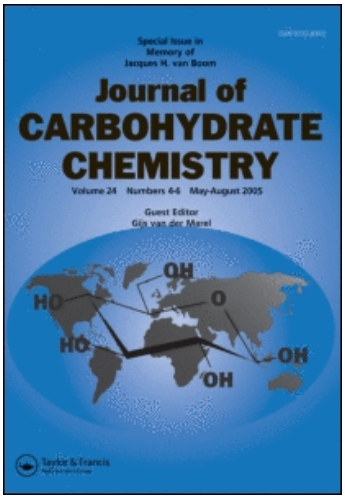

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Synthesis of Lacto- and Neolacto-series Ganglioside Analogs Containing *N*-Glycolylneuraminic Acid: Probes for Investigation of Specific Receptor Structures Recognized by Influenza A Viruses

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Synthesis of Lacto- and Neolacto-series Ganglioside Analogs Containing *N*-Glycolylneuraminic Acid: Probes for Investigation of Specific Receptor Structures Recognized by Influenza A Viruses[#]

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ABSTRACT

Sialic acids are essential components of host-cell surface receptors for infection of influenza virus. To investigate the specific receptor structures recognized by various influenza A viruses, a series of lacto- and neolacto-series ganglioside analogs containing *N*-glycolylneuraminic acid (Neu5Gc) have been synthesized. The pentasaccharide structures of Neu5Gc-α-(2→3)/(2→6)-lactotetraose ($IV^{3(6)}$Neu5GcLcOse) and Neu5Gc-α-(2→3)/(2→6)-neolactotetraose ($IV^{3(6)}$Neu5GcnLcOse) were constructed by glycosylation of the suitably protected trisaccharide acceptors (**2A** and **2B**) with the Neu5Gc-α-(2→3)/(2→6)-Gal trichloroacetimidate donors (**1** and **21**), respectively. Transformation of the 2-(trimethylsilyl)ethyl group at the reducing end in **4**, **11**, **23**, and **30** into the trichloroacetimidate group gave a series of Neu5Gc-α-(2→3)/(2→6)-lacto- and neolactotetraose donors (**7**, **13**, **26**, and **33**), which were

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coupled with 2-(tetradecyl)hexadecanol (**8**), to give the corresponding glycolipids (**9**, **14**, **27**, and **34**). Finally, the complete removal of the *O*-acyl groups and saponification of the methyl ester group gave the desired ganglioside analogs (**10**, **15**, **28**, and **35**).

Key Words: Sialic acid; Ganglioside; Influenza; Glycosylation; Carbohydrate.

INTRODUCTION

Influenza virus possesses both the receptor-binding protein (hemagglutinin: HA) and the receptor-destroying enzyme (neuraminidase: NA) on the cell surface, which are responsible for viral infection and budding from the host cells. It has been reported that the sialyl-lacto- and neolacto-series sugar chains, such as sialyl-α-(2→3)/(2→6)-Gal-β-(1→3)/(1→4)-GlcNAc in both glycolipids and glycoproteins, are the functional receptors for HA of influenza A virus.[1−4] It has also been suggested that HA discriminates the species of sialic acid molecules as well as the linkage form of sialyl-galactose on these sialoglycoconjugates.[1−3,5] These receptors differ among humans and the other animals,[3,4] so that it has been speculated that HA might continue some mutations for succession of the binding ability against these receptors on the occasion of infection between different animal species.[3−6]

We have achieved a systematic synthesis of gangliosides to elucidate the structure and functions of sialoglycoconjugates.[7,8] The sialyl lacto-(type I) and sialyl neolacto-(type II) tetraosyl ceramides containing *N*-acetylneuraminic acid[9,10] or KDN[11] have successfully been synthesized by our established method.

In this paper, we describe the synthesis of four kinds of Neu5Gc-α-(2→3)/(2→6)-Gal-β-(1→3)/(1→4)-GlcNAc-β-(1→3)-Gal-β-(1→4)-Glc-β-(1→1)-OR probes containing *N*-glycolylneuraminic acid (Neu5Gc), which are widely found in many animals but have not yet been detected in normal human tissues,[12,13] to investigate the receptor specificity of influenza A virus HA at the molecular level.

RESULTS AND DISCUSSION

For an efficient construction of a series of pentasaccharide structures, we employed the Neu5Gc-α-(2→3)/(2→6)-Gal trichloroacetimidate derivatives (**1**[14] and **21**) as the common glycosyl donors and two kinds of the suitably protected trisaccharide acceptors (**2A**[9] for lacto-series and **2B**[11] for neolacto-series).

As shown in Scheme 1, Neu5Gc-α-(2→3)-Gal trichloroacetimidate donor **1**, previously reported by Tanahashi et al.[14] was coupled with the lacto-series acceptor **2A** in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf) in CH_2Cl_2 to give the desired pentasaccharide **3** in 95% yield. In the ^{1}H NMR spectrum of **3**, one-proton doublet (J = 8.1 Hz) appeared at δ 5.11 indicating the newly formed glycosidic linkage to be β. Hydrogenolytic removal of the benzyl and benzylidene groups in **3** over 20% $Pd(OH)_2$ on carbon in EtOH, followed by complete acetylation of the resulting free hydroxyl groups with Ac_2O-pyridine, afforded the fully acylated pentasaccharide **4** in 86% yield. Removal of the *O*-acyl groups and saponification of the methyl ester group in **4** afforded **5** in a quantitative yield. Significant signals in the ^{1}H NMR spectrum of **5**

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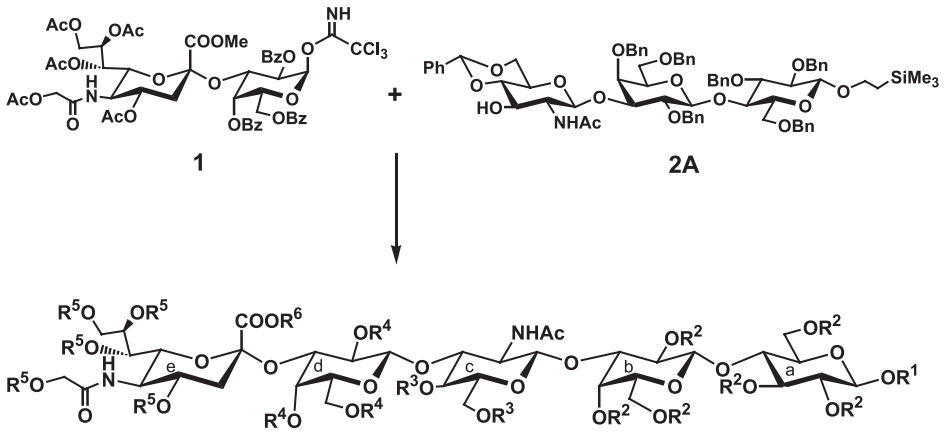
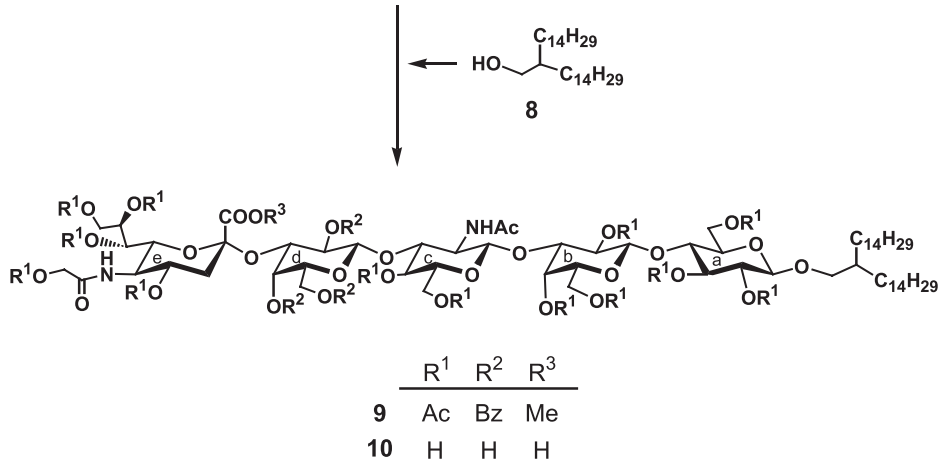


1 + **2A**

	R^1	R^2	R^3	R^4	R^5	R^6
3	$CH_2CH_2SiMe_3$	Bn	Benzylidene	Bz	Ac	Me
4	$CH_2CH_2SiMe_3$	Ac	Ac	Bz	Ac	Me
5	$CH_2CH_2SiMe_3$	H	H	H	H	H
6	H (α, β mixture)	Ac	Ac	Bz	Ac	Me
7	$C(NH)CCl_3$ (α only)	Ac	Ac	Bz	Ac	Me



	R^1	R^2	R^3
9	Ac	Bz	Me
10	H	H	H

Scheme 1. Synthesis of Neu5Gc-α-(2-3)lactotetraosyl lipid.

were two-proton multiplets (δ 1.00, TMS CH_2-), one-proton triplet (δ 1.77, H-3ax of NeuGc), three-proton singlet (δ 2.00, AcN), one-proton doublet of doublets (δ 2.75, H-3eq of NeuGc), and four one-proton doublets (δ 4.41 ∼ 4.70, J = 7.7 ∼ 8.4 Hz) comprised of four β-glycosidic linkages, clearly showing the desired structure.

The 2-(trimethylsilyl)ethyl group in **4** was selectively cleaved by treatment[15,16] with trifluoroacetic acid (TfOH) in CH_2Cl_2 to give the 1-hydroxy derivative **6**, which

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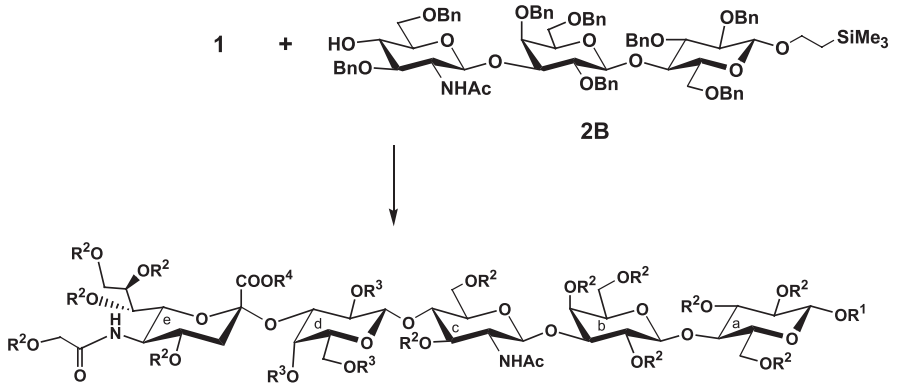
upon further treatment[17] with trichloroacetonitrile under 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in CH_2Cl_2 afforded the trichloroacetimidate donor **7** in 86% yield. In the same way, the neolacto-series pentasaccharide **11**,[14] which was prepared by coupling of **1** with **2B** (Scheme 2), was also converted to **13** in 85% yield. In the ^1H NMR spectra of **7** and **11**, a significant one-proton doublet was observed at δ 6.48 (J = 3.7 Hz) and δ 6.47 (J = 3.6 Hz), respectively, showing the anomeric configuration of the imidate to be α. Coupling of **7** with 2-(tetradecyl)hexadecanol **8**,[18] a mimic of ceramide, was performed in the presence of TMSOTf in CH_2Cl_2 at about 20°C to give the desired glycolipid derivative **9** in 54% yield. The coupling of **13** with **8** in the same manner afforded the desired glycolipid **14** in 50% yield. Finally, removal of the *O*-acyl groups and saponification of the methyl ester group in **9** and **14** gave the target Neu5Gc-α-(2→3)-lacto- and -neolacto-series ganglioside analogs (**10** and **15**) in high yields after column chromatography on Sephadex LH-20.



	R^1	R^2	R^3	R^4
11	$CH_2CH_2SiMe_3$	Ac	Bz	Me
12	H (α, β mixture)	Ac	Bz	Me
13	$C(NH)CCl_3$ (α only)	Ac	Bz	Me

	R^1	R^2	R^3
14	Ac	Bz	Me
15	H	H	H

Scheme 2. Synthesis of Neu5Gc-α-(2-3)neolactotetraosyl lipid.

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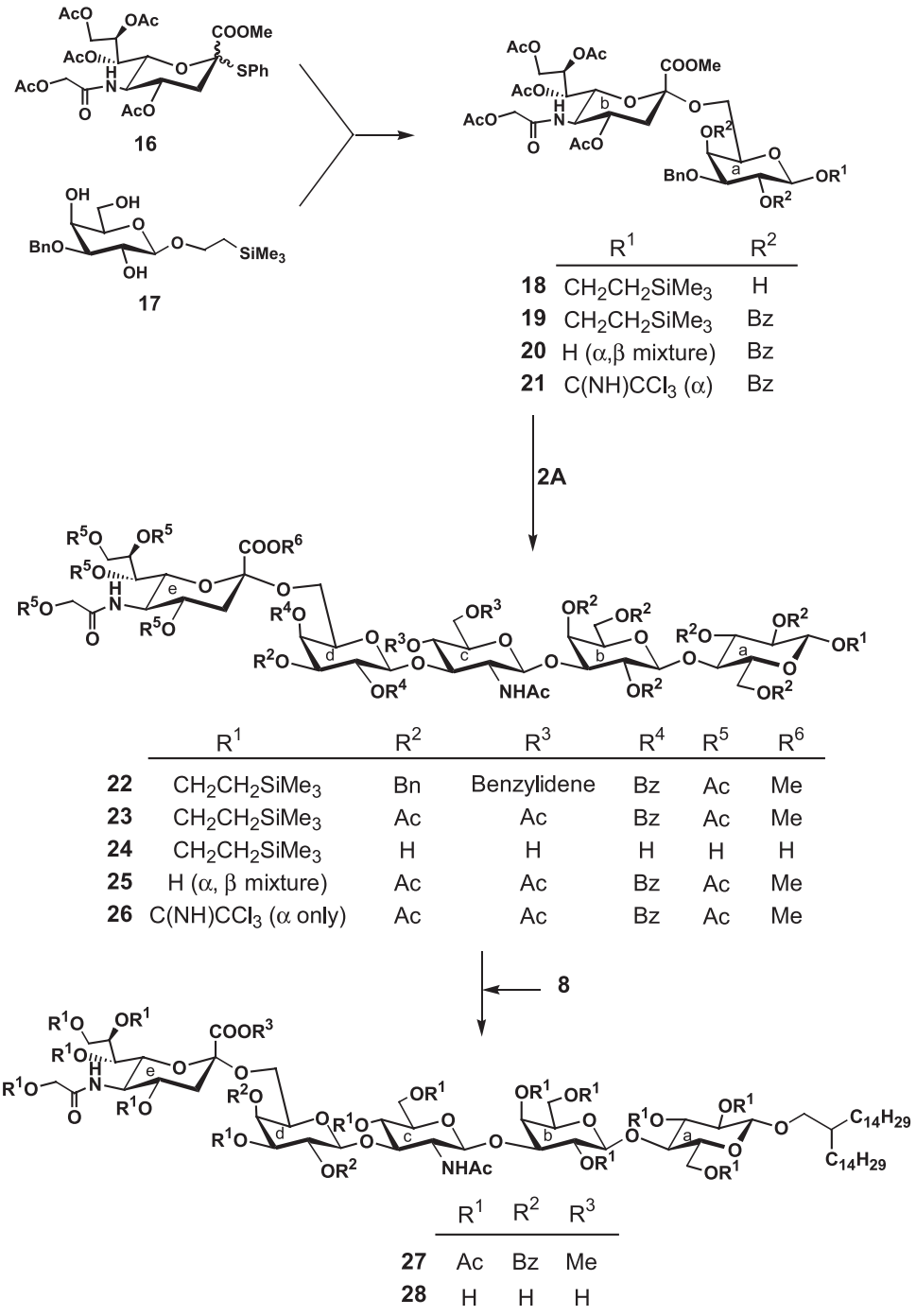

Scheme 3. Synthesis of Neu5Gc-α-(2-6)lactotetraose and its glycolipid.

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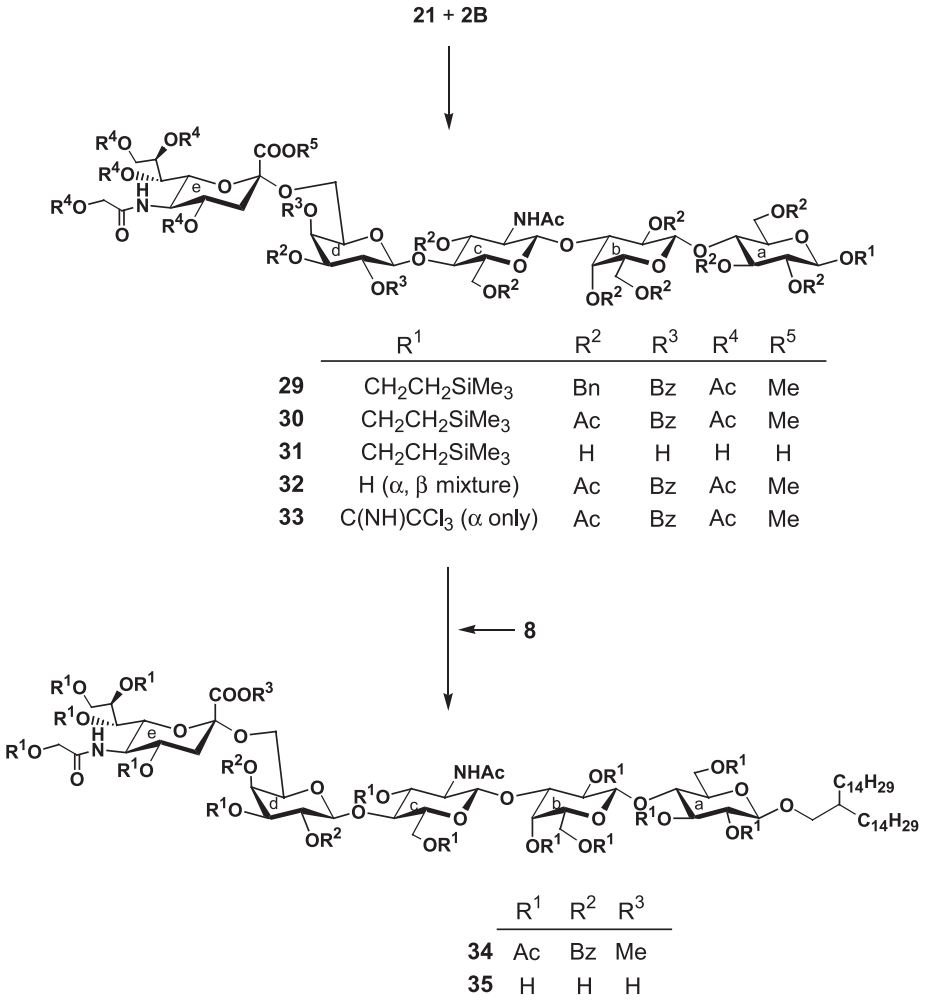

	R^1	R^2	R^3	R^4	R^5
29	$CH_2CH_2SiMe_3$	Bn	Bz	Ac	Me
30	$CH_2CH_2SiMe_3$	Ac	Bz	Ac	Me
31	$CH_2CH_2SiMe_3$	H	H	H	H
32	H (α, β mixture)	Ac	Bz	Ac	Me
33	$C(NH)CCl_3$ (α only)	Ac	Bz	Ac	Me

	R^1	R^2	R^3
34	Ac	Bz	Me
35	H	H	H

Scheme 4. Synthesis of Neu5Gc-α-(2-6)neolactotetraose and its glycolipid.

The synthetic routes of Neu5Gc-α-(2→6)-lactotetraose and neolactotetraose derivatives are shown in Schemes 3 and 4.

For the preparation of Neu5Gc-α-(2→6)-Gal donor, methyl (phenyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosid)onate **16**[19] was coupled with 2-(trimethylsilyl)ethyl 3-*O*-benzyl-β-D-galactopyranoside **17**[20] in the presence of *N*-iodosuccinimide (NIS) and TfOH in CH_3CN at − 35°C to give Neu5Gc-α-(2→6)-Gal derivative **18** in 67% yield (Scheme 3). Benzoylation of **18** with benzoic anhydride (Bz_2O) and 4-dimethylaminopyridine (DMAP) afforded **19** which was converted, by cleavage of the 2-(trimethylsilyl)ethyl group and trichloroacetimidate formation, to the desired Neu5Gc-α-(2→6)-Gal donor **21** in good

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yield. Couplings of trichloroacetimidate donor **21** with **2A** and **2B** were carried out in the presence of TMSOTf in CH_2Cl_2 to afford the corresponding pentasaccharides **22** (51%) and **29** (82%), respectively. Hydrogenolytic removal of the benzyl and benzylidene groups from **22** and **29**, and complete acetylation of the resulting free hydroxyl groups afforded the fully acylated pentasaccharides **23** and **30**. Removal of the *O*-acyl groups and saponification of the methyl ester group in **23** and **30** afforded the Neu5Gc-α-(2→6)-lactotetraose and neolactotetraose derivatives (**24** and **31**), quantitatively. In the ^{1}H NMR spectra of **24** and **31**, four one-proton doublets (J = 8.0–8.2 Hz), each corresponding to the β-glycosidic linkages, were clearly observed at δ 4.36–4.71, indicating the desired structures. The pentasaccharide donors **26** and **33** were prepared from **23** and **30** as described for **7** and **13**, and coupled with **8** to give the desired glycolipid derivatives **27** and **34** in 55% and 51% yields, respectively. Removal of the *O*-acyl groups and saponification of the methyl ester group in **27** and **34** gave the target Neu5Gc-α-(2→6)-lactotetraosyl and neolactotetraosyl glycolipids (**28** and **35**), quantitatively.

The synthetic ganglioside analogs (**10**, **15**, **28**, **35**) have successfully been utilized as the molecular probes for analyzing the recognition specificity of influenza A virus hemagglutinin,[21] demonstrating that a few amino acid residues in hemagglutinin affect binding reactivity to the molecular species of sialic acid (Neu5Ac/Neu5Gc).

It has also been shown that both sialic acid species (Neu5Ac/Neu5Gc) and the sialoside linkage to galactose (α2→3/α2→6) are critically associated with intestinal replication of influenza A virus in ducks[22] as well as the host range restriction in viral infection among different animals.[23]

EXPERIMENTAL

General procedures. Specific 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 at 400 MHz with a Varian Inova 400, or 200 MHz with a Varian Gemini-2000 spectrometer. TLC was performed on Silica Gel 60 (E. Merck), and column chromatography on silica gel (Fuji Silysia Co., 300 mesh) was accomplished with the solvent systems (v/v) specified. Concentrations and evaporations were conducted in vacuo.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-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)-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (3). To a solution of **1** (408 mg, 0.36 mmol) and **2A** (365 mg, 0.29 mmol) in CH_2Cl_2 (4 mL) was added MS4Å (600 mg), the reaction mixture was stirred for 3 h at room temperature and then cooled to 0°C. To the stirred mixture TMSOTf (11 μL, 58 μmol) was added, and the stirring was continued for 48 h at 0°C, being monitored by TLC. The solids were collected and washed with $CHCl_3$, and the combined filtrate and washings were washed with sat. Na_2CO_3 and water, dried (Na_2SO_4), and concentrated. Column chromatography ($CHCl_3$:MeOH = 80:1) of the

residue on silica gel gave **3** (610 mg, 95%) as an amorphous mass; $[\alpha]_D$ + 2.9 (*c* 0.34, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1550, 860, 840, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.44 (s, 3H, AcN), 1.59 (t, 1H, J = 12.8 Hz, H-3e(ax)), 1.79, 1.88, 2.03, 2.13, 2.16 (5s, 15H, 5AcO), 2.44 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.81 (s, 3H, MeO), 4.78 (dd, 1H, J = 9.9, 2.9 Hz, H-3d), 5.11 (d, 1H, J = 8.1 Hz, H-1d), 5.16 (dd, 1H, J = 2.6, 9.5 Hz, H-7e), 5.29 (d, 1H, J = 2.9 Hz, H-4d), 5.37 (dd, 1H, J = 8.1, 9.9 Hz, H-2d), 5.57 (s, 1H, PhCH), 5.61 (m, 1H, H-8e), 5.66 (d, 1H, J = 10.3 Hz, NH), 7.10–8.18 (m, 50H, 10Ph).

Anal. Calcd for $C_{123}H_{138}N_2O_{38}Si$: C, 64.78; H, 6.10; N, 1.23. Found: C, 64.70; H, 5.88; N, 1.21.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-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)-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (4). A solution of **3** (610 mg, 0.27 mmol) in acetic acid (1 mL) and EtOH (10 mL) was treated with hydrogen over $Pd(OH)_2$ (600 mg) overnight. The solids were filtered off and the filtrate was concentrated. The residue was treated with acetic anhydride (0.1 mL) in pyridine (0.5 mL) for 12 h at room temperature and worked up. The residue was taken up in $CHCl_3$, washed with 2N HCl and water, dried (Na_2SO_4) and concentrated. Column chromatography ($CHCl_3$:MeOH = 50:1) of the residue on silica gel gave **4** (457 mg, 86%) as an amorphous mass; $[\alpha]_D$ + 14.5 (*c* 1.2, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1550, 860, 840, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.93 (m, 2H, $Me_3SiCH_2CH_2$), 1.51 (s, 3H, AcN), 1.60 (t, 1H, J = 12.8 Hz, H-3e(ax)), 1.87, 1.91, 1.97, 1.98, 2.00, 2.03, 2.04, 2.057, 2.058, 2.06, 2.10, 2.12, 2.16 (13s, 39H, 13AcO), 2.44 (dd, 1H, J = 12.8, 4.6 Hz, H-3e(eq)), 3.81 (s, 3H, MeO), 4.19, 4.45 (2d, 2H, J = 15.3 Hz, NHC(O)CH_2OAc), 5.18 (dd, 1H, J = 2.8, 9.8 Hz, H-7e), 5.30 (dd, 1H, J = 8.0, 10.1 Hz, H-2d), 5.33 (d, 1H, J = 3.2 Hz, H-4d), 5.60 (m, 1H, H-8e), 5.75 (d, 1H, NH), 7.40–8.17 (m, 15H, 3Ph).

Anal. Calcd for $C_{90}H_{114}N_2O_{46}Si$: C, 54.38; H, 5.78; N, 1.41. Found: C, 54.22; H, 5.73; N, 1.21.

2-(Trimethylsilyl)ethyl (3,5-dideoxy-5-glycolylamino-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-(β-D-galactopyranosyl)-(1→3)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (5). To a solution of **4** (70 mg, 36 μmol) in MeOH (1 mL) was added a catalytic amount of 28% sodium methoxide in MeOH, the reaction mixture was stirred for 24 h at room temperature, and then water (0.1 mL) was added. After completion of the reaction, the solution was neutralized with Amberlite IR-120 (H^+) resin. The resin was filtered off and washed with MeOH, and the combined filtrate and washings was concentrated. Column chromatography (MeOH:H_2O = 1:1) of the residue on Sephadex LH-20 gave **5** (34 mg, 95%) as an amorphous mass; $[\alpha]_D$ − 15 (*c* 0.8, MeOH); IR (KBr) 3400, 2950, 1660, 1550, 860, 840cm^{-1}; ^{1}H NMR (D_2O): δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.77 (t, 1H, J = 12.1 Hz, H-3e(ax)), 2.00 (s, 3H, AcN), 2.75 (dd, 1H, J = 12.1, 4.4 Hz, H-3e(eq)), 4.41 (J = 8.1 Hz), 4.47 (J = 8.1 Hz), 4.48 (J = 7.7 Hz), 4.70 (J = 8.4 Hz) (4d, 4H, four anomeric protons).

Anal. Calcd for $C_{42}H_{74}N_2O_{30}Si$: C, 45.24; H, 6.69; N, 2.51. Found: C, 44.97; H, 6.48; N, 2.39.

(Methyl 5-acetoxyacetamido-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)-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (7). A solution of **4** (150 mg, 78 μmol) in CH_2Cl_2 (1.0 mL) was cooled to 0°C. TFA (1.0 mL) was added to the solution, and the mixture was stirred at room temperature. After 1 h, the mixture was concentrated at 35°C. Column chromatography ($CHCl_3$:MeOH = 45:1) of the residue on silica gel gave **6** (129 mg, 91%) as an amorphous mass; IR (film) 3400, 2950, 1750, 1660, 1550, 700cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 1.53 (s, 3H, AcN), 1.62 (t, 1H, J = 12.6 Hz, H-3e(ax)), 1.89–2.18 (13s, 39H, 13AcO), 2.46 (t, 1H, J = 12.6, 4.3 Hz, H-3e(eq)), 3.83 (s, 3H, MeO), complete loss of the TMS ethyl group. To a solution of **6** (116 mg, 63 μmol) in CH_2Cl_2 (1 mL) were added trichloroacetonitrile (0.19 mL, 1.8 mmol) and DBU (10 μL, 69 μmol) at 0°C. The reaction mixture was stirred at 0°C for 45 min. After completion of the reaction, the mixture was chromatographed ($CHCl_3$:MeOH = 50:1) on a column of silica gel gave **7** (108 mg, 86%) as an amorphous mass; $[\alpha]_D$ + 38.6 (*c* 0.76, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.52 (s, 3H, AcN), 1.62 (t, 1H, J = 12.8 Hz, H-3e(ax)), 1.89, 1.93, 1.94, 1.99, 2.00, 2.02, 2.05, 2.06, 2.080, 2.083, 2.11, 2.14, 2.18 (13s, 39H, 13AcO), 2.46 (dd, 1H, J = 12.8, 4.6 Hz, H-3e(eq)), 3.83 (s, 3H, MeO), 4.21, 4.47 (2d, 2H, J = 15.3 Hz, NHC(O)CH_2OAc), 5.16 (d, 1H, J = 8.0 Hz, H-1d), 5.18 (dd, 1H, J = 2.5, 9.8 Hz, H-7e), 5.32 (dd, 1H, J = 8.0, 10.0 Hz, H-2d), 5.35 (d, 1H, J = 3.2 Hz, H-4d), 5.62 (m, 1H, H-8e), 5.70 (d, 1H, J = 9.8 Hz, NH), 6.48 (d, 1H J=3.7 Hz, H-1a), 7.42–8.19 (m, 15H, 3Ph), 8.66 (s, 1H, C═NH).

Anal. Calcd for $C_{87}H_{102}Cl_3N_3O_{46}$: C, 51.42; H, 5.06; N, 2.07. Found: C, 51.23; H, 4.76; N, 2.00.

2-(Tetradecyl)hexadecyl (methyl 5-acetoxyacetamido-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)-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (9). To a solution of **7** (108 mg, 54 μmol) and 2-(tetradecyl)hexadecanol **8** (59 mg, 135 μmol) in CH_2Cl_2 (0.7 mL) was added MS4Å (160 mg), the reaction mixture was stirred for 3 h at room temperature and then cooled to 0°C. To the mixture was added TMSOTf (0.62 μL, 3.3 μmol), and the reaction mixture was stirred for 12 h at 20°C. Work-up as described for **3** gave **9** (66 mg, 54%) as an amorphous mass; $[\alpha]_D$ + 19.4 (*c* 1.3, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 6H, 2*Me*CH_2), 1.25 (s, 53H, 26CH_2, C*H*), 1.52 (s, 3H, AcN), 1.62 (t, 1H, J = 12.6 Hz, H-3e(ax)), 1.69–2.17 (13s, 39H, 13AcO), 2.46 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.83 (s, 3H, MeO), 4.21, 4.48 (2d, 2H, J = 15.3 Hz, NHC(O)CH_2OAc), 5.32 (dd, 1H, J = 8.0, 9.6 Hz, H-2d), 5.63 (m, 1H, H-8e), 5.67 (d, 1H, NH), 7.42–8.19 (m, 15H, 3Ph).

Anal. Calcd for $C_{115}H_{162}N_2O_{46}$: C, 59.83; H, 7.07; N, 1.21. Found: C, 59.57; H, 6.95; N, 0.98.

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2-(Tetradecyl)hexadecyl (3,5-dideoxy-5-glycolylamino-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-(β-D-galactopyranosyl)-(1→3)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (10). To a solution of **9** (66 mg, 33 μmol) in MeOH (3 mL) was added a catalytic amount of 28% sodium methoxide in MeOH, the reaction mixture was stirred for 24 h at room temperature, and then water (0.1 mL) was added. After completion of the reaction, the solution was neutralized with Amberlite IR-120 (H^+) resin and filtered. The resin was washed with MeOH, and combined filtrate and washings was concentrated. Column chromatography ($CHCl_3$:MeOH:H_2O = 4:1:0.1) of the residue on Sephadex LH-20 gave **10** (35 mg, 96%) as an amorphous mass; $[\alpha]_D$ + 7.7 (*c* 0.39, $CHCl_3$:MeOH:H_2O = 4:1:0.1); IR (KBr) 3400, 2950, 1650, 1550cm^{-1}; ^{1}H NMR (DMSO–d_6): δ 0.86 (t, 6H, 2*Me*CH_2), 1.24 (s, 53H, 26C*H*$_2$, C*H*), 1.52 (t, 1H, J = 12.6 Hz, H-3e(ax)), 1.79 (s, 3H, AcN), 2.79 (dd, 1H, J = 12.6, 4.4 Hz, H-3e(eq)).

Anal. Calcd for $C_{67}H_{122}N_2O_{30}$: C, 56.05; H, 8.57; N, 1.95. Found: C, 56.00; H, 8.53; N, 1.89.

(Methyl 5-acetoxyacetamido-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→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (13). A solution of **11**[14] (240 mg, 0.12 mmol) in CH_2Cl_2 (2 mL) was cooled to 0°C. TFA (2 mL) was added to the solution, and the mixture was stirred at room temperature. After 1 h, the mixture was concentrated at 35°C. Column chromatography ($CHCl_3$:MeOH = 35:1) of the residue on silica gel gave **12** (220 mg, 98%) as an amorphous mass; IR (film) 3400, 2950, 1750, 1650, 1550, 700cm^{-1}. To a solution of **12** (220 mg, 0.12 mmol) in CH_2Cl_2 (1 mL) were added trichloroacetonitrile (0.1 mL, 3.6 mmol) and DBU (21 μL, 0.14 mmol) at 0°C. The mixture was stirred at 0°C for 45 min. After completion of the reaction, the mixture was chromatographed ($CHCl_3$:MeOH = 50:1) on a column of silica gel gave **13** (201 mg, 85%) as an amorphous mass; $[\alpha]_D$ + 38.9 (*c* 0.38, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.89 (s, 3H, AcN), 1.94–2.14 (13s, 39H, 13AcO), 2.48 (dd, 1H, J = 12.6, 4.2 Hz, H-3e(eq)), 3.70 (s, 3H, MeO), 5.01 (dd, 1H, J = 3.6, 10.3 Hz, H-2a), 6.47 (d, 1H J = 3.6 Hz, H-1a), 7.43–8.19 (m, 15H, 3Ph), 8.65 (s, 1H, C═NH).

Anal. Calcd for $C_{87}H_{102}Cl_3N_3O_{46}$: C, 51.42; H, 5.06; N, 2.07. Found: C, 51.22; H, 4.90; N, 1.97.

2-(Tetradecyl)hexadecyl (methyl 5-acetoxyacetamido-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→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (14). To a solution of **13** (195 mg, 97 μmol) and **8** (85 mg, 190 μmol) in CH_2Cl_2 (1 mL) was added MS4Å (130 mg), the reaction mixture was stirred for 3 h at room temperature and then cooled to 0°C. To the mixture was added TMSOTf (1.1 μL, 5.8 μmol), and the reaction mixture was stirred for 12 h at 20°C. Work-up as described for **3** gave **14** (110 mg, 50%) as an amorphous mass; $[\alpha]_D$ + 35.2 (*c* 1.3, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 6H, 2*Me*CH_2), 1.25 (s, 53H, 26C*H*$_2$, C*H*), 1.52 (s, 3H, AcN), 1.62 (t, 1H,

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J = 12.6 Hz, H-3e(ax)), 1.69–2.17 (13s, 39H, 13AcO), 2.46 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.83 (s, 3H, MeO), 4.21, 4.48 (2d, 2H, J = 15.3 Hz, NHC(O)CH_2OAc), 5.32 (dd, 1H, J = 8.0, 9.6 Hz, H-2d), 5.63 (m, 1H, H-8e), 5.67 (d, 1H, NH), 7.42–8.19 (m, 15H, 3Ph).

Anal. Calcd for $C_{115}H_{162}N_2O_{46}$: C, 59.83; H, 7.07; N, 1.21. Found: C, 59.76; H, 7.03; N, 0.92.

2-(Tetradecyl)hexadecyl (3,5-dideoxy-5-glycolylamino-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-(β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (15). Complete *O*-deacylation and saponification of the methyl ester group in **14** (60 mg) were carried out as described for **10** to give **15** (33 mg, 90%) as an amorphous mass; $[\alpha]_D$ + 9.8 (*c* 0.51, $CHCl_3$:MeOH:H_2O = 4:1:0.1); IR (KBr) 3400, 2950, 1650, 1550cm^{-1}; ^{1}H NMR (DMSO–d_6): δ 0.86 (t, 6H, 2*Me*CH_2), 1.24 (s, 53H, 26CH_2, C*H*), 1.52 (t, 1H, J = 12.4 Hz, H-3e(ax)), 1.79 (s, 3H, AcN), 2.79 (dd, 1H, J = 12.4, 4.6 Hz, H-3e(eq)).

Anal. Calcd for $C_{67}H_{122}N_2O_{30}$: C, 56.05; H, 8.57; N, 1.95. Found: C, 55.92; H, 8.46; N, 1.76.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(3-*O*-benzyl-β-D-galactopyranoside (18). To a solution of **16**[19] (7.8 g, 12.2 mmol) and **17**[20] (3.0 g, 8.1 mmol) in CH_3CN (70 mL) was added MS3Å (11 g), the reaction mixture was stirred for 6 h at room temperature and then cooled to − 35°C. To the mixture were added NIS (4.1 g, 18.2 mmol) and TfOH (0.11 mL, 1.2 mmol), and the reaction mixture was stirred for 12 h at − 35°C, being monitored by TLC. The solids were collected and washed with $CHCl_3$, and the combined filtrate and washings was washed with sat. Na_2CO_3 and sat. $Na_2S_2O_3$, dried (Na_2SO_4), and concentrated. Column chromatography ($CHCl_3$:MeOH = 90:1) of the residue on silica gel gave **18** (4.9 g, 67%) as an amorphous mass; $[\alpha]_D$ − 18.6 (*c* 0.97, $CHCl_3$); IR (film) 3500, 3300, 2950, 1750, 1650, 860, 840, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.01 (m, 2H, $Me_3SiCH_2CH_2$), 2.01–2.18 (5s, 15H, 5AcO), 2.61 (dd, 1H, J = 12.7, 4.4 Hz, H-3b(eq)), 3.81 (s, 3H, MeO), 4.30, 4.59 (2d, 2H, J = 15.0, Hz, NHC(O)CH_2OAc), 4.72 (dd, 2H, J = 11.7 Hz, PhCH_2O), 4.93 (m, 1H, H-4b), 5.27 (dd, 1H, J = 1.5, 7.7 Hz, H-7e), 5.36 (m, 1H, H-8b), 5.94 (d, 1H, J = 9.7 Hz, NH), 7.28–7.47 (m, 5H, Ph).

Anal. Calcd for $C_{40}H_{59}NO_{20}Si$: C, 53.26; H, 6.59; N, 1.55. Found: C, 53.08; H, 6.31; N, 1.53.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-2,4-di-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranoside (19). To a solution of **18** (3.9 g, 4.3 mmol) in pyridine (40 mL) were added Bz_2O (3.9 g, 17.2 mmol) and DMAP (0.52 g, 4.3 mmol), and the reaction mixture was stirred at room temperature overnight. The mixture was diluted with $CHCl_3$ and washed with 2N HCl and water. The organic layer was dried over Na_2SO_4 and concentrated. Column chromatography ($CHCl_3$:MeOH = 100:1) of the residue on silica gel gave **19** (4.3 g, 91%) as an amorphous mass; $[\alpha]_D$ + 31 (*c* 0.97, $CHCl_3$); IR (film) 3300, 2950, 1750, 1660, 1550, 860, 840, 700cm^{-1}; ^{1}H NMR

($CDCl_3$): δ 0.89 (m, 2H, $Me_3SiCH_2CH_2$), 2.10, 2.11, 2.19, 2.21, 2.26 (5s, 15H, 5AcO), 2.60 (dd, 1H, J = 12.6, 4.4 Hz, H-3b(eq)), 3.29 (s, 3H, MeO), 3.89 (dd, 1H, J = 10.1, 3.4 Hz, H-3a), 4.29, 4.53 (2d, 2H, J = 15.4 Hz, NHC(O)CH_2OAc), 4.59, 4.75 (dd, 2H, J = 12.5 Hz, PhCH_2O), 4.70 (d, 1H, J = 8.2 Hz, H-1a), 4.85 (m, 1H, H-4b), 5.24 (dd, 1H, J = 1.5, 7.7 Hz, H-7b), 5.38 (m, 1H, H-8b), 5.46 (dd, 1H, J = 8.2, 10.1 Hz, H-2a), 6.00 (d, 1H, J = 9.8 Hz, NH), 6.02 (d, 1H, J = 3.4 Hz, H-4a), 7.13–8.25 (m, 15H, 3Ph).

Anal. Calcd for $C_{54}H_{67}NO_{22}Si$: C, 58.42; H, 6.08; N, 1.26. Found: C, 58.29; H, 5.83; N, 1.15.

(Methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-2,4-di-*O*-benzoyl-3-*O*-benzyl-α-D-galactopyranosyl trichloroacetimidate (21). A solution of **19** (825 mg, 0.7 mmol) in CH_2Cl_2 (5 mL) was cooled to 0°C. TFA (5 mL) was added to the solution, and the reaction mixture was stirred at room temperature. After 2 h, the mixture was concentrated at 35°C. Column chromatography ($CHCl_3$:MeOH = 50:1) of the residue on silica gel gave **20** (749 mg, 97%) as an amorphous mass; IR (film) 3400, 2950, 1750, 1660, 1550, 700cm^{-1}. To a solution of **20** (100 mg, 92 μmol) in CH_2Cl_2 (0.8 mL) were added trichloroacetonitrile (279 μL, 2.8 mmol) and DBU (15 μL, 102 μmol) at 0°C. The reaction mixture was stirred at 0°C for 45 min. After completion of the reaction, the mixture was chromatographed ($CHCl_3$:MeOH = 70:1) on a column of silica gel gave **21** (111 mg, 96%) as an amorphous mass; $[\alpha]_D$ + 55.7 (*c* 1.1, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1550, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.01, 2.02, 2.06, 2.12, 2.17 (5s, 15H, 5AcO), 2.39 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.26 (s, 3H, MeO), 4.28, 4.57 (2d, 2H, J = 12.5 Hz, NHC(O)CH_2OAc), 4.62, 4.79 (2d, 2H, J = 12.5 Hz, PhCH_2), 4.85 (m, 1H, H-4b), 5.25 (dd, 1H, J = 2.2, 8.4 Hz, H-7b), 5.37 (m, 1H, H-8b), 5.63 (dd, 1H, J = 3.3, 10.3 Hz, H-2a), 5.86 (d, 1H, NH), 6.06 (d, 1H, J = 2.9 Hz, H-4a), 6.77 (d, 1H, J = 3.3 Hz, H-1a), 7.14–8.17 (m, 15H, 3Ph), 8.46 (s, 1H, C═NH).

Anal. Calcd for $C_{51}H_{55}Cl_3N_2O_{22}$: C, 53.07; H, 4.80; N, 2.43. Found: C, 52.77; H, 4.58; N, 2.42.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(2,4-di-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→3)-(2-acetamido-4,6-*O*-benzylidene-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (22). To a solution of **21** (111 mg, 90 μmol) and **2A** (138 mg, 108 μmol) in CH_2Cl_2 (0.7 mL) was added MS4Å (250 mg), the reaction mixture was stirred for 3 h at room temperature and then cooled to 0°C. To the mixture was added TMSOTf (1.4 μL, 7.2 μmol), and the reaction mixture was stirred for 12 h at 0°C, being monitored by TLC. Work-up as described for **3** gave **22** (108 mg, 51%) as an amorphous mass; $[\alpha]_D$ + 21 (*c* 1.6, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1550, 860, 840, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.70 (s, 3H, AcN), 1.89, 2.00, 2.02, 2.10, 2.17 (5s, 15H, 5AcO), 2.58 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.06 (s, 3H, MeO), 4.28, 4.59 (2d, 2H, J = 15.7, Hz, NHC(O)CH_2OAc), 4.80 (m, 1H, H-4e), 5.27 (dd, 1H, J = 2.8, 9.2 Hz, H-7e), 5.34 (dd, 1H, J = 8.2, 10.1 Hz, H-2d), 5.42 (m, 1H, H-8e), 5.75 (d, 1H, J = 3.3 Hz, H-4d), 5.78 (s, 1H, PhC*H*), 5.80 (d, 1H, NH), 6.94–8.16 (m, 50H, 10Ph).

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Anal. Calcd for $C_{123}H_{140}N_2O_{37}Si$: C, 65.18; H, 6.23; N, 1.24. Found: C, 64.88; H, 6.06; N, 1.23.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (23). A solution of **22** (100 mg, 42.7 mmol) in EtOH (5 mL) and AcOH (0.1 mL) was treated with hydrogen over $Pd(OH)_2$ (100 mg) overnight. Work-up and acetylation as described for **4** gave **23** (55 mg, 65%) as an amorphous mass; $[\alpha]_D$ + 9.3 (*c* 1.1, $CHCl_3$); IR (film) 3400, 3100–2900, 1750, 1660, 1540, 860, 840, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.95 (m, 2H, $Me_3SiCH_2CH_2$), 1.84 (s, 3H, AcN), 1.85, 2.00, 2.01 × 2, 2.02, 2.029 × 2, 2.034, 2.05, 2.09, 2.11 × 2, 2.175, 2.181 (14s, 42H, 14AcO), 2.52 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.30 (s, 3H, MeO), 4.30, 4.60 (2d, 2H, J = 15.6 Hz, NHC(O)CH_2OAc), 5.71 (d, 1H, J = 3.3 Hz, H-4d), 5.86 (d, 1H, NH), 7.45–8.12 (m, 10H, 2Ph).

Anal. Calcd for $C_{85}H_{112}N_2O_{46}Si$: C, 53.01; H, 5.86; N, 1.45. Found: C, 52.94; H, 5.58; N, 1.28.

2-(Trimethylsilyl)ethyl (3,5-dideoxy-5-glycolylamino-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→6)-(β-D-galactopyranosyl)-(1→3)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (24). To a solution of **23** (30 mg, 20 μmol) in MeOH (2 mL) was added a catalytic amount of 28% sodium methoxide in MeOH, the reaction mixture was stirred for 24 h at room temperature, and then water (0.1 mL) was added. Work-up as described for **5** gave **24** (18 mg, 98%) as an amorphous mass; $[\alpha]_D$ − 17 (*c* 0.4, MeOH); IR (KBr) 3400, 2950, 1660, 1550, 860, 840cm^{-1}; ^{1}H NMR (D_2O) : δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.69 (t, 1H, J = 12.4 Hz, H-3e(ax)), 2.00 (s, 3H, AcN), 2.69 (dd, 1H, J = 12.4, 4.6 Hz, H-3e(eq)), 4.36 (J = 8.0 Hz), 4.42 (J = 8.0 Hz), 4.47 (J = 8.0 Hz), 4.71 (J = 8.2 Hz) (4d, 4H, four anomeric protons).

Anal. Calcd for $C_{42}H_{74}N_2O_{30}Si$: C, 45.24; H, 6.69; N, 2.51. Found: C, 45.01; H, 6.48; N, 2.30.

(Methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (26). A solution of **23** (100 mg, 50 μmol) in CH_2Cl_2 (1 mL) was cooled to 0°C. TFA (1 mL) was added to the solution, and the reaction mixture was stirred at room temperature. After 1 h, the mixture was concentrated at 35°C. Column chromatography ($CHCl_3$:MeOH = 35:1) of the residue on silica gel gave **25** (83 mg, 88%) as an amorphous mass; IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.85 (s, 3H, AcN), 2.01–2.18 (14s, 42H, 14AcO), 2.52 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.29 (s, 3H, MeO), 4.30, 4.58 (2d, 2H, J = 15.4 Hz, NHC(O)CH_2OAc), 5.70 (d, 1H, J = 3.3 Hz, H-4d), 5.85 (d, 1H, J = 9.9 Hz, NH), 7.47–8.12 (m, 10H, 2Ph). To a solution of **25** (83 mg, 44 μmol) in CH_2Cl_2 (0.3 mL) were added trichloroacetonitrile (131 μL, 1.3 mmol) and DBU (7.2

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μL, 48 μmol) at 0°C. The reaction mixture was stirred at 0°C for 1 h. Work-up as described for **7** gave **26** (86 mg, 97%) as an amorphous mass; $[\alpha]_D$ + 33.2 (*c* 1.7, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.85 (s, 3H, AcN), 2.00–2.18 (14s, 42H, 14AcO), 2.53 (dd, 1H, J = 13.0, 4.6 Hz, H-3e(eq)), 3.31 (s, 3H, MeO), 4.28, 4.57 (2d, 2H, J = 15.3 Hz, NHC(O)CH_2OAc), 4.91 (m, 1H, H-4e), 5.12 (d, 1H, J = 8.0 Hz, H-1d), 5.31 (dd, 1H, J = 3.2, 10.5 Hz, H-3d), 5.34 (m, 1H, H-8e), 5.38 (dd, 1H, J = 8.0, 10.5 Hz, H-2d), 5.71 (d, 1H, J = 3.2 Hz, H-4d), 5.83 (d, 1H, NH), 6.47 (d, 1H, J = 3.7 Hz, H-1a), 7.50–8.12 (m, 10H, 2Ph), 8.66 (s, 1H, C═NH).

Anal. Calcd for $C_{82}H_{100}Cl_3N_3O_{46}$: C, 49.99; H, 5.12; N, 2.13. Found: C, 49.83; H, 4.92; N, 1.99.

2-(Tetradecyl)hexadecyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→3)-(2-acetamido-4,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (27). To a solution of **26** (86 mg, 42 μmol) and **8** (42 mg, 97 μmol) in CH_2Cl_2 (0.3 mL) was added MS4Å (140 mg), the reaction mixture was stirred for 3 h at room temperature and then cooled to 0°C. To the mixture was added TMSOTf (0.45 μL, 2.3 μmol), and the reaction mixture was stirred for 12 h at 0°C, being monitored by TLC. Work-up as described for **3** gave **27** (53 mg, 55%) as an amorphous mass; $[\alpha]_D$ + 26.3 (*c* 0.75, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.88 (t, 6H, 2*Me*CH_2), 1.26 (s, 53H, 26CH_2, C*H*), 1.84 (s, 3H, AcN), 1.88 (t, 1H, H-3e(ax)), 1.85–2.18 (14s, 42H, 14AcO), 2.52 (dd, 1H, J = 13.0, 4.6 Hz, H-3e(eq)), 3.29 (s, 3H, MeO), 4.30, 4.59 (2d, 2H, J = 15.3 Hz, NHC(O)CH_2OAc), 5.12 (d, 1H, J = 8.2 Hz, H-1d), 5.31 (dd, 1H, J = 3.2, 10.3 Hz, H-3d), 5.35 (m, 1H, H-8e), 5.71 (d, 1H, J = 3.2 Hz, H-4d), 5.81 (d, 1H, NH), 7.47–8.12 (m, 10H, 2Ph).

Anal. Calcd for $C_{110}H_{160}N_2O_{46}$: C, 58.81; H, 7.18; N, 1.25. Found: C, 58.59; H, 6.95; N, 1.04.

2-(Tetradecyl)hexadecyl (3,5-dideoxy-5-glycolylamino-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→6)-(β-D-galactopyranosyl)-(1→3)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (28). To a solution of **27** (37 mg, 16 μmol) in MeOH (2 mL) and THF (1.5 mL) was added a catalytic amount of 28% sodium methoxide in MeOH, the reaction mixture was stirred for 24 h at room temperature, and then water (0.1 mL) was added. Work-up as described for **5** gave **28** (21 mg, 98%); $[\alpha]_D$ + 10.8 (*c* 0.61, $CHCl_3$:MeOH:H_2O = 4:1:0.1); IR (KBr) 3400, 2950, 1650, 1550cm^{-1}; ^{1}H NMR (DMSO–d_6): δ 0.86 (t, 6H, 2*Me*CH_2), 1.24 (s, 53H, 26CH_2, C*H*), 1.82 (s, 3H, AcN), 2.64 (dd, 1H, J = 11.7, 4.4 Hz, H-3e(eq)).

Anal. Calcd for $C_{67}H_{122}N_2O_{30}$: C, 56.05; H, 8.57; N, 1.95. Found: C, 56.05; H, 8.46; N, 1.78.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(2,4-di-*O*-benzoyl-3-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-benzyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (29). To a solution of **21** (334 mg, 271 μmol) and **2B** (204 mg, 149 μmol) in CH_2Cl_2 (1.5 mL) was added MS4Å (200 mg), the reaction

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mixture was added TMSOTf (5.3 μL, 27 μmol), and the reaction mixture was stirred for 12 h at 0°C, being monitored by TLC. Work-up as described for **3**, and column chromatography (*n*-hexane:AcOEt = 1:2) of the residue on silica gel gave **29** (296 mg, 82%) as an amorphous mass; $[\alpha]_D$ + 6.2 (*c* 0.45, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 860, 840, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.50 (s, 3H, AcN), 1.94, 2.00, 2.05, 2.07, 2.17 (5s, 15H, 5AcO), 2.52 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.25 (s, 3H, MeO), 4.28, 4.58 (2d, 2H, J = 15.4 Hz, NHC(O)CH_2OAc), 5.26 (dd, 1H, J = 1.8, 8.4 Hz, H-7e), 5.37 (m, 1H, H-8e), 5.40 (dd, 1H, J=8.1, 10.9 Hz, H-2d), 5.83 (d, 1H, NH), 5.84 (d, 1H, J = 3.3 Hz, H-4d), 7.07–8.07 (m, 55H, 11Ph).

Anal. Calcd for $C_{130}H_{148}N_2O_{37}Si$: C, 66.20; H, 6.32; N, 1.19. Found: C, 65.98; H, 6.24; N, 1.05.

2-(Trimethylsilyl)ethyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (30). A solution of **29** (220 mg, 90 μmol) in EtOH (10 mL) was hydrogenated over $Pd(OH)_2$ (220 mg) overnight. The solid was filtered off and the filtrate was concentrated. The residue was acetylated with acetic anhydride (0.1 mL) in pyridine (0.5 mL) for 12 h at room temperature. Work-up as described for **3** gave **30** (145 mg, 82%) as an amorphous mass; $[\alpha]_D$ + 1.0 (*c* 1.2, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1550, 860, 840, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.95 (m, 2H, $Me_3SiCH_2CH_2$), 1.84 (s, 3H, AcN), 1.91–2.18 (14s, 42H, 14AcO), 2.53 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.43 (s, 3H, MeO), 4.30, 4.59 (2d, 2H, J = 15.4 Hz, NHC(O)CH_2OAc), 5.33 (dd, 1H, J = 3.1, 10.6 Hz, H-3d), 5.38 (m, 1H, H-8e), 5.46 (dd, 1H, J = 8.1, 10.6 Hz, H-2d), 5.59 (d, 1H, NH), 5.78 (d, 1H, J = 3.1 Hz, H-4d), 5.90 (d, 1H, NH), 7.43–8.11 (m, 10H, 2Ph).

Anal. Calcd for $C_{85}H_{112}N_2O_{46}Si$: C, 53.01; H, 5.86; N, 1.45. Found: C, 52.77; H, 5.69; N, 1.19.

2-(Trimethylsilyl)ethyl (3,5-dideoxy-5-glycolylamino-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→6)-(β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (31). To a solution of **30** (35 mg, 18 μmol) in MeOH (2 mL) was added a catalytic amount of 28% sodium methoxide in MeOH, the reaction mixture was stirred for 24 h at room temperature, and then water (0.1 mL) was added. Work-up as described for **5** gave **31** (20 mg, 98%) as an amorphous mass; $[\alpha]_D$ − 12.8 (*c* 0.4, MeOH); IR (KBr) 3400, 2950, 1660, 1550, 860, 840cm^{-1}; ^{1}H NMR (D_2O) : δ 1.00 (m, 2H, $Me_3SiCH_2CH_2$), 1.71 (t, 1H, J = 12.4 Hz, H-3e(ax)), 2.03 (s, 3H, AcN), 2.66 (dd, 1H, J = 12.4, 4.6 Hz, H-3e(eq)), 4.41 (J = 8.2 Hz), 4.43 (J = 8.0 Hz), 4.47 (J = 8.0 Hz), 4.70 (J = 8.0 Hz) (4d, 4H, four anomeric protons).

Anal. Calcd for $C_{42}H_{74}N_2O_{30}Si$: C, 45.24; H, 6.69; N, 2.51. Found: C, 45.04; H, 6.67; N, 2.34.

(Methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-galacto-mixture was stirred for 3 h at room temperature and then cooled to 0°C. To the

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pyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-α-D-glucopyranosyl trichloroacetimidate (33). A solution of **30** (80 mg, 40 μmol) in CH_2Cl_2 (1 mL) was cooled to 0°C. TFA (1 mL) was added to the solution, and the reaction mixture was stirred at room temperature. After 1 h, the mixture was concentrated at 35°C. Column chromatography ($CHCl_3$:MeOH = 35:1) of the residue on silica gel gave **32** (73 mg, 96%) as an amorphous mass; IR (film) 3400, 2950, 1750, 1660, 1550, 700cm^{-1}. To a solution of **32** (73 mg, 38 μmol) in CH_2Cl_2 (0.7 mL) were added trichloroacetonitrile (115 μL, 1.1mmol) and DBU (6.3 μL, 42 μmol) at 0°C. The reaction mixture was stirred at 0°C for 1 h. Work-up as described for **7** gave **33** (69 mg, 88%) as an amorphous mass; $[\alpha]_D$ + 25.5 (*c* 1.2, $CHCl_3$); IR (film) 3400, 2950, 1750, 1680, 1550, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.84 (s, 3H, AcN), 1.91–2.18 (14s, 42H, 14AcO), 2.52 (dd, 1H, J = 12.8, 4.6 Hz, H-3e(eq)), 3.43 (s, 3H, MeO), 4.29, 4.60 (2d, 2H, J = 15.3 Hz, NHC(O)CH_2OAc), 4.82 (d, 1H, J = 7.8 Hz, H-1d), 4.89 (m, 1H, H-4e), 5.33 (dd, 1H, J = 3.2, 10.5 Hz, H-3d), 5.37 (m, 1H, H-8e), 5.45 (dd, 1H, J = 7.8, 10.5 Hz, H-2d), 5.78 (d, 1H, J = 3.2 Hz, H-4d), 5.86 (d, 1H, NH), 6.46 (d, 1H, J = 3.7 Hz, H-1a), 7.43–8.11 (m, 10H, 2Ph), 8.66 (s, 1H, C═NH).

Anal. Calcd for $C_{82}H_{100}Cl_3N_3O_{46}$: C, 49.99; H, 5.12; N, 2.13. Found: C, 49.76; H, 4.88; N, 2.06.

2-(Tetradecyl)hexadecyl (methyl 5-acetoxyacetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→6)-(3-*O*-acetyl-2,4-di-*O*-benzoyl-β-D-galactopyranosyl)-(1→4)-(2-acetamido-3,6-di-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-(1→3)-(2,4,6-tri-*O*-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-*O*-acetyl-β-D-glucopyranoside (34). To a solution of **33** (61 mg, 30 μmol) and 2-(tetradecyl)hexadecanol **8** (30 mg, 68 μmol) in CH_2Cl_2 (0.3 mL) was added MS4Å (100 mg), the reaction mixture was stirred for 3 h at room temperature and then cooled to 0°C. To the mixture was added TMSOTf (0.29 μL, 1.5 μmol), and the reaction mixture was stirred for 12 h at 0°C, being monitored by TLC. Work-up as described for **3** gave **34** (36 mg, 51%) as an amorphous mass; $[\alpha]_D$ + 16.4 (*c* 0.71, $CHCl_3$); IR (film) 3400, 2950, 1750, 1660, 1540, 700cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.89 (t, 6H, 2*Me*CH_2), 1.25 (s, 53H, 26CH_2, C*H*), 1.84 (s, 3H, AcN), 1.91–2.18 (14s, 42H, 14AcO), 2.52 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)), 3.43 (s, 3H, MeO), 4.30, 4.6 (2d, 2H, J = 15.4 Hz, NHC(O)CH_2OAc), 4.82 (d, 1H, J = 7.7 Hz, H-1d), 4.94 (m, 1H, H-4e), 5.32 (dd, 1H, J = 3.3, 10.3 Hz, H-3d), 5.37 (m, 1H, H-8e), 5.46 (dd, 1H, J = 7.7, 10.3 Hz, H-2d), 5.77 (d, 1H, J = 3.3 Hz, H-4d), 5.83 (d, 1H, NH), 7.43–8.11 (m, 10H, 2Ph).

Anal. Calcd for $C_{110}H_{160}N_2O_{46}$: C, 58.81; H, 7.18; N, 1.25. Found: C, 58.67; H, 6.97; N, 1.16.

2-(Tetradecyl)hexadecyl (3,5-dideoxy-5-glycolylamino-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→6)-(β-D-galactopyranosyl)-(1→4)-(2-acetamido-2-deoxy-β-D-glucopyranosyl)-(1→3)-(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranoside (35). To a solution of **34** (36 mg, 15 μmol) in MeOH (2 mL) and THF (3 mL) was added a catalytic amount of 28% sodium methoxide in MeOH, the reaction mixture was stirred for 24 h at room temperature, and then water (0.1 mL) was added. Work-up as

described for **5** gave **36** (20 mg, 97%); $[\alpha]_D$ + 8.1 (*c* 0.57, $CHCl_3$:MeOH:H_2O = 4:1:0.1); IR (KBr) 3400, 2950, 1660, 1550cm^{-1}; ^1H NMR (DMSO–d_6): δ 0.82 (t, 6H, 2*Me*CH_2), 1.21 (s, 53H, 26C*H*$_2$, C*H*), 1.81 (s, 3H, AcN), 2.62 (dd, 1H, J = 12.8, 4.4 Hz, H-3e(eq)).

Anal. Calcd for $C_{67}H_{122}N_2O_{30}$: C, 56.05; H, 8.57; N, 1.95. Found: C, 56.02; H, 8.38; N, 1.94.

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