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Synthetic studies on glycosphingolipids from the parasite *Echinococcus multilocularis*

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Abstract

Novel neutral glycosphingolipids isolated from the metacestodes of *Echinococcus multilocularis* by Persat, may be expected to be involved in host–parasite interactions. We have synthesized these glycosphingolipid analogues containing 2-branched fatty alkyl residues in place of ceramide. The glycosylation of galactosyl donors **4** and **5** with each of the acceptors **2** and **11** in the presence of *N*-iodosuccinimide (NIS)/TfOH, and the glycosylation of fucosyl donor **13** with acceptors **12** and **20** in the presence of dimethyl(methylthio)sulfonium triflate (DMTST) gave the desired oligosaccharide derivatives at good yield. The fully per-*O*-acylated 2-(trimethylsilyl)ethyl glycosides **6**, **15**, **21**, and **26** were converted to glycosylimidates **7**, **16**, **22**, and **27**, which were condensed with 2-(tetradecyl)hexadecanol and subsequently deacylated give four target glycosphingolipid analogues.

Keywords: Glycosphingolipids; *Echinococcus mululocularis*; Chemical synthesis

1. Introduction

Over the past few years we have seen great interest in the preparation of oligosaccharides containing sialic acids, such as sialyl Lewis X in mammalian membranes, in order to elucidate the biological function of carbohydrates on the cell surface [1,2]. A number of sialyl-oligosaccharides and their mimetics have been synthesized by many carbohydrate chemists [3–5]. On the other hand, synthetic studies of oligosaccharides from invertebrate animal species that do not have gangliosides have been neglected, in spite of their having interesting structures [6,7].

We have been interested in the structure and biological function of glycolipids from invertebrate animal species and have so far synthesized an octasaccharide of the *Hyriopsis schlegelii* glycosphingolipid in order to elucidate the mechanism of its fertilization [8]. We have now turned our attention to a glycolipid from a parasite that may be involved in host–parasite interactions such as species-related infestation and stage development or the choice of target organs that parasites preferentially invade. There are some reports that patients infected with *Taenia* [9], *Leishmania* [10], or *Schistosoma* [11] were shown to express antibodies directed against parasite glycolipid. However, the structural characteristics of these immunogenic glycolipids have not been established.

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Table 1
Major glycosphingolipid structures in *E. multilocularis* metacestodes

β-D-Gal*p*-(1→6)-β-D-Gal*p*-(1↔1)-Cer	A
α-L-Fuc*p*-(1→3)-β-D-Gal*p*-(1→6)-β-D-Gal*p*-(1↔1)-Cer	B
β-D-Gal*p*-(1→6)-β-D-Gal*p*-(1→6)-β-D-Gal*p*-(1↔1)-Cer	C
β-D-Gal*p*-(1→6)-[α-L-Fuc*p*-(1→3)]-β-D-Gal*p*-(1→6)-β-D-Gal*p*-(1↔1)-Cer	D

Recently, Persat et al. have reported glycosphingolipids with β-D-Gal*p*-(1→6)-D-Gal*p* sequences in metacestodes of the parasite, *Echinococcus mululocularis* (Table 1) [12]. In this study they demonstrated for the first time that metacestodes of *E. multilocularis* contained glycolipids that were recognized by serum antibodies from different patients with alveolar hydatid disease [12].

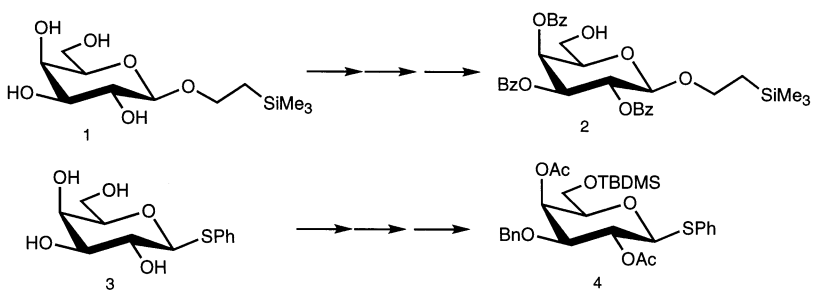
The glycolipids related to this binding were specifically bound to the neutral glycosphingolipid. It is interesting that no reaction was observed with acid glycolipids such as GM_1, GM_3 and GD_{1a}. In addition, fucose has been shown to form at least seven types of linkages, but none is of the two novel fucolipid structures of the α-(1→3)-Gal*p* type. The two novel fucolipids have structures α-L-Fuc*p*-(1→3)-β-D-Gal*p*-(1→6)-β-D-Gal*p*-(1↔1)-Cer and β-D-Gal*p*-(1→6)-[α-L-Fuc*p*-(1→3)]-β-D-Gal*p*-(1→6)-β-D-Gal*p*-(1↔1)-Cer. The oligosaccharides of four glycolipids were the target for the synthetic studies described herein as part of our investigation into synthetic oligosaccharides of structural and biological interest. We chose a systematic, integrated approach for the synthesis of tetrasaccharides and have synthesized these glycolipid analogues containing 2-branched fatty alkyl residues in place of ceramide [13].

2. Results and discussion

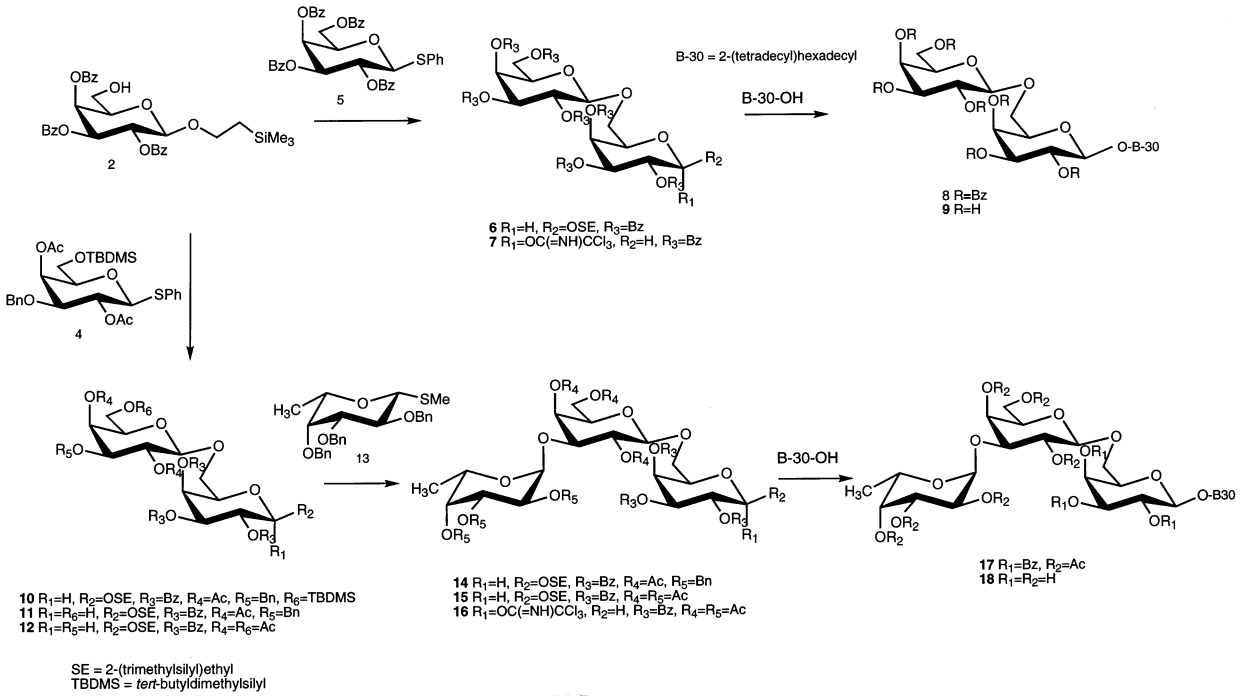
Syntheses of monosaccharide derivatives.—Syntheses of the additional galactopyranosyl building blocks **2** and **4** were carried out as depicted in Scheme 1. 2-(Trimethylsilyl)ethyl 2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside (**2**) was prepared from known 2-(trimethylsilyl)ethyl β-D-galactopyranoside (**1**) [14] following a three-step procedure. Regioselective silyl ation of the starting material with *tert*-butyldimethylsilyl chloride (TBDMS-Cl), followed by benzoylation and subsequent acid hydrolysis of the silyl group, gave compound **2**. On the other hand, donor **4** was obtained from phenyl 1-thio-β-D-galactopyranoside (**3**) [15] by regioselective benzylation of the in situ prepared stannylidene derivative [16] of **3** with benzyl bromide and subsequent regioselective silylation with TBDMS-Cl, followed by acetylation.

Systematic syntheses of the each of the glycolipid analogues.—In this work, four kinds of target glycolipid analogues **9**, **18**, **24** and **29** were synthesized by stepwise condensation [17] of suitably protected monosaccharide units. A systematic plan for these compounds was designed as shown in Schemes 2 and 3.

First, we chose compounds **6**, **15**, **21** and **26**, which were the per-*O*-acylated 2-(trimethylsilyl)ethyl glycoside derivatives, as the intermediates. The glycosylation of **2** with phenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside (**5**) [18] in the presence of *N*-iodosuccinimide (NIS)/TfOH (cat.) [19] and 4 Å molecular sieves in dichloromethane for 30 min at 0 °C gave the desired disaccharide **6** (70%) as evidenced by ^{1}H NMR spectroscopy (H-1′ 4.91 ppm, *J* 7.9 Hz). On the other hand, the common donor **4** was chosen for the

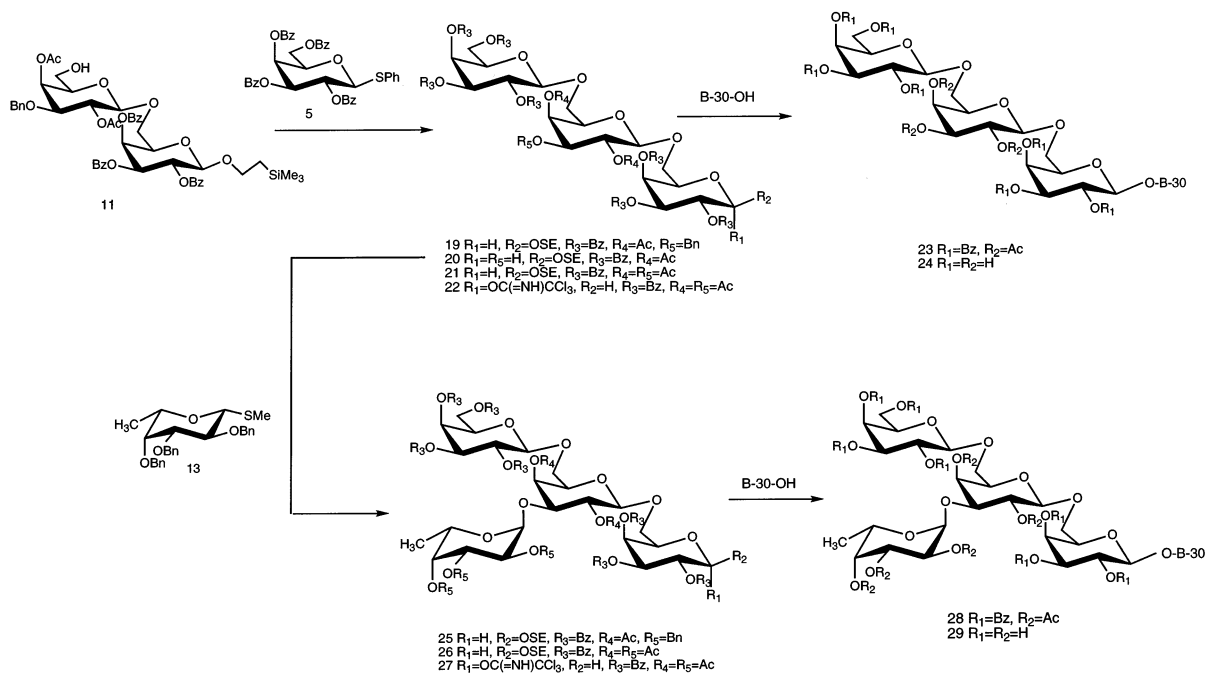


Scheme 1.



Scheme 2.

target compounds **15**, **21** and **26**, which was condensed with **2** under the agency of NIS/TfOH (cat) to yield disaccharide **10** (58%) as evidenced by ^{1}H NMR spectroscopy (H-1′ 4.42 ppm, J 8.0 Hz). Selective removal of the TBDMS group in **10** with 3:1:1 AcOH–THF–H_2O gave the partially protected compound **11**, a part of which was converted by O-acetylation with Ac_2O and followed by hydrogenation over 10% Pd–C to give the disaccharide derivative **12**. The glycosylation of compound **12** with methyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside (**13**) [3] in the presence of dimethyl(methythio)sulfonium triflate



Scheme 3.

Table 2
^{13}C NMR data (δ) for selected compounds

Carbon atom	Compound				
	6	**10**	**14**	**19**	**25**
C-l(Gal^{I})	101.1	101.0	100.9 (157.3)	101.0	101.1 (159.3)
2	69.6	69.9	69.8	69.9	70.0
3	71.9	72.0	71.9	72.0	72.0
4	68.6	68.7	68.6	68.6	68.5
5	73.0	73.1	73.1	72.7	73.2
6	67.6	67.8	67.4	67.4	67.5
C-1 (Gal^{II})	100.9	101.2	101.0 (161.4)	101.0	101.1 (161.4)
2	69.8	70.6	70.7	70.2	70.9
3	71.7	77.0	75.4	76.8	77.3
4	68.0	65.5	69.0	65.8	69.4
5	71.3	73.7	71.4	72.2	72.6
6	61.7	60.6	61.9	66.8	67.1
C-1 (Fuc)			99.4 (169.7)		99.1 (171.7)
2			75.8		750.8
3			78.6		78.7
4			74.7		74.9
5			77.4		77.7
6			16.4		16.5
C-1 (Gal^{III})				101.0	101.2 (159.3)
2				69.8	69.8
3				71.7	71.6
4				68.0	68.1
5				71.4	71.3
6				62.0	62.0
Si(*tert*-Bu)$(CH_3)_2$		137.7			
		25.7			
		−5.6			
$CH_2CH_2Si(CH_3)_3$	67.5	67.7	67.5	67.7	67.7
	17.5	18.0	18.0	18.0	18.0
	−1.5	−1.4	−1.5	−1.5	−1.5
CH_2Ph		71.2	74.7	71.2	74.7
			73.0		72.9
			72.8		72.8

(DMTST) [20] as the glycosyl promoter and 4 Å molecular sieves in dichloromethane for 5 h at 0 °C gave the desired α-glycoside **14** in 89% yield. Significant signals of the fucose unit in the ^1H NMR spectrum showed a signal for the anomeric hydrogen atoms at δ 4.96 (d, J 3.7 Hz). The α-L configuration of the newly formed glycosidic bond was also indicated by the $J_{C,H}$ value of 169.7 Hz in the ^{13}C NMR spectrum. Catalytic hydrogenolysis (10%, Pd–C) in methanol–AcOH of the benzyl groups in **14** and subsequent O-acetylation gave the trisaccharide **15** (81%) (Table 2).

On the other hand, the glycosylation of **11** with **5** in the presence of NIS/TfOH as described for compound **6** gave the trisaccharide derivative **19** (78%), as evidenced by ^1H NMR spectroscopy (H-1″ 4.84 ppm, J 7.9 Hz). Removal of the 3′-*O*-benzyl group from **19** by catalytic hydrogenolysis over Pd–C gave the accepter **20** (82%) for the tetrasaccharide derivative, and subsequent acetylation gave the trisaccharide **21**. Furthermore the glycosylation of **20** with **13** in the presence of DMTST as described for **14** gave the tetrasaccharide derivative **25** (90%), as evidenced by ^1H NMR spectroscopy (H-1 of Fuc 4.96 ppm, J 3.7 Hz). Then **25** was converted by O-debenzylation and subsequent acetylation, to give the tetrasaccharide **26**.

Next, for the selective removal of the 2-(trimethylsilyl)ethyl group, the fully acylated

oligosaccharides **6**, **15**, **21** and **26** were treated [21] with trifluoroacetic acid in dichloromethane for 30 min at 0 °C to give the 1-hydroxy compounds, which, on further treatment with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane for 2 h at 0 °C, gave the corresponding receptor carbohydrates **7**, **16**, **22** and **27**. Glycosylation of 2-(tetradecyl)hexadecanol with each of the glycosyl donors, which was carried out in the presence of BF_3·OEt and AW300 molecular sieves for 5 h at 0 °C, afforded the desired β-glycosides **8** (36%), **17** (37%), **23** (49%) and **28** (29%) in low yield. Following this lead, we attempted a similar coupling of donor **27** with the acceptor, 2-(tetradecyl)hexadecanol, in the presence of Me_3SiOTf to give **28** in a more acceptable yield of 53%. Finally, removal of all acyl groups with sodium methoxide in 3:1 methanol–1,4-dioxane for 5 h at room temperature afforded the desired glycolipid (A–D) analogues (**9**, **18**, **24** and **29**). Biological results using sera from patients with alveolar hydatid disease for these compounds will be reported in detail elsewhere.

3. Experimental

General.—Optical rotations were determined with a Jasco digital polarimeter. ^1H NMR and ^{13}C NMR spectra were recorded with a JNM A 500 FT NMR spectrometer with Me_4Si as the internal standard for solutions in $CDCl_3$. MALDI-TOFMS was recorded on a Perceptive Voyager RP mass spectrometer. TLC was performed on Silica Gel 60 F_{254} (E. Merck) with detection by quenching of UV fluorescence and by spraying with 10% H_2SO_4. Column chromatography was carried out on Silica Gel 60 (E. Merck). 2-(Trimethylsilyl)ethyl β-D-galactopyranoside (**1**), phenyl 1-thio-β-D-galactopyranoside (**3**), phenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside (**5**) and methyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside (**13**) were prepared by literature methods [14,15,18,3].

2-(Trimethylsilyl)ethyl 2,3,4-tri-O-*benzoyl-β-*D-*galactopyranoside* (**2**).—To a solution of 2-(trimethylsilyl)ethyl β-D-galactopyranoside (**1**) (5.0 g, 17.8 mmol) in DMF (30 mL) were added at 0 °C imidazole (2.42 g, 35.6 mmol) and *tert*-butyldimethylsilyl chloride (2.82 g, 18.7 mmol). The reaction mixture was stirred at room temperature (rt) for 6 h, then diluted with $CHCl_3$ and washed with 5% HCl, aq $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 10:1 $CHCl_3$–MeOH as eluent to give 2-(trimethylsilyl)ethyl-6-*O*-(*tert*-butyldimethylsilyl)-β-D-galactopyranoside (**5**, 87 g, 83.1%). To a solution of this compound in pyridine (50 mL) was added benzoyl chloride (7 mL), and the mixture was stirred for 4 h at 0 °C. Extractive isolation gave 2-(trimethylsilyl)ethyl 6-*O*-(*tert*-butyldimethylsilyl)-2,3,4-tri-*O*-benzoyl-β-D-galactopyranoside quantitatively. This compound was treated with 80% AcOH (50 mL) at 40 °C for 3 h, and following removal of acetic acid and water by coevaporation with toluene, was purified by column chromatography (3:2 hexane–EtOAc) on silica gel to give compound **2** (9.37 g, 89%): $[\alpha]_D + 180°$ (*c* 0.9 $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.12–7.22 (m, 15 H, 3 × Ph), 5.84 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.3 Hz, H-2), 5.82 (d, 1 H, $J_{3,4}$ 2.4 Hz, H-4), 5.58 (dd, 1 H, H-3), 4.83 (d, 1 H, H-1), 4.12–4.02 (m, 2 H, H-6a, $-OCH_2CH_2-$), 3.85 (ddd, 1 H, H-5), 3.67–3.62 (m, 2 H, H-6b, $-OCH_2CH_2-$), 2.71 (t, 1 H, OH), 0 97–0 86 (m, 2 H, $-OCH_2CH_2-$), −0.06 (s, 9 H, $Si(CH_3)_3$); Anal. Calcd for $C_{32}H_{36}O_9Si$ (592.7) C, 64.85; H, 6.12. Found: C, 64.59; H, 6.10.

Phenyl 2,4-di-O-*acetyl-3*-O-*benzyl-6*-O-*(tert-butyldimethylsilyl)-1-thio-β-*D-*galactopyranoside* (**4**).—A mixture of phenyl 1-thio-β-D-galactopyranoside (**3**) (500 mg, 2.08 mmol), dibutyltin oxide (570 mg, 2.30 mmol) and 30 mL of dry benzene was stirred under reflux for 5 h. Benzene (15 mL) was distilled off, and the solution was cooled to 50 °C and treated with Bu_4NBr (804 mg) and BnBr (0.6 mL). After the reaction mixture was stirred for 5 h, the solution was concentrated. Purification of the residue by column chromatography (10:1 $CHCl_3$–MeOH) on silica gel gave phenyl 3-*O*-benzyl-1-thio-β-D-galactopyranoside (374 mg, 50%). To a solution of this compound (583 mg, 1.61 mmol) in DMF (7 mL) were added

imidazole (219 mg, 3.22 mmol) and *tert*-butyldimethylsilyl chloride (292 mg, 1.93 mmol) at 0 °C. The reaction mixture was stirred at rt for 3 h and then diluted with $CHCl_3$, washed with 5% HCl, aq $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The product was chromatographed on silica gel using 2:1 hexane–EtOAc as eluent to provide phenyl 3-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-1-thio-β-D-galactopyranoside. To a solution of this compound in pyridine (20 mL) was added acetic anhydride (15 mL), and the mixture was stirred for 4 h at 0 °C. The reaction mixture was poured into ice-water and extracted with $CHCl_3$. The extract was washed sequentially with 5% HCl, aq $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 4:1 hexane–ethyl acetate as eluent to give **4** (830 mg, 92%, 2 steps): $[\alpha]_D + 55.0°$ (*c* 0.6, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.49–7.25 (m, 10 H, 2 × Ph), 5.61 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 5.16 (t, 1 H, $J_{1,2,2,3}$ 9.7 Hz, H-2), 4.71 and 4.42 (each d, 2 H, J_{gem} 12.2 Hz, benzylic methylene), 4.64 (d, 1 H, H-1), 3.74 (dd, 1 H, $J_{5,6a}$ 9.2 Hz, $J_{6a,6b}$ 11.2 Hz, H-6a), 3.67–3.64 (m, 2 H, H-5, H-6b), 3.55 (dd, 1 H, H-3), 2.12 and 2.05 (each s, 6 H, 2 × OAc), 0.88 (s, 9H, 3 × CH_3), −0.04 (s, 6 H, $-Si(CH_3)_2-$); Anal. Calcd for $C_{29}H_{40}O_7SSi$ (560.8): C, 62.11; H, 7.19. Found: C, 61.85; H, 7.25.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-O-*benzoyl*-β-D-*galactopyranosyl*(1→6)-*2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**6**).—To a solution of **2** (300 mg, 0.51 mmol) and phenyl 2,3,4,6-tetra-*O*-benzoyl-1-thio-β-D-galactopyranoside **5** (421 mg, 0.61 mmol) in dry CH_2Cl_2 (5 mL) was added powdered 4 Å molecular sieves (1 g), and the mixture was stirred for 2 h at rt, then cooled to 0 °C. *N*-Iodosuccinimide (NIS; 160 mg, 0.73 mmol) and trifluoromethanesulfonic acid (TfOH; 5.3 μL 0.06 mmol) were added to the mixture, which was stirred for 30 min at 0 °C, then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings were successively washed with aq $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated. The product was chromatographed on silica gel using 3:2 hexane–EtOAc as eluent to give **6** (416 mg, 70%): $[\alpha]_D + 63.2°$ (*c* 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.11–7.21 (m, 35 H, 7 × Ph), 5.94 (d, 1 H, $J_{3,4}$ 3.7 Hz, H-4′), 5.92 (d, 1 H, $J_{3',4'}$ 3.7 Hz, H-4′), 5.77 (dd, 1 H, $J_{1',2'}$, 7.9 Hz, $J_{2',3'}$ 10.4 Hz, H-2′), 5.72 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.4 Hz, H-2), 5.57 (dd, 1 H, H-3′), 5.51 (dd, 1 H, H-3), 4.91 (d, 1 H, H-1′), 4.70 (d, 1 H, H-1), 4.39 (dd, 1 H, $J_{5',6'a}$, 8.5 Hz, $J_{6'a,6'b}$ 13.5 Hz, H-6a′), 4.27–4.23 (m, 2 H, H-5′,6b′), 4.20–4.16 (m, 2H, H-5, 6a), 3.94–3.89 (m, 2 H, $-CH_2CH_2Si$, H-6b), 3.46 (dt, 1 H, $-CH_2CH_2Si$), 0.85–0.71 (m, 2 H, $-CH_2CH_2Si$), −0.08 (s, 9 H, $Si(CH_3)_3$); Anal. Calcd for $C_{66}H_{62}O_{18}Si$ (1171.3): C, 67.68; H, 5.34. Found: C, 67.63; H, 5.31.

2,3,4,6-Tetra-O-*benzoyl*-β-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-α-D-*galactopyranosyl trichloroacetimidate* (**7**).—To a solution of **6** (52 mg, 44 mmol) in CH_2Cl_2 (2.5 mL) cooled to 0 °C was added CF_3COOH (1.5 mL), and the mixture was stirred for 30 min. at rt and concentrated. Ethyl acetate and toluene (1:2) were added and then evaporated to give the 1-hydroxy compound. To a solution of the residue in CH_2Cl_2 (0.8 mL) cooled to 0 °C were added trichloroacetonitrile (132 μL 132 mmol) and DBU (7.3 μL 48 mmol). The mixture was stirred for 2 h at 0 °C. After completion of the reaction, the mixture was concentrated. Column chromatography (3:2 hexane–EtOAc) of the residue on silica gel gave **7** (38 mg, 70%) as an amorphous mass: $[\alpha]_D + 116.9°$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.33 (s, 1 H, NH), 8.09–7.20 (m, 35 H, 7 × Ph), 6.76 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 6.08 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 6.01 (dd, 1 H, $J_{2,3}$ 10.0 Hz, H-3), 5.92 (d, 1 H, $J_{3',4'}$ 3.1 Hz, H-4′), 5.85 (dd, 1 H, $J_{2,3}$ 10.4 Hz, H-2), 5.74 (dd, 1 H, $J_{1',2'}$ 7.9 Hz, $J_{2',3'}$ 10.4 Hz, H-2′), 5.53 (dd, 1 H, H-3′), 4.90 (d, 1 H, H-1′), 4.69–3.88 (m, 6 H, H-5, 5′, 6a, 6b, 6′a, 6′b); MALDI-TOFMS: Calcd for $C_{63}H_{50}Cl_3NO_{18}$: *m*/*z* 1214.7. Found: *m*/*z* 1237.5 $[M + Na]^+$, 1253.7 $[M + K]^+$.

2-(Tetradecyl)hexadecyl 2,3,4,6-tetra-O-*benzoyl*-β-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**8**).—To a solution of the trichloroacetimidate **7** (90 mg, 74 μmol) and 2-(tetradecyl)hexadecanol (65 mg, 148 μmol) in CH_2Cl_2 (1 mL) were

added AW300 molecular sieves (300 mg) and the mixture was stirred for 3 h at rt, then cooled to 0 °C. Boron trifluoride etherate (45 μL) was added, and mixture was stirred for 5 h at 0 °C then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings was successively washed with water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 3:2 hexane–EtOAc as eluent to give **8** (46 mg, 36%): $[\alpha]_D + 82.5°$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.10–7.21 (m, 35 H, 7 × Ph), 5.93 (1 H, d, $J_{3',4'}$ 3.0 Hz, H-4′), 5.91 (d, 1 H, $J_{3,4}$ 3.7 Hz, H-4), 5.77 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.5 Hz, H-2), 5.72 (dd, 1 H, $J_{1',2'}$ 7.9 Hz, $J_{2',3'}$ 10.4 Hz, H-2′), 5.57 (dd, 1 H, H-3), 5.51 (dd, 1 H, H-3′), 4.92 (1 H, d, 1 H, H-1′), 4.62 (d, 1 H, H-1), 4.39 (dd, 1 H, $J_{5',6'a}$ 8.5 Hz, $J_{6'a,6'b}$ 13.5 Hz, H-6′a), 4.25–4.16 (m, 3 H, H-5′,6′b, $-OCH_2-$), 3.91 (ddd, 1 H, H-5), 3.69 (dd, 1 H, H-6b), 3.17, (dd, 1 H, $-OCH_2-$), 1.34 (br.s, 52 H, 26 × CH_2), 0.96 (t, 6 H, 2 × $-CH_2CH_3$); MALDI-TOFMS: Calcd for $C_{91}H_{110}O_{18}$: *m*/*z* 1490.8. Found: *m*/*z* 1513.7 $[M + Na]^+$, 1529.9 $[M + K]^+$.

*2-(Tetradecyl)hexadecyl β-*D*-galactopyranosyl-(1→6)-β-*D*-galactopyranoside* (**9**).—To a solution of **8** (40 mg, 27 μmol) in 3:1 MeOH–1,4-dioxane (2 mL) was added NaOMe (20 mg), and the mixture was stirred for 5 h at rt, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with 1:1 $CHCl_3$–MeOH. The filtrate and washings were combined and concentrated. Column chromatography (1:1 $CHCl_3$–MeOH) of the residue on Sephadex LH-20 gave **9** (20 mg, 94%): $[\alpha]_D$ −22.2° (*c* 0.5, 1:1 $CHCl_3$–MeOH); ^1H NMR ($CDCl_3$–CD_3OD): δ 4.30 (d, 1 H, *J* 8.0 Hz, H-la), 4.19 (d, 1 H, *J* 7.5 Hz, H-lb); MALDI-TOFMS: Calcd for $C_{42}H_{82}O_{11}$: *m*/*z* 762.6. Found: *m*/*z* 785.3 $[M + Na]^+$, 801.4 $[M + K]^+$.

*2-(Trimethylsilyl)ethyl 2,4-di-*O*-acetyl-3-*O*-benzyl-6-*O*-(*tert*-butyldimethylsilyl)-β-*D*-galactopyranosy-(1→6)-2,3,4-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**10**).—To a solution of **2** (1.39 g, 2.35 mmol) and **4** (1.58 g, 2.82 mmol) in dry CH_2Cl_2 (15 mL) was added powdered 4 Å molecular sieves (3 g), and the mixture was stirred for 2 h at rt, then cooled to 0 °C. NIS (630 mg, 2.82 mmol) and TfOH (50 μL, 0.56 mmol) were added to the mixture, which was stirred for 20 min at 0 °C, then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings was successively washed with aq $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 2:1 hexane–EtOAc as eluent to give **10** (1.42 g, 58%): $[\alpha]_D = +105.6°$ (*c* 0.6 $CHCl_3$) ^1H NMR ($CDCl_3$): δ 8.07–7.21 (m, 20 H, 4 × Ph), 5.84 (d, 1 H, $J_{3,4}$ 2.4 Hz, H-4), 5.74 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.4 Hz, H-2), 5.58 (d, 1 H, $J_{3'4'}$ 3.0 Hz, H-4′), 5.21 (dd, 1 H, H-3), 5.11 (dd, 1 H, $J_{1'2'}$ 8.0 Hz, $J_{2'3'}$ 10.4 Hz, H-2′) 4.77 (d, 1 H, H-1), 4.72 and 4.40 (each d, 2 H, J_{gem} 12.2 Hz, benzylic methylene), 4.42 (d, 1 H, H-1′), 4.14–4.07 (m, 2 H, H-5, $-OCH_2CH_2-$), 3.98 (dd, 1 H, $J_{5,6a}$ 4.7 Hz, $J_{6a,6b}$ 11.0 Hz, H-6a), 3.82 (dd, 1 H, $J_{5,6b}$ 7.3 Hz, H-6b), 3.67–13.56 (m, 4 H, H-5′, 6′a, 6′b, $-OCH_2CH_2-$), 3.50(dd, 1 H, H-3′), 2.16 and 2.13 (each s, 6 H, 2 × OAc), 1.00–0.90 (m, 2 H, $-OCH_2CH_2-$), 0.85 (s, 9 H, 3 × CH_3), −0.04 (s, 6 H, $-Si(CH_2)_2-$), −0.05(S, 9 H, $-Si(CH_3)_3$). Anal. Calcd for $C_{55}H_{70}O_{16}Si_2$ (1043.3): C, 63.32; H, 6.76. Found: C, 63.08; H, 6.78.

*2-(Trimethylsilyl)ethyl 2,4-di-*O*-acetyl-3-*O*-benzyl-β-*D*-galactopyranosyl-(1→6)-2,3,4-tri-*O*-benzoyl-β-*D*-galactopyranoside* (**11**).—Compound **11** (438 mg, 0.42 mmol) was dissolved in 3:1:1 AcOH–THF–H_2O (50 mL). After stirring for 3 h at 50 °C, the reaction mixture was concentrated, and the remaining solvents were removed by evaporation with toluene. The product was purified by silica gel column chromatography using 3:2 hexane–EtOAc as eluent to give **11** (291 mg, 75%): $[\alpha]_D = +95.7°$ (*c* 4.1 $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.07–7.21 (m, 20 H, 4 × Ph), 5.91 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 5.72 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.4 Hz, H-2), 5.51 (dd, 1 H, H-3), 5.40 (d, 1 H, $J_{3',4'}$ 3.6 Hz, H-4′), 5.15 (dd, 1 H, $J_{1',2'}$ 8.5 Hz, $J_{2'3'}$ 9.8 Hz, H-2′) 4.76 (d, 1 H, H-1), 4.63 and 4.39 (each d, 2 H, J_{gem} 12.2 Hz, benzylic methylene), 4.40 (d, 1 H, H-1′), 4.13–4.08 (m, 2 H, H-5, $-OCH_2CH_2-$), 3.95 (dd, 1 H, $J_{5,6a}$ 5.5 Hz, $J_{6a,6b}$ 10.4 Hz, H-6a), 3 84 (dd, 1 H, $J_{5,6b}$ 6.1 Hz, H-6b), 3.63 (m, 2 H, H-6′a, $-OCH_2CH_2-$), 3.54 (t, 1 H, H-5′), 3.50 (dd, 1

H, H-3′), 2.25 (br.d, 1 H, OH), 2.17 and 2.05 (each s, 6 H, 2 × OAc) 0.95–0.87 (m, 2 H, $-OCH_2CH_2-$), −0.06 (s, 9 H, $-Si(CH_3)_3$). Anal. Calcd for $C_{49}H_{56}O_{16}Si$ (929.1): C, 63.35; H, 6.08. Found: C, 63.15; H, 6.04.

2-(Trimethylsilyl)ethyl 2,4,6-tri-O-*acetyl-β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl-β*-D-*galactopyranoside* (**12**).—To a solution of **11** (104 mg, 0.11 mmol) in pyridine (3 mL) was added Ac_2O (2 mL), and the mixture was stirred for 2 h at rt. At the end of this time MeOH was added, and the remaining solvents were removed by evaporation with toluene. Hydrogenolysis of this residue in MeOH (4 mL) and AcOH (1 mL) in the presence of 10% Pd–C (60 mg) was carried out for 2 h at rt. (**Caution: Pd–C and MeOH in admixture are extremely pyrophoric**.) After removing the Pd–C by filtration, the filtrate was concentrated. Column chromatography (10:1 benzene–acetone) of the residue on silica gel gave **12** (90 mg, 93%): $[\alpha]_D + 90.0°$ (*c* 0.6 $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.07–7.21 (m, 15 H 3 × Ph), 5.87 (d, 1 H, $J_{3,4}$ 3.1 Hz, H-4), 5.75 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.4 Hz, H-2), 5.55 (dd, 1 H, H-3), 5.29 (d, 1 H, $J_{3'4'}$ 3.0 Hz, H-4′), 4.96 (dd, 1 H, $J_{1'2'}$ 7.9 Hz, $J_{2'3'}$ 9.8 Hz, H-2′) 4.80 (d, 1 H, H-1), 4.51 (d, 1 H, H-1′), 4.19–3.63 (m, 9 H, H-3′, 5, 5′, 6a,6b,6′a,6′b, $-OCH_2CH_2-$), 2.86 (br.s, 1 H, OH), 2.15, 2.13 and 1.97 (each s, 9 H, 3 × OAc) 0.98–0.89 (m, 2 H, $-OCH_2CH_2-$), −0.05 (s, 9 H, $-Si(CH_3)_3$); Anal. Calcd for $C_{44}H_{52}O_{17}Si$ (881.0): C, 59.99; H, 5.75. Found: C, 59.82; H, 5.88.

2-(Trimethylsilyl)ethyl 2,3,4-tri-O-*benzyl-α*-L-*fucopyranosyl*-(1→3)-*2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl-β*-D-*galactopyranoside* (**14**).—To a solution of **12** (97 mg, 0.11 mmol) and **13** (77 mg, 0.17 mmol) in CH_2Cl_2 (2 mL) was added 4 Å molecular sieves (300 mg), and the mixture was stirred for 2 h at rt, then cooled to 0 °C. Dimethyl(methylthio)sulfonium triflate (DMTST; 130 mg, 0.50 mmol) was added to the mixture, which was stirred for 5 h at 0 °C, then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings were successively washed with water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 15:1 benzene–acetone as eluent to give **14** (127 mg, 89%): $[\alpha]_D + 48.9°$ (*c* 0.9, $CHCl_3$); ^1H NMR($CDCl_3$): δ 8.07–7.20 (m, 30 H, 6 × Ph), 5.85 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 5.74 (dd, 1 H, $J_{1,2}$ 7.9 Hz, $J_{2,3}$ 10.3 Hz, H-2), 5.52 (dd, 1 H, H-3), 5.26–5.22 (m, 1 H, H-2′, 4′), 4.96 (d, 1 H, $J_{1'',2''}$ 3.7 Hz, H-1″), 4.94–4.60 (m, 6 H, 3 × benzylic methylene), 4.77 (d, 1 H, H-1), 4.44 (d, 1H, $J_{1'2'}$ 7.9 Hz, H-1′), 4.14–4.07 (m, 2 H, $-CH_2CH_2Si$, H-3″), 4.02–3.91 (m, 3 H, H-2″, 5′, 6a), 3.83–3.79 (m, 5H, H-3′, 4″, 6b, 6′a, 6′b), 3.67–3.62 (m, 2H, $-CH_2CH_2Si$, H-5″), 0.85–0.71 (m, 2 H, $-CH_2CH_2Si$), −0.08 (s, 9 H, $Si(CH_3)_3$). Anal. Calcd for $C_{71}H_{80}O_{21}Si$ (1297.5): C, 65.73; H, 6.21. Found: C, 65.52; H, 6.33.

2-(Trimethylsilyl)ethyl 2,3,4-tri-O-*acetyl-α*-L-*fucopyranosy*-(1→3)-*2,4,6-tri*-O-*acetyl-β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl-β*-D-*galactopyranoside* (**15**).—A solution of **14** (125 mg, 0.10 mol) in MeOH (5 mL) and AcOH (0.1 mL) was hydrogenolysed in the presence of 10% Pd–C (80 mg) for 3 h at room temperature, then filtered and concentrated. The residue was acetylated with Ac_2O (3 mL) in pyridine (4 mL) for 3 h at rt. The mixture was poured into ice-water and extracted with $CHCl_3$. The extract was washed sequentially with 5% HCl, aq $NaHCO_3$ and water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 10:1 benzene–acetone as eluent to give **15** (90 mg, 81%, 2 steps): $[\alpha]_D + 15.2°$ (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.09–7.21 (m, 15 H, 3 × Ph), 5.84 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 5.74 (dd, 1 H, $J_{1,2}$ 8.5 Hz, $J_{2,3}$ 10.3 Hz, H-2), 5.52 (dd, 1 H, H-3), 5.29–5.16 (m, 4 H, H-2′, 4′, 3″, 4″), 5.26 (d, 1 H, $J_{1'',2''}$ 3.7 Hz, H-1″), 4.93 (dd, 1 H, H-2″), 4.77 (d, 1 H, H-1), 4.39 (d, 1 H, $J_{1',2'}$ 8.6 Hz, H-1′), 3.93 (dd, 1 H, H-3′), 0.85–0.71 (m, 2 H, $-CH_2CH_2Si$), −0.08 (s, 9 H, $Si(CH_3)_3$); Anal. Calcd for $C_{56}H_{68}O_{24}Si$ (1153.2): C, 58. 32; H, 5. 94. Found: C, 57.91; H, 5.83.

2,3,4-Tri-O-*acetyl-α*-L-*fucopyranosyl*-(1→3)-*2,4,6-tetra*-O-*acetyl-β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl-α*-D-*galactopyranosyl trichloroacetimidate* (**16**).—To a solution of **15** (81 mg, 0.07 mmol) in CH_2Cl_2 (3 mL) cooled to 0 °C, was added CF_3COOH (2 mL),

and the mixture was stirred for 30 min at rt and concentrated. Ethyl acetate and toluene (1:2) were added and then evaporated to give the 1-hydroxy compound. To a solution of the residue in CH_2Cl_2 (0.8 mL) cooled to 0 °C were added trichloroacetonitrile (210 μL, 2.10 mmol) and DBU (12.7 μL, 84 μmol). The mixture was stirred for 2 h at 0 °C. After completion of the reaction, the mixture was concentrated. Column chromatography (3:2 hexane–EtOAc) of the residue on silica gel gave **16** (66 mg, 79%) as an amorphous mass: $[\alpha]_D + 45.8°$ (*c* 1.7, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.61 (s, 1 H, NH), 6.87 (d, 1 H, $J_{1,2}$ 3.7 Hz, H-1), 5.26 (d, 1 H, $J_{1'',2''}$ 3.7 Hz, H-1″), 4.38 (d, 1 H, $J_{1',2'}$ 8.6 Hz, H-1′); MALDI-TOFMS: Calcd for $C_{53}H_{56}Cl_3NO_{24}$: *m/z* 1196.7. Found: *m/z* 1219.5 $[M + Na]^+$, 1235.9 $[M + K]^+$.

2-(Tetradecyl)hexadecyl 2,3,4-tri-O-*acetyl*-α-L-*fucopyranosyl*-(1→3)-*2,4,6-tetra*-O-*acetyl*-β-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**17**).—To a solution of the trichloroacetimidate **16** (66 mg, 55 μmol) and 2-(tetradecyl)hexadecanol (36 mg, 83 μmol) in CH_2Cl_2 (1 mL) were added AW300 molecular sieves (300 mg) and the mixture was stirred for 3 h at rt, then cooled to 0 °C. Boron trifluoride etherate (30 μL) was added, and mixture was stirred for 5 h at 0 °C then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings was successively washed with water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 3:2 hexane–EtOAc as eluent to give **17** (46 mg, 37%): $[\alpha]_D + 15.2°$ (*c* 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.25 (d, 1 H, $J_{1'',2''}$ 3.7 Hz, H-1″), 4.69 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.38 (d, 1 H, $J_{1',2'}$ 7.9 Hz, H-1′), 3.92 (dd, 1 H, $-OCH_2-$), 3.34 (dd, 1H, $-OCH_2-$), 1.34 (br.s, 52 H, $26 \times CH_2$), 0.96 (t, 6 H, $2 \times -CH_2CH_3$); MALDI-TOFMS: Calcd for $C_{81}H_{116}O_{24}$: *m/z* 1472.8. Found: *m/z* 1495.6 $[M + Na]^+$, 1511.8 $[M + K]^+$.

2-(Tetradecyl)hexadecyl α-L-*fucopyranosyl*-(1→3)-β-D-*galactopyranosyl*-(1→6)-β-D-*galactopyranoside* (**18**).—To a solution of **17** (20 mg, 13 μmol) in 3:1 MeOH–1,4-dioxane (2 mL) was added NaOMe (20 mg), and the mixture was stirred for 5 h at rt, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with 1:1 $CHCl_3$–MeOH. The filtrate and washings were combined and concentrated. Column chromatography (1:1 $CHCl_3$–MeOH) of the residue on Sephadex LH-20 gave **18** (12 mg, 97%): $[\alpha]_D$ −46.3° (*c* 0.1, 1:1 $CHCl_3$–MeOH); ^1H NMR ($CDCl_3$–CD_3OD): δ 5.16 (d, 1 H, *J* 4.3 Hz, H-1″), 4.36 (d, 1 H, *J* 7.9 Hz, H-1), 4.19 (d, 1 H, *J* 7.9 Hz, H-1′); MALDI-TOFMS: Calcd for $C_{48}H_{92}O_{15}$: *m/z* 908.6. Found: *m/z* 931.4 $[M + Na]^+$, 947.4 $[M + K]^+$.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-O-*benzoyl*-β-D-*galactopyranosyl*-(1→6)-*2,4-di*-O-*acetyl*-*3*-O-*benzyl*-β-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-β-D-*galactopyranoside* (**19**).—To a solution of **11** (108 mg, 0.12 mmol) and **5** (120 mg, 0.17 mmol) in dry CH_2Cl_2 (2 mL) was added powdered 4 Å molecular sieves (300 mg), and the mixture was stirred for 2 h at rt, then cooled to 0 °C. NIS (57 mg, 0.25 mmol) and TfOH (3 μL, 35 μmol) were added to the mixture, which was stirred for 20 min at 0 °C, then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings were successively washed with aq $Na_2S_2O_3$ and water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 2:1 hexane–EtOAc as eluent to give **19** (128 mg, 78%): $[\alpha]_D + 84.5°$ (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.12–7.20 (m, 40H, $8 \times$ Ph), 5.99 (d, 1 H, $J_{3'',4''}$ 3.7 Hz, H-4″), 5.82 (d, 1 H, $J_{3,4}$ 3.0 Hz, H-4), 5.77–5.72 (m, 2 H, H-2, 2″), 5.61 (dd, 1 H, $J_{2'',3''}$ 10.3 Hz, H-3″), 5.53 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-4′), 5.52 (dd, 1 H, H-3), 5.07 (dd, 1 H, $J_{1',2'}$ 7.9 Hz, $J_{2',3'}$ 9.8 Hz, H-2′), 4.84 (d, 1 H, $J_{1'',2''}$ 7.9 Hz, H-1″), 4.76 (d, 1 H, H-1), 4.67 (dd, 1 H, $J_{5'',6''a}$ 6.7 Hz, $J_{6''a,6''b}$ 11.0 Hz, H-6″a), 4.61 and 4.26 (each d, 2 H, J_{gem} 12.2 Hz, benzylic methylene) 4.42 (dd, 1 H, $J_{5'',6''}$ 6.7 Hz, H-6″), 4.33 (d, 1 H, H-1′), 4.32 (t, 1 H, H-5″), 4.25–4.07 (m, 2 H, H-5, $-CH_2CH_2Si$), 3.95–3.60 (m, 6 H, H-5′, 6a, 6b, 6′a, 6′b, $-CH_2CH_2Si$), 3.37 (dd, 1 H, H-3′), 2.09 and 2.01 (each s, 6 H, $2 \times$ OAc), 0.95–0.85 (m, −2 H, CH_2CH_2Si), −0.08 (9 H, s, $Si(CH_3)_3$). Anal. Calcd for $C_{83}H_{82}O_{25}Si$ (1507.7): C, 66.12; H, 5.48. Found: C, 65.92; H, 5.35.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,4-di*-O-*acetyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*β*-D-*galactopyranoside* (**20**).—A solution of **19** (367 mg, 0.24 mol) in MeOH (8 mL) and AcOH (2 mL) was hydrogenolysed in the presence of 10% Pd–C (200 mg) for 18 h at rt, then filtered and concentrated. (**Caution: Pd–C and MeOH in admixture are extremely pyrophoric**.) The product was purified by silica gel column chromatography using 3:2 hexane–ethyl acetate as eluent to give **20** (284 mg, 82%) $[\alpha]_D + 97.8°$ (*c* 1.5, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.10–7.21 (m, 35 H, 7 × Ph), 5.98 (d, 1 H, $J_{3'',4''}$ 3.0 Hz, H-4″), 5.83 (d, 1 H, $J_{3,4}$ 3.7 Hz, H-4), 5.76–5.70 (m, 2 H, H-2, 2″), 5.59 (dd, 1 H, $J_{2'',3''}$ 10.4 Hz, H-3″), 5.53 (dd, 1 H, H-3), 5.29 (d, 1 H, $J_{3',4'}$ 3.0 Hz, H-4′), 4.89 (dd, 1 H, $J_{1',2'}$ 7.9 Hz, $J_{2',3'}$ 10.4 Hz, H-2′), 4.83 (d, 1 H, H-1″), 4.82 (d, 1 H, H-1), 4.64 (dd, 1 H, $J_{5'',6''a}$ 6.7 Hz, $J_{6''a,6''b}$ 11.7 Hz, H-6″a), 4.42 (dd, 1 H, $J_{5'',6''}$ 6.7 Hz, H-6″), 4.38 (d, 1 H, H-1′), 4.30 (t, 1 H, H-5″), 4.13–4.07 (m, 2 H, H-5, $-CH_2CH_2Si$), 3.95–3.58 (m, 7 H, H-3′, 5′, 6a, 6b, 6′a, 6′b, $-CH_2CH_2Si$), 2.52 (d, 1 H, *J* 6.1 Hz, OH), 2.02 and 2.01 (each s, 6 H, 2 × OAc), 0.96–0.87 (m, 2 H, $-CH_2CH_2Si$), −0.08 (s, 9 H, $Si(CH_3)_3$). Anal. Calcd for $C_{76}H_{76}0_{25}Si$ (1417.5): C, 64.40; H, 5.40. Found: C, 63.97; H, 5.45.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*acetyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*β*-D-*galactopyranoside* (**21**).—Compound **20** (100 mg, 0.07 mmol) was acetylated with Ac_2O (2 mL) in pyridine (3 mL) for 3 h at rt. Workup as described for **15** gave **21** (98 mg, 96%): $[\alpha]_D + 84.5°$ (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 4.81 (d, 1 H, $J_{1'',2''}$ 7.3 Hz, H-1″), 4.80 (d, 1 H, $J_{1,2}$ 8.0 Hz, H-1), 4.38 (d, 1 H, $J_{1',2'}$ 8.0 Hz, H-1′), 2.08, 2.06 and 1.96 (each s, 9 H, 3 × OAc). Anal. Calcd for $C_{78}H_{78}O_{26}Si$ (1459.6): C, 64.19; H, 5.39. Found: C, 64.02; H, 5.42.

2,3,4,6-Tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*acetyl*-*α*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*α*-D-*galactopyranosyl trichloroacetimidate* (**22**).—To a solution of **21** (185 mg, 0.16 mmol) in CH_2Cl_2 (4 mL), cooled to 0 °C, was added CF_3COOH (3 mL), and the mixture was stirred for 30 min at rt and concentrated. Ethyl acetate and toluene (1:2) were added and then evaporated to give the 1-hydroxy compound. To a solution of the residue in CH_2Cl_2 (2 mL) cooled at 0 °C were added trichloroacetonitrile (380 μL, 3.80 mmol) and DBU (23 μL, 152 μmol). The mixture was stirred for 2 h at 0 °C. After completion of the reaction, the mixture was concentrated. Column chromatography of the residue on silica gel (3:2 hexane–EtOAc) gave **22** (105 mg, 55%) as an amorphous mass: $[\alpha]_D + 61.4°$ (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 8.63 (s, 1 H, NH), 6.85 (d, 1 H, *J* 3.7 Hz, H-1), 4.74 (d, 1 H, *J* 7.9 Hz, H-1″), 4.41 (d, 1 H, *J* 7.9 Hz, H-1′); MALDI-TOFMS: Calcd for $C_{75}H_{66}Cl_3NO_{26}$: *m*/*z* 1502.7. Found: *m*/*z* 1525.6 $[M + Na]^+$, 1541.8 $[M + K]^+$.

2-(Tetradecyl)hexadecyl 2,3,4,6-tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*acetyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*β*-D-*galactopyranoside* (**23**).—To a solution of the trichloroacetimidate **22** (50 mg, 33 μmol) and 2-(tetradecyl)hexadecanol (30 mg, 68 μmol) in CH_2Cl_2 (1 mL) were added AW300 molecular sieves (300 mg), and the mixture was stirred for 3 h at rt, then cooled to 0 °C. Boron trifluoride etherate (19 μL) was added, and the mixture was stirred for 5 h at 0 °C then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings was successively washed with water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 3:2 hexane–EtOAc as eluent to give **23** (46 mg, 49%): $[\alpha]_D + 64.4°$ (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 4.77 (d, 1 H, $J_{1'',2''}$ 7.4 Hz, H-1″), 4.70 (d, 1 H, $J_{1,2}$ 7.9 Hz, H-1), 4.43 (d, 1 H, $J_{1',2'}$, 7.9 Hz, H-1′), 3.92 (dd, 1 H, $-OCH_2-$), 3.33 (dd, 1 H, $-OCH_2-$), 1.34 (br.s, 52 H, 26 × CH_2), 0.96 (t, 6 H, 2 × $-CH_2CH_3$); MALDI-TOFMS: Calcd for $C_{103}H_{126}O_{26}$: *m*/*z* 1778.8. Found: *m*/*z* 1801.7 $[M + Na]^+$, 1817.7 $[M + K]^+$.

2-(Tetradecyl)hexodecyl β-D-*galactopyranosyl*-(1→6)-*β*-D-*galactopyranosyl*-(1→6)-

β-D-*galactopyranoside* (**24**).—To a solution of **23** (29 mg, 16.3 μmol) in 3:1 MeOH–1,4-dioxane (2 mL) was added NaOMe (20 mg), and the mixture was stirred for 5 h at rt, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with 1:1 $CHCl_3$–MeOH. The filtrate and washings were combined and concentrated. Column chromatography (1:1 $CHCl_3$–MeOH) of the residue on Sephadex LH-20 gave **24** (14 mg, 93%): $[\alpha]_D$ −23.8° (*c* 0.2, 1:1 $CHCl_3$–MeOH); ^1H NMR ($CDCl_3$–CD_3OD): *δ* 4.30 (d, 1 H, *J* 8.0 Hz, H-1), 4.19 (d, 1 H, *J* 7.5 Hz, H-1′), 4.10 (d, 1 H, *J* 7.5 Hz, H-1″); MALDI-TOFMS: Calcd for $C_{48}H_{92}O_{16}$: *m*/*z* 924.6. Found: *m*/*z* 947.3 $[M + Na]^+$, 963.5 $[M + K]^+$.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*[2,3,4-tri*-O-*benzyl*-*α*-L-*fucopyranosyl*-(1→3)*]-2,4,-di*-O-*acetyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*β*-D-*galactopyranoside* (**25**).—To a solution of **20** (180 mg, 0.13 mmol) and **13** (88 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) was added 4 Å molecular sieves (300 mg), and the mixture was stirred for 2 h at rt, then cooled to 0 °C. DMTST (147 mg, 0.57 mmol) was added to the mixture, which was stirred for 5 h at 0 °C, then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings were successively washed with water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 15:1 benzene–acetone as eluent to give **25** (209 mg, 90%): $[\alpha]_D + 57.2°$ (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): *δ* 4.96 (d, 1 H, *J* 3.7 Hz, H-1 of Fuc), 4.79 (d, 1 H, *J* 7.9 Hz, H-1a), 4.79 (d, 1 H, *J* 7.9 Hz, H-1c), 4.33 (d, 1 H, *J* 7.9 Hz, H-1b). Anal. Calcd for $C_{103}H_{104}O_{29}Si$ (1834.1): C, 67.45; H, 5.72. Found: C, 67.20; H, 5.77.

2-(Trimethylsilyl)ethyl 2,3,4,6-tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*[2,3,4-tri*-O-*acetyl*-*α*-L-*fucopyranosyl*-(1→3)*]-2,4,-di*-O-*acetyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*β*-D-*galactopyranoside* (**26**).—A solution of **25** (278 mg, 0.17 mol) in MeOH (4 mL), THF (1 mL) and AcOH (0.1 mL) was hydrogenolysed in the presence of 10% Pd–C (200 mg) for 18 h at rt, then filtered and concentrated. The residue was acetylated with Ac_2O (3 mL) in pyridine (4 mL) for 3 h at rt. Workup was carried out as described for **15** and the product was purified by silica gel column chromatography using 1:1 hexane–EtOAc as an eluent to give **26** (235 mg, 92%, 2 steps): $[\alpha]_D + 42.3°$ (*c* 1.7, $CHCl_3$); ^1H NMR ($CDCl_3$): *δ* 5.22 (d, 1 H, *J* 3.7 Hz, H-1 of Fuc), 4.79 (d, 1 H, *J* 7.9 Hz, H-1c), 4.76 (d, 1 H, *J* 7.9 Hz, H-la), 4.26 (d, 1 H, *J* 8.0 Hz, H-1b). Anal. Calcd for $C_{88}H_{92}O_{32}Si$ (1689.8): C, 62.55; H, 5.49. Found: C, 62.25; H, 5.46.

2,3,4,6-Tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*[2,3,4-tri*-O-*benzyl*-*α*-L-*fucopyranosyl*-(1→3)*]-[2,4-di*-O-*acetyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*β*-D-*galactopyranosyl trichloroacetimidate* (**27**).—To a solution of **26** (165 mg, 98 μmol) in CH_2Cl_2 (3 mL) cooled to 0 °C was added CF_3COOH (2 mL), and the mixture was stirred for 30 min at rt and concentrated. Ethyl acetate and toluene (1:2) were added and then removed to give the 1-hydroxy compound. To a solution of the residue in CH_2Cl_2 (2 mL) cooled to 0 °C were added trichloroacetonitrile (300 μL, 3 mmol) and DBU (18 μL, 0.12 mmol). The mixture was stirred for 2 h at 0 °C. After completion of the reaction, the mixture was concentrated. Column chromatography (20:1 benzene–acetone) of the residue on silica gel gave **27** (162 mg, 95%) as an amorphous mass: $[\alpha]_D + 45.8°$ (*c* 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$): *δ* 8.61 (s, 1H, NH), 6.85 (d, 1 H, *J* 3.7 Hz, H-1a), 5.20 (d, 1 H, *J* 3.7 Hz, H-1 of Fuc), 4.73 (d, 1 H, *J* 7.9 Hz, H-1c), 4.24 (d, 1 H, *J* 7.9 Hz, H-1b); MALDI-TOFMS: Calcd for $C_{85}H_{80}Cl_3NO_{32}$: *m*/*z* 1732.8. Found: *m*/*z* 1755.9 $[M + Na]^+$, 1771.8 $[M + K]^+$.

2-(Tetradecyl)hexadecyl 2,3,4,6-tetra-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*[2,3,4-tri*-O-*acetyl*-*α*-L-*fucopyranosyl*-(1→3)*]-2,4,-di*-O-*benzoyl*-*β*-D-*galactopyranosyl*-(1→6)-*2,3,4-tri*-O-*benzoyl*-*β*-D-*galactopyranoside* (**28**).—(a) To a solution of the trichloroacetimidate **27** (30 mg, 17 μmol) and 2-(tetradec-

yl)hexadecanol (15 mg, 34 μmol) in CH_2Cl_2 (1 mL) were added AW300 molecular sieves (300 mg), and the mixture was stirred for 3 h at rt, then cooled to 0 °C. Boron trifluoride etherate (25 μL) was added, and the mixture was stirred for 5 h at 0 °C, then neutralized with Et_3N. The solids were filtered off and washed with $CHCl_3$. The combined filtrate and washings was successively washed with water, dried (Na_2SO_4), and concentrated. The product was purified by silica gel column chromatography using 8:1 benzene–acetone as an eluent to give **28** (10 mg, 29%). (b) To a solution of the trichloroacetimidate **27** (95 mg, 55 μmol) and 2-(tetradecyl)hexadecanol (48 mg, 110 μmol) in CH_2Cl_2 (1 mL) were added 4 Å molecular sieves (300 mg), and the mixture was stirred for 3 h at rt, then cooled to 0 °C. Me_3SiOTf (13 μL, 66 μmol) was added, and the mixture was stirred for 5 h at 0 °C, then neutralized with Et_3N. Workup as described for (a) gave **28** (59 mg, 53%): $[\alpha]_D + 23.2°$ (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.21 (d, 1 H, *J* 3.7 Hz, H-1 of Fuc), 4.77 (d, 1 H, *J* 7.9 Hz, H-1c), 4.68 (d, 1 H, *J* 7.9 Hz, H-la), 4.25 (d, 1 H, *J* 8.6 Hz, H-1b), 3.92 (dd, 1 H, $-OCH_2-$), 3.33 (dd, 1 H, $-OCH_2-$), 1.34 (br.s, 52 H, $26 \times CH_2$), 0.96 (t, 6 H, $2 \times -CH_2CH_3$); MALDI-TOFMS: Calcd for $C_{113}H_{150}O_{32}$: *m*/*z* 2019.0. Found: *m*/*z* 2042.1 $[M + Na]^+$, 2058.2 $[M + K]^+$.

*2-(Tetradecyl)hexadecyl β-*D*-galactopyranosyl-(1→6)-[α-*L*-fucopyranosyl-(1→3)]-β-*D*-galactopyranosyl-(1→6)-β-*D*-galactopyranoside* (**29**).—To a solution of **28** (59 mg, 29.2 μmol) in 3:1 MeOH–l,4-dioxane (2 mL) was added NaOMe (20 mg), and the mixture was stirred for 5 h at rt, then neutralized with Amberlite IR-120 (H^+) resin. Workup as described for **18** gave **29** (30 mg, 96%): $[\alpha]_D$ −46.3° (*c* 0.1, 1:1 $CHCl_3$–MeOH); ^1H NMR ($CDCl_3$–CD_3OD): δ 5.14 (d, 1 H, *J* 4.3 Hz, H-1 of Fuc), 4.35 (d, 1 H, *J* 8.0 Hz, H-1a), 4.29 (d, 1 H, *J* 7.3 Hz, H-1c), 4.17 (d, 1 H, *J* 6.6 Hz, H-1b); MALDI-TOFMS: Calcd for $C_{54}H_{102}O_{20}$: *m*/*z* 1070.7. Found: *m*/*z* 1093.7 $[M + Na]^+$, 1109.5 $[M + K]^+$.

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