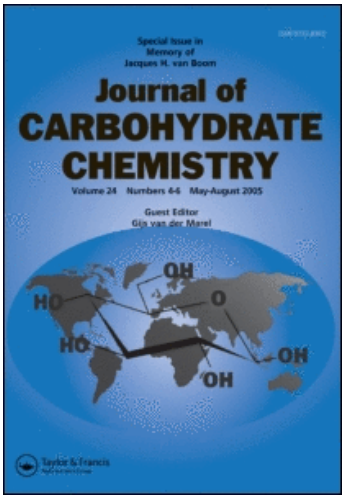

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Synthetic Studies on Sialoglycoconjugates 85: Synthesis of Sialyl Lewis X Ganglioside Analogs Containing a Variety of Anionic Substituents in Place of Sialic Acid

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To cite this Article Yoshida, Masahiro , Kawakami, Yukiko , Ishida, Hideharu , Kiso, Makoto and Hasegawa, Akira(1996) 'Synthetic Studies on Sialoglycoconjugates 85: Synthesis of Sialyl Lewis X Ganglioside Analogs Containing a Variety of Anionic Substituents in Place of Sialic Acid', Journal of Carbohydrate Chemistry, 15: 4, 399 — 418
To link to this Article: DOI: 10.1080/07328309608005662
URL: http://dx.doi.org/10.1080/07328309608005662

J. CARBOHYDRATE CHEMISTRY, 15(4), 399-418 (1996)

SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 85: SYNTHESIS OF SIALYL LEWIS X GANGLIOSIDE ANALOGS CONTAINING A VARIETY OF ANIONIC SUBSTITUENTS IN PLACE OF SIALIC ACID

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Received October 14, 1995 - Final Form January 23, 1996

ABSTRACT

Three sialyl-Le^x ganglioside analogs containing carboxymethyl, sulfate, and phosphate groups in place of the sialic acid moiety, have been synthesized. Glycosylation of 2-(trimethylsilyl)ethyl *O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2, 4, 6-tri-*O*-benzyl-β-D-galactopyranoside (**10**) with methyl 2,4,6-tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-1-thio-β-D-galactopyranoside (**6**) or methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-levulinoyl-1-thio-β-D-galactopyranoside (**9**) using dimethyl(methylthio)sulfonium triflate (DMTST) as a promoter, afforded the corresponding tetrasaccharide derivatives **11** and **19**. Compounds **11** and **19** were converted into the α-trichloroacetimidates **14** and **23**, *via* reductive removal of the benzyl and benzylidene groups, *O*-acetylation, removal of the 2-(trimethylsilyl)ethyl group, and treatment with trichloroacetonitrile, which, on coupling with (2*S*, 3*R*, 4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**15**) or 2-(tetradecyl)hexadecan-1-ol (**24**), gave the lipophilic derivatives **16** and **25**. Compound **16** was transformed, *via* selective reduction of the azido group, condensation with octadecanoic acid, *O*-deacylation, and hydrolysis of the methyl ester group, into the title compound **18** in good yield. Compound **25** was treated with hydrazine acetate to give compound **26**, which in turn was transformed, *via* sulfation or phosphorylation, and *O*-deacylation, into the target compounds **28** and **31**.

INTRODUCTION

Sialyl-Le^x was first isolated[1] from human kidney and found[2] to be widespread as the tumor-associated antigen. Recently, it has been demonstrated that the selectins [3-6], such as E-, P-, and L-selectin, recognize the sialyl-Le^x determinant, α-Neu5Ac-(2→3)-β-D-Gal-(1→4)-[α-L-Fuc-(1→3)]-β-D-GlcNAc, which is found as the terminal carbohydrate structure of both cell membrane glycolipids and glycoproteins.

Previously, we reported[7] the synthesis of sulfo-Le^x analogs containing a ceramide or 2-(tetradecyl)hexadecyl residue, and examined[8] their competitive inhibition as well as binding activity to selectin-mediated adhesion. Interestingly, these sulfo-Le^x analogs, inhibited strongly the binding between the selectins and the sialyl-Le^x ganglioside, indicating an important influence for this reaction. In view of these facts, we describe herein the synthesis of sialyl-Le^x ganglioside analogs containing a variety of anionic substituents in place of sialic acid in sialyl-Le^x ganglioside, to clarify the effect of anionic groups for the selectin recognition.

RESULTS AND DISCUSSION

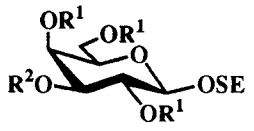
For the synthesis of carboxymethyl-, sulfo-, and phosphono-Le^x lipophilic derivatives, we selected 2-(trimethylsilyl)ethyl *O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside[9] (**10**) as the glycosyl acceptor, and methyl 2,4,6-tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-1-thio-β-D-galactopyranoside (**6**) and methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-3-*O*-levulinoyl-1-thio-β-D-galactopyranoside (**9**) as the key glycosyl donors.

2-(Trimethylsilyl)ethyl 2,4,6-tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranoside (**3**) was obtained in good yield from 2-(trimethylsilyl)ethyl β-D-galactopyranoside[10] (**1**) *via* dibutyltin oxide-mediated selective 3-*O*-(methoxycarbonyl)methylation using methyl bromoacetate and tetrabutylammonium bromide and subsequent *O*-benzoylation. Treatment[10] of **3** with trifluoroacetic acid in

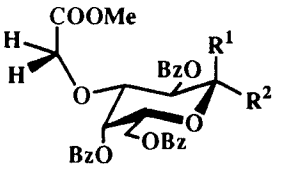
dichloromethane at room temperature gave the 1-hydroxy compound **4**. When treated with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 1 h at 0 °C, **4** gave the α-trichloroacetimidate **5** in quantitative yield. The glycosyl donor **6** was prepared from **5** with methylthiotrimethylsilane in the presence of boron trifluoride etherate, in 85% yield.

Selective 3-*O*-levulinoylation of methyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside[11] (**7**) with levulinic anhydride in pyridine-dichloromethane at -50 °C, and subsequent *O*-benzoylation afforded the another glycosyl donor **9** in good yield.

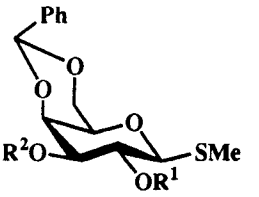
The glycosylation of **10** with **6** in dichloromethane using dimethyl(methylthio)sulfonium triflate[12,13] (DMTST) as the glycosyl promoter, gave the desired Le^x tetrasaccharide derivative **11** in 89% yield. Significant signals in the ^1H NMR spectrum of the **11** were a three-proton singlet at δ 3.56 (*O*-methyl) and a one-proton doublet of doublets at δ 5.44 ($J_{1,2}$ = 8.6 Hz, $J_{2,3}$ = 9.5 Hz, H-2c), indicating the newly formed glycosidic linkage to be β. In essentially the same way, reaction of **10** with **9** afforded the expected Le^x tetrasaccharide **19** in 46% yield. H-2 proton of the galactose residue at the non-reducing end in the ^1H NMR spectrum of **19** appeared at δ 5.59 ($J_{1,2}$ = 8.4 Hz), indicating the structure assigned. Catalytic hydrogenolysis in methanol-acetic acid at 45 °C of the benzyl groups of **11**, or in ethanol-acetic acid at 40 °C of the benzyl and benzylidene groups of **19**, and subsequent *O*-acetylation gave the per-*O*-acyl compounds **12** and **21**, which, on treatment with trifluoroacetic acid in dichloromethane for 1 h at room temperature gave the 1-hydroxy compounds **13** and **22** in 93% and 89% yields, respectively. When treated with trichloroacetonitrile in dichloromethane in the presence of DBU for 1 h at 0 °C, **13** and **22** gave the corresponding α-trichloroacetimidates **14** and **23** in quantitative yields, respectively. The ^1H NMR data for the reducing end Gal unit in **14** [δ 6.50 ($J_{1,2}$ = 3.7 Hz, H-1) and 8.64 (C=NH)] and **23** [δ 6.48 ($J_{1,2}$ = 3.9 Hz, H-1) and 8.63 (C=NH)] indicated the imidates to be α.



	R^1	R^2
1	H	H
2	H	CH_2COOMe
3	Bz	CH_2COOMe



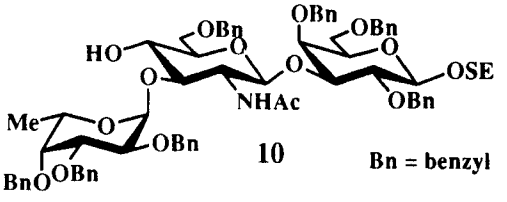
	R^1	R^2
4	H, OH	
5	$OC(=NH)CCl_3$	H
6	H	SMe



	R^1	R^2
7	H	H
8	H	Lev
9	Bz	Lev

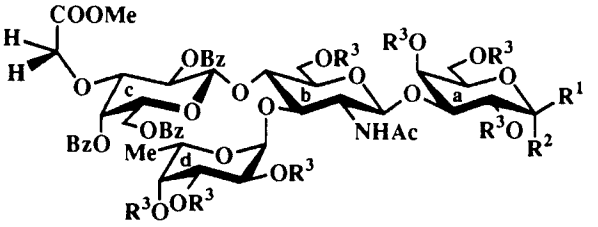
SE = 2-(trimethylsilyl)ethyl
Bz = benzoyl

Lev = levulinoyl

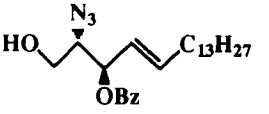


10

Bn = benzyl



	R^1	R^2	R^3
11	OSE	H	Bn
12	OSE	H	Ac
13	H, OH		Ac
14	H	$OC(=NH)CCl_3$	Ac



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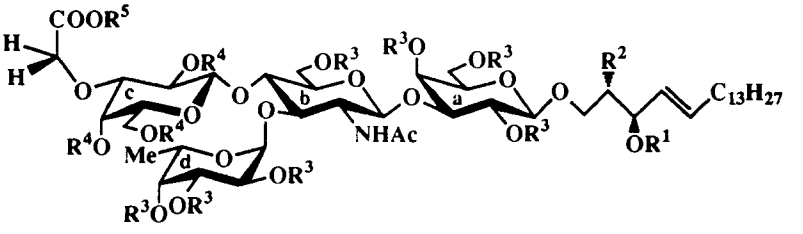
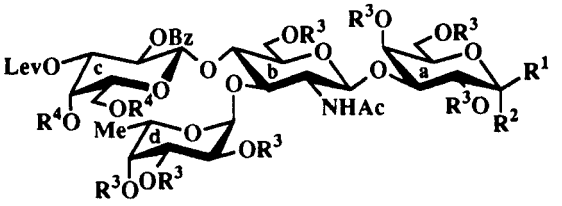
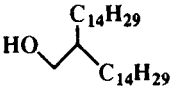


	R^1	R^2	R^3	R^4	R^5
16	Bz	N_3	Ac	Bz	Me
17	Bz	$NHCOC_{17}H_{35}$	Ac	Bz	Me
18	H	$NHCOC_{17}H_{35}$	H	H	H



	R^1	R^2	R^3	R^4
19	OSE	H	Bn	benzylidene
20	OSE	H	Ac	benzylidene
21	OSE	H	Ac	Ac
22	H, OH		Ac	Ac
23	H	$OC(=NH)CCl_3$	Ac	Ac



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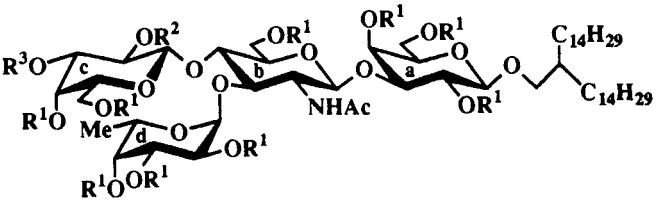
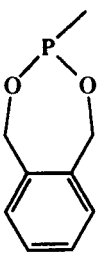
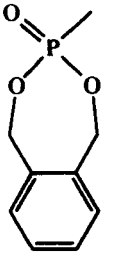


	R^1	R^2	R^3
25	Ac	Bz	Lev
26	Ac	Bz	H
27	Ac	Bz	SO_3•pyr.
28	H	H	SO_3Na
29	Ac	Bz	XEP
30	Ac	Bz	XEPO
31	H	H	$P(O)(ONa)_2$

XEP = 

XEPO = 

The condensation[14,15] of (2*S*, 3*R*, 4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[16,17] (**15**) with **14** in dichloromethane in the presence of boron trifluoride etherate for 2 h at 0 °C afforded the expected β-glycoside **16** in 38% yield. Selective reduction[18,19] of the azido group in **16** with hydrogen sulfide in aqueous pyridine for 50 h at 0 °C gave the syrupy amine, which, on coupling with octadecanoic acid using 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (WSC) in dichloromethane, gave the ceramide derivative **17** in 61% yield.

O-Deacylation of **17** with sodium methoxide in methanol, and subsequent saponification of the methyl ester group, yielded the target carboxymethyl-Le^x **18** in good yield after chromatography on a column of Sephadex LH-20. The ^{1}H NMR data of the product thus obtained are consistent with the structure assigned.

The glycosylation[14,15] of 2-(tetradecyl)hexadecan-1-ol[20] (**24**) with **23** in dichloromethane in the presence of boron trifluoride etherate for 21 h at 7 °C afforded the desired lipophilic derivative **25** in 37% yield. Selective removal of the levulinoyl group of **25** performed with hydrazine acetate in ethanol gave the monohydroxy derivative **26** in 87% yield.

Treatment of **26** with sulfur trioxide-pyridine complex in *N*,*N*-dimethylformamide (DMF) for 4 h at room temperature gave the sulfo derivative as its pyridine salt **27**, and this was transformed, by *O*-deacylation with sodium methoxide in methanol and tetrahydrofuran, into the title sulfo-Le^x sodium salt **28** in good yield.

Treatment of **26** with *o*-xylylene *N*,*N*-diethylphosphoramidite[21,22] (XEPA) in dichloromethane in the presence of 1*H*-tetrazole for 13 h at room temperature gave **29**, and this was transformed, *via* oxidation of phosphorus atom with 3-chloroperoxybenzoic acid in dichloromethane, followed by catalytic hydrogenolysis (10% Pd-C) in methanol of the *o*-xylylene group, and *O*-deacylation with sodium methoxide in methanol and tetrahydrofuran, into the target phosphono-Le^x **31** as its sodium salt in high yield.

The synthesized carboxymethyl- (**18**), sulfo- (**28**), and phosphono-Le^x (**31**) ganglioside analogs showed significant competitive inhibition activity between the selectins (E-, P-, and L-selectin) and sialyl-Le^x ganglioside. These results suggest that

the sialic acid part may be replaced by other anionic substituents. The detailed biological results will be published in *J. Med. Chem.*[8]

EXPERIMENTAL

General Procedures. Specific rotations were determined with a Union PM-201 polarimeter at 25 °C and IR spectra were recorded with a Jasco A-100 spectrophotometer. ^{1}H NMR spectra were recorded with a JEOL JNM-GX 270 spectrometer. Electroscopy mass spectra were recorded on an API-III triple quadrupole mass spectrometer (Perkin-Elmer Sciex Instruments, Thornhill, Canada) fitted with an atmospheric pressure ionization source. Preparative chromatography was performed on silica gel (Fuji Silysia Co., 127 mesh) with the solvent systems specified. Concentrations were conducted *in vacuo*.

2-(Trimethylsilyl)ethyl 3-*O*-(Methoxycarbonyl)methyl-β-D-galactopyranoside (2). A suspension of 2-(trimethylsilyl)ethyl β-D-galactopyranoside[10] (**1**; 1.0 g, 3.6 mmol) and dibutyltin oxide (1.3 g) in MeOH (10 mL) was heated, with stirring, for 6 h at 70 °C then concentrated. To a solution of the residue in benzene (10 mL) were added methyl bromoacetate (1 mL) and tetrabutylammonium bromide (0.6 g), and the mixture was stirred under reflux for 15 min then concentrated. Column chromatography (3:2 AcOEt-hexane) of the residue on silica gel (80 g) gave **2** (870 mg, 69%) as an amorphous mass: $[\alpha]_D$ -31.0° (*c* 1.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 3.32 (dd, 1H, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 3.4 Hz, H-3), 3.50 (m, 1H, H-5), 3.57, 3.98 (m, 2H, $Me_3SiCH_2CH_2$), 3.75 (s, 3H, MeO), 4.25 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), and 4.28 (m, 2H, $MeOCOCH_2$).

Anal. Calcd for $C_{14}H_{28}O_8Si$ (352.5): C, 47.71; H, 8.01. Found: C, 47.56; H, 7.78.

2-(Trimethylsilyl)ethyl 2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranoside (3). To a solution of **2** (910 mg, 2.6 mmol) in pyridine (13 mL) was added benzoyl chloride (1.3 mL, 11.2 mmol), and the mixture was stirred for 2 h at room temperature. After completion of the reaction,

MeOH (3 mL) was added, and the mixture was stirred for 30 min at room temperature, concentrated, and extracted with CH_2Cl_2. The extract was successively washed with 2M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:3 AcOEt-hexane) of the residue on silica gel (80 g) gave **3** (1.4 g, 82%) as an amorphous mass: $[\alpha]_D$ +38.4° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.94 (m, 2H, $Me_3SiCH_2CH_2$), 3.48 (s, 3H, MeO), 3.62 (m, 1H, Me_3SiCH_2CH), 4.18 (d, 2H, J_{gem} = 7.1 Hz, $MeOCOCH_2$), 4.43 (dd, 1H, J_{gem} = 11.4 Hz, $J_{5,6}$ = 6.1 Hz, H-6), 4.63 (dd, 1H, $J_{5,6'}$ = 7.0 Hz, H-6'), 4.73 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 5.54 (dd, 1H, $J_{2,3}$ = 9.9 Hz, H-2), 5.92 (d, 1H, $J_{3,4}$ = 2.8 Hz, H-4), and 7.26-8.17 (m, 15H, 3Ph).

Anal. Calcd for $C_{35}H_{40}O_{11}Si$ (664.8): C, 63.24; H, 6.07. Found: C, 63.15; H, 5.93.

2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-D-galactopyranose (4). To a solution of **3** (2.3 g, 3.5 mmol) in CH_2Cl_2 (15 mL) was added trifluoroacetic acid (10 mL), and the mixture was stirred for 1 h at room temperature and concentrated. Column chromatography (1:2 AcOEt-hexane) of the residue on silica gel (100 g) gave **4** (1.9 g, 95%) as an amorphous mass: IR (film) 3300 (OH), 1750 and 1250 (ester), and 700 cm^{-1} (Ph).

Anal. Calcd for $C_{30}H_{28}O_{11}$ (564.5): C, 63.83; H, 5.00. Found: C, 63.66; H, 4.97.

2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-α-D-galactopyranosyl trichloroacetimidate (5). To a solution of **4** (820 mg, 1.5 mmol) in CH_2Cl_2 (10 mL) and trichloroacetonitrile (4.4 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 0.22 mL) at 0 °C, and the mixture was stirred for 1 h at 0 °C, then concentrated. Column chromatography (2:5 AcOEt-hexane) of the residue on silica gel (100 g) gave **5** (1.0 g, quantitative) as an amorphous mass: $[\alpha]_D$ +123.2° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 3.59 (s, 3H, MeO), 4.29 (m, 2H, $MeOCOCH_2$), 4.45 (m, 2H, H-3 and H-6), 4.55 (dd, 1H, J_{gem} = 11.4 Hz, $J_{5,6'}$ = 6.5 Hz, H-6'), 4.69 (m, 1H, H-5), 5.74 (dd, 1H, $J_{1,2}$ = 3.8 Hz, $J_{2,3}$ = 10.4 Hz, H-

2), 6.12 (d, 1H, $J_{3,4}$ = 2.6 Hz, H-4), 6.84 (d, 1H, H-1), 7.26-8.15 (m, 15H, 3Ph), and 8.59 (s, 1H, C=NH).

Anal. Calcd for $C_{32}H_{28}NO_{11}Cl_3$ (708.9): C, 54.22; H, 3.98; N, 1.98. Found: C, 54.05; H, 3.77; N, 1.69.

Methyl 2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-1-thio-β-D-galactopyranoside (6). To a solution of **5** (786 mg, 1.1 mmol) in $ClCH_2CH_2Cl$ (11 mL) were added, with stirring, methylthiotrimethylsilane (0.63 mL, 4.5 mmol) and boron trifluoride etherate (0.55 mL), and the mixture was stirred for 3 h at room temperature. CH_2Cl_2 (100 mL) was added, and the solution was washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:4 AcOEt-hexane) of the residue on silica gel (80 g) gave **6** (561 mg, 85%) as an amorphous mass: $[\alpha]_D$ +68.7° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.31 (s, 3H, MeS), 3.48 (s, 3H, MeO), 4.13 (dd, 1H, $J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 3.2 Hz, H-3), 4.21 (d, 1H, J_{gem} = 7.3 Hz, $MeOCOCH_2$), 4.42 (dd, 1H, J_{gem} = 11.4 Hz, $J_{5,6}$ = 6.0 Hz, H-6), 4.62 (dd, 1H, $J_{5,6'}$ = 6.8 Hz, H-6'), 4.67 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 5.67 (t, 1H, H-2), 6.01 (d, 1H, H-4), and 7.26-8.13 (m, 15H, 3Ph).

Anal. Calcd for $C_{31}H_{30}O_{10}S$ (594.6): C, 62.62; H, 5.09. Found: C, 62.32; H, 4.94.

Methyl 4,6-*O*-Benzylidene-3-*O*-levulinoyl-1-thio-β-D-galactopyranoside (8). To a solution of methyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside[11] (**7**; 100 mg, 0.34 mmol) in pyridine (3 mL) and CH_2Cl_2 (3 mL), cooled to -50 °C, were added, with stirring, a solution of levulinic anhydride (179 mg, 0.84 mmol) in CH_2Cl_2 (1 mL) and 4-dimethylaminopyridine (41 mg), and the stirring was continued for 30 min at -50 °C. MeOH (3 mL) was added to the mixture, concentrated and extracted with CH_2Cl_2. The extract was successively washed with 2M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:1 AcOEt-hexane) of the residue on silica gel (50 g) gave **8** (85 mg, 64%) as an amorphous mass: $[\alpha]_D$ +40.1° (*c* 1.7, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 2.10 (s, 3H, $MeCOCH_2CH_2$), 2.26 (s, 3H, MeS), 2.52-2.88 (m, 4H, $MeCOCH_2CH_2$), 3.58 (s, 1H, H-5), 4.01 (dd, 1H, J_{gem} = 12.6 Hz, $J_{5,6}$ = 1.3 Hz, H-6), 4.09 (dd, 1H, $J_{1,2}$ =

9.3 Hz, $J_{2,3}$ = 9.7 Hz, H-2), 4.33 (d, 1H, H-6'), 4.35 (d, 1H, $J_{3,4}$ = 3.5 Hz, H-4), 4.36 (d, 1H, H-1), 4.94 (dd, 1H, H-3), and 7.34-7.51 (m, 5H, Ph).

Anal. Calcd for $C_{19}H_{24}O_7S$ (396.5): C, 57.56; H, 6.10. Found: C, 57.32; H, 6.02.

Methyl 2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-levulinoyl-1-thio-β-D-galactopyranoside (9). To a solution of **8** (104 mg, 0.26 mmol) in pyridine (1 mL) was added benzoyl chloride (80 μL, 0.69 mmol), and the mixture was stirred for 3 h at room temperature. MeOH (0.5 mL) was added to the mixture, concentrated and extracted with CH_2Cl_2. The extract was successively washed with 2M HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:2 AcOEt-hexane) of the residue on silica gel (50 g) gave **9** (111 mg, 85%) as an amorphous mass: $[\alpha]_D$ +55.9° (*c* 1.2, CH_2Cl_2); ^1H NMR ($CDCl_3$) δ 1.88 (s, 3H, *Me*$COCH_2CH_2$), 2.27 (s, 3H, MeS), 2.41-2.58 (m, 4H, $MeCOCH_2CH_2$), 3.62 (s, 1H, H-5), 4.01 (near d, 1H, J_{gem} = 12.5 Hz, H-6), 4.33 (d, 1H, H-6'), 4.41 (d, 1H, $J_{3,4}$ = 3.5 Hz, H-4), 4.54 (d, 1H, $J_{1,2}$ = 9.9 Hz, H-1), 5.20 (dd, 1H, $J_{2,3}$ = 9.9 Hz, H-3), 5.51 (s, 1H, PhC*H*), 5.73 (t, 1H, H-2), and 7.25-8.02 (m, 10H, 2Ph).

Anal. Calcd for $C_{26}H_{28}O_8S$ (500.6): C, 62.39; H, 5.64. Found: C, 62.16; H, 5.55.

2-(Trimethylsilyl)ethyl *O*-[2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranosyl]-(1→4)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside (11). To a solution of 2-(trimethylsilyl)ethyl *O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside (**10**; 118 mg, 94 μmol) and **6** (100 mg, 0.17 mmol) in CH_2Cl_2 (0.5 mL) were added molecular sieves 4Å (MS-4Å; 218 mg), and the mixture was stirred for 8 h at room temperature. Dimethyl(methylthio)sulfonium triflate (DMTST; 266 mg) and MS-4Å (266 mg) were added to the stirred mixture at 7 °C, and the stirring was continued for 12 h at 7 °C. The precipitate was filtered off and washed with CH_2Cl_2. The filtrate and washings

were combined, and the solution was washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:2 AcOEt-hexane) of the residue on silica gel (50 g) gave **11** (150 mg, 89%) as an amorphous mass: $[\alpha]_D$ -17.2° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.95 (m, 2H, $Me_3SiCH_2CH_2$), 1.23 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.65 (s, 3H, AcN), 3.56 (s, 3H, MeO), 5.30 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1d), 5.44 (dd, 1H, $J_{1,2}$ = 8.6 Hz, $J_{2,3}$ = 9.5 Hz, H-2c), 5.76 (d, 1H, NH), 5.81 (bd, 1H, $J_{3,4}$ = 3.5 Hz, H-4c), and 7.11-8.14 (m, 50H, 10Ph).

Anal. Calcd for $C_{104}H_{115}NO_{25}Si$ (1807.1): C, 69.12; H, 6.41; N, 0.78. Found: C, 68.83; H, 6.31; N, 0.61.

2-(Trimethylsilyl)ethyl *O*-[2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranosyl]-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (12). A solution of **11** (94 mg, 52 μmol) in MeOH (15 mL) and AcOH (2.6 mL) was hydrogenolyzed in the presence of 10% Pd-C (113 mg) for 22 h at 45 °C, then filtered and concentrated. The residue was acetylated with Ac_2O (1.5 mL)-pyridine (3 mL) for 48 h at 40 °C. The product was purified by chromatography on a column of silica gel (50 g) with 2:1 AcOEt-hexane afforded **12** (47 mg, 62%) as an amorphous mass: $[\alpha]_D$ -26.2° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.92 (m, 2H, $Me_3SiCH_2CH_2$), 1.30 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6d), 1.89-2.17 (7s, 24H, 7AcO and AcN), 3.50 (s, 3H, MeO), 3.59 (dd, 1H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 3.9 Hz, H-3a), 5.24 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1d), 5.42 (d, 1H, H-4a), 5.45 (t, 1H, $J_{1,2}$ = $J_{2,3}$ = 8.6 Hz, H-2c), 5.55 (d, 1H, NH), 5.91 (bd, 1H, $J_{3,4}$ = 3.3 Hz, H-4c), and 7.46-8.13 (m, 15H, 3Ph).

Anal. Calcd for $C_{69}H_{87}NO_{32}Si$ (1470.5): C, 56.36; H, 5.96; N, 0.95. Found: C, 56.27; H, 5.80; N, 0.74.

***O*-[2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranosyl]-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-acetyl-D-galactopyranose (13).** Selective removal of the 2-(trimethylsilyl)ethyl group in **12** (121 mg, 82 μmol) with trifluoroacetic acid (1 mL) in

CH_2Cl_2 (1.4 mL) as described for **4**, gave compound **13** (105 mg, 93%) as an amorphous mass: IR (film) 3500 (OH), 3350 (NH), 1720 and 1250 (ester), 1680 and 1530 (amide), and 710 cm^{-1} (Ph).

Anal. Calcd for $C_{64}H_{75}NO_{32}$ (1370.3): C, 56.10; H, 5.52; N, 1.02. Found: C, 55.81; H, 5.41; N, 0.77.

***O*-[2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranosyl]-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate (14).** To a solution of **13** (105 mg, 77 μmol) in CH_2Cl_2 (1.3 mL) and trichloroacetonitrile (0.23 mL) was added DBU (12 mg) at 0 °C. A similar processing, as described for **5**, gave compound **14** (115 mg, quantitative) as an amorphous mass: $[\alpha]_D$ +3.6° (*c* 2.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.30 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.88-2.17 (8s, 24H, 7AcO and AcN), 3.49 (s, 3H, MeO), 5.44 (m, 1H, H-2c), 5.45 (d, 1H, $J_{3,4}$ = 3.8 Hz, H-4a), 5.64 (d, 1H, NH), 5.92 (bd, 1H, $J_{3,4}$ = 3.3 Hz, H-4c), 6.50 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1a), 7.46-8.12 (m, 15H, 3Ph), and 8.64 (s, 1H, C=NH).

Anal. Calcd for $C_{66}H_{75}N_2O_{32}Cl_3$ (1514.7): C, 52.34; H, 4.99; N, 1.85. Found: C, 52.16; H, 4.94; N, 1.58.

***O*-[2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranosyl]-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1 → 1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (16).** To a solution of **14** (117 mg, 77 μmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[16,17] (**15**; 66 mg, 0.15 mmol) in CH_2Cl_2 (2.6 mL) was added MS-4Å (type AW-300; 2.7 g), and the mixture was stirred for 3 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (57 μL) was added, and the mixture was stirred for 2 h at 0 °C and then filtered. The insoluble material was washed with CH_2Cl_2, and the combined filtrate and washings was washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (2:1 AcOEt-hexane) of the residue on silica gel (80 g) gave **16** (52

mg, 38%) as an amorphous mass: $[\alpha]_D$ -20.8° (*c* 1.0, $CHCl_3$); IR (film) 3350 (NH), 3150-2800 (Me and methylene), 2100 (N_3), 1740 and 1230 (ester), 1680 and 1550 (amide), and 710 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.88 (t, 3H, *Me*CH_2), 1.24 (s, 22H, 11CH_2), 1.30 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.88-2.16 (8s, 24H, 7AcO and AcN), 3.50 (s, 3H, MeO), 5.24 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-1d), 5.42 (m, 1H, H-4a), 5.49 (m, 1H, H-2c), 5.54 (d, 1H, NH), 5.89 (m, 1H, H-4c), 5.90 (m, 1H, H-5 of sphingosine), and 7.41-8.13 (m, 20H, 4Ph).

Anal. Calcd for $C_{89}H_{112}N_4O_{34}$ (1781.9): C, 59.99; H, 6.34; N, 3.14. Found: C, 59.96; H, 6.31; N, 2.88.

***O*-[2,4,6-Tri-*O*-benzoyl-3-*O*-(methoxycarbonyl)methyl-β-D-galactopyranosyl]-(1→4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1→3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (17).** Hydrogen sulfide was bubbled through a stirred solution of **16** (52 mg, 29 μmol) in aqueous 83% pyridine (6 mL) for 50 h at 0 °C. The mixture was concentrated, and the residue was stirred with octadecanoic acid (35 mg, 0.12 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (35 mg) in CH_2Cl_2 (2.9 mL) for 13 h at room temperature. CH_2Cl_2 (50 mL) was added, and the mixture was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (2:1 AcOEt-hexane) of the residue on silica gel (40 g) gave **17** (36 mg, 61%) as an amorphous mass: $[\alpha]_D$ -7.4° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, 2*Me*CH_2), 1.26 (s, 52H, 26CH_2), 1.28 (m, 3H, H-6d), 1.89-2.16 (8s, 24H, 7AcO and AcN), 3.50 (s, 3H, MeO), 5.20 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1d), 5.80 (m, 1H, H-5 of sphingosine), and 7.40-8.12 (m, 20H, 4Ph).

Anal. Calcd for $C_{107}H_{148}N_2O_{35}$ (2022.3): C, 63.55; H, 7.38; N, 1.39. Found: C, 63.45; H, 7.32; N, 1.31.

***O*-(3-*O*-Carboxymethyl-β-D-galactopyranosyl)-(1→4)-*O*-[α-L-fucopyranosyl-(1→3)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-*O*-(β-D-galactopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-**

octadecene-1,3-diol (18). To a solution of **17** (36 mg, 18 μmol) in MeOH (5 mL) was added sodium methoxide (60 mg), and the mixture was stirred for 17 h at 40 °C, and water (1 mL) was added. The solution was stirred for 24 h at 40 °C, then treated with Amberlite IR-120 (H^+) resin and filtered. The resin was washed with 1:1 $CHCl_3$-MeOH, and the combined filtrate and washings were concentrated. Column chromatography (1:1 $CHCl_3$-MeOH) of the residue on Sephadex LH-20 (70 g) gave **18** (22 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -19.2° (*c* 0.7, 1:1 $CHCl_3$-MeOH); ^1H NMR (1:1 $CDCl_3$-CD_3OD) δ 0.89 (t, 6H, 2*Me*CH_2), 1.21 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6d), 1.27 (s, 52H, 26CH_2), 2.00 (s, 3H, AcN), 2.17 (t, 2H, CO*C*$H_2$$CH_2$), 4.48 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1 of Gal), 5.09 (d, 1H, $J_{1,2}$ = 3.5 Hz, H-1d), 5.45 (dd, 1H, $J_{3,4}$ = 7.3 Hz, $J_{4,5}$ = 15.4 Hz, H-4 of sphingosine), and 5.70 (dt, 1H, $J_{5,6}$ = $J_{5,6'}$ = 7.1 Hz, H-5 of sphingosine).

Anal. Calcd for $C_{64}H_{116}N_2O_{24}$ (1297.6): C, 59.24; H, 9.01; N, 2.16. Found: C, 59.18; H, 8.77; N, 1.99.

2-(Trimethylsilyl)ethyl *O*-(2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-[(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside (19). Glycosylation of **10** (150 mg, 0.12 mmol) with **9** (110 mg, 0.22 mmol) in CH_2Cl_2 (1 mL) in the presence of DMTST and MS-4Å (650 mg, 52% DMTST by weight) for 84 h at 7 °C, as described for **11**, gave compound **19** (94 mg, 46%) as an amorphous mass: $[\alpha]_D$ +0.2° (*c* 1.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.92 ($Me_3SiCH_2CH_2$), 1.26 (d, 3H, $J_{5,6}$ = 7.0 Hz, H-6d), 1.95 (s, 3H, AcN), 2.03 (s, 3H, *Me*$COCH_2CH_2$), 2.48-2.76 (m, 4H, MeCOCH_2CH_2), 4.96 (dd, 1H, $J_{2,3}$ = 9.9 Hz, $J_{3,4}$ = 3.7 Hz, H-3c), 4.98 (d, 1H, $J_{1,2}$ = 3.3 Hz, H-1d), 5.56 (s, 1H, PhC*H*), 5.59 (dd, 1H, $J_{1,2}$ = 8.4 Hz, H-2c), and 7.15-8.08 (m, 45H, 9Ph).

Anal. Calcd for $C_{99}H_{113}NO_{23}Si$ (1713.1): C, 69.41; H, 6.65; N, 0.82. Found: C, 69.21; H, 6.48; N, 0.55.

2-(Trimethylsilyl)ethyl *O*-(2-*O*-Benzoyl-4,6-*O*-benzylidene-3-*O*-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α

-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (20). A solution of **19** (100 mg, 58 μmol) in EtOH (15 mL) and AcOH (2.6 mL) was hydrogenolyzed in the presence of 10% Pd-C (120 mg) for 48 h at 40 °C, and subsequent acetylation with Ac_2O (2 mL) in pyridine (4 mL) as described for **12**, gave compound **20** (65 mg, 81%) as an amorphous mass: $[\alpha]_D$ -24.3° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.73 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6d), 0.91 (m, 2H, $Me_3SiCH_2CH_2$), 1.97-2.12 (9s, 27H, 7AcO, AcN and $MeCOCH_2CH_2$), 2.39-2.64 (m, 4H, $MeCOCH_2CH_2$), 3.50 and 3.93 (m, 2H, $Me_3SiCH_2CH_2$), 3.67 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 3.6 Hz, H-3a), 4.39 and 4.74 (2d, 2H, $J_{1,2}$ = 8.1 Hz, $J_{1,2}$ = 8.3 Hz, H-1a and H-1c), 5.57 (s, 1H, PhCH), and 7.28-8.05 (m, 10H, 2Ph).

Anal. Calcd for $C_{64}H_{85}NO_{30}Si$ (1376.5): C, 55.85; H, 6.22; N, 1.02. Found: C, 55.76; H, 6.14; N, 0.98.

2-(Trimethylsilyl)ethyl *O*-(4,6-Di-*O*-acetyl-2-*O*-benzoyl-3-*O*-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (21). Hydrogenolysis of **20** (140 mg, 0.10 mmol) in EtOH (16 mL) and AcOH (4 mL) in the presence of $PdCl_2$ (150 mg) for 24 h at 40 °C, and subsequent acetylation with Ac_2O (1.5 mL)-pyridine (3 mL) as described for **12**, gave compound **21** (87 mg, 62%) as an amorphous mass: $[\alpha]_D$ -47.5° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.92 (m, 2H, $Me_3SiCH_2CH_2$), 1.31 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.92-2.22 (10s, 33H, 9AcO, AcN and $MeCOCH_2CH_2$), 2.27-2.67 (m, 4H, $MeCOCH_2CH_2$), 3.50 (m, 1H, Me_3SiCH_2CH), 3.63 (dd, 1H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 3.6 Hz, H-3a), 4.30 and 4.73 (2d, 2H, $J_{1,2}$ = 7.9 Hz, $J_{1,2}$ = 8.1 Hz, H-1a and H-1c), and 7.29-8.02 (m, 5H, Ph).

Anal. Calcd for $C_{61}H_{85}NO_{32}Si$ (1372.4): C, 53.39; H, 6.24; N, 1.02. Found: C, 53.36; H, 6.01; N, 0.97.

***O*-(4,6-Di-*O*-acetyl-2-*O*-benzoyl-3-*O*-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-**

2,4,6-tri-*O*-acetyl-D-galactopyranose (22). Selective removal of the 2-(trimethylsilyl)ethyl group in **21** (209 mg, 0.15 mmol) with trifluoroacetic acid (1.7 mL) in CH_2Cl_2 (2.4 mL) as described for **4**, gave compound **22** (173 mg, 89%) as an amorphous mass: IR (film) 3500 (OH), 3350 (NH), 1750 and 1240 (ester), 1680 and 1530 (amide), and 710 cm^{-1} (Ph).

Anal. Calcd for $C_{56}H_{73}NO_{32}$ (1272.2): C, 52.87; H, 5.78; N, 1.10. Found: C, 52.59; H, 5.71; N, 0.88.

***O*-(4,6-Di-*O*-acetyl-2-*O*-benzoyl-3-*O*-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-acetyl-α-D-galactopyranosyl trichloroacetimidate (23).** To a stirred solution of **22** (169 mg, 0.13 mmol) in CH_2Cl_2 (2.1 mL), cooled to 0 °C, were added trichloroacetonitrile (0.4 mL) and DBU (20 mg), and the mixture was stirred for 1 h at 0 °C. A similar processing, as described for **5**, gave compound **23** (187 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -7.4° (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.30 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.98-2.22 (10s, 33H, 9AcO, AcN and $MeCOCH_2CH_2$), 2.27-2.66 (m, 4H, $MeCOCH_2CH_2$), 6.48 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1a), 7.46-8.02 (m, 5H, Ph), and 8.63 (s, 1H, C=NH).

Anal. Calcd for $C_{58}H_{73}N_2O_{32}Cl_3$ (1416.6): C, 49.18; H, 5.19; N, 1.98. Found: C, 49.07; H, 5.18; N, 1.81.

2-(Tetradecyl)hexadecyl *O*-(4,6-Di-*O*-acetyl-2-*O*-benzoyl-3-*O*-levulinoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (25). Coupling of **23** (187 mg, 0.13 mmol) and 2-(tetradecyl)hexadecan-1-ol[20] (**24**; 120 mg, 0.27 mmol) in CH_2Cl_2 (2.6 mL), as described for **16**, gave compound **25** (83 mg, 37%) as an amorphous mass: $[\alpha]_D$ -34.7° (*c* 1.5, $CHCl_3$); IR (film) 3350 (NH), 3150-2800 (Me and methylene), 1720 and 1250 (ester), 1650 and 1560 (amide), and 700 cm^{-1} (Ph); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2MeCH_2$), 1.26 (s, 52H, $26CH_2$), 1.31 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.92-2.22 (10s, 33H, 9AcO, AcN and

*Me*COCH$_2$CH$_2$), 2.27-2.67 (m, 4H, MeCOC*H$_2$*C*H$_2$*), 3.09 (m, 1H, H-1 of lipophilic part), 3.63 (dd, 1H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 3.5 Hz, H-3a), 4.73 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1 of Gal), and 7.45-8.02 (m, 5H, Ph).

Anal. Calcd for $C_{86}H_{133}NO_{32}$ (1693.0): C, 61.01; H, 7.92; N, 0.83. Found: C, 60.95; H, 7.92; N, 0.64.

2-(Tetradecyl)hexadecyl *O*-(4,6-Di-*O*-acetyl-2-*O*-benzoyl-β-D-galactopyranosyl)-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (26). To a solution of **25** (83 mg, 49 μmol) in EtOH (1.6 mL) was added hydrazine acetate (5.4 mg, 59 μmol) and the mixture was stirred for 2 h at room temperature then concentrated. Column chromatography (3:2 AcOEt-hexane) of the residue on silica gel (50 g) gave **26** (68 mg, 87%) as an amorphous mass: $[\alpha]_D$ -42.0° (*c* 1.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 6H, 2*Me*CH$_2$), 1.25 (s, 52H, 26CH$_2$), 1.30 (d, 3H, $J_{5,6}$ = 5.9 Hz, H-6d), 1.91-2.23 (10s, 30H, 9AcO and AcN), 3.65 (dd, 1H, $J_{2,3}$ = 10.1 Hz, $J_{3,4}$ = 3.5 Hz, H-3a), 4.25 and 4.65 (2d, 2H, $J_{1,2}$ = 7.9 Hz, $J_{1,2}$ = 8.2 Hz, H-1a and H-1c), and 7.45-8.06 (m, 5H, Ph).

Anal. Calcd for $C_{81}H_{127}NO_{30}$ (1594.9): C, 61.00; H, 8.03; N, 0.88. Found: C, 60.83; H, 7.93; N, 0.78.

2-(Tetradecyl)hexadecyl *O*-(3-*O*-Sulfo-β-D-galactopyranosyl)-(1→4)-*O*-[α-L-fucopyranosyl-(1→3)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-β-D-galactopyranoside sodium salt (28). To a solution of **26** (29 mg, 18 μmol) in *N*,*N*-dimethylformamide (0.3 mL) was added sulfur trioxide-pyridine complex (30 mg, 0.19 mmol) and the mixture was stirred for 4 h at room temperature; the course of the reaction was monitored by TLC. MeOH (1 mL) was added, and the mixture was concentrated at 25 °C. Column chromatography (5:1 CH_2Cl_2-MeOH) of the residue on silica gel (50 g) gave the pyridine salt (**27**; 30 mg, quantitative) as an amorphous mass, and subsequently to a solution of **27** (30 mg, 17 μmol) in MeOH (2.5 mL) and tetrahydrofuran (2.5 mL) was added sodium methoxide (60 mg) and the mixture was stirred for 92 h at room temperature then concentrated at

25 °C. Column chromatography (5:4:0.7 $CHCl_3$-MeOH-water) of the residue on Sephadex LH-20 (80 g) gave **28** (19 mg, quantitative) as an amorphous mass: ^1H NMR (C_5D_5N) δ 0.88 (t, 6H, $2MeCH_2$), 1.15 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.28 (s, 52H, $26CH_2$), 1.96 (s, 3H, AcN), and 5.09 (bd, 1H, H-1d). The mass spectrum of **28** (negative ion mode) showed the base peak at *m/z* 1190.7 $(M-H)^-$.

2-(Tetradecyl)hexadecyl *O*-[4,6-Di-*O*-acetyl-2-*O*-benzoyl-3-*O*-(*o*-xylylenedioxyphosphinyl)-β-D-galactopyranosyl]-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (29). A suspension of **26** (32 mg, 20 μmol) and 1*H*-tetrazole (4 mg) in CH_2Cl_2 (0.3 mL) was added *o*-xylylene *N*,*N*-diethylphosphoramidite (20 mg, 84 μmol), and the mixture was stirred for 13 h at room temperature; the course of the reaction was monitored by TLC. The resulting solution was directly applied for preparative thin layer chromatography (20 x 20 cm, 2 mm, Merck Co.; 15:1 CH_2Cl_2-MeOH) gave **29** (24 mg, 69%) as an amorphous mass: $[\alpha]_D$ -7.5° (*c* 0.8, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, $2MeCH_2$), 1.26 (s, 52H, $26CH_2$), 1.34 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.92-2.24 (10s, 30H, 9AcO and AcN), 3.63 (dd, 1H, $J_{3,4}$ = 3.3 Hz, H-3a), 4.09, 4.47, 5.47, and 5.62 [4dd, 4H, J_{gem} = 10.3 Hz, $J_{P,H}$ = 13.6 Hz, $P(OCH_2)_2$], 4.24 and 4.69 (2d, 2H, $J_{1,2}$ = 8.1 Hz, $J_{1,2}$ = 8.1 Hz, H-1a and H-1c), 5.62 (bd, 1H, $J_{3,4}$ = 3.5 Hz, H-4c), and 7.00-8.07 (m, 9H, aromatic protons).

Anal. Calcd for $C_{89}H_{134}NO_{32}P$ (1761.0): C, 60.70; H, 7.67; N, 0.86. Found: C, 60.56; H, 7.53; N, 0.65.

2-(Tetradecyl)hexadecyl *O*-[4,6-Di-*O*-acetyl-2-*O*-benzoyl-3-*O*-(*o*-xylylenedioxyphosphoryl)-β-D-galactopyranosyl]-(1 → 4)-*O*-[(2,3,4-tri-*O*-acetyl-α-L-fucopyranosyl)-(1 → 3)]-*O*-(2-acetamido-6-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1 → 3)-2,4,6-tri-*O*-acetyl-β-D-galactopyranoside (30). To a solution of **29** (24 mg, 14 μmol) in CH_2Cl_2 (0.25 mL), cooled to 0 °C, was added dropwise, with stirring, a solution of 3-chloroperoxybenzoic acid (50-60% by weight; 5 mg, 14 μmol) in CH_2Cl_2 (0.1 mL), and the stirring was continued for 1 h at room temperature. CH_2Cl_2 (50 mL) was added, and the solution

was washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (50:1 CH_2Cl_2-MeOH) of the residue on silica gel (40 g) gave **30** (20 mg, 83%) as an amorphous mass: $[\alpha]_D$ -13.5° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (t, 6H, 2*Me*CH_2), 1.26 (s, 52H, 26CH_2), 1.92-2.22 (10s, 30H, 9AcO and AcN), 3.63 (dd, 1H, $J_{3,4}$ = 3.5 Hz, H-3a), 4.24 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1 of Gal), 4.63-4.77 and 4.94-5.05 [m, 4H, P(OC*H*$_2$)2], 5.39 (m, 1H, H-2c), 5.68 (bd, 1H, $J_{3,4}$ = 3.5 Hz, H-4c), and 6.96-8.14 (m, 9H, aromatic protons).

Anal. Calcd for $C_{89}H_{134}NO_{33}P$ (1777.0): C, 60.16; H, 7.60; N, 0.79. Found: C, 60.11; H, 7.41; N, 0.57.

2-(Tetradecyl)hexadecyl *O*-(3-*O*-Phosphono-β-D-galactopyranosyl)-(1 → 4)-*O*-[α-L-fucopyranosyl-(1→3)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-β-D-galactopyranoside sodium salt (31). A solution of **30** (20 mg, 11 μmol) in MeOH (1 mL) was stirred for 8 h at room temperature in the presence of 10% Pd-C (17 mg) under hydrogen, then filtered and concentrated at 25 °C. To a solution of the residue in MeOH (3 mL) and tetrahydrofuran (3 mL) was added sodium methoxide (60 mg), and the mixture was stirred for 6 days at room temperature then concentrated at 25 °C. Column chromatography (5:4:0.7 $CHCl_3$-MeOH-water) of the residue on Sephadex LH-20 (80 g) gave **31** (12 mg, quantitative) as an amorphous mass: ^1H NMR (C_5D_5N) δ 0.88 (t, 6H, 2*Me*CH_2), 1.13 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.30 (s, 52H, 26CH_2), 2.00 (s, 3H, AcN), and 5.13 (bd, 1H, H-1d). The mass spectrum of **31** (negative ion mode) showed the base peak at *m/z* 1234.6 $(M-H)^-$, 1212.7 $(M-Na)^-$, and 1190.7 $(M-2Na+H)^-$.

ACKNOWLEDGMENT

This work was supported in part by Grant-in-Aid (No. 07273226 and No. 05274102) for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture of Japan.

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