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Efficiently Synthesizing Lacto-Ganglio-Series Gangliosides by Using a Glucosyl Ceramide Cassette Approach: The Total Synthesis of Ganglioside X2**

Shinya Nakashima,[a, b] Hiromune Ando,*[a, b] Risa Saito,[a] Hideki Tamai,[a, b] Hideharu Ishida,[a] and Makoto Kiso*[a, b]

Abstract: The first total synthesis of the hybrid ganglioside X2, which consisted of a highly branched octasaccharide and ceramide moieties, was accomplished by using a glucosyl ceramide cassette approach. With a disaccharyl donor, the heptasaccharide could not be constructed by glycosylation of the C4 hydroxy group of galactose at the reducing end of the pentasaccharide. In contrast, through an alternative approach with two branched glycan units, a GM2-core trisaccharide, and a lacto-ganglio tetrasaccharide, the heptasaccharyl donor could be prepared and subsequently joined with a glucosyl ceramide cassette to afford the protected ganglioside, X2. Finally, global deprotection completed the synthesis, thus affording the pure ganglioside X2.

Keywords: amyotrophic lateral sclerosis · gangliosides · oligosaccharides · sialic acid · total synthesis

Introduction

Amyotrophic lateral sclerosis (ALS) is characterized by the progressive and selective degeneration of motor neurons in the brain and spinal cord, and the etiology and pathogenesis of this debilitating disease are still unknown. However, an ALS-like disorder was found to be induced by the therapeutic intramuscular administration of a mixture of bovine brain gangliosides to a patient with a neurological disorder.[1] Because an extremely high concentration of anti-GM2 IgM was detected in the patient's serum and because the recovery was rapid after plasmapheresis,[1,2] anti-GM2 IgM was thought to be the main cause of the ALS-like disorder. The target molecule of this study, ganglioside X2 (**2**), which contains a GM2 core, was identified in bovine brain gangliosides by using the patient's IgM together with ganglioside X1 (**1**)[3] (Scheme 1). These hybrid gangliosides are lacto-ganglio-series gangliosides in which the core sequences of lacto- and ganglio-series gangliosides, namely, Galβ-(1,3)GlcNAcβ(1,3)Gal and Galβ(1,3)GalNAcβ(1,4)Gal, are hybridized in their glycan moieties. Their unusual structures are hypothesized to be immunogenic in humans or to be targets of autoantibodies in some patients who are misdiagnosed with ALS. In this context, the gangliosides should be useful for identifying such patients, who can be treated with immunotherapy. However, isolating enough gangliosides of sufficient quality is difficult from natural sources because they are structurally diverse and present in the cell membrane in very small amounts. To obtain a pure ganglioside, we recently synthesized ganglioside X1; furthermore, we confirmed that serum IgM binds to synthetic ganglioside X1.[4] Accordingly, our next goal was to chemically synthesize ganglioside X2 to provide access to the complete set of these hybrid gangliosides, which are expected to be useful in distinguishing treatable patients with an ALS-like disorder from patients diagnosed with ALS. Herein, we report the total synthesis of ganglioside X2.

[a] S. Nakashima, Dr. H. Ando, R. Saito, H. Tamai, Dr. H. Ishida, Dr. M. Kiso
Department of Applied Bioorganic Chemistry
Gifu University
1-1 Yanagido, Gifu-shi, Gifu 501-1193 (Japan)
Fax: (+81) 58-293-3452
hando@ gifu-u.ac.jp

[b] S. Nakashima, Dr. H. Ando, H. Tamai, Dr. M. Kiso
Institute for Integrated Cell-Material Sciences
WPI-iCeMS
Kyoto University
Yoshida Ushinomiya-cho, Sakyo-ku
Kyoto 606-8501 (Japan)

[**] Part 156 in the series: Synthetic studies on sialoglycoconjugates. For part 155, see: Synthesis of the disialic acid-embedded glycan part of ganglioside HPG-1, Ref. [16].

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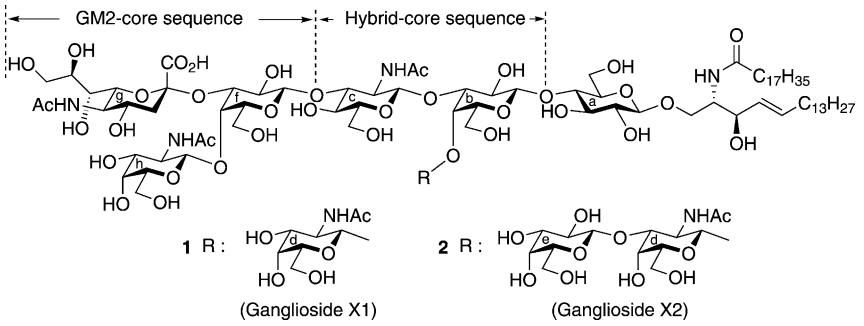
Results and Discussion

We wanted to establish a synthetic route that provided easy access to both gangliosides X1 (**1**) and X2 (**2**) for their use in advanced immunological and diagnostic studies. In our synthesis of ganglioside X1, the final coupling between the heptasaccharide and the ceramide provided a low yield of the desired product (26%), which was accompanied by the hemiacetal (61%) and trichloroacetylaminoglycoside (10%) by-products from the heptasaccharyl trichloroacetimidate donor. Because the aminoglycoside and ganglioside X1 had

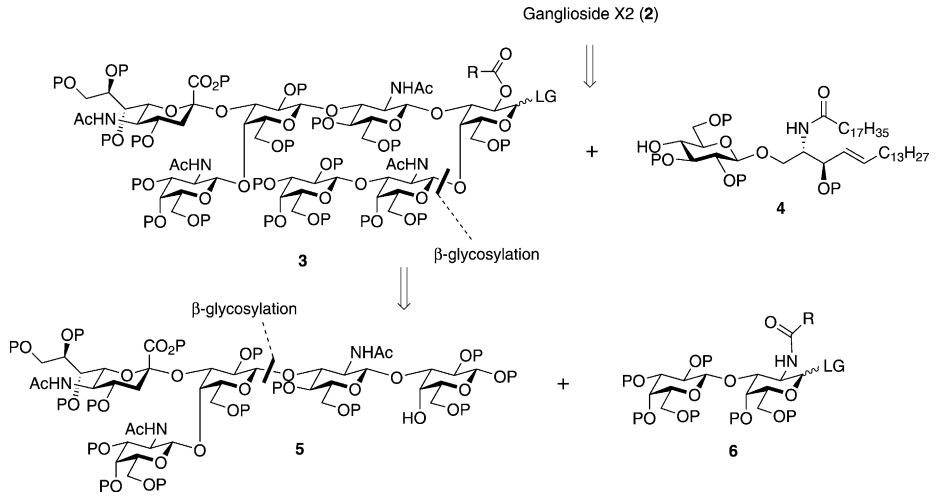


Scheme 1. Structures of gangliosides X1 (**1**) and X2 (**2**) found in bovine brain.

similar mobilities on silica gel, chromatographic separation was challenging and some fractions of eluent that contained the desired compound were inevitably lost. In addition, with the previous synthetic route developed for ganglioside X1, common synthetic intermediates could not be fully applied to the preparation of both gangliosides X1 and X2. Taking into account the major drawbacks of the previous route, we envisaged a new approach to ganglioside X2 (Scheme 2). To avoid the loss of the valuable oligosaccharyl donor during the coupling of the self-aggregating, bulky, and unreactive ceramide, we recently developed a glucosyl ceramide (Glc-Cer) cassette approach.[5] This approach was used to construct the very complicated framework of the target compound, with the aim of improving the coupling yields and efficiency of the chromatographic purification. Thus, retrosynthetic analysis of the target molecule (**2**) first provided heptasaccharide **3** and Glc-Cer cassette **4**. Heptasaccharide **3** was disconnected at the β(1,4)-linkage between galactosamine and galactose to give disaccharyl donor **6** and pentasaccharyl acceptor **5**, which could also be used for the synthesis of ganglioside X1. Pentasaccharide **5** should be accessible from the known GM2-core donor[6] plus a suitably protected disaccharide acceptor.

For the pentasaccharyl acceptor (**5**), we chose a set of orthogonal protecting groups for the latent glycosylation positions on the inner disaccharide unit (GlcNAcβ(1,3)Gal). The 2,2,2-trichloroethoxycarbonyl (Troc) group was chosen for protection of the C3 hydroxy group of the glucosaminyl donor, and the di-*tert*-butylsilyl (DTBS) group was chosen for the simultaneous protection of the C4 and C6 hydroxy groups of the galactosyl acceptor, thereby providing glucosaminyl unit **7**[4] and galactosaminyl unit **8**,[7] respectively (Scheme 3). First, inner disaccharide unit **9** was prepared in good yield by the straightforward glycosidation of compound **7** with compound **8**, followed by conversion into the corresponding disaccharyl acceptor (**10**) by the selective deprotection of the Troc groups and *N*-acetylation. Next, the glycosylation of compound **10** (1.0 equiv) with GM2-core donor **11**[6] (1.0 equiv; TMSOTf, CH_2Cl_2, 0 °C) produced pentasaccharide **12** in 77 % yield. For conversion into acceptor **13**, the DTBS moiety in compound **12** was selectively removed by treatment with tributylamine hydrofluoride (TBAHF)[8] to deprotect the C4 and C6 hydroxy groups, and the C6 hydroxy group was selectively protected with an acetyl group under mild conditions. Next, pentasaccharide acceptor **13** was subjected to glycosylation with glycosyl donor **14**.[9] However, the glycosylation reaction, promoted by *N*-iodosuccinimide (NIS) and trifluoromethanesulfonic acid (TfOH),[10] could not produce the desired compound (**16**). By using trichloroacetimidate donor **15**, the heptasaccharide was generated in very poor yield (ca. 10–20 %). To our disappointment, we were unable to improve the glycosylation yield.

Because of the poor yield from the glycosylation of the pentasaccharyl acceptor, an alternative route was devised to synthesize ganglioside X2 (Scheme 4). Although the common synthetic route to gangliosides X1 and X2 became shorter than that in the first attempt, the heptasaccharide moiety (**3**) in the target molecule was disassembled at the β-glycosidic linkage between Gal and GlcN, thereby providing the GM2-core unit (**11**) and the tetrasaccharide (hybrid-core) unit (**17**), which further fragmented into disaccharide units **6** and **18**.



Scheme 2. Retrosynthetic analysis of target compound **2**. P = protecting group, LG = leaving group.

Hybrid-core unit **17** was suitably protected to give compound **24** in high overall yield (Scheme 5). First, disaccharyl acceptor **20** was synthesized from compound **9** with the protecting groups being manipulat-

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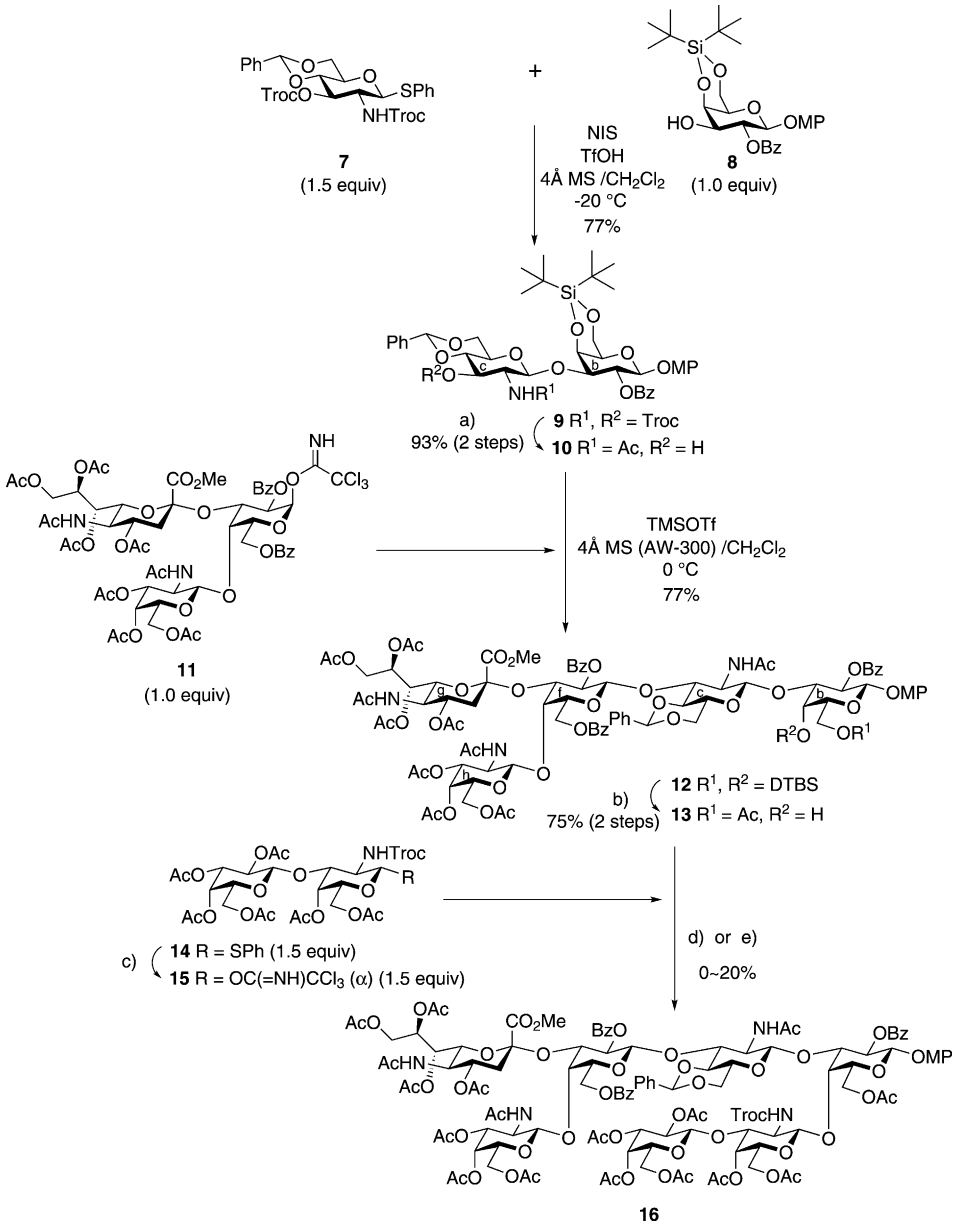


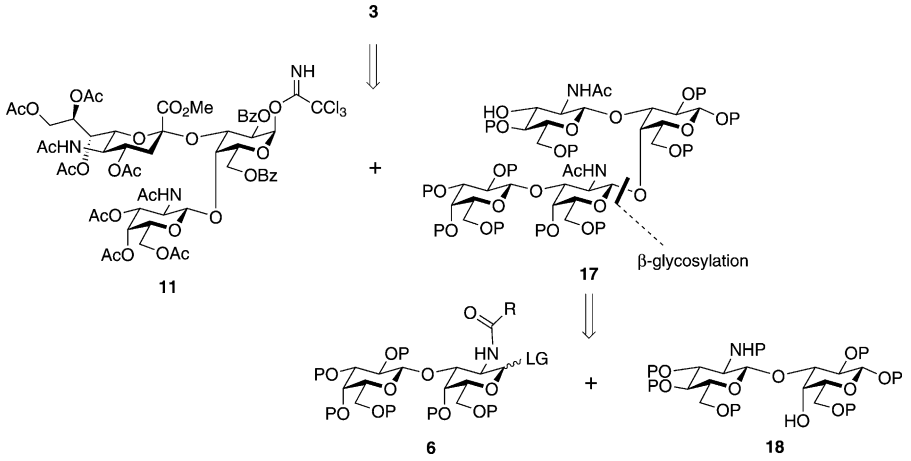
Scheme 3. First approach to the heptasaccharide fragment: a) (i) Zn, AcOH/MeCN, RT; (ii) Ac_2O, CH_2Cl_2/MeOH 2:1, RT, 93% (2 steps); b) (i) TBAHF, RT; (ii) Ac_2O, pyridine, THF, −20°C to RT, 75% (2 steps); c) (i) NBS, H_2O/acetone 1:20, RT; (ii) CCl_3CN, DBU, CH_2Cl_2, RT, 91% (2 steps); d) compound **14**, NIS, TfOH, CH_2Cl_2, 4 Å M.S., −20°C; e) compound **15**, TMSOTf, CH_2Cl_2, 4 Å M.S. (AW-300), 0°C to RT. Troc = 2,2,2-trichloroethoxycarbonyl, MP = *p*-methoxyphenyl, Bz = benzoyl, NIS = *N*-iodosuccinimide, TfOH = trifluoromethanesulfonic acid, M.S. = molecular sieves, TMSOTf = trimethylsilyl trifluoromethanesulfonate, TBAHF = tri-*n*-butylamine hydrofluoride, NBS = *N*-bromosuccinimide, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DTBS = di-*tert*-butylsilylene.

ed in a similar manner to the conversion of compound **12** into compound **13**. Next, the NIS/TfOH-mediated coupling of acceptor **20** with Gal-GalN donor **14** was performed to yield tetrasaccharide **23** in 82% yield. By using GalN donor **21**,[11] compound **20** was converted into the hybrid-core structure of ganglioside X1 in high yield. In the final step, deprotection of the Troc groups and subsequent acetylation of the resulting amine group in compound **23** produced hybrid-core acceptor **24** in 93% yield over two steps. A comparison of the results from the glycosylation of heptasaccharide **13** and disaccharide **20** with compound **14** suggested that the reactivity of the C4 hydroxy group in compound **13** was attenuated by the steric bulk of the GlcN residue.

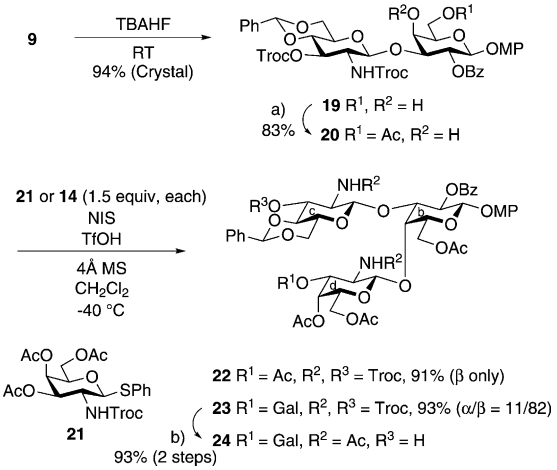
In line with our expectations, glycosyl acceptor **24** was a good coupling partner for GM2-core donor **11**, and generated highly branched heptasaccharide **25** in 81% yield (Scheme 6). Then, compound **25** was converted into the corresponding glycosyl imidate donor. To replace the acid-labile benzylidene acetal moiety with acetyl groups, compound **25** was treated with 90% AcOH (aq.) at 60°C and then with Ac_2O and DMAP in pyridine to afford compound **26**. Finally, the *p*-methoxyphenyl group at the anomeric position of compound **26** was selectively cleaved by treatment with CAN and water,[12] and the resulting hemiacetal was treated with CCl_3CN in the presence of DBU[13] to furnish heptasaccharyl imidate donor **27** in good yield.

In our previous study on the synthesis of GQ1b,[5a] we found that Glc-Cer cassette **34** could accept highly branched oligosaccharyl donors to provide ganglioside frameworks in high yields. However, the moderate yield (48%) from the coupling of the Glc donor (1.5 equiv) and the Cer acceptor (1.0 equiv) limited the scope of its applications in ganglioside synthesis. Herein, we improved the glycosylation yield by introducing a *tert*-butyldimethylsilyl (TBS) group at the C4 hydroxy group of the Glc donor. Phenylthioglycoside donor **30** and imidate donor **31**, which were derived from compound **28**[14] through a sequence of conventional reactions, provided high yields (77% and 78%) of Glc-Cer **33** from the glycosidation reaction with ceramide acceptor **32**[15] (Scheme 7). Next, the TBS group was cleaved to afford Glc-Cer cassette **34** in 95% yield.

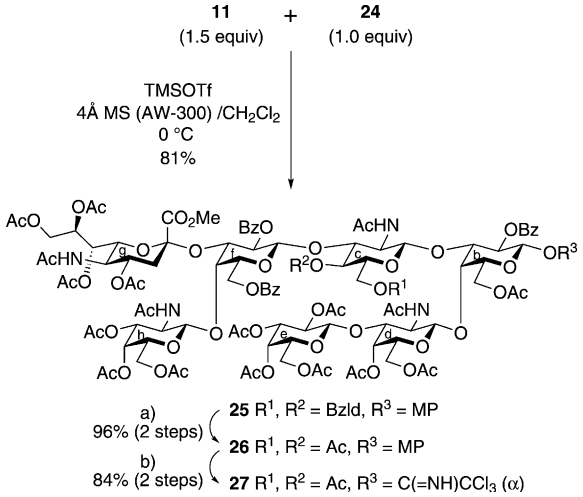
In the final stage of this synthesis, to build the glycolipid framework of ganglioside X2, the coupling reaction between



Scheme 4. Revised retrosynthetic analysis of the heptasaccharide part.



Scheme 5. Synthesis of inner-hyprid-core acceptor **24**: a) Ac_2O, pyridine, THF, −20 °C to RT, 83 %; b) (i) Zn, AcOH, THF, RT; (ii) Ac_2O, CH_2Cl_2/MeOH 2:1, RT, 93 % (2 steps). Gal = 2,3,4,6-tetra-*O*-acetyl-β-D-galactopyranosyl.

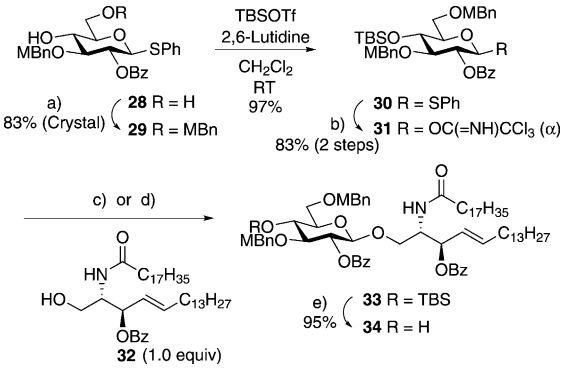


Scheme 6. Assembly of heptasaccharide and conversion into the glycosyl donor: a) (i) 90 % AcOH (aq.), 60 °C; (ii) Ac_2O, DMAP, pyridine, RT, 96 % (2 steps); b) (i) CAN, MeCN/toluene/H_2O 6:5:3, 0 °C; (ii) CCl_3CN, DBU, CH_2Cl_2, RT, 84 % (2 steps). Bzld = benzylidene, DMAP = 4-dimethylaminopyridine, CAN = ceric(IV) ammonium nitrate.

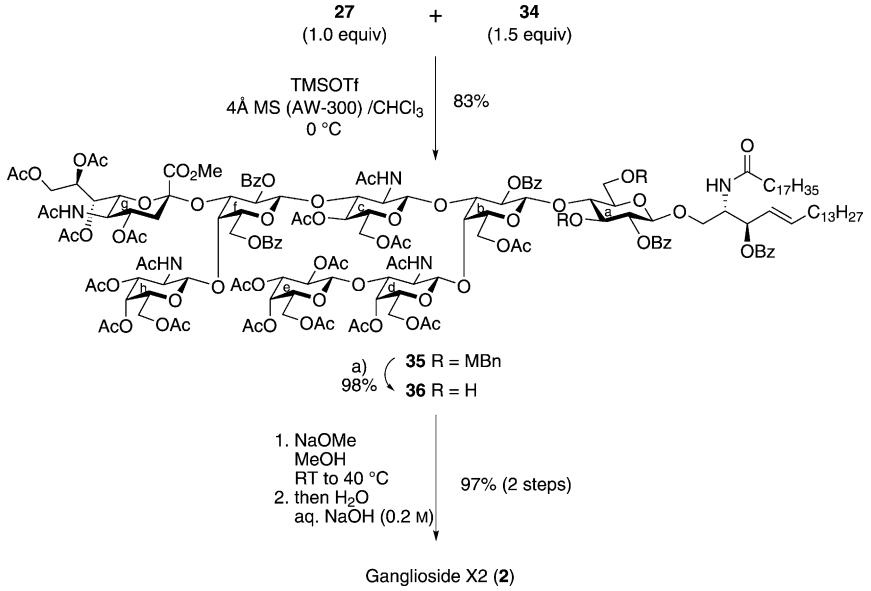
heptasaccharyl donor (**27**) and the Glc-Cer cassette (**34**) was promoted by a catalytic amount of TMSOTf in $CHCl_3$ at 0 °C, thus providing compound **35** in 83 % yield together with the trichloroactylaminoglycoside analogue of compound **27** (about 7 %; Scheme 8). Chromatographic separation of the reaction mixture was straightforward owing to the large difference in mobility on silica gel between the heptasaccharyl byproduct and the desired octasaccharyl ceramide **35**. The Glc-Cer cassette method afforded a high yield, and, more importantly, allowed for the efficient production of pure ganglioside with a high degree of reproducibility. Finally, *p*-methoxybenzyl groups were removed under acidic conditions (TFA, CH_2Cl_2, 0 °C, 98 %), followed by deacylation under Zemplén conditions and subsequent saponification of methyl ester in sialic acid (97 % yield over two steps). This global deprotection successfully provided 30.6 mg of pure ganglioside X2 (**2**), which is a sufficient amount for use in immunological and diagnostic studies.

Conclusions

Although our first attempted route was unsuccessful, we successfully completed the first total synthesis of the hybrid ganglioside X2 by using a modified convergent route. By applying the Glc-Cer cassette approach, the assembly of the glycolipid framework, which is critical in ganglioside synthe-



Scheme 7. Synthesis of the Glc-Cer acceptor **34**. a) DBTO, toluene, reflux, then MBnCl, TBAB, 83 % (crystal); b) (i) NBS, H_2O/acetone 1:20, RT; (ii) CCl_3CN, DBU, CH_2Cl_2, RT, 83 % (2 steps); c) compound **30** (1.0 equiv), DMTST, CH_2Cl_2, 4 Å M.S., RT, 77 %; d) compound **31** (1.0 equiv), TMSOTf, CH_2Cl_2, 4 Å M.S. (AW-300), RT, 78 %; e) TBAF, AcOH, THF, RT, 95 %. MBn = *p*-methoxybenzyl, DBTO = dibutyltin(IV) oxide, TBAB = *n*-tetrabutylammonium bromide, TBSOTf = *tert*-butyldimethylsilyl trifluoromethanesulfonate, DMTST = dimethyl(methylthio)-sulfonium trifluoromethanesulfonate, TBAF = *n*-tetrabutylammonium fluoride.



Scheme 8. Final coupling and global deprotection to afford ganglioside X2 (**2**): a) TFA, CH_2Cl_2, 0 °C, 98 %. TFA = trifluoroacetic acid.

sis, was successfully performed. The quantity of X2 prepared from this first synthesis (30.6 mg) accentuated the efficacy and practicality of this synthetic route. Based on the synthesized compounds X1 and X2, we are currently working to develop a diagnostic method for distinguishing between patients with ALS and treatable patients with an ALS-like disorder.

Experimental Section

General Procedures

^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECA500 and 600 spectrometers. ^{1}H NMR chemical shifts are expressed in ppm (δ) relative to Me_4Si as an internal standard. ^{13}C NMR chemical shifts are expressed in ppm (δ) relative to the solvent as a standard. High-resolution mass spectrometry (HRMS) was performed on a Bruker Daltonics micrOTOF (ESI-TOF) mass spectrometer. Specific rotations were measured with a Horiba SEPA-300 high-sensitivity polarimeter. Melting points were determined by using an AS ONE ATM-01. Molecular sieves were purchased from Wako Chemicals Inc. and dried at 300 °C for 2 h in a muffle furnace prior to use. Reactions were carried out under an argon atmosphere unless otherwise specified. Solvents as reaction media were dried over molecular sieves and used without further purification. TLC analysis was performed on Merck TLC plates (silica gel $60F_{254}$ on glass). Compounds were visualized either by exposure to UV light (254 nm), or by spraying with a 10 % H_2SO_4 solution in EtOH or ninhydrin, followed by heating. Flash column chromatography on silica gel (Fuji Silysia Co., 80 mesh, 300 mesh and Mitsubishi Chemical Medience Co., Iatrobeads 6RS-8060) or Sephadex (Pharmacia LH-20) was performed with the solvent systems (v/v) specified. Evaporation and concentration were conducted in vacuo.

*4-Methoxyphenyl-4,6-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-3-O-(2,2,2-trichloroethoxycarbonyl)-β-*D*-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-di-tert-butylsilylene-β-*D*-galactopyranoside (**9**)*

Molecular sieves (4 Å, 500 mg) were added to a solution of compounds **7** (192 mg, 271 μmol) and **8** (96 mg, 181 μmol) in CH_2Cl_2 (4.5 mL). The suspension was stirred for 30 min at −20 °C, whereupon NIS (91 mg, 407 μmol) and TfOH (3.6 μL, 40.7 μmol) were added. Stirring was continued for 30 min at −20 °C (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 2:5). The reaction mixture was quenched with saturated aqueous $NaHCO_3$, filtered through celite, and the 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 $Na_2S_2O_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/toluene, 1:4→1:3) and column chromatography on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give compound **9** (157 mg, 77 %). $[\alpha]_D = +3.5$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.08$–7.32 (m, 10H; 2×Ph), 6.89–6.72 (m, 4H; Ar), 5.80 (dd, $J(1,2) = 7.6$ Hz, $J(2,3) = 9.6$ Hz, 1H; H-2b), 5.63 (t, $J(2,3) = J(3,4) = 9.6$ Hz, 1H; H-3c), 5.51 (s, 1H; PhC*H*), 5.30 (d, $J(1,2) = 8.2$ Hz, 1H; H-1c), 5.21 (d, $J(2,NH) = 6.1$ Hz, 1H; NH), 4.92 (d, 1H; H-1b), 4.69 (d, $J(3,4) = 2.8$ Hz, 1H; H-4b), 4.67–4.65 (m, 2H; CH_2), 4.46 (d, $J(gem) = 11.7$ Hz, 1H; CH_2), 4.34 (dd, $J(5,6) = 4.8$ Hz, $J(gem) = 10.3$ Hz, 1H; H-6c), 4.31–4.28 (m, 2H; H-6b, H-6′b), 3.82 (dd, 1H; H-3b), 3.75–3.69 (m, 2H; H-4c, H-6′c), 3.73 (s, 3H; OMe), 3.61 (m, 1H; H-5c), 3.52 (s, 1H; H-5b), 3.36–3.34 (m, 2H; CH_2, H-2c), 1.15 and 1.09 ppm (2 s, 18H; 2×*t*Bu); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 165.2$, 155.6, 153.4, 151.4, 136.6, 133.3, 129.8, 129.2, 128.7, 128.2, 126.1, 119.6, 114.3, 101.6, 101.4, 100.8, 95.2, 94.2, 81.3, 78.8, 74.4, 73.3, 72.3, 71.4, 70.3, 68.6, 67.0, 65.7, 57.5, 55.5, 27.5, 27.5, 23.5, 20.7 ppm; HRMS (ESI): *m*/*z* calcd for $C_{47}H_{55}Cl_6NO_{16}Si+Na^+$: 1150.1313 $[M+Na]^+$; found: 1150.1313.

*4-Methoxyphenyl 2-acetamido-4,6-O-benzylidene-2-deoxy-β-*D*-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-di-tert-butylsilylene-β-*D*-galactopyranoside (**10**)*

Zinc powder (1.5 g) was added to a solution of compound **9** (296 mg, 262 μmol) in MeCN (8.0 mL) and AcOH (2.0 mL) and the mixture was stirred for 20 min at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 20:1). The reaction mixture was filtered through celite and the zinc powder was washed with EtOAc. The combined filtrate and washings were extracted with EtOAc, and the organic layer was washed with saturated aqueous Na_2CO_3 and brine, dried (Na_2SO_4), concentrated under vacuum, and exposed to high vacuum for 14 h. The residue was treated with a solution of Ac_2O (74 μL, 786 μmol) in CH_2Cl_2/MeOH (1.7 mL:0.9 mL) for 30 min at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 20:1). The mixture was concentrated under vacuum and the residue was purified by column chromatography on silica gel ($CHCl_3$/acetone, 80:1→50:1) to give compound **10** (201 mg, 93 %). $[\alpha]_D = -5.0$ ($c = 1.3$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.07$–7.31 (m, 10H; 2×Ph), 6.92–6.74 (m, 4H; Ar), 5.90 (br s, 1H; NH), 5.79 (dd, $J(1,2) = 7.6$ Hz, $J(2,3) = 10.0$ Hz, 1H; H-2b), 5.55 (s, 1H; PhC*H*), 4.98 (d, 1H; H-1b), 4.85 (d, $J(1,2) = 7.6$ Hz, 1H; H-1c), 4.77 (s, 1H; OH), 4.65 (d, $J(3,4) = 2.7$ Hz, 1H; H-4b), 4.33–4.27 (m, 3H; H-6b, H-6′b, H-6c), 4.11 (t, $J(2,3) = J(3,4) = 9.0$ Hz, 1H; H-3c), 3.84 (dd, 1H; H-3b), 3.74 (s, 3H; OMe), 3.73 (t, $J(5,6') = J(gem) = 10.0$ Hz, 1H; H-6′c), 3.53 (s, 1H; H-5b), 3.53 (t, $J(4,5) = 9.0$ Hz, 1H; H-4c), 3.44 (ddd, $J(5,6) = 4.8$ Hz, 1H; H-5c), 3.30 (ddd, $J(2,NH) = 4.1$ Hz, 1H; H-2c), 1.70 (s, 3H; Ac), 1.14 and 1.09 ppm (2 s, 18H; 2×*t*Bu); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 172.6$, 166.0, 155.7, 151.3, 136.9, 129.7, 129.3, 129.2, 128.8, 128.2, 126.3, 119.6, 114.4, 101.9, 101.4, 101.3, 81.5, 80.1, 72.5, 71.5, 71.3, 70.3, 68.6, 66.9, 66.3, 60.2, 55.6,

27.5, 27.4, 23.4, 22.8, 20.7 ppm; HRMS (ESI): *m/z* calcd for $C_{43}H_{55}NO_{13}Si+Na^+$: 844.3335 $[M+Na]^+$; found: 844.3334.

*4-Methoxyphenyl (methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-{2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl-(1→4)}-2,6-di-O-benzoyl-β-D-galactopyranosyl-(1→3)-2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-4,6-O-di-tert-butylsilylene-β-D-galactopyranoside (**12**)*

AW-300 molecular sieves (4 Å, 300 mg) were added to a solution of compounds **11** (104 mg, 77.9 μmol) and **10** (64 mg, 77.9 μmol) in CH_2Cl_2 (1.6 mL). The suspension was stirred for 30 min at 0 °C, whereupon TMSOTf (0.7 μL, 3.90 μmol) was added. Stirring was continued for 30 min at 0 °C (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/acetone, 1:1). The reaction mixture was quenched with saturated aqueous $NaHCO_3$, filtered through celite, and the 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 under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/acetone, 5:2→2:1) and column chromatography on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give compound **12** (120 mg, 77 %). $[\alpha]_D = +10.5$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.99$–7.07 (m, 20H; 4× Ph), 6.87–6.70 (m, 4H; Ar), 6.03 (d, J(2,NH) = 6.9 Hz, 1H; NHh), 5.72 (dd, $J(1,2) = 8.3$ Hz, $J(2,3) = 9.6$ Hz, 1H; H-2b), 5.61 (dd, $J(2,3) = 11.0$ Hz, $J(3,4) = 3.5$ Hz, 1H; H-3h), 5.50 (s, 1H; PhC*H*), 5.43 (d, J(2,NH) = 6.8 Hz, 1H; NHc), 5.36 (m, 1H; H-8g), 5.32 (d, $J(1,2) = 7.5$ Hz, 1H; H-1c), 5.31–5.28 (m, 2H; H-2f, H-4h), 5.21 (dd, $J(6,7) = 2.1$ Hz, $J(7,8) = 10.3$ Hz, 1H; H-7g), 5.07 (d, $J(1,2) = 8.3$ Hz, 1H; H-1h), 5.05 (d, $J(1,2) = 9.6$ Hz, 1H; NHg), 4.90–4.86 (m, 2H; H-1b, H-4g), 4.84 (d, $J(1,2) = 8.3$ Hz, 1H; H-1f), 4.70 (t, $J(2,3) = J(3,4) = 9.3$ Hz, 1H; H-3c), 4.66 (d, $J(3,4) = 3.4$ Hz, 1H; H-4b), 4.64 (dd, $J(5,6) = 8.2$ Hz, J(gem) = 11.0 Hz, 1H; H-6f), 4.29–4.20 (m, 4H; H-6b, H-6′b, H-6c, H-3f), 4.07–3.99 (m, 3H; H-6′f, H-9g, H-9g), 3.92 (t, $J(5,6) = J(5,6') = 6.9$ Hz, 1H; H-5h), 3.89–3.75 (m, 6H; H-4f, H-5g, H-6g, H-2h, H-6h, H-6h), 3.74 and 3.72 (2 s, 6H; 2× OMe), 3.70–3.68 (m, 3H; H-3b, H-4c, H-6′c), 3.55 (ddd, $J(4,5) = J(5,6) = 9.6$ Hz, $J(5,6') = 4.8$ Hz, 1H; H-5c), 3.47 (s, 1H; H-5b), 3.43 (dd, $J(5,6) = 4.2$ Hz, 1H; H-5f), 2.99 (ddd, 1H; H-2c), 2.39 (dd, $J(3_{eq},4) = 4.1$ Hz, J(gem) = 13.1 Hz, 1H; H-3g_{eq}), 2.14, 2.10, 2.01, 2.00, 1.99, and 1.92 (6 s, 18H; 6× Ac), 1.86–1.73 (m, 10H; H-3g_{ax}, 3× Ac), 1.62 (s, 3H; Ac), 1.13 and 1.08 ppm (2 s, 18H; 2× *t*Bu); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 171.2, 170.6, 170.6, 170.5, 170.4, 170.3, 170.3, 170.1, 169.6, 169.5, 168.1, 165.3, 165.1, 164.5, 155.5, 151.4, 137.1, 133.3, 133.2, 133.2, 129.9, 129.7, 129.6, 129.4, 128.7, 128.4, 128.4, 128.1, 126.1, 119.6, 114.2, 101.6, 101.3, 100.4, 100.3, 100.1, 98.0, 81.1, 81.0, 75.9, 74.5, 73.7, 72.3, 71.9, 71.4, 71.4, 70.7, 70.2, 69.9, 69.7, 69.0, 68.8, 67.1, 67.0, 66.9, 66.2, 65.5, 62.7, 62.0, 61.4, 58.6, 55.5, 52.9, 52.2, 49.0, 36.2, 27.5, 27.4, 23.5, 23.4, 23.1, 21.4, 21.2, 20.8, 20.7, 20.6, 20.5, 20.2 ppm; HRMS (ESI): *m/z* calcd for $C_{97}H_{119}N_3O_{40}Si+Na^+$: 2016.7031 $[M+Na]^+$; found: 2016.7030.

*4-Methoxyphenyl (methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-{2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl-(1→4)}-2,6-di-O-benzoyl-β-D-galactopyranosyl-(1→3)-2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosyl-(1→3)-6-O-acetyl-2-O-benzoyl-β-D-galactopyranoside (**13**)*

Compound **12** (61 mg, 30.6 μmol) was treated with a solution of tributylamine hydrofluoride (1.0 M in THF; 1.0 mL, 1.00 mmol) for 1 h at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 12:1). The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with H_2O and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 30:1→25:1) and column chromatography on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give the diol derivative. The derivative was treated with a solution of Ac_2O (2.7 μL, 28.0 μmol) and pyridine (11.5 μL, 140 μmol) in THF (930 μL). The mixture was stirred for 1 h 15 min at −20 °C, for 2.5 h at 0 °C, and for 2.5 h at room temperature (monitored by TLC analysis; $CHCl_3$/MeOH, 15:1; developed twice). Next, Ac_2O (24.3 μL, 252 μmol) and pyridine (46.0 μL, 560 μmol) were added to the mixture and stirring was continued for 84 h at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 15:1; developed twice). Then the reaction mixture was quenched with MeOH and concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 40:1→30:1, then $CHCl_3$/acetone, 3:2→1:2) to give compound **13** (43 mg, 75 %). $[\alpha]_D = -12.1$ ($c = 0.7$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.01$–7.09 (m, 20H; 4× Ph), 6.87–6.70 (m, 4H; Ar), 6.07 (d, J(2,NH) = 6.8 Hz, 1H; NHh), 5.60 (dd, $J(1,2) = 8.3$ Hz, $J(2,3) = 9.7$ Hz, 1H; H-2b), 5.57 (dd, $J(2,3) = 11.0$ Hz, $J(3,4) = 3.4$ Hz, 1H; H-3h), 5.49 (br s, 1H; NHc), 5.48 (s, 1H; PhC*H*), 5.37 (m, 1H; H-8g), 5.29 (d, 1H; H-4h), 5.28–5.25 (m, 2H; H-1c, H-2f), 5.19 (dd, $J(6,7) = 2.1$ Hz, $J(7,8) = 10.3$ Hz, 1H; H-7g), 5.10 (d, J(5,NH) = 8.3 Hz, 1H; NHg), 5.05 (d, $J(1,2) = 9.0$ Hz, 1H; H-1h), 4.89 (ddd, $J(3_{eq},4) = 4.2$ Hz, $J(3_{ax},4) = J(4,5) = 10.4$ Hz, 1H; H-4g), 4.86 (d, $J(1,2) = 8.3$ Hz, 1H; H-1f), 4.85 (d, 1H; H-1b), 4.64 (dd, $J(5,6) = 6.9$ Hz, J(gem) = 11.0 Hz, 1H; H-6c), 4.48 (t, $J(2,3) = J(3,4) = 9.3$ Hz, 1H; H-3c), 4.44 (dd, $J(5,6) = 7.6$ Hz, J(gem) = 11.7 Hz, 1H; H-6f), 4.40 (dd, $J(5,6') = 4.8$ Hz, 1H; H-6′f), 4.24–4.21 (m, 2H; H-6b, H-3f), 4.08–4.03 (m, 3H; H-4b, H-6′c, H-9g), 3.99 (dd, $J(8,9') = 5.5$ Hz, J(gem) = 12.4 Hz, 1H; H-9g), 3.95 (t, $J(5,6) = J(5,6') = 6.5$ Hz, 1H; H-5h), 3.91–3.83 (m, 4H; H-3b, H-5g, H-2h, H-6h), 3.81 (dd, 1H; H-5f), 3.79–3.74 (m, 3H; H-4f, H-6g, H-6h), 3.76 and 3.72 (2 s, 6H; 2× OMe), 3.71–3.68 (m, 2H; H-6′b, H-4c), 3.53–3.49 (m, 2H; H-5b, H-5c), 3.12 (ddd, $J(1,2) = J$(2,NH) = 8.3 Hz, 1H; H-2c), 2.86 (s, 1H; OH), 2.37 (dd, J(gem) = 13.0 Hz, 1H; H-3g_{eq}), 2.15, 2.11, 2.09, 2.00, 2.00, 1.95 and 1.92 (7 s, 21H; 7× Ac), 1.84–1.73 (m, 10H; H-3g_{ax}, 3× Ac), 1.63 ppm (s, 3H; Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 171.3, 170.9, 170.7, 170.6, 170.6, 170.4, 170.4, 170.3, 170.1, 169.8, 169.7, 168.1, 165.4, 165.0, 164.6, 155.5, 151.3, 136.9, 133.3, 133.3, 133.2, 129.9, 129.7, 129.6, 129.4, 128.8, 128.5, 128.4, 128.1, 126.1, 118.9, 114.3, 101.4, 101.0, 100.4, 100.2, 100.0, 98.1, 80.6, 80.2, 76.3, 74.8, 73.7, 72.1, 71.9, 71.7, 70.9, 70.7, 70.0, 69.8, 68.8, 68.6, 68.2, 67.1, 66.9, 66.4, 66.0, 63.1, 63.0, 62.2, 61.4, 57.8, 55.6, 53.0, 52.0, 49.0, 36.2, 23.4, 23.1, 21.8, 21.2, 20.8, 20.7, 20.7, 20.6, 20.4, 20.3 ppm; HRMS (ESI): *m/z* calcd for $C_{91}H_{105}N_3O_{41}+Na^+$: 1918.6116 $[M+Na]^+$; found: 1918.6116.

*2,3,4,6-Tetra-O-acetyl-β-D-galactopyranosyl-(1→3)-4,6-di-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-α-D-galactopyranosyl trichloroacetimidate (**15**)*

N-Bromosuccinimide (125 mg, 697 μmol) was added to a solution of compound **14** (300 mg, 348 μmol) in acetone/H_2O (3.3 mL:0.2 mL). The mixture was stirred for 15 min at room temperature (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 5:2), then the reaction mixture was extracted with $CHCl_3$ and the organic layer was washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:1→3:2) to give the 1-OH derivatives. The derivatives were treated with a solution of trichloroacetonitrile (700 μL, 6.97 mmol) and DBU (10.0 μL, 69.7 μmol) in CH_2Cl_2 (3.5 mL) for 30 min at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 25:1). The mixture was concentrated under vacuum and the residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:2→2:3) to give compound **15** (289 mg, 91 %). $[\alpha]_D = +75.0$ ($c = 0.6$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.75$ (s, 1H; C=NH), 6.57 (d, $J(1,2) = 3.5$ Hz, 1H; H-1d), 5.44 (d, $J(3,4) = 2.8$ Hz, 1H; H-4d), 5.42 (d, J(2,NH) = 7.6 Hz, 1H; NH), 5.39 (d, $J(3,4) = 3.1$ Hz, 1H; H-4e), 5.25 (dd, $J(1,2) = 8.2$ Hz, $J(2,3) = 10.3$ Hz, 1H; H-2e), 4.99 (dd, 1H; H-3e), 4.84 (d, J(gem) = 12.1 Hz, 1H; CH_2), 4.76 (d, 1H; H-1e), 4.62 (d, 1H; CH_2), 4.39 (ddd, $J(2,3) = 10.3$ Hz, 1H; H-2d), 4.31 (t, $J(5,6) = J(5,6') = 6.6$ Hz, 1H; H-5e), 4.22–4.16 (m, 4H; H-3d, H-6d, H-6′d, H-6e), 4.14–3.97 (m, 2H; H-5d, H-6′e), 2.19, 2.14, 2.10, 2.04, 2.04, and 1.98 ppm (6 s, 18H; 6× Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta =$ 170.4, 170.2, 170.1, 170.0, 169.9, 169.6, 160.3, 154.1, 99.7, 95.3, 91.0, 74.6, 71.3, 70.9, 69.8, 68.0, 67.5, 66.4, 61.7, 60.4, 50.5, 20.8, 20.7, 20.7, 20.6, 20.5 ppm; HRMS (ESI): *m/z* calcd for $C_{29}H_{36}Cl_6N_2O_{18}+Na^+$: 932.9986 $[M+Na]^+$; found: 932.9986.

*4-Methoxyphenyl 4,6-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-glucopyranosyl-(1→3)-2-O-benzoyl-β-D-galactopyranoside (**19**)*

Compound **9** (257 mg, 227 μmol) was treated with a solution of tributylamine hydrofluoride (1.0 M in THF; 2.3 mL, 2.30 mmol) for 1 h at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 20:1). The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with 2 M aqueous HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was recrystallized from $CHCl_3$/*n*-hexane to give compound **19** (210 mg, 94%). M.p. 276 °C; $[\alpha]_D = -8.0$ ($c = 0.5$, THF); ^{1}H NMR (600 MHz, [D$_6$]acetone): $\delta = 8.08$–7.33 (m, 10H; 2×Ph), 6.95 (d, J(2,NH) = 9.0 Hz, 1H; NH), 6.89–6.73 (m, 4H; Ar), 5.71 (dd, $J(1,2) = 8.2$ Hz, $J(2,3) = 9.6$ Hz, 1H; H-2b), 5.68 (s, 1H; PhC*H*), 5.24 (d, $J(1,2) = 8.3$ Hz, 1H; H-1c), 5.21 (t, $J(2,3) = J(3,4) = 9.6$ Hz, 1H; H-3c), 5.12 (d, 1H; H-1b), 4.88 (d, J(gem) = 12.3 Hz, 1H; CH_2), 4.71 (d, 1H; CH_2), 4.43 (d, J(gem) = 12.3 Hz, 1H; CH_2), 4.37 (t, $J(3,4) = J(4,OH) = 3.5$ Hz, 1H; H-4b), 4.34 (dd, $J(5,6) = 5.2$ Hz, J(gem) = 10.7 Hz, 1H; H-6c), 4.26 (dd, 1H; H-3b), 3.99 (d, 1H; OH-4b), 3.98–3.96 (m, 2H; H-6b, CH_2), 3.90–3.84 (m, 5H; H-5b, H-6′b, OH-6b, H-4c, H-6′c), 3.77 (ddd, 1H; H-2c), 3.69 (s, 3H; OMe), 3.62 ppm (ddd, $J(4,5) = J(5,6) = 9.8$ Hz, 1H; H-5c); ^{13}C NMR (150 MHz, [D$_6$]acetone): $\delta = 165.7$, 156.2, 154.8, 154.5, 152.6, 138.5, 133.8, 131.4, 130.6, 129.7, 129.3, 128.8, 127.1, 119.0, 115.1, 103.2, 101.9, 101.8, 96.8, 95.5, 81.9, 79.3, 77.4, 77.3, 76.3, 74.2, 71.9, 69.6, 69.0, 66.8, 62.1, 57.2, 55.7 ppm; HRMS (ESI): m/z calcd for $C_{39}H_{39}Cl_6NO_{16}$+Na$^+$: 1010.0292 [M+Na]$^+$; found: 1010.0292.

*4-Methoxyphenyl 4,6-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-glucopyranosyl-(1→3)-6-O-acetyl-2-O-benzoyl-β-D-galactopyranoside (**20**)*

Ac_2O (4.0 μL, 42.4 μmol) and pyridine (10.5 μL, 127 μmol) were added to a solution of compound **19** (42 mg, 42.4 μmol) in THF (850 μL). The mixture was stirred for 69 h at room temperature (monitored by TLC analysis; $CHCl_3$/MeOH, 20:1), then Ac_2O (6.0 μL, 63.6 μmol) and pyridine (5.2 μL, 63.6 μmol) were added to the mixture and stirring was continued for 81 h at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 20:1). Then, the reaction mixture was quenched with MeOH and concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/acetone, 15:1→10:1) to give compound **20** (36 mg, 83%). $[\alpha]_D = -2.5$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.06$–7.28 (m, 10H; 2×Ph), 6.83–6.65 (m, 4H; Ar), 5.83 (d, J(2,NH) = 7.6 Hz, 1H; NH), 5.69 (dd, $J(1,2) = 7.5$ Hz, $J(2,3) = 9.7$ Hz, 1H; H-2b), 5.38 (t, $J(2,3) = J(3,4) = 9.6$ Hz, 1H; H-3c), 5.33 (s, 1H; PhC*H*), 5.20 (d, $J(1,2) = 8.3$ Hz, 1H; H-1c), 4.88 (d, 1H; H-1b), 4.78 (d, J(gem) = 11.7 Hz, 1H; CH_2), 4.57 (d, 1H; CH_2), 4.46 (dd, $J(5,6) = 7.6$ Hz, J(gem) = 11.7 Hz, 1H; H-6b), 4.43 (dd, $J(5,6′) = 4.8$ Hz, 1H; H-6′b), 4.29 (dd, $J(5,6) = 4.8$ Hz, J(gem) = 11.0 Hz, 1H; H-6c), 4.21 (br s, 1H; H-4b), 4.11 (d, J(gem) = 11.7 Hz, 1H; CH_2), 4.05 (dd, $J(3,4) = 3.5$ Hz, 1H; H-3b), 3.88 (dd, 1H; H-5b), 3.79 (d, 1H; CH_2), 3.73 (dd, $J(5,6′) = 10.0$ Hz, 1H; H-6′c), 3.68 (s, 3H; OMe), 3.63–3.55 (m, 2H; H-2c, H-5c), 3.51 (t, $J(4,5) = 9.6$ Hz, 1H; H-4c), 2.94 (br s, 1H; OH), 2.09 ppm (s, 3H; Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.7$, 165.5, 155.5, 153.8, 153.8, 151.1, 136.5, 133.5, 129.9, 129.4, 129.1, 128.7, 128.3, 126.0, 118.7, 114.3, 101.5, 101.1, 100.8, 95.4, 94.2, 81.3, 78.2, 75.0, 73.5, 72.1, 70.8, 68.3, 68.3, 66.2, 63.1, 56.6, 55.5, 20.8 ppm; HRMS (ESI): m/z calcd for $C_{41}H_{41}Cl_6NO_{17}$+Na$^+$: 1052.0398 [M+Na]$^+$; found: 1052.0395.

*4-Methoxyphenyl 4,6-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-glucopyranosyl-(1→3)-{3,4,6-tri-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-β-D-galactopyranosyl-(1→4)}-6-O-acetyl-2-O-benzoyl-β-D-galactopyranoside (**22**)*

Molecular sieves (4 Å, 300 mg) were added to a solution of compounds **21** (38 mg, 65.4 μmol) and **20** (45 mg, 43.6 μmol) in CH_2Cl_2 (1.1 mL). The suspension was stirred for 30 min at −40 °C, whereupon NIS (22 mg, 98.1 μmol) and TfOH (0.9 μL, 9.8 μmol) were added. Stirring was continued for 15 min at −40 °C (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 3:2). The reaction mixture was quenched with saturated aqueous $NaHCO_3$, filtered through celite and the 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 $Na_2S_2O_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 2:3, then $CHCl_3$/acetone, 20:1→15:1) and column chromatography on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give compound **22** (59 mg, 91%). $[\alpha]_D = -10.0$ ($c = 0.5$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.07$–7.35 (m, 10H; 2×Ph), 6.89–6.73 (m, 4H; Ar), 5.96 (d, J(2,NH) = 8.9 Hz, 1H; NHd), 5.64–5.61 (m, 2H; H-2b, PhC*H*), 5.41 (d, $J(3,4) = 2.7$ Hz, 1H; H-4d), 5.28 (d, $J(1,2) = 8.2$ Hz, 1H; H-1d), 5.21 (dd, $J(2,3) = 9.6$ Hz, 1H; H-3d), 5.08–4.94 (m, 4H; H-3c, NHc, CH_2, CH_2), 4.91 (d, $J(1,2) = 8.2$ Hz, 1H; H-1b), 4.81 (d, J(gem) = 11.7 Hz, 1H; CH_2), 4.71–4.56 (m, 4H; H-1c, CH_2, CH_2), 4.43–4.40 (m, 2H; H-6c, H-6d), 4.35 (dd, $J(5,6) = 7.5$ Hz, J(gem) = 11.7 Hz, 1H; H-6′d), 4.30–4.25 (m, 2H; H-4b, H-6b), 4.20–3.98 (m, 3H; H-3b, H-6b, H-2d), 3.93 (t, $J(5,6) = J$(gem) = 10.4 Hz, 1H; H-6′c), 3.91–3.88 (m, 2H; H-5b, H-5d), 3.82 (t, $J(3,4) = J(4,5) = 9.6$ Hz, 1H; H-4c), 3.74 (s, 3H; OMe), 3.64 (q, $J(1,2) = J(2,3) = J$(2,NH) = 8.9 Hz, 1H; H-2c), 3.51 (m, 1H; H-5c), 2.21, 2.10, 2.09, and 2.02 ppm (4 s, 12H; 4×Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.9$, 170.5, 170.3, 170.3, 170.2, 164.6, 155.5, 154.9, 154.4, 154.0, 151.2, 136.4, 133.6, 129.7, 129.4, 129.3, 128.8, 128.2, 126.1, 118.8, 114.4, 102.5, 101.5, 100.8, 100.4, 96.0, 95.2, 93.9, 79.1, 78.3, 74.6, 74.6, 74.4, 73.1, 72.2, 70.8, 70.6, 70.4, 68.2, 66.5, 66.4, 63.7, 61.0, 57.0, 55.6, 52.7, 29.7, 20.9, 20.8, 20.6 ppm; HRMS (ESI): m/z calcd for $C_{56}H_{59}Cl_9N_2O_{26}$+Na$^+$: 1513.0445 [$M$+Na]$^+$; found: 1513.0445.

*4-Methoxyphenyl 4,6-O-benzylidene-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-3-O-(2,2,2-trichloroethoxycarbonyl)-β-D-glucopyranosyl-(1→3)-[{2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1→3)}-4,6-di-O-acetyl-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-β-D-galactopyranosyl-(1→4)]-6-O-acetyl-2-O-benzoyl-β-D-galactopyranoside (**23**)*

Molecular sieves (4 Å, 300 mg) were added to a solution of compounds **14** (88 mg, 102 μmol) and **20** (70 mg, 67.8 μmol) in CH_2Cl_2 (1.7 mL). The suspension was stirred for 30 min at −40 °C, whereupon NIS (34 mg, 153 μmol) and TfOH (1.4 μL, 15.3 μmol) were added. Stirring was continued for 15 min at −40 °C (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 1:1; developed twice). The reaction mixture was quenched with saturated aqueous $NaHCO_3$, filtered through celite, and the 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 $Na_2S_2O_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:1) to give compound **23** (99 mg, 82%). $[\alpha]_D = +7.0$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 8.07$–7.35 (m, 10H; 2×Ph), 6.83–6.72 (m, 4H; Ar), 5.95 (d, J(2,NH) = 9.0 Hz, 1H; NHd), 5.62–5.57 (m, 2H; H-2b, PhC*H*), 5.42 (d, $J(3,4) = 3.5$ Hz, 1H; H-4d), 5.36 (d, $J(3,4) = 2.7$ Hz, 1H; H-4e), 5.26 (d, $J(1,2) = 8.2$ Hz, 1H; H-1d), 5.21–5.12 (m, 2H; H-3c, H-2e), 5.11 (d, J(2,NH) = 8.9 Hz, 1H; NHc), 4.97–4.85 (m, 4H; H-1b, H-3e, CH_2), 4.77 (m, 3H; H-1c, H-1e, CH_2), 4.67 (d, J(gem) = 11.6 Hz, 1H; CH_2), 4.56 (d, J(gem) = 12.4 Hz, 1H; CH_2), 4.46–4.29 (m, 4H; H-4b, H-6c, H-6e, CH_2), 4.21–4.16 (m, 5H; H-5b, H-6b, H-6′b, H-3d, H-6d), 4.07 (dd, $J(5,6) = 6.9$ Hz, J(gem) = 11.0 Hz, 1H; H-6′d), 4.01 (dd, $J(2,3) = 10.3$ Hz, $J(3,4) = 2.8$ Hz, 1H; H-3b), 3.92–3.79 (m, 6H; H-4c, H-6′c, H-2d, H-5d, H-5e, H-6′e), 3.73 (s, 3H; OMe), 3.60 (q, $J(1,2) = J(2,3) = 8.9$ Hz, 1H; H-2c), 3.53 (m, 1H; H-5c), 2.19, 2.16, 2.12, 2.10, 2.09, 2.04, and 1.97 ppm (7 s, 21H; 7×Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 170.8$, 170.6, 170.3, 170.2, 170.1, 170.0, 169.9, 169.5, 164.6, 155.6, 154.7, 154.5, 153.7, 151.2, 136.3, 133.6, 129.6, 129.4, 129.3, 128.8, 128.2, 126.0, 118.8, 114.3, 102.2, 101.5, 101.3, 100.8, 99.6, 95.8, 95.2, 93.9, 79.3, 78.6, 74.8, 74.6, 74.5, 74.4, 72.5, 72.2, 71.2, 70.8, 70.8, 70.6, 68.5, 68.1, 66.7, 66.3, 63.7, 62.0, 60.7, 57.0, 55.6, 54.6, 20.9, 20.8, 20.8, 20.8, 20.6, 20.5 ppm; HRMS (ESI): m/z calcd for $C_{68}H_{75}Cl_9N_2O_{34}$+Na$^+$: 1801.1290 [$M$+Na]$^+$; found: 1801.1290.

*4-Methoxyphenyl 2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosyl-(1→3)-[[2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1→3)]-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-D-galactopyranosyl-(1→4)]-6-O-acetyl-2-O-benzoyl-β-D-galactopyranoside (**24**)*

Zinc powder (860 mg) was added to a solution of compound **23** (86 mg, 48.2 μmol) in THF (1.6 mL) and AcOH (0.4 mL) and the mixture was stirred for 40 min at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 20:1). The reaction mixture was filtered through celite and the zinc powder was washed with EtOAc. The combined filtrate and washings were extracted with EtOAc, and the organic layer was washed with saturated aqueous Na_2CO_3 and brine, dried (Na_2SO_4), concentrated under vacuum and exposed to high vacuum for 2 h. The residue was treated with a solution of Ac_2O (23 μL, 241 μmol) in CH_2Cl_2/MeOH (1.0 mL:0.5 mL) for 50 min at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 20:1; developed twice). The mixture was concentrated under vacuum and the residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 50:1→30:1) to give compound **24** (60 mg, 93%). $[\alpha]_D = -12.0$ ($c = 0.5$, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): $\delta =$ 8.04–7.36 (m, 10H; 2×Ph), 6.89–6.72 (m, 4H; Ar), 6.51 (br s, 1H; NHd), 5.67 (br s, 1H; NHc), 5.60 (dd, $J(1,2) = 8.3$ Hz, $J(2,3) = 9.7$ Hz, 1H; H-2b), 5.59 (s, 1H; PhC*H*), 5.38 (d, $J(3,4) = 3.5$ Hz, 1H; H-4d), 5.36 (d, $J(3,4) = 2.8$ Hz, 1H; H-4e), 5.23 (d, $J(1,2) = 8.2$ Hz, 1H; H-1d), 5.12 (dd, $J(1,2) = 7.5$ Hz, $J(2,3) = 10.3$ Hz, 1H; H-2e), 4.97 (dd, 1H; H-3e), 4.87 (d, 1H; H-1b), 4.74(d, 1H; H-1e), 4.64 (d, $J(1,2) = 8.3$ Hz, 1H; H-1c), 4.38–4.30 (m, 4H; H-6c, H-3d, H-6e, H-6′e), 4.22–4.19 (m, 2H; H-4b, H-6d), 4.15–4.09 (m, 3H; H-6b, H-6′b, H-6′d), 3.97–3.85 (m, 5H; H-3b, H-3c, H-2d, H-5d, H-5e), 3.82–3.78 (m, 2H; H-5b, H-6′c), 3.74 (s, 3H; OMe), 3.62 (ddd, $J(2,3) = 9.6$ Hz, $J(2,NH) = 7.6$ Hz, 1H; H-2c), 3.55 (t, $J(3,4) = J(4,5) = 9.0$ Hz, 1H; H-4c), 3.46 (ddd, $J(5,6) = 9.7$ Hz, $J(5,6') = 4.9$ Hz, 1H; H-5c), 3.25 (br s, 1H; OH), 2.16, 2.15, 2.14, 2.11, 2.10, 2.08, 2.03, 1.98, and 1.77 ppm (9 s, 27H; 9×Ac); ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 171.6$, 171.2, 170.9, 170.7, 170.6, 170.4, 170.3, 170.2, 169.6, 169.4, 155.6, 151.0, 136.7, 133.7, 129.6, 129.4, 128.8, 128.4, 126.3, 119.2, 114.4, 102.5, 102.0, 100.9, 100.8, 99.9, 81.6, 79.0, 74.6, 73.4, 72.4, 71.5, 71.0, 70.8, 70.5, 69.9, 68.7, 68.4, 66.8, 66.4, 63.8, 62.4, 60.8, 57.6, 55.6, 52.9, 23.6, 23.3, 20.9, 20.8, 20.8, 20.7, 20.7, 20.6 ppm; HRMS (ESI): m/z calcd for $C_{63}H_{76}N_2O_{30}+Na^+$: 1363.4375 $[M+Na]^+$; found: 1363.4375.

*4-Methoxyphenyl (methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-[2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl-(1→4)]-2,6-di-O-benzoyl-β-D-galactopyranosyl-(1→3)-2-acetamido-4,6-O-benzylidene-2-deoxy-β-D-glucopyranosyl-(1→3)-[[2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1→3)]-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-D-galactopyranosyl-(1→4)]-6-O-acetyl-2-O-benzoyl-β-D-galactopyranoside (**25**)*

AW-300 molecular sieves (4 Å, 600 mg) were added to a solution of compounds **11** (174 mg, 132 μmol) and **24** (118 mg, 88.0 μmol) in CH_2Cl_2 (2.2 mL). The suspension was stirred for 30 min at 0°C, whereupon TMSOTf (1.2 μL, 6.60 μmol) was added. The mixture was stirred for 3 h at 0°C (monitored by TLC analysis; $CHCl_3$/MeOH, 18:1; developed twice), TMSOTf (1.2 μL, 6.60 μmol) was added to the mixture, and stirring was continued for 1 h at 0°C (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 18:1; developed twice). The reaction mixture was quenched with saturated aqueous $NaHCO_3$, filtered through celite, and the 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 under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 25:1) and column chromatography on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give compound **25** (179 mg, 81%). $[\alpha]_D = -11.5$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3CN): $\delta = 7.95$–7.13 (m, 20H; 4×Ph), 6.90 (d, $J(2,NH) =$ 10.3 Hz, 1H; NHd), 6.83–6.75 (m, 4H; Ar), 6.35 (d, $J(2,NH) = 9.7$ Hz, 1H; NHh), 6.07 (d, $J(5,NH) = 9.7$ Hz, 1H; NHg), 5.93 (d, $J(2,NH) =$ 9.7 Hz, 1H; NHc), 5.59 (s, 1H; PhC*H*), 5.31 (d, $J(3,4) = 3.5$ Hz, 1H; H-4e), 5.29 (d, $J(3,4) = 2.7$ Hz, 1H; H-4d), 5.28 (dd, $J(1,2) = 7.6$ Hz, $J(2,3) =$ 9.7 Hz, 1H; H-2b), 5.22 (d, $J(3,4) = 3.5$ Hz, 1H; H-4h), 5.12 (dd, $J(6,7) =$ 1.4 Hz, $J(7,8) = 9.7$ Hz, 1H; H-7g), 5.11 (m, 1H; H-8g), 5.07 (dd, $J(2,3) =$ 11.6 Hz, 1H; H-3h), 5.05 (dd, $J(2,3) = 10.3$ Hz, 1H; H-3e), 5.02 (dd, $J(1,2) = 8.2$ Hz, $J(2,3) = 10.3$ Hz, 1H; H-2f), 4.97 (dd, $J(1,2) = 7.6$ Hz, 1H; H-2e), 4.94 (d, 1H; H-1b), 4.93 (m, 1H; H-4g), 4.89 (d, 1H; H-1f), 4.88 (d, $J(1,2) = 8.9$ Hz, 1H; H-1d), 4.83 (d, $J(1,2) = 8.9$ Hz, 1H; H-1h), 4.71 (d, 1H; H-1e), 4.54–4.50 (m, 2H; H-3f, H-6f), 4.44 (br s, 1H; H-1c), 4.24 (dd, $J(5,6) = 4.9$ Hz, $J(\text{gem}) = 10.4$ Hz, 1H; H-6c), 4.21–3.74 (m, 27H; H-3b, H-4b, H-5b, H-6b, H-6′b, H-2c, H-3c, H-4c, H-6′c, H-2d, H-3d, H-5d, H-6d, H-6′d, H-5e, H-6e, H-6′e, H-4f, H-6′f, H-5g, H-6g, H-9g, H-9g, H-2h, H-5h, H-6h, H-6h), 3.73 and 3.69 (2s, 6H; 2×OMe), 3.59 (t, $J(5,6) = J(5,6') = 6.2$ Hz, 1H; H-5f), 3.36 (ddd, $J(4,5) = J(5,6') = 9.0$ Hz, 1H; H-5c), 2.15–1.76 ppm (m, 56H; H-3g_{eq}, H-3g_{ax}, 18×Ac); ^{13}C NMR (150 MHz, CD_3CN): $\delta = 171.7$, 171.4, 171.2, 171.1, 171.1, 170.9, 170.9, 170.8, 170.7, 170.6, 170.5, 169.3, 166.5, 165.9, 165.3, 156.5, 152.0, 138.5, 134.4, 134.4, 134.2, 131.0, 130.7, 130.6, 130.6, 130.5, 130.2, 129.7, 129.6, 129.5, 129.4, 129.0, 127.1, 119.2, 115.4, 104.1, 103.2, 102.1, 102.1, 102.0, 101.3, 101.2, 100.2, 81.4, 80.1, 79.4, 79,1, 79.0, 78.3, 74.9, 74.1, 73.2, 72.6, 72.5, 72.2, 72.2, 71.8, 71.8, 71.6, 71.4, 71.0, 70.6, 70.3, 69.5, 69.2, 68.6, 68.2, 67.9, 67.6, 67.3, 64.4, 63.9, 63.7, 63.0, 62.2, 62.0, 56.1, 54.0, 51.3, 50.8, 48.7, 35.8, 23.6, 23.3, 23.1, 23.0, 21.4, 21.3, 21.2, 21.1, 21.1, 21.0, 20.9, 20.9, 20.8, 20.6 ppm; HRMS (ESI): m/z calcd for $C_{117}H_{140}N_4O_{57}+Na^+$: 2535.8072 $[M+Na]^+$; found: 2535.8072.

*4-Methoxyphenyl (methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-[2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-D-galactopyranosyl-(1→4)]-2,6-di-O-benzoyl-β-D-galactopyranosyl-(1→3)-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-D-glucopyranosyl-(1→3)-[[2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl-(1→3)]-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-D-galactopyranosyl-(1→4)]-6-O-acetyl-2-O-benzoyl-β-D-galactopyranoside (**26**)*

Compound **25** (82 mg, 32.6 μmol) was treated with a solution of 90% aqueous AcOH (3.3 mL) for 12 h at 60°C (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 18:1; developed three times). The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous Na_2CO_3, dried (Na_2SO_4), concentrated under vacuum, and exposed to high vacuum for 2 h. The diol derivative was treated with a solution of Ac_2O (62 μL, 652 μmol) and DMAP (1.0 mg, 8.15 μmol) in pyridine (1.1 mL). The mixture was stirred for 7 h at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 18:1; developed three times). Then the reaction mixture was quenched with MeOH and concentrated under vacuum. Then, the mixture was extracted with $CHCl_3$, and the organic layer was washed with 2M aqueous HCl and saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 30:1→25:1) to give compound **26** (79 mg, 96%). $[\alpha]_D = -10.0$ ($c = 1.3$, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3CN): $\delta = 8.06$–7.48 (m, 15H; 3×Ph), 6.83–6.75 (m, 5H; NHd, Ar), 6.32 (d, $J(2,NH) = 8.9$ Hz, 1H; NHc), 6.26 (d, $J(2,NH) = 9.6$ Hz, 1H; NHh), 6.04 (d, $J(5,NH) = 10.3$ Hz, 1H; NHg), 5.30–5.27 (m, 2H; H-2b, H-4h), 5.21–5.20 (m, 2H; H-4d, H-4e), 5.16–5.13 (m, 2H; H-7g, H-8g), 5.12 (dd, $J(2,3) = 11.0$ Hz, $J(3,4) = 3.5$ Hz, 1H; H-3h), 4.98 (d, $J(1,2) = 8.2$ Hz, 1H; H-1b), 4.97 (dd, $J(1,2) = 7.5$ Hz, $J(2,3) =$ 10.3 Hz, 1H; H-2f), 4.91–4.86 (m, 5H; H-4c, H-2e, H-3e, H-4g, H-1h), 4.76 (d, $J(1,2) = 8.9$ Hz, 1H; H-1d), 4.74 (d, 1H; H-1f), 4.53 (dd, $J(5,6) =$ 5.5 Hz, $J(\text{gem}) = 11.7$ Hz, 1H; H-6f), 4.49–4.45 (m, 3H; H-3f, H-6′f, H-1e), 4.26–4.24 (m, 2H; H-1c, H-6e), 4.19 (dd, $J(5,6) = 5.5$ Hz, $J(\text{gem}) =$ 12.3 Hz, 1H; H-6c), 4.17–4.09 (m, 4H; H-4b, H-2d, H-2h, H-6h), 4.07–3.98 (m, 9H; H-6b, H-6′c, H-6d, H-5e, H-6′e, H-5g, H-9g, H-9g, H-5h), 3.97 (d, $J(3,4) = 2.8$ Hz, 1H; H-4f), 3.94 (dd, $J(2,3) = 10.3$ Hz, $J(3,4) =$ 2.7 Hz, 1H; H-3b), 3.92–3.77 (m, 9H; H-6′b, H-2c, H-3c, H-3d, H-5d, H-6′d, H-5f, H-6g, H-6h), 3.75, and 3.70 (2 s, 6H; 2×OMe), 3.51 (t, $J(5,6) =$ $J(5,6') = 6.2$ Hz, 1H; H-5b), 3.39 (m, 1H; H-5c), 2.15–1.61 ppm (m, 62H; H-3g_{eq}, H-3g_{ax}, 20×Ac); ^{13}C NMR (150 MHz, CD_3CN): $\delta = 171.6$, 171.4, 171.4, 171.4, 171.3, 171.2, 171.2, 171.1, 170.9, 170.9, 170.9, 170.8, 170.5, 170.5, 170.4, 169.2, 167.0, 165.9, 165.4, 156,5, 152.0, 134.5, 134.5, 131.1, 130.8, 130.7, 130.6, 130.5, 130.4, 129.7, 129.6, 129.5, 119.2, 115.4, 104.0, 103.0, 102.4, 102.2, 101.3, 100.8, 100.2, 80.7, 78.5, 76.6, 75.6, 74.5, 73.2, 73.0, 72.6, 72.3, 72.2, 72.1, 72.0, 71.6, 71.5, 71.3, 71.1, 70.5, 70.4, 69.9, 69.3, 68.5, 68.1, 68.0, 67.5, 64.5, 63.3, 62.9, 62.4, 61.8, 56.1, 55.2, 54.0, 51.2, 51.0,

48.7, 35.8, 23.5, 23.3, 23.1, 21.4, 21.1, 21.1, 21.1, 21.0, 20.9, 20.9, 20.8, 20.8 ppm; HRMS (ESI): *m/z* calcd for $C_{114}H_{140}N_4O_{59}$+Na^+: 2531.7970 [*M*+Na]$^+$; found: 2531.7970.

*Methyl-5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate-(2→3)-{2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1→4)}-2,6-di-O-benzoyl-β-*D*-galactopyranosyl-(1→3)-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-*D*-glucopyranosyl-(1→3)-[{2,3,4,6-tetra-O-acetyl-β-*D*-galactopyranosyl-(1→3)}-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1→4)]-6-O-acetyl-2-O-benzoyl-α-*D*-galactopyranosyl trichloroacetimidate (**27**)*

Diammonium cerium(IV) nitrate (137 mg, 250 mmol) was added to a solution of compound **26** (63 mg, 25.0 μmol) in MeCN/toluene/H_2O (1.1 mL:0.9 mL:0.5 mL) and the mixture was stirred for 1 h at 0 °C (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 10:1). The reaction mixture was extracted with EtOAc, and the organic layer was washed with H_2O, saturated aqueous $NaHCO_3$, and brine, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 25:1→20:1) and column chromatography on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give 1-OH derivatives. The derivatives were treated with a solution of trichloroacetonitrile (64 μL, 625 μmol) and DBU (3.0 μL, 20.0 μmol) in CH_2Cl_2 (500 μL) for 30 min at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 10:1). The mixture was concentrated under vacuum and the residue was purified by column chromatography on silica gel ($CHCl_3$/acetone, 1:1) to give **27** (54 mg, 84 %). $[\alpha]_D$ = +3.6 (*c* = 0.7, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3CN): δ = 8.88 (s, 1H; C=NH), 8.10–7.45 (m, 15H; 3×Ph), 6.66 (d, *J*(2,NH) = 10.3 Hz, 1H; NHd), 6.48 (d, *J*(1,2) = 3.4 Hz, 1H; H-1b), 6.33 (d, *J*(2,NH) = 9.0 Hz, 1H; NHc), 6.26 (d, *J*(2,NH) = 9.0 Hz, 1H; NHh), 6.04 (d, *J*(5,NH) = 9.6 Hz, 1H; NHg), 5.33 (dd, *J*(2,3) = 10.3 Hz, 1H; H-2b), 5.28 (d, *J*(3,4) = 2.7 Hz, 1H; H-4h), 5.21–5.20 (m, 2H; H-4d, H-4e), 5.17–5.14 (m, 2H; H-7g, H-8g), 5.13 (dd, *J*(2,3) = 11.0 Hz, 1H; H-3h), 4.97 (dd, *J*(1,2) = 8.3 Hz, *J*(2,3) = 9.7 Hz, 1H; H-2f), 4.91–4.84 (m, 5H; H-4c, H-2e, H-3e, H-4g, H-1h), 4.78–4.75 (m, 2H; H-1d, H-1f), 4.56–4.49 (m, 3H; H-1e, H-6f, H-6′f), 4.48 (dd, *J*(3,4) = 2.8 Hz, 1H; H-3f), 4.31–4.25 (m, 3H; H-4b, H-1c, H-6e), 4.23–4.09 (m, 4H; H-3b, H-6c, H-2d, H-2h), 4.07–3.97 (m, 13H; H-6b, H-2c, H-6′c, H-6d, H-5e, H-6′e, H-4f, H-5g, H-9g, H-9g, H-5h, H-6h, H-6h), 3.88–3.77 (m, 7H; H-6′b, H-3c, H-3d, H-5d, H-6′d, H-5f, H-6g), 3.75 (s, 3H; OMe), 3.58 (t, *J*(5,6) = *J*(5,6′) = 6.6 Hz, 1H; H-5b), 3.40 (m, 1H; H-5c), 2.15–1.74 ppm (m, 62H; H-3g_{eq}, H-3g_{ax}, 20×Ac); ^{13}C NMR (150 MHz, CD_3CN): δ = 171.5, 171.4, 171.3, 171.2, 171.2, 171.1, 171.0, 170.9, 170.8, 170.5, 170.5, 170.4, 169.2, 167.0, 166.1, 165.4, 160.8, 134.6, 134.5, 134.4, 131.2, 130.8, 130.7, 130.5, 130.5, 130.4, 130.1, 129.7, 129.7, 129.6, 129.5, 104.2, 103.1, 102.4, 102.2, 100.9, 100.2, 94.6, 91.7, 78.5, 78.4, 77.9, 76.8, 76.2, 74.5, 73.0, 72.7, 72.3, 72.3, 72.2, 72.0, 72.0, 71.6, 71.3, 71.1, 70.5, 70.4, 69.8, 69.3, 69.3, 68.5, 68.1, 68.0, 67.5, 64.8, 64.4, 63.3, 63.0, 62.5, 61.8, 55.2, 54.0, 51.3, 51.0, 48.7, 35.9, 23.4, 23.3, 23.3, 23.1, 21.4, 21.1, 21.1, 21.0, 21.0, 20.9, 20.9, 20.8, 20.8 ppm; HRMS (ESI): *m/z* calcd for $C_{109}H_{134}Cl_3N_3O_{58}$+$Na^+$: 2568.6648 [*M*+Na]$^+$; found: 2568.6648.

*Phenyl 2-O-benzoyl-3,6-di-O-4-methoxybenzyl-1-thio-β-*D*-glucopyranoside (**29**)*

Dibutyltin (IV) oxide (3.02 g, 12.1 mmol) was added to a solution of **28** (5.02 g, 10.1 mmol) in toluene (101 mL). The mixture was stirred for 6 h under reflux conditions, then 4-methoxybenzyl chloride (1.6 mL, 12.1 mmol) and tetrabutylammonium bromide (3.26 g, 10.1 mmol) were added to the reaction mixture at room temperature. The mixture was stirred for 13 h under reflux conditions (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 1:1), then triethylamine was added and the mixture was concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 150:1). And the residue was recrystallized from EtOAc/*n*-hexane to give **29** (5.16 g, 83 %). M.p. 104 °C; $[\alpha]_D$ = +19.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.05–6.68 (m, 18H; 2 Ph, 2 Ar), 5.53 (t, *J*(1,2) = *J*(2,3) = 9.2 Hz, 1H; H-2), 4.79 (d, 1H; H-1), 4.64 (d, *J*(gem) = 11.2 Hz, 1H; CH_2), 4.58 (d, 1H; CH_2), 4.54 (d, *J*(gem) = 11.5 Hz, 1H; CH_2), 4.50 (d, 1H; CH_2), 3.82 (s, 3H; OMe), 3.80–3.73 (m, 3H; H-4, H-6, H-6′), 3.71 (s, 3H; OMe), 3.67 (t, *J*(3,4) = 9.2 Hz, 1H; H-3), 3.58 (ddd, *J*(4,5) = *J*(5,6) = 9.2 Hz, *J*(5,6′) = 4.6 Hz, 1H; H-5), 2.72 ppm (s, 1H; OH); ^{13}C NMR (150 MHz, $CDCl_3$): δ = 165.2, 159.3, 159.2, 133.2, 133.0, 132.3, 130.0, 129.9, 129.7, 129.4, 128.8, 128.4, 127.7, 113.8, 113.8, 86.4, 83.2, 78.3, 74.3, 73.4, 72.1, 72.0, 70.1, 55.3, 55.1 ppm; HRMS (ESI): *m/z* calcd for $C_{35}H_{36}O_8S$+Na^+: 639.2023 [*M*+Na]$^+$; found: 639.2023.

*Phenyl 2-O-benzoyl-4-O-tert-butyldimethylsilyl-3,6-di-O-4-methoxybenzyl-1-thio-β-*D*-glucopyranoside (**30**)*

2,6-Lutidine (283 μL, 2.43 mmol) and TBSOTf (280 μL, 1.22 mmol) were added to a solution of **29** (500 mg, 811 μmol) in CH_2Cl_2 (2.7 mL). The mixture was stirred for 1 h at room temperature (monitored by TLC analysis; EtOAc/*n*-hexane, 1:3), 2,6-lutidine (190 μL, 1.62 mmol) and TBSOTf (186 μL, 811 μmol) were added to the mixture and stirring was continued for 20 min at room temperature (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 1:3). Then the reaction mixture was quenched with MeOH. The mixture was extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane, 1:7) to give **30** (572 mg, 97 %). $[\alpha]_D$ = +60.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99–6.62 (m, 18H; 2 Ph, 2 Ar), 5.27 (t, *J*(1,2) = *J*(2,3) = 9.2 Hz, 1H; H-2), 4.82 (d, 1H; H-1), 4.60–4.53 (m, 3H; CH_2, CH_2), 4.46 (d, *J*(gem) = 11.4 Hz, 1H; CH_2), 3.81 (s, 3H; OMe), 3.79 (m, 1H; H-6), 3.71–3.57 (m, 7H; H-3, H-4, H-5, H-6′, OMe), 0.86 (s, 9H; *t*Bu), 0.01 ppm (s, 6H; 2 Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.2, 159.1, 158.8, 133.6, 133.1, 131.9, 130.5, 130.0, 129.9, 129.8, 129.2, 128.7, 128.3, 127.4, 113.7, 113.4, 86.2, 84.4, 80.9, 74.8, 73.1, 72.8, 71.2, 69.2, 55.3, 55.0, 25.9, 18.0, −3.7, −4.7 ppm; HRMS (ESI): *m/z* calcd for $C_{41}H_{50}O_8SSi$+Na^+: 753.2888 [*M*+Na]$^+$; found: 753.2889.

*2-O-Benzoyl-4-O-tert-butyldimethylsilyl-3,6-di-O-4-methoxybenzyl-α-*D*-glucopyranosyl trichloroacetimidate (**31**)*

N-Bromosuccinimide (75 mg, 417 μmol) was added to a solution of **30** (203 mg, 278 μmol) in acetone (2.7 mL)/H_2O (0.1 mL). The mixture was stirred for 15 min at room temperature (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 1:3), then the reaction mixture was extracted with EtOAc and the organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/toluene, 1:7) to give the 1-OH derivatives. The derivatives were treated with a solution of trichloroacetonitrile (560 μL, 5.56 mmol) and DBU (50.0 μL, 334 μmol) in CH_2Cl_2 (2.8 mL) for 45 min at room temperature (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/acetone, 20:1). The mixture was concentrated under vacuum and the residue was purified by column chromatography on silica gel ($CHCl_3$/acetone, 70:1→60:1) to give compound **31** (180 mg, 83 %). $[\alpha]_D$ = +93.0 (*c* = 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.46 (s, 1H; C=NH), 7.92–6.63 (m, 13H; Ph, 2×Ar), 6.59 (d, *J*(1,2) = 3.5 Hz, 1H; H-1), 5.35 (dd, *J*(2,3) = 9.7 Hz, 1H; H-2), 4.69 (s, 2H; CH_2), 4.54 (d, *J*(gem) = 11.4 Hz, 1H; CH_2), 4.46 (d, 1H; CH_2), 4.03, (t, *J*(3,4) = 9.7 Hz, 1H; H-3), 3.99 (m, 1H; H-5), 3.90 (t, *J*(3,4) = 9.7 Hz, 1H; H-4), 3.81 (s, 3H; OMe), 3.71–3.69 (m, 5H; H-6, H-6′, OMe), 0.88 (s, 9H; *t*Bu), 0.05 ppm (s, 6H; 2×Me); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.4, 160.6, 159.1, 158.8, 133.2, 130.2, 130.2, 129.7, 129.3, 129.2, 129.0, 128.3, 113.7, 113.4, 94.1, 91.1, 79.6, 75.0, 74.7, 73.0, 72.9, 70.4, 68.1, 55.2, 55.1, 26.0, 18.1, −3.7, −4.9 ppm; HRMS (ESI): *m/z* calcd for $C_{37}H_{46}Cl_3NO_9Si$+Na^+: 804.1900 [*M*+Na]$^+$; found: 804.1900.

*2-O-Benzoyl-4-O-tert-butyldimethylsilyl-3,6-di-O-4-methoxybenzyl-β-*D*-glucopyranosyl-(1→1)-(2*S*,3*R*,4*E*)-3-O-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (**33**)*

AW-300 molecular sieves (4 Å, 200 mg) were added to a solution of compounds **31** (47 mg, 60.0 μmol) and **32** (40 mg, 60.0 μmol) in CH_2Cl_2 (1.2 mL). The suspension was stirred for 30 min at room temperature, whereupon TMSOTf (1.1 μL, 6.00 μmol) was added. Stirring was continued for 30 min at room temperature (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 1:3; developed twice). The reaction mixture was filtered through celite and the 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 under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/toluene, 1:10) and column chromatography on Sephadex LH-20 ($CHCl_3$/MeOH, 1:1) to give compound **33** (61 mg, 78%). $[\alpha]_D = +30.0$ ($c = 1.0$, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 8.04$–7.39 (m, 10H; 2 Ph), 7.17–6.63 (m, 8H; 2×Ar), 5.83 (dt, $J(4,5) = 14.9$ Hz, $J(5,6) = J(5,6') = 6.9$ Hz, 1H; H-5^{Cer}), 5.78 (d, $J(2,NH) = 9.2$ Hz, 1H; NH), 5.54 (t, $J(2,3) = J(3,4) = 7.4$ Hz, 1H; H-3^{Cer}), 5.46 (dd, 1H; H-4^{Cer}), 5.23 (t, $J(1,2) = J(2,3) = 8.0$ Hz, 1H; H-2a), 4.61 (d, $J(gem) = 10.8$ Hz, 1H; CH_2), 4.57 (d, 1H; CH_2), 4.52 (d, 1H; H-1a), 4.43–4.39 (m, 2H; H-2^{Cer}, CH_2), 4.28 (d, $J(gem) = 12.0$ Hz, 1H; CH_2), 4.14 (dd, $J(1,2) = 2.8$ Hz, $J(gem) = 9.7$ Hz, 1H; H-1^{Cer}), 3.80 and 3.70 (2 s, 6H; 2×OMe), 3.69–3.63 (m, 3H; H-3a, H-4a, H-6a), 3.60 (dd, $J(1',2) = 3.4$ Hz, 1H; H-1$'^{Cer}$), 3.51–3.45 (m, 2H; H-5a, H-6′a), 1.99 (m, 2H; H-6^{Cer}, H-6$'^{Cer}$), 1.72 (m, 2H; NHCOCH_2), 1.44–1.09 (m, 52H; 26×CH_2), 0.90 (t, $J(gem) = 6.9$ Hz, 6H; 2×CH_3), 0.85 (s, 9H; *t*Bu), 0.02 and 0.02 ppm (2 s, 6H; 2×Me); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 172.7$, 165.3, 165.2, 159.1, 158.8, 137.1, 133.2, 132.8, 130.4, 130.1, 129.7, 129.6, 129.2, 129.1, 128.4, 128.3, 124.9, 113.7, 113.4, 100.7, 82.8, 74.5, 74.5, 73.1, 71.1, 68.9, 66.9, 55.2, 55.0, 50.5, 36.4, 32.3, 31.9, 29.7, 29.7, 29.6, 29.6, 29.5, 29.4, 29.4, 29.3, 29.2, 29.0, 25.9, 25.5, 22.7, 17.9, 14.1, −3.8, −4.8 ppm; HRMS (ESI): *m*/*z* calcd for $C_{78}H_{119}NO_{12}Si+Na^+$: 1312.8394 $[M+Na]^+$; found: 1312.8395.

*2-O-Benzoyl-3,6-di-O-4-methoxybenzyl-β-*D*-glucopyranosyl-(1→1)-(2S,3R,4E)-3-O-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (**34**)*

TBAF (1.0 M in THF; 140 μL, 140 μmol) and AcOH (2.7 μL, 46.5 μmol) were added to a solution of compound **33** (60 mg, 46.5 μmol) in THF (930 μL) and the mixture was stirred for 2.5 h at room temperature (completion of the reaction was confirmed by TLC analysis; EtOAc/*n*-hexane, 2:3). The reaction mixture was extracted with EtOAc, and the organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel (EtOAc/*n*-hexane >, 2:3) to give compound **34** (52 mg, 95%).

The spectropic data of compound **34** were indentical to those reported previously.[5a]

*Methyl-5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate-(2→3)-{2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1→4)}-2,6-di-O-benzoyl-β-*D*-galactopyranosyl-(1→3)-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-*D*-glucopyranosyl-(1→3)-[{2,3,4,6-tetra-O-acetyl-β-*D*-galactopyranosyl-(1→3)}-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1→4)]-6-O-acetyl-2-O-benzoyl-β-*D*-galactopyranosyl-(1→4)-2-O-benzoyl-3,6-di-O-4-methoxybenzyl-β-*D*-glucopyranosyl-(1→1)-(2S,3R,4E)-3-O-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (**35**)*

AW-300 molecular sieves (4 Å, 200 mg) were added to a solution of compounds **27** (50 mg, 19.6 μmol) and **34** (35 mg, 29.4 μmol) in $CHCl_3$ (700 μL). The suspension was stirred for 30 min at 0 °C, whereupon TMSOTf (0.55 μL, 2.94 μmol) was added. Stirring was continued for 1 h at 0 °C (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 20:1). The reaction mixture was quenched with saturated aqueous $NaHCO_3$, filtered through celite and the molecular sieves were washed with $CHCl_3$. The combined filtrate and washings were extracted with $CHCl_3$, and the organic layer was washed with brine, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 30:1) to give compound **35** (58 mg, 83%). $[\alpha]_D = -7.0$ ($c = 0.5$, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3CN): $\delta = 8.07$–7.41 (m, 25H; 5×Ph), 7.24–6.63 (m, 9H; NHd, 2×Ar), 6.26 (d, $J(2,NH) = 8.9$ Hz, 1H; NHc), 6.26 (d, $J(2,NH) = 8.9$ Hz, 1H; NHh), 6.07 (d, $J(2,NH) = 8.9$ Hz, 1H; NH^{Cer}), 6.04 (d, $J(5,NH) = 9.6$ Hz, 1H; NHg), 5.61 (dt, $J(4,5) = 14.5$ Hz, $J(5,6) = J(5,6') = 7.1$ Hz, 1H; H-5^{Cer}), 5.37–5.33 (m, 2H; H-3^{Cer}, H-4^{Cer}), 5.27 (d, $J(3,4) = 2.7$ Hz, 1H; H-4h), 5.21 (d, $J(3,4) = 3.5$ Hz, 1H; H-4d), 5.18 (d, $J(3,4) = 1.4$ Hz, 1H; H-4e), 5.16–5.10 (m, 4H; H-2b, H-7g, H-8g, H-3h), 4.98 (dd, $J(1,2) = 7.6$ Hz, $J(2,3) = 9.6$ Hz, 1H; H-2f), 4.92 (dd, $J(1,2) = 8.2$ Hz, $J(2,3) = 9.7$ Hz, 1H; H-2a), 4.89–4.80 (m, 5H; H-4c, H-2e, H-3e, H-4g, H-1h), 4.75 (d, $J(1,2) = 8.3$ Hz, 1H; H-1d), 4.75 (d, 1H; H-1f), 4.70 (d, $J(gem) = 10.3$ Hz, 1H; CH_2), 4.57 (dd, $J(5,6) = 4.8$ Hz, $J(gem) = 11.7$ Hz, 1H; H-6f), 4.51 (d, $J(1,2) = 8.2$ Hz, 1H; H-1b), 4.48–4.43 (m, 5H; H-1a, H-1e, H-3f, H-6′f, CH_2), 4.39 (d, 1H; CH_2), 4.29–4.25 (m, 2H; H-6e, H-2^{Cer}), 4.22–4.08 (m, 8H; H-4b, H-1c, H-6c, H-2d, H-2h, H-6h, H-6h, CH_2), 4.06–3.95 (m, 8H; H-6b, H-6d, H-5e, H-6′e, H-4f, H-5g, H-9g, H-5h), 3.90–3.87 (m, 2H; H-4a, H-2c), 3.83–3.76 (m, 15H; H-6′b, H-6′c, H-3d, H-5d, H-6′d, H-5f, H-6g, H-9g, H-1^{Cer}, 2×OMe), 3.70–3.68 (m, 4H; H-3b, OMe), 3.63–3.59 (m, 3H; H-3a, H-3c, H-5c), 3.51–3.48 (m, 2H; H-5b, H-1$'^{Cer}$), 3.45 (dd, $J(5,6) = 3.9$ Hz, $J(gem) = 10.7$ Hz, 1H; H-6a), 3.30 (d, 1H; H-6′a), 3.19 (m, 1H; H-5a), 2.15–1.74 (m, 66H; H-3g$_{eq}$, H-3g$_{ax}$, H-6^{Cer}, H-6$'^{Cer}$, NHCOCH_2, 20×Ac), 1.39–1.07 (m, 52H; 26×CH_2), 0.87 ppm (t, $J = 6.9$ Hz, 6H; 2×CH_3); ^{13}C NMR (150 MHz, CD_3CN): $\delta = 173.3$, 171.5, 171.4, 171.4, 171.3, 171.2, 171.2, 171.1, 171.1, 171.0, 171.0, 170.9, 170.9, 170.8, 170.8, 170.4, 170.4, 169.2, 167.0, 166.1, 165.9, 165.5, 165.5, 160.3, 160.0, 137.5, 134.5, 134.4, 134.3, 134.0, 131.6, 131.4, 131.1, 130.9, 130.9, 130.7, 130.6, 130.5, 130.4, 129.8, 129.7, 129.6, 129.4, 125.4, 114.8, 114.1, 103.9, 103.0, 102.4, 102.4, 102.2, 101.4, 100.8, 100.2, 80.9, 80.8, 78.5, 78.5, 76.6, 76.5, 75.7, 75.4, 75.3, 74.7, 74.5, 73.9, 73.5, 73.0, 72.9, 72.7, 72.3, 72.3, 72.2, 72.1, 72.0, 71.6, 71.3, 71.1, 70.6, 70.4, 70.0, 69.3, 68.5, 68.3, 68.2, 68.1, 68.0, 67.5, 64.6, 64.5, 63.6, 63.3, 63.0, 62.4, 61.8, 56.0, 55.7, 54.0, 51.4, 51.0, 48.7, 36.7, 35.9, 32.8, 32.6, 30.4, 30.2, 30.1, 30.1, 29.8, 29.5, 26.4, 23.5, 23.4, 23.3, 23.1, 21.4, 21.2, 21.1, 21.0, 20.9, 20.8, 20.8, 14.4 ppm; HRMS (ESI): *m*/*z* calcd for 1/2 ($C_{179}H_{237}N_5O_{69}$)+Na$^+$: 1803.2487 $[1/2M+Na]^+$; found: 1803.2487.

*Methyl 5-acetamido-4,7,8,9-tetra-O-acetyl-3,5-dideoxy-*D*-glycero-α-*D*-galacto-2-nonulopyranosylonate-(2→3)-{2-acetamido-3,4,6-tri-O-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1→4)}-2,6-di-O-benzoyl-β-*D*-galactopyranosyl-(1→3)-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-*D*-glucopyranosyl-(1→3)-[{2,3,4,6-tetra-O-acetyl-β-*D*-galactopyranosyl-(1→3)}-2-acetamido-4,6-di-O-acetyl-2-deoxy-β-*D*-galactopyranosyl-(1→4)]-6-O-acetyl-2-O-benzoyl-β-*D*-galactopyranosyl-(1→4)-2-O-benzoyl-β-*D*-glucopyranosyl-(1→1)-(2S,3R,4E)-3-O-benzoyl-2-octadecanamido-4-octadecene-1,3-diol (**36**)*

TFA (200 μL) was added to a solution of compound **35** (22.5 mg, 6.32 μmol) in CH_2Cl_2 (400 μL) and the mixture was stirred for 40 min at 0 °C (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH, 15:1; developed twice). The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with saturated aqueous Na_2CO_3 and brine, dried (Na_2SO_4), and concentrated under vacuum. The residue was purified by column chromatography on silica gel ($CHCl_3$/MeOH, 80:1→20:1) to give compound **36** (20.6 mg, 98%). $[\alpha]_D = -6.0$ ($c = 2.0$, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3CN): $\delta = 8.07$–7.42 (m, 25H; 5×Ph), 6.71 (d, $J(2,NH) = 10.3$ Hz, 1H; NHd), 6.25 (d, $J(2,NH) = 8.9$ Hz, 1H; NHc), 6.25 (d, $J(2,NH) = 8.9$ Hz, 1H; NHh), 6.09 (d, $J(2,NH) = 8.9$ Hz, 1H; NH^{Cer}), 6.04 (d, $J(5,NH) = 10.3$ Hz, 1H; NHg), 5.62 (m, 1H; H-5^{Cer}), 5.40–5.36 (m, 2H; H-3^{Cer}, H-4^{Cer}), 5.27 (d, $J(3,4) = 2.8$ Hz, 1H; H-4h), 5.20 (br s, 1H; H-4e), 5.19 (d, $J(3,4) = 3.4$ Hz, 1H; H-4d), 5.17–5.10 (m, 4H; H-2b, H-7g, H-8g, H-3h), 4.96 (dd, $J(1,2) = 8.2$ Hz, $J(2,3) = 9.6$ Hz, 1H; H-2f), 4.91 (dd, $J(1,2) = 7.9$ Hz, $J(2,3) = 9.3$ Hz, 1H; H-2a), 4.89–4.83 (m, 5H; H-4c, H-2e, H-3e, H-4g, H-1h), 4.73 (d, 1H; H-1f), 4.68 (d, $J(1,2) = 9.7$ Hz, 1H; H-1d), 4.66 (d, $J(1,2) = 8.2$ Hz, 1H; H-1b), 4.57 (d, 1H; H-1a), 4.54 (dd, $J(5,6) = 4.9$ Hz, $J(gem) = 11.7$ Hz, 1H; H-6f), 4.48–4.45 (m, 3H; H-1e, H-3f, H-6′f), 4.39 (d, $J(3,OH) = 2.1$ Hz, 1H; OH_{3a}), 4.35 (m, 1H; H-2^{Cer}), 4.26–3.97 (m, 16H; H-4b, H-6b, H-1c, H-6c, H-6′c, H-2d, H-6d, H-5e, H-6e, H-6′e, H-4f, H-5g, H-9g, H-2h, H-5h, H-6h), 3.92–3.89 (m, 3H; H-3b, H-2c, H-6h), 3.87–3.73 (m, 13H; H-3a, H-6′b, H-3c, H-3d, H-5d, H-6′d, H-5f, H-6g, H-9g, H-1^{Cer}, OMe), 3.56–3.50 (m, 3H; H-4a, H-5b, H-1$'^{Cer}$), 3.39 (m, 1H; H-5c), 3.28 (m, 1H; H-5a), 3.18 (m, 1H; H-6a), 3.12 (m, 1H; H-6′a), 2.56 (br t, 1H; OH_{6a}), 2.15–1.74 (m, 66H; H-3g$_{eq}$, H-3g$_{ax}$, H-6^{Cer}, H-6$'^{Cer}$, NHCOCH_2, 20×Ac), 1.41–1.10 (m, 52H; 26×CH_2), 0.88 ppm (t, $J = 6.9$ Hz, 6H; 2×CH_3); ^{13}C NMR (150 MHz, CD_3CN): $\delta = 173.5$, 171.5, 171.5, 171.4, 171.3, 171.3, 171.2, 171.2, 171.2, 171.1, 171.0, 170.9, 170.9, 170.8, 170.8, 170.5, 170.5, 170.4, 169.2, 167.0, 166.3, 166.1, 165.8, 165.5, 137.8, 134.5, 134.5, 134.2, 134.1, 131.3, 131.2, 131.0, 130.9, 130.8, 130.5, 130.5, 130.4, 130.3, 129.8, 129.6, 129.6, 129.4, 125.1, 103.9, 103.1, 102.8, 102.5, 102.2, 101.1, 100.8, 100.2,

82.8, 80.6, 78.6, 78.5, 76.7, 75.4, 75.3, 74.6, 74.5, 74.1, 73.1, 73.0, 72.7, 72.3, 72.2, 72.1, 72.0, 71.6, 71.4, 71.3, 71.1, 70.4, 69.9, 69.3, 68.5, 68.4, 68.1, 68.0, 67.5, 64.5, 64.3, 63.2, 63.0, 62.5, 61.8, 61.2, 55.1, 54.0, 51.4, 51.2, 51.0, 48.7, 36.8, 35.9, 32.8, 32.6, 30.4, 30.3, 30.2, 30.1, 30.1, 29.8, 29.5, 26.5, 23.5, 23.4, 23.3, 23.2, 23.1, 21.4, 21.1, 21.0, 20.9, 20.8, 20.8, 20.7, 14.4 ppm; HRMS (ESI): *m*/*z* calcd for 1/2 ($C_{163}H_{221}N_5O_{67}$)+Na^+: 1683.1912 $[1/2M+Na]^+$; found: 1683.1912.

*Ganglioside X2 (**2**)*

A solution of sodium methoxide (28% in MeOH, 1.0 mg) was added to a solution of compound **36** (49.8 mg, 15.0 μmol) in MeOH (1.0 mL). The mixture was stirred for 75 h at room temperature (monitored by TLC analysis; $CHCl_3$/MeOH/12 mM $MgCl_2$ (aq.), 5:4:1), H_2O was added to the mixture, and stirring was continued for 93 h at 40 °C (monitored by TLC analysis; $CHCl_3$/MeOH/12 mM $MgCl_2$ (aq.), 5:4:1). Then 0.2 M NaOH (aq.) was added to the mixture and stirring was continued for 72 h at 40 °C (completion of the reaction was confirmed by TLC analysis; $CHCl_3$/MeOH/12 mM $MgCl_2$ (aq.), 5:4:1). After neutralization with Dowex-50 (H^+), the mixture was filtered through cotton wool, and the resin was washed with MeOH. The combined filtrate and washings were concentrated under vacuum. The residue was purified by column chromatography on Sephadex LH-20 (MeOH) and column chromatography on Iatrobeads 6RS-8060 ($CHCl_3$/MeOH/H_2O, 5:4:0.8→5:4:1) to give compound **2** (30.6 mg, 97%). $[\alpha]_D = -3.0$ ($c = 0.5$, MeOH); ^{1}H NMR (600 MHz, CD_3OD): $\delta = 5.68$ (dt, $J(4,5) = 15.2$ Hz, $J(5,6) = J(5,6') = 6.9$ Hz, 1H; H-5^{Cer}), 5.44 (dd, $J(3,4) = 7.6$ Hz, 1H; H-4^{Cer}), 4.94 (d, $J = 9.0$ Hz, 1H; anomeric H), 4.86–4.85 (m, 1H; anomeric H), 4.60 (d, $J = 8.9$ Hz, 1H; anomeric H), 4.49 (d, $J = 7.6$ Hz, 1H; anomeric H), 4.44 (d, $J = 8.3$ Hz, 1H; anomeric H), 4.32 (d, $J = 8.3$ Hz, 1H; anomeric H), 4.29 (d, $J = 7.5$ Hz, 1H; anomeric H), 2.75 (dd, $J(3_{eq},4) = 4.9$ Hz, J(gem) = 12.4 Hz, 1H; H-3g$_{eq}$), 2.16 (t, $J = 7.6$ Hz, 2H; NHCOCH_2), 2.02–1.99 (m, 14H; H-6^{Cer}, H-6′^{Cer}, 4×Ac), 1.89 (t, $J(3_{ax},4) = 12.4$ Hz, 1H; H-3g$_{ax}$), 1.57 (m, 2H; NHCOCH$_2$CH_2), 1.39 (m, 2H; H-7^{Cer}, H-7′^{Cer}), 1.33–1.29 (m, 48H; 24×CH_2), 0.90 ppm (t, $J = 6.9$ Hz, 6H; 2×CH_3); ^{13}C NMR (150 MHz, CD_3OD): $\delta = 175.9$, 175.7, 175.0, 174.7, 174.7, 135.1, 131.4, 106.4, 105.3, 104.6, 104.4, 104.3, 104.1, 103.3, 103.2, 84.4, 83.2, 81.9, 80.9, 78.9, 77.7, 76.7, 76.7, 76.5, 76.5, 76.3, 76.1, 76.0, 75.9, 75.9, 75.1, 74.9, 74.6, 74.3, 73.3, 73.0, 72.6, 71.3, 70.8, 70.4, 70.1, 70.0, 69.9, 69.6, 65.4, 63.1, 62.9, 62.8, 62.4, 62.0, 61.9, 61.7, 55.9, 54.7, 54.3, 53.8, 52.7, 49.6, 38.8, 37.4, 33.5, 33.1, 33.1, 30.9, 30.8, 30.8, 30.8, 30.7, 30.6, 30.5, 30.5, 30.4, 27.2, 23.8, 23.6, 23.6, 22.6, 14.5 ppm; HRMS (ESI): *m*/*z* calcd for $C_{95}H_{167}N_5O_{46}$-H: 2113.0809 $[M-H]^-$; found: 2113.0810.

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[1] N. Yuki, S. Sato, T. Miyatake, K. Sugiyama, T. Katagiri, H. Sasaki, *Lancet* **1991**, *337*, 1109–1110.
[2] N. Yuki, T. Miyatake, Y. Ichihashi, S. Sato, T. Katagiri, *Muscle Nerve* **1992**, *15*, 1371–1373.
[3] T. Nakao, K. Kon, S. Ando, T. Miyatake, N. Yuki, Y.-T. Li, S. Furuya, Y. Hirabayashi, *J. Biol. Chem.* **1993**, *268*, 21028–21034.
[4] S. Nakashima, H. Ando, A. Imamura, N. Yuki, H. Ishida, M. Kiso, *Chem. Eur. J.* **2011**, *17*, 588–597.
[5] a) A. Imamura, H. Ando, H. Ishida, M. Kiso, *J. Org. Chem.* **2009**, *74*, 3009–3023; b) K. Fujikawa, T. Nohara, A. Imamura, H. Ando, H. Ishida, M. Kiso, *Tetrahedron Lett.* **2010**, *51*, 1126–1130; c) K. Fujikawa, S. Nakashima, M. Konishi, T. Fuse, N. Komura, T. Ando, H. Ando, N. Yuki, H. Ishida, M. Kiso, *Chem. Eur. J.* **2011**, *17*, 5641–5651.
[6] T. Fuse, H. Ando, A. Imamura, S. Sawada, H. Ishida, M. Kiso, T. Ando, S.-C. Li, Y.-T. Li, *Glycoconjugate J.* **2006**, *23*, 329–343.
[7] J.-C. Jacquinet, *Carbohydr. Res.* **2006**, *341*, 1630–1644.
[8] K. Furusawa, *Chem. Lett.* **1989**, 509–510.
[9] T. Yoshikawa, Y. Kato, N. Yuki, T. Yabe, H. Ishida, M. Kiso, *Glycoconjugate J.* **2008**, *25*, 545–553.
[10] a) P. Konradsson, U. E. Udodong, B. Fraser-Reid, *Tetrahedron Lett.* **1990**, *31*, 4313–4316; b) P. Konradsson, D. R. Mootoo, R. E. McDevitt, B. Fraser-Reid, *J. Chem. Soc. Chem. Commun.* **1990**, 270–272; c) G. H. Veeneman, S. H. Van Leeuwen, J. H. Van Boom, *Tetrahedron Lett.* **1990**, *31*, 1331–1334.
[11] M. Nitz, D. R. Bundle, *J. Org. Chem.* **2000**, *65*, 3064–3073.
[12] Y. Matsuzaki, Y. Ito, Y. Nakahara, T. Ogawa, *Tetrahedron Lett.* **1993**, *34*, 1061–1064.
[13] a) K. K. Sadozai, T. Nukada, Y. Ito, Y. Nakahara, T. Ogawa, *Carbohydr. Res.* **1986**, *157*, 101–123; b) T. Ogawa, M. Sugimoto, T. Kitajima, K. K. Sadozai, T. Nukada, *Tetrahedron Lett.* **1986**, *27*, 5739–5742.
[14] K. Fujikawa, A. Imamura, H. Ishida, M. Kiso, *Carbohydr. Res.* **2008**, *343*, 2729–2734.
[15] a) M. Kiso, A. Nakamura, Y. Tomita, A. Hsegawa, *Carbohydr. Res.* **1986**, *158*, 101–111; b) M. Kiso, A. Nakamura, J. Nakamura, Y. Tomita, A. Hsegawa, *J. Carbohydr. Chem.* **1986**, *5*, 335–340.
[16] H. Shimizu, Y. Iwayama, A. Imamura, H. Ando, H. Ishida, M. Kiso, *Biosci. Biotechnol. Biochem.* **2011**, *75*, 2079-2082.

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