{II}), 5.30–5.20 (d, 1 H), 5.15-5.05 (m, 2 H, H-4^{IV}, H-1^{III}, $J_{1,2}$ 8.6 Hz), 5.01-4.98 (dd, 1 H, H-2^{IV}), 4.96-4.92 (d, 1 H, J_{gem} 12.6 Hz, OCHAr), 4.90-4.84 (d, 1 H, J₁, 7.8 Hz, H-1^{II}), 4.84–4.75 (m, 3 H, OCHAr, H-1^I, H-3^{IV}), 4.75–4.64 (m, 3 H, H-1^{IV}, H-3^{III}, OCHAr), 4.64-4.60 (m, 2 H, H-5^V), 4.60-4.52 (d, 1 H, J_{gem} 12.4 Hz, OCHPh), 4.04-4.32 (m, 2 H, H-2^{III}), 4.32–4.24 (dd, 2 H, OCH₂Ph), 4.20–4.12 (t, 1 H, H-4^{III}), 4.12– 4.04 (m, 2 H), 4.04–3.96 (t, H-5^{II}), 3.92–3.84 $(m, 2 H, H-3^{I}), 3.84-3.76 (m, 1 H), 3.76-3.69$ $(dd, 1 H, H-2^{I}), 3.69-3.48 (m, 7 H, H-5^{III}),$ 3.12-3.04 (t, 1 H), 2.90-2.84 (t, 1 H), 2.84 (s, 3 H, OCH₃), 1.92 (s, 3 H, Ac), 1.84 (s, 3 H, Ac), 1.80 (s, 3 H, Ac), 1.79 (s, 3 H, Ac), 1.20 (d, 3 H, J 6.4 Hz, CH₃^V), 1.12 (s, 9 H, t-Bu); ¹³C NMR (CDCl₃, 100.6 MHz): δ 176.85 (C=O), 170.25 (C=O), 170.00 (C=O), 169.93 (C=O), 168.91 (C=O), 166.85 (C=O), 165.78 (C=O), 165.01 (C=O), 135.13, 134.23, 134.00,

133.61, 133.48, 133.41, 133.25, 130.27, 130.01, 129.86, 128.89, 128.76, 128.47, 128.40, 128.32, 128.24, 128.18, 128.16, 128.05, 127.82, 127.62, 127.36, 127.25, 126.63, 126.31, 126.04, 123.61, 102.35, 99.86, 99.08, 98.52, 97.81, 80.08, 79.86, 75.66, 75.45, 75.21, 75.05, 74.52, 74.23, 73.21, 72.55, 71.89, 71.40, 70.50, 70.34, 69.35, 69.20, 68.83, 68.57, 68.08, 67.86, 67.81, 66.75, 61.08, 60.31, 56.56, 54.87, 48.50, 38.85, 27.51, 22.53 (Ac), 20.58 (3 Ac), 16.35 (CH₃).

Methyl (β - D - galactopyranosyl) - (1 \rightarrow 4)- $[(\alpha - L - fucopyranosyl) - (1 \rightarrow 3)] - 2 - acetamido - 2 - ac$ $deoxy-6-O-sulfo-\beta-D-glucopyranosyl)-(1 \rightarrow 6) [(6-O-sulfo-\beta-D-galactopyranosyl)-(1 \rightarrow 3)]-2$ acetamido-2-deoxy-a-D-galactopyranoside disodium salt (2).—A soln of compound 32 (90 mg) and 10% Pd-C (200 mg) in 3:1 CH₂Cl₂-MeOH (6 mL) was stirred overnight at rt under a H₂ atmosphere. The filtrate was concd under reduced pressure to give a crude residue was treated for 4-6 h in that 1:5 $NH_2NH_2H_2O-MeOH$ (12 mL) at 80-85 °C. The reaction mixture was then concd and treated overnight with 1:1 Ac₂O-pyridine (6 mL) in the presence of a catalytic amount of DMAP at rt. The mixture was concd and purified by a short column of silica gel and eluted with 6:1 CH₂Cl₂-MeOH to give pure compound 33. Compound 33 was dissolved in 1:1 MeOH-water (3 mL), treated for 24 h with 1 M CH₃ONa (80 µL) at rt, and then concd. The crude residue was applied to a short column of silica gel and eluted with 3:1:1 $n-C_{3}H_{7}OH-HOAc$ -water to give compound 2 (6 mg, 26%) as an amorphous solid. R_{f} 0.16 $(3:1:1 n-C_3H_7OH-HOAc-water);$ ¹H NMR (D₂O, 600 MHz): δ 5.16–5.10 (d, 1 H, $J_{1,2}$ 3.5 Hz, H-1^V), 4.90–4.79 (dd, 1 H, H-5^V), 4.78– 4.60 (d, 1 H, $J_{1,2}$ 3.0 Hz, H-1^I), 4.64–4.60 (d, 1 H, $J_{1,2}$ 8.8 Hz, H-1^{III}), 4.60–4.58 (d, 1 H, $J_{1,2}$ 7.8 Hz, H-1^{IV}), 4.46–4.44 (d, 1 H, J₁, 7.6 Hz, H-1^{II}), 4.44-4.40 (d 1 H, J 2.8 Hz, H-4^{IV}), 4.40–4.30 (dd, 1 H, H-2^I), 4.30–4.28 (dd, 1 H, J 2.8 Hz, H-4^I), 4.22–4.18 (m, 2 H, H-6b^{II}) H-5^I), 4.14–3.80 (m, 11 H, H-3^I, H-6b^I, H-4^{II}. H-2¹¹¹, H-3^v, H-6a^I, H-5^{1v}, H-4^v), 3.80-3.46 (m, 12 H, $H-5^{III}$, $H-2^{V}$, $H-5^{II}$, $H-3^{IV}$, $H-3^{II}$, H-4^{III}, H-2^{IV}, H-2^{II}), 3.36 (s, 3 H, OCH₃), 2.13 (s, 3 H, Ac), 2.02 (s, 3 H, Ac), 1.20 (d, 3 H, J 6.4 Hz, CH_{3}^{V}); ¹³C NMR (D₂O, 100.6 MHz): δ 173.50 (C=O), 173.20 (C=O), 104.50, 102.30,

101.60, 98.60, 98.40, 77.52, 75.20, 75.00, 73.30, 72.90, 72.75, 72.65 (2 C), 72.25, 71.50, 71.25, 70.60, 69.50 (2 C), 69.25, 68.60, 68.50, 68.00, 67.50, 67.00, 66.30, 62.65, 56.00, 55.28, 48.90, 23.00 (Ac), 22.50 (Ac), 15.50 (CH₃^V); FABMS (m/z) (positive ion mode): Calcd for $C_{35}H_{58}O_{31}N_2Na_2S_2$: 1112.3; found: 1113.9 [M⁺ + 1].

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