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Study on systematizing the synthesis of the a-series ganglioside glycans GT1a, GD1a, and GM1 using the newly developed *N*-Troc-protected GM3 and GalN intermediates ☆

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Dedicated to Professor Dr. Hans Kamerling on the occasion of his 65th birthday

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ABSTRACT

A first systematic synthesis of the glycan parts of the a-series gangliosides (GT1a, GD1a, and GM1) utilizing the newly developed *N*-Troc-protected GM3 and galactosaminyl building blocks is described. The key processes, including the assembly of the GM2 sequence and its conversion into the 3-hydroxy acceptor, were facilitated mainly by the high degree of participation and chemoselective cleavability of the Troc group in the galactosaminyl unit. Furthermore, the novel GM2 acceptor served as a good coupling partner during glycosylation with galactosyl, sialyl galactosyl, and disialyl galactosyl donors, successfully producing the GM1, GD1a, and GT1a glycans.

1. Introduction

There has been explosive growth in the field of glycobiology in the last two decades. The surfaces of animal cells are covered with glycolipids whose oligosaccharide chains are positioned outermost from the cell surface and often function as recognition molecules. Among the glycolipids, glycosphingolipids (GSLs) are the most abundant and intriguing molecules. GSLs contribute to the glycocalyx of the cell and provide binding sites for toxins, viruses, and bacteria, as well as mediate cell adhesion processes and other intercellular communication events. Gangliosides are distinguished from other GSLs by containing one or more sialic acid residues, which are considered as crucial structural and/or electronic elements for interplay with biological molecules or receptors on cells. Since gangliosides are extremely minor constituents in living organisms and are a huge family composed of diverse congeners at the functionality level, large quantities of homogeneous gangliosides are not available from natural sources. Therefore, the chemical reconstruction of gangliosides from monosaccharides that are abundant in nature has been needed. The a-series (GM2,[1] GM1,[1a,2] GD1a,[2a] and GT1a[3]) and b-series (GD2, GT1b, and GQ1b)[4] have been synthesized by several approaches, including those developed by our group, and very recently, the synthesis of the GP1c glycan has also been achieved.[5] However, the synthetic methods cannot always deliver a large amount of ganglioside for molecular biology or medicinal studies.

Also, in our earlier reports on the synthesis of GM1, GD1a, and GT1a,[2a,3] the low degree of accessibility of the GM2 tetrasaccharide acceptor (GM2 acceptor) impeded the efficient assembly of the glycan parts, decreasing the overall yields. The critical considerations in the synthesis of the GM2 acceptor are as follows: (1) α-selective sialylation of the C-3′ hydroxyl group of lactose and chromatographic separation of the α-sialylated product (GM3 glycan); (2) β-selective and efficient incorporation of the galactosamine moiety into the C-4′ hydroxyl group of the GM3 glycan, which is hampered by the adjacent sialyl moiety; and (3) the manipulation of protecting groups to convert GM2 glycan into the corresponding acceptor. After completion of the first total syntheses of gangliosides GD1a and GT1a, our efforts have turned to systematizing the synthesis of the a-series gangliosides with solutions for the above-mentioned synthetic problems aimed at obtaining a sufficient supply for cross-disciplinary studies. Meanwhile, we have devised a highly reactive *N*-Troc-sialyl donor,[6] with which we recently demon-

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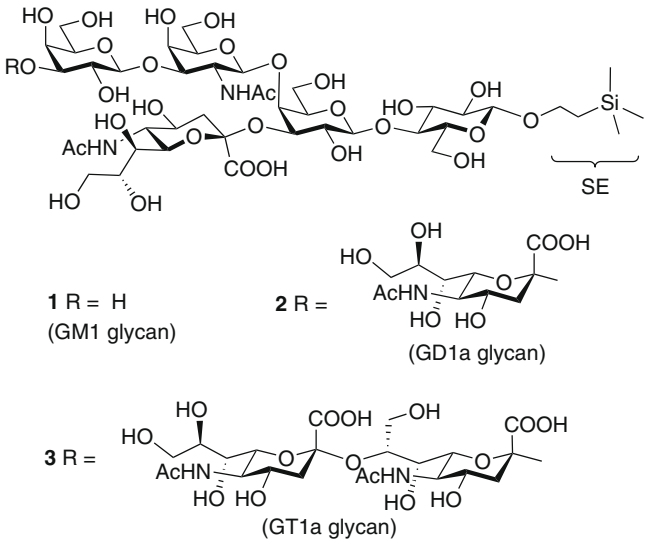


Figure 1. Structure of target glycans **1** (GM1), **2** (GD1a), and **3** (GT1a).

strated an efficient assembly of GM3 glycan.[7] Here, we report on the systematic syntheses of the a-series ganglioside glycans GM1 (**1**), GD1a (**2**), and GT1a (**3**), all of which feature the effective construction of the GM2 glycan and its conversion into the corresponding key acceptor (Fig. 1).

2. Results and discussion

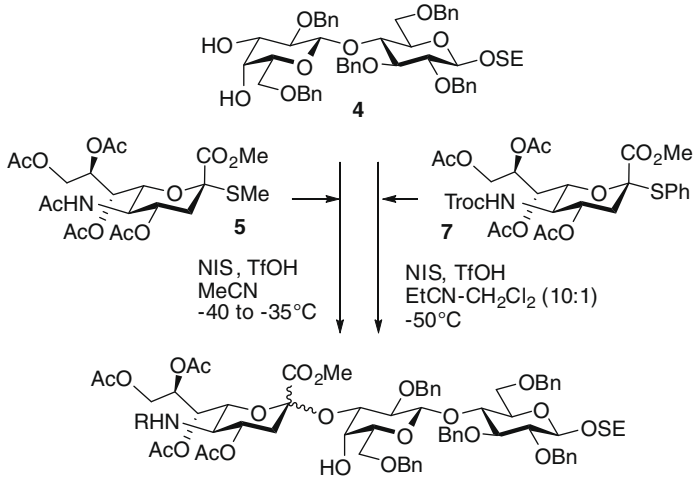
2.1. Lessons from our earlier results, and new synthetic strategy

Our revised strategy includes using an *N*-Troc sialyl lactose acceptor (GM3 acceptor) and novel galactosamine unit that is able to be glycosidated with a less reactive C-4′ hydroxyl group within the GM3 acceptor to fashion a GM2 glycan and then accept mono-, di-, and trisaccharyl glycosyl units at the C-3 hydroxyl group in the next elongation step toward the GM1, GD1a, and GT1a glycans. As we reported recently, the highly reactive *N*-Troc sialyl donor **7** improved the efficiency of the production of GM3 glycan.[7] In our original method of GM2 synthesis, GM3 acceptor **6** was produced in moderate yields (69%, α:β = 59:10) by the coupling of the *N*-acetyl sialyl donor **5** and 3′,4′-diol lactose acceptor **4**, which was promoted by NIS–TfOH in MeCN (Scheme 1).[1b] However, silica gel column chromatography was repeatedly conducted to separate the desired α-isomer from an anomeric mixture that also contained a 2,3-en sialic acid derivative, thereby making the GM3 assembly demanding and insufficient. In contrast, the *N*-Troc sialyl donor **7** improved, not only the yield of GM3 **8** (83%, α:β = 69:14) trisaccharide production, but also its chromatographic purification.[7]

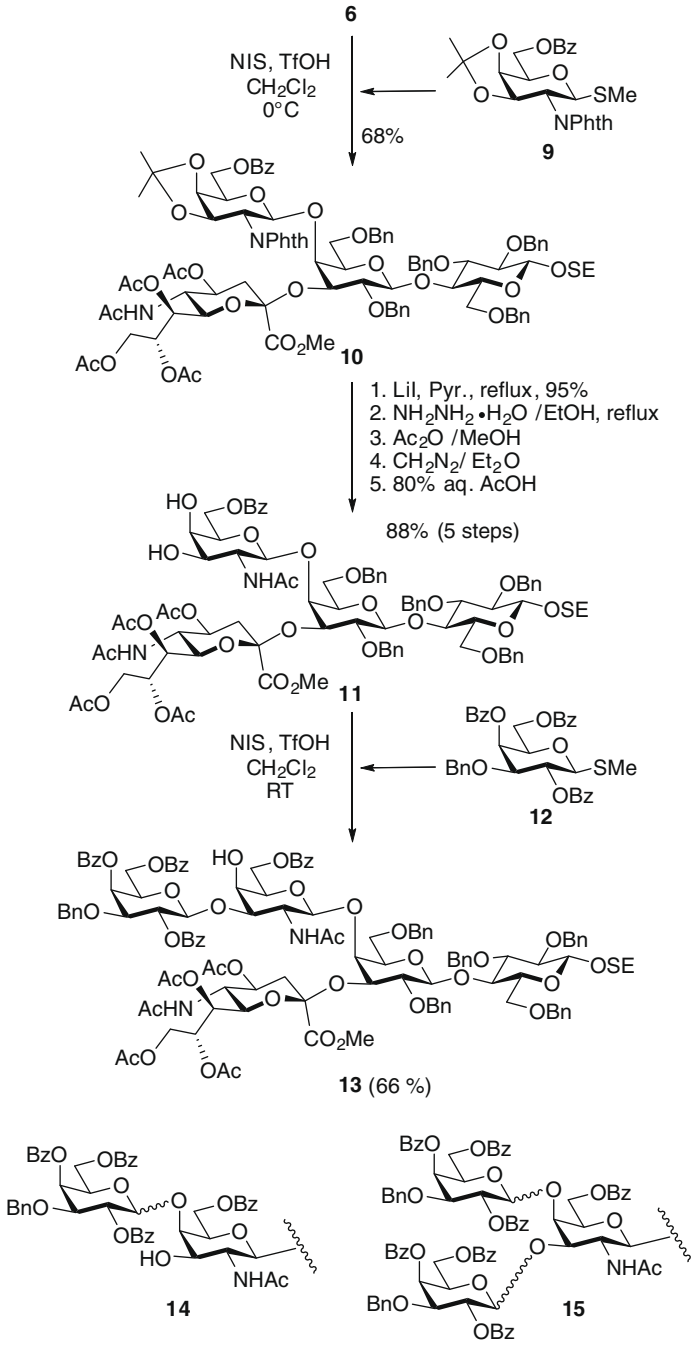
Given the high degree of accessibility of GM3 acceptor **8**, we next examined the design of a linchpin unit, the GM2 acceptor, which is expected to be readily accessible through the minimum number of reaction steps and to possess a reactive hydroxyl group at the C-3 position. Therefore, the structure of the galactosaminyl donor (GalN donor) was considered. In the earlier report,[1b,2a,3] a phthaloyl group was employed as a β-directing functionality with the combination of a methyl sulfide group as an anomeric leaving group to establish the GM2 sequence (Scheme 2). That is, *N*-phthaloylgalactosaminyl donor **9**, which was derived from methylsulfenyl *N*-phthaloylgalactosamine in a 61% yield over two reactions, was reacted with GM3 acceptor **6** in the presence of NIS–TfOH to afford GM2 **10** in 68% yield. Then, the GM2 glycan was converted into the corresponding 3,4-diol acceptor **11** through protecting group manipulations, including demethylation, dephthaloylation, N-acetylation, remethylation, and acid hydrolysis of the isopropylidene group (57% over six reactions from **6**). Next, the coupling reaction with galactosyl donor **12** afforded GM1 **13**.[2a] Although the C-3 hydroxyl group in the *cis*-diol system was reactive to fashion the GM1 glycan sequence, the adjacent axial C-4 hydroxyl was also unexpectedly glycosylated, thereby producing 4-*O*-galactosyl and 3,4-di-*O*-galactosyl derivatives, **14** and **15**, as competitive products.

2.2. Assembly of a key GM2 unit

In this study, keeping these lessons in mind, a Troc group was chosen as a stereo-directing element in a novel GalN donor, which was first utilized in GM2 synthesis by Schmidt and co-workers,[1c] due to its compatible deprotection with ester groups present in the sialic acid residue at the C-3′ position after glycosylation. Furthermore, the C-4 hydroxyl group was designed to be protected as a benzylidene with a C-6 hydroxyl group in order to prevent the hydroxyl group from over-glycosylation at the next elongation



Scheme 1. Sialylations of the C′-3 hydroxyl group of lactose with *N*-Ac (**5**) or *N*-Troc-sialyl donor (**7**).



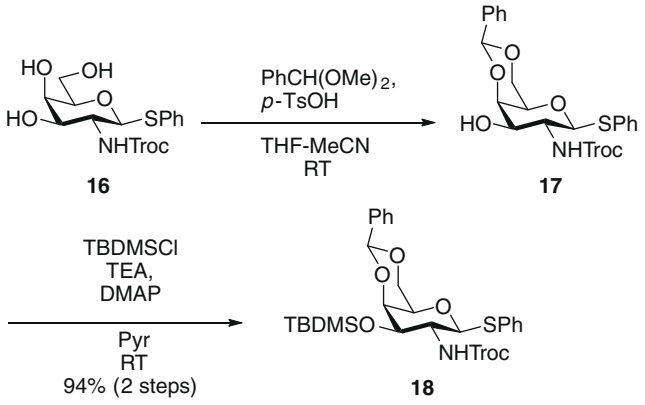
Scheme 2. Synthesis of GM1 glycan reported by our group.

stage. Finally, the C-3 hydroxyl group was designed to be temporally capped with a substituent that is able to be selectively cleaved among other functionalities within the GM2 tetrasaccharide.

According to the design of the GalN moiety, the preparation of GalN donor **18** commenced with a known phenylthioglycoside of *N*-Trocgalactosamine **16**,[8] which, upon treatment with $PhCH(OMe)_2$ and *p*-TsOH in THF–MeCN, was converted into product **17** (Scheme 3). Unexpectedly, compound **17** was hard to dissolve in an apolar solvent such as CH_2Cl_2. In order to enhance the solubility, a lipophilic and selectively cleavable *tert*-butyldimethylsilyl (TBDMS) group was chosen to cap the C-3 hydroxyl group. Compound **17** was reacted with TBDMSCl in the presence of triethylamine and a catalytic amount of 4-dimethylaminopyridine (DMAP) in pyridine at room temperature to afford compound **18** in a high yield (94% from **16**).

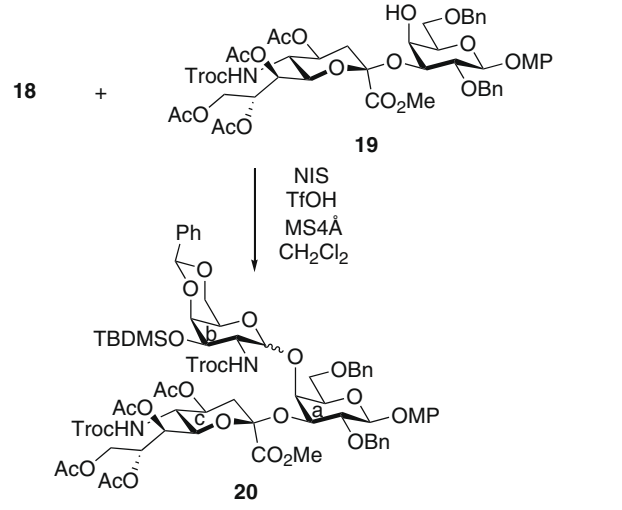
Novel galactosaminyl donor **18**, however, showed insufficient anomeric selectivity in the model coupling reaction with sialyl-α-(2→3)-galactosyl acceptor **19**[6] in the presence of NIS–TfOH[9] in CH_2Cl_2, as shown in Table 1. The α/β ratio of glycosyl product **20** ranged from 1:1 to 1:2.4, depending on the reaction temperature. Presumably, a rigidifying effect is imposed by the benzylidene group which influences the conformational mobility of the pyranose ring, which is similar to the results reported by Chen and Kong.[10]

To improve the poor selectivity of the *N*-Trocgalactosamine donor, the benzylidene group in compound **18** was reductively opened by the action of $PhBCl_2$ and Et_3SiH[11] to furnish a benzyl group at the C-4 oxygen, and the resulting free hydroxyl group at the C-6 position was successively acetylated to give another galac-



Scheme 3. Synthesis of novel *N*-Troc-carrying galactosaminyl donor **18**.

Table 1
Glycosylation of model acceptor **19** with donor **18**

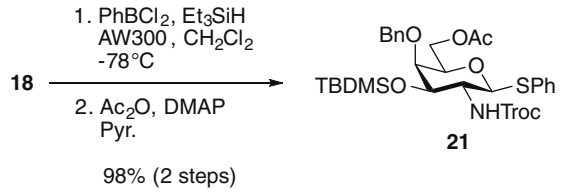


Entry	Temp (°C)	Yield[a] (%)	α/β ratio[b]
1	rt	90	1/1.0
2	0	81	1/1.3
3	−50	70	1/2.4

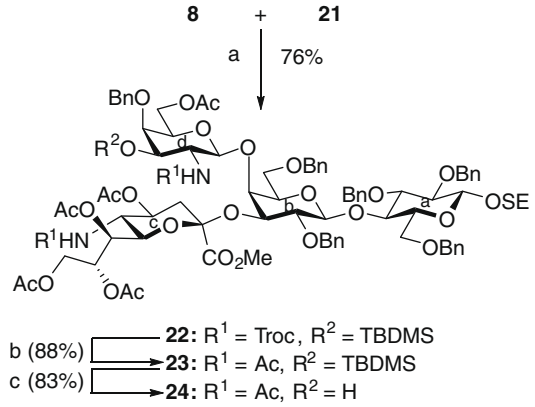
[a] Isolated yield.
[b] α/β ratio was estimated by ^{1}H NMR spectrum.

tosamine donor **21** (98% over two steps; 92% from compound **16**) (Scheme 4).

The glycosylation of GM3 acceptor **8** was then performed with donor **21** under conditions similar to those described above (Scheme 5). According to our expectations, the reaction produced GM2 tetrasaccharide **22** as a single anomer in a much higher yield than for the model case of donor **18**. Compound **22** then underwent conversion into the corresponding 3-hydroxy acceptor, compound **24**. First, the two Troc groups within compound **22** were cleaved by



Scheme 4. Conversion of **18** into another galacotsaminyl donor **21**.

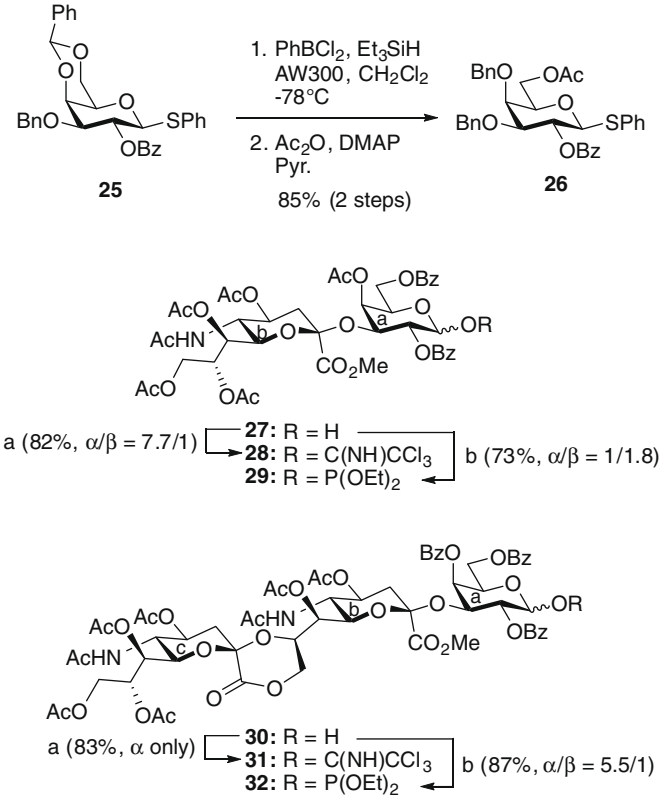


Scheme 5. Assembly of GM2 tetrasaccharide **22** and its conversion into the corresponding acceptor **24**. Reagents and conditions: (a) NIS, TfOH, CH_2Cl_2, 4 Å MS, −20 °C, 76%; (b) (i) Zn–Cu, 2:1 AcOH–1,2-dichloroethane, 40 °C; (ii) Ac_2O, DMAP, Pyr. rt, 88% (two steps); (c) TASF, DMF, rt, 83%.

the action of a zinc–copper couple, and the generated amino groups were acetylated to yield compound **23** in 88% yield. Next, O-desilylation was completed by the use of excess tris(dimethylamino)sulfonium difluorotrimethylsilicate (TASF) (10 equiv) in DMF,[12] affording GM2 acceptor **24** in 83% yield (56% over four reactions from compound **8**).

2.3. Synthesis of GM1, GD1a, and GT1a glycans

As coupling partners for GM2 acceptor **24**, a set of mono-, di-, and trisaccharide glycosyl donors were prepared to construct GM1, GD1a, and GT1a glycans, respectively (Scheme 6). For the

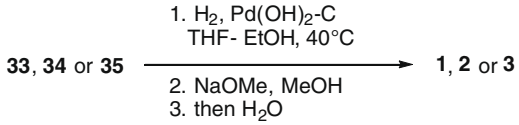


Scheme 6. Preparation of glycosyl donors for the assembly of GM1, GD1a, and GT1a glycans. Reagents and conditions: (a) CCl_3CN, DBU, CH_2Cl_2, 0 °C to rt; (b) $ClP(OEt)_2$, DIEA, CH_3CN, O °C to RT.

GM1 glycan, the original 3-*O*-benzyl-4-*O*-benzoylated galactosyl donor **12**[2a] was transformed into the 3,4-di-O-benzylated form **26** to prevent the remote participation of the C-4 benzoyl group to the β-face of the anomeric carbon during glycosylation. Compound **26** was prepared from known galactose derivative **25**[13] via the reductive opening of the benzylidene acetal ring and subsequent acetylation of the resulting 6-OH group. As sialyl galactose (for GD1a) and disialyl galactose (for GT1a) donors, the corresponding diethylphosphite derivatives,[14] compounds **29** and **32**, were chosen for the first time, together with known trichloroacetimidate derivatives **28**[15] and **31**,[4e] respectively, which were reported by our group. Thus, the suitably protected sialyl galactose **27**[15] and disialyl galactose **30**[4e] were converted into diethylphosphite forms **29** and **32**, upon reaction with $ClP(OEt)_2$ and DIPEA, respectively.

Final connections between GM2 acceptor **24** and nonreducing end blocks **26**, **28**, **29**, **31**, and **32** were made. The optimized coupling yields with each glycosyl donor are summarized in Table 2. In all events, glycosylation produced exclusively β-glycosides. In entry 1, GM1 glycan **33** was obtained in 75% yield by the coupling of compounds **24** and **26**, promoted by NIS–TfOH. In the case of coupling with sialyl galactosyl donors, the phosphite **29** compared favorably with the imidate **28**; thus, the phosphite **29** provided GD1a glycan **34** in 60% yield, whilst the imidate **28** provided a 38% yield (entries 2 and 3). This tendency increased in the coupling of disialyl galactosyl donors. In entry 6, GT1a glycan **35** was obtained in 68% yield when phosphite donor **32** was used. Conversely, imidate **31** produced compound **35** in 26% yield.

Finally, the successfully obtained compounds **33** (GM1 glycan), **34** (GD1a glycan), and **35** (GT1a glycan) were subjected to the manipulation for global deprotection, including hydrogenolysis on $Pd(OH)_2$-on-charcoal and O-deacylation[16] and saponification, thereby delivering GM1, GD1a, and GT1a glycans **1**, **2**, and **3**, respectively (Scheme 7).



Scheme 7. Global deprotection of **33**, **34**, and **35**.

2.4. Conclusions

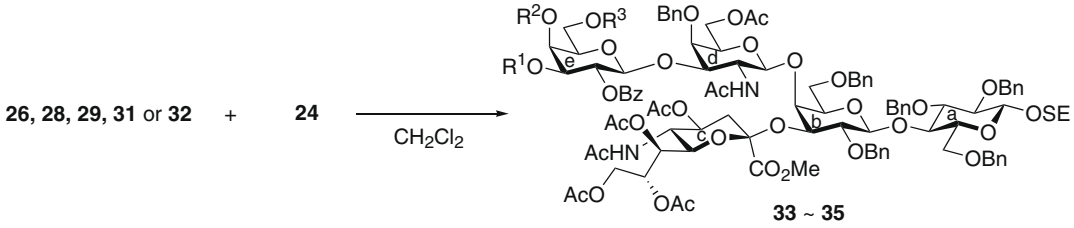
In conclusion, we first demonstrated a systematic assembly of the a-series ganglioside glycans GM1, GD1a, and GT1a. From the results of the connection of newly developed GM3 acceptor **8** and GalN-Troc donors **18** and **21**, 4,6-*O*-benzylidene group in **18** turned out to be a mismatch protecting group for β-selective glycosylation, probably due to its sterically hindering the reaction at the β face of the anomeric center. Conversely, 6-*O*-acetyl-4-*O*-benzyl protection afforded complete β selectivity, with a high yield of glycosylated product. Furthermore, the suitable choice of Troc and TBDMS groups for C-2 amino and C-3 hydroxyl protection within the galactosamine moiety allowed an efficient conversion of GM2 tetrasaccharide **22** into the key pivotal acceptor compound **24**, which then served as a good coupling partner for compounds **26**, **29**, and **32**, leading to a successful synthesis of the GM1, GD1a, and GT1a glycans.

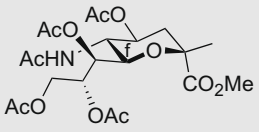
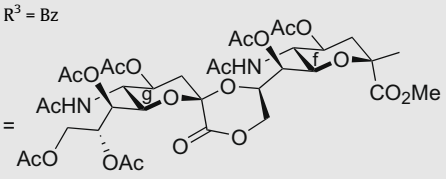
3. Experimental

3.1. General methods

All reactions were carried out under a positive pressure of argon, unless otherwise noted. All chemicals were purchased from commercial suppliers and used without further purification, unless otherwise noted. Molecular sieves were purchased from Wako

Table 2



Entry[a]	Donor (equiv)	Promotor (equiv for donor)	Temp (°C)	Product	Yield (%)
1	**26** (2.0)	NIS (2.0) TfOH (0.2)	0	**33** R^1, R^2 = Bn, R^3 = Ac	75
2	**28** (2.0)	TMSOTf (0.2)	0	**34** R^1 =  R^2 = Ac, R^3 = Bz	38
3	**29** (2.0)	TMSOTf (0.2)	0	R^2 = Ac, R^3 = Bz	60
4	**31** (1.5)	TMSOTf (0.2)	0	**35** R^1 =  R^2, R^3 = Bz	26
5	**32** (2.0)	TMSOTf (0.2)	0		46
6	**32** (2.0)	TMSOTf (0.2)	15		68

[a] MS 4 Å (entry 1) or AW-300 (entries 2–6) was used as a drying reagent.

Chemicals Inc. and dried at 300 °C for 2 h in muffle furnace prior to use. ^{1}H and ^{13}C NMR spectra were recorded at 300 K with a JEOL ECA 500/600 spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from Me_4Si. MALDI-TOF mass spectra were recorded in the positive-ion mode on a Bruker Autoflex with the use of α-cyano-4-hydroxy-cinnamic acid (CHCA) as a matrix. Specific rotations were determined with a Horiba SEPA-300 high-sensitive polarimeter. Silica gel (300 mesh) manufactured by Fuji Silysia Co. was used for flash column chromatography. TLC analysis was conducted on E. Merck TLC (Silica Gel 60-F_{254} on glass plates). Compounds were visualized either by exposure to UV light or by spraying with a solution of 10% H_2SO_4 in EtOH followed by heating. Organic solutions were concentrated by rotary evaporation below 40 °C under reduced pressure. Solvent systems in chromatography are specified in v/v.

3.2. Phenyl 4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-1-thio-2-(2,2,2-trichloroethoxycarbamoyl)-β-D-galactopyranoside (18)

To a solution of compound **16** (2.0 g, 4.47 mmol) in 2:5 THF–MeCN (28 mL) were added benzaldehyde dimethylacetal (2.0 mL, 13.4 mmol) and *p*-TsOH (170 mg, 0.900 mmol), and the mixture was stirred at room temperature for 1 h, with monitoring of the reaction by TLC (5:1 $CHCl_3$–MeOH). The mixture was neutralized with Et_3N and concentrated. The residue was dissolved in pyridine (20 mL), and Et_3N (1.9 mL, 13.4 mmol), DMAP (600 mg, 4.92 mmol), and TBDMSCl (2.0 g, 13.4 mmol) were added. The reaction mixture was stirred at room temperature for 4 h, with monitoring of the reaction by TLC (1:4 EtOAc–toluene). Then MeOH was added at 0 °C, the reaction mixture was co-evaporated with toluene, and diluted with $CHCl_3$. The organic layer was washed with 2 M HCl, H_2O, satd $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1:4 EtOAc–hexane) to give **18** (2.7 g, 94%); $[\alpha]_D$ −8.5 (*c* 0.44, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.62–7.18 (m, 10H, 2Ph), 5.51 (s, 1H, PhC*H*), 5.24 (d, 1H, NH), 5.08 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1), 4.73 and 4.63 (2d, 2H, J_{gem} = 12.3 Hz, OCH_2), 4.38 (dd, 1H, J_{gem} = 12.3 Hz, H-6), 4.35 (br d, 1H, H-3), 4.08 (d, 1H, H-4), 4.02 (d, 1H, J_{gem} = 12.3 Hz, H-6′), 3.56 (m, 1H, H-2), 3.54 (s, 1H, H-5), 0.84 (s, 9H, ^{t}Bu), 0.05 and 0.03 (2s, 6H, $SiMe_2$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 153.4, 137.9, 132.9, 132.1, 128.8, 128.8, 128.0, 127.7, 126.2, 100.7, 95.2, 84.3, 76.3, 74.5, 70.7, 70.0, 69.4, 53.3, 25.6, 18.0, −4.5, −4.6; MALDI-TOFMS: calcd for $[C_{28}H_{36}Cl_3NO_6SSi+Na]^+$: *m/z* 670.09. Found: *m/z* 670.15.

3.3. 4-Methoxyphenyl 4,6-*O*-benzylidene-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-D-galacto-pyranosyl-(1→4)-{methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-(2,2,2-trichloroethoxycarbamoyl)-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)}-2,6-di-*O*-benzyl-β-D-galactopyranoside (20)

A suspension of compound **18** (60 mg, 93 μmol), compound **19** (50 mg, 46 μmol), and 4 Å molecular sieves (120 mg) in dry CH_2Cl_2 (1.5 mL) was stirred at room temperature for 1 h. To the mixture was added NIS (42 mg, 186 μmol). After the mixture was cooled to −50 °C, TfOH (1.6 μL, 18 μmol) was added. The reaction mixture was stirred at −50 °C for 1.5 h, with monitoring of the reaction by TLC (1:2 EtOAc–toluene). Et_3N was added to quench the reaction. The mixture was filtered through Celite. The combined filtrate and washings were diluted with $CHCl_3$, and the organic layer was washed with satd $NaHCO_3$, satd $Na_2S_2O_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1:6 EtOAc–toluene) to give **20** (52 mg, 70%) as an anomeric mixture (α:β = 1:2.4).

3.3.1. β Isomer

$[\alpha]_D$ +9.5 (*c* 1.4, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3CN): δ 7.53–7.23 (m, 15H, 3Ph), 7.03 and 6.83 (2d, 4H, Ar), 6.02 (d, 1H, $J_{2,NH}$ = 9.6 Hz, NH-b), 5.82 (d, 1H, $J_{5,NH}$ = 9.6 Hz, NH-c), 5.61 (s, 1H, PhC*H*), 5.17 (m, 3H, H-7c, 8c, 4c), 4.98 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1a), 4.91 (d, 1H, $J_{1,2}$ = 8.9 Hz, H-1b), 4.86 and 4.64 (2d, 2H, J_{gem} = 10.9 Hz, OCH_2), 4.85 and 4.56 (2d, 2H, J_{gem} = 11.6 Hz, OCH_2), 4.78 and 4.61 (2d, 2H, J_{gem} = 12.3 Hz, OCH_2), 4.59 and 4.53 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 4.34 (dd, 1H, $J_{2,3}$ = 10.3 Hz, $J_{3,4}$ = 2.7 Hz, H-3a), 4.15 (d, 1H, $J_{3,4}$ = 2.7 Hz, H-4a), 4.13–3.99 (m, 6H, H-6b, 6′b, 9c, 9′c, 3b, 4b), 3.97 (near d, 1H, $J_{5,6}$ = 10.9 Hz, H-6c), 3.90 (m, 4H, H-6a, OMe), 3.80–3.75 (m, 3H, H-5a, 5b, 2b), 3.73 (s, 3H, OMe), 3.67–3.62 (m, 3H, H-6′a, 5c, 2a), 2.35 (dd, 1H, J_{gem} = 13.7 Hz, $J_{3eq,4}$ = 4.8 Hz, H-3*eq*-c), 2.21 (near t, 1H, J_{gem} = 13.7 Hz, $J_{3ax,4}$ = 11.6 Hz, H-3*ax*-c), 2.17, 2.07, 1.95 and 1.83 (4s, 12H, 4Ac), 0.89 (s, 9H, ^{t}Bu), 0.17 and 0.15 (2s, 6H, $SiMe_2$); ^{13}C NMR (150 MHz, CD_3CN): δ 171.1, 170.6, 170.6, 170.5, 169.8, 156.2, 155.7, 155.1, 152.4, 139.7, 139.7, 139.6, 138.8, 129.8, 129.8, 129.2, 129.2, 129.1, 129.1, 128.7, 128.5, 128.4, 128.4, 127.2, 126.2, 119.0, 115.5, 103.0, 102.9, 101.5, 100.5, 96.7, 96.5, 79.2, 78.9, 77.0, 76.3, 76.0, 75.1, 74.9, 74.0, 73.8, 73.3, 72.1, 70.3, 70.0, 69.8, 68.8, 67.7, 67.0, 62.8, 56.1, 55.5, 54.1, 51.6, 35.3, 26.1, 21.4, 21.3, 21.0, 20.9, 20.9, 18.7, −4.2, −4.5; MALDI-TOFMS: calcd for $[C_{70}H_{86}Cl_6N_2O_{26}Si+Na]^+$: *m/z* 1631.32. Found: *m/z* 1631.32.

3.3.2. α Isomer

$[\alpha]_D$ +27.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.55–7.16 (m, 15H, 3Ph), 7.02 and 6.79 (2d, 4H, Ar), 5.61 (m, 1H, $J_{7,8}$ = 8.2 Hz, $J_{8,9}$ = 5.4 Hz, H-8c), 5.53 (s, 1H, PhC*H*), 5.49 (d, 1H, $J_{2,NH}$ = 10.2 Hz, NH-b), 5.39 (dd, 1H, $J_{6,7}$ = 2.7 Hz, $J_{7,8}$ = 8.2 Hz, H-7c), 5.06 (d, 1H, $J_{1,2}$ = 3.4 Hz, H-1b), 5.04 (d, 1H, $J_{1,2}$ = 6.8 Hz, H-1a), 4.92 and 4.85 (2d, 2H, J_{gem} = 13.0 Hz, OCH_2), 4.91 (m, 1H, H-4c), 4.89 and 4.46 (2d, 2H, J_{gem} = 11.6 Hz, OCH_2), 4.80 (d, 1H, $J_{5,NH}$ = 9.6 Hz, NH-c), 4.77 and 4.51 (2d, 2H, J_{gem} = 12.3 Hz, OCH_2), 4.51 and 4.43 (2d, 2H, J_{gem} = 11.6 Hz, OCH_2), 4.33 (td, 1H, $J_{1,2}$ = 3.4 Hz, $J_{2,3}$ = $J_{2,NH}$ = 10.2 Hz, H-2a), 4.30 (m, 2H, H-3a, 9c), 4.24 (near d, 1H, J_{gem} = 11.6 Hz, H-6b), 4.07 (d, 1H, $J_{3,4}$ = 2.7 Hz, H-4b), 4.02 (dd, 1H, J_{gem} = 13.0 Hz, $J_{8,9}$ = 5.4 Hz, H-9′c), 3.99 (near d, 1H, J_{gem} = 11.6 Hz, H-6′b), 3.96 (s, 1H, H-5b), 3.95 (dd, 1H, $J_{2,3}$ = 10.2 Hz, $J_{3,4}$ = 2.7 Hz, H-3b), 3.91 (dd, 1H, $J_{5,6}$ = 10.9 Hz, $J_{6,7}$ = 2.7 Hz, H-6c), 3.76 (m, 9H, H-4a, 5a, 5c, 2OMe), 3.63 (m, 2H, H-2a, 6a), 3.58 (dd, 1H, J_{gem} = 9.6 Hz, $J_{5,6}$ = 6.1 Hz, H-6′a), 2.56 (dd, 1H, J_{gem} = 12.3 Hz, $J_{3eq,4}$ = 4.8 Hz, H-3*eq*-c), 2.12, 2.03, 1.96 and 1.85 (4s, 12H, 4Ac), 1.85 (t, 1H, J_{gem} = -$J_{3ax,4}$ = 12.3 Hz, H-3*ax*-c), 0.87 (s, 9H, ^{t}Bu), 0.08 and 0.07 (2s, 6H, $SiMe_2$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.6, 170.1, 170.1, 169.9, 167.8, 155.4, 154.1, 154.0, 151.3, 139.2, 137.8, 137.7, 137.5, 128.9, 128.6, 128.3, 128.1, 128.0, 128.0, 127.7, 127.5, 127.4, 127.2, 126.1, 125.2, 119.2, 118.6, 114.4, 103.1, 100.5, 99.2, 97.2, 95.3, 95.2, 76.4, 74.9, 74.6, 74.5, 74.2, 73.0, 72.9, 72.0, 71.8, 69.4, 68.9, 68.7, 68.3, 67.3, 67.0, 66.5, 63.0, 62.1, 55.5, 53.0, 52.2, 51.2, 37.5, 25.5, 21.4, 21.3, 20.8, 20.6, 20.4, 18.0, −4.2, −4.5; MALDI-TOFMS: calcd for $[C_{70}H_{86}Cl_6N_2O_{26}Si+Na]^+$: *m/z* 1631.32. Found: *m/z* 1631.31.

3.4. Phenyl 6-*O*-acetyl-4-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-1-thio-2-(2,2,2-trichloroethoxycarbamoyl)-β-D-galactopyranoside (21)

A suspension of compound **18** (111 mg, 171 μmol) and AW-300 molecular sieves (256 mg) in dry CH_2Cl_2 (2.0 mL) was stirred at room temperature for 3 h. After the mixture was cooled to −78 °C, Et_3SiH (82 μL, 513 μmol) and $PhBCl_2$ (75 μL, 581 μmol) were added, and the mixture was stirred at −78 °C for 1 h, with monitoring of the reaction by TLC (1:3 EtOAc–toluene). Et_3N and MeOH were added to quench the reaction. The mixture was filtered through Celite. The combined filtrate and washings were diluted with $CHCl_3$, and the organic layer was washed with satd $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The residue was

dissolved in pyridine (2.0 mL), Ac_2O (0.8 mL) and a catalytic amount of DMAP were added, and the mixture was stirred at room temperature for 1 h. Then MeOH was added at 0 °C, the reaction mixture was co-evaporated with toluene, and diluted with $CHCl_3$. The organic layer was washed with 2 M HCl, H_2O, satd $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1:5 EtOAc–hexane) to give **21** (116 mg, 98%); $[\alpha]_D$ −2.0 (*c* 0.52, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$): δ 7.51–7.19 (m, 10H, 2Ph), 5.06–5.01 (m, 3H, H-1, NH, OCH_2), 4.73 and 4.64 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 4.53 (d, 1H, J_{gem} = 11.7 Hz, OCH_2), 4.25 (dd, 1H, J_{gem} = 11.7 Hz, H-6), 4.14 (dd, 1H, J_{gem} = 11.7 Hz, H-6′), 4.07 (br d, 1H, H-3), 3.81 (q, 1H, H-2), 3.72 (t, 1H, H-5), 3.70 (d, 1H, H-4), 2.01 (s, 3H, Ac), 0.91 (s, 9H, ^{t}Bu), 0.15 and 0.09 (2s, 6H, $SiMe_2$); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.6, 153.6, 138.2, 133.3, 131.9, 128.7, 128.2, 127.6, 127.6, 127.4, 95.1, 85.7, 76.6, 76.0, 75.0, 74.7, 73.8, 63.5, 54.0, 25.7, 20.7, 17.9, −3.9, −5.0; MALDI-TOFMS: calcd for $[C_{30}H_{40}Cl_3NO_7SSi+Na]^+$: *m/z* 714.12. Found: *m/z* 714.15.

3.5. 2-(Trimethylsilyl)ethyl 6-*O*-acetyl-4-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-2-(2,2,2-trichloroethoxycarbamoyl)-β-D-galactopyranosyl-(1→4)-{methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-(2,2,2-trichloroethoxycarbamoyl)-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)}-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (22)

A suspension of compound **21** (116 mg, 167 μmol), compound **8** (126 mg, 84 μmol), and 4 Å molecular sieves (262 mg) in dry CH_2Cl_2 (2.5 mL) was stirred at room temperature for 1 h. To the mixture was added NIS (75 mg, 334 μmol). After the mixture was cooled to −20 °C, TfOH (3.0 μL, 33 μmol) was added, and the reaction mixture was stirred at −20 °C for 1.5 h, with monitoring of the reaction by TLC (1:3 EtOAc–toluene). Et_3N was added to quench the reaction. The mixture was filtered through Celite. The combined filtrate and washings were diluted with $CHCl_3$, and the organic layer was washed with satd $NaHCO_3$, satd $Na_2S_2O_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1:6 EtOAc–toluene) to give **22** (132 mg, 76%); $[\alpha]_D$ +12.7 (*c* 1.1, $CHCl_3$); Ratio of rotamer A:B: 2.06:1 ($CDCl_3$), 3.72:1 (acetone-d_6), 6.76:1 (THF-d_8), 10.5:1 (CD_3CN); rotamer A: ^1H NMR (600 MHz, CD_3CN): δ 7.44–6.74 (m, 30H, 6Ph), 5.80 (d, 1H, NH-c), 5.68 (d, 1H, NH-d), 5.26 (d, 1H, H-7c), 5.16 (td, 1H, $J_{3eq,4}$ = 5.4 Hz, H-4c), 5.11 (m, 1H, H-8c), 5.05 and 4.62 (2d, 2H, J_{gem} = 11.0 Hz, OCH_2), 4.87 and 4.56 (2d, 2H, J_{gem} = 9.6 Hz, OCH_2), 4.81 (d, 1H, $J_{1,2}$ = 10.9 Hz, H-1d), 4.80–4.75 (m, 5H, $5OCH_2$), 4.61 (d, 1H, OCH_2), 4.57–4.55 (m, 2H, $2OCH_2$), 4.49 and 4.42 (2d, 2H, J_{gem} = 12.3 Hz, OCH_2), 4.47 (d, 1H, $J_{1,2}$ = 9.6 Hz, H-1b), 4.36 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1a), 4.32 (d, 1H, OCH_2), 4.22 (m, 2H, H-6d, 6′d), 4.18–4.02 (m, 7H, H-3b, 9c, 9′c, 2d, 3d, 5d, OCH_2), 3.95–3.88 (m, 6H, H-6c, 4d, COOMe, CH_2CH$_2$SiMe$_3$), 3.82 (t, 1H, H-4a), 3.79 (br s, 1H, H-4b), 3.69 (dd, 1H, H-6b), 3.66–3.58 (m, 4H, H-6a, 6′b, 5c, CH_2CH$_2$SiMe$_3$), 3.49–3.41 (m, 4H, H-3a, 5a, 2b, 5b), 3.33 (dd, 1H, H-6′a), 3.10 (t, 1H, $J_{1,2}$ = 7.5 Hz, H-2a), 2.33 (dd, 1H, J_{gem} = 13.7 Hz, $J_{3eq,4}$ = 5.4 Hz, H-3*eq*-c), 2.20 (t, 1H, J_{gem} = 13.7 Hz, H-3*ax*-c), 2.13, 2.08, 1.90, 1.89, 1.88 (5s, 15H, 5Ac), 0.95 (m, 2H, CH$_2$CH_2SiMe$_3$), 0.91 (s, 9H, ^{t}Bu), 0.24 and 0.22 (2s, 6H, $SiMe_2$), 0.00 (s, 9H, CH$_2$Si*Me*$_3$); ^{13}C NMR (125 MHz, CD_3CN): δ 171.2, 170.7, 170.5, 170.3, 170.2, 155.4, 155.1, 140.2, 140.0, 139.6, 139.6, 139.6, 130.3, 129.8, 129.3, 129.1, 129.1, 129.0, 128.9, 128.9, 128.7, 128.7, 128.5, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.1, 128.1, 126.2, 103.5, 102.6, 100.7, 96.7, 96.6, 83.3, 82.5, 80.0, 79.6, 78.6, 76.5, 76.4, 76.3, 76.1, 76.1, 75.4, 75.2, 75.1, 75.0, 74.8, 74.4, 73.7, 73.6, 72.5, 71.8, 70.7, 70.2, 69.0, 67.6, 67.1, 64.4, 62.1, 55.9, 54.4, 51.6, 34.9, 26.3, 21.4, 21.3, 21.1, 21.0, 20.9, 20.9, 18.9, 18.5, −1.3, −3.9, −4.4; MALDI-TOFMS: calcd for $[C_{97}H_{124}Cl_6N_2O_{31}Si_2+Na]^+$: *m/z* 2101.57. Found: *m/z* 2101.85.

3.6. 2-(Trimethylsilyl)ethyl 2-acetamido-6-*O*-acetyl-4-*O*-benzyl-3-*O*-*tert*-butyldimethylsilyl-2-deoxy-β-D-galactopyranosyl-(1→4)-{methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)}-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (23)

To a solution of compound **22** (127 mg, 61 μmol) in 2:1 AcOH–1,2-dichloroethane (3.0 mL) was added Zn–Cu couple (665 mg). The suspension was vigorously stirred at 40 °C for 1.5 h and monitored by TLC (20:1 $CHCl_3$–MeOH). The mixture was filtered through Celite. The combined filtrate and washings were evaporated and diluted with $CHCl_3$, and the organic layer was washed with satd Na_2CO_3 and brine, dried over Na_2SO_4, and concentrated. The residue was dissolved in pyridine (1.5 mL), Ac_2O (0.5 mL) and a catalytic amount of DMAP were added at 0 °C, and the resulting mixture was stirred at room temperature for 16 h. Then MeOH was added at 0 °C, and the reaction mixture was co-evaporated with toluene and diluted with $CHCl_3$. The organic layer was washed with 2 M HCl, H_2O, satd $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (50:1 $CHCl_3$–MeOH) to give **23** (98 mg, 88%); $[\alpha]_D$ +17.2 (*c* 0.93, $CHCl_3$); Ratio of rotamer A:B: 1.65:1 ($CDCl_3$), 2.77:1 (THF-d_8), 10.9:1 (CD_3CN), 12.0:1 (DMSO-d_6); rotamer A: ^1H NMR (500 MHz, CD_3CN): δ 7.43–6.75 (m, 30H, 6Ph), 6.34 (d, 1H, NH-d), 6.11 (d, 1H, $J_{5,NH}$ = 10.0 Hz, NH-c), 5.21 (d, 1H, H-7c), 5.14–5.08 (m, 2H, H-4c, 8c), 5.02 and 4.60 (2d, 2H, J_{gem} = 11.5 Hz, OCH_2), 4.87 and 4.58 (2d, 2H, J_{gem} = 9.5 Hz, OCH_2), 4.82 and 4.74 (2d, 2H, J_{gem} = 11.5 Hz, OCH_2), 4.76 and 4.53 (2d, 2H, J_{gem} = 11.5 Hz, OCH_2), 4.74 (d, 1H, $J_{1,2}$ = 10.9 Hz, H-1d), 4.48 and 4.40 (2d, 2H, J_{gem} = 11.5 Hz, OCH_2), 4.46 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1b), 4.36 (d, 1H, $J_{1,2}$ = 8.5 Hz, H-1a), 4.29–4.25 (m, 2H, H-2d, OCH_2), 4.21 (d, 2H, H-6d, 6′d), 4.11–4.04 (m, 6H, H-3b, 9c, 9′c, 3d, 5d, OCH_2), 4.02 (q, 1H, $J_{5,NH}$ = 10.0 Hz, H-5c), 3.93–3.87 (m, 6H, H-6c, 4d, COOMe, CH_2CH$_2$SiMe$_3$), 3.78 (t, 1H, H-4a), 3.76 (br s, 1H, H-4b), 3.67 (dd, 1H, H-6b), 3.62–3.55 (m, 3H, H-6a, 6′b, CH_2CH$_2$SiMe$_3$), 3.49 (t, 1H, H-3a), 3.46 (t, 1H, H-5b), 3.43 (m, 1H, H-5a), 3.37 (t, 1H, $J_{1,2}$ = 8.0 Hz, H-2b), 3.28 (dd, 1H, H-6′a), 3.10 (t, 1H, $J_{1,2}$ = 8.5 Hz, H-2a), 2.32 (dd, 1H, J_{gem} = 14.5 Hz, H-3*eq*-c), 2.20 (t, 1H, J_{gem} = 14.5 Hz, H-3*ax*-c), 2.18, 2.07, 1.94, 1.91, 1.87, 1.85, 1.78 (7s, 21H, 7Ac), 0.94 (m, 2H, CH$_2$CH_2SiMe$_3$), 0.93 (s, 9H, ^{t}Bu), 0.22 and 0.20 (2s, 6H, $SiMe_2$), 0.00 (s, 9H, CH$_2$Si*Me*$_3$); ^{13}C NMR (125 MHz, CD_3CN): δ 171.3, 171.2, 170.8, 170.7, 170.5, 170.3, 170.2, 170.0, 140.2, 140.1, 139.7, 139.6, 139.6, 130.3, 129.3, 129.2, 129.1, 129.1, 129.0, 128.9, 128.9, 128.7, 128.5, 128.5, 128.4, 128.3, 128.2, 128.0, 104.0, 103.5, 102.8, 100.7, 83.2, 82.5, 79.9, 78.7, 76.8, 76.4, 76.3, 76.1, 75.8, 75.4, 75.3, 75.0, 74.4, 73.7, 73.6, 72.4, 70.7, 70.6, 69.0, 67.6, 67.3, 64.4, 62.3, 54.0, 49.2, 35.0, 26.3, 26.2, 24.1, 23.1, 21.3, 21.1, 21.0, 20.9, 20.8, 18.9, 18.5, −1.3, −3.8, −4.5; MALDI-TOFMS: calcd for $[C_{95}H_{126}N_2O_{29}Si_2+Na]^+$: *m/z* 1837.78. Found: *m/z* 1837.70.

3.7. 2-(Trimethylsilyl)ethyl 2-acetamido-6-*O*-acetyl-4-*O*-benzyl-2-deoxy-β-D-galactopyranosyl-(1→4)-{methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)}-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (24)

To compound **23** (34 mg, 19 μmol) in a round-bottomed flask was added TASF (52 mg, 187 μmol) in DMF (0.8 mL), and the resulting mixture was stirred at room temperature for 1.5 h. The progress of the reaction was monitored by TLC (20:1 $CHCl_3$–MeOH). The reaction mixture was extracted with $CHCl_3$, and the organic layer was washed with H_2O, satd $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (25:25:1 EtOAc–toluene–MeOH) to give **24** (27 mg, 83%); $[\alpha]_D$ −12.2 (*c* 0.46, $CHCl_3$);

^{1}H NMR (600 MHz, $CDCl_3$): δ 7.43–6.89 (m, 30H, 6Ph), 7.11 (d, 1H, NH-d), 5.28 (d, 1H, OH-3d), 5.25 (d, 1H, H-7c), 5.19–5.17 (m, 2H, H-8c, NH-c), 5.11 and 4.71 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 5.07 (td, 1H, H-4c), 4.91 and 4.79 (2d, 2H, J_{gem} = 11.0 Hz, OCH_2), 4.90 and 4.75 (2d, 2H, J_{gem} = 9.6 Hz, OCH_2), 4.84 and 4.49 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 4.73 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1d), 4.59 and 4.49 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 4.49 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 4.38 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1a), 4.26–4.17 (m, 5H, H-2d, 6d, 6′d, OCH_2), 4.08 (dd, 1H, H-9c), 4.02–3.95 (m, 6H, H-5c, 6c, 9′c, 4d, 5d, $CH_2CH_2SiMe_3$), 3.94–3.91 (m, 2H, H-4a, 3b), 3.84 (s, 3H, COOMe), 3.80–3.77 (m, 3H, H-6a, 4b, 3d), 3.72 (dd, 1H, H-6′a), 3.68 (m, 1H, H-6b), 3.59 (m, 1H, $CH_2CH_2SiMe_3$), 3.57 (t, 1H, H-3a), 3.48 (t, 1H, $J_{1,2}$ = 7.5 Hz, H-2b), 3.42 (m, 1H, H-5a), 3.38–3.35 (m, 3H, H-2a, 6′b, 5b), 2.24 (m, 2H, H-3*eq*-c, 3-*ax*-c), 2.06, 2.02, 1.98, 1.96, 1.91, 1.88 and 1.86 (7s, 21H, 7Ac), 1.03 (m, 2H, $CH_2CH_2SiMe_3$), 0.00 (s, 9H, CH_2SiMe_3); ^{13}C NMR (150 MHz, $CDCl_3$): δ 173.1, 170.5, 170.3, 170.2, 169.5,169.1, 168.0, 138.7, 138.6, 138.5, 138.4, 138.2, 137.8, 128.6, 128.3, 128.2, 128.2, 128.1, 127.9, 127.5, 127.5, 127.4, 127.4, 127.3, 127.2, 102.9, 102.4, 101.7, 99.3, 82.5, 81.9, 78.8, 78.3, 77.0, 76.6, 76.2, 75.8, 75.6, 75.3, 75.3, 75.1, 74.9, 73.4, 73.3, 73.2, 72.3, 71.6, 68.8, 68.6, 68.5, 67.7, 67.2, 66.4, 63.1, 61.5, 55.4, 53.1, 49.0, 35.3, 29.6, 23.1, 22.7, 20.9, 20.7, 20.6, 20.4, 20.4, 18.4, −1.4; MALDI-TOFMS: calcd for $[C_{89}H_{112}N_2O_{29}Si+Na]^+$: *m/z* 1723.70. Found: *m/z* 1723.40.

3.8. Phenyl 6-*O*-acetyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-1-thio-β-D-galactopyranoside (26)

The suspension of compound **25** (560 mg, 1.00 mmol) and AW-300 molecular sieves (1.9 g) in dry CH_2Cl_2 (10 mL) was stirred at room temperature for 2 h. After the suspension was cooled to −78 °C, Et_3SiH (0.48 mL, 3.02 mmol) and $PhBCl_2$ (0.45 mL, 3.43 mmol) were added, and the mixture was stirred at −78 °C for 1.5 h. The progress of the reaction was monitored by TLC (1:4 EtOAc–toluene). Et_3N and MeOH were added to quench the reaction, and the mixture was filtered through Celite. The combined filtrate and washings were diluted with $CHCl_3$, and the organic layer was washed with satd $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. The residue was dissolved in pyridine (10 mL), Ac_2O (0.48 mL, 5.04 mmol) and a catalytic amount of DMAP were added, and the reaction mixture was stirred at room temperature for 14 h. Then MeOH was added at 0 °C, the reaction mixture was co-evaporated with toluene, and diluted with $CHCl_3$. The organic layer was washed with 2 M HCl, H_2O, satd $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (1:20 EtOAc–toluene) to give **26** (512 mg, 85%); $[\alpha]_D$ +32.0 (*c* 0.35, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.03–7.14 (m, 20H, 4Ph), 5.70 (t, 1H, $J_{1,2}$ = $J_{2,3}$ = 9.6 Hz, H-2), 5.00 and 4.64 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 4.75 (d, 1H, H-1), 4.66 and 4.54 (2d, 2H, J_{gem} = 12.3 Hz, OCH_2), 4.29 (dd, 1H, J_{gem} = 10.9 Hz, H-6), 4.13 (dd, 1H, J_{gem} = 10.9 Hz, H-6′), 3.91 (d, 1H, H-4), 3.71 (dd, 1H, $J_{2,3}$ = 9.6 Hz, H-3), 3.68 (t, 1H, H-5), 2.00 (s, 3H, Ac); ^{13}C NMR (150 MHz, $CDCl_3$): δ 170.5, 165.2, 137.9, 137.3, 133.4, 133.0, 132.1, 129.9, 129.8, 128.6, 128.3, 128.3, 128.2, 127.8, 127.7, 127.7, 127.5, 86.7, 81.2, 76.2, 74.1, 72.3, 72.2, 70.2, 63.4, 20.7; MALDI-TOFMS: calcd for $[C_{35}H_{34}O_7S+Na]^+$: *m/z* 621.19. Found: *m/z* 621.19.

3.9. Methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)-4-*O*-acetyl-2,6-di-*O*-benzoyl-D-galactopyranosyl diethylphosphite (29)

To a solution of compound **27** (120 mg, 132 μmol) in MeCN (2.5 mL) were added *N*,*N*-diisopropylethylamine (69 μL, 398 μmol) and $ClP(OEt)_2$ (39 μL, 266 μmol), and the reaction mixture was stirred at 0 °C to room temperature for 1 h and monitored by TLC (15:1 $CHCl_3$–MeOH). After completion of the reaction, the solvent was evaporated, and the resulting residue was purified by column chromatography on silica gel (60:1 $CHCl_3$–MeOH) to give **29** (98 mg, 73%, α:β = 1:1.8); ^{1}H NMR (500 MHz, $CDCl_3$): β isomer; δ 8.15 and 8.05 (2d, 4H, Ph), 7.62–7.15 (m, 6H, Ph), 5.61 (m, 1H, H-8b), 5.38 (d, 1H, $J_{1,2}$ = 9.0 Hz, H-1a), 5.38 (t, 1H, H-2a), 5.19 (dd, 1H, H-7b), 5.14 (d, 1H, H-4a), 4.99 (d, 1H, $J_{5,NH}$ = 10.0 Hz, NH-b), 4.91–4.81 (m, 2H, H-3a, 4b), 4.44 (dd, 1H, J_{gem} = 11.0 Hz, H-6a), 4.29 (dd, 1H, J_{gem} = 12.5 Hz, H-9b), 4.25 (dd, 1H, J_{gem} = 11.0 Hz, H-6′a), 4.16 (t, 1H, H-5a), 3.96 (dd, 1H, J_{gem} = 12.5 Hz, H-9′b), 3.77 (s, 3H, COOMe), 3.65–3.54 (m, 3H, H-6b, $2CH_2CH_3$), 2.56 (dd, 1H, J_{gem} = 12.6 Hz, $J_{3eq,4}$ = 4.5 Hz, H-3*eq*-b), 2.16, 2.16, 2.07, 1.96, 1.78, 1.43 (6s, 18H, 6Ac), 1.73 (t, 1H, J_{gem} = 12.6 Hz, H-3*ax*-b), 1.13 and 0.84 (2t, 6H, $2CH_2CH_3$); MALDI-TOFMS: calcd for $[C_{46}H_{58}NO_{23}P+K]^+$: *m/z* 1062.27. Found: *m/z* 1062.18.

3.10. [Methyl 5-acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosyl-ono-1′,9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate]-(2→3)-2,4,6-tri-*O*-benzoyl-D-galactopyranosyl diethylphosphite (32)

To a solution of compound **30** (80 mg, 60 μmol) in MeCN (1.5 mL) were added *N*,*N*-diisopropylethylamine (32 μL, 181 μmol) and $ClP(OEt)_2$ (22 μL, 151 μmol), and the reaction mixture was stirred at 0 °C to room temperature for 1 h and monitored by TLC (15:1 $CHCl_3$–MeOH). After the completion of the reaction, the solvent was evaporated. The residue was purified by column chromatography on silica gel (40:1 $CHCl_3$–MeOH) to give **32** (76 mg, 87%, α:β = 5.5:1); ^{1}H NMR (600 MHz, $CDCl_3$): α-isomer; δ 8.07, 8.05 and 8.00 (3d, 6H, Ph), 7.60–7.39 (m, 9H, Ph), 6.03 (dd, 1H, $J_{1,2}$ = 4.1 Hz, H-2a), 5.87 (d, 1H, $J_{3,4}$ = 3.4 Hz, H-4a), 5.58 (td, 1H, $J_{3eq,4}$ = 5.5 Hz, H-4c), 5.56 (d, 1H, $J_{1,2}$ = 4.1 Hz, H-1a), 5.56 (d, 1H, $J_{5,NH}$ = 10.3 Hz, NH-b), 5.48 (dd, 1H, $J_{3,4}$ = 3.4 Hz, H-3a), 5.44 (d, 1H, $J_{5,NH}$ = 10.3 Hz, NH-c), 5.35 (dd, 1H, $J_{6,7}$ = 2.1 Hz, H-7c), 5.26 (td, 1H, $J_{3eq,4}$ = 5.5 Hz, H-4b), 5.19 (m, 1H, H-8c), 5.01 (dd, 1H, $J_{6,7}$ = 1.3 Hz, H-7b), 4.72 (m, 1H, H-8b), 4.72 (dd, 1H, H-6a), 4.66 (t, 1H, H-5a), 4.45–4.38 (m, 2H, H-6′a, 9b), 4.29 (dd, 1H, J_{gem} = 13.0 Hz, H-9c), 4.23 (q, 1H, $J_{5,6}$ = $J_{5,NH}$ = 10.3 Hz, H-5b), 4.13 (q, 1H, $J_{5,6}$ = $J_{5,NH}$ = 10.3 Hz, H-5c), 4.06 (dd, 1H, H-9′b), 4.02 (dd, 1H, J_{gem} = 13.0 Hz, H-9′c), 3.94 (dd, 1H, $J_{5,6}$ = 10.3 Hz, $J_{6,7}$ = 1.3 Hz, H-6b), 3.92 (dd, 1H, $J_{5,6}$ = 10.3 Hz, $J_{6,7}$ = 2.1 Hz, H-6c), 3.84–3.79 (m, 2H, $2CH_2CH_3$), 3.78–3.69 (m, 2H, $2CH_2CH_3$), 3.20 (s, 3H, COOMe), 2.50 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 5.5 Hz, H-3*eq*-c), 2.22 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 5.5 Hz, H-3*eq*-b), 2.16 (t, 1H, J_{gem} = 13.0 Hz, H-3*ax*-b), 2.12, 2.11, 2.10, 2.05, 2.05, 1.94, 1.89 and 1.88 (8s, 24H, 8Ac), 1.62 (t, 1H, J_{gem} = 13.0 Hz, H-3*ax*-c), 1.08 and 1.01 (2t, 6H, $2CH_2CH_3$); MALDI-TOFMS: calcd for $[C_{66}H_{79}N_2O_{32}P+Na]^+$: *m/z* 1465.42. Found: *m/z* 1465.54.

3.11. 2-(Trimethylsilyl)ethyl 6-*O*-acetyl-2-*O*-benzoyl-3,4-di-*O*-benzyl-β-D-galactopyranosyl-(1→3)-2-acetamido-6-*O*-acetyl-4-*O*-benzyl-2-deoxy-β-D-galactopyranosyl-(1→4)-{methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)}-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (33)

A suspension of compound **26** (42 mg, 69 μmol), compound **24** (59 mg, 34 μmol), and 4 Å molecular sieves (160 mg) in dry CH_2Cl_2 (2.0 mL) was stirred at room temperature for 1 h. NIS (39 mg, 173 μmol) was added to the mixture. The mixture was then cooled to 0 °C, and TfOH (1.5 μL, 17 μmol) was added. The mixture was stirred at 0 °C for 2 h, with monitoring by TLC (20:1 $CHCl_3$–MeOH). Et_3N was added to quench the reaction. The mixture was filtered through Celite. The combined filtrate and washings were diluted

with $CHCl_3$, and the organic layer was washed with satd $NaHCO_3$, satd $Na_2S_2O_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (30:30:1 EtOAc–toluene–MeOH) to give **33** (57 mg, 75%); $[\alpha]_D$ −5.5 (*c* 1.0, $CHCl_3$); Ratio of rotamer A:B: 1.80:1 ($CDCl_3$), 9.62:1 (CD_3CN), 10.4:1 (THF-d_8); rotamer A: ^{1}H NMR (600 MHz, THF-d_8): δ 8.00–6.81 (m, 46H, NH-d, 9Ph), 6.77 (d, 1H, NH-c), 5.69 (t, 1H, $J_{1,2}$ = 8.2 Hz, H-2e), 5.62 (m, 1H, H-8c), 5.29 (dd, 1H, H-7c), 5.11 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1d), 5.06 and 4.76 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 5.04 (d, 1H, $J_{1,2}$ = 10.9 Hz, H-1a), 5.01 and 4.61 (2d, 2H, J_{gem} = 11.6 Hz, OCH_2), 4.96 and 4.62 (2d, 2H, J_{gem} = 12.3 Hz, OCH_2), 4.86 and 4.69 (2d, 2H, J_{gem} = 11.6 Hz, OCH_2), 4.85 and 4.59 (2d, 2H, J_{gem} = 10.3 Hz, OCH_2), 4.82 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1e), 4.75 (td, 1H, $J_{3eq,4}$ = 4.8 Hz, H-4c), 4.70 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 4.67 and 4.54 (2d, 2H, J_{gem} = 11.7 Hz, OCH_2), 4.43 (d, 1H, OCH_2), 4.32–4.25 (m, 5H, H-3b, 3d, 6e, 2OCH_2), 4.17–4.13 (m, 2H, H-9c, 6′e), 4.11–4.03 (m, 6H, H-4b, 5c, 6d, 6′d, 4e, OCH_2), 3.98–3.92 (m, 2H, H-9′c, $CH_2CH_2SiMe_3$), 3.84–3.80 (m, 2H, H-3e, 6c), 3.78–3.75 (m, 5H, H-6a, 5e, COOMe), 3.67 (t, 1H, H-5d), 3.60–3.54 (m, 5H, H-4a, 6′a, 6b, 4d, $CH_2CH_2SiMe_3$), 3.54 (t, 1H, $J_{1,2}$ = 7.5 Hz, H-2b), 3.47 (t, 1H, H-5b), 3.45 (t, 1H, H-3a), 3.39 (m, 1H, H-5a), 3.26 (dd, 1H, H-6′b), 3.22–3.17 (m, 2H, H-2a, 2d), 2.93 (dd, 1H, J_{gem} = 13.7 Hz, $J_{3eq,4}$ = 4.8 Hz, H-3*eq*-c), 2.01, 1.95, 1.91, 1.82, 1.74, 1.68, 1.65 and 1.44 (8s, 24H, 8Ac), 1.81 (t, 1H, J_{gem} = 13.7 Hz, H-3*ax*-c), 0.96 (m, 2H, CH_2SiMe_3), 0.00 (s, 9H, CH_2SiMe_3); ^{13}C NMR (150 MHz, THF-d_8): δ 170.4, 170.3, 170.3, 170.1, 170.1, 169.8, 169.6, 169.4, 165.0, 140.8, 140.4, 140.3, 140.2, 139.9, 139.6, 139.0, 133.4, 131.6, 130.5, 129.5, 129.2, 128.9, 128.7, 128.6, 128.6, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 128.0, 128.0, 127.9, 127.9, 127.7, 127.7, 127.6, 127.5, 127.4, 127.3, 127.3, 103.6, 103.3, 100.1, 99.0, 83.7, 83.0, 81.4, 80.4, 78.6, 77.9, 77.0, 76.5, 76.0, 75.6, 75.1, 74.8, 74.8, 74.2, 74.2, 73.8, 73.3, 73.2, 73.1, 72.9, 72.9, 72.6, 72.2, 70.2, 69.8, 69.0, 67.7, 67.7, 67.6, 67.4, 63.9, 63.5, 62.8, 55.6, 52.8, 49.5, 38.5, 30.5, 25.6, 25.5, 25.3, 23.7, 22.6, 21.1, 20.6, 20.5, 20.4, 20.4, 20.3, 18.9, −1.2; MALDI-TOFMS: calcd for $[C_{118}H_{140}N_2O_{36}Si+Na]^+$: *m/z* 2211.88. Found: *m/z* 2211.77.

3.12. 2-(Trimethylsilyl)ethyl (methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate)-(2→3)-4-*O*-acetyl-2,6-di-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-acetamido-6-*O*-acetyl-4-*O*-benzyl-2-deoxy-β-D-galactopyranosyl-(1→4)-{methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)}-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (34)

A suspension of compound **29** (48 mg, 46 μmol), compound **24** (40 mg, 23 μmol), and AW-300 molecular sieves (203 mg) in dry CH_2Cl_2 (2.0 mL) was stirred at room temperature for 1 h. The mixture was cooled to 0 °C, TMSOTf (1.7 μL, 9.2 μmol) was added, and the reaction mixture was stirred at 0 °C for 2 h with monitoring by TLC (40:1 $CHCl_3$–MeOH). Et_3N was added to quench the reaction. The mixture was filtered through Celite. The combined filtrate and washings were diluted with $CHCl_3$ and the organic layer was washed with satd $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (50:1→35:1 $CHCl_3$–MeOH) to give **34** (36 mg, 60%); $[\alpha]_D$ −5.9 (*c* 0.84, $CHCl_3$); Ratio of rotamer A:B: 2.83:1 ($CDCl_3$), 8.60:1 (THF-d_8), 14.7:1 (CD_3CN); rotamer A: ^{1}H NMR (600 MHz, CD_3CN): δ 8.08–6.77 (m, 40H, 8Ph), 6.10 (d, 1H, NH-c), 6.08 (d, 1H, NH-d), 5.97 (d, 1H, NH-f), 5.47 (m, 1H, H-8f), 5.35–5.31 (m, 2H, H-2e, 4e), 5.21 (dd, 1H, H-7f), 5.20 (dd, 1H, H-7c), 5.18 (m, 1H, H-8c), 5.01 (dt, 1H, $J_{3eq,4}$ = 4.8 Hz, H-4c), 5.00 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1e), 4.97 and 4.69 (2d, 2H, J_{gem} = 11.0 Hz, OCH_2), 4.85 and 4.51 (2d, 2H, J_{gem} = 9.6 Hz, OCH_2), 4.81 and 4.73 (2d, 2H, J_{gem} = 11.0 Hz, OCH_2), 4.81 (dd, 1H, H-3e), 4.77 (dt, 1H, H-4f), 4.67 and 4.52 (2d, 2H, J_{gem} = 10.3 Hz, OCH_2), 4.67 (d, 1H, $J_{1,2}$ = 10.3 Hz, H-1d), 4.46 (dd, 1H, J_{gem} = 11.7 Hz, H-6e), 4.43 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1b), 4.41 (q, 2H, OCH_2), 4.34 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1a), 4.33 (dd, 1H, J_{gem} = 11.7 Hz, H-6′e), 4.29 (dd, 1H, H-9f), 4.26 (d, 1H, OCH_2), 4.19 (t, 1H, H-5e), 4.16–4.12 (m, 2H, H-3d, 6d), 4.08–3.85 (m, 13H, H-3b, 2d, 6′d, 5c, 6c, 9c, 9′c, 9′f, OCH_2, COOMe, $CH_2CH_2SiMe_3$), 3.80 (t, 1H, H-5d), 3.76–3.67 (m, 8H, H-4a, 4b, 4d, 5f, 6f, COOMe), 3.63–3.56 (m, 3H, H-6a, 6′a, $CH_2CH_2SiMe_3$), 3.51 (dd, 1H, J_{gem} = 10.9 Hz, H-6b), 3.45 (t, 1H, $J_{2,3}$ = 8.9 Hz, H-3a), 3.43 (t, 1H, H-5b), 3.39 (m, 1H, H-5a), 3.31 (t, 1H, $J_{1,2}$ = 7.5 Hz, H-2b), 3.23 (dd, 1H, J_{gem} = 10.9 Hz, H-6′b), 3.07 (t, 1H, $J_{1,2}$ = 7.5 Hz, $J_{2,3}$ = 8.9 Hz, H-2a), 2.43 (dd, 1H, $J_{3eq,4}$ = 4.8 Hz, H-3*eq*-c), 2.37 (dd, 1H, J_{gem} = 12.3 Hz, H-3*eq*-f), 2.15, 2.07, 2.07, 2.04, 2.00, 1.93, 1.92, 1.84, 1.84, 1.80, 1.76, 1.73 and 1.67 (13s, 39H, 13Ac), 2.07 (t, 1H, H-3*ax*-c), 1.49 (t, 1H, J_{gem} = 12.3 Hz, H-3*ax*-f), 0.96 (m, 2H, CH_2SiMe_3), 0.00 (s, 9H, CH_2SiMe_3); ^{13}C NMR (150 MHz, CD_3CN): δ 171.4, 171.3, 171.2, 171.1, 171.0, 170.8, 170.7, 170.7, 170.6, 170.5, 170.2, 169.5, 168.9, 166.6, 165.7, 140.2, 140.1, 140.0, 139.9, 139.6, 139.6, 134.3, 134.1, 131.0, 130.8, 130.7, 130.4, 130.3, 129.7, 129.5, 129.5, 129.2, 129.2, 129.1, 129.1, 129.0, 129.0, 129.0, 128.9, 128.7, 128.5, 128.5, 128.3, 128.3, 128.3, 128.2, 128.1, 128.0, 103.7, 103.5, 103.4, 102.8, 100.4, 98.4, 83.3, 82.5, 81.7, 79.9, 78.7, 77.0, 76.9, 76.4, 76.2, 75.7, 75.4, 75.3, 75.3, 74.3, 73.6, 73.5, 72.7, 72.5, 72.4, 72.0, 71.6, 71.5, 70.6, 70.5, 70.2, 69.4, 69.1, 68.9, 68.8, 67.8, 67.6, 67.3, 64.5, 63.2, 62.9, 62.3, 53.8, 53.7, 52.4, 49.3, 49.1, 38.0, 35.8, 30.3, 23.3, 23.1, 23.0, 21.6, 21.4, 21.2, 21.1, 21.0, 20.9, 20.9, 20.9, 20.9, 20.8, 18.9, 1.9, −1.3; MALDI-TOFMS: calcd for $[C_{131}H_{159}N_3O_{49}Si+Na]^+$: *m/z* 2608.97. Found: *m/z* 2608.31.

3.13. 2-(Trimethylsilyl)ethyl [methyl 5-acetamido-8-*O*-(5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylono-1′,9-lactone)-4,7-di-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate]-(2→3)-2,4,6-tri-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-acetamido-6-*O*-acetyl-4-*O*-benzyl-2-deoxy-β-D-galactopyranosyl-(1→4)-{methyl 5-acetamido-4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonate-(2→3)}-2,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3,6-tri-*O*-benzyl-β-D-glucopyranoside (35)

A suspension of compound **32** (74 mg, 51 μmol), compound **24** (44 mg, 25 μmol), and AW-300 molecular sieves (155 mg) in dry CH_2Cl_2 (2.0 mL) was stirred at room temperature for 1 h. After the suspension was cooled to 15 °C, TMSOTf (1.9 μL, 10 μmol) was added, and the reaction mixture was stirred at 15 °C for 5.5 h. The progress of the reaction was monitored by TLC (5:5:1 EtOAc–toluene–MeOH). After quenching the reaction, the mixture was worked up as described for compound **34**. The resulting residue was chromatographed on silica gel (12:12:1→5:5:1 EtOAc–toluene–MeOH) to give **35** (52 mg, 68%); $[\alpha]_D$ −17.5 (*c* 0.37, $CHCl_3$); Ratio of rotamer A:B: 2.18:1 ($CDCl_3$), 11.0:1 (THF-d_8), 12.4:1 (CD_3CN); rotamer A: ^{1}H NMR (600 MHz, THF-d_8): δ 8.07–6.73 (m, 47H, NH-d, NH-g, 9Ph), 6.99 (d, 1H, NH-f), 6.79 (d, 1H, NH-c), 5.88 (d, 1H, H-4e), 5.65 (t, 1H, $J_{1,2}$ = 7.5 Hz, H-2e), 5.63 (m, 1H, H-8c), 5.52 (td, 1H, $J_{3eq,4}$ = 5.5 Hz, H-4g), 5.35 (dd, 1H, H-7g), 5.30 (dd, 1H, H-7c), 5.26 (d, 1H, $J_{1,2}$ = 10.9 Hz, H-1d), 5.22 (dd, 1H, H-7f), 5.17 (d, 1H, $J_{1,2}$ = 7.5 Hz, H-1e), 5.14 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1a), 5.08 (m, 1H, H-8g), 5.04 (td, 1H, H-4f), 4.98 and 4.62 (2d, 2H, J_{gem} = 12.3 Hz, OCH_2), 4.88–4.83 (m, 3H, 3OCH_2), 4.78 (td, 1H, $J_{3eq,4}$ = 4.1 Hz, H-4c), 4.74–4.71 (m, 5H, H-1b, 3e, 8f, 2OCH_2), 4.69 (d, 1H, OCH_2), 4.61 (d, 1H, OCH_2), 4.56 (dd, 1H, J_{gem} = 11.7 Hz, H-6e), 4.44 (dd, 1H, J_{gem} = 11.7 Hz, H-6′e), 4.44 (d, 1H, OCH_2), 4.36 (t, 1H, H-5e), 4.35–4.21 (m, 6H, H-3b, 3d, 9f, 9g, 2OCH_2), 4.18–4.02 (m, 6H, H-5c, 9c, 6d, 6′d, 5f, 5g), 4.01–3.94 (m, 4H, H-4b, 9′c, 9′g, $CH_2CH_2SiMe_3$), 3.85–3.75 (m, 8H, H-6a, 6c, 6f, 9′f, 6g, COOMe), 3.72 (t, 1H, H-5d), 3.60–3.55 (m, 5H, H-4a, 6′a, 6b, 4d, $CH_2CH_2SiMe_3$), 3.54 (t, 1H,

H-2b), 3.48 (t, 1H, H-5b), 3.46 (t, 1H, H-3a), 3.40 (m, 1H, H-5a), 3.26 (dd, 1H, H-6′b), 3.24–3.20 (m, 2H, H-2a, 2d), 3.14 (s, 3H, COOMe), 2.96 (dd, 1H, $J_{3eq,4}$ = 4.1 Hz, H-3*eq*-c), 2.56 (dd, 1H, J_{gem} = 13.0 Hz, $J_{3eq,4}$ = 5.5 Hz, H-3*eq*-g), 2.12–1.68 (m, 3H, H-3*ax*-c, 3*eq*-f, 3*ax*-f), 2.03, 2.02, 1.98, 1.95, 1.94, 1.85, 1.80, 1.79, 1.69, 1.68, 1.68 and 1.41 (12s, 45H, 15Ac), 1.46 (t, 1H, J_{gem} = 13.0 Hz, H-3*ax*-g), 0.96 (m, 2H, $CH_2CH_2SiMe_3$), 0.00 (s, 9H, CH_2SiMe_3); ^{13}C NMR (150 MHz, CD_3CN): δ 171.3, 171.2, 171.2, 170.9, 170.8, 170.7, 170.6, 170.6, 170.5, 170.4, 170.2, 170.1, 169.6, 168.5, 166.7, 166.5, 165.2, 165.1, 140.2, 140.1, 139.9, 139.6, 134.3, 134.3, 130.7, 130.6, 130.6, 130.5, 130.2, 129.7, 129.6, 129.5, 129.4, 129.2, 129.1, 129.1, 129.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 117.0, 103.8, 103.5, 103.2, 102.8, 100.5, 98.6, 83.3, 82.5, 82.3, 79.9, 78.8, 77.4, 76.8, 76.4, 76.3, 75.8, 75.7, 75.4, 75.3, 74.3, 73.6, 73.5, 72.7, 72.7, 72.4, 72.4, 71.8, 70.9, 70.6, 70.4, 69.7, 69.2, 69.0, 68.7, 67.6, 67.3, 64.5, 63.9, 62.6, 62.3, 53.8, 53.2, 52.5, 49.4, 49.3, 48.4, 39.3, 36.0, 35.8, 30.3, 23.1, 23.1 23.0, 23.0, 21.4, 21.1, 21.1, 21.0, 21.0, 20.9, 20.9, 20.9, 20.8, 18.9, 2.7, 2.5, 1.8, −1.3; MALDI-TOFMS: calcd for $[C_{151}H_{180}N_4O_{58}Si+Na]^+$: *m/z* 3028.09. Found: *m/z* 3028.78.

3.14. 2-(Trimethylsilyl)ethyl β-D-galactopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranosyl-(1→4)-{5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid-(2→3)}-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (1)

To a solution of compound **33** (57 mg, 26 μmol) in 1:1 EtOH–THF (4.0 mL) was added 20% $Pd(OH)_2$-on-charcoal (53 mg). The suspension was stirred at 40 °C under an H_2 atmosphere for 19 h. The progress of the reaction was monitored by TLC (5:1 $CHCl_3$–MeOH). The reaction mixture was filtered through Celite, and the combined filtrate and washings were concentrated. The residue was dissolved in MeOH, a catalytic amount of NaOMe (28% MeOH solution) was added, and the resulting mixture was stirred at room temperature for 3 days and at 40 °C for another 2 days. H_2O was then added to the mixture, and the mixture was stirred at 40 °C for 1 day (TLC; 2:1:1 *n*-BuOH–MeOH–5% aq $CaCl_2$). The mixture was cooled to room temperature and neutralized with IR-120 (H^+) resin, filtered through cotton, and the combined filtrate and washings were concentrated. The residue was purified by gel-filtration column chromatography on Sephadex LH-20 (1:1 MeOH–H_2O) to give **1** (25 mg, 87%); $[\alpha]_D$ +9.7 (*c* 0.41, 1:1 MeOH–H_2O); ^{1}H NMR (500 MHz, 1:1 CD_3OD–D_2O): δ 2.65 (dd, 1H, J_{gem} = 12.5 Hz, H-3*eq*-c), 2.01 and 1.97 (2s, 6H, 2NAc), 1.88 (t, 1H, J_{gem} = 12.5 Hz, H-3*ax*-c), 0.99 (m, 2H, CH_2SiMe_3), 0.00 (s, 9H, CH_2SiMe_3); ^{13}C NMR (125 MHz, 1:1 CD_3OD–D_2O): δ 176.0, 175.4, 175.0, 105.9, 103.9, 103.6, 102.9, 81.8, 80.1, 78.5, 76.0, 75.8, 75.8, 75.6, 75.4, 75.2, 74.4, 74.0, 73.8, 73.2, 71.9, 71.0, 69.8, 69.5, 69.4, 69.1, 68.9, 64.2, 62.3, 62.0, 61.6, 61.2, 53.0, 52.2, 38.0, 23.6, 22.8, 18.7, −1.4; MALDI-TOFMS: calcd for $[C_{42}H_{74}N_2O_{29}Si+Na]^+$: *m/z* 1121.40. Found: *m/z* 1121.59.

3.15. 2-(Trimethylsilyl)ethyl (5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-β-D-galactopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranosyl-(1→4)-{5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid-(2→3)}-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (2)

To a solution of compound **34** (23 mg, 8.8 μmol) in 1:1 EtOH–THF (2.0 mL) was added 20% $Pd(OH)_2$-on-charcoal (20 mg). The suspension was stirred at 40 °C under an H_2 atmosphere for 15 h. The progress of the reaction was monitored by TLC (10:1 $CHCl_3$–MeOH). The reaction mixture was filtered through Celite, and the combined filtrate and washings were concentrated. The residue was dissolved in MeOH, and a catalytic amount of NaOMe (28% MeOH solution) was added. The resulting mixture was stirred at room temperature for 2 days and at 50 °C for another 3 days. Then H_2O was added, and the mixture was stirred at 40 °C for 1 day (TLC; 2:1:1 *n*-BuOH–MeOH–5% aq $CaCl_2$). The mixture was cooled to room temperature and neutralized with IR-120 (H^+) resin and filtered through cotton, and the combined filtrate and washings were concentrated. The residue was purified by gel-filtration column chromatography on Sephadex LH-20 (1:1 MeOH–H_2O) to give **2** (10 mg, 81%); $[\alpha]_D$ +6.9 (*c* 1.0, 1:1 MeOH–H_2O); ^{1}H NMR (500 MHz, 1:1 CD_3OD–D_2O): δ 2.73 (dd, 1H, H-3*eq*^{Neu}), 2.67 (dd, 1H, H-3*eq*^{Neu}), 2.01, 2.00 and 1.97 (3s, 9H, 3NAc), 1.86 (t, 1H, H-3*ax*^{Neu}), 1.77 (t, 1H, H-3*ax*^{Neu}), 0.99 (m, 2H, $CH_2CH_2SiMe_3$), 0.00 (s, 9H, CH_2SiMe_3); ^{13}C NMR (125 MHz, 1:1 CD_3OD–D_2O): δ 176.0, 175.8, 175.3, 175.0, 174.9, 105.7, 103.9, 103.7, 102.8, 102.7, 100.8, 81.9, 80.0, 78.2, 76.7, 75.8, 75.8, 75.7, 75.6, 75.4, 75.2, 74.3, 74.0, 74.0, 73.2, 72.8, 71.0, 70.3, 69.5, 69.4, 68.9, 68.5, 64.2, 63.7, 62.3, 62.1, 61.6, 61.2, 53.1, 53.0, 52.1, 41.0, 38.3, 23.6, 22.8, 18.7, −1.4; MALDI-TOFMS: calcd for $[C_{53}H_{87}N_3O_{37}Si+3Na]^+$: *m/z* 1456.46. Found: *m/z* 1456.63.

3.16. 2-(Trimethylsilyl)ethyl (5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→8)-(5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid)-(2→3)-β-D-galactopyranosyl-(1→3)-2-acetamido-2-deoxy-β-D-galactopyranosyl-(1→4)-{5-acetamido-3,5-dideoxy-D-*glycero*-α-D-*galacto*-2-nonulopyranosylonic acid-(2→3)}-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (3)

To a solution of compound **35** (96 mg, 31 μmol) in 1:1 EtOH–THF (4 mL) was added 20% $Pd(OH)_2$-on-charcoal (95 mg). The suspension was stirred at 40 °C under an H_2 atmosphere for 13 h, with monitoring of the reaction by TLC (10:1 $CHCl_3$–MeOH). The reaction mixture was filtered through Celite and the combined filtrate and washings were concentrated. The residue was dissolved in MeOH, and a catalytic amount of NaOMe (28% MeOH solution) was added. The resulting mixture was stirred at room temperature for 2.5 days and at 50 °C for another 3 days. Then H_2O was added, and the mixture was stirred at 40 °C for 1 day, with monitoring of the reaction by TLC (2:1:1 *n*-BuOH–MeOH5% aq $CaCl_2$). The mixture was cooled to room temperature, neutralized with IR-120 (H^+) resin, and filtered through cotton, and the combined filtrate and washings were concentrated. The residue was purified by gel-filtration column chromatography on Sephadex LH-20 (1:1 MeOH–H_2O) to give **3** (49 mg, 92%); $[\alpha]_D$ −4.7 (*c* 1.1, 1:1 MeOH–H_2O); ^{1}H NMR (500 MHz, 1:1 CD_3OD–D_2O): δ 2.97 (br d, 1H, H-3*eq*-^{Neu}), 2.66 (br d, 2H, 2H-3*eq*^{Neu}), 2.01, 2.00 and 2.00 (3s, 12H, 4NAc), 1.89 (t, 1H, H-3*ax*^{Neu}), 1.68 (t, 2H, 2H-3*ax*^{Neu}), 0.99 (m, 2H, CH_2SiMe_3), 0.00 (s, 9H, CH_2SiMe_3); ^{13}C NMR (125 MHz, 1:1 CD_3OD–D_2O): δ 176.3, 176.1, 175.6, 175.5, 175.4, 174.4, 174.3, 105.4, 103.9, 103.5, 102.9, 101.8, 101.0, 81.6, 80.0, 78.8, 78.2, 75.9, 75.8, 75.6, 75.4, 75.2, 75.1, 74.7, 74.4, 74.3, 74.0, 73.2, 72.7, 70.9, 70.5, 69.6, 69.5, 69.4, 69.0, 69.0, 68.9, 68.8, 68.6, 67.9, 64.3, 63.9, 62.7, 62.3, 62.1, 61.5, 61.2, 54.0, 53.4, 53.2, 52.4, 42.5, 41.5, 37.9, 23.8, 23.0, 22.9, 22.8, 18.7, −1.4; MALDI-TOFMS: calcd for $[C_{64}H_{102}N_4Na_4O_{45}Si+4Na]^+$: *m/z* 1769.54. Found: *m/z* 1769.59.

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References

1. (a) Sugimoto, M.; Numata, M.; Koike, K.; Nakahara, Y.; Ogawa, T. *Carbohydr. Res.* **1986**, *156*, c1–c5; (b) Hasegawa, A.; Nagahama, T.; Ohki, H.; Kiso, M. *J. Carbohydr. Chem.* **1992**, *11*, 699–714; (c) Castro-Palomino, J. C.; Ritter, G.;

Fortunato, S. R.; Reinhardt, S.; Old, L. J.; Schmidt, R. R. *Angew. Chem., Int. Ed.* **1997**, *36*, 1998–2001.
2. (a) Hasegawa, A.; Nagahama, T.; Kiso, M. *Carbohydr. Res.* **1992**, *235*, C13–C17; (b) Stauch, T.; Greilich, U.; Schmidt, R. R. *Liebigs Ann. Chem.* **1995**, 2101–2111; (c) Greilich, U.; Brescello, R.; Jung, K.-H.; Schmidt, R. R. *Liebigs Ann. Chem.* **1996**, 663–672.
3. Ishida, H.-K.; Ando, H.; Ito, H.; Ishida, H.; Kiso, M.; Hasegawa, A. *J. Carbohydr. Chem.* **1997**, *16*, 413–428.
4. (a) Hasegawa, A.; Ishida, H.; Isogai, Y.; Ishida, H.; Kiso, M. *J. Carbohydr. Chem.* **1993**, *12*, 1217–1222; (b) Ishida, H.; Ohta, Y.; Tsukada, Y.; Isogai, Y.; Ishida, H.; Kiso, M.; Hasegawa, A. *Carbohydr. Res.* **1994**, *252*, 283–290; (c) Ishida, H.-K.; Ishida, H.; Kiso, M.; Hasegawa, A. *Carbohydr. Res.* **1994**, *260*, C1–C6; (d) Ishida, H.-K.; Ishida, H.; Kiso, M.; Hasegawa, A. *Tetrahedron: Asymmetry* **1994**, *5*, 2493–2512; (e) Imamura, A.; Ando, H.; Ishida, H.; Kiso, M. *J. Org. Chem.* **2009**, *74*, 3009–3023.
5. Tanaka, H.; Nishiura, Y.; Takahashi, T. *J. Am. Chem. Soc.* **2008**, *130*, 17244–17245.
6. (a) Ando, H.; Koike, Y.; Ishida, H.; Kiso, M. *Tetrahedron Lett.* **2003**, *44*, 6883–6886; (b) Fuse, T.; Ando, H.; Imamura, A.; Sawada, N.; Ishida, H.; Kiso, M.; Ando, T.; Li, S.-C.; Li, Y.-T. *Glycoconjugate J.* **2006**, *23*, 329–343; Other groups also reported *N*-Troc sialyl donor: (c) Ren, C.-T.; Chen, C.-S.; Wu, S.-H. *J. Org. Chem.* **2002**, *67*, 1376–1379; (d) Adachi, M.; Tanaka, H.; Takahashi, T. *Synlett* **2004**, 609–614; (e) Tanaka, H.; Adachi, M.; Takahashi, T. *Chem. Eur. J.* **2005**, *11*, 849–862; (f) Hanashima, S.; Castanger, B.; Esposito, D.; Nokami, T.; Seeberger, P. H. *Org. Lett.* **2007**, *9*, 1777–1779.
7. Komori, T.; Ando, T.; Imamura, A.; Li, Y.-T.; Ishida, H.; Kiso, M. *Glycoconjugate J.* **2008**, *25*, 647–661.
8. Imamura, A.; Ando, H.; Ishida, H.; Kiso, M. *Org. Lett.* **2005**, *7*, 4415–4418.
9. Konradsson, P.; Udodong, U. E.; Fraser-Reid, B. *Tetrahedron Lett.* **1990**, *31*, 4313–4316.
10. Chen, L.; Kong, F. *Tetrahedron Lett.* **2003**, *44*, 3691–3695.
11. Sakagami, M.; Hamana, H. *Tetrahedron Lett.* **2000**, *41*, 5547–5551.
12. Fürstner, A.; Nagano, T. *J. Am. Chem. Soc.* **2007**, *129*, 1906–1907.
13. Malet, C.; Hindsgaul, O. *Carbohydr. Res.* **1997**, *303*, 51–65.
14. Martin, T. J.; Schmidt, R. R. *Tetrahedron Lett.* **1992**, *33*, 6123–6126.
15. Imamura, A.; Yoshikawa, T.; Komori, T.; Ando, M.; Ando, H.; Wakao, M.; Suda, Y.; Ishida, H.; Kiso, M. *Glycoconjugate J.* **2008**, *25*, 269–278.
16. Zemplén, G. *Ber. Dtsch. Chem. Ges.* **1927**, *60*, 1555–1564.
17. Yamaguchi, M.; Ishida, H.; Kiso, M. *Heterocycles* **2009**, *77*, 333–349.