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The First Total Synthesis of Ganglioside GalNAc-GD1a, a Target Molecule for Autoantibodies in Guillain–Barré Syndrome**

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Abstract: The first synthesis of ganglioside GalNAc-GD1a, featuring efficient glycan assembly and a cyclic glucosyl ceramide as a versatile unit for ganglioside synthesis is described. Although ganglioside GalNAc-GD1a was first found as a brain ganglioside, IgG autoantibodies to GalNAc-GD1a were subsequently found to be closely related to a human peripheral-nerve disorder, Guillain–Barré syndrome, which is the commonest cause of acute flaccid paralysis worldwide. In this study, the characteristic hexasaccharide part carrying two sialic acid residues was synthesized efficiently by use of a readily accessible GM2-core unit as a common unit. The potentially difficult coupling of the oligosaccharide and ceramide moieties was carried out by using a cyclic glucosyl ceramide as a coupling partner for the hexasaccharide part, thereby successfully providing the framework of the target compound. Global deprotection delivered the homogenous ganglioside GalNAc-GD1a. An enzyme-linked immunosorbent assay showed that sera from patients with Guillain–Barré syndrome reacted both with natural and with synthetic GalNAc-GD1a.

Keywords: gangliosides · Guillain–Barré syndrome · natural products · sialic acids · total synthesis

Introduction

Gangliosides are a family of sialic acid containing glycosphingolipids that are highly concentrated in nervous tissues. Autoantibodies to gangliosides are useful diagnostic markers in autoimmune neuropathies, at least some of which are involved in pathogenesis.[1] The ceramide portion of the ganglioside is anchored in the lipid bilayer membrane with the carbohydrate structure exposed outside the cell, where it acts as an autoantibody target. Guillain–Barré syndrome (GBS) is now the most frequent cause of acute flaccid paralysis worldwide because the incidence of poliomyelitis has been much reduced by immunization. GBS is mainly divided into two subtypes: acute inflammatory demyelinating polyneuropathy and acute motor axonal neuropathy.[2] IgG autoantibodies against gangliosides GM1, GM1b, GD1a, and GalNAc-GD1a are strongly associated with the latter subtype. In other words, IgG anti-GM1, -GM1b, -GD1a, and -GalNAc-GD1a antibodies are diagnostic markers of GBS. Currently, anti-GM1 and -GD1a antibodies are measured at some commercial laboratories, and the measurement kits are also available for investigators. The antigens GM1 and GD1a are abundant and are easily purified from bovine brain gangliosides. GM1b and GalNAc-GD1a are not as readily available, being difficult to isolate from mixtures of bovine brain gangliosides. Few researchers are able to test the autoantibodies against GM1b or GalNAc-GD1a antigens. However, there are some GBS patients who have only anti-GM1b and -GalNAc-GD1a antibodies, and not anti-GM1 or -GD1a antibodies.[3] The aim of this study was to provide a method of synthesizing large quantities of GalNAc-GD1a.[4] Very recently, we briefly reported the assembly of GalNAc-GD1a as an example of the application of a new synthetic method for the synthesis of gangliosides.[5] Here we present a detailed report of the first total synthesis of GalNAc-GD1a.

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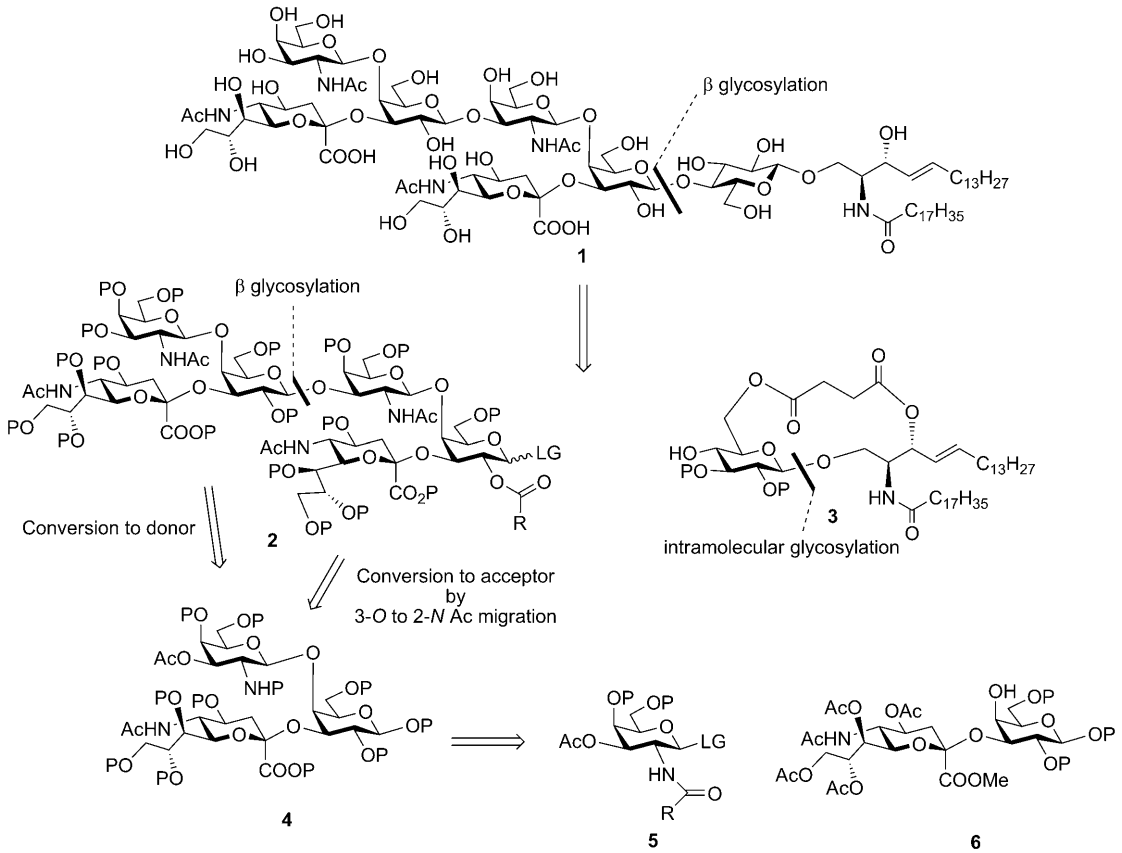
Results and Discussion

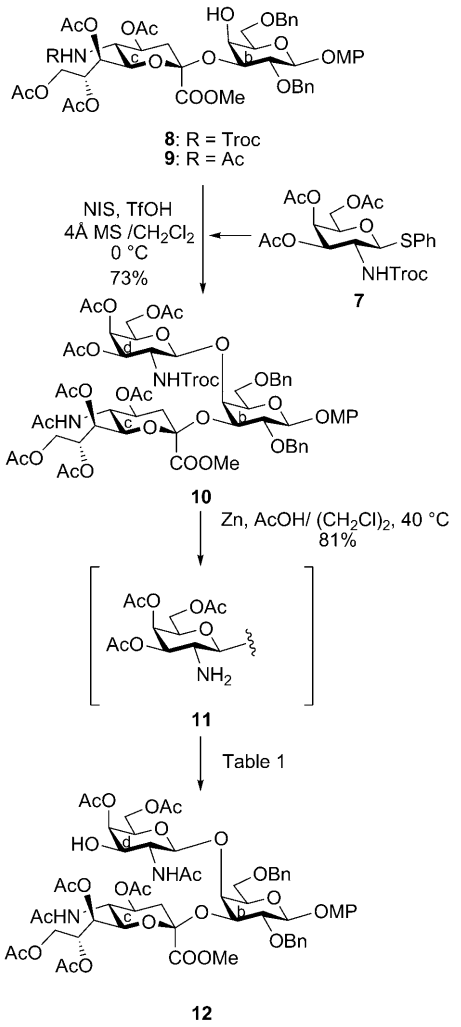
The structure and retrosynthetic analysis of the target compound **1** is illustrated in Scheme 1. The target molecule was disassembled at the β(1,4)-linkage between galactose (Gal) and glucose (Glc) by an approach based on the use of the glucosyl–ceramide (Glc–Cer) cassette **3**, which was developed by our research group,[5,6] thus providing **3** and the hexasaccharide fragment **2**. The approach based on use of the Glc–Cer cassette is useful in that it avoids loss of the valuable oligosaccharide unit in a coupling reaction with the lipophilic, self-aggregating, bulky, and unreactive ceramide moiety. The physical properties of Cer were much improved by combining Glc with Cer. It was also demonstrated that the steric bulk of the Cer moiety did not reduce the reactivity of the C4 hydroxy group in glycosylation with the oligosaccharyl donor. However, in view of the overall efficiency of the chemical synthesis, the low yield of the coupling between Glc and Cer needed to be improved. This issue was very recently overcome by the development of an intramolecular glycosylation system, and the resulting cyclic Glc–Cer acceptor was shown to be capable of accepting a variety of oligosaccharide donors.[5] In this study, we attempted to elaborate the design and synthetic process of the cyclic Glc–Cer acceptor **3** further from the perspective of overall efficiency.

To access the hexasaccharide moiety **2**, that is, the tandem sequence of the GM2-core trisaccharide, we designed a convergent approach in which the GM2-core trisaccharide **4** could serve as a pivotal common unit. We envisaged a one-step conversion of **4** into the corresponding glycosyl acceptor through the 3-*O* to 2-*N* migration of the acetyl group upon deprotection of the C2 amine group. The unit **4** was further disconnected into the 3-*O*-acetyl galactosaminyl donor **5** and the sialyl galactose unit **6**.

To achieve migration of the acetyl group from O to N, we chose a selectively removable 2,2,2-trichloroethoxycarbonyl (Troc) group for the protection of the C2 amine group and as a stereodirecting element during the glycosylation reaction. The C4 and C6 hydroxy groups would be protected by acetate, leading to the triacetate galactosamine (GalN) derivative **7**, which could easily be produced from galactosamine (Scheme 2).[7] The structure of the coupling partner for the GalN donor **7** was designed according to a previously reported GM2-core trisaccharide synthesis.[7a] The *N*-Troc sialyl galactoside **8**,[8] which can be produced on a large scale because it can be purified by crystallization, was converted in high yield into the corresponding *N*-acetyl compound **9** by treatment with zinc in acetic anhydride.[9] The C4 free hydroxy group of **9** was then glycosylated with the GalN donor **7**, by use of *N*-iodosuccinimide (NIS)/trifluoromethanesulfonic acid (TfOH)[10] in CH_2Cl_2 at 0 °C, to pro-



Scheme 1. Retrosynthetic analysis of the target compound **1**. P = protecting group, LG = leaving group.



Scheme 2. Synthesis of the GM2-core acceptor **12**. Bn = benzyl, Troc = 2,2,2-trichloroethoxycarbonyl, MP = *p*-methoxyphenyl, NIS = *N*-iodosuccinimide, TfOH = trifluoromethanesulfonic acid, MS = molecular sieves.

duce the GM2-core structure **10**. The core structure was divided into separate portions, which were then converted into the corresponding glycosyl donor and acceptor.

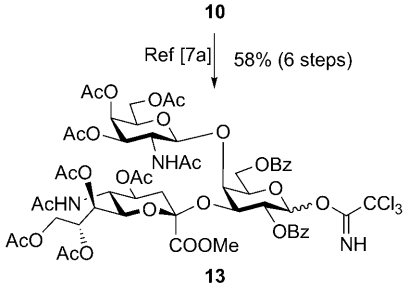
To achieve rapid liberation of the GalN C3 hydroxy group by migration of the acetyl group from O to N, we first removed the Troc protection with zinc in acetic acid to obtain the amino GM2-core unit **11** in 81% yield. The acetyl migration was next investigated and the results are summarized in Table 1. Under basic conditions, the migration of the acetyl group at the C3 position was very sluggish, providing poor to marginal yields (Table 1, entries 1 and 2). In addition, the methyl ester moiety of the sialic acid was hydrolyzed to afford a carboxylic acid derivative (Table 1, entry 1). In contrast, acidic conditions provided a much better yield (74%), which demonstrated the validity of our strategy. In the next step, we attempted a conversion of **10** into **12** in a one-pot reaction. As a result, the *N*-Troc-protected compound **10** could be converted into **12** in 70% yield by treatment with zinc in AcOH/DMF (1:9) at 60°C (Table 1, entry 4).

Table 1. Examination of 3-*O* to 2-*N* acetyl migration to produce the GM2-core acceptor **12**.

Entry	Reagent/solvent	*T* [°C]	*t* [h]	Yield [%]
1	TEA/DMF 1:1	60	48	trace
2	Pyr/DCE 1:1	60	24	58
3	AcOH/1,4-dioxane 1:4	60	48	74
4[a]	Zn, AcOH/DMF (1:9)	60	15	70

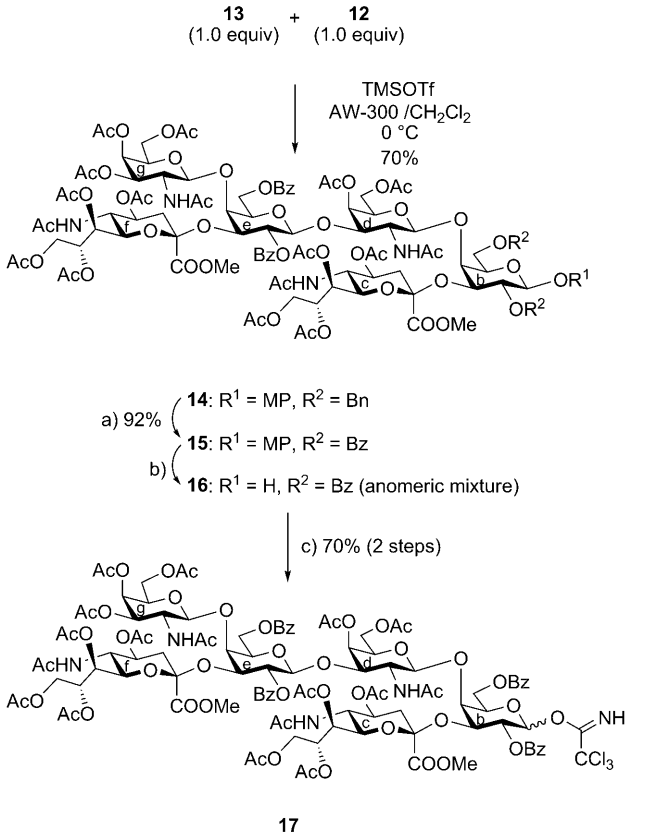
[a] One-pot reaction from compound **10**. TEA = triethylamine, Pyr = pyridine, DCE = 1,2-dichloroethane.

On the other hand, the trisaccharide **10** was also transformed into the corresponding trichloroacetimidate donor **13** through a six-step reaction sequence by a previously reported procedure[7a] (58% overall yield) as shown in Scheme 3.



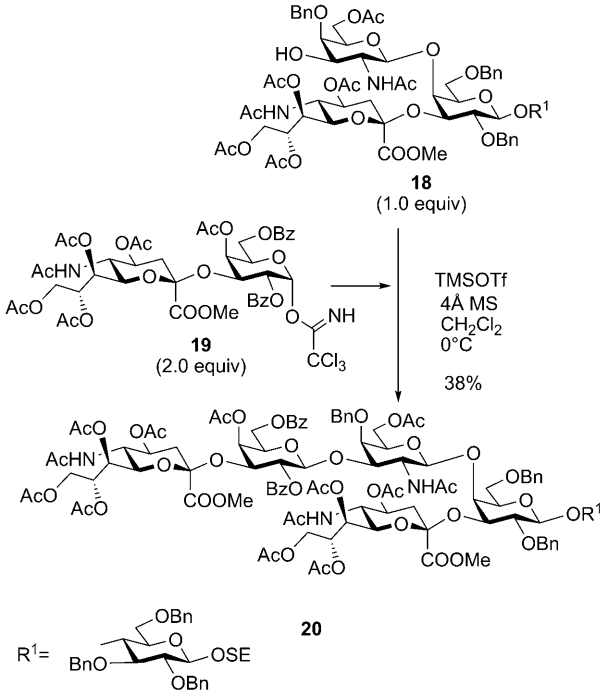
Scheme 3. Synthesis of the GM2-core donor **13**. a) i) Zn, AcOH/MeOH (1:1), RT; ii) Ac_2O/Pyr, RT, 81%; b) i) H_2, $Pd(OH)_2$-C/1,4-dioxane, RT; ii) Bz_2O, DMAP/Pyr, RT, 95%; c) i) CAN, MeCN/PhMe/H_2O (6:5:3), RT; ii) CCl_3CN, DBU/CH_2Cl_2, RT, 75%. Bz = benzoyl, CAN = ceriu-m(IV) ammonium nitrate.

To assemble the tandem sequence of the GM2-core trisaccharides, the trisaccharyl donor **13** (1.0 equiv) and the acceptor **12** (1.0 equiv) were coupled in CH_2Cl_2 at 0°C in the presence of a catalytic amount of TMSOTf (0.16 equiv), yielding the highly branched disialoside **14** as a single β-isomer in 70% yield (Scheme 4). This encouraging result suggests that compound **12** could be usable as a common acceptor for the construction of other core sequences of a series of gangliosides such as GM1, GD1a, and GT1a. For comparison, the coupling yield of **12** and **13** is much higher than those of similar glycosylations performed in our research group: the coupling of the 6-*O*-acetyl-4-*O*-benzyl GM2 acceptor **18** with the small sialyl galactosyl imidate donor **19**, for example, afforded a lower yield (38%) of **20**, even when two equivalents of the donor were used (Scheme 5).[11] This suggests that coupling through the C3 hydroxy group is disfavored by the presence of a bulky substituent, rather than an electron-withdrawing one, at the C4 position. The hexasaccharide **14** (Scheme 4) was then converted into the imidate donor **17** in three steps: replacement of the benzyl groups with benzoyl groups (i) H_2, $Pd(OH)_2$-C; ii) Bz_2O, DMAP, Pyr, 92%), removal of the *p*-methoxyphenyl group (CAN, H_2O, 70%), and conversion of the resulting



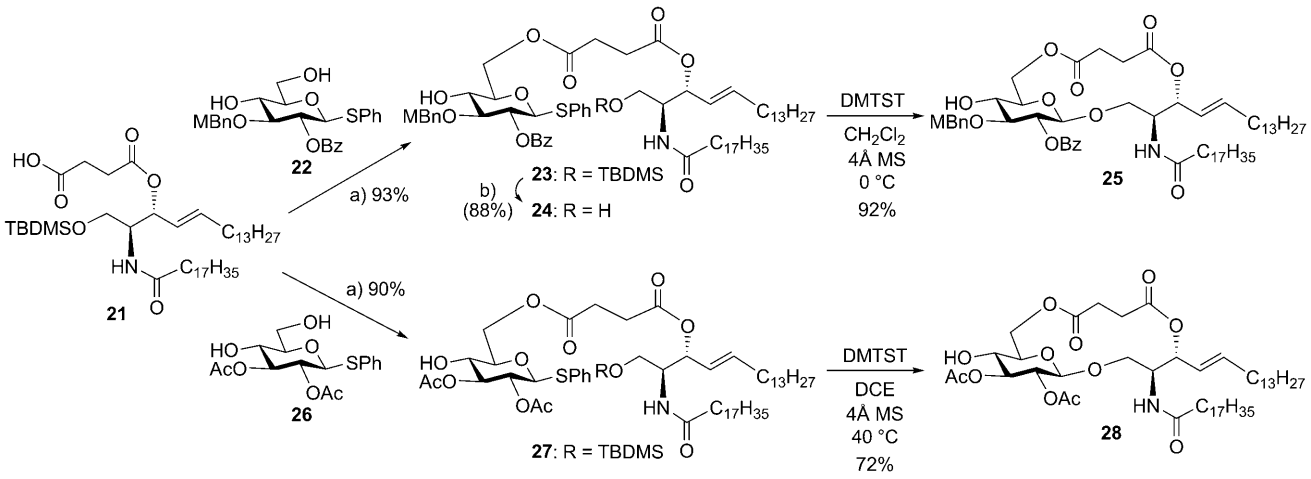
Scheme 4. Assembly of the GM2-core tandem sequence and conversion into the corresponding glycosyl donor **17**. a) i) H_2, $Pd(OH)_2$-C/1,4-dioxane, RT; ii) Bz_2O, DMAP/Pyr, RT, 92%; b) CAN, MeCN/PhMe/H_2O (6:5:3), RT, 70%; c) CCl_3CN, DBU/CH_2Cl_2, RT, 70% (2 steps). TMSOTf = trimethylsilyl trifluoromethanesulfonate, DMAP = 4-dimethylaminopyridine, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene.

hydroxy group into a trichloroacetimidate group (quantitative),[12] to give the hexasaccharyl donor **17** in high yields.



Scheme 5. Previously obtained result for the glycosylation of the GM2 tetrasaccharide acceptor **18** with the sialyl galactosyl donor **19**. SE = 2-(trimethylsilyl)ethyl.

The cyclic Glc–Cer acceptor **25** was synthesized as the first coupling partner for the hexasaccharide **17** (Scheme 6). This synthesis began with tethering of the Glc donor and Cer through a succinoyl bridge.[13] The succinoylated Cer derivative **21**[14] and the 4,6-diol thioglucoside **22**[15] could thus be condensed with the aid of a carbodiimide coupling reagent (EDC·HCl) and a catalytic amount of DMAP to give the tethered compound **23**. The free hydroxy group at the C1 position of the Cer moiety was retrieved by exposure to TBAF. Then, intramolecular coupling within **24**, promoted

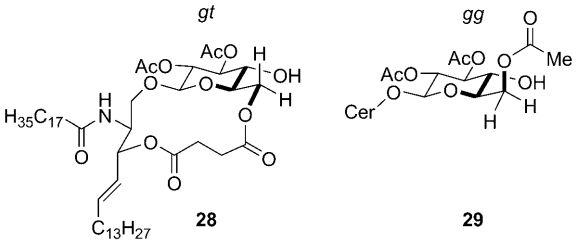


Scheme 6. Synthesis of the cyclic Glc–Cer acceptors **25** and **28** through intramolecular glycosylation. a) EDC·HCl, DMAP/CH_2Cl_2, RT, 93%; b) TBAF, AcOH/THF, 0°C to RT, 88%. TBDMS = *tert*-butyldimethylsilyl, MBn = *p*-methoxybenzyl, EDC = 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide, TBAF = *n*-tetrabutylammonium fluoride, DMTST = dimethyl(methylthio)sulfonium trifluoromethanesulfonate, DCE = 1,2-dichloroethane.

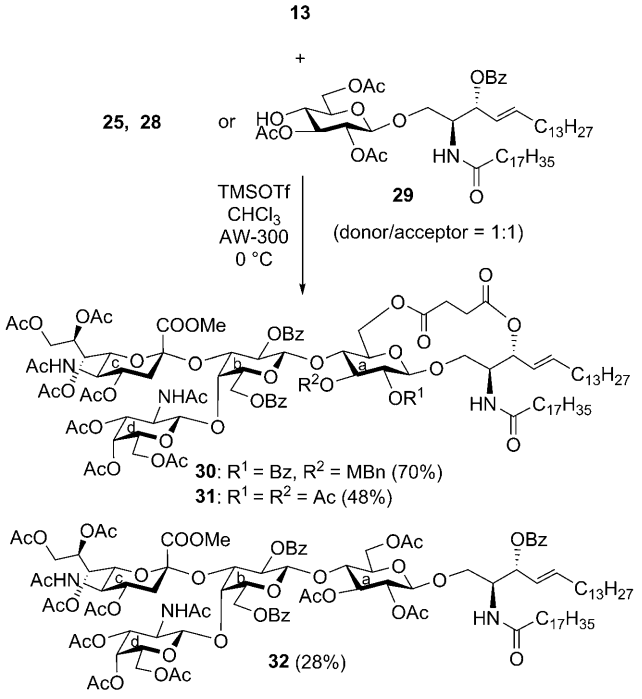
by DMTST,[16] successfully produced the cyclic Glc–Cer acceptor **25** in very high yield without affecting the C4–C5 olefin moiety (use of NIS/TfOH as the promoter did not leave the olefin intact).

In the next step, the 2,3-diacetyl Glc–Cer **28** was designed as a more easily accessible version of the cyclic Glc–Cer **25**. The 2,3-diacetyl thioglucoside **26**[17] was tethered to the Cer unit **21** in a similar way to compound **23**, producing **27** in high yield. To reduce the number of reaction steps, compound **27**, with the TBDMS-protected C1 hydroxy group, was subjected to direct DMTST-promoted intramolecular glycosylation. At room temperature, this reaction was complete after 3 h and gave the cyclic Glc–Cer **28** in 36% yield. In contrast, at 40°C the reaction gave a yield of 72%. During this reaction, the acetyl group at C3 did not migrate to the adjacent C4 hydroxy group; to the best of our knowledge this is the first example of intramolecular glycosylation of a TBDMS-protected hydroxy group.[18] It is unlikely that compound **23**, with an acid-labile MBn group, would undergo such a direct glycosylation. The cyclic Glc–Cer **28** was synthesized more efficiently than **25** with respect to the overall yields based on glucose pentaacetate: the overall yield for **28** was 43% (seven steps), whereas that of **25** was 27% (nine steps).

The above cyclic Glc–Cer acceptors were next subjected to model glycosylation reactions with the GM2-core donor **13** to evaluate their potentials as glycosyl acceptors (Scheme 7). Equimolar amounts of the glycosyl donor **13** and the Glc–Cer acceptor (**25** or **28**) were allowed to react in the presence of a TMSOTf catalyst in $CHCl_3$ at 0°C. This model experiment revealed distinct differences in reactivity between the two cyclic Glc–Cer acceptors. Compound **25** gave the glycosidated product in 70% yield, almost 1.5 times that achieved with **28** (48%). Furthermore, use of a linear analogue (**29**) of compound **28** reduced the coupling yield to 28%. It was observed that the presence of an electron-donating group was more suitable for protection of the C3 hydroxy group even if it was bulky. In addition, the results for cyclic versus linear acceptors indicated that the C4 hydroxy group in the cyclic structure was more reactive than that in the linear analogue. In the ^{1}H NMR spectrum for compound **28**, the coupling constants between H5 and H6 or H6′ were 9.7 and 2.3 Hz, respectively. These coupling constants were used to estimate the population of rotamers about the C5−C6 bond by a previously reported method based on Karplus relationships.[19] The estimation showed that the *gauche*/*trans* (*gt*) rotamer was predominant (83%) over the *gauche*/*gauche* (*gg*) (19%) and *trans*/*gauche* (*tg*) rotamers (−2%). The *gt* rotamer of **28** is illustrated in Scheme 8. In contrast, the *gg* rotamer was favored (71%) over the *gt* (26%) and *tg* (3%) rotamers about the C5−C6 bond in **29** ($J(5,6)=4.1$ Hz and $J(5,6')=2.0$ Hz), due to the *gauche* effect[20] between σ_{C5-H5} and σ^*_{C6-O6}. These results are consistent with those reported for the conformational analysis of the 6-*O*-acetyl glucose derivative.[19b] This comparison of conformations about the C5−C6 bonds of **28** and **29** suggests that the acetyl group at the C6 position reduced the reactivity of the C4 hydroxy group through steric hindrance rather than through its electron-withdrawing effect.

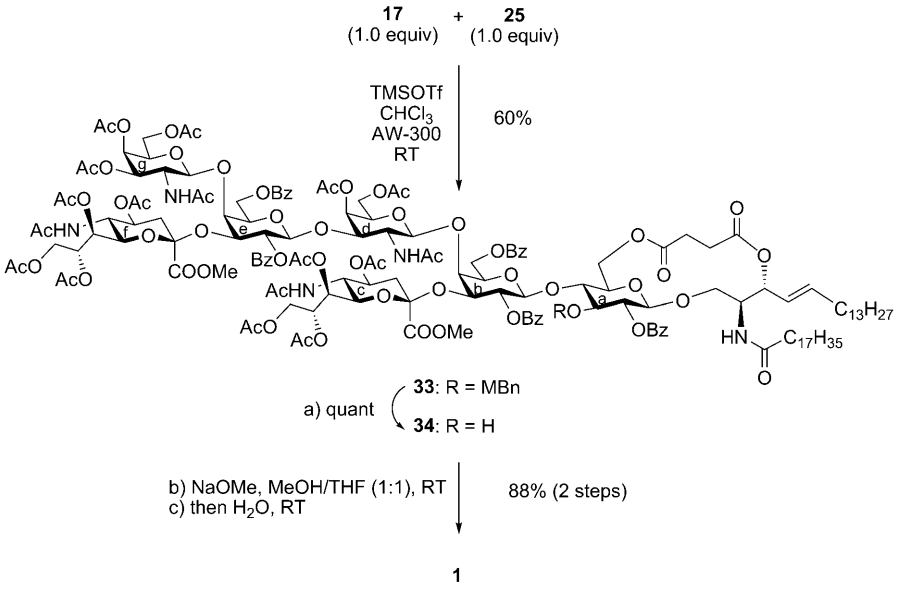


Scheme 8. Structures of predominant rotamers about C5−C6 bonds within compounds **28** and **29** based on estimation with the aid of Karplus relationships.



Scheme 7. Examination of the glycosylation of the Glc–Cer acceptors **25**, **28**, and **29**.

Although we could have used the easily accessible Glc–Cer acceptor **28**, as mentioned above, the Glc–Cer acceptor **25** was chosen as the coupling partner for the hexasaccharyl donor **17**, to take advantage of the high coupling yield. To our delight, the most challenging coupling reaction in this study, between **17** (1.0 equiv) and **25** (1.0 equiv) in the presence of catalytic TMSOTf in $CHCl_3$ at room temperature, successfully delivered the glycolipid framework **33** in 60% yield, as shown in Scheme 9. Next, compound **33** was converted into compound **34** (TFA, 0°C). Compound **34** was then deacylated by the Zemplén method, and saponification of the methyl ester group gave the target compound **1**. The first attempt at this synthetic route produced 20 mg of ho-



Scheme 9. Final approach to target compound **1**. a) TFA/CH_2Cl_2, 0 °C, quant. TFA = trifluoroacetic acid.

mogenous ganglioside GalNAc-GD1a **1**, which was then subjected to reaction with serum IgG antibodies from patients with GBS.

Natural GalNAc-GD1a was isolated from bovine brain gangliosides as previously reported.[3c] Sera were selected from 24 patients with GBS: twelve had high titers of IgG antibodies against the natural GalNAc-GD1a, whereas the remaining 12, who did not, acted as negative controls. IgG antibodies against the natural and synthetic GalNAc-GD1a (5 pmol per well) were measured in sera (1:500 dilution) from the patients by means of an enzyme-linked immunosorbent assay, as described previously.[3d] Figure 1 shows that the 12 sera with positive IgG antibodies against the natural GalNAc-GD1a bound to the synthetic GalNAc-GD1a, whereas none of the controls did. These results suggest that synthetic GalNAc-GD1a could be useful in autoantibody testing.

Conclusion

We have achieved the first total synthesis of ganglioside GalNAc-GD1a in sufficient quantities for biological study. The highly branched glycan structure comprising the tandem sequence of GM2-core trisaccharides was successfully constructed by an efficient route that used the highly accessible GM2-core unit **10** as a pivotal intermediate. The successful coupling of the huge hexasaccharyl donor **17** and the cyclic Glc–Cer **25** consequently led to delivery of the refined target molecule in sufficient quantities for biological study. With this total synthesis of the intricate ganglioside, the efficacy of the glucosyl ceramide cassette approach with the cyclic Glc–Cer was confirmed. Furthermore, the reactivity of the synthetic GalNAc-GD1a towards serum IgG from GBS patients was confirmed to be comparable to that of natural GalNAc-GD1a.

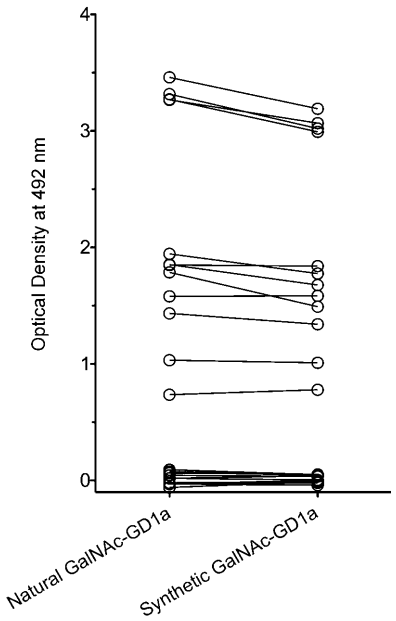


Figure 1. Enzyme-linked immunosorbent assay results in 24 patients with Guillain–Barré syndrome. Sera from 12 patients who had IgG antibodies to natural GalNAc-GD1a reacted with synthetic GalNAc-GD1a, whereas sera from 12 patients who had no IgG antibodies to the natural GalNAc-GD1a did not react with the synthetic GalNAc-GD1a.

Experimental Section

General procedures: ^1H and ^{13}C NMR spectra were recorded with JEOL JNM-ECA400, JNM-ECA500, and JNM-ECA600 spectrometers. ^1H NMR chemical shifts are expressed in ppm (δ) relative to the signal of Me_4Si as an internal standard. ^{13}C NMR chemical shifts are expressed in ppm (δ) relative to the signal of the solvent as a standard. High-resolution mass spectrometry (HRMS) was performed with a Bruker Daltonics micrOTOF (ESI-TOF) mass spectrometer. Specific rotations were measured with a Horiba SEPA-300 high-sensitivity polarimeter. Molecular sieves were purchased from Wako Chemicals and dried at 300 °C for 2 h in a muffle furnace prior to use. Reactions were carried out under argon unless otherwise specified. Solvents as reaction media were dried over molecular sieves and used without further purification. TLC analysis was performed with Merck TLC plates (silica gel $60F_{254}$ on glass). Compounds were visualized by exposure to UV light (254 nm) or by spraying either with H_2SO_4 solution in EtOH (10%) or with ninhydrin reagent, followed by heating. Flash column chromatography on silica gel (Fuji Silysia, 80 mesh and 300 mesh) was performed

with the solvent systems (v/v) specified. Evaporation and concentration were conducted in vacuo.

Compound 9: Zinc powder (1.0 g) was added at RT to a solution of **8** (1.00 g, 932 μmol) in a mixture of AcOH (10.0 mL), THF (10.0 mL), and Ac_2O (10.0 mL). The mixture was stirred for 3 h at RT (completion of the reaction was confirmed by TLC, $CHCl_3$/MeOH 18:1). The reaction mixture was filtered through Celite and the removed zinc powder was washed with EtOAc. The combined filtrate and washings were concentrated by co-evaporation with toluene. The residue was extracted with EtOAc and the organic layer was washed with saturated aqueous Na_2CO_3 and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane 5:2→3:1) to give **9** (786 mg, 90%). $[\alpha]_D=-14.9°$ ($c=0.9$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.42$–6.78 (m, 14H; 3×Ph), 5.42 (m, 1H; H-8c), 5.31 (dd, $J_{6,7}=2.1$ Hz, $J_{7,8}=8.3$ Hz, 1H; H-7c), 5.11 (d, $J_{5,NH}=9.6$ Hz, 1H; NH), 4.94 (d, $J_{1,2}=8.2$ Hz, 1H; H-1b), 4.92 (d, $J_{gem}=12.4$ Hz, 1H; PhCH_2), 4.87 (m, 1H; H-4c), 4.82 (d, 1H; PhCH_2), 4.60–4.55 (m, 2H; PhCH_2), 4.32 (dd, $J_{8,9}=2.4$ Hz, $J_{gem}=12.4$ Hz, 1H; H-9c), 4.26 (dd, $J_{2,3}=9.6$ Hz, $J_{3,4}=3.4$ Hz, 1H; H-3b), 4.09 (q, $J_{4,5}=J_{5,6}=9.6$ Hz, 1H; H-5c), 4.04 (dd, 1H; H-6c), 3.96 (dd, $J_{8,9'}=6.2$ Hz, 1H; H-9′c), 3.86–3.76 (m, 11H; H-2b, H-4b, H-5b, H-6b, H-6′b, OMe, COOMe), 2.77 (s, 1H; OH), 2.58 (dd, $J_{3eq,4}=4.2$ Hz, $J_{gem}=13.1$ Hz, 1H; H-3c$_{eq}$), 2.10–1.86 ppm (m, 16H; H-3c$_{ax}$, 5×Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=170.8$, 170.5, 170.2, 170.1, 169.9, 168.5, 155.1, 151.6, 138.8, 138.1, 128.3, 128.1, 127.8, 127.6, 127.5, 127.4, 118.4, 114.4, 102.7, 97.9, 75.6, 74.9, 73.5, 73.0, 72.7, 69.3, 69.0, 68.8, 68.1, 67.3, 62.3, 55.6, 53.0, 49.1, 36.9, 23.1, 21.1, 20.7, 20.7, 20.6 ppm; HRMS: m/z: calcd for $C_{47}H_{57}NO_{19}Na^+$: 962.3417 $[M+Na]^+$; found: 962.3417.

Compound 10: Molecular sieves (4 Å, 10 g) were added to a solution of **7** (2.2 g, 3.94 mmol) and **9** (3.7 g, 3.94 mmol) in CH_2Cl_2 (80.0 mL). The suspension was stirred for 1 h at RT, after which NIS (2.3 g, 10.2 mmol) and TfOH (90 μL, 1.02 mmol) were added at 0°C. Stirring was continued for 1 h at 0°C (completion of the reaction was confirmed by TLC, EtOAc/hexane 3:1). The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$, saturated aqueous $Na_2S_2O_3$, and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane 2:1) to give **10** (4.0 g, 73%). $[\alpha]_D=-16.0°$ ($c=1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.28$ (m, 10H; 2×Ph), 7.07–6.81 (2×d, 4H; MeO*Ar*), 6.20 (d, $J_{NH,2}=8.3$ Hz, 1H; NHd), 5.36 (m, 1H; H-4d), 5.23 (m, 4H; H-8c, H-7c, NHc, H-3d), 5.13 (m, 2H; H-4c, CH_2), 4.99 (d, $J_{1,2}=8.9$ Hz, 1H; H-1d), 4.95 (d, 1H; CH_2), 4.89 (d, $J_{1,2}=8.2$ Hz, 1H; H-1b), 4.57 (m, 3H; 2×CH_2), 4.33 (m, 2H; H-6d, CH_2), 4.21 (near t, $J_{6,6'}=11.0$ Hz, $J_{5,6'}=8.3$ Hz, 1H; H-6′d), 4.16 (m, 1H; H-2d), 4.09–3.97 (m, 6H; H-5d, H-4b, H-3b, H-9c, H-9′c, H-5c), 3.94 (s, 3H; OMe), 3.90 (dd, $J_{6,6'}=10.3$ Hz, $J_{6,5}=5.5$ Hz, 1H; H-6b), 3.78 (m, 6H; H-6c, H-6′b, H-2b, OMe), 3.67 (m, 1H; H-5b), 3.24 (m, 1H; H-3c$_{eq}$), 2.18–1.88 ppm (m, 25H; 8×Ac, H-3c$_{ax}$); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=170.6$, 170.4, 170.3, 170.3, 170.2, 169.6, 169.5, 168.5, 155.3, 154.5, 151.3, 138.2, 138.0, 128.3, 128.2, 127.8, 127.7, 127.6, 118.7, 118.5, 114.5, 102.9, 101.8, 99.2, 96.0, 78.6, 77.7, 75.6, 74.2, 73.6, 72.2, 71.9, 70.0, 69.4, 69.0, 67.5, 67.1, 66.6, 62.1, 61.2, 55.6, 53.5, 52.9, 49.0, 35.2, 23.1, 21.0, 20.7, 20.6, 20.5 ppm; HRMS: m/z calcd for $C_{62}H_{75}Cl_3N_2O_{28}Na^+$: 1423.3469 $[M+Na]^+$; found: 1423.3470.

Compound 12: Zinc powder (1.0 g) was added at RT to a solution of **10** (100 mg, 71 μmol) in a mixture of DMF (6.4 mL) and AcOH (0.7 mL). The mixture was stirred for 15 h at 60°C (completion of the reaction was confirmed by TLC, EtOAc/MeOH 20:1). The reaction mixture was filtered through Celite and the removed zinc powder was washed with EtOAc. The combined filtrate and washings were extracted with EtOAc. The organic layer was washed with H_2O, saturated aqueous Na_2CO_3, and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/MeOH 50:1) to give **12** (62 mg, 70%). $[\alpha]_D=-12.5°$ ($c=0.4$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=7.28$ (m, 10H; 2×Ph), 7.08–6.81 (m, 3H; NHd, MeO*Ar*), 5.33 (d, $J_{3,OH}=3.4$ Hz, 1H; OH), 5.25 (m, 4H; H-8c, H-7c, H-4d, NHc), 5.08 (m, 2H; H-4c, PhCH_2), 4.92 (d, $J_{1,2}=7.6$ Hz, 1H; H-1b), 4.78 (d, $J_{1,2}=8.3$ Hz, 1H; H-1d), 4.56 (m, 3H; PhCH_2, PhCH_2), 4.18 (m, 2H; H-9c, H-3b), 4.11 (m, 2H; H-6d, H-4b), 4.05–3.96 (m, 5H; H-6′d, H-2d, H-3d, H-9′c, H-5c), 3.87 (m, 4H; OMe, H-6b), 3.78 (m, 7H; H-5d, H-6′b, H-2b, H-6c), 3.68 (m, 1H; H-5b), 2.30 (m, 2H; H-3c$_{eq}$, H-3c$_{ax}$), 2.16–1.91 ppm (8 s, 24H; 8×Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=173.4$, 170.6, 170.5, 170.3, 169.6, 169.4, 168.0, 155.4, 151.1, 138.1, 137.7, 128.4, 128.3, 127.9, 127.8, 127.7, 127.6, 118.6, 114.5, 103.0, 101.5, 99.3, 78.5, 77.7, 77.3, 75.7, 75.5, 74.0, 73.8, 73.7, 72.4, 70.4, 69.5, 68.7, 68.6, 67.5, 66.7, 62.0, 61.9, 55.6, 55.3, 53.2, 49.0, 35.5, 29.7, 23.2, 22.6, 21.0, 20.9, 20.7, 20.7, 20.5 ppm; HRMS: m/z calcd for $C_{59}H_{74}N_2O_{26}Na^+$: 1249.4421 $[M+Na]^+$; found: 1249.4428.

Compound 14: Molecular sieves (AW-300, 4 Å, 2.0 g) were added to a solution of **12** (390 mg, 320 μmol) and **13** (424 mg, 320 μmol) in CH_2Cl_2 (10.0 mL). The suspension was stirred for 1 h at RT, after which TMSOTf (7.0 μL, 38 μmol) was added at 0°C. Stirring at 0°C was continued for 2 h (completion of the reaction was confirmed by TLC, EtOAc/MeOH 20:1). The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/MeOH 50:1) to give **14** (534 mg, 70%). $[\alpha]_D=-8.5°$ ($c=1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3CN): $\delta=8.04$–7.23 (m, 20H; 4×Ph), 6.98–6.77 (2×d, 4H; Ar), 6.37 (d, $J_{2,NH}=9.6$ Hz, 1H; NHg), 6.07 (m, 3H; NHc, NHd, NHf), 5.40 (m, 1H; H-4d), 5.26 (m, 1H; H-4g), 5.18 (m, 4H; H-8f, H-7f, H-7c, H-3g), 5.08 (m, 2H; H-8c, H-2e), 5.00 (td, $J_{3eq,4}=4.8$ Hz, $J_{3ax,4}=J_{4,5}=11.0$ Hz, 1H; H-4f), 4.93 (td, $J_{3eq,4}=3.8$ Hz, $J_{3ax,4}=J_{4,5}=8.3$ Hz, 1H; H-4c), 4.86 (m, 3H; H-1g, H-1b, H-1e), 4.74 (d, 1H; PhCH_2), 4.62 (d, $J_{1,2}=8.2$ Hz, 1H; H-1d), 4.52 (m, 3H; H-3e, H-6′e, PhCH_2), 4.44 (q, 2H; PhCH_2), 4.34 (dd, $J_{gem}=11.7$ Hz, $J_{6,5}=6.8$ Hz, 1H; H-6e), 4.24 (m, 2H; H-3b, H-9′f), 4.14 (m, 1H; H-2g), 4.05–3.97 (m, 7H; H-9f, H-9c, H-9′c, H-5f, H-4b, H-3d, H-4e), 3.97–3.70 (m, 18H; 2×OMe, H-5d, H-6d, H-6′d, H-5g, H-6g, H-6g, H-2d, H-5e, H-5c, H-6f, H-6c, H-6b), 3.55 (m, 2H; H-5b, H-6′b), 3.42 (m, 1H; H-2b), 2.37 (dd, $J_{gem}=13.7$ Hz, $J_{3eq,4}=5.5$ Hz, 1H; H-3f$_{eq}$), 2.15–1.74 ppm (m, 54H; 17×Ac, H-3c$_{eq}$, H-3c$_{ax}$, H-3f$_{ax}$); ^{13}C NMR (150 MHz, CD_3CN): $\delta=171.3$, 171.3, 171.2, 171.2, 171.1, 171.0, 171.0, 170.8, 170.7, 170.7, 170.5, 170.4, 170.3, 169.5, 169.2, 166.8, 164.9, 156.2, 152.4, 139.8, 139.7, 134.2, 134.1, 131.1, 130.8, 130.6, 130.2, 129.5, 129.5, 129.2, 129.0, 128.4, 128.3, 119.0, 115.4, 103.2, 103.2, 102.2, 102.8, 100.5, 100.3, 79.4, 79.3, 79.1, 78.8, 75.8, 75.7, 74.2, 73.5, 72.6, 72.6, 72.5, 72.0, 71.8, 71.2, 71.2, 71.0, 70.9, 70.5, 70.4, 69.1, 68.6, 68.0, 67.5, 67.4, 64.8, 64.2, 62.8, 62.4, 62.4, 56.1, 53.9, 53.8, 52.1, 51.0, 49.3, 48.7, 35.8, 35.7, 23.3, 23.0, 23.0, 21.4, 21.3, 21.1, 21.0, 21.0, 20.9, 20.8, 20.7, 20.7 ppm; HRMS: m/z calcd for $C_{113}H_{138}N_4O_{53}Na^+$: 2421.8118 $[M+Na]^+$; found: 2421.8119.

Compound 15: Pd(OH)$_2$/C (20%, 412 mg) was added to a solution of compound **14** (412 mg, 170 μmol) in 1,4-dioxane (8.6 mL) and the suspension was stirred under a hydrogen stream for 16 h at RT (completion of the reaction was confirmed by TLC, EtOAc/MeOH 10:1). The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were concentrated and exposed to high vacuum. The residue was then treated with a solution of Bz_2O (156 mg, 690 μmol) and DMAP (11.0 mg, 86 μmol) in pyridine (6.0 mL) for 12 h at RT (completion of the reaction was confirmed by TLC, EtOAc/MeOH 10:1). The reaction mixture was then co-evaporated with toluene. The residue was extracted with $CHCl_3$ and the solution was washed with aqueous HCl (2M), H_2O, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/MeOH 25:1) to give **15** (384 mg, 92%). $[\alpha]_D=+1.3°$ ($c=1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=8.14$–7.42 (m, 20H; 4×Ph), 6.87–6.60 (2×d, 4H; Ar), 6.41 (d, $J_{NH,5}=6.9$ Hz, 1H; NHf), 5.67 (m, 2H; NHg, NHd), 5.56 (m, 1H; H-8f), 5.43 (m, 3H; H-8c, H-2e, H-4g), 5.34 (m, 1H; H-4d), 5.30 (near t, $J_{1,2}=J_{2,3}=7.6$ Hz, 1H; H-2b), 5.22 (m, 2H; H-3g, NHc), 5.14 (m, 3H; H-7f, H-7c, H-1e), 5.07 (d, $J_{1,2}=9.6$ Hz, 1H; H-1g), 4.97 (td, $J_{3eq,4}=3.4$ Hz, $J_{3ax,4}=J_{4,5}=8.2$ Hz, 1H; H-4f), 4.93 (d, $J_{1,2}=10.3$ Hz, 1H; H-1d), 4.80 (d, 1H; H-1b), 4.76 (td, $J_{3ax,4}=J_{4,5}=8.3$ Hz, $J_{3eq,4}=3.5$ Hz, 1H; H-4c), 4.62 (m, 2H; H-6′e, H-6′b), 4.49 (dd, $J_{3,4}=2.8$ Hz, $J_{2,3}=9.6$ Hz, 1H; H-3e), 4.41 (m, 2H; H-6e, H-6b), 4.32 (dd, $J_{3,4}=2.7$ Hz, $J_{2,3}=9.7$ Hz, 1H; H-3b), 4.16 (m, 2H; H-9′f, H-3d), 4.06 (m, 3H;

H-9′c, H-6d, H-6′d), 3.96–3.87 (m, 7H; H-9f, H-9c, H-5f, H-4b, H-5e, H-6g, H-5d), 3.86–3.75 (m, 10H; 2×OMe, H-5c, H-2d, H-5b, H-6g), 3.75–3.66 (m, 7H; OMe, H-4e, H-5g, H-6f, H-6c), 3.13 (m, 1H; H-2g), 2.82 (dd, J_{gem}=13.0 Hz, $J_{3eq,4}$=4.1 Hz, 1H; H-3f$_{eq}$), 2.42 (dd, J_{gem}=13.7 Hz, $J_{3eq,4}$=4.8 Hz, 1H; H-3c$_{eq}$), 2.16–1.62 ppm (m, 53H; 17×Ac, H-3c$_{ax}$, H-3f$_{ax}$); ^{13}C NMR (150 MHz, $CDCl_3$): δ=172.0, 171.1, 170.5, 170.3, 170.2, 170.1, 170.1, 170.0, 169.8, 169.7, 169.6, 168.1, 168.0, 167.6, 165.7, 165.6, 165.0, 164.3, 155.3, 151.3, 133.3, 133.0, 132.9, 132.2, 130.7, 129.9, 129.9, 129.8, 129.6, 129.4, 129.4, 128.6, 128.4, 128.3, 128.2, 119.2, 118.9, 114.2, 114.1, 100.9, 100.0, 98.2, 98.0, 97.3, 76.8, 76.8, 74.2, 73.2, 72.9, 72.7, 72.4, 71.9, 71.8, 71.7, 71.6, 70.6, 70.5, 70.3, 69.8, 69.7, 69.6, 68.7, 68.0, 67.2, 67.1, 66.9, 66.4, 66.3, 63.5, 63.1, 62.8, 62.2, 62.1, 61.3, 60.2, 55.3, 55.1, 52.8, 52.5, 52.0, 48.9, 38.5, 36.7, 36.2, 30.2, 29.4, 28.7, 23.5, 23.2, 22.9, 22.8, 22.7, 21.1, 20.9, 20.7, 20.5, 20.5, 20.2, 20.2, 19.9, 14.0, 13.9, 13.8, 10.7 ppm; HRMS: *m/z* calcd for $C_{113}H_{134}N_4O_{55}Na^+$: 2449.7710 $[M+Na]^+$; found: 2449.7709.

Compound 16: Diammonium cerium (IV) nitrate (1.1 g, 2.04 mmol) was added at 0°C to a solution of **15** (495 mg, 200 μmol) in a mixture of MeCN (1.7 mL), toluene (1.5 mL), and H_2O (0.9 mL). The mixture was stirred at 0°C for 20 min (completion of the reaction was confirmed by TLC, EtOAc/MeOH 10:1). The reaction mixture was diluted with Et_2O, and the solution was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH 20:1) to give **16** (330 mg, 70%). HRMS: *m/z* calcd for $C_{106}H_{128}N_4O_{54}Na^+$: 2343.7295 $[M+Na]^+$; found: 2343.7291.

Compound 17: Trichloroacetonitrile (60 μL, 600 μmol) and DBU (0.9 μL, 5.9 μmol) were added at 0°C to a solution of **16** (69 mg, 30 μmol) in CH_2Cl_2 (2.0 mL). The mixture was stirred for 10 h at RT (completion of the reaction was confirmed by TLC, $CHCl_3$/MeOH 15:1). The reaction mixture was concentrated and the residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH 20:1) to give **17** (73 mg, quant). HRMS: *m/z* calcd for $C_{108}H_{128}Cl_3N_5O_{54}Na^+$: 2486.6386 $[M+Na]^+$; found: 2486.6387.

Compound 23: Compound **22** (29.0 mg, 58 μmol), DMAP (3.0 mg, 18 μmol), and EDC·HCl (12.0 mg, 64 μmol) were added at 0°C to a solution of **21** (45.5 mg, 58 μmol) in CH_2Cl_2 (1.2 mL). The mixture was stirred for 5 h at RT (completion of the reaction was confirmed by TLC, toluene/EtOAc 2:1). The reaction mixture was diluted with $CHCl_3$, and the solution was washed with H_2O and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (Et_2O/hexane 1:4) to give **23** (68 mg, 93%). $[\alpha]_D$=+4.9° (*c*=1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$): δ=8.00–7.20 (m, 10H; 2×Ph), 7.03–6.60 (2×d, 4H; Ar), 5.70 (m, $J_{NH,2}$=8.2 Hz, 2H; NH, H-5^{Cer}), 5.40 (t, 1H; H-4^{Cer}), 5.33 (m, 1H; H-3^{Cer}), 5.16 (t, $J_{1,2}$=10.1 Hz, $J_{2,3}$=9.2 Hz, 1H; H-2a), 4.73 (d, 1H; H-1a), 4.59 (s, 2H; ArCH_2), 4.39 (m, 2H; H-6a, H-6′a), 4.20 (m, 1H; H-2^{Cer}), 3.97 (d, $J_{4,OH}$=4.0 Hz, 1H; OH), 3.60 (m, 6H; OMe, H-4a, H-3a, H-1^{Cer}), 3.53 (m, 2H; H-5a, H-1′^{Cer}), 2.60 (s, 4H; OCOCH_2CH_2COO), 2,11 (t, 2H; NHCOCH_2), 1.96 (m, 2H; H-6^{Cer}, H-6′^{Cer}), 1.53 (m, 2H; NHCOCH$_2$CH_2), 1.21 (m, 50H; 25×CH_2), 0.83 (m, 15H; 5×CH_3), 0.01 ppm (m, 6H; Si(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$); δ=173.0, 172.5, 170.7, 165.1, 159.2, 136.7, 133.1, 132.8, 132.5, 130.0, 129.8, 129.7, 128.7, 128.4, 127.8, 124.4, 113.7, 86.4, 82.9, 77.9, 77.3, 74.4, 74.0, 72.0, 69.7, 63.2, 61.7, 60.4, 55.1, 51.8, 36.9, 32.4, 31.9, 29.7, 29.5, 29.5, 29.4, 29.3, 29.3, 29.2, 29.1, 29.0, 25.8, 22.7, 18.2, 14.1, −5.5, −5.6 ppm; HRMS: *m/z* calcd for $C_{73}H_{115}NO_{12}SSiNa^+$: 1280.7805 $[M+Na]^+$; found: 1280.7807.

Compound 24: AcOH (38.0 μL, 640 μmol) and TBAF (1.0 M solution in THF, 644.0 μL, 640 μmol) were added at 0°C to a solution of **23** (270 mg, 220 μmol) in THF (2.2 mL). The mixture was stirred for 3 h at RT (completion of the reaction was confirmed by TLC, EtOAc/hexane 1:1). The reaction mixture was diluted with $CHCl_3$, and the solution was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane 1:1.3) to give **24** (219 mg, 88%). $[\alpha]_D$=−6.1° (*c*=1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.03–7.24 (m, 10H; 2×Ph), 7.08–6.64 (2×d, 4H; Ar), 6.15 (d, $J_{NH,2}$=8.9 Hz, 1H; NH), 5.77 (m, 1H; H-5^{Cer}), 5.42 (m, 1H; H-4^{Cer}), 5.37 (t, 1H; H-3^{Cer}), 5.20 (dd, $J_{1,2}$=10.3 Hz, $J_{2,3}$=8.7 Hz, 1H; H-2a), 4.79 (d, 1H; H-1a), 4.64 (q, 2H; PhCH_2), 4.50 (dd, $J_{5,6}$=4.1 Hz, $J_{6,6'}$=12.4 Hz, 1H; H-6a), 4.37 (dd, 1H; H-6′a), 4.17 (m, 1H; H-2^{Cer}), 4.10 (d, $J_{4,OH}$=3.4 Hz, 1H; OHa), 3.71–3.57 (m, 8H; OMe, H-4a, H-3a, H-5a, H-1^{Cer}, H-1′^{Cer}), 3.16 (t, $J_{1,OH}$=$J_{1',OH}$=6.1 Hz, 1H; OH^{Cer}), 2.66 (m, 4H; OCOCH$_2$CH$_2$COO), 2,17 (m, 2H; NHCOCH_2), 2.00 (m, 2H; H-6^{Cer}, H-6′^{Cer}), 1.59 (m, 2H; NHCOCH$_2$CH_2), 1.31 (m, 50H; 25×CH_2), 0.88 ppm (t, 6H; 2×CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ=173.7, 172.8, 171.5, 165.1, 159.3, 137.4, 133.2, 132.7, 132.5, 129.8, 129.8, 128.8, 128.4, 127.9, 124.4, 113.7, 86.4, 83.1, 77.7, 74.6, 74.5, 72.0, 69.5, 63.3, 61.6, 55.1, 52.9, 36.7, 32.3, 31.9, 29.7, 29.53, 29.47, 29.4, 29.3, 29.2, 29.1, 28.9, 25.7, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{67}H_{101}NO_{12}SNa^+$: 1166.6945 $[M+Na]^+$; found: 1166.6942.

Compound 25: Molecular sieves (4 Å, 85 mg) were added to a solution of **24** (85.0 mg, 740 μmol) in CH_2Cl_2 (15.0 mL). The suspension was stirred for 1 h at RT, after which DMTST (120.0 mg, 220 μmol) was added at 0°C. Stirring was continued for 2 h at 0°C (completion of the reaction was confirmed by TLC, toluene/EtOAc 1:1). The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$ and H_2O, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH 130:1) to give **25** (71 mg, 92%). $[\alpha]_D$=−29.2° (*c*=0.5, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ=8.03–7.45 (m, 5H; Ph), 7.19–6.78 (2×d, 4H; Ar), 5.78 (m, 1H; H-5^{Cer}), 5.70 (d, $J_{NH,2}$=8.9 Hz, 1H; NH), 5.26 (m, 2H; H-3^{Cer}, H-4^{Cer}), 5.17 (t, $J_{1,2}$=$J_{2,3}$=7.6 Hz, 1H; H-2a), 4.63 (2d, 2H; ArCH_2), 4.54 (d, 1H; H-1a), 4.41 (near t, $J_{5,6}$=8.9 Hz, $J_{6,6'}$=11.7 Hz, 1H; H-6a), 4.26 (m, 2H; H-6′a, H-2^{Cer}), 3.88 (dd, J_{gem}=9.6 Hz, $J_{1,2}$=3.4 Hz, 1H; H-1^{Cer}), 3.75 (s, 3H; OMe), 3.69–3.59 (m, 4H; H-3a, H-4a, H-5a, H-1′^{Cer}), 2.75–2.51 (m, 4H; OCOCH$_2$CH$_2$COO), 2.50 (d, $J_{4,OH}$=2.7 Hz, 1H; OH), 2.04 (t, 2H; NHCOCH_2), 1.95 (m, 2H; H-6^{Cer}, H-6′^{Cer}), 1.48 (m, 2H; NHCOCH$_2$CH_2), 1.26 (m, 50H; 25×CH_2), 0.88 ppm (t, 6H; 2×CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ=172.7, 171.9, 170.6, 165.2, 159.5, 138.3, 133.4, 129.9, 129.7, 129.6, 128.5, 124.8, 114.0, 100.0, 82.0, 73.9, 73.7, 73.4, 72.9, 70.9, 66.7, 64.1, 55.2, 50.0, 36.7, 32.3, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 29.2, 28.9, 25.6, 22.7, 14.1 ppm; HRMS: *m/z* calcd for $C_{61}H_{95}NO_{12}Na^+$: 1056.6751 $[M+Na]^+$; found: 1056.6752.

Compound 27: Compound **26** (61 mg, 171 μmol), DMAP (2 mg, 17.1 μmol), and EDC·HCl (36 mg, 188 μmol) were added at 0°C to a solution of **21** (133 mg, 171 μmol) in CH_2Cl_2 (3.4 mL). The mixture was stirred for 2 h at RT (completion of the reaction was confirmed by TLC, EtOAc/hexane 1:1). The reaction mixture was diluted with $CHCl_3$, and the solution was washed with aqueous HCl (2 M) and H_2O, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel [i) EtOAc/hexane 1:5, ii) $CHCl_3$/MeOH 200:1] to give **27** (171 mg, 90%). $[\alpha]_D$=−20.4° (*c*=1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ=7.49–7.29 (m, 5H; Ph), 5.74 (m, 2H; H-5^{Cer}, NH), 5.39 (m, 2H; H-3^{Cer}, H-4^{Cer}), 5.11 (t, $J_{2,3}$=$J_{3,4}$=9.5 Hz, 1H; H-3a), 4.94 (t, $J_{1,2}$=9.8 Hz, 1H; H-2a), 4.73 (d, 1H; H-1a), 4.65 (d, $J_{4,OH}$=4.6 Hz, 1H; OH), 4.48 (dd, $J_{5,6}$=3.5 Hz, J_{gem}=12.0 Hz, 1H; H-6a), 4.34 (dd, $J_{5,6'}$=2.0 Hz, 1H; H-6′a), 4.19 (m, 1H; H-2^{Cer}), 3.75 (m, 1H; H-4a), 3.66 (dd, $J_{1,2}$=2.9 Hz, J_{gem}=10.4 Hz, 1H; H-1^{Cer}), 3.56 (m, 2H; H-5a, H-1′^{Cer}), 2.71–2.57 (m, 4H; OCOCH$_2$CH$_2$COO), 2.15 (m, 2H; NHCOCH_2), 2.09 (s, 3H; Ac), 2.08 (s, 3H; Ac), 2.02 (m, 2H; H-6^{Cer}, H-6′^{Cer}), 1.57 (m, 2H; NHCOCH$_2$CH_2), 1.25 (m, 50H; 25×CH_2), 0.89 (m, 15H; *t*Bu, 2×CH_3), 0.04 ppm (m, 6H; Si(CH_3)$_2$); ^{13}C NMR (100 MHz, $CDCl_3$): δ=173.2, 172.4, 170.8, 170.4, 169.6, 136.8, 132.6, 132.3, 128.9, 128.1, 124.3, 85.9, 77.8, 77.3, 76.5, 73.9, 70.1, 67.7, 62.9, 61.7, 51.7, 36.9, 32.4, 31.9, 29.7, 29.5, 29.5, 29.4, 29.4, 29.3, 29.2, 29.1, 29.0, 25.8, 25.7, 22.7, 20.8, 18.2, 14.1, −5.6, −5.7 ppm; HRMS: *m/z* calcd for $C_{62}H_{107}NO_{12}SSiNa^+$: 1140.7176 $[M+Na]^+$; found: 1140.7175.

Compound 28: Molecular sieves (4 Å, 130 mg) were added to a solution of **27** (62 mg, 55.5 μmol) in $(CH_2Cl)_2$ (11.0 mL). The suspension was stirred for 1 h at RT, after which DMTST (90 mg, 167 μmol) was added. Stirring was continued for 1 h at 40°C (completion of the reaction was confirmed by TLC, acetone/hexane 1:2). TFA (5.5 mL) was added at 0°C to the reaction mixture. Stirring was continued for 2 h at 0°C. The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings

were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous Na_2CO_3, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (acetone/hexane 1:5) to give **28** (36 mg, 72%). $[\alpha]_D = -16.1°$ ($c = 0.7$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 5.80$ (m, 1H; H-5^{Cer}), 5.72 (d, $J_{2,NH} = 9.8$ Hz, 1H; NH), 5.30 (m, 2H; H-3^{Cer}, H-4^{Cer}), 4.95 (t, $J_{2,3} = J_{3,4} = 8.3$ Hz, 1H; H-3a), 4.88 (t, $J_{1,2} = 7.5$ Hz, 1H; H-2a), 4.47 (m, 2H; H-1a, H-6a), 4.32 (m, 1H; H-2^{Cer}), 4.27 (dd, $J_{5,6'} = 2.3$ Hz, $J_{gem} = 12.0$ Hz, 1H; H-6′a), 3.87 (dd, $J_{1,2} = 4.9$ Hz, $J_{gem} = 10.0$ Hz, 1H; H-1^{Cer}), 3.77 (dd, $J_{1',2} = 4.0$ Hz, 1H; H-1′^{Cer}), 3.62 (m, 2H; H-4a, H-5a), 2.83 (d, $J_{4,OH} = 4.6$ Hz, 1H; OH), 2.73–2.56 (m, 4H; $OCOCH_2CH_2COO$), 2.16 (m, 2H; $NHCOCH_2$), 2.12 (s, 3H; Ac), 2.05 (s, 3H; Ac), 1.96 (m, 2H; H-6^{Cer}, H-6′^{Cer}), 1.59 (m, 2H; $NHCOCH_2CH_2$), 1.25 (m, 50H; 25×CH_2), 0.88 ppm (2×t, 6H; 2×CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.8$, 172.0, 171.9, 170.4, 169.4, 138.0, 124.5, 99.6, 76.6, 73.5, 71.2, 70.4, 66.4, 63.7, 50.0, 36.8, 32.3, 31.9, 29.7, 29.7, 29.5, 29.5, 29.4, 29.2, 28.9, 25.7, 22.7, 20.9, 20.8, 14.1 ppm; HRMS: m/z calcd for $C_{50}H_{87}NO_{12}Na^+$: 916.6121 $[M+Na]^+$; found: 916.6120.

Compound 30: Molecular sieves (AW-300, 4 Å, 200 mg) were added to a solution of **25** (25.0 mg, 24 μmol) and **13** (32.0 mg, 24 μmol) in $CHCl_3$ (800 μL). The suspension was stirred for 1 h at RT, after which TMSOTf (0.4 μL, 1.9 μmol) was added at 0°C. Stirring was continued for 2 h at 0°C (completion of the reaction was confirmed by TLC, toluene/EtOAc/MeOH 5:5:1). The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (toluene/EtOAc/MeOH 10:10:1) to give **30** (37 mg, 70%). $[\alpha]_D = +1.8°$ ($c = 0.8$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.10$–7.43 (m, 15H; 3×Ph), 7.20–6.70 (2×d, 4H; Ar), 6.04 (d, $J_{NH,2} = 8.2$ Hz, 1H; NHd), 5.73 (m, 1H; H-5^{Cer}), 5.58 (d, $J_{NH,2} = 9.6$ Hz, 1H; NH^{Cer}), 5.40 (m, 3H; H-3d, H-2b, H-8c), 5.34 (m, 1H; H-4d), 5.26–5.11 (m, 5H; H-7c, NHc, H-2a, H-3^{Cer}, H-4^{Cer}), 5.07 (m, 1H; H-4c), 5.02 (d, $J_{1,2} = 8.3$ Hz, 1H; H-1d), 4.84 (d, $J_{gem} = 11.0$ Hz, 1H; ArCH_2), 4.82 (d, $J_{1,2} = 8.2$ Hz, 1H; H-1b), 4.69 (dd, $J_{gem} = 11.7$ Hz, $J_{5,6} = 6.2$ Hz, 1H; H-6b), 4.64 (d, 1H; ArCH_2), 4.45 (d, $J_{1,2} = 6.9$ Hz, 1H; H-1a), 4.33 (dd, $J_{2,3} = 10.3$ Hz, $J_{3,4} = 2.8$ Hz, 1H; H-3b), 4.25–4.03 (m, 9H; H-2d, H-6d, H-6′d, H-5d, H-6′a, H-9c, H-9′c, H-6′b, H-2^{Cer}), 4.02–3.74 (m, 11H; OMe, H-4b, H-5b, H-6a, H-5a, H-4a, H-5c, H-6c, H-1^{Cer}), 3.64 (s, 3H; OMe), 3.54 (near t, 1H; H-3a), 3.50 (dd, $J_{gem} = 9.6$ Hz, $J_{1',2} = 3.4$ Hz, 1H; H-1′^{Cer}), 2.55–2.35 (m, 4H; $OCOCH_2CH_2COO$), 2.25 (dd, $J_{gem} = 13.1$ Hz, $J_{3eq,4} = 4.8$ Hz, 1H; H-3c$_{eq}$), 2.15–1.84 (m, 32H; 9×Ac, H-3c$_{ax}$, H-6^{Cer}, H-6′^{Cer}, $NHCOCH_2$), 1.45 (m, 2H; $NHCOCH_2CH_2$), 1.25 (m, 50H; 25×CH_2), 0.88 ppm (t, 6H; 2×CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 172.6$, 171.1, 170.8, 170.5, 170.3, 170.2, 169.9, 169.7, 168.1, 165.9, 165.1, 164.3, 158.9, 138.2, 133.3, 133.1, 130.5, 130.1, 129.9, 129.7, 129.6, 129.5, 129.4, 129.2, 128.4, 124.9, 113.5, 101.5, 101.2, 99.5, 98.6, 80.5, 79.0, 76.5, 74.1, 73.9, 73.3, 73.0, 72.3, 72.0, 70.9, 70.7, 70.1, 68.7, 67.4, 67.0, 66.6, 66.5, 63.5, 63.1, 62.1, 61.4, 55.0, 53.2, 51.3, 49.9, 49.3, 36.6, 36.4, 35.9, 32.2, 31.9, 29.7, 29.7, 29.5, 29.5, 29.4, 29.3, 29.3, 28.9, 25.5, 23.3, 23.2, 22.7, 21.1, 20.8, 20.7, 20.6, 20.5, 20.4, 14.1 ppm; HRMS: m/z calcd for $C_{115}H_{159}N_3O_{39}Na^+$: 2229.0448 $[M+Na]^+$; found: 2229.0448.

Compound 31: Molecular sieves (AW-300, 4 Å, 300 mg) were added to a solution of **28** (40 mg, 44.8 μmol) and **13** (60 mg, 44.8 μmol) in $CHCl_3$ (448 μL). The suspension was stirred for 1 h at RT, after which TMSOTf (0.8 μL, 4.48 μmol) was added at 0°C. Stirring was continued for 1 h at 0°C (completion of the reaction was confirmed by TLC, acetone/hexane 1:1). TFA (224 μL) was added to the reaction mixture. Stirring was continued for 2 h at 0°C. The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous Na_2CO_3, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (acetone/hexane 2:3) to give **31** (45 mg, 48%). $[\alpha]_D = -13.7°$ ($c = 0.7$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.11$–7.43 (m, 10H; 2×Ph), 6.42 (d, $J_{2,NH} = 7.6$ Hz, 1H; NHd), 5.75 (m, 2H; H-5^{Cer}, H-3d), 5.67 (d, $J_{2,NH} = 9.6$ Hz, 1H; NH^{Cer}), 5.53 (m, 1H; H-8c), 5.33 (m, 2H; H-4d, H-2b), 5.24 (m, 3H; H-3^{Cer}, H-4^{Cer}, H-7c), 5.14 (m, 3H; H-1d, H-3a, NHc), 4.88 (m, 1H; H-4c), 4.82 (t, $J_{1,2} = J_{2,3} = 7.6$ Hz, 1H; H-2a), 4.73 (d, $J_{1,2} = 7.6$ Hz, 1H; H-1b), 4.67 (dd, $J_{5,6} = 6.6$ Hz, $J_{gem} = 11.3$ Hz, 1H; H-6b), 4.42 (dd, $J_{2,3} = 10.3$ Hz, $J_{3,4} = 2.8$ Hz, 1H; H-3b), 4.33 (m, 2H; H-1a, H-6′b), 4.27 (m, 3H; H-6a, H-9c, H-2^{Cer}), 4.14 (near d, 1H; H-6′a), 4.03–3.95 (m, 4H; H-9′c, H-6d, H-6′d, H-5d), 3.89 (m, 2H; H-5b, H-5c), 3.83–3.78 (m, 5H; H-4b, H-6c, $COOCH_3$), 3.74–3.67 (m, 4H; H-4a, H-2d, H-1^{Cer}, H-1′^{Cer}), 3.49 (near t, 1H; H-5a), 2.61–2.48 (m, 5H; $OCOCH_2CH_2COO$, H-3c$_{eq}$), 2.16–1.82 (11×s, 33H; 11×Ac), 2.13–1.84 (m, 5H; H-3c$_{ax}$, H-6^{Cer}, H-6′^{Cer}, $NHCOCH_2$), 1.57 (m, 2H; $NHCOCH_2CH_2$), 1.23 (m, 50H; 25×CH_2), 0.88 ppm (2×t, 6H; 2×CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 172.7$, 171.3, 170.6, 170.3, 170.3, 170.2, 170.2, 170.1, 169.9, 169.4, 168.2, 165.8, 164.6, 137.6, 133.4, 133.3, 130.2, 129.8, 129.5, 129.2, 128.6, 128.5, 124.5, 100.7, 100.1, 99.3, 98.0, 76.7, 74.3, 73.4, 73.3, 73.1, 72.2, 72.0, 71.8, 71.7, 70.5, 70.1, 69.4, 68.7, 67.3, 66.9, 66.5, 66.3, 63.0, 62.7, 62.3, 61.4, 53.0, 52.4, 50.0, 49.1, 36.7, 36.4, 32.2, 31.9, 29.7, 29.6, 29.5, 29.4, 29.3, 29.3, 29.2, 28.8, 25.6, 23.4, 23.1, 22.6, 21.2, 20.8, 20.7, 20.6, 20.4, 20.3, 14.1 ppm; HRMS: m/z calcd for $C_{104}H_{151}N_3O_{39}Na^+$: 2088.9818 $[M+Na]^+$; found: 2088.9817.

Compound 32: Molecular sieves (AW-300, 4 Å, 200 mg) were added to a solution of **29** (39 mg, 41.1 μmol) and **13** (55 mg, 41.1 μmol) in $CHCl_3$ (820 μL). The suspension was stirred for 30 min at RT, after which TMSOTf (0.8 μL, 4.11 μmol) was added at 0°C. Stirring was continued for 1 h at 0°C (completion of the reaction was confirmed by TLC, acetone/hexane 1:1). The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (acetone/hexane 1:1) to give **32** (24 mg, 28%). $[\alpha]_D = -3.5°$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.09$–7.39 (m, 15H; 3×Ph), 6.40 (d, 1H; $J_{2,NH} = 7.5$ Hz, NHd), 5.85–5.79 (m, 2H; H-3d, H-5^{Cer}), 5.70 (d, $J_{2,NH} = 9.6$ Hz, 1H; NH^{Cer}), 5.52–5.41 (m, 3H; H-8c, H-3^{Cer}, H-4^{Cer}), 5.35 (d, $J_{3,4} = 3.5$ Hz, 1H; H-4d), 5.29–5.24 (m, 2H; H-2b, H-7c), 5.21 (d, $J_{1,2} = 8.3$ Hz, 1H; H-1d), 5.13 (t, $J_{2,3} = J_{3,4} = 9.3$ Hz, 1H; H-3a), 4.99 (d, $J_{5,NH} = 9.6$ Hz, 1H; NHc), 4.89–4.82 (m, 2H; H-2a, H-4c), 4.70 (d, $J_{1,2} = 8.2$ Hz, 1H; H-1b), 4.65 (dd, $J_{5,6} = 6.2$ Hz, $J_{gem} = 11.0$ Hz, 1H; H-6b), 4.42 (m, 1H; H-2^{Cer}), 4.39 (dd, $J_{2,3} = 10.3$ Hz, $J_{3,4} = 2.1$ Hz, 1H; H-3b), 4.35–4.32 (m, 2H; H-1a, H-6′b), 4.31 (dd, $J_{8,9} = 2.4$ Hz, $J_{gem} = 12.7$ Hz, 1H; H-9c), 4.09–3.90 (m, 7H; H-6a, H-6′a, H-9′c, H-5d, H-6d, H-6′d, H-1^{Cer}), 3.88–3.81 (m, 3H; H-4a, H-5b, H-5c), 3.78 (s, 3H; $COOCH_3$), 3.77–3.75 (m, 2H; H-4b, H-6c), 3.59–3.53 (m, 2H; H-2d, H-1′^{Cer}), 3.35 (m, 1H; H-5a), 2.61 (dd, $J_{3eq,4} = 4.9$ Hz, $J_{gem} = 13.0$ Hz, 1H; H-3c$_{eq}$), 2.15, 2.14, and 2.13 (3×s, 9H; 3×Ac), 2.12–2.08 (m, 4H; $NHCOCH_2$), 2.06–1.98 (m, 17H; H-6^{Cer}, H-6′^{Cer}, 5 Ac), 1.96 and 1.88 (2×s, 6H; 2×Ac), 1.82–1.78 (m, 7H; H-3c$_{ax}$, 2 Ac), 1.57 (m, 2H; $NHCOCH_2CH_2$), 1.30–1.22 (m, 50H; 25×CH_2), 0.88 ppm (2×t, $J = 6.6$ Hz, 6H; 2×CH_2CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 172.7$, 171.5, 170.7, 170.4, 170.4, 170.2, 170.2, 170.1, 170.1, 169.8, 169.6, 168.3, 165.9, 165.2, 164.6, 137.4, 133.5, 133.3, 130.0, 130.2, 130.2, 129.7, 129.6, 129.5, 129.2, 128.7, 128.5, 128.3, 124.6, 100.5, 100.2, 99.6, 97.8, 74.5, 74.2, 73.5, 73.4, 72.7, 72.6, 71.9, 71.6, 71.4, 70.6, 70.1, 69.0, 68.8, 67.3, 66.9, 66.2, 62.8, 61.9, 61.8, 61.4, 52.9, 52.8, 50.7, 49.2, 36.8, 36.6, 32.3, 31.9, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 29.3, 29.2, 28.9, 25.7, 23.4, 23.1, 22.7, 21.3, 20.9, 20.7, 20.7, 20.7, 20.5, 20.4, 20.3, 14.1 ppm; HRMS: m/z calcd for $^1/_2(C_{104}H_{151}N_3O_{39})+Na^+$: 1088.0011 $[^1/_2M+Na]^+$; found: 1088.0014.

Compound 33: Molecular sieves (AW-300, 4 Å, 100 mg) were added to a solution of **25** (20.0 mg, 20 μmol) and **17** (48.0 mg, 20 μmol) in $CHCl_3$ (0.96 mL). The suspension was stirred for 1 h at RT, after which TMSOTf (0.7 μL, 3.9 μmol) was added at 0°C. Stirring was continued for 2 h at RT (completion of the reaction was confirmed by TLC, $CHCl_3$/EtOAc/MeOH 3:3:1). The reaction mixture was filtered through Celite and the removed molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$/EtOAc/MeOH 8:8:1) to give **33** (39 mg, 60%). $[\alpha]_D = +3.5°$ ($c = 0.2$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.15$–7.35 (m, 25H; 5×Ph), 7.10–6.64 (2×d, 4H; Ar), 6.41 (d, $J_{NH,5} = 7.6$ Hz, 1H; NHf), 5.65 (m, 5H; H-5^{Cer}, NH^{Cer}, H-8f, NHg, NHd), 5.41 (m, 2H; H-4d, H-8c), 5.33 (m, 1H; H-4g), 5.29 (m, 2H; H-2b, H-2e), 5.19 (m, 4H; H-3^{Cer}, H-

4^{Cer}, H-7f, H-7c), 5.10 (m, 4H; NHc, H-1d, H-2a, H-3g), 4.95 (m, 3H; H-1e, H-1g, H-4f), 4.77 (m, 3H; H-1b, H-4c, ArCH_2), 4.62 (m, 2H; H-6e, H-6b), 4.55 (d, 1H; ArCH_2), 4.46 (dd, $J_{3,4}=2.8$ Hz, $J_{3,2}=9.6$ Hz, 1H; H-3e), 4.39 (m, 2H; H-1a, H-6′b), 4.29 (m, 2H; H-3b, H-9′f), 4.15 (m, 4H; H-6a, H-6′a, H-9c, H-2^{Cer}), 4.06–4.01 (m, 4H; H-6d, H-3d, H-9f, H-9′c), 4.01–3.86 (m, 4H; H-6′d, H-6g, H-6′e, H-4b), 3.85–3.68 (m, 20H; H-5b, H-5e, H-2d, H-5f, H-5c, H-3a, H-4a, H-5a, H-6g, H-6f, H-6c, H-4e, H-5g, H-5d, 2×OMe), 3.60 (s, 3H; OMe), 3.52 (m, 1H; H-1^{Cer}), 3.48 (m, 1H; H-$1'^{Cer}$), 3.22 (m, 1H; H-2g), 2.72 (dd, $J_{gem}=13.7$ Hz, $J_{3eq,4}=4.8$ Hz, 1H; H-3f_{eq}), 2.60–2.44 (m, 4H; OCOCH_2CH_2COO), 2.37 (m, 1H; H-3c_{eq}), 2.20–1.52 (m, 57H; 17×Ac, NHCOCH_2, H-3f_{ax}, H-3c_{ax}, H-6^{Cer}, H-$6'^{Cer}$), 1.42 (m, 2H; NHCOCH$_2$CH_2), 1.25 (m, 50H; 25×CH_2), 0.86 ppm (t, 6H; 2×CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=172.7$, 171.1, 170.8, 170.8, 170.7, 170.6, 170.5, 170.4, 170.3, 170.2, 170.2, 170.1, 170.0, 169.8, 168.3, 168.2, 165.9, 165.6, 165.1, 164.4, 158.9, 133.3, 133.2, 132.9, 130.4, 130.3, 130.0, 129.9, 129.7, 129.7, 129.5, 129.3, 129.2, 129.0, 128.8, 128.7, 128.5, 128.3, 128.2, 113.5, 101.1, 100.2, 99.5, 98.1, 97.7, 80.9, 78.5, 73.9, 73.7, 73.5, 73.3, 73.2, 72.6, 72.3, 72.0, 71.9, 71.0, 70.9, 70.6, 70.0, 69.8, 68.9, 68.8, 67.3, 66.9, 66.5, 66.5, 63.2, 63.1, 63.0, 62.6, 62.2, 61.4, 55.0, 54.9, 53.0, 52.7, 49.9, 49.3, 37.4, 37.4, 37.1, 36.7, 36.5, 36.3, 34.4, 32.7, 32.2, 31.9, 31.2, 30.4, 30.3, 30.1, 30.0, 29.9, 29.7, 29.7, 29.5, 29.5, 29.4, 29.3, 29.3, 28.8, 27.4, 27.1, 25.5, 24.8, 24.5, 23.4, 23.2, 23.1, 23.1, 23.0, 22.7, 21.3, 21.2, 20.8, 20.7, 20.7, 20.4, 20.4, 20,2, 20.1, 19.7, 14.4, 14.1, 11.4 ppm; HRMS: m/z calcd for $C_{167}H_{221}N_5O_{65}Na^+$: 3359.4032 $[M+Na]^+$; found: 3359.4039.

Compound 34: Trifluoroacetic acid (180 μL) was added at 0°C to a solution of **33** (18.0 mg, 54 μmol) in CH_2Cl_2 (360 μL). The mixture was stirred for 50 min at 0°C (completion of the reaction was confirmed by TLC, $CHCl_3$/EtOAc/MeOH 3:3:1). The reaction mixture was diluted with $CHCl_3$, and the solution was washed with ice-cooled H_2O, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$/EtOAc/MeOH 8:8:1) to give **34** (17 mg, quant). $[\alpha]_D=-17.0°$ ($c=0.2$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta=8.17$–7.26 (m, 25H; 5×Ph), 6.47 (d, $J_{NH,5}=7.6$ Hz, 1H; NHf), 5.75–5.58 (m, 5H; H-5^{Cer}, NH^{Cer}, H-8f, NHg, NHd), 5.42 (m, 2H; H-4d, H-8c), 5.38–5.27 (m, 3H; H-4g, H-2b, H-2e), 5.25–5.01 (m, 8H; H-3^{Cer}, H-4^{Cer}, H-7f, H-7c, NHc, H-1d, H-2a, H-3g), 5.01–4.90 (m, 3H; H-1e, H-1g, H-4f), 4.85–4.72 (m, 2H; H-1b, H-4c), 4.70–4.62 (m, 2H; H-6e, H-6b), 4.52 (m, 1H; H-3e), 4.41 (m, 4H; H-1a, H-6′b, H-3b, H-9f), 4.31–4.12 (m, 4H; H-6a, H-6′a, H-9c, H-2^{Cer}), 4.10–3.85 (m, 8H; H-6d, H-3d, H-9′f, H-9′c, H-6′d, H-6g, H-6′e, H-4b), 3.85–3.68 (m, 20H; H-5b, H-5e, H-2d, H-5f, H-5c, H-3a, H-4a, H-5a, H-6g, H-6f, H-6c, H-4e, H-5g, H-5d, 2×OMe), 3.65–3.47 (m, 2H; H-1^{Cer}, H-$1'^{Cer}$), 3.21 (m, 1H; H-2g), 2.70 (dd, $J_{gem}=13.7$ Hz, $J_{3eq,4}=4.8$ Hz, 1H; H-3f_{eq}), 2.60–2.44 (m, 4H; OCOCH_2CH_2COO), 2.40 (m, 1H; H-3c_{eq}), 2.20–1.41 (m, 59H; 17×Ac, NHCOCH_2, H-3f_{ax}, H-3c_{ax}, H-6^{Cer}, H-$6'^{Cer}$, NHCOCH$_2$CH_2), 1.29 (m, 50H; 25×CH_2), 0.86 ppm (t, 6H; 2×CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=172.7$, 171.9, 171.3, 170.9, 170.8, 170.5, 170.4, 170.2, 170.0, 169.9, 169.7, 168.2, 166.2, 165.9, 165.4, 164.9, 164.4, 137.9, 133.3, 133.1, 130.9, 130.2, 130.1, 129.8, 129.8, 129.7, 129.6, 129.5, 129.2, 128.8, 128.6, 128.5, 128.4, 124.7, 101.3, 101.1, 100.3, 99.7, 98.7, 98.2, 97.8, 82.7, 78.1, 78.0, 77.7, 77.3, 73.5, 73.2, 73.1, 72.9, 72.7, 72.5, 72.0, 71.9, 71.6, 70.9, 70.7, 70.5, 70.4, 70.1, 70.0, 69.6, 68.8, 67.3, 66.9, 66.6, 66.5, 64.1, 63.2, 63.0, 62.6, 62.2, 61.7, 61.4, 53.1, 52.8, 52.2, 50.0, 49.2, 49.1, 37.4, 37.1, 36.7, 36.6, 36.4, 34.4, 32.7, 32.2, 31.9, 31.7, 30.8, 30.4, 30.0, 29.7, 29.5, 29.5, 29.4, 29.3, 29.2, 28.8, 27.1, 26.7, 25.5, 23.4, 23.1, 23.1, 22.7, 21.4, 21.2, 20.8, 20.8, 20.7, 20.5, 20.4, 20.4, 20.3, 19.7, 14.1 ppm; HRMS: m/z calcd for $C_{159}H_{213}N_5O_{64}Na^+$: 3239.3460 $[M+Na]^+$; found: 3239.3464.

Ganglioside GalNAc-GD1a (1): A catalytic amount of sodium methoxide (28% in MeOH) was added at RT to a solution of **34** (13.0 mg, 4.0 μmol) in a mixture of MeOH (200 μL) and THF (200 μL). The mixture was stirred for 5 days at RT. Water (10 μL) was added and stirring was continued for 2 days at RT (completion of the reaction was confirmed by TLC, $CHCl_3$/MeOH/H_2O 5:4:1), the reaction mixture was neutralized with Dowex-50 (H^+), the mixture was filtered through cotton, and removed resin was washed with mixed solvent ($CHCl_3$/MeOH 1:1). The combined filtrate and washings were concentrated. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH/H_2O 5:4:0.5) to give **1** (7 mg, 88%). $[\alpha]_D=-3.5°$ ($c=0.1$, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$/CD_3OD 1:1): $\delta=5.60$ (m, 1H; H-5^{Cer}), 5.37 (m, 1H; H-4^{Cer}), 2.69 (m, 2H; H-3c_{eq}, H-3f_{eq}), 2.10 (t, 2H; NHCOCH_2), 1.95 (s, 14H; H-6^{Cer}, H-$6'^{Cer}$, 4×Ac), 1.82 (m, 2H; H-3c_{ax}, H-3f_{ax}), 1.50 (m, 2H; NHCOCH$_2$CH_2), 1.25 (m, 50H; 25×CH_2), 0.81 ppm (t, 6H; 2×CH_3); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta=177.9$, 175.9, 175.6, 175.6, 175.1, 174.6, 170.5, 135.6, 131.6, 104.9, 104.4, 104.2, 103.2, 101.3, 101.3, 101.1, 88.9, 84.7, 84.1, 81.4, 79.5, 79.2, 76.4, 76.2, 76.1, 75.9, 75.8, 75.1, 74.1, 73.9, 73.8, 73.5, 72.9, 71.6, 71.0, 70.6, 70.5, 69.9, 69.7, 69.0, 68.8, 65.5, 65.3, 63.0, 62.9, 61.7, 60.5, 57.5, 57.3, 57.2, 57.1, 56.0, 54.5, 53.8, 50.3, 50.1, 49.9, 49.6, 49.4, 49.3, 49.1, 48.9, 48.8, 48.7, 48.6, 48.1, 48.0, 47.9, 43.3, 38.8, 37.4, 36.9, 36.1, 33.5, 33.1, 31.0, 30.9, 30.8, 30.7, 30.7, 30.6, 30.5, 30.4, 27.2, 24.0, 23.8, 23.7, 23.6, 23.4, 22.6, 17.4, 16.3, 14.9, 14.7, 14.5 ppm; HRMS: m/z calcd for $C_{92}H_{161}N_5O_{44}^{2-}$:1019.0815 $[1/2M-2H]^{2-}$; found: 1019.0815.

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