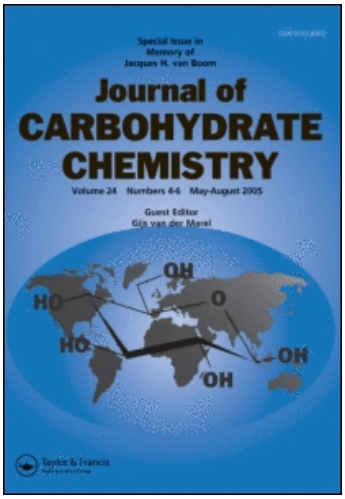

Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Synthetic Studies on Sialoglycoconjugates 65: Stereocontrolled Synthesis of Positional Isomers of Tumor-Associated Ganglioside Antigens, Sialyl Lewis X and Sialyl Paragloboside

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To cite this Article Hotta, Kenji , Itoh, Ken-Ichi , Kameyama, Akihiko , Ishida, Hideharu , Kiso, Makoto and Hasegawa, Akira(1995) 'Synthetic Studies on Sialoglycoconjugates 65: Stereocontrolled Synthesis of Positional Isomers of Tumor-Associated Ganglioside Antigens, Sialyl Lewis X and Sialyl Paragloboside', Journal of Carbohydrate Chemistry, 14: 1, 115 — 133
To link to this Article: DOI: 10.1080/07328309508006440
URL: http://dx.doi.org/10.1080/07328309508006440

J. CARBOHYDRATE CHEMISTRY, 14(1), 115-133 (1995)

SYNTHETIC STUDIES ON SIALOGLYCOCONJUGATES 65: STEREOCONTROLLED SYNTHESIS OF POSITIONAL ISOMERS OF TUMOR-ASSOCIATED GANGLIOSIDE ANTIGENS, SIALYL LEWIS X AND SIALYL PARAGLOBOSIDE

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Received August 17, 1994 - Final Form September 26, 1994

ABSTRACT

Stereocontrolled synthesis of neolacto series ganglioside analogs containing GlcNAcβ1-6Gal substituted for the GlcNAcβ1-3Gal residue in sialyl Lewis X and sialyl neolactotetraosyl ceramide is described. Tri- and tetra- saccharides **7** and **10** containing GlcNAcβ1→6Gal residue were obtained by glycosylation of 2-(trimethylsilyl)ethyl *O*-(2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**2**) with methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**4**) for the synthesis of sialyl paragloboside or methyl *O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**6**) for sialyl Le^x synthesis. Compounds **7** and **10** were transformed *via* removal of the phthaloyl group followed by *N*-acetylation, *O*-acetylation and reductive ring-opening of the benzylidene acetal into the acceptors **9** and **12**. Dimethyl (methylthio)sulfonium triflate (DMTST)-promoted coupling of **9** or **12** with methyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside (**13**) gave the desired pentasaccharide **14** and hexasaccharide **18**, respectively, which were converted *via* reductive removal of the benzyl groups, *O*-acetylation, removal of the 2-(trimethylsilyl)ethyl group and treatment with trichloroacetonitrile, into the α-trichloroacetimidates **17** and **21**. Condensation of **17** or **21** with (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (**22**) gave the β-glycosides **23** and **26**, which were transformed *via* reduction of the azido group, coupling with octadecanoic acid, *O*-deacylation and saponification of the methyl ester group, into the desired positional isomers of sialyl neolactotetraosyl ceramide **25** and of sialyl Le^x gangliosides **28**, respectively.

INTRODUCTION

Numerous carbohydrates are present as important constituents of glycoproteins and glycolipids[1] of cell membranes. Many lines of evidence have demonstrated[2-5] that these are directly or indirectly involved in the regulation of cellular growth, cell differentiation, and oncogenesis and in intracellular recognition such as adhesion, receptor functions for viruses and bacterial toxins, and ligand activities for E-, P-, and L-selectins.[6] In order to investigate the function of sialoglycoconjugates at the molecular level, we have synthesized a series of gangliosides and their analogs using our newly developed methods for ganglioside synthesis.[7]

Lacto-series gangliosides[8a] (sialyl lactotetraosyl ceramide) and neolacto-series gangliosides[8b,9] (sialyl paragloboside and sialyl Le^x) have been well known as tumor-associated ganglioside antigens. Especially sialyl Le^x, Neu5Ac α(2→3)Galβ(1→4) [Fucα(1→3)]GlcNAc-, which is found as the terminal carbohydrate structure in both glycolipids and glycoproteins has been reported to be recognized by selectin family[6] (E, P- or L-selectin). On the other hand, I- and sialyl I-antigens, containing the biantennary structure, GlcNAc β(1→6) [GlcNAc β(1→3)] Gal, in the molecules which belong to neolacto-series, have been recognized and characterized by specific markers for differentiated type cells in the developing lung of human embryos[10] and in lung cancers.[11] In view of these facts, it is of interest to elucidate the relationship between tumor associated ganglioside antigens, sialyl Le^x and sialyl paragloboside, and GlcNAc β(1→6)Gal structure belonging to I-active antigens.

Previously, we have synthesized[12-14] sialyl Le^x and sialyl paragloboside gangliosides and their analogs by use of the methyl β-thioglycosides of sialyl α(2→3)-galactose derivative[15] as the glycosyl donor which is easily prepared according to our newly developed procedure for the α-glycoside synthesis of sialic acid.[7b,16] Here we describe the stereocontrolled synthesis of the positional isomers of tumor-associated neolactoseries gangliosides, sialyl paragloboside, Neu5Acα(2→3)Galβ(1→4)GlcNAc β(1→6)Galβ(1→4)Glcβ(1→1)Cer, and sialyl Le^x, Neu5Acα(2→3)Galβ(1→4)[Fuc α(1→3)]GlcNAc β(1→6)Galβ(1→4)Glcβ(1→1)Cer.

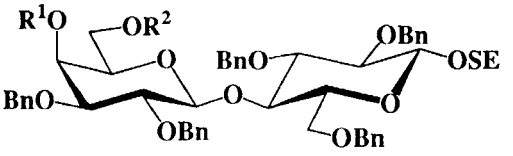
RESULTS AND DISCUSSION

For the synthesis of the title gangliosides, we have selected 2-(trimethylsilyl)ethyl *O*- (2-acetamido-3-*O*-acetyl-6-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→ 6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4) -2,3,6-tri-*O*-benzyl-β-D-glucopy-

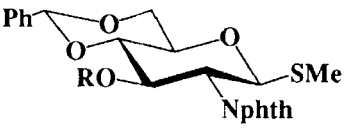
ranoside (**9**) and 2-(trimethylsilyl)ethyl *O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-*O*-2-acetamido-6-*O*-benzyl-2-deoxy- β -D-glucopyranosyl)- (1→ 6) -*O*-(4-*O*-acetyl-2,3- d i -*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**12**) as glycosyl acceptors which have the key structure, GlcNAc β1-6 Gal, obtained by condensation of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[17] (**4**) or methyl *O*-(2,3,4-tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (**6**), which was prepared by dimethyl (methylthio) sulfonium triflate[18] (DMTST)-promoted condensation of methyl 4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[17] (**3**) and methyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside[15] (**5**) at 0 °C, with 2-(trimethylsilyl)ethyl *O*-(2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**2**) prepared by removal of the benzylidene group of 2-(trimethylsilyl)ethyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[19] (**1**), followed by transformation of the phthalimide into acetamide and reductive ring-opening of the benzylidene group. We have employed methyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside[13] (**13**) as the glycosyl donor.

The glycosylation of **2** with **4** in dichloromethane in the presence of *N*-iodosuccinimide (NIS) - trifluoromethanesulfonic acid (TfOH) gave the desired β-glycoside **7** in 67% yield. Heating of **7** with hydrazine hydrate in aqueous 95% ethanol followed by acetylation afforded 2-(trimethylsilyl)ethyl *O*-(2-acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)- (1→6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**8**) in 78% yield. A significant signal of the GlcN unit in the ^{1}H NMR spectrum of **8** was at δ 5.62 (d, $J_{1,2}$ = 8.4 Hz, H-1) indicating the newly formed glycosidic linkage to be β. Reductive ring opening[20] of the benzylidene acetal of **8** with sodium cyanoborohydride-hydrogen chloride in tetrahydrofuran gave the tetrasaccharide acceptor **9** in 95% yield.

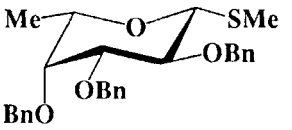
In order to prepare the fucosyl lactotriose derivative for the synthesis of sialyl Le^x, glycosylation of **2** with **6** gave the desired β-glycoside **10** in 58% yield. A significant signal of the GlcNAc unit in the ^{1}H NMR spectrum of **10** was at δ 5.36 (d, $J_{1,2}$ = 8.3 Hz, H-1) indicating the newly formed glycosidic linkage to be β. Compound **10** was transformed into **12** in good yield, *via* conversion of the phthalimide group into an acetamido group and reductive ring-opening of the benzylidene group as described for **9**.



	R^1	R^2
1	benzylidene	
2	H	H



3 R = H
4 R = Bn



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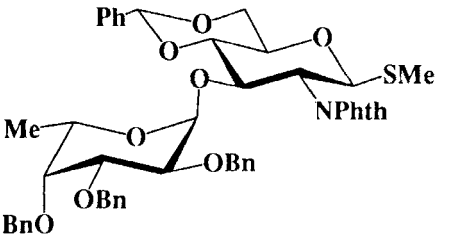
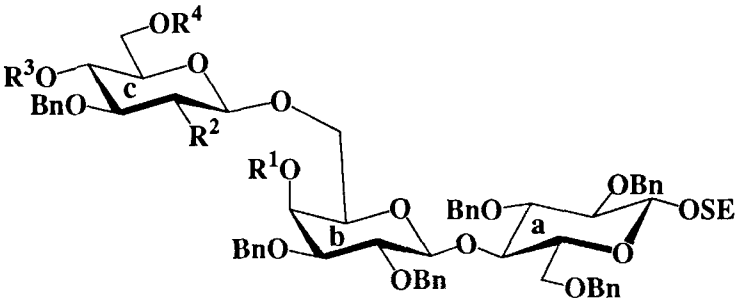
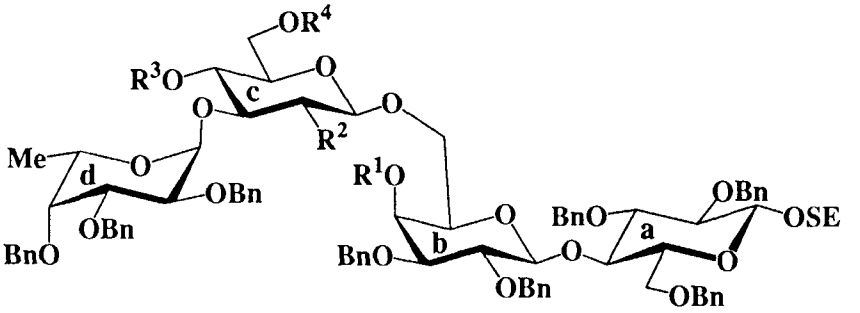


6

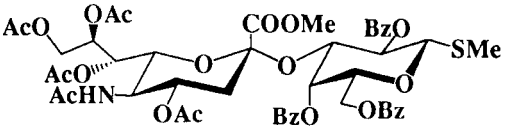
SE = 2-(trimethylsilyl)ethyl
Bn = benzyl
Phth = phthaloyl



	R^1	R^2	R^3	R^4
7	H	NPhth	benzylidene	
8	Ac	NHAc	benzylidene	
9	Ac	NHAc	H	Bn



	R^1	R^2	R^3	R^4
10	H	NPhth	benzylidene	
11	Ac	NHAc	benzylidene	
12	Ac	NHAc	H	Bn



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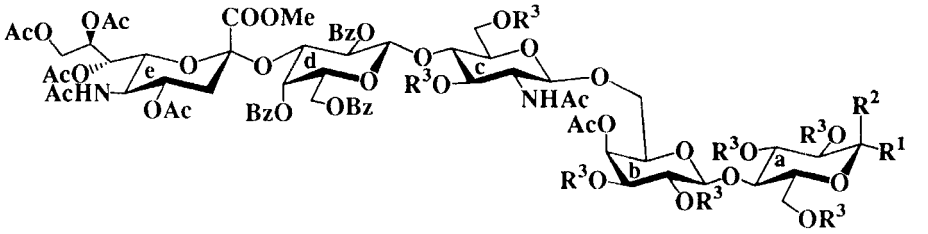
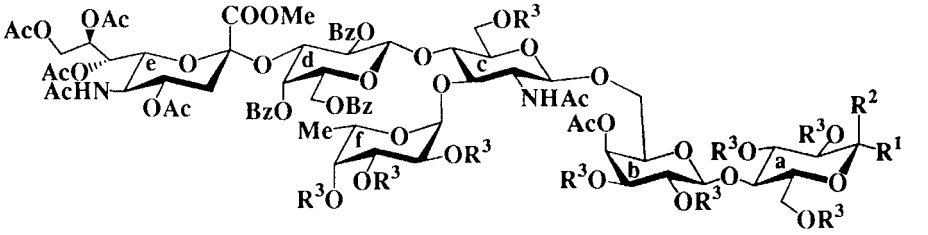
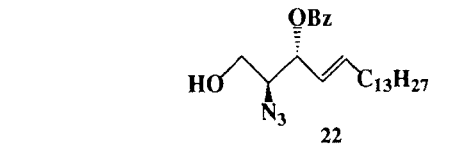


	R^1	R^2	R^3
14	OSE	H	Bn
15	OSE	H	Ac
16	OH , H		Ac
17	H	$OC(=NH)CCl_3$	Ac



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



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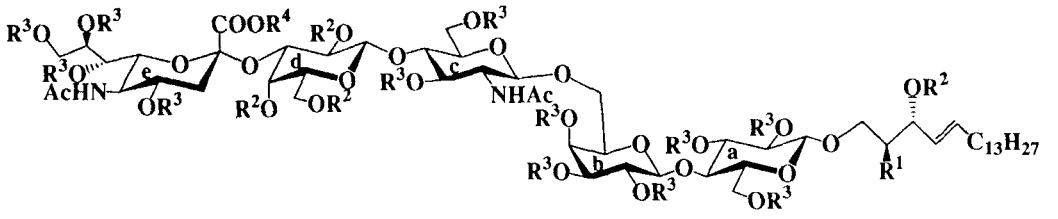
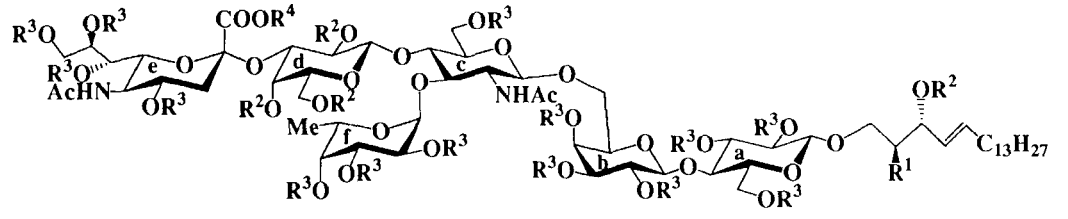


	R^1	R^2	R^3	R^4
23	N_3	Bz	Ac	Me
24	$NHCO(CH_2)_{16}CH_3$	Bz	Ac	Me
25	$NHCO(CH_2)_{16}CH_3$	H	H	H



	R^1	R^2	R^3	R^4
26	N_3	Bz	Ac	Me
27	$NHCO(CH_2)_{16}CH_3$	Bz	Ac	Me
28	$NHCO(CH_2)_{16}CH_3$	H	H	H

Glycosylation of **9** with **13** in dichloromethane for 45 h at 6 °C in the presence of 4.0 equiv of DMTST to the glycosyl donor as the glycosyl promoter and powdered molecular sieves 4Å (MS-4Å) gave the pentasaccharide **14** in 65% yield. Catalytic hydrogenolysis (10% Pd-C) of the benzyl groups in **14** in ethanol-acetic acid for 10 h at 45 °C and subsequent *O*-acetylation gave the per-*O*-acyl compound **15** in 81% yield. The ^1H NMR data for Neu5Acα(2-3)Gal unit in **15** indicated the newly formed glycosidic linkage to be β. Treatment[19] of **15** with trifluoroacetic acid in dichloromethane for 30 min at 0 °C gave the 1-hydroxy compound **16**. When treated with trichloroacetonitrile in dichloromethane in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) for 3 h at 0 °C, **16** gave the α-trichloroacetimidate **17** in 95% yield.

The ^1H NMR data for the Glc unit in **17** [δ 6.47 ($J_{1,2}$ = 3.7 Hz, H-1) and 8.65 (C=NH)] indicated the trichloroacetimidate to be α. In essentially the same way, glycosylation of **12** with **13** gave the desired β-glycoside **18** which was converted into **21** *via* removal of benzyl groups followed by acetylation, selective removal of 2-(trimethylsilyl)ethyl group and formation of α-trichloroacetimidate.

The final glycosylation of (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[21] (**22**) with **17** and **21** thus obtained, in dichloromethane in the presence of boron trifluoride etherate[21b,22] for 5 h at 0 °C afforded the expected β-glycoside **23** (47%) and **26** (64%), respectively. Selective reduction[21b,23] of the azide group in **23** and **26** with hydrogen sulfide in aqueous pyridine for 3 days at 0 °C gave the amines, which, on condensation with octadecanoic acid, using 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide (WSC) in dichloromethane, gave the corresponding acylated gangliosides **24** and **27** in good yields, after chromatography.

Finally, *O*-deacylation of **24** and **27** with sodium methoxide in methanol, with subsequent saponification of the methyl ester group, yielded the title gangliosides **25** and **27** in good yields after chromatography on a column of Sephadex LH-20. The ^1H NMR data of the products are consistent with the structure assigned.

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. ^1H NMR spectra were recorded with a JEOL JNM-GX 270 spectrometer. Preparative chromatography was performed on silica gel (Wako Chemical Co., 200 mesh) with the solvent systems specified. Concentrations were conducted *in vacuo*.

2-(Trimethylsilyl)ethyl *O*-(2,3-Di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (2). A solution of 2-(trimethylsilyl)ethyl *O*-(2,3-di-*O*-benzyl-4,6-*O*-benzylidene-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[19] (**1**; 1.0 g, 1.01 mmol) in aqueous 80% acetic acid (40 mL) was heated for 24 h at 60 °C and concentrated. Column chromatography (1:2 ethyl acetate-hexane) of the residue on silica gel (50 g) gave **2** (0.9 g, quant.) as an amorphous mass: $[\alpha]_D$ +20.2° (*c* 1.08, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$) and 7.15-7.85 (m, 25H, 5Ph).

Anal. Calcd for $C_{52}H_{64}O_{11}Si$ (893.2): C, 69.93; H, 7.22. Found: C, 69.80; H, 7.01.

Methyl *O*-(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside (6). To a solution of methyl 4,6-

O-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[17](**3**; 113 mg, 0.26 mmol) and methyl 2,3,4-tri-*O*-benzyl-1-thio-β-L-fucopyranoside[15] (**5**; 134 mg, 0.29 mmol) in dry benzene (1 mL) were added powdered molecular sieves 4 Å (MS-4Å, 500 mg), and the mixture was stirred for 5 h at room temperature then cooled to 7 °C. Dimethyl(methylthio)sulfonium triflate (DMTST; 201 mg, 0.78 mmol) and MS-4Å (200 mg) were added to the mixture, and the mixture was stirred for 2 h at 5~10 °C; the course of the reaction was monitored by TLC. The mixture was diluted with dichloromethane, the precipitate was collected and washed with dichloromethane, and the combined filtrate and washings were washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (1:5 ethyl acetate-hexane) of the residue on silica gel (10 g) gave **6** (200 mg, 90%) as an amorphous mass: $[\alpha]_D$ -14.8° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.86 (d, 3H, $J_{5',6'}$ = 6.4 Hz, H-6'), 2.18 (s, 3H, SMe), 4.42 (d, 1H, $J_{1',2'}$ = 2.7 Hz, H-1'), 5.37 (d, 1H, $J_{1,2}$ = 10.7 Hz, H-1), 5.56 (s, 1H, PhC*H*), and 7.00-7.96 (m, 24H, 5Ph).

Anal. Calcd for $C_{49}H_{49}NO_{10}S$ (843.99): C, 69.73; H, 5.85; N, 1.66. Found: C, 69.54; H, 5.76; N, 1.65.

2-(Trimethylsilyl)ethyl *O*-(3-*O*-Benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-*O*-(2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (7). To a solution of **2** (200 mg, 0.22 mmol) and methyl 3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-2-phthalimido-1-thio-β-D-glucopyranoside[17] (**4**; 125 mg, 0.24 mmol) in dry dichloromethane (4 mL) was added MS-4Å (400 mg), and the mixture was stirred for 5 h at room temperature then cooled to 0 °C. To the cooled mixture were added, with stirring, *N*-iodosuccinimide (NIS; 121 mg, 0.54 mmol) and trifluoromethanesulfonic acid (TfOH; 6 μL, 0.07 mmol), and the stirring was continued for 3 h at 0 °C. The precipitate was filtered off, and washed thoroughly with dichloromethane. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3, M $Na_2S_2O_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:4 ethyl acetate-hexane) of the residue on silica gel (10 g) gave **7** (204 mg, 67%) as an amorphous mass: $[\alpha]_D$ +26.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 5.53 (s, 1H, PhC*H*), and 7.15-7.59 (m, 39H, 8Ph)

Anal. Calcd for $C_{80}H_{87}NO_{17}Si$ (1362.65): C, 70.52; H, 6.44; N, 1.03. Found: C, 70.37; H, 6.29; N, 0.92.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-3-*O*-benzyl-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (8). A solution of **7** (330 mg, 0.25 mmol) in aqueous 95% ethanol (20 mL) was treated with hydrazine hydrate (0.12 mL) for 2 h under reflux. The precipitate was collected and washed with ethanol, and

the combined filtrate and washings was concentrated. The residue was treated with acetic anhydride (0.5 mL) in pyridine (1.0 mL) for 2 h at room temperature, methanol (2 mL) was added, the mixture was concentrated, and a solution of the residue in dichloromethane was successively washed with 2 M hydrochloric acid, water, and M sodium carbonate, dried (Na_2SO_4) and concentrated. Column chromatography (1:2 ethyl acetate-hexane) of the residue on silica gel (10 g) afforded **8** (250 mg, 78%) as an amorphous mass: $[\alpha]_D$ +47.6° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.87 (s, 3H, AcN), 2.10 (s, 3H, AcO), 5.37 (d, 1H, $J_{3,4}$ = 2.8 Hz, H-4b), 5.48 (s, 1H, PhC*H*), 5.62 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1c) and 7.21-7.46 (m, 35H, 7Ph)

Anal. Calcd for $C_{76}H_{89}NO_{17}Si$ (1316.62): C, 69.33; H, 6.81; N, 1.06. Found: C, 69.04; H, 6.69; N, 0.96.

2-(Trimethylsilyl)ethyl *O*-(2-Acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (9). To a solution of **8** (280 mg, 0.21 mmol) in dry tetrahydrofuran (5 mL) was added MS-3Å (500 mg), and the mixture was stirred for 5 h at room temperature, and sodium cyanoborohydride (280 mg) was gradually added. After the reagent had dissolved, hydrogen chloride in ether was added dropwise at room temperature until the evolution of gas ceased. TLC indicated that the reaction was complete after 5 min. The mixture was neutralized with triethylamine and filtered, the residue was washed with methanol and the combined filtrate and washings was concentrated then extracted with dichloromethane. The extract was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (1:2 ethyl acetate-hexane) of the residue on silica gel (10 g) afforded **9** (266 mg, 95%) as an amorphous mass: $[\alpha]_D$ +9.65° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.02 (m, 2H, $Me_3SiCH_2CH_2$), 1.89 (s, 3H, AcN), 2.05 (s, 3H, AcO), 5.02 (d, 1H, $J_{1,2}$ = 10.8 Hz, H-1c), 5.37 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-4b), and 7.21-7.41 (m, 35H, 7Ph).

Anal. Calcd for $C_{76}H_{91}NO_{17}Si$ (1318.64): C, 69.23; H, 6.96; N, 1.06. Found: C, 69.16; H, 6.89; N, 0.93.

2-(Trimethylsilyl)ethyl *O*-(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-*O*-(4,6-*O*-benzylidene-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-(1→6)-*O*-(2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (10). To a solution of **2** (200 mg, 0.22 mmol) and **6** (189 mg, 0.22 mmol) in dry dichloromethane (4 mL) was added MS-4Å (400 mg), and the mixture was stirred for 5 h at room temperature then cooled to 0 °C. To the cooled mixture were added, with stirring, NIS (121 mg, 0.54 mmol) and TfOH (6 μL, 0.07 mmol), and the stirring was continued for 3 h at 0 °C, and then worked-up as described for **7**. Column chromatography (1:4 ethyl acetate-hexane) of the residue on silica gel (10 g) gave **10**

(215 mg, 57%) as an amorphous mass: $[\alpha]_D$ -0.1° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.88 (d, 3H, $J_{5,6}$ = 6.6 Hz, H-6d), 1.02 (m, 2H, $Me_3SiCH_2CH_2$), 5.36 (d, 1H, $J_{1,2}$ = 8.6 Hz, H-1c), 5.50 (s, 1H, PhC*H*), and 7.13-7.50 (m, 49H, 10Ph).

Anal. Calcd for $C_{100}H_{109}NO_{21}Si$ (1689.04): C, 71.11; H, 6.50; N, 0.83. Found: C, 71.00; H, 6.23; N, 0.61.

2-(Trimethylsilyl)ethyl *O*-(2,3,4-Tri-*O*-benzyl-α-L-fucopyranosyl)-(1→3)-*O*-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (11). A solution of **10** (410 mg, 0.24 mmol) in aqueous 95% ethanol (10 mL) was treated with hydrazine hydrate (0.12 mL) for 2 h under reflux. The precipitate was collected and washed with ethanol, and the combined filtrate and washings was concentrated. The residue was treated with acetic anhydride (0.5 mL) in pyridine (1.0 mL) for 10 h at room temperature, methanol (2 mL) was added, and then worked-up as described for **8**. Column chromatography (1:3 ethyl acetate-hexane) of the residue on silica gel (10 g) afforded **11** (220 mg, 55%) as an amorphous mass: $[\alpha]_D$ -25.7° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.80 (d, 3H, $J_{5,6}$ = 6.2 Hz, H-6d), 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.24 (s, 3H, AcN), 2.09 (s, 3H, AcO), 5.10 (d, 1H, $J_{3,4}$ = 2.8 Hz, H-4b), 5.43 (s, 1H, PhC*H*), and 7.18-7.70 (m, 45H, 9Ph).

Anal. Calcd for $C_{96}H_{111}NO_{21}Si$ (1643.02): C, 70.18; H, 6.81; N, 0.85. Found: C, 69.98; H, 6.80; N, 0.75.

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→6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (12). To a solution of **11** (460 mg, 0.28 mmol) in dry tetrahydrofuran (10 mL) was added MS-3Å (1 g), and the mixture was stirred for 5 h at room temperature, and sodium cyanoborohydride (264 mg) was gradually added. After the reagent had dissolved, hydrogen chloride in ether was added dropwise at room temperature until the evolution of gas ceased. TLC indicated that the reaction was complete after 5 min, and then worked-up, as described for **9**. Column chromatography (1:3 ethyl acetate-hexane) of the residue on silica gel (10 g) afforded **12** (329 mg, 71%) as an amorphous mass: $[\alpha]_D$ -12.1° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.15 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6d), 1.20 (s, 3H, AcN), 2.06 (s, 3H, AcO), and 7.23-7.40 (m, 45H, 7Ph).

Anal. Calcd for $C_{96}H_{113}NO_{21}Si$ (1645.03): C, 70.09; H, 6.92; N, 0.85. Found: C, 70.08; H, 6.86; N, 0.68.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-ben-

zoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (14). To a solution of **9** (782 mg, 0.59 mmol) and methyl *O*-(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside[13] (**13**; 871 mg, 0.89 mmol) in dry dichloromethane (10 mL) was added MS-4Å (1.5 g), and the mixture was stirred for 5 h at room temperature and cooled to 0 °C. DMTST (1.78 g, 3.99 mmol) was added to the mixture, and the mixture was stirred for 48 h at 6 °C, filtered, washed with dichloromethane. The combined filtrate and washings were washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (20 g) gave **14** (880 mg, 65%) as an amorphous mass: $[\alpha]_D$ +17.9° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.02 (m, 2H, $Me_3SiCH_2CH_2$), 1.47, 1.75, 1.87, 1.88, 1.95, 2.00, 2.03 (7s, 21H, 5AcO and 2AcN), 2.42 (dd, 1H, Jgem = 8.1 Hz, $J_{3eq,4}$ = 4.2 Hz, H-3e-*eq*), 3.78 (s, 3H, MeO), 5.52 (dd, 1H, $J_{6,7}$ = 2.6 Hz, $J_{7,8}$ = 7.5 Hz, H-7e), 5.67 (m, 1H, H-8e), and 7.00-8.31 (m, 50H, 10Ph).

Anal. Calcd for $C_{123}H_{140}N_2O_{37}Si$ (2266.54): C, 65.18; H, 6.23, N, 1.24. Found: C, 65.13; H, 6.20; N, 1.04.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (15). A solution of **14** (660 mg, 0.29 mmol) in ethanol (24 mL) and acetic acid (6 mL) was hydrogenated in the presence of 10% Pd-C (700 mg) for 48 h at 45 °C, then filtered and concentrated. The residue was acetylated with acetic anhydride (2.0 mL)-pyridine (4.0 mL) for 10 h at room temperature, methanol (2 mL) was added, the mixture was concentrated, and a solution of the residue in dichloromethane was successively washed with 2 M hydrochloric acid, water, and M sodium carbonate, dried (Na_2SO_4) and concentrated. The product was purified by chromatography on a column of silica gel (20 g) with 40:1 dichloromethane-methanol afforded **15** (454 mg, 81%) as an amorphous mass: $[\alpha]_D$ +0.6° (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.93 (m, 2H, $Me_3SiCH_2CH_2$), 1.52, 1.77, and 1.92-2.23 (14s, 42H, 12AcO and 2AcN), 2.47 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 3.5 Hz, H-3e-*eq*), 3.79 (1s, 3H, MeO), 5.62 (m, 1H, H-8e), and 7.25-8.20 (m, 15H, 3Ph).

Anal. Calcd for $C_{88}H_{112}N_2O_{44}Si$ (1929.92): C, 54.77; H, 5.85, N, 1.45. Found: C, 54.50; H, 5.63; N, 1.16.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyrano-**

syl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranose (16). To a solution of **15** (454 mg, 0.24 mmol) in dichloromethane (1 mL) was added trifluoroacetic acid (3 mL) at 0 °C, the mixture was stirred for 30 min at 0 °C, then ethyl acetate (5 mL) was added, and concentrated. Column chromatography (20:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **16** (391 mg, 90%) as an amorphous mass: $[\alpha]_D$ +17.3° (*c* 1.1, $CHCl_3$); IR (KBr) δ 3600-3300 (OH,NH), 1730 and 1230 (ester), 1680 and 1550 (amide), and 740 and 710 (ph).

Anal. Calcd for $C_{83}H_{100}N_2O_{44}$ (1829.68): C, 54.49; H, 5.51, N, 1.53. Found: C, 54.28; H, 5.28; N, 1.40.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl Trichloroacetimidate (17).** To a solution of **16** (393 mg, 0.21 mmol) in dichloromethane (4 mL) and trichloroacetonitrile (0.84 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 30 mg) at -5 °C, and the mixture was stirred for 1 h at 0 °C, then concentrated. Column chromatography (20:1 dichloromethane-methanol) of the residue on silica gel (20 g) gave **17** (432 mg, quantitative) as an amorphous mass: $[\alpha]_D$ +23.9° (*c* 0.96, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.52-2.13 (14s, 42H, 12AcO and 2AcN), 2.47 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3e-*eq*), 3.82 (1s, 3H, MeO), 4.91 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1d), 5.27 (dd, 1H, $J_{6,7}$ = 2.7 Hz, $J_{7,8}$ = 10.0 Hz, H-7e), 5.50 (t, 1H, $J_{2,3}$ = 9.5 Hz, H-2d), 5.64 (m, 1H, H-8e), 6.47 (d, 1H, $J_{1,2}$ = 3.7 Hz, H-1a), and 7.27-8.20 (m, 15H, 3Ph).

Anal. Calcd for $C_{85}H_{100}N_3O_{44}Cl_3$ (1974.07): C, 51.72; H, 5.11, N, 2.13. Found: C, 51.65; H, 4.82; N, 1.90.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-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→6)-*O*-(4-*O*-acetyl-2,3-di-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (18). To a solution of **12** (329 mg, 0.20 mmol) and **13** (334 mg, 0.34 mmol) in dry dichloromethane (2 mL) was added MS-4Å (1.5 g), and the mixture was stirred for 5 h at room temperature and cooled to 0 °C. DMTST (439 mg, 1.70 mmol) was added to the mixture, the mixture was stirred for 48 h at 6 °C, filtered, and then worked-up, as described for **14**. Column chromatography (60:1 dichloromethane-methanol) of the residue on silica gel (20 g) gave **18** (178 mg, 42%) as an amorphous mass: $[\alpha]_D$ -2.7° (*c* 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$),

1.12 (d, 3H, $J_{5,6}$ = 6.4 Hz, H-6f), 1.48 - 2.00 (7s, 21H, 5AcO and 2AcN), 2.38 (dd, 1H, Jgem = 12.4 Hz, $J_{3eq,4}$ = 4.7 Hz, H-3e-*eq*), 3.71 (s, 3H, MeO), 5.15 (d, 1H, $J_{1,2}$ = 2.1 Hz, H-1f), 5.21 (dd, 1H, $J_{6,7}$ = 2.8 Hz, $J_{7,8}$ = 10.3 Hz, H-7e), 5.67 (m, 1H, H-8e), and 7.04-8.31 (m, 60H, 12Ph).

Anal. Calcd for $C_{143}H_{162}N_2O_{41}Si$ (2592.93): C, 66.24; H, 6.30, N, 1.08. Found: C, 66.09; H, 6.29; N, 0.96.

2-(Trimethylsilyl)ethyl *O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*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→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (19). A solution of **18** (178 mg, 0.08 mmol) in ethanol (12 mL) and acetic acid (3 mL) was hydrogenated in the presence of 10% Pd-C (200 mg) for 48 h at 45 °C, then filtered and concentrated. The residue was acetylated with acetic anhydride (2 mL)-pyridine (4 mL) for 10 h at room temperature, methanol (2 mL) was added, and then worked-up, as described for **15**. The product was purified by chromatography on a column of silica gel (10 g) with 50:1 dichloromethane-methanol to afford **19** (142 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -28.9° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.90 (m, 2H, $Me_3SiCH_2CH_2$), 1.42-2.10 (16s, 48H, 14AcO and 2AcN), 2.47 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 3.5 Hz, H-3e-*eq*), 3.81 (1s, 3H, MeO), 4.48 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1d), 5.27 (d, 1H, $J_{1,2}$ = 3.9 Hz, H-1f), and 7.47-8.14 (m, 15H, 3Ph).

Anal. Calcd for $C_{98}H_{126}N_2O_{50}Si$ (2160.14): C, 54.49; H, 5.88, N, 1.30. Found: C, 54.23; H, 5.83; N, 1.01.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*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→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-D-glucopyranose (20).** To a solution of **19** (87 mg, 0.05 mmol) in dichloromethane (0.5 mL) was added trifluoroacetic acid (0.7 mL) at 0 °C, the mixture was stirred for 30 min at 0 °C, and then worked-up, as described for **16**. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **20** (68 mg, 84%) as an amorphous mass: $[\alpha]_D$ -17.9° (*c* 1.4, $CHCl_3$); IR (KBr) δ 3600-3300 (OH,NH), 1730 (ester), 1680 and 1550 (amide), and 740 and 710 (Ph).

Anal. Calcd for $C_{93}H_{114}N_2O_{50}$ (2059.90): C, 54.23; H, 5.58, N, 1.36. Found: C, 54.11; H, 5.51; N, 1.18.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyrano-**

syl)-(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→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl Trichloroacetimidate (21). To a solution of **20** (68 mg, 0.04 mmol) in dichloromethane (2 mL) and trichloroacetonitrile (0.1 mL) was added DBU (10 mg) at -5 °C, and the mixture was stirred for 1 h at 0 °C, then concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **21** (63 mg, 86%) as an amorphous mass: $[\alpha]_D$ +35.3° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.21 (d, 3H, $J_{5,6}$ = 6.8 Hz, H-6f), 1.67-2.14 (16s, 48H, 14AcO and 2AcN), 2.47 (dd, 1H, J_{gem} = 12.2 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3e-*eq*), 3.75 (1s, 3H, MeO), 6.55 (d, 1H, $J_{1,2}$ = 3.8 Hz, H-1a), and 7.44-8.14 (m, 15H, 3Ph).

Anal. Calcd for $C_{95}H_{114}N_3O_{50}Cl_3$ (2204.29): C, 51.76; H, 5.21, N, 1.91. Found: C, 51.55; H, 5.06; N, 1.78.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (23).** To a solution of **17** (432 mg, 0.22 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol[21] (**22**; 375 mg, 0.48 mmol) in dichloromethane (2 mL) were added MS-4Å (AW-300, 0.8 g) and the mixture was stirred for 5 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (176 μL) was added, and the mixture was stirred for 5 h at 0 °C and then filtered. The insoluble material was washed with dichloromethane, and the combined filtrate and washings were washed with M sodium hydrogen carbonate and water, dried (Na_2SO_4) and concentrated. Column chromatography (40:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **23** (231 mg, 47%) as an amorphous mass: $[\alpha]_D$ +0.40° (*c* 0.98, $CHCl_3$); ^1H NMR ($CDCl_3$) (aglycon) δ 0.88 (s, 3H, *Me*CH_2), 1.24 (s, 22H, 11CH_2), 5.90 (m, 1H, H-5), and (pentasaccharide) δ 1.51-2.13 (14s, 42H, 12AcO and 2AcN), 2.46 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 4.6 Hz, H-3e-*eq*), 3.81(1s, 3H, MeO), 4.40 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1a), and 7.26-8.19 (m, 20H, 4Ph).

Anal. Calcd for $C_{108}H_{137}N_5O_{46}$ (2241.3): C, 57.88; H, 6.16, N, 3.12. Found: C, 57.69; H, 6.01; N, 3.11.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol**

(24). Hydrogen sulfide was bubbled through a stirred solution of **23** (231 mg, 0.10 mmol) in aqueous 83% pyridine (10 mL) for 2 days at 0 °C. The mixture was concentrated, and the residue was stirred with octadecanoic acid (59 mg, 0.21 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride(59 mg, 0.31 mmol) in dry dichloromethane (2.0 mL) for 24 h at room temperature. Dichloromethane (50 mL) was added, and the mixture was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (20 g) gave **24** (149 mg, 59%) as an amorphous mass: $[\alpha]_D$ +4.9° (*c* 1.03, $CHCl_3$);^{1}H NMR ($CDCl_3$) (aglycon) δ 0.88 (t, 6H, 2*Me*CH_2), 1.25 (s, 52H, 26CH_2), and (pentasaccharide) δ 1.51-2.13 (14s, 42H, 12AcO and 2AcN), 2.46 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3\text{-}eq,4}$ = 4.6 Hz, H-3e-*eq*), 3.82 (1s, 3H, MeO), 4.44 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1a), 4.84 (d, 1H, $J_{1,2}$ = 9.5 Hz, H-1d), 5.00 (d, 1H, $J_{1,2}$ = 9.5 Hz, H-1c), and 7.41-8.20 (m, 20H, 4Ph).

Anal. Calcd for $C_{126}H_{173}N_3O_{47}$ (2481.74): C, 60.98; H, 7.03; N, 1.69. Found: C, 60.69; H, 6.77; N, 1.41

***O*-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-(β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-octadecene-1,3-diol (25).** To a solution of **24** (149 mg, 0.06 mmol) in methanol (5 mL) was added sodium methoxide (5 mg), and the mixture was stirred for 24 h at 40 °C, and water (0.8 mL) was added. The solution was stirred for 10 h at room temperature, then treated with Amberlite IR-120 (H^+) resin, and filtered. The resin was washed with methanol, and the combined filtrate and washings was concentrated. Column chromatography (7:40:50 H_2O-MeOH-$CHCl_3$) of the residue on Sephadex LH-20 (20 g) gave **25** (90 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -2.2° (*c* 0.92, 7:40:50 H_2O-MeOH-$CHCl_3$); ^{1}H NMR [98:2 $(CD_3)_2SO$-D_2O] δ 0.85 (t, 6H, 2*Me*CH_2), 1.24 (s, 52H, 26CH_2), 1.83,1.89 (2s, 6H, 2AcN), 2.27 (dd, 1H, H-3e-*eq*), 4.23 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1a), 4.55 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1b), 4.63 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1d), 4.88 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1c), 5.56 (dd, 1H, $J_{3,4}$ = 6.3 Hz, $J_{4,5}$ = 13.1 Hz,H-4 for sphingoshine), and 5.98 (dt, 1H, $J_{5,6}$ = $J_{5',6}$ = 6.9 Hz, H-5 for sphingoshine)

Anal. Calcd for $C_{80}H_{135}N_3O_{32}$ (1650.95): C, 58.20; H, 8.24, N, 2.55. Found: C, 58.06; H, 8.10; N, 2.47.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*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→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galac-**

topyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-benzoyl-4-octadecene-1,3-diol (26). To a solution of **21** (70 mg, 30 μmol) and **22** (375 mg, 34 μmol) in dichloromethane (1 mL) were added MS-4Å (AW-300, 0.3 g) and the mixture was stirred for 5 h at room temperature, then cooled to 0 °C. Boron trifluoride etherate (15 μL) was added, and the mixture was stirred for 5 h at 0 °C and then worked-up, as described for **23**. Column chromatography (40:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **26** (50 mg, 64%) as an amorphous mass: $[\alpha]_D$ -29.0° (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) (aglycon) δ 0.87 (s, 3H, *Me*CH_2), 1.24 (s, 22H, 11CH_2), 5.91 (m, 1H, H-5), and (pentasaccharide) δ 1.59-2.08 (16s, 48H, 14AcO and 2AcN), 2.41 (dd, 1H, J_{gem} = 12.5 Hz, $J_{3\text{-}eq,4}$ = 4.4 Hz, H-3e-*eq*), 3.81(1s, 3H, MeO), and 7.26-8.19 (m, 20H, 4Ph).

Anal. Calcd for $C_{118}H_{151}N_5O_{52}$ (2471.49): C, 57.35; H, 6.16, N, 2.83. Found: C, 57.08; H, 5.87; N, 2.71.

***O*-(Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-*O*-(2,4,6-tri-*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→6)-*O*-(2,3,4-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (27).** Hydrogen sulfide was bubbled through a stirred solution of **26** (50 mg, 20 μmol) in aqueous 83% pyridine (6 mL) for 2 days at 0 °C. The mixture was concentrated, and the residue was stirred with octadecanoic acid (12 mg, 43 μmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (12 mg, 64 μmol) in dry dichloromethane (1.5 mL) for 24 h at room temperature, and then worked-up, as described for **24**. Column chromatography (30:1 dichloromethane-methanol) of the residue on silica gel (10 g) gave **27** (34mg, 62%) as an amorphous mass: $[\alpha]_D$ -22.1° (*c* 0.7, $CHCl_3$); ^1H NMR ($CDCl_3$) (aglycon) δ 0.88 (t, 6H, 2*Me*CH_2), 1.26 (s, 52H, 26CH_2), 5.87 (m, 1H, H-5), and (pentasaccharide) δ 1.59-2.10 (16s, 48H, 14AcO and 2AcN), 2.41 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.6 Hz, H-3e-*eq*), 3.81 (s, 3H, MeO), 4.62 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1a), 4.85 (d, 1H, $J_{1,2}$ = 8.6 Hz, H-1d), 5.13 (d, 1H, $J_{1,2}$ = 9.4 Hz, H-1c), and 7.41-8.20 (m, 20H, 4Ph).

Anal. Calcd for $C_{136}H_{187}N_3O_{53}$ (2711.96): C, 60.23; H, 6.95; N, 1.55. Found: C, 60.05; H, 6.82; N, 1.31

***O*-(5-Acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-*O*-(β-D-galactopyranosyl)-(1→4)-[*O*-(α-L-fucopyranosyl)-(1→3)]-*O*-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→6)-*O*-(β-D-galactopyranosyl)-(1→4)-*O*-(β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-octadecanamido-4-octadecene-1,3-diol (28).** Deacylation and saponification of **27** (34 mg, 0.013 mmol), as

described for **25**, yielded **28** (18 mg, quantitative) as an amorphous mass: $[\alpha]_D$ -28.3° (*c* 0.60, 5:4:0.7 $CHCl_3$-MeOH-H_2O); ^1H NMR [49:1 $(CD_3)_2SO$-D_2O] δ 0.90 (t, 6H, 2*Me*CH_2), 1.07 (d, 3H, $J_{5,6}$ = 6.1 Hz, H-6f), 1.29 (s, 52H, 26CH_2), 1.82, 1.86 (2s, 6H, 2AcN), 2.10 (t, 2H, CO*C*$H_2$$CH_2$), 2.80 (dd, 1H, H-3e-*eq*), 4.23 (d, 1H, $J_{1,2}$ = 6.4 Hz, H-1d), 4.37 (d, 1H, $J_{1,2}$ = 6.6 Hz, H-1b), 4.72 (d, 1H, $J_{1,2}$ = 6.2 Hz, H-1c), 4.90 (d, 1H, $J_{1,2}$ = 3.1 Hz, H-1f), 5.42 (m, 1H, H-4 for sphingosine), and 5.60 (m 1H, H-5 for sphingosine).

Anal. Calcd for $C_{79}H_{141}N_3O_{35}$ (1693.0): C, 56.04; H, 8.40; N, 2.48. Found: C, 56.01; H, 8.25; N, 2.32.

ACKNOWLEDGMENT

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

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