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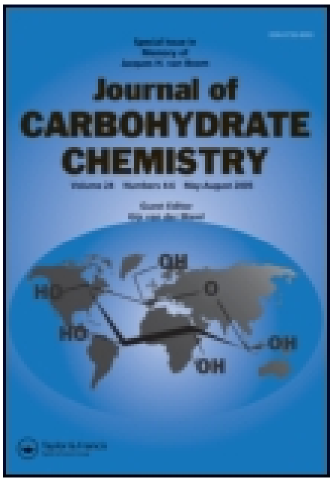

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A HIGHLY EFFICIENT TOTAL SYNTHETIC ROUTE TO α-SERIES GANGLIOSIDES: GM1α, GD1α, AND GT1α

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A HIGHLY EFFICIENT TOTAL SYNTHETIC ROUTE TO α-SERIES GANGLIOSIDES: GM1α, GD1α, AND GT1α[1,2]

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Dedicated to Professor Joachim Thieru on the occassion of his 60th birthday.

ABSTRACT

A highly efficient total synthetic route to α-series gangliosides GM1α, GD1 α and GT1α is described. The suitably protected gangliotriose (GgOse3) derivatives, i.e., 2-(trimethylsilyl)ethyl (2-acetamido-2-deoxy-3-*O*-*p*-methoxybenzyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**8**) and the corresponding III^3-levulinoyl derivative (**9**), were regioselectively glycosylated with the phenyl 2-thioglycoside of *N*-acetylneuraminic acid (Neu5Ac) promoted by *N*-iodosuccinimide (NIS)-trimethylsilyl trifluoromethanesulfonate (TMSOTf) or trifluoromethanesulfonic acid (TfOH) in acetonitrile, to give the desired α-Neu5Ac-(2→6)-gangliotriose (III^{6}Neu5AcGgOse3) derivatives as the major products (**11** and **12**). The *p*-methoxybenzyl (MPM) group in **11** or the levulinoyl group in **12** was selectively removed, and the resulting 2-(trimethylsilyl)ethyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-

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galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**13**), a key glycosyl acceptor, was systematically glycosylated with the galactose donor (**14**), α-Neu5Ac-(2→3)-galactose donor (**15**) and α-Neu5Ac-(2→8)-α-Neu5Ac-(2→3)-galactose donor (**20**) to give the protected GM1α (**16**, 70%), GD1α (**17**, 80%) and GT1α (**21**, 87%) oligosaccharides, respectively, which can be converted to the target gangliosides by the introduction of ceramide and then complete deprotection.

INTRODUCTION

Gangliosides are a group of sialylated glycosphingolipids widely present in mammalian tissues and are involved in various biological phenomena such as cell-cell recognition, cell growth, differentiation, transformation, and neural functions.

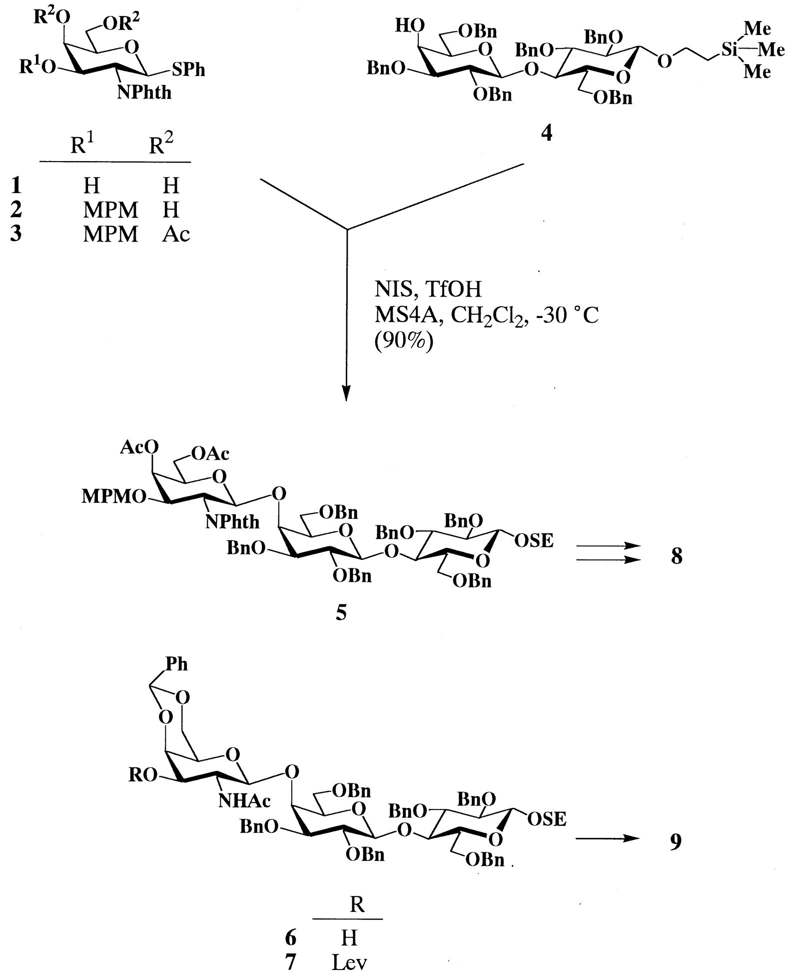
A new family (α-series) of gangliosides, which have in common one sialic acid residue α(2→6)-linked to the *N*-acetylgalactosamine (GalNAc) moiety of the gangliotetraose core structure, have been characterized as cholinergic neuron-specific gangliosides.[3–11] Among them, GQ1bα[12] has been found[13–16] to be an extremely high affinity ligand of myelin-associated glycoprotein (MAG), which is a transmembrane cell surface glycoprotein of myelin-forming oligodendrocytes and a member of sialic acid-binding immunoglobulin superfamily lectins (siglecs), previously termed sialoadhesins or I-type lectins.[17–20] The binding activities of GT1aα[21,22] and GD1α[23] to MAG were also much higher than those of parent GD1α and GM1b, suggesting a special importance of the Neu5Ac residue α(2→6)-linked to GalNAc for siglec-binding. Very recently, a brain-specific GD1α synthase (ST6GalNAc V) has been cloned.[24] We describe herein a highly efficient total synthetic route to three α-series gangliosides GM1α, GD1α and GT1α by use of a facile, regio- and α-stereoselective method for the sialyl glycoside synthesis.[25–29]

RESULTS AND DISCUSSION

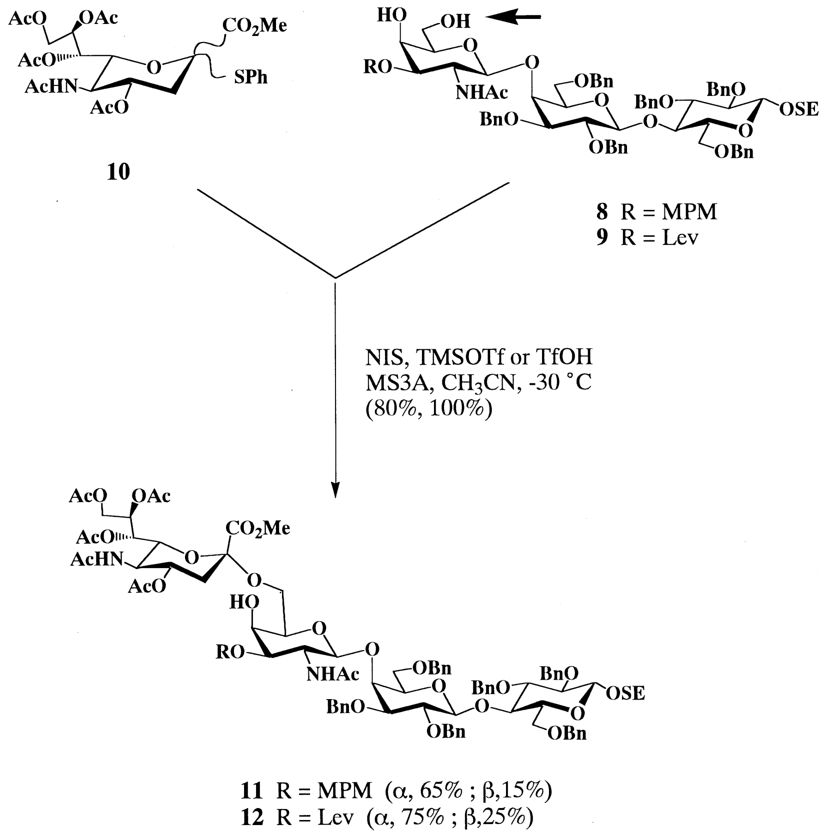
In our previous synthesis of ganglioside GM1α[30] and GD1α,[31] the gangliotetraose (GgOse4) and α-Neu5Ac-(2→3)-gangliotetraose (IV^{3}Neu5Ac GgOse4; GM1b oligosaccharide) core structures were first constructed, and then the regio- and α-stereoselective sialylation on O-6 of the *N*-acetylgalactosamine (GalNAc) residue was conducted, raising a critical problem in the separation of the resulting diastereoisomers. For the systematic synthesis of the α-series gangliosides GM1α, GD1α and GT1α, we have now selected the suitably protected α-Neu5Ac-(2→6)-gangliotriose (III^{6}Neu5Ac GgOse3) derivative **13** as a common key glycosyl acceptor.

Coupling of **3**, which was prepared by regioselective *p*-methoxybenzylation of phenyl 2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (**1**) and the following 4,6-di-*O*-acetylation, with 2-(trimethylsilyl)ethyl (2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside[32,33] (**4**) was carried out in the presence of NIS and TfOH in dichloromethane at −30°C to give **5** in 90% yield (Scheme 1). The *N*-phthaloyl and *O*-acetyl groups in **5** were simultaneously cleaved by treatment with hydrazine monohydrate in ethanol, and the resulting free amino group was selectively acetylated to afford one trisaccharide acceptor **8** in high yield. 3-*O*-Levinoylation of **6**[30] and cleavage of the 4,6-*O*-benzylidene group gave another trisaccharide acceptor **9**.

Iodonium-ion promoted,[34,35] regio- and α-stereocontrolled glycosylation of **8** and **9** with a Neu5Ac donor **10**[36] was performed[25–29] at −30°C in a solution of acetonitrile to give the desired tetrasaccharides **11** (65%) and **12** (75%) containing the sialyl α(2→6)GalNAc structure (Scheme 2). The total sialylation yields were 80%



Scheme 1. MPM = *p*-methoxybenzyl, NPhth = phthalimido, NIS = *N*-iodosuccinimide, TfOH = trifluoromethanesulfonic acid, SE = 2-(timethylsilyl)ethyl, Lev = levulinyl.

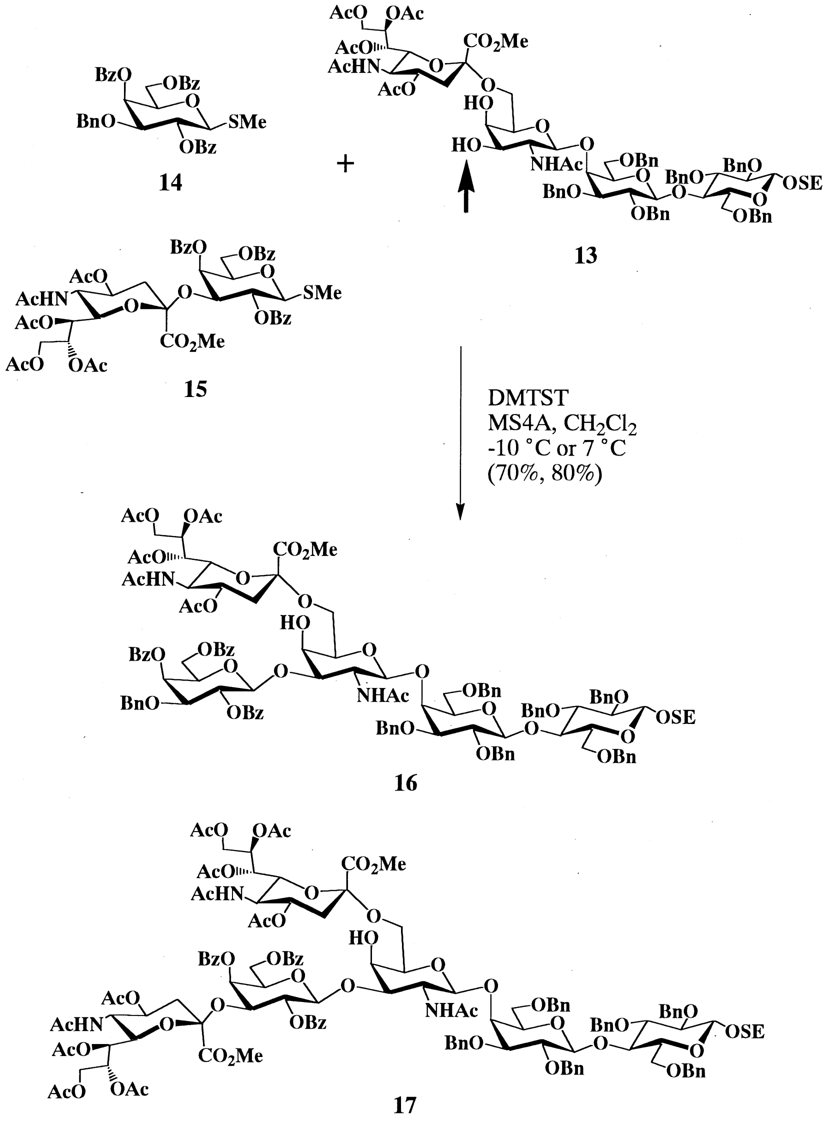


Scheme 2. TMSOTf = trimethylsilyl trifluoromethanesulfonate.

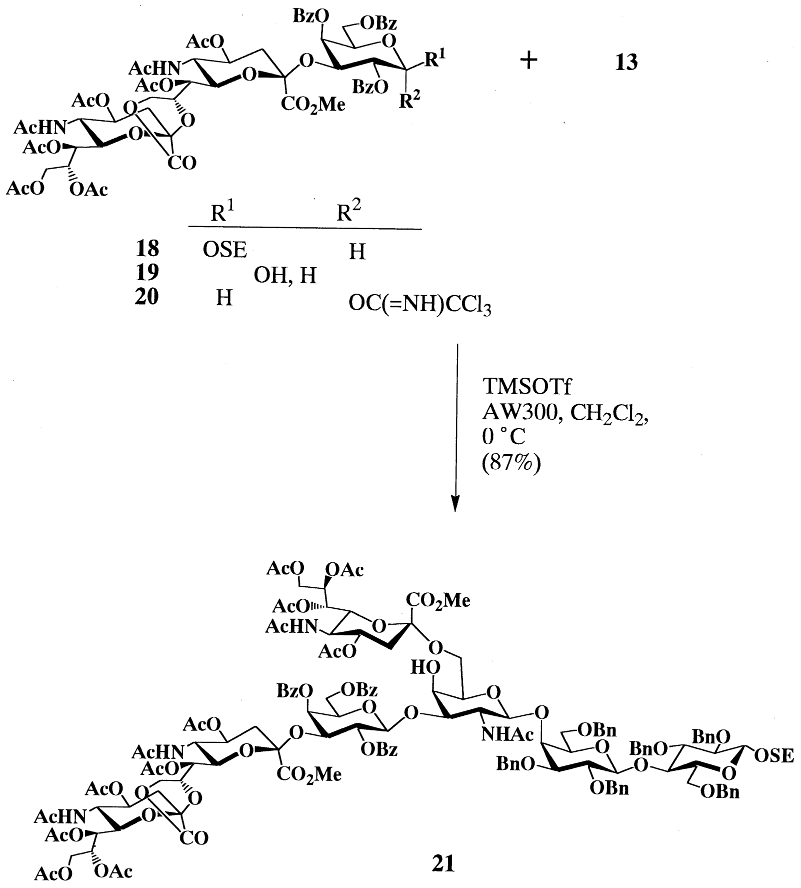
and 100% including the β isomer 15% and 25%, respectively. Selective removal of the MPM or Lev group afforded the key glycosyl acceptor **13**, which was systematically glycosylated with methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside[37] (**14**), methyl (5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-2,4,6-tri-*O*-benzoyl-1-thio-β-D-galactopyranoside[38] (**15**) and methyl 5-acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α D-*galacto*-2-nonulopyranosylono-1′,9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate]-(2→3)-2,4,6-tri-*O*-benzoyl-D-glucopyranosyl trichloroacetimidate (**20**).

Regio- and stereoselective glycosylations at O-3 of the GalNAc residue in **13** were carried out (Scheme 3) by employing **14** and **15** as the glycosyl donors and DMTST[25,39,40] as the glycosyl promoter in dichloromethane to yield the desired **16**[30] (70%) and **17**[31] (80%), respectively, which had been transformed into gangliosides GM1α[30] and GD1α.[31] On the other hand, the glycosylation of **13** with **20** was performed at 0°C in the presence of TMSOTf and MS4A (AW-300) in dichloromethane to give the heptasaccharide derivative **21** (87%) as a precursor of ganglioside GT1α (Scheme 4).

Hydrogenolytic removal of the benzyl groups in **17** over $Pd(OH)_2$ in 10 : 1 ethanol-acetic acid, followed by complete acetylation of the resulting free hydroxyls with Ac_2O-pyridine, afforded the fully acylated oligosaccharide **22** in 85% yield. Selective removal of the 2-(trimethylsilyl)ethyl (SE) group[32,41] was achieved by treatment of **22** with trifluoroacetic acid in dichloromethane to give



Scheme 3. DMTST = dimethyl(methylthio)sulfonium triflate.



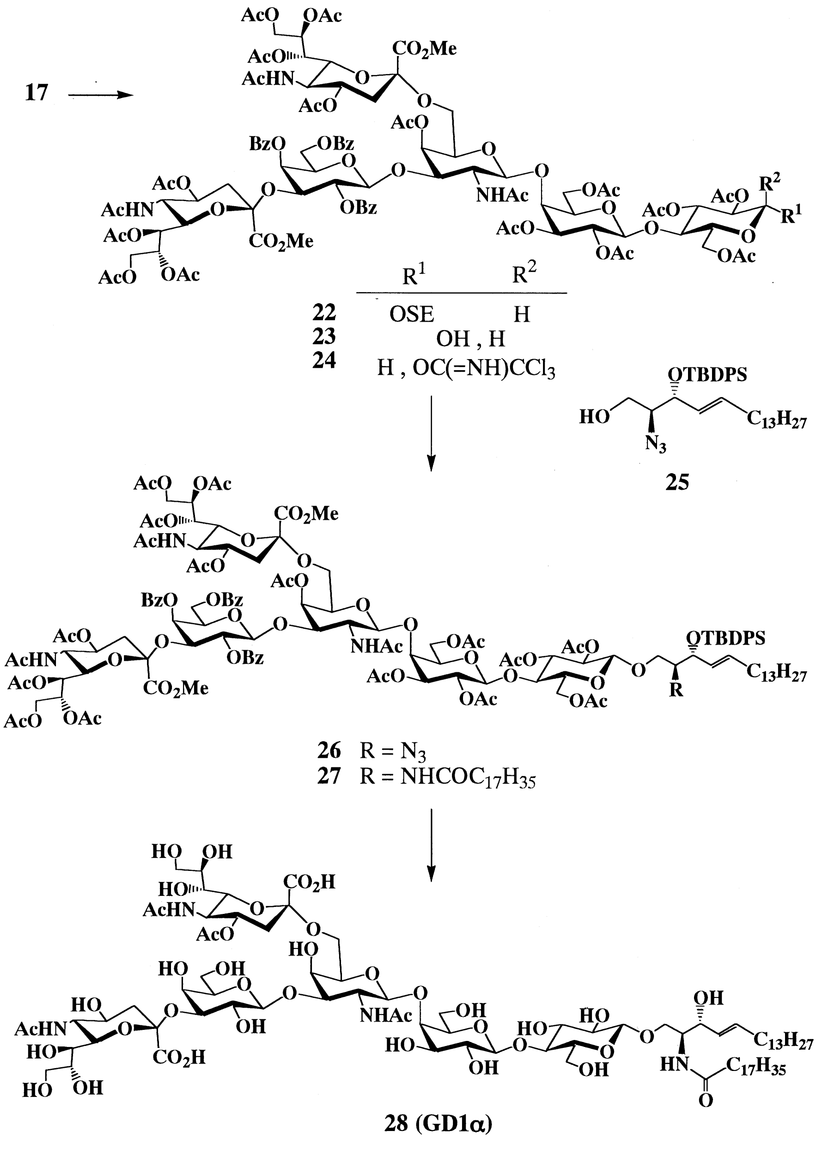
Scheme 4.

the 1-hydroxy compound **23** (93%), which upon further treatment[42] with trichloroacetonitrile in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in dichloromethane, gave the trichloroacetimidate **24** in high yield.

Coupling of **24** with (2*S*,3*R*,4*E*)-2-azido-3-*O*-(*tert*-butyldiphenylsilyl)-4-octadecene-1,3-diol[22] (**25**) was carried out in the presence of TMSOTf and MS-4Å (AW300) in dichloromethane to give **26** in 64% yield. Selective reduction of the azido group in **26** with triphenylphosphine in 5 : 1 benzene-water gave the amine, which on condensation with stearic acid using 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (WSC) in dichloromethane, afforded the fully protected ganglioside GD1α (**27**) in 53% yield. Finally, removal of the *tert*-butyldiphenylsilyl group in **27** with 1.0 M tetrabutylammonium fluoride in acetonitrile, *O*-deacetylation with sodium methoxide in methanol, and subsequent saponification of the methyl ester group gave ganglioside GD1α (**28**) as an amorphous mass in a quantitative yield, after chromatography on a column of

Sephadex LH-20 with 5 : 5 : 1 chloroform-methanol-water (Scheme 5). The physicochemical properties and spectral data were identical with those reported[31] previously.

In conclusion, a highly efficient total synthetic route to α-series gangliosides GM1α, GD1α and GT1α was developed by using the key glycosyl acceptor **13** and the suitably protected glycosyl donors **14**, **15** and **20**. Ganglioside GD1α has been found to be a high affinity ligand of myelin-associated glycoprotein (MAG).[23,43]



Scheme 5.

EXPERIMENTAL

General Procedures. Optical rotations were determined with a Union PM-201 polarimeter at 25°C, and IR spectra were recorded with a Jasco IRA-100 spectrophotometer. ^{1}H NMR spectra were recorded on Varian Unity Inova (400 MHz) spectrometer with TMS as the internal standard. All reactions were monitored by TLC (Merck silica gel aluminium plate 60F-254) and preparative chromatography was performed on silica gel (Fuji Silysia Co. 300 mesh) with the solvent systems specified. Concentrations were conducted *in vacuo*.

Phenyl 2-Deoxy-2-phthalimido-1-thio-β-**D-galactopyranoside (1).** To a solution of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-2-phthalimido-D-galactopyranose (6.1 g, 12.7 mmol) in CH_2Cl_2 (50 mL) were added thiophenol (1.44 mL, 13.9 mmol) and BF_3•OEt_2 (3.94 mL, 31.8 mmol) and the mixture was stirred for 24 h at room temperature. The solution was extracted with chloroform, and the extract was successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (1 : 3 ethyl acetate-hexane) of the residue on silica gel gave phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (6.5 g, 97%) as an amorphous mass. To a solution of phenyl 3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-1-thio-β-D-galactopyranoside (6.5 g, 12.3 mmol) in methanol (50 mL) was added a catalytic amount of sodium methoxide, and the mixture was stirred for 5 h at room temperature, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with methanol, and the combined filtrate and washings were concentrated. Column chromatography (15:1 chloroform -methanol) of the residue on silica gel gave **1** (4.8 g, 98%) as an amorphous mass; $[\alpha]_D$ +33.6° (*c* 0.2, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.72 (m, 1H, H-5), 3.94 (m, 2H, H-6 and H-6′), 4.17 (d, 1H, $J_{3,4}$ = 3.0 Hz, H-4), 4.40 (dd, 1H, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 4.47 (t, 1H, $J_{1,2}$ = $J_{2,3}$ = 10.3 Hz, H-2), 5.61 (d, 1H, $J_{1,2}$ = 10.3 Hz, H-1), and 7.22–7.85 (m, 9H, 2Ph).

Anal. Calcd for $C_{20}H_{19}NO_6S$ (401.4): C, 59.84; H, 4.77; N, 3.49. Found: C, 59.72; H, 4.51; N, 3.40.

Phenyl 2-Deoxy-3-*O*-*p*-methoxybenzyl-2-phthalimido-1-thio-β-D-galactopyranoside (2). To a solution of **1** (4.0 g, 10 mmol) in MeOH (50 mL) was added dibutyltin oxide (5.0 g, 20 mmol), and the mixture was boiled under reflux for 5 h, and concentrated to dryness. The residue was treated with 4-methoxybenzyl chloride (3.37 mL, 25 mmol) and tetrabutylammonium bromide (1.6 g, 5.0 mmol) in benzene (40 mL) under reflux for 1 h. The mixture was concentrated and the residual syrup was washed with hexane to remove the excess reagents. Column chromatography (1 : 1 ethyl acetate-hexane) of the residue on silica gel gave amorphous **2** (3.12 g, 58%) : $[\alpha]_D$ +131.2° (*c* 0.5, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.62 (s, 3H, MeO), 3.68 (m, 1H, H-5), 3.82 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5,6}$ = 4.4 Hz, H-6), 4.00 (dd, 1H, J_{gem} = 11.7 Hz, $J_{5,6}$ = 6.6 Hz, H-6′), 4.13 (d, 1H, $J_{3,4}$ = 3.3 Hz, H-4), 4.23 (dd, 1H, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 4.49 (dd, 1H, $J_{1,2}$ = $J_{2,3}$ = 10.6 Hz, H-2), 5.50 (d, 1H, $J_{1,2}$ = 10.6 Hz, H-1), and 6.40–7.85 (m, 13H, 3Ph).

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Anal. Calcd for $C_{28}H_{27}NO_7S$ (521.6): C, 64.48; H, 5.22; N, 2.69. Found: C, 64.38; H, 5.21; N, 2.58.

Phenyl 4,6-Di-*O*-acetyl-2-deoxy-3-*O*-*p*-methoxybenzyl-2-phthalimido-1-thio-β-D-galactopyranoside (3). To a stirred solution of **2** (3.12 g, 5.98 mmol) in pyridine (10 mL) was added acetic anhydride (1.5 mL) at 0°C. The mixture was stirred for 8 h at room temperature, and methanol (5 mL) was added. The solution was concentrated to a syrup which was extracted with chloroform. The extract was successively washed with 2 M HCl, water, M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (2:3 ethyl acetate-hexane) of the residue on silica gel gave **3** (3.60 g, 99%) as an amorphous mass: $[\alpha]_D$ +111.7° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 2.04 and 2.16 (2s, 6H, 2AcO), 3.63 (s, 3H, MeO), 3.98 (m, 1H, H-5), 4.19 (m, 2H, H-6, H-6′), 4.27 (dd, 1H, $J_{2,3}$ = 10.6 Hz, $J_{3,4}$ = 3.3 Hz, H-3), 4.44 (dd, 1H, $J_{1,2}$ = $J_{2,3}$ = 10.6 Hz, H-2), 5.51 (d, 1H, $J_{1,2}$ = 10.6 Hz, H-1), 5.55 (d, 1H, $J_{3,4}$ = 3.3 Hz, H-4), and 6.36–7.83 (m, 13H, 3Ph).

Anal. Calcd for $C_{32}H_{31}NO_9S$ (605.7): C, 63.46; H, 5.16; N, 2.31. Found: C, 63.38; H, 4.87; N, 2.17.

2-(Trimethylsilyl)ethyl (4,6-Di-*O*-acetyl-2-deoxy-3-*O*-*p*-methoxybenzyl-2-phthalimido-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (5). To a solution of 2-(trimethylsilyl)ethyl (2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**4**; 4.45 g, 4.66 mmol) and **3** (3.39 g, 5.60 mmol) in dichloromethane (30 mL) were added molecular sieves 4Å (5 g) and the mixture was stirred for 3 h at room temperature, then cooled to −30°C. To the stirred mixture were added NIS (1.84 g, 8.40 mmol) and TfOH (34 μL, 0.39 mmol), and the stirring was continued for 30 min at −30°C. The precipitates were filtered off and washed with chloroform. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3 and M $Na_2S_2O_3$, dried (Na_2SO_4) and concentrated. Column chromatography (1:3 ethyl acetate-hexane) of the residue on silica gel gave **5** (6.20 g, 90%) as an amorphous mass: $[\alpha]_D$ +25.8° (*c* 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 2.03, 2.19 (2s, 6H, 2AcO), 3.29 (dd, 1H, $J_{1,2}$ = 8.1 Hz, $J_{2,3}$ = 9.2 Hz, H-2a), 3.52 (t, 1H, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, H-3a), 3.60 (s, 3H, MeO), 3.62 (m, 1H, H-4b), 3.74 (t, 1H, $J_{3,4}$ = $J_{4,5}$ = 9.2 Hz, H-4a), 4.18 (d, 1H, $J_{1,2}$ = 7.6 Hz, H-1b), 4.35 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1a), 5.18 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1c), 5.60 (d, 1H, $J_{3,4}$ = 3.7 Hz, H-4c), and 6.40–7.84 (m, 34H, 7Ph).

Anal. Calcd for $C_{85}H_{95}NO_{20}Si$ (1478.8): C, 69.04; H, 6.48; N, 0.95. Found: C, 68.75; H, 6.35; N, 0.76.

2-(Trimethylsilyl)ethyl (2-Acetamido-4,6-*O*-benzylidene-2-deoxy-3-*O*-levulinyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (7). To a solution of 2-(trimethylsilyl)ethyl (2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (**6**; 540 mg, 0.42 mmol) in pyridine (10 mL) was added levulinic anhydride (181 mg, 0.84 mmol). The mixture was stirred for 2 h at room temperature, and methanol (5 mL) was added. The solution was concentrated then extracted with chloroform. The extracted was successively washed with 2M HCl, water, M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (1:3 ethyl acetate-hexane) of the residue on silica gel gave **7** (476 mg, 82%) as an amorphous mass: $[\alpha]_D$ +34.3° (*c* 2.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.80 (s, 3H, AcN), 2.18 (1s, 3H, $CH_3COCH_2CH_2$), 2.43–2.76 (m, 4H, $CH_3COCH_2CH_2$), 5.59 (s, 1H, PhC*H*), and 7.22–7.58 (m, 35H, 7Ph).

Anal. Calcd for $C_{79}H_{93}NO_{18}Si$ (1372.7): C, 69.12; H, 6.83; N, 1.02. Found: C, 68.84; H, 6.64; N, 1.00.

2-(Trimethylsilyl)ethyl (2-Acetamido-2-deoxy-3-*O*-*p*-methoxybenzyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (8). A solution of **5** (6.05 g, 4.09 mmol) in ethanol (100 mL) and hydrazine monohydrate (4.36 mL) was heated for 30 h under reflux. After cooling, insoluble materials were filtered off and washed with ethanol. The filtrate and washings were combined and concentrated to dryness. The residue was treated with acetic anhydride (7.6 mL) and methanol (100 mL) for 8 h at room temperature, and the solution was concentrated. Column chromatography (40:1 dichloromethane-methanol) of the residue on silica gel gave **8** (4.85 g, 85%) as an amorphous mass; $[\alpha]_D$ +56.1° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.60 (s, 3H, AcN), 3.26 (dd, 1H, $J_{2,3}$ = 9.5 Hz, $J_{3,4}$ = 2.6 Hz, H-3b), 3.37 (dd, 1H, $J_{1,2}$ = 7.3 Hz, $J_{2,3}$ = 8.5 Hz, H-2a), 3.47 (dd, 1H, $J_{1,2}$ = 8.4 Hz, $J_{2,3}$ = 9.5 Hz, H-2b), 3.52 (t, 1H, $J_{2,3}$ = $J_{3,4}$ =8.5 Hz, H-3a), 3.80 (s, 3H, MeO), 3.92 (m, 1H, H-4b), 4.32 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1b), 4.35 (d, 1H, $J_{1,2}$ = 7.3 Hz, H-1a), 5.28 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1c), and 6.83–7.42 (m, 34H, 7Ph).

Anal. Calcd for $C_{75}H_{91}NO_{17}Si$ (1306.6): C, 68.94; H, 7.02; N, 1.07. Found: C, 68.86; H, 6.79; N, 0.96.

2-(Trimethylsilyl)ethyl (2-Acetamido-2-deoxy-3-*O*-levulinyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→ 4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (9). A solution of **7** (417 mg, 0.30 mmol) in aqueous 80% acetic acid (5 mL) was heated, with stirring, for 24 h at 50°C, then concentrated. Column chromatography (2:1 ethyl acetate-hexane) of the residue on silica gel gave **9** (390 mg, quantitative) as an amorphous mass: $[\alpha]_D$ +15.4° (*c* 3.1, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.03 (m, 2H, $Me_3SiCH_2CH_2$), 1.60 (s, 3H, AcN), 2.14 (1s, 3H, $CH_3COCH_2CH_2$), 2.43–2.76 (m, 4H, $CH_3COCH_2CH_2$), 5.57 (d, 1H, $J_{1,2}$ = 7.7 Hz, H-1c), and 7.22–7.42 (m, 30H, 6Ph).

Anal. Calcd for $C_{72}H_{89}NO_{18}Si$ (1286.4): C, 67.32; H, 6.98; N, 1.09. Found: C, 67.17; H, 6.78; N, 0.95.

2-(Trimethylsilyl)ethyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(2-acetamido-2-deoxy-3-*O*-*p*-methoxybenzyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyra noside (11). To a solution of **8** (500 mg, 0.38 mmol) and methyl (phenyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-2-thio-D-*glycero*-D-*galacto*-2-nonulopyranosid)onate (**10**; 458 mg, 0.76 mmol) in acetonitrile (7 mL) were added molecular sieves 3Å (3 g), and the mixture was stirred for 6 h at room temperature, then cooled to −30°C. To the stirred mixture were added NIS(353 mg, 1.52 mmol) and TMSOTf (15 μL, 0.076 mmol), and the stirring was continued for 40 h at −30°C. The precipitates were filtered off and washed with chloroform. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3 and M $Na_2S_2O_3$, dried (Na_2SO_4) and concentrated. Column chromatography (50:1 chloroform-methanol) of the residue on silica gel gave **11** (445 mg, 65%) accompanied by the β-isomer (103 mg, 15%) as an amorphous mass: ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.63, 1.86, 1.93, 2.01, 2.05, and 2.10 (6s, 18H, 2AcN and 4AcO), 2.59 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.8 Hz, H-3*eq* of Neu5Ac), 3.77 and 3.80 (2s, 6H, 2MeO), and 6.83–7.40 (m, 34H, 7Ph).

Anal. Calcd for $C_{95}H_{118}N_2O_{29}Si$ (1780.1): C, 64.10; H, 6.68; N, 1.57. Found: C, 63.98; H, 6.51; N, 1.53.

2-(Trimethylsilyl)ethyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(2-acetamido-2-deoxy-3-*O*-levulinyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (12). Glycosylation of **9** (1.58 g, 1.22 mmol) with **10** (1.44 g, 2.44 mmol) in acetonitrile (13 mL) in the presence of NIS (1.11 g, 4.88 mmol), TfOH (22 μg, 0.24 mmol), and MS 3Å (1.7 g) for 36 h at −30°C, then work up as described for **11**, gave **12** (1.62 mg, 75%) accompanied by the β-isomer (0.51 mg, 25%) as an amorphous mass: $[\alpha]_D$ +20.3° (*c* 2.4, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.02 (m, 2H, $Me_3SiCH_2CH_2$), 1.87–2.14 (7s, 21H, 2AcN, 4AcO, and $CH_3COCH_2CH_2$), 2.53 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 5.2 Hz, H-3d*eq*), 3.76 (s, 3H, MeO), 5.39 (m, 1H, H-4d), and 7.32–7.65 (m, 30H, 6Ph).

Anal. Calcd for $C_{92}H_{116}N_2O_{30}Si$ (1758.0): C, 62.86; H, 6.65; N, 1.59. Found: C, 62.63; H, 6.60; N, 1.44.

2-(Trimethylsilyl)ethyl (Methyl 5-Acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (13). To a solution of **11** (400 mg, 0.225 mmol) in 9 : 1 ethyl acetate - H_2O (4 mL) was added ammonium cerium(IV) nitrate (250 mg, 0.45 mmol), and the mixture was stirred for 3 h at room temperature. Ethyl acetate was added and mixture was successively washed with water, M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (40:1 chloroform-methanol) of the residue on silica gel afforded **13** (360 mg, 95%) as an amorphous mass: $[\alpha]_D$ +8.9° (*c* 2.0, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 1.51, 1.86, 1.96, 2.03, 2.12, and 2.13 (6s, 18H, 2AcN and 4AcO), 2.60 (dd, 1H, $J_{gem} = 12.6$ Hz, $J_{3,4} = 4.7$ Hz, H-3*eq* of Neu5Ac), 3.77 (s, 3H, MeO), and 7.23–7.42 (m, 30H, 6Ph).

Anal. Calcd for $C_{87}H_{110}N_2O_{28}Si$ (1659.9): C, 62.95; H, 6.68; N, 1.69. Found: C, 62.81; H, 6.53; N, 1.65.

2-(Trimethylsilyl)ethyl (2,4,6-Tri-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)]-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (16). To a solution of **13** (300 mg, 0.18 mmol) and methyl 2,4,6-tri-*O*-benzoyl-3-*O*-benzyl-1-thio-β-D-galactopyranoside (**14**; 133 mg, 0.21 mmol) in CH_2Cl_2 (10 mL) were added molecular sieves 4Å (1.2 g) and the mixture was stirred for 5 h at room temperature and cooled to −10°C. DMTST (196 mg, 0.43 mmol) was added, and the stirring was continued for 24 h. After reaction was over, the precipitates were filtered off and washed with chloroform. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (50:1 chloroform-methanol) of the residue on silica gel gave **16** (273 mg, 68%) as an amorphous mass: $[\alpha]_D$ +26.8° (*c* 1.4, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.02 (m, 2H, $Me_3SiCH_2CH_2$), 1.80–2.20 (6s, 18H, 4AcO and 2AcN), 2.50 (m, 1H, H-3e-*eq*), 3.74 (s, 3H, MeO), 4.80 (m, 1H, H-4e), 5.30 (m, 1H, H-8e), 5.34 (d, 1H, $J_{7,8} = 10.1$ Hz, H-7e), 5.50 (dd, 1H, $J_{1,2} = 9.9$ Hz, $J_{2,3} = 8.8$ Hz, H-2d), 5.91 (d, 1H, $J_{3,4} = 3.3$ Hz, H-4d), and 7.03–8.31 (m, 50H, 10Ph)

Anal. Calcd for $C_{121}H_{138}N_2O_{36}Si$ (2224.5): C, 65.33; H, 6.25; N, 1.26. Found: C, 65.18; H, 6.02; N, 1.14.

2-(Trimethylsilyl)ethyl (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-β-D-galactopyranosyl)-(1→3)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)]-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (17). To a solution of **13** (1.5 g, 0.90 mmol) and methyl (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 (**15**; 1.8 g, 1.80 mmol) in CH_2Cl_2 (20 mL) were added molecular sieves 4Å (2.2 g) and the mixture was stirred for 6 h at room temperature and cooled to 0°C. DMTST (1.94 g, 4.50 mmol) was added, and the stirring was continued for 24 h. After reaction was over, the precipitates were filtered off and washed with chloroform. The filtrate and washings were combined, and the solution was successively washed with M Na_2CO_3 and water, dried (Na_2SO_4) and concentrated. Column chromatography (40:1 chloroform-methanol) of the residue on silica gel gave **17** (2.01 g, 86%) as an amorphous mass: $[\alpha]_D$ +17.3° (*c* 1.7, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 2.42 (dd, 1H, $J_{3,4}$ = 4.4 Hz, H-3e-*eq*), 2.56 (dd, 1H, $J_{3,4}$ = 4.4 Hz, H-3f-*eq*), 3.69 and 3.79 (2s, 6H, 2MeO), 5.33 (d, 1H, $J_{3,4}$ = 3.2 Hz, H-4d), 5.44 (dd, 1H, $J_{1,2} = J_{23}$ = 7.7 Hz, H-2d), and 7.18–8.17 (m, 45H, 9Ph).

Anal. Calcd for $C_{134}H_{159}N_3O_{48}Si$ (2607.8): C, 61.72; H, 6.15; N, 1.61. Found: C, 61.57; H, 6.02; N, 1.33.

[Methyl 5-Acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylono-1′,9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate]-(2→3)-2,4,6-tri-*O*-benzoyl-D-glucopyranosyl Trichloroacetimidate (20). To a solution of **18**[44] (380 mg, 0.27 mmol) in dichloromethane (1.9 mL) was added trifluoroacetic acid (1.7 mL) at 0°C, and the mixture was stirred for 2 h at room temperature and concentrated. Column chromatography (25:1 dichloromethane-methanol) of the residue on silica gel gave **19** (320 mg, 91%) as an amorphous mass. To a solution of **19** (320 mg, 0.24 mmol) in dichloromethane (5.5 mL) and trichloroacetonitrile (1 mL, 7.20 mmol) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 50 μL, 0.30 mmol) at 0°C, and the mixture was stirred for 2 h at 0°C, then concentrated. Column chromatography (20:1 dichloromethane-methanol) of the residue on silica gel gave **20** (320 mg, 90%) as an amorphous mass: $[\alpha]_D$ +23.6° (*c* 1.1, $CHCl_3$); ^{1}HNMR ($CDCl_3$): δ 1.88–2.12 (8s, 24H, 2AcN and 6AcO), 2.59 (dd, 1H, $J_{3ax,3eq}$ = 13.5, $J_{3eq,4}$ = 6.6 Hz, H-3b*eq*), 3.36 (s, 3 H, MeO), 5.00 (d, 1H, $J_{7,8}$ = 10.0 Hz, H-7b), 5.37 (d, 1H, $J_{7,8}$ = 10.0 Hz, H-7c), 5.57 (m, 1H, H-4c), 5.69 (dd, 1H, $J_{1,2}$ = 3.4, $J_{2,3}$ = 7.0 Hz, H-2a), 5.94 (d, 1H, $J_{3,4}$ = 3.1 Hz, H-4a), 6.84 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1a), 7.30–8.11 (m, 15H, 3Ph) and 8.63 (s, 1H, C=NH).

Anal. Calcd for $C_{64}H_{70}Cl_3N_3O_{30}$ (1467.6): C, 52.38; H, 4.81; N, 2.86. Found: C, 52.15; H, 4.54; N, 2.82.

2-(Trimethylsilyl)ethyl [Methyl 5-Acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylono-1′,9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate]-(2→3)-(2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)]-(2-acetamido-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (21). To a solution of **13** (321 mg, 0.19 mmol) and **20** (380 mg, 0.26 mmol) in dichloromethane (7 mL) were added molecular sieves 4Å (AW-300; 5.6 g), and the mixture was stirred for 12 h at room temperature, then cooled to 0°C. TMSOTf (13 μL, 0.066 mmol) was added, and the mixture was stirred for 24 h at 0°C, then filtered. The insoluble materials were washed with chloroform, and the combined filtrate and washings were washed with M $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (40:1 chloroform-methanol) of the residue on silica gel gave **21** (500 mg, 87%) as an amorphous mass:$[\alpha]_D$ +10.8° (*c* 1.8, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.82–2.18 (14s, 42H, 10AcO and 4AcN), 2.37–2.60 (m, 3H, H-3e-*eq*, H-3f-*eq*, and H-3g-*eq*), 3.47 and 3.80 (2s, 6H, 2MeO), and 7.21–8.13 (m, 45H, 9Ph).

Anal. Calcd for $C_{149}H_{178}N_4O_{57}Si$ (2965.1): C, 60.36; H, 6.05; N, 1.89. Found: C, 60.24; H, 5.84; N, 1.88.

2-(Trimethylsilyl)ethyl (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-β-D-galactopyranosyl)-(1→3)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)]-(2-acetamido-4-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (22). Compound **17** (1.2 g, 0.46 mmol) in ethanol (30 mL) and acetic acid (3 mL) was hydrogenolyzed in the presence of 20% $Pd(OH)_2$ (1.2 g) for 96 h at 40°C, and the reaction mixture was filtered. The filtrate was concentrated to a residue which was acetylated with acetic anhydride (5 mL) and pyridine (10 mL) for 20 h at 40°C. The mixture was concentrated, and a solution of the residue in chloroform was successively washed with 2 M HCl and M Na_2CO_3, dried (Na_2SO_4) and concentrated. Column chromatography (30:1 chloroform-methanol) of the residue on silica gel gave **22** (935 mg, 85%) as an amorphous mass: $[\alpha]_D$ +6.0° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.53–2.18 (18s, 54H, 15AcO and 3AcN), 2.39 (dd, 1H, H-3e-*eq*), 2.53 (dd, 1H, H-3f-*eq*), 2.74 (m, 1H, H-2c), 3.74 and 3.79 (2s, 6H, 2MeO), 5.44 (dd, 1H, $J_{1,2} = J_{2,3} = 7.7$ Hz, H-2d), 5.46 (d, 1H, $J_{3,4} = 3.3$ Hz, H-4c), 5.80 (d, 1H, NH-c), and 7.40–8.19 (m, 15H, 3Ph).

Anal. Calcd for $C_{106}H_{137}N_3O_{55}Si$ (2361.31): C, 53.92; H, 5.85; N, 1.78. Found: C, 53.85; H, 5.68; N, 1.60.

(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-β-D-galactopyranosyl)-(1→3)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)]-(2-acetamido-4-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-*O*-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-D-glucopyranosyl Trichloroacetimidate (24). To a solution of **22** (935 mg, 0.396 mmol) in dichloromethane (7 mL) was added trifluoroacetic acid (3 mL) at 0°C, and the mixture was stirred for 3 h at room temperature and concentrated. Column chromatography (20:1 chloroform-methanol) of the residue on silica gel gave **23** (838 mg, 93%) as an amorphous mass: IR (KBr) 3600-3100 (OH, NH), 1740 and 1220 (ester), 1670 and 1550 (amide), and 720 (Ph).

To a solution of **23** (300 mg, 0.12 mmol) in dichloromethane (2 mL) and trichloroacetonitrile (590 μL, 0.36 mmol) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU; 22 μL, 0.15 mmol) at 0°C, and the mixture was stirred for 1 h at 0°C, then concentrated. Column chromatography (20:1 chloroform-methanol) of the residue on silica gel gave **24** (317 mg, quantitative) as an amorphous mass: $[\alpha]_D$ +22.9° (*c* 0.3 $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 1.52–2.19 (18s, 54H, 15AcO and 3AcN), 2.40 (dd, 1H, H-3e-*eq*), 2.51 (dd, 1H, H-3f-*eq*), 2.98 (m, 1H, H-2c), 3.77 and 3.80 (2s, 6H, 2MeO), 5.44 (d, 1H, $J_{3,4}$ = 3.3 Hz, H-4c), 6.11 (d, 1H, NH-c), 6.51 (d, 1H, $J_{1,2}$ = 3.6 Hz, H-1a), 7.41–8.23 (m, 15H, 3Ph), and 8.73 (s, 1H, C=NH).

Anal. Calcd for $C_{103}H_{125}Cl_3N_4O_{55}$ (2405.47): C, 51.43; H, 5.24; N, 2.33. Found: C, 51.25; H, 5.14; N, 2.06.

(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-β-D-galactopyranosyl)-(1→3)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)]-(2-acetamido-4-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-2-azido-3-*O*-(*tert*-butyldiphenylsilyl)-4-octadecene-1,3-diol (26). To a solution of **24** (90 mg, 0.037 mmol) and (2*S*,3*R*,4*E*)-2-azido-3-*O*-(*tert*-butyldiphenylsilyl)-4-octadecene-1,3-diol[1] (**25**, 94 mg, 0.068 mmol) in dichloromethane (1.1 mL) were added molecular sieves 4Å (AW-300; 1.0 g), and the mixture was stirred for 12 h at room temperature, then cooled to 0°C. TMSOTf (2 μL, 0.010 mmol) was added, and the mixture was stirred for 36 h at 0°C, then filtered. The insoluble materials were washed with chloroform, and the combined filtrate and washings was washed with M $NaHCO_3$ and water, dried (Na_2SO_4) and concentrated. Column chromatography (25:1 chloroform-methanol) of the residue on silica gel gave **26** (66 mg, 64%) as an amorphous mass: $[\alpha]_D$ +0.47° (*c* 0.4 $CHCl_3$); IR (KBr) 3300 (NH), 3100-2900 (CH), 2100 (azide), 1740 and 1220 (ester), 1670 and 1550 (amide), 710 and 700 cm^{-1} (phenyl); ^{1}H NMR ($CDCl_3$) δ 0.88 (t, 3H, $J_{Me,CH2}$ = 6.6 Hz, $MeCH_2$), 1.04 (s, 9H, Me_3C), 1.26 (s, 22H, $11CH_2$), 1.53–2.03 (18s, 54H, 3AcN and 15AcO), 2.44 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.8 Hz, H-3e*eq*), 2.50 (dd, 1H, J_{gem} = 12.8 Hz, $J_{3eq,4}$ = 4.6 Hz, H-3f*eq*), 2.95 (m, 1H, H-2c), 3.75 and 3.81 (2s, 6H, 2MeO), 6.19 (d, 1H, NH-c), and 7.24–8.16 (m, 25H, 5Ph).

Anal. Calcd for $C_{135}H_{176}N_6O_{56}Si$ (2806.97): C, 57.75; H, 6.32; N, 2.99. Found: C,57.58; H, 6.19; N, 2.75.

(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-β-D-galactopyranosyl)-(1→3)-[(methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)]-(2-acetamido-4-*O*-acetyl-2-deoxy-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tri-*O*-acetyl-β-D-glucopyranosyl)-(1→1)-(2*S*,3*R*,4*E*)-3-*O*-(*tert*-butyldiphenylsilyl)-2-octadecanamido-4-octadecene-1,3-diol (27). To a solution of **26** (200 mg, 0.071 mmol) in benzene (6.5 mL) and water (0.26 mL) was added triphenylphosphine (34 mg, 0.13 mmol), and the mixture was stirred for 48 h at 30°C and concentrated. To a solution of the residue in dichloromethane (5 mL) were added octadecanoic acid (57 mg, 0.20 mmol) and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (38 mg, 0.20 mmol), and the mixture was stirred for 20 h at 30°C. The mixture was diluted with chloroform and the solution was washed with water, dried (Na_2SO_4) and concentrated. Column chromatography (25:1 chloroform-methanol) of the residue on silica gel gave **27** (113 mg, 52%) as an amorphous mass: $[\alpha]_D$ $+3.0°$ (*c* 1.3 $CHCl_3$); ^1H NMR ($CDCl_3$) δ 0.84 (t, 3H, $J_{vic} = 6.6$ Hz, $MeCH_2$), 0.97 (s, 9H, Me_3C), 1.22 (s, 50H, $25CH_2$), 1.74–2.10 (18s, 54H, 15AcO and 3AcN), 2.41 (dd, 1H, $J_{gem} = 12.3$ Hz, $J_{3eq,4} = 4.1$ Hz, H-3e-*eq*), 2.48 (dd, 1H, $J_{gem} = 12.8$ Hz, $J_{3eq,4} = 3.5$ Hz, H-3f-*eq*), 2.90 (m, 1H, H-2c), 3.72 and 3.78 (2s, 6H, 2MeO), 6.36 (d, 1H, NH-c), and 7.24–8.16 (m, 25H, 5Ph).

Anal. Calcd for $C_{153}H_{212}N_4O_{57}Si$ (3047.44): C, 60.30; H, 7.01; N, 1.84. Found: C,60.11; H, 6.83; N, 1.65.

Ganglioside GD1α (28). To a solution of **27** (113 mg, 0.037 mmol) in acetonitrile (3 mL) was added 1.0 M tetrabutylammonium fluoride in tetrahydrofuran (1 mL), and the mixture was stirred for 48 h at room temperature, then concentrated. To a solution of the residue in methanol (2 mL) was added a catalytic amount of sodium methoxide, and the mixture was stirred for 48 h at room temperature. Water (0.5 mL) was added and the solution was stirred for 24 h at room temperature, then neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with 1:1 chloroform-methanol, and the combined filtrate and washings were concentrated. Column chromatography (5:5:1 chloroform-methanol-water) of the residue on Sephadex LH-20 gave **28** (63 mg, 92%) as an amorphous mass: $[\alpha]_D$ $+3.4°$ (*c* 0.3, 5:5:1 $CHCl_3$-MeOH-H_2O); ^1H NMR ($(CD_3)_2SO$-D_2O) δ 0.84 (t, 6H, $2MeCH_2$), 1.23 (s, 50H, $25CH_2$), 1.82, 1.87, 1.88 (3s, 9H, 3AcN), 1.93 (q, 2H, $CH{=}CH_2CH_2$), 2.01 (t, 2H, $COCH_2$), 2.64 (dd, 1H, $J_{3eq,4} = 4.4$ Hz, H-3f-*eq*), 2.51 (dd, 1H, $J_{3eq,4} = 4.4$ Hz, H-3e-*eq*), 3.03 (t, 1H, H-2a), 3.84 (br d, 1H, H-4b), 4.15 (d, 1H, $J_{1,2} = 8.0$ Hz, H-1a), 4.20 (d, 1H, $J_{1,2} = 8.1$ Hz, H-1b), 4.23 (d, 1H, $J_{1,2} = 7.3$ Hz, H-1d), 4.50 (d, 1H, $J_{1,2} = 8.8$ Hz, H-1c), 5.32 (m, 1H, H-4 of ceramide), and 5.51 (m, 1H, H-5 of ceramide);

Anal. Calcd for $C_{84}H_{148}N_4O_{39}$ (1838.10): C, 54.89; H, 8.12; N, 3.05. Found: C, 54.63; H, 7.96; N, 3.01.

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