CHEMISTRY
AN ASIAN JOURNAL

DOI: 10.1002/asia.200600424

Total Synthesis of Sialylated Glycans Related to Avian and Human Influenza Virus Infection

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Abstract: Human and avian influenza type A viruses bind sialylated pentasaccharides. Herein, the total synthesis of four of these glycans is reported. Efficient sialylations relied on two *N*-Troc-protected (Troc = 2,2,2-trichloroethoxycarbonyl) sialic acid building blocks. The first, a thiophenyl glycoside, readily produced the sialyl-α(2-6)galactose disaccharide. Combination of the second building block, a novel glycosyl phosphite, and a benzylidene-protected galactoside produced the best results for the formation of the sialyl-α(2-3)galactose. Two common trisaccharides were assembled by the introduction of glucose, galactose, and glucosamine building blocks followed by selective deprotection. Two sets of pentasaccharides were obtained by the union of two sialylgalactose *N*-phenyl trifluoroacetimidate building blocks with the two trisaccharides above. Global deprotection furnished the desired pentasaccharides. The products of these total syntheses are currently employed on the surface of carbohydrate microarrays to detect and type different strains of the influenza virus.

Keywords: glycosylation · influenza · oligosaccharides · sialic acid · total synthesis

Introduction

The influenza virus poses a severe threat for a worldwide pandemic.[1] The strain H5N1, a highly virulent avian influenza virus, has been spreading in eastern Asia and Europe. The remarkable similarity between the strain responsible for the Spanish influenza pandemic in 1918 and H5N1 has been described based on gene-sequence analysis and reconstruction of the virus.[2] Viral strains are classified by differences in the surface antigens hemagglutinin and neuraminidase.

Cell-surface glycans that carry a terminal *N*-acetylneuraminic acid (Neu5Ac) play an essential role for viral infection.[3] Binding of the virus correlates with the type of sialic acid and the glycan sequence.[3d] The tertiary structure of hemagglutinin trimer in its interaction with sialylated glycans has been studied by combining X-ray crystallography and computational analysis.[4,5]

Human and avian viruses differ significantly in the way they interact with Neu5Ac on the surface of the host cells. Whereas the human influenza virus preferentially recognizes the Neu5Acα(2-6)Gal linkage, the avian flu virus binds to the Neu5Acα(2-3)Gal motif.[4–6] The epithelial cells of the human respiratory tract express both sequences, but differential distribution renders the direct infection of humans with avian viruses unlikely.[7]

To avoid the spread of pandemic influenza viruses, highly sensitive and rapid detection methods are urgently needed to identify potential hosts immediately. Carbohydrate-microarray technology holds great potential for the identification and typing of different viral strains.[6,8] Access to pure oligosaccharides in a form that allows for attachment to a microarray surface is the limiting step for the production of such carbohydrate arrays. Herein we report the synthesis of four viral receptor sialoglycans: **1a**, **1b**, **2a**, and **2b** (Scheme 1a).[3–6] These four pentasaccharides[9] represent all the permutations of the sialic acid α(2-3) or α(2-6) galactose bond and the glucosamine β(1-3) or β(1-4) galactose linkage found in nature.

Results and Discussion

The sialylated glycans **1a**, **1b**, **2a**, and **2b** were systematically assembled by using five building blocks (Scheme 1b). *N*-

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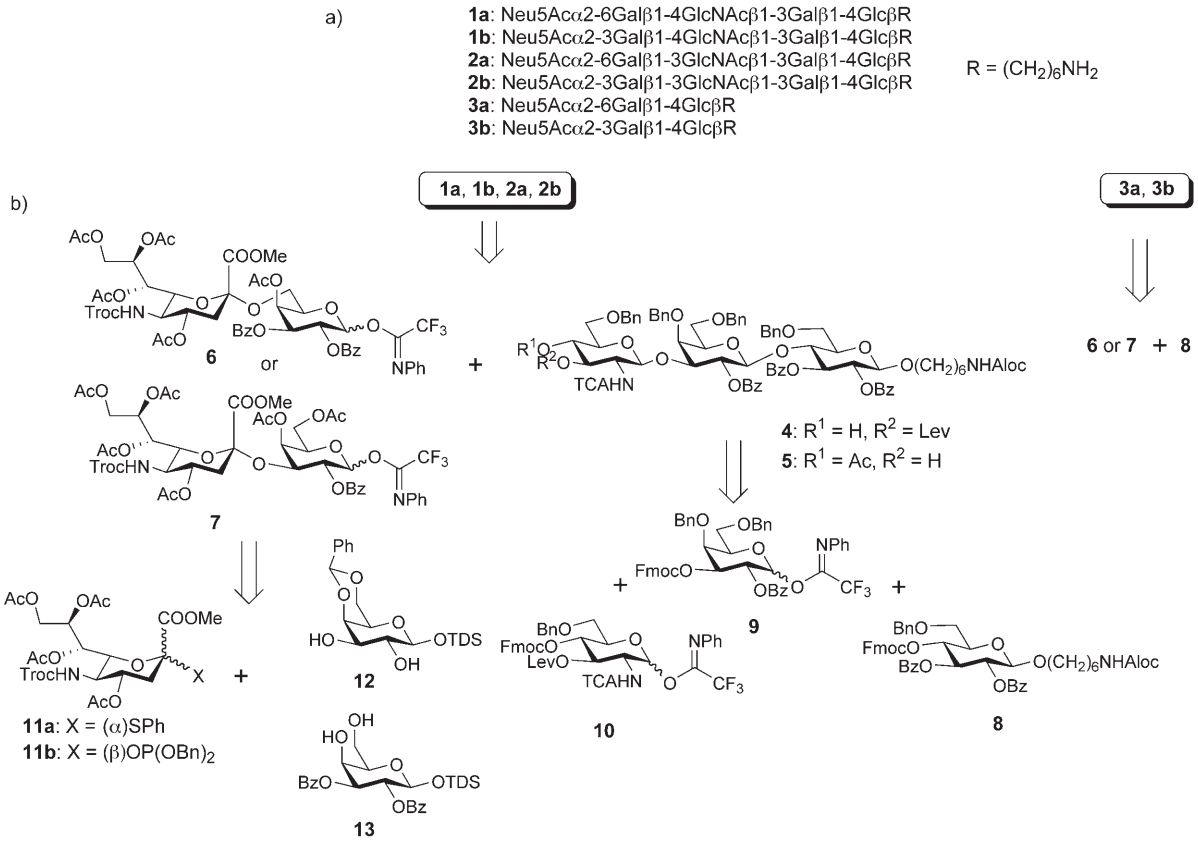
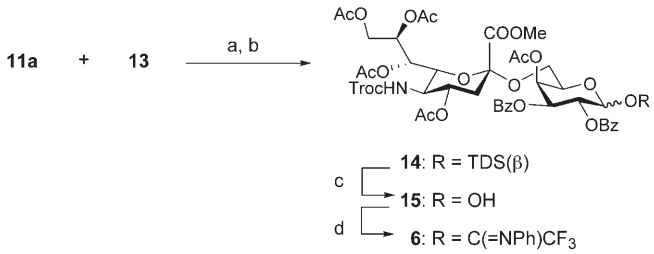


Scheme 1. a) Sialylated pentasaccharides that bind to influenza hemagglutinins. b) Linier synthetic plan and building blocks for assembling the pentasaccharides **1a**, **1b**, **2a**, and **2b**. Aloc = allyloxycarbonyl, Bn = benzyl, Bz = benzoyl, Fmoc = 9-fluorenylmethoxycarbonyl, Lev = levulinoyl, TCA = trichloroacetyl, TDS = thexyldimethylsilyl, Troc = 2,2,2-trichloroethoxycarbonyl.

Phenyl trifluoroacetimidate served as the anomeric leaving group for most of the glycosylations except for the sialylations. This leaving group circumvents rearrangements that result in acetamidate by-products.[10]

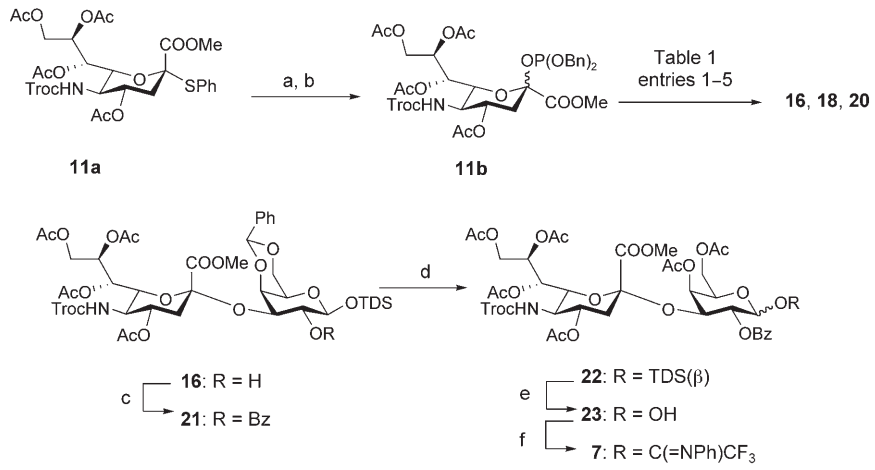
Neu5Ac-capped glycans **1a**, **1b**, **2a**, and **2b** of the neolacto and lacto series were synthesized from sialyl-α(2-6)galactose and sialyl-α(2-3)galactose building blocks **6** and **7** by coupling with trisaccharides **4** and **5**. All glycans were equipped with an amine handle connected to the reducing terminus by a C6 alkyl spacer. Sialylation of galactoside **12** and **13** was achieved with the *N*-Troc-protected phenylthio and phosphitidyl glycoside building blocks **11a**[11] or **11b** to furnish **6** and **7**. Few examples for the use of *N*-Troc sialic acid phosphite to create sialyl-α(2-3)galactose linkages exist.[15a] We explored this particular type of building block owing to its reactivity and the possibility of deriving various sialic acid species.[12c] Trisaccharide **4** was assembled from glucose **8**, galactose **9**, and glucosamine **10**. Selective manipulation of the protecting groups of **4** furnished building block **5**, which carries a C3 hydroxy group.

Initially, chemical sialylation reactions that involve building blocks **6** and **7** were explored (Scheme 2).[12,13] Neu5Acα-(2-6)Gal *N*-phenyl trifluoroacetimidate disaccharide **6** was synthesized from *N*-Troc sialyl phenylthioglycoside **11a**. Union with galactose diol **13** in acetonitrile at −40 °C produced the disaccharide,[14] before acetylation gave **14** in 71% yield (α/β = 6:1). At this stage, the anomeric TDS group was removed by treatment with HF/pyridine, before introduction of an anomeric *N*-phenyl trifluoroacetimidate produced the key sialyl-α(2-6)galactose building block **6** in 92% yield.



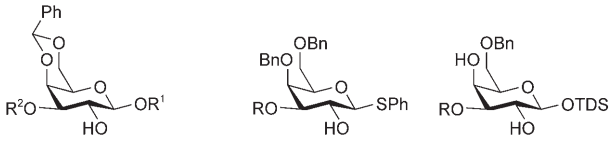
Scheme 2. Synthesis of sialyl-α(2-6)galactose building block **6**. Reagents and conditions: a) NIS, TfOH, CH_3CN, 4-Å molecular sieves, −40 °C; b) Ac_2O, pyridine, 71% (α/β = 6:1); c) HF/pyridine, DMF, 40 °C, 80%; d) $CF_3C(NPh)Cl$, Cs_2CO_3, CH_2Cl_2, 92%. DMF = *N*,*N*-dimethylformamide, NIS = *N*-iodosuccinimide, TfOH = trifluoromethanesulfonic acid.

The synthesis of the sialyl-α(2-3)galactose *N*-phenyl trifluoroacetimidate building block **7** is depicted in Scheme 3 and Table 1. Sialylation of **12**[16] with building block **11a** as



Scheme 3. Synthesis of sialyl-α(2-3)galactose building block **7**. Reagents and conditions: a) NBS, acetone, H_2O, 90%; b) $Et_2NP(OBn)_2$, tetrazole, CH_3CN, 86% (α/β = 1:8); c) BzCl (excess), pyridine, dichloroethane, 60°C, 89%; d) i) PPTS, CH_3CN/MeOH, reflux; ii) Ac_2O, pyridine, 92%; e) HF/pyridine, DMF, 45°C, 93%; f) $CF_3C(NPh)Cl$, Cs_2CO_3, CH_2Cl_2, 85%. NBS = *N*-bromosuccinimide, PPTS = pyridinium *p*-toluenesulfonate.

Table 1. Sialylation of galactoses **12**, **17**, and **19** with **11**.



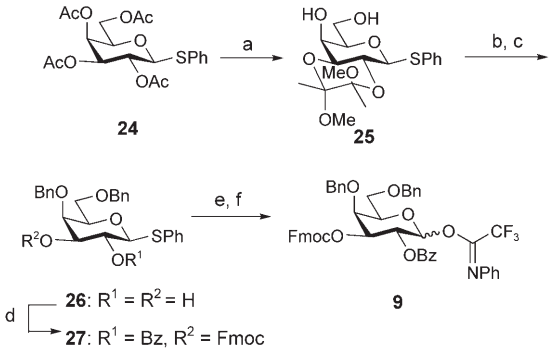
Entry	Sialic acid building block	Nucleophile	Conditions[a]	Product	Yield[b] [%]
1	**11a**	**12**	A	**16**	33
2	**11b**	**17**	B	**18**	32
3	**11b**	**19**	B	**20**	30
4	**11b**	**12**	B	**16**	51
5	**11b**	**12**	C	**16**	65

[a] A: NIS (1.5 equiv), TfOH (0.2 equiv), 4-Å molecular sieves, −35°C in CH_3CN; B: TMSOTf (0.1 equiv), 4-Å molecular sieves, −35°C in CH_3CN; C: TMSOTf (0.1 equiv), 4-Å molecular sieves, −78°C in CH_3CH_2CN. [b] Yield of the isolated α anomer. Sia = sialyl, TMS = trimethylsilyl.

well as NIS and TfOH furnished **16** in low yield (Table 1, entry 1). The TDS group was partially cleaved under these conditions. Consequently, **11a** was transformed into phosphite **11b** to explore other activating conditions. The phenylthio glycoside **11a** was hydrolyzed by treatment with NBS in aqueous acetone prior to the introduction of bisbenzylphosphite by *N*,*N*-bisethylaminophosphoramidite to afford **11b**.[15] Although glycosyl phosphite **11b** was successfully coupled with nucleophiles **12**, **17**, and **19** in the presence of TMSOTf in acetonitrile, disaccharides **16**, **18**, and **20** were obtained in low to moderate yield (Table 1, entries 2–4). Careful optimization identified reaction conditions that produced satisfying yields (Table 1, entry 5). The reaction proceeded smoothly even at −78°C in propionitrile to provide disaccharide **16** in 65% yield.[17]

After benzoylation of **16** by treatment with excess benzoyl chloride, the 4,6-benzylidene was replaced by acetates to avoid the undesired formation of α isomers during subsequent glycosylations.[18] To put this plan to practice, **21** was treated with PPTS in protic media followed by reacetylation to give **22** in 92% yield. The anomeric TDS group of **22** was then removed by HF/pyridine to afford **23**. Finally, placement of the anomeric *N*-phenyl trifluoroacetimidate provided **7**.

The synthesis of galactose building block **9** (Scheme 4)

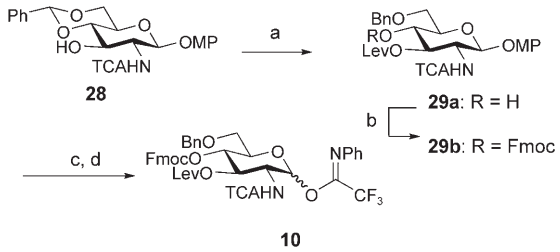


Scheme 4. Synthesis of galactose building block **9**. Reagents and conditions: a) i) NaOMe, MeOH; ii) butane-2,3-dione, $HC(OMe)_3$, CSA, MeOH, reflux, 64%; b) BnBr, NaH, DMF, 91%; c) 90% TFA/H_2O, 94%; d) i) FmocCl, pyridine, CH_2Cl_2, −40°C; ii) BzCl, pyridine, CH_2Cl_2, 43%; e) NBS, acetone, H_2O, 86%; f) $CF_3C(NPh)Cl$, Cs_2CO_3, CH_2Cl_2, 93%. CSA = camphor-10-sulfonic acid, TFA = trifluoroacetic acid.

employed the cyclic-ketal protection of Ley and co-workers to mask the C2 and C3 hydroxy groups.[19] Initially, sodium methoxide removed the acetyl protection of **24**, following which treatment with butane-2,3-dione, orthomethylformate, and catalytic amounts of CSA produced **25** in 64% yield. The remaining hydroxy groups of **25** were benzylated. Subsequent acidic removal of cyclic ketal produced diol **26**. Next, the C3 hydroxy group of **26** was equipped with a temporary Fmoc carbonate group. Treatment of **26** with Fmoc chloride resulted in an inseparable mixture of C2 and C3 *O*-Fmoc isomers even at −40°C.

This mixture was benzoylated, and chromatographic separation gave **27** in 43% yield. Hydrolysis of the thiophenyl glycoside **27** produced the hemiacetal in 86% yield, before introduction of the anomeric *N*-phenyl trifluoroacetimidate group afforded building block **9** in 93% yield.

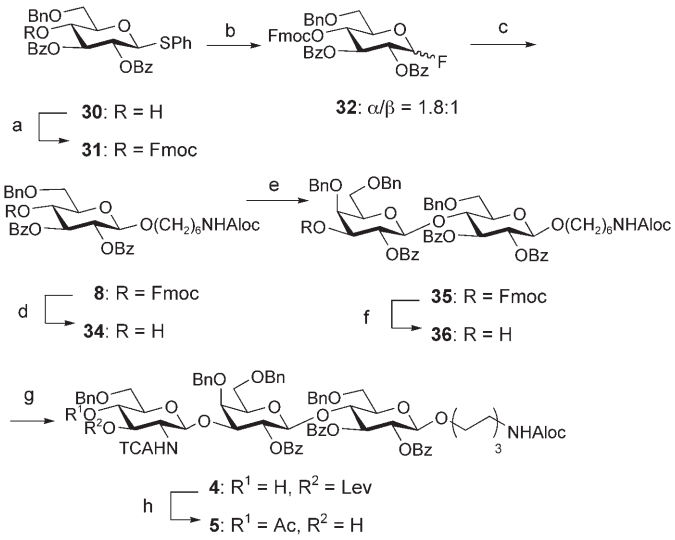
Glucosamine building block **10**, which carries both Lev and Fmoc protection, was prepared from **28**[20] (Scheme 5). Placement of the Lev group by esterification and reductive



Scheme 5. Synthesis of glucosamine building block **10**. Reagents and conditions: a) i) LevOH, DIC, DMAP, CH_2Cl_2; ii) TFA, Et_3SiH, CH_2Cl_2, 93%; b) FmocCl, pyridine, CH_2Cl_2, 81%; c) CAN, CH_3CN, H_2O, 88%; d) $CF_3C(NPh)Cl$, Cs_2CO_3, CH_2Cl_2, 71%. CAN = ammonium cerium nitrate, DIC = diisopropyl carbodiimide, DMAP = 4-dimethylaminopyridine, MP = *p*-methoxyphenyl.

benzylidene opening by TFA and triethylsilane provided the glucosamine derivative **29a** in good yield. Next, the Fmoc group was introduced to produce **29b** in 81% yield. The anomeric *N*-phenyl trifluoroacetimidate was installed after oxidative removal of MP ether with CAN to provide **10**.

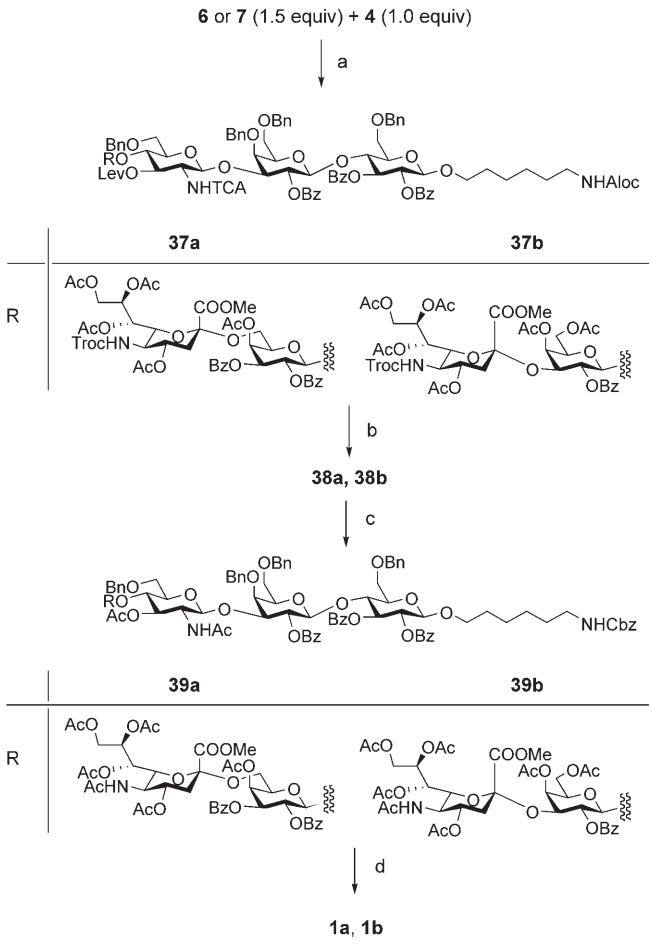
Trisaccharides **4** and **5** were both synthesized from glucoside **34** (Scheme 6). This common precursor was in turn de-



Scheme 6. Synthesis of trisaccharides **4** and **5**. Reagents and conditions: a) FmocCl, pyridine, CH_2Cl_2, 94%; b) NBS, DAST, CH_2Cl_2, 0°C, 80%; c) $HO(CH_2)_6NHAloc$ **33**, AgOTf, $[Cp_2HfCl_2]$, toluene, 4-Å molecular sieves, 50°C, 80%; d) Et_3N, THF, 97%; e) **9**, TMSOTf, CH_2Cl_2, 0°C, 91%; f) Et_3N, THF, 82%; g) i) **10**, TMSOTf, CH_2Cl_2, 0°C; ii) Et_3N, THF, 69%; h) i) Ac_2O, pyridine; ii) hydrazine acetate, DMF, 95%. Cp = cyclopentadienyl, DAST = diethylaminosulfur trifluoride.

rived from **30**.[21] Fmoc protection and replacement of the phenylthio group with fluoride gave **32**.[22] Union of alcohol **33**, which carries an Aloc-protected amine terminal, with fluoride **32** was initiated by $Cp_2HfCl_2/AgOTf$[23] to produce **8** in 80% yield. Under mild basic conditions, the Fmoc group of **8** was removed to yield **34** (97%) and set the stage for glycosylation with galactose building block **9**, which produced lactose derivative **35** in 91% yield. Again, removal of temporary Fmoc protection afforded **36**. Glycosylation of **36** with glucosamine building block **10** and subsequent Fmoc cleavage furnished key trisaccharide **4** in 69% yield. To synthesize the β(1-3)GlcNAc backbone, the liberated hydroxy group was acetylated. Cleavage of the Lev ester with hydrazine acetate produced key trisaccharide **5** in 95% yield.[24]

With the key trisaccharides in hand, the final assembly and global deprotection of pentasaccharides **1a** and **1b** was undertaken (Scheme 7). The 2+3 coupling strategy to pro-



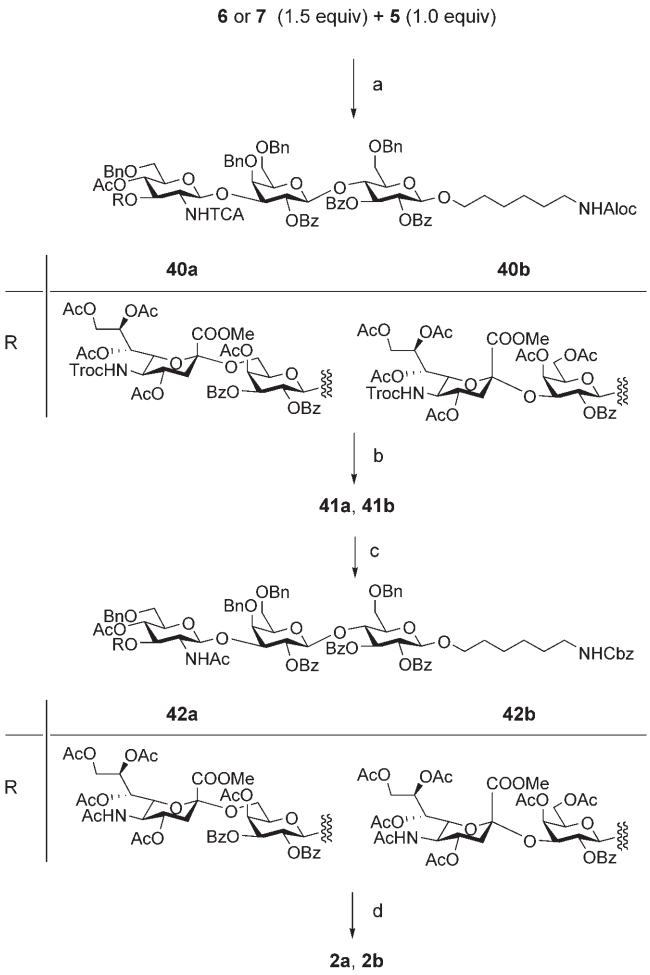
Scheme 7. Synthesis of pentasaccharides **1a** and **1b**. Reagents and conditions: a) TMSOTf, CH_2Cl_2, 0°C, **37a**: 90%, **37b**: 89%; b) i) $[Pd(PPh_3)_4]$, *p*-toluenesulfinic acid, CH_2Cl_2, ii) CbzOSu, Et_3N, **38a**: 80%, **38b**: 85%; c) i) H_2NNH_2, AcOH, DMF, ii) Zn/Cu couple, 40°C, 2 days; iii) Ac_2O, pyridine, **39a**: 55%, **39b**: 40%; d) i) 0.05 M NaOMe in MeOH, then H_2O; ii) H_2, 20% $Pd(OH)_2/C$, MeOH, H_2O, AcOH, **1a**: 45%, **1b**: 58%. Cbz = carbyloxybenzoyl, Su = succinimidyl.

duce sialylated pentasaccharides **37a** and **37b** relied on the reaction of trisaccharide **4** with sialyl-α(2-6)galactose and sialyl-α(2-3)galactose building blocks **6** and **7**. *N*-phenyl trifluoroacetimidates **6** and **7** were activated with catalytic amounts of TMSOTf, and the glycosylation reactions proceeded smoothly to give pentasaccharides **37a** and **37b**.

While examining the global deprotection conditions of **37a** and **37b**, it became clear that the Aloc protection at the terminal amine group did not stand up to the reductive con-

ditions. Therefore, the Aloc group was replaced by a Cbz moiety. Treatment of **37a/b** with $[Pd(PPh_3)_4]$ and *p*-toluenesulfinic acid resulted in the ready removal of the Aloc moiety,[25] and addition of Cbz succinate and triethylamine produced **38a/b** in a one-pot manner. Reduction of the *N*-trichloroacetyl group to the corresponding acetate did not proceed in a satisfactory manner when zinc powder was employed.[26,27] After careful optimization, the use of a Zn/Cu couple with gentle heating allowed for complete TCA reduction.[28] The Troc group was removed simultaneously, and subsequent acetylation produced **39a** and **39b** in moderate yield. Basic treatment with sodium methoxide in methanol cleaved all the acetates and benzoates. Addition of water induced hydrolysis of the sialic acid methyl ester. Palladium-catalyzed hydrogenolysis of the benzyl ethers and the Cbz group provided target pentasaccharides **1a** and **1b**.

The synthesis of pentasaccharides **2a** and **2b** was planned on the basis of the lessons learned from the synthesis of **1a** and **1b** (Scheme 8). Glycosylation of trisaccharide **5** with sialylgalactose building blocks **6** and **7** produced the desired pentasaccharides **40a** and **40b** in good yield. Replacement of the Aloc groups by Cbz provided **41a** and **41b** in 74 and 81% yield, respectively. Treatment with Zn/Cu couple and acetylation furnished **42a** and **42b** in moderate yield. Global deprotection by ester hydrolysis and hydrogenolysis gave the pentasaccharides **2a** and **2b**. The four pentasaccharides contain a terminal amine group for ready immobilization onto carbohydrate arrays and conjugation to protein carriers.



Scheme 8. Synthesis of pentasaccharides **2a** and **2b**. Reagents and conditions: a) TMSOTf, CH_2Cl_2, 0 °C, **40a**: 94%, **40b**: 94%; b) i) $[Pd(PPh_3)_4]$, *p*-toluenesulfinic acid, CH_2Cl_2; ii) CbzOSu, Et_3N, **41a**: 74%, **41b**: 81%; c) i) Zn/Cu couple, 40 °C, 2 days; ii) Ac_2O, pyridine, **42a**: 59%, **42b**: 62%; d) i) 0.05 M NaOMe in MeOH, then H_2O; ii) H_2, 20% $Pd(OH)_2/C$, MeOH, H_2O, AcOH, **2a**: 64%, **2b**: 59%.

Conclusions

We have described the synthesis of four sialylated glycans (**1a**, **1b**, **2a**, and **2b**) equipped with an amine group attached to the reducing terminus by a C6 spacer. The core trisaccharide, which is common to all four molecules, was assembled from three building blocks (**8**–**10**) in a linear fashion. Orthogonal deprotection produced two trisaccharides, **4** and **5**, for the construction of the target pentasaccharides. *N*-Troc-protected sialic acid phenylthioglycoside **11a** served in the construction of the sialyl-α(2-6)galactose linkage. To install the sialyl-α(2-3)galactose unit, sialic acid phosphite **11b** produced the best results.

The four pentasaccharides have been attached to microarray slides, and binding experiments with different influenza virus hemagglutinin proteins as well as different viral strains are currently ongoing.

Experimental Section

General

^1H and ^{13}C NMR spectra were recorded on Varian Mercury-300 and Gemini-300 spectrometers. ^1H and ^{13}C NMR chemical shifts in $CDCl_3$ are reported in ppm relative to $CHCl_3$ (7.24 ppm) and $CDCl_3$ (77.0 ppm), respectively. Chemical shifts in D_2O are relative to DOH (4.65 ppm; ^1H). Optical rotations were measured with a JASCO DIP-370 polarimeter. High-resolution MALDI and ESI mass spectra were recorded on an IonSpec Ultra mass spectrometer.

Syntheses

13: BzCl (1.65 mL, 14.2 mmol) was added to a solution of **12** (2.35 g, 5.96 mmol) in CH_2Cl_2 (3 mL)/pyridine (3 mL). After stirring for 2.5 h at room temperature, the mixture was concentrated and redissolved in EtOAc. The organic phase was washed with 10% citric acid, and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude dibenzoate produced was dissolved in MeOH (60 mL), and TsOH/H_2O (566 mg, 2.98 mmol) was added. After stirring for 4.5 h, the mixture was diluted with EtOAc and neutralized with aqueous $NaHCO_3$. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification with flash silica-gel column chromatography (hexanes/EtOAc = 4:1–3:2) gave thexyldimethylsilyl 2,3-di-*O*-benzoyl-β-D-galactopyranoside (**13**; 2.13 g, 4.01 mmol, 67%). $[\alpha]_D^{25} = +61$ ($c = 1.00$, chloroform); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.99$–7.94 (m, 4H), 7.54–7.34 (m, 6H), 5.70 (dd, $J = 7.5$, 10.3 Hz, 1H, 2-H), 5.27 (dd, $J = 3.1$, 10.3 Hz, 1H, 3-H), 4.96 (d, $J = 7.8$ Hz, 1H, 1-H), 4.37–4.35 (m, 1H, 4-H), 4.04–4.01 (m, 1H, 6a-H), 3.91–3.89 (m, 1H, 6b-H), 3.79–3.77 (m, 1H, 5-H), 2.59 (d, $J = 4.7$ Hz, 1H, OH), 2.02–2.00 (m, 1H, OH), 1.54–1.52 (m,

1H), 0.75–0.72 (m, 12H), 0.18 (s, 3H), 0.08 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 165.7, 165.1, 133.3, 129.7, 129.5, 128.9, 128.3, 128.1, 96.4, 74.3, 71.5, 68.3, 62.4, 33.9, 24.8, 20.0, 19.9, 18.5, −1.6, −3.2 ppm; MS (ESI): *m/z* calcd for $C_{28}H_{42}NO_8Si$: 548.3 $[M+NH_4]^+$; found: 548.0; elemental analysis: calcd (%) for $C_{28}H_{38}O_8Si$: C 63.37, H 7.22; found: C 63.26, H 7.26.

14: NIS (231 mg, 1.03 mmol) and TfOH (10 μL, 0.113 mmol) were added to a solution of **11a** (501 mg, 0.699 mmol) and **13** (555 mg, 1.05 mmol) in CH_3CN (15 mL) with 4-Å molecular sieves (2.1 g) at −40 °C, and the mixture was stirred for 4 h at −40 °C under Ar atmosphere. The mixture was then neutralized with Et_3N, filtered through celite to remove the molecular sieves, and diluted with EtOAc. The organic phase was washed with aqueous $NaHCO_3$. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude product was then dissolved in pyridine (5 mL), and Ac_2O (2.5 mL) was added in an ice bath. After stirring for 17 h at room temperature under an atmosphere of nitrogen, the mixture was concentrated and coevaporated with toluene. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 4:1–2:1, then toluene/EtOAc = 6:1) gave thexyldimethylsilyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranoside (**14**; 583 mg, 0.495 mmol, 71 % α/β = 6:1). α anomer: $[\alpha]_D^{23}$ = +18 (*c* = 0.66, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98–7.96 (m, 2H), 7.88–7.86 (m, 2H), 7.52–7.32 (m, 6H), 5.67 (d, *J* = 2.8 Hz, 1H), 5.60 (dd, *J* = 7.5, 10.3 Hz, 1H), 5.42 (dd, *J* = 3.4, 10.6 Hz, 1H), 5.40–5.35 (m, 2H), 5.00 (d, *J* = 7.8 Hz, 1H), 4.98–4.96 (m, 1H), 4.90 (d, *J* = 12.4 Hz, 1H), 4.85 (d, *J* = 9.6 Hz, 1H), 4.48 (d, *J* = 12.1 Hz, 1H), 4.35 (dd, *J* = 1.9, 12.1 Hz, 1H), 4.20–4.14 (m, 2H), 4.06 (t, *J* = 6.2 Hz, 1H), 3.86–3.83 (m, 1H), 3.81 (s, 3H), 3.61 (dd, *J* = 10.3, 20.5 Hz, 1H), 3.43 (dd, *J* = 6.5, 10.3 Hz, 1H), 2.60 (dd, *J* = 4.7, 13.1 Hz, 1H), 2.19 (s, 3H), 2.14 (s, 3H), 2.13 (s, 3H), 2.06 (s, 3H), 2.01 (s, 3H), 1.85 (t, *J* = 12.5 Hz, 1H), 1.54–1.51 (m, 1H), 0.74–0.71 (m, 12H), 0.21 (s, 3H), 0.13 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.9, 170.6, 170.6, 170.3, 169.7, 167.9, 165.7, 165.5, 154.2, 133.3, 133.1, 129.9–128.4, 99.0, 96.3, 95.6, 77.4, 74.7, 72.2, 72.1, 72.0, 71.8, 16.4, 67.9, 67.8, 67.4, 63.5, 62.5, 53.1, 51.7, 38.2, 34.0, 24.9, 21.2, 21.2, 21.0, 20.8, 20.0, 18.6, −1.6, −3.3 ppm; HRMS (MALDI): *m/z* calcd for $C_{51}H_{66}NO_{22}Cl_3SiNa$: 1200.2809 $[M+Na]^+$; found: 1200.2782; β anomer: $[\alpha]_D^{23}$ = +3.5 (*c* = 0.14 M, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96–7.93 (m, 2H), 7.89–7.86 (m, 2H), 7.52–7.34 (m, 6H), 5.78 (d, *J* = 2.8 Hz, 1H), 5.61 (dd, *J* = 7.5, 10.6 Hz, 1H), 5.47 (dd, *J* = 3.4, 10.3 Hz, 1H), 5.38 (dd, *J* = 2.2, 6.2 Hz, 1H), 5.30–5.28 (m, 1H), 5.24 (d, *J* = 10.0 Hz, 1H), 5.22–5.20 (m, 1H), 4.95 (d, *J* = 7.5 Hz, 1H), 4.80 (d, *J* = 11.8 Hz, 1H), 4.63 (dd, *J* = 2.5, 12.5 Hz, 1H), 4.55 (d, *J* = 12.1 Hz, 1H), 4.08–4.06 (m, 1H), 3.84 (s, 3H), 3.84–3.81 (m, 1H), 3.68 (dd, *J* = 2.2, 10.6 Hz, 1H), 3.58–3.56 (m, 1H), 3.41 (t, *J* = 9.3 Hz, 1H), 2.56 (dd, *J* = 5.0, 13.1 Hz, 1H), 2.31 (s, 3H), 2.16 (s, 3H), 2.14 (s, 3H), 2.03 (s, 3H), 1.98 (s, 3H), 1.80 (t, *J* = 12.5 Hz, 1H), 1.52–1.50 (m, 1H), 0.74–0.71 (m, 12H), 0.17 (s, 3H), 0.07 ppm (s, 3H).

6: HF/pyridine (800 μL) was added to a solution of **14** (396 mg, 0.336 mmol) in DMF (8 mL), and the mixture was stirred at 45 °C for 15 h. The mixture was then carefully neutralized with aqueous $NaHCO_3$ in an ice bath, and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 4:1–3:2) gave **15** (278 mg, 0.268 mmol, 80 %). Next, **15** (276 mg, 0.266 mmol) was dissolved in CH_2Cl_2 (4 mL) before addition of $CF_3C(NPh)Cl$ (168 mg, 0.809 mmol) and Cs_2CO_3 (178 mg, 0.546 mmol) at 0 °C. After stirring for 2.5 h at 0 °C to room temperature under Ar atmosphere, the mixture was filtered through celite, and the filtrate was concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 4:1–3:2) gave methyl (4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranose *N*-phenyl trifluoroacetimidate (**6**; 295 mg, 0.244 mmol, 92 %). $[\alpha]_D^{23}$ = +37 (*c* = 0.32, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.86 (m, 4H), 7.57–7.09 (m, 6H), 6.73 (d, *J* = 8.1 Hz, 1H), 5.90–5.34 (m, 4H), 5.00–4.79 (m, 2H), 4.48 (d, *J* = 12.1 Hz, 1H), 4.31 (dd, *J* = 2.5, 12.8 Hz, 1H), 4.21–3.77 (m, 3H), 3.81 (s, 3H), 3.69–3.67 (m, 1H), 3.54–3.51 (m, 1H), 2.59 (dd, *J* = 4.7, 13.1 Hz, 1H), 2.18–2.00 (m, 1H), 1.87 ppm (t, *J* = 12.5 Hz, 1H); ^{13}C NMR (75 MHz): δ = 170.3–165.3, 153.8, 142.8, 133.2–132.8, 129.7–128.2, 126.3, 120.3, 119.1, 98.9, 95.9, 95.3, 91.0, 74.5, 72.4–71.5, 69.4, 68.4–67.1, 63.4–62.8, 53.0, 51.7, 38.0, 21.1–20.8 ppm; HRMS (MALDI): *m/z* calcd for $C_{51}H_{52}N_2O_{22}Cl_3F_3Na$: 1229.1921 $[M+Na]^+$; found: 1229.1934.

16: TMSOTf (10 μL, 51 μmol) was added to a solution of **11b** (441 mg, 0.517 mmol) and **12** (323 mg, 0.787 mmol) in EtCN (10 mL) with 4-Å molecular sieves (1.10 g) at −78 °C, and the mixture was stirred for 75 min at −78 °C under argon atmosphere. The mixture was then neutralized with Et_3N, filtered through celite to remove the molecular sieves, and diluted with EtOAc. The organic phase was washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, concentrated, and purified by flash silica-gel column chromatography (toluene/EtOAc = 3:2) to give thexyldimethylsilyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4,6-*O*-benzylidene-β-D-galactopyranoside (**16**; 340 mg, 0.334 mmol, 65 %). $[\alpha]_D^{22}$ = +19 (*c* = 1.27, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52–7.49 (m, 2H), 7.36–7.34 (m, 3H), 5.43–5.40 (m, 2H), 5.35 (s, 2H), 5.05–4.91 (m, 2H), 4.90 (d, *J* = 12.1 Hz, 1H), 4.67 (d, *J* = 7.5 Hz, 1H), 4.68 (d, *J* = 12.1 Hz, 1H), 4.27 (dd, *J* = 12.1, 14.0 Hz, 1H), 4.23–4.18 (m, 3H), 3.97 (d, *J* = 3.4 Hz, 1H), 3.78–3.76 (m, 1H), 3.58 (s, 3H), 3.42 (s, 1H), 2.76 (dd, *J* = 8.4, 12.8 Hz, 1H), 2.56 (s, 1H), 2.19 (s, 3H), 2.17 (s, 3H), 2.05 (s, 3H), 2.00 (s, 3H), 1.95 (t, *J* = 12.5 Hz, 1H), 1.70–1.68 (m, 1H), 0.91–0.85 (m, 12H), 0.21 (s, 3H), 0.20 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6, 170.3, 170.0, 169.9, 168.2, 153.9, 138.0, 128.8, 128.0, 126.4, 100.8, 97.9, 97.0, 95.3, 74.9, 74.4, 73.8, 71.9, 70.4, 69.2, 67.8, 67.7, 67.0, 66.1, 62.0, 60.3, 52.7, 51.6, 38.5, 34.0, 24.9, 21.2, 20.7, 20.1, 20.0, 18.5, 18.4, 14.1, −1.9, −2.7 ppm; HRMS (MALDI): *m/z* calcd for $C_{42}H_{60}NO_{19}Cl_3SiNa$: 1138.2492 $[M+Na]^+$; found: 1138.2469.

21: BzCl (380 μL, 3.28 mmol) was added to a solution of **16** (220 mg, 0.216 mmol) in dichloroethane (2.5 mL) and pyridine (2.5 mL), and the mixture was stirred for 22 h at 60 °C under nitrogen atmosphere. The solvent was then evaporated, and the precipitate was redissolved in EtOAc and washed with 10 % citric acid, H_2O, aqueous $NaHCO_3$, and brine. The organic phase was dried over Na_2SO_4, filtered, concentrated, and purified by flash silica-gel column chromatography (toluene/EtOAc = 8:1–4:1) to give thexyldimethylsilyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4,6-*O*-benzylidene-2-*O*-benzoyl-β-D-galactopyranoside (**21**; 213.4 mg, 0.1903 mmol, 89 %). $[\alpha]_D^{23}$ = +32 (*c* = 0.57, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.11–8.08 (m, 2H), 7.61–7.32 (m, 8H), 5.55–5.53 (m, 1H), 5.39 (dd, *J* = 7.8, 10.3 Hz, 1H), 5.36 (br s, 1H), 5.32 (dd, *J* = 2.2, 9.7 Hz, 1H), 4.95 (d, *J* = 7.5 Hz, 1H), 4.85 (d, *J* = 12.1 Hz, 1H), 4.84–4.75 (m, 2H), 4.48 (dd, *J* = 3.7, 10.3 Hz, 1H), 4.43 (d, *J* = 11.8 Hz, 1H), 4.34 (dd, *J* = 2.5, 12.5 Hz, 1H), 4.25 (dd, *J* = 1.3, 13.4 Hz, 1H), 4.11 (d, *J* = 12.8 Hz, 1H), 4.06 (dd, *J* = 5.6, 12.5 Hz, 1H), 4.00–3.80 (m, 2H), 3.56–3.45 (m, 2H), 3.54 (s, 3H), 2.66 (dd, *J* = 4.7, 12.8 Hz, 1H), 2.22 (s, 3H), 2.07 (s, 3H), 1.93 (s, 3H), 1.82 (s, 3H), 1.66 (t, *J* = 12.8 Hz, 1H), 1.52–1.49 (m, 1H), 0.72–0.69 (m, 12H), 0.18 (s, 3H), 0.09 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6, 170.2, 170.1, 170.0, 168.5, 164.9, 153.9, 137.8, 133.5, 132.6, 130.6–128.1, 100.9, 96.5, 96.1, 95.2, 74.5, 73.5, 72.2, 72.1, 71.8, 69.3, 68.4, 67.5, 67.1, 66.1, 62.5, 52.7, 51.3, 38.5, 33.9, 24.7, 21.5, 20.8, 20.6, 20.0, 18.5, −1.6, −2.8 ppm; HRMS (MALDI): *m/z* calcd for $C_{49}H_{64}NO_{20}Cl_3NSiNa$: 1142.2754 $[M+Na]^+$; found: 1142.2733.

22: PPTS (163 mg, 0.648 mmol) was added to a solution of **21** (294 mg, 0.262 mmol) in CH_3CN (4 mL) and MeOH (4 mL), and the mixture was stirred for 5 h at 75 °C. The mixture was then cooled to room temperature, neutralized with Et_3N, concentrated, and dried under reduced pressure. The crude product was dissolved in pyridine (6 mL), and Ac_2O (3 mL) was added. After stirring for 10 h at room temperature, the mixture was concentrated and redissolved in EtOAc. The organic phase was washed with 10 % citric acid. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, concentrated, and purified by flash silica-gel column chromatography (toluene/EtOAc = 6:1–3:1) to give thexyldimethylsilyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5- trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulo-

pyranosylonate)-(2→3)-4,6-di-*O*-acetyl-2-*O*-benzoyl-β-D-galactopyranoside (**22**; 268 mg, 0.240 mmol, 92%). $[\alpha]_D^{23}=+29$ ($c=1.55$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=8.14$–8.12 (m, 2H), 7.58–7.43 (m, 3H), 5.63–5.61 (m, 1H), 5.26–5.17 (m, 2H), 4.98–4.88 (m, 3H), 4.81 (d, $J=11.8$ Hz, 1H), 4.66–4.62 (m, 2H), 4.38 (d, $J=12.1$ Hz, 1H), 4.33 (dd, $J=2.2$, 12.5 Hz, 1H) 4.07 (d, $J=7.2$ Hz, 2H), 3.97 (dd, $J=6.5$, 12.5 Hz, 1H), 3.90–3.87 (m, 1H), 3.85 (s, 3H), 3.66 (dd, $J=2.5$, 10.6 Hz, 1H), 3.43 (dd, $J=10.3$, 21 Hz, 1H), 2.60 (dd, $J=4.7$ Hz, 12.5 Hz, 1H), 2.21 (s, 3H), 2.15 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 1.95 (s, 3H), 1.68 (t, $J=12.5$ Hz, 1H), 1.47–1.45 (m ,1H), 1.40–1.24 (m, 9H), 0.14 (s, 3H), 0.06 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=170.5$, 170.3, 170.3, 170.1, 170.1, 169.9, 167.8, 165.1, 153.9, 153.9, 132.8, 130.3, 130.1, 128.1, 96.6, 96.0, 95.2, 77.2, 74.5, 73.0, 71.4, 71.3, 70.8, 69.0, 68.1, 67.4, 66.8, 62.5, 62.4, 53.2, 51.0, 37.6, 33.8, 24.7, 21.6, 20.9, 20.9, 20.8, 20.3, 20.0, 19.8, 18.5, 18.4, −1.8, −3.2 ppm; HRMS (MALDI): *m/z* calcd for $C_{46}H_{64}NO_{22}Cl_3SiNa$: 1138.2653 $[M+Na]^+$; found: 1138.2626.

7: HF/pyridine (600 μL) was added to a solution of **22** (246 mg, 0.220 mmol) in DMF (6 mL), and the mixture was stirred at 45°C for 20 h. The mixture was then carefully neutralized with aqueous $NaHCO_3$ in an ice bath, and the aqueous phase was extracted with EtOAc. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, concentrated, and purified by silica-gel column chromatography (hexanes/EtOAc=2:1–1:1) to give the hemiacetal (199 mg, 0.204 mmol, 93%). The hemiacetal (196 mg, 0.201 mmol) was dissolved in CH_2Cl_2 (3 mL), and $CF_3C(NPh)Cl$ (128 mg, 0.618 mmol) and Cs_2CO_3 (129 mg, 0.396 mmol) were added at 0°C. After stirring for 2.5 h at 0°C to room temperature under an atmosphere of argon, the mixture was filtered through celite, and the filtrate was concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc=3:1–3:2) gave methyl (4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4,6-di-*O*-acetyl-2-*O*-benzoyl-β-D-galactopyranose *N*-phenyl trifluoroacetimidate (**7**; 217 mg, 0.171 mmol, 85%). $[\alpha]_D^{23}=+40$ ($c=0.95$, chloroform) ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=8.15$ (dd, $J=6.2$, 13.4 Hz, 2H), 7.65–6.78 (m, 8H), 6.45 (d, $J=7.5$ Hz, 1H), 6.16–6.14 (m, 1H), 5.49 (t, $J=9.6$ Hz, 1H), 5.17 (dd, $J=2.5$, 11.8 Hz, 1H), 5.04–4.71 (m, 5H), 4.38 (d, $J=12.1$ Hz, 1H), 4.30 (dd, $J=2.2$, 12.1 Hz, 1H), 4.21–3.79 (m, 3H), 3.86 (s, 3H), 3.66 (dd, $J=2.5$, 10.6 Hz, 1H), 3.47 (m, 1H), 2.63 (dd, $J=4.7$, 12.1 Hz, 1H), 2.20–1.91 (m, 1H), 1.73 ppm (t, $J=12.1$ Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=171.0$–169.8, 167.7, 164.9, 153.9, 143.2, 133.6, 133.3, 130.1–128.4, 126.2, 124.3, 120.4, 119.3, 119.0, 96.7, 95.2, 74.5, 71.8, 71.6, 70.9, 70.2, 69.0, 67.4, 67.4, 66.9, 62.6, 62.3, 61.8, 60.5, 53.3, 50.9, 37.5, 21.6–20.7, 14.3 ppm; HRMS (MALDI): *m/z* calcd for $C_{46}H_{50}N_2O_{22}F_3Cl_3Na$: 1167.1765 $[M+Na]^+$; found: 1167.1760.

25: NaOMe (103 mg, 1.91 mmol) was added to a solution of **24** (8.30 g, 18.9 mmol) in MeOH (80 mL), and the mixture was stirred at room temperature under N_2 atmosphere. After stirring for 7 h, the reaction mixture was neutralized with Amberlite IR-120 resin. The resin was removed by filtration, and the filtrate was concentrated and dried under reduced pressure. The residue was dissolved in MeOH (60 mL), and butane-2,3-dione (2.0 mL, 23 mmol), trimethylorthoformate (6.2 mL, 57 mmol), and CSA (438 mg, 1.89 mmol) were added. The mixture was stirred while heated under reflux for 12 h. After cooling to room temperature, the mixture was neutralized with Et_3N and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc=1:1–1:2) gave phenylthio-1-deoxy-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-β-D-galactopyranoside (**25**; 4.66 g, 12.1 mmol, 64%). $[\alpha]_D^{25}=-146$ ($c=1.18$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.55$–7.50 (m, 2H), 7.31–7.23 (m, 3H), 4.78 (d, $J=10.0$ Hz, 1H, 1-H), 4.15–3.93 (m, 3H), 3.85–3.76 (m, 2H), 3.64–3.62 (m, 1H, 5-H), 3.26 (s, 3H), 3.18 (s, 3H), 2.59 (br s, 1H, OH), 2.15 ppm (br s, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=133.3$, 131.4, 128.7, 127.2, 100.4, 85.4, 78.8, 71.7, 68.3, 65.3, 62.7, 48.1, 17.8, 17.7 ppm; MS (ESI): *m/z* calcd for $C_{18}H_{30}NO_7S$: 404.2 $[M+NH_4]^+$; found: 404.0; HRMS (MALDI): *m/z* calcd for $C_{18}H_{26}O_7SNa$: 409.1297 $[M+Na]^+$; found: 409.1295.

26a: Benzylbromide (3.4 mL, 29 mmol) and NaH (60% in mineral oil; 1.12 g, 28.0 mmol) were added to a solution of **25** (4.48 g, 11.6 mmol) in DMF (40 mL), and the mixture was stirred for 9.5 h at room temperature under an atmosphere of nitrogen. Et_3N (4.0 mL) was then added to remove any remaining benzyl bromide. After further stirring for 30 min, the mixture was poured into iced water. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc=9:1–4:1) gave phenylthio-1-deoxy-4,6-di-*O*-benzyl-2,3-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-β-D-galactopyranoside (**26a**; 5.96 g, 10.5 mmol, 91%). $[\alpha]_D^{23}=-126$ ($c=0.82$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.55$–7.16 (m, 15H), 5.00 (d, $J=11.5$ Hz, 1H), 4.77 (d, $J=9.9$ Hz, 1H, 1-H), 4.60 (d, $J=11.5$ Hz, 1H), 4.48 (d, $J=11.5$ Hz, 1H), 4.42 (d, $J=11.5$ Hz, 1H), 4.26 (t, $J=9.9$ Hz, 1H, 2-H), 3.86–3.62 (m, 5H, 3-H, 4-H, 5-H, 6a-H, 6b-H), 3.27 (s, 3H), 3.17 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=138.8$, 137.9, 133.9, 133.2–126.8, 100.0, 99.7, 85.6, 78.1, 73.9, 73.5, 73.2, 68.9, 65.5, 47.9, 47.8, 17.7, 17.6 ppm; MS (ESI): *m/z* calcd for $C_{32}H_{42}NO_7S$: 584.3 $[M+NH_4]^+$; found: 584.2; HRMS (MALDI): *m/z* calcd for $C_{32}H_{38}O_7Na$: 589.2236 $[M+Na]^+$; found: 589.2231.

26b: A solution of **26a** (5.74 g, 10.1 mmol) in aqueous TFA (90%, 30 mL) was stirred at room temperature for 30 min. The solvent was removed by evaporation and coevaporated with toluene. The remaining residue was purified by flash silica-gel column chromatography (CH_2Cl_2/EtOAc=20:1–6:1) to give phenylthio-1-deoxy-4,6-di-*O*-benzyl-β-D-galactopyranoside (**26b**; 4.32 g, 9.55 mmol, 94%). $[\alpha]_D^{25}=-32$ ($c=0.61$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=7.57$–7.53 (m, 2H), 7.37–7.23 (m, 13H), 4.74 (d, $J=11.6$ Hz, 1H), 4.67 (d, $J=11.8$ Hz, 1H), 4.54 (d, $J=11.8$ Hz, 1H), 4.51 (d, $J=9.3$ Hz, 1H, 1-H), 4.48 (d, $J=11.6$ Hz, 1H), 3.95–3.93 (m, 1H, 4-H), 3.76–3.65 (m, 4H, 2-H, 3-H, 6a-H, 6b-H), 3.65–3.62 (m, 1H, 5-H), 2.57 (br s, 1H, OH), 2.43 ppm (d, $J=6.2$ Hz, 1H, OH); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=138.2$, 137.6, 132.4, 132.0, 128.8, 128.3–127.5, 88.4, 77.6, 76.0, 75.3, 75.0, 73.5, 70.3, 68.5 ppm; MS (ESI): *m/z* calcd for $C_{26}H_{32}NO_5S$: 470.2 $[M+NH_4]^+$; found: 470.0; elemental analysis: calcd (%) for $C_{26}H_{28}O_5S$: C 69.00, H 6.24; found: C 68.71, H 6.31.

27: Pyridine (700 μL, 8.65 mmol) was added to a solution of **26** (392 mg, 0.867 mmol) in CH_2Cl_2 (10 mL), and the mixture was cooled to −40°C. FmocCl (243 mg, 0.94 mmol) was added as three portions at 2-h intervals at −40°C. After stirring overnight at −40°C to room temperature, the mixture was diluted with CH_2Cl_2 and neutralized with 10% citric acid. The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc=5:1–3:1) gave an inseparable mixture of regioisomers (417 mg, 0.617 mmol). The mixture was dissolved in CH_2Cl_2 (4 mL) and pyridine (4 mL), and benzoyl chloride (100 μL, 0.86 mmol) was added. The mixture was stirred at room temperature under N_2 atmosphere. After stirring for 15 h, the mixture was diluted with CH_2Cl_2 and washed with HCl (0.5 M). The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc=10:1–6:1) gave phenylthio-1-deoxy-4,6-di-*O*-benzyl-2-*O*-benzoyl-3-*O*-(9-fluorenylmethyl)oxycarbonyl-β-D-galactopyranoside (**27**; 293 mg, 0.376 mmol, 43%). $[\alpha]_D^{25}=+39$ ($c=0.92$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta=8.07$–8.04 (m, 2H), 7.70–7.07 (m, 26H), 5.76 (t, $J=10.0$ Hz, 1H, 2-H), 5.09 (dd, $J=3.1$, 10.0 Hz, 1H, 3-H), 4.88 (d, $J=10.0$ Hz, 1H, 1-H), 4.79 (d, $J=11.2$ Hz, 1H) 4.53 (d, $J=11.8$ Hz, 1H), 4.50 (d, $J=11.5$ Hz, 1H), 4.46 (d, $J=11.8$ Hz, 1H), 4.33–4.04 (m, 4H, 4-H, 6a-H, 6b-H, Fmoc), 3.87–3.85 (m, 1H, 5-H), 3.76–3.74 ppm (m, 2H, Fmoc); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta=165.3$, 154.7, 143.4, 143.0, 141.4, 138.0, 137.9, 133.4–127.3, 125.4, 125.1, 120.1, 86.9, 79.2, 77.5, 75.2, 74.1, 73.8, 70.3, 68.8, 68.5, 46.6 ppm; MS (ESI): *m/z* calcd for $C_{48}H_{46}NO_8S$: 796.3 $[M+NH_4]^+$; found: 796.2; elemental analysis: calcd (%) for $C_{48}H_{42}O_8S$: C 74.02, H 5.43; found: C 73.82, H 5.32.

9: NBS (256 mg, 1.44 mmol) was added to a solution of **27** (269 mg, 0.346 mmol) in acetone/H_2O (6 mL/1 mL). The mixture was stirred at room temperature for 30 min, diluted with EtOAc, and washed with 5% $Na_2S_2O_3$. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography

(hexanes/EtOAc = 5:1–3:1) gave the hemiacetal (204 mg, 0.297 mmol, 86%). $CF_3(NPh)Cl$ (190 mg, 0.918 mmol) and Cs_2CO_3 (190 mg, 0.584 mmol) were added to a solution of the hemiacetal (197 mg, 0.287 mmol) in CH_2Cl_2 (5 mL) at 4 °C. After stirring for 4 h at 4 °C to room temperature under an atmosphere of nitrogen, the solid salt was removed by filtration through celite. The filtrate was concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 3:1) gave 4,6-di-*O*-benzyl-2-*O*-benzoyl-3-*O*-(9-fluorenylmethyl)oxycarbonyl-β-D-galactopyranose *N*-phenyl trifluoroacetimidate (**9**; 229 mg, 0.267 mmol, 93%): $[\alpha]_D^{23} = +63$ ($c = 0.61$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.07$ (d, $J = 6.5$ Hz, 2H), 7.72–7.06 (m, 24H), 6.69 (d, $J = 7.2$ Hz, 2H), 5.98–5.95 (m, 2H), 5.10 (br s, 1H), 4.80 (d, $J = 11.2$ Hz, 1H), 4.57–4.09 (m, 7H), 3.72 ppm (br s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 164.7$, 154.3, 143.1, 143.0, 142.7, 141.1, 141.0, 137.5, 133.3, 129.8, 129.1, 128.6, 128.4, 128.3, 127.9, 127.8, 127.1, 125.1, 124.9, 124.3, 119.9, 119.1, 95.2, 77.4, 75.4, 74.5, 73.6, 73.4, 70.3, 69.4, 67.7 ppm; HRMS (MALDI): *m/z* calcd for $C_{50}H_{42}O_9NF_3Na$: 880.2709 $[M+Na]^+$; found: 880.2763.

29a: Levulinic acid (1.3 mL, 13 mmol), diisopropylcarbodiimide (DIC; 1.6 mL, 10 mmol), and DMAP (536 mg, 4.39 mmol) were added to a solution of **28** (4.30 g, 8.29 mmol) in CH_2Cl_2 (35 mL). After stirring at room temperature for 3.5 h, the mixture was diluted with CH_2Cl_2 and 10% citric acid. The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. Treatment with hexane/EtOAc gave precipitation. The dried precipitate was dissolved in CH_2Cl_2 (35 mL), and Et_3SiH (6.6 mL, 41 mmol) and TFA (3.2 mL, 42 mmol) were added in an ice bath under N_2 atmosphere. The mixture was stirred for 7 h at 0 °C, then more Et_3SiH (2.2 mL, 14 mmol) and TFA (1.2 mL, 16 mmol) were added to complete the reaction. After stirring for 1.5 h at 0 °C to room temperature, the mixture was neutralized with cold aqueous $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 2:1–1:2) gave *p*-methoxyphenyl 2-deoxy-6-*O*-benzyl-3-*O*-levulinoyl-2-trichloroacetamidyl-α-D-glucopyranoside (**29a**; 4.79 g, 7.74 mmol, 93%). $[\alpha]_D^{23} = -27$ ($c = 0.43$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.41$ (d, $J = 9.0$ Hz, 1H, NH), 7.33–7.25 (m, 5H), 6.99–6.97 (m, 2H), 6.78–6.75 (m, 2H), 5.35 (dd, $J = 8.4$, 10.5 Hz, 1H, 3-H), 5.06 (d, $J = 8.4$ Hz, 1H), 4.61 (d, $J = 11.7$ Hz, 1H), 4.56 (d, $J = 11.7$ Hz, 1H, 1-H), 4.22–4.20 (m, 1H), 3.90–3.70 (m, 4H), 3.75 (s, 3H), 3.39 (d, $J = 3.1$ Hz, 1H), 2.80–2.46 (m, 4H), 2.11 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 207.5$, 173.3, 162.1, 155.4, 151.1, 137.7, 128.4, 127.7, 127.6, 118.6, 114.5, 100.4, 75.1, 74.7, 73.7, 70.0, 69.6, 55.7, 55.6, 38.5, 29.8, 28.3 ppm; elemental analysis: calcd (%) for $C_{27}H_{30}Cl_3NO_9$: C 52.40, H 4.89, N 2.26; found: C 52.32, H 4.93, N 2.42.

29b: FmocCl (2.40 g, 9.28 mmol) and pyridine (6.3 mL, 78 mmol) were added to a solution of **29a** (4.79 g, 7.74 mmol) in CH_2Cl_2 (30 mL). After stirring at room temperature for 1 h, the mixture was diluted with CH_2Cl_2 and 10% citric acid. The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with 10% citric acid and brine, dried over Na_2SO_4, filtered, concentrated, and purified by silica-gel column chromatography (hexanes/EtOAc = 6:1–2:1) to give *p*-methoxyphenyl 2-deoxy-6-*O*-benzyl-4-*O*-(9-fluorenylmethyl)oxycarbonyl-3-*O*-levulinoyl-2-trichloroacetamidyl-α-D-glucopyranoside (**29b**; 5.27 g, 6.27 mmol, 81%); $[\alpha]_D^{23} = -18$ ($c = 0.74$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.76$ (d, $J = 7.8$ Hz, 2H), 7.54 (dd, $J = 0.6$, 7.5 Hz, 1H), 7.41–7.16 (m, 10H), 7.13 (d, $J = 9.0$ Hz, 1H, NH), 7.00–6.98 (m, 2H), 6.72–6.70 (m, 2H), 5.60 (dd, $J = 9.3$, 10.5 Hz, 1H, 3-H), 5.16 (d, $J = 8.1$ Hz, 1H, 1-H), 5.10 (t, $J = 9.3$ Hz, 1H, 4-H), 4.55 (d, $J = 12.3$ Hz, 1H), 4.50 (d, $J = 12.3$ Hz, 1H), 4.47–4.17 (m, 3H), 3.98–3.95 (m, 1H, 5-H), 3.75–3.65 (m, 3H), 3.69 (s, 3H), 2.68–2.43 (m, 4H), 2.02 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 205.7$, 172.5, 162.0, 155.6, 153.9, 150.9, 143.2, 143.0, 141.2, 137.6, 128.3–127.1, 125.1, 120.0, 118.8, 114.4, 100.0, 73.7, 73.2, 73.0, 71.8, 70.5, 68.8, 56.3, 55.6, 46.6, 37.9, 29.6, 28.1 ppm; elemental analysis: calcd (%) for $C_{42}H_{40}Cl_3NO_{11}$: C 59.97, H 4.79, N 1.67; found: C 59.83, H 4.86, N 1.79.

10: CAN (4.70 g, 8.57 mmol) was added to a solution of **29b** (1.46 g, 1.74 mmol) in CH_3CN (32 mL) and H_2O (5 mL). After stirring at room temperature for 30 min, the mixture was diluted with EtOAc and water. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, concentrated, and purified by flash silica-gel column chromatography (hexanes/EtOAc = 4:1–3:2) to give the corresponding hemiacetal (1.12 g, 1.53 mmol, 88%). The hemiacetal (1.12 g, 1.53 mmol) was dissolved in CH_2Cl_2 (10 mL), and $CF_3C(NPh)Cl$ (969 mg, 4.67 mmol) and Cs_2CO_3 (1.02 g, 3.14 mmol) were added at 0 °C. After stirring for 2 h at room temperature under argon atmosphere, the mixture was filtered through celite. The filtrate was concentrated and purified by silica-gel column chromatography (hexanes/EtOAc = 8:1–3:1) to give 2-deoxy-6-*O*-benzyl-4-*O*-(9-fluorenylmethyl)oxycarbonyl-3-*O*-levulinoyl-2-trichloroacetamidyl-D-glucopyranose *N*-phenyl trifluoroacetimidate (**10**; 989 mg, 1.09 mmol, 71%); $[\alpha]_D^{23} = +53$ ($c = 0.90$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.78$ (dd, $J = 0.62$, 7.5 Hz, 2H), 7.59 (d, $J = 7.5$ Hz, 2H), 7.45–7.19 (m, 10H), 7.17–7.14 (m, 2H), 6.76 (d, $J = 7.2$ Hz, 1H), 6.52 (br s, 1H), 5.52 (dd, $J = 9.7$, 10.8 Hz, 1H), 5.25 (t, $J = 10.0$ Hz, 1H), 4.61–4.41 (m, 3H), 4.39–4.37 (m, 1H), 4.36 (t, $J = 10.2$ Hz, 1H), 4.25 (t, $J = 7.2$ Hz, 1H), 4.15–4.12 (m, 1H), 3.70–3.67 (m, 2H), 2.68–2.49 (m, 4H), 2.07 ppm (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 205.3$, 173.5, 162.0, 153.8, 143.2–141.1, 137.3, 128.8–127.6, 125.1, 124.7, 120.1, 119.2, 92.6, 91.7, 73.7, 71.4, 71.2, 70.6, 70.2, 67.8, 53.9, 46.7, 37.8, 29.6, 28.0 ppm; HRMS (MALDI): *m/z* calcd for $C_{43}H_{38}N_2O_{10}Cl_3F_3Na$: 927.1442 $[M+Na]^+$; found: 927.1435.

31: FmocCl (1.14 g, 4.41 mmol) and pyridine (2.8 mL, 34.6 mmol) were added to a solution of **30** (1.91 g, 3.35 mmol) in CH_2Cl_2 (15 mL), and the mixture was stirred for 2 h at room temperature under an atmosphere of nitrogen. After completion of the reaction, the mixture was diluted with CH_2Cl_2, and the organic layer was washed with 10% citric acid and brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 10:1–4:1) gave phenylthio-1-deoxy-2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(9-fluorenylmethyl)oxycarbonyl-β-D-glucopyranoside (**31**; 2.48 g, 3.13 mmol, 94%). $[\alpha]_D^{23} = +40$ ($c = 1.29$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.99$ (d, $J = 7.5$ Hz, 2H), 7.87 (d, $J = 7.5$ Hz, 2H), 7.73–7.16 (m, 24H), 5.81 (t, $J = 9.3$ Hz, 1H, 3-H), 5.47 (t, $J = 9.6$ Hz, 1H, 2-H), 5.21 (t, $J = 9.6$ Hz, 1H, 4-H), 5.00 (d, $J = 9.9$ Hz, 1H), 4.63 (d, $J = 12.3$ Hz, 1H), 4.57 (d, $J = 12.3$ Hz, 1H), 4.25 (dd, $J = 7.2$, 10.2 Hz, 1H), 4.11 (dd, $J = 7.2$, 10.2 Hz, 1H), 4.02–4.00 (m, 2H), 3.79–3.77 ppm (m, 2H, 6-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.5$, 164.9, 154.0, 143.1, 142.8, 141.1, 141.0, 132.7–127.0, 124.9, 119.9, 86.3, 77.4, 74.4, 73.7, 73.2, 70.5, 70.4, 69.0, 46.5 ppm; elemental analysis: calcd (%) for $C_{48}H_{38}O_9S$: C 72.90, H 4.84; found: C 72.88, H 5.12.

32: NBS (671 mg, 3.77 mmol) and DAST (500 μL, 3.79 mmol) were added to a solution of **31** (2.48 g, 3.13 mmol) in CH_2Cl_2 (20 mL) at 0 °C. After stirring for 2.5 h at 4 °C under argon atmosphere, the mixture was diluted with CH_2Cl_2 and washed with aqueous $NaHCO_3$. The aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 8:1–4:1) gave 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(9-fluorenylmethyl)oxycarbonyl-D-glucopyranosyl fluoride (**32**; 1.76 g, 2.50 mmol, 80%; α/β = 1.8:1). **32**(α): $[\alpha]_D^{23} = +75$ ($c = 1.93$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.03$–7.92 (m, 4H), 7.74–7.70 (m, 2H), 7.57–7.17 (m, 26H), 6.10 (t, $J = 10.2$ Hz, 1H), 6.02 (dd, $^3J_{H,H} = 2.8$ Hz, $^2J_{F,H} = 51.4$ Hz, 1H), 5.45 (t, $J = 9.9$ Hz, 1H), 5.35 (ddd, $^3J_{H,H} = 2.8$, 10.5 Hz, $^3J_{F,H} = 23.9$ Hz, 1H), 4.64 (d, $J = 12.1$ Hz, 1H), 4.55 (d, $J = 12.1$ Hz, 1H), 4.42–4.40 (m, 1H), 4.27 (dd, $J = 7.1$, 10.4 Hz, 1H), 3.95 (dd, $J = 7.4$, 7.4 Hz, 1H), 3.77–3.75 ppm (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.5$, 153.9, 143.1, 142.7, 141.1, 137.3, 133.6, 133.3, 129.9, 129.8, 128.7, 128.4, 128.3, 127.8, 127.7, 127.0, 125.1, 124.8, 119.8, 103.9 ($^1J_{C,F} = 230$ Hz), 73.6, 71.7, 71.3, 70.9, 70.8, 70.3, 69.9, 67.4, 46.3 ppm; HRMS (MALDI): *m/z* calcd for $C_{42}H_{35}O_9FK$: 741.1902 $[M+K]^+$; found: 741.1903.

8: Compounds **32** (1.75 g, 2.50 mmol) and **33** (392 mg, 1.95 mmol) were coevaporated with toluene and dried under reduced pressure. The mixture was dissolved in toluene (23 mL), and 4-Å molecular sieves (2.1 g) were added. After stirring for 10 min at room temperature under argon atmosphere, AgOTf (857 mg, 3.34 mmol) and $[Cp_2HfCl_2]$ (618 mg,

1.66 mmol) were added. After stirring for 16 h at 50 °C, the mixture was cooled to room temperature and filtered through celite. The filtrate was then washed with aqueous $NaHCO_3$. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 4:1–3:2) gave allyloxycarbonylaminohexyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-4-*O*-(9-fluorenylmethyl)-oxycarbonyl-β-D-glucopyranoside (**8**; 1.37 g, 1.55 mmol, 80 %). $[\alpha]_D^{23} = +24$ ($c = 1.43$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.99$–7.68 (m, 4H), 7.55–7.49 (m, 2H), 7.46–7.15 (m, 17H), 5.93–5.91 (m, 1H, $CH_2CH{=}CH_2$), 5.78 (t, $J = 9.6$ Hz, 1H, 3-H), 5.45 (t, $J = 7.8$, 9.9 Hz, 1H, 2-H), 5.34–5.18 (m, 3H, 4-H, $CH_2CH{=}CH_2$), 4.72 (d, $J = 7.7$ Hz, 1H, 1-H), 4.64–4.54 (m, 5H), 4.23 (dd, $J = 7.4$, 10.4 Hz, 1H), 4.07 (dd, $J = 7.7$, 10.4 Hz, 1H), 3.97–3.89 (m, 4H), 3.76–3.73 (m, 2H, 6-H), 3.52–3.51 (m, 1H), 3.01–2.99 (m, 2H), 1.63–1.18 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.7$, 164.9, 156.1, 154.0, 143.1, 142.8, 141.0, 141.0, 137.7, 133.2, 133.1, 133.0, 129.8–127.6, 125.1, 124.9, 119.8, 117.5, 101.1, 73.6, 73.5, 73.0, 71.7, 70.2, 70.0, 68.8, 65.3, 46.3, 40.7, 29.6, 29.1, 26.1, 25.4 ppm; elemental analysis: calcd (%) for $C_{52}H_{53}NO_{12}$: C 70.65, H 6.04, N 1.58; found: C 70.67, H 6.13, N 1.55.

34: Et_3N (5 mL) was added to a solution of **8** (785 mg, 0.888 mmol) in THF (20 mL). After stirring at room temperature for 3.5 h, the reaction mixture was concentrated and purified by flash silica-gel column chromatography (hexanes/EtOAc = 3:1–3:2) to afford allyloxycarbonylaminohexyl 2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**34**; 569 mg, 0.860 mmol, 97 %). $[\alpha]_D^{23} = +38$ ($c = 0.79$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.99$–7.94 (m, 4H), 7.53–7.27 (m, 11H), 5.90–5.89 (m, 1H, $CH_2CH{=}CH_2$), 5.45–5.43 (m, 2H, 2-H, 3-H), 4.67–4.53 (m, 6H), 3.98–3.85 (m, 5H), 3.71–3.69 (m, 1H), 3.50–3.48 (m, 1H), 3.35–3.33 (m, 2H), 3.00–2.98 (m, 2H), 1.53–1.16 (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 167.0$, 165.1, 156.0, 137.6, 133.3, 133.1, 133.0, 129.9–127.7, 117.5, 101.1, 74.6, 73.8, 71.6, 71.2, 70.1, 70.0, 65.4, 40.9, 29.8, 29.3, 26.3, 25.6 ppm; elemental analysis: calcd (%) for $C_{37}H_{43}NO_{10}$: C 67.16, H 6.55, N 2.12; found: C 66.98, H 6.68, N 2.15.

36: TMSOTf (5 μL, 0.03 mmol) was added to a solution of **9** (218 mg, 0.254 mmol) and **34** (113 mg, 0.171 mmol) in CH_2Cl_2 (4 mL) at 4 °C. After stirring for 1 h at 4 °C under argon atmosphere, the mixture was neutralized by a few drops of Et_3N and diluted with CH_2Cl_2. The organic phase was washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 4:1–2:1) gave allyloxycarbonylaminohexyl-2-*O*-benzoyl-4,6-di-*O*-benzyl-3-(9-fluorenylmethyl)oxycarbonyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glycopyranoside (**35**; 207 mg, 0.156 mmol, 91 %). Et_3N (3 mL) was added to a solution of **35** (892 mg, 0.671 mmol) in THF (12 mL), and the mixture was stirred for 3 h. Concentration and purification by flash silica-gel column chromatography (hexanes/EtOAc = 3:1–3:2) afforded allyloxycarbonylaminohexyl 2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**36**; 612 mg, 0.552 mmol, 82 %). $[\alpha]_D^{23} = +8.2$ ($c = 1.53$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.97$–7.92 (m, 6H), 7.58–7.18 (m, 24H), 5.93–5.91 (m, 1H, $CH_2CH{=}CH_2$), 5.60 (t, $J = 9.6$ Hz, 1H), 5.35 (dd, $J = 8.1$, 10.0 Hz, 1H), 5.32–5.17 (m, 2H), 5.11 (dd, $J = 7.8$, 10.0 Hz, 1H), 4.62–4.51 (m, 8H), 4.36 (d, $J = 12.1$ Hz, 1H), 4.14–3.87 (m, 3H), 3.86–3.84 (m, 1H), 3.74–3.69 (m, 2H), 3.61 (dd, $J = 1.6$, 10.9 Hz, 1H), 3.56–3.48 (m, 3H), 3.45–3.43 (m, 1H), 3.33–3.31 (m, 1H), 2.98–2.96 (m, 3H), 2.85 (t, $J = 9.0$ Hz, 1H), 2.21 (d, $J = 10.6$ Hz, 1H), 1.49–1.13 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 166.0$, 165.1, 165.1, 156.0, 138.1, 137.6, 133.1, 133.0, 132.5, 130.3, 129.8, 129.7, 129.5, 128.4–127.5, 117.5, 101.0, 100.5, 76.6, 75.6, 75.1, 74.7, 74.3, 73.6, 73.5, 73.1, 72.9, 72.7, 72.0, 69.9, 67.8, 66.9, 65.4, 40.9, 29.8, 29.3, 26.3, 25.6 ppm; HRMS (MALDI): *m/z* calcd for $C_{64}H_{69}NO_{16}Na$: 1130.4514 $[M+Na]^+$; found: 1130.4494.

4: TMSOTf (12 μL, 0.06 mmol) was added to a solution of **10** (559 mg, 0.617 mmol) and **36** (486 mg, 0.439 mmol) in CH_2Cl_2 (15 mL) at 4 °C. After stirring for 50 min at 4 °C under argon atmosphere, the mixture was neutralized with a few drops of Et_3N and diluted with CH_2Cl_2. The organic phase was washed with aqueous $NaHCO_3$, the aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. The crude trisaccharide was then dissolved in THF (12 mL), and Et_3N (3 mL) was added. After stirring for 3 h, the mixture was concentrated and purified by silica-gel column chromatography (hexanes/EtOAc = 1:1–1:2) to give allyloxycarbonylaminohexyl 2-deoxy-6-*O*-benzyl-3-*O*-levulinoyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**4**; 488 mg, 0.071 mmol, 69 %). $[\alpha]_D^{23} = -10.7$ ($c = 1.48$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.93$–7.82 (m, 6H), 7.61–7.12 (m, 29H), 6.35 (d, $J = 9.1$ Hz, 1H, NH), 5.93–5.91 (m, 1H), 5.54 (t, $J = 9.6$ Hz, 1H), 5.38 (dd, $J = 7.7$, 9.3 Hz, 1H), 5.34–5.18 (m, 2H), 4.86 (d, $J = 11.8$ Hz, 1H), 4.80 (dd, $J = 8.8$, 10.7 Hz, 1H), 4.59–4.44 (m, 9H), 4.38 (d, $J = 11.7$ Hz, 1H), 4.28 (d, $J = 12.6$ Hz, 1H), 4.13–4.02 (m, 3H), 3.88–3.25 (m, 15H), 2.96–2.72 (m, 7H), 2.54–2.35 (m, 2H), 2.14 (s, 3H), 1.45–1.12 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 207.7$, 172.8, 165.1, 164.3, 161.9, 156.0, 138.9, 138.1, 137.9, 137.6, 133.5, 132.9, 132.3, 130.4, 129.7–127.0, 117.5, 100.9, 100.6, 100.5, 91.9, 78.4, 77.3, 75.7, 75.2, 75.0, 75.0, 74.8, 74.6, 73.7, 73.4, 73.1, 72.9, 72.0, 70.0, 69.8, 69.7, 67.5, 67.2, 65.4, 55.6, 40.9, 38.4, 29.9, 29.7, 29.3, 28.2, 26.3, 25.6 ppm; HRMS (MALDI): *m/z* calcd for $C_{84}H_{91}N_2O_{23}Cl_3K$: 1639.4715 $[M+K]^+$; found: 1639.4709.

5: Ac_2O (1.5 mL) was added to a solution of **4** (159 mg, 0.099 mmol) in pyridine (3 mL), and the mixture was stirred for 16 h at room temperature under nitrogen atmosphere. The mixture was concentrated, coevaporated with toluene, and dried under reduced pressure. The dried crude material was dissolved in DMF (3 mL), and hydrazine acetate (14.0 mg, 0.152 mmol) was added. After stirring for 19 h at room temperature, the mixture was diluted with EtOAc, and the organic phase was washed with 10 % citric acid. The aqueous phase was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 2:1–1:1) gave allyloxycarbonylaminohexyl 2-deoxy-4-*O*-acetyl-6-*O*-benzyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**5**; 146 mg, 0.094 mmol, 95 %). $[\alpha]_D^{22} = -1.8$ ($c = 1.97$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.90$–7.83 (m, 6H), 7.57–7.13 (m, 29H), 6.83 (d, $J = 6.2$ Hz, 1H, NH), 5.92–5.90 (m, 1H), 5.55 (t, $J = 10.0$ Hz, 1H), 5.39 (dd, $J = 7.8$, 10.0 Hz, 1H), 5.34–5.18 (m, 3H), 4.81 (t, $J = 8.7$ Hz, 1H), 4.76 (d, $J = 11.8$ Hz, 1H), 4.61–4.37 (m, 9H), 4.28 (d, $J = 12.5$ Hz, 1H), 4.08–4.05 (m, 4H), 3.90–3.33 (m, 14H), 3.18 (d, $J = 5.9$ Hz, 1H), 2.98–2.88 (m, 2H), 2.80 (t, $J = 8.7$ Hz, 1H), 1.96 (s, 3H), 1.44–1.12 ppm (m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.4$, 165.1, 164.9, 163.2, 162.4, 156.0, 138.8, 138.1, 137.8, 137.4, 133.4, 132.9, 132.4, 130.3–126.9, 117.5, 100.9, 100.4, 99.5, 91.8, 78.4, 77.3, 75.8, 75.0, 74.8, 74.6, 73.6, 73.4, 73.2, 73.1, 72.8, 72.1, 72.0, 69.8, 69.2, 67.5, 67.1, 65.4, 60.5, 59.7, 40.9, 36.6, 29.7, 29.3, 26.3, 25.6, 21.2, 20.9, 14.4 ppm; HRMS (MALDI): *m/z* calcd for $C_{81}H_{87}N_2O_{22}Cl_3K$: 1583.4453 $[M+K]^+$; found: 1583.4437.

37a: TMSOTf (1.0 μL, 5.2 μmol) was added to a solution of **4** (51 mg, 0.032 mmol) and **6** (50 mg, 0.041 mmol) in CH_2Cl_2 (1.2 mL) at 0 °C, and the mixture was stirred for 1 h at 0 °C under argon atmosphere. After dilution with CH_2Cl_2 and washing with aqueous $NaHCO_3$, the aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexanes/EtOAc = 3:2–1:1) gave allyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2-deoxy-6-*O*-benzyl-3-*O*-levulinoyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**37a**; 76 mg, 0.029 mmol, 90 %). $[\alpha]_D^{23} = -1.6$ ($c = 0.82$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.92$–7.80 (m, 9H), 7.57–7.07 (m, 38H), 6.40 (d, $J = 9.1$ Hz, 1H), 5.91–5.89 (m, 1H), 5.63 (d, $J = 3.0$ Hz, 1H), 5.53 (t, $J = 9.3$ Hz, 1H), 5.46 (dd, $J = 7.8$, 10.4 Hz, 1H), 5.34–5.17 (m, 7H), 5.02–4.86 (m, 5H), 4.76 (d, $J = 7.7$ Hz, 1H), 4.54–3.23 (m, 42H), 3.79 (s, 3H), 2.96 (br s, 2H), 2.89–2.87 (m, 1H), 2.80 (t, $J = 8.8$ Hz, 1H), 2.68–2.52 (m, 5H), 2.17 (s, 3H), 2.14 (s, 3H), 2.10 (s, 1H), 2.05 (s, 1H), 2.00 (s, 3H), 1.99 (s, 3H), 1.86 (t, $J = 12.6$ Hz, 1H), 1.41 (br s, 2H), 1.25–1.10 ppm (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 205.7$, 172.4, 170.5, 170.2, 170.2, 169.5,

169.4, 167.3, 165.1, 165.0, 164.6, 164.1, 161.7, 153.8, 138.8, 138.0, 137.8, 137.6, 133.3, 132.8, 132.2, 130.3–127.0, 117.4, 100.7, 100.4, 98.9, 95.3, 91.8, 78.8–71.5, 69.8, 69.7, 65.7, 63.3, 62.6, 62.4, 56.0, 53.0, 51.5, 56.0, 53.1, 51.5, 40.8, 37.8, 29.7–25.5, 20.9, 20.6 ppm; HRMS (MALDI): *m/z* calcd for $C_{127}H_{137}N_3O_{44}Cl_6Na$: 2640.6598 $[M+Na]^+$; found: 2640.6651.

38a: Toluenesulfinic acid sodium salt (8 mg, 0.046 mmol) and $[Pd(PPh_3)_4]$ (2 mg, 18 μmol) were added to a solution of **37a** (49 mg, 0.019 mmol) in degassed THF/MeOH (2:1, 3 mL), and the mixture was stirred for 1 h at room temperature under argon atmosphere. After deprotection, CbzOSu (10 mg, 0.04 mmol) and Et_3N (11 μL, 0.08 mmol) were added. The mixture was stirred for another 3 h and concentrated. Purification by preparative TLC (toluene/acetone = 3:1) gave benzyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2-deoxy-6-*O*-benzyl-3-*O*-levulinoyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**38a**; 40 mg, 0.015 mmol, 80%). $[\alpha]_D^{23} = -1.8$ ($c = 0.3$, chloroform); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.91–7.80$ (m, 7H), 7.61–6.91 (m, 38H), 6.37 (d, $J = 9.1$ Hz, 1H), 5.65–5.63 (m, 1H), 5.53 (t, $J = 9.3$ Hz, 1H), 5.46 (dd, $J = 7.7$, 10.2 Hz, 1H), 5.38–5.25 (m, 4H), 5.07–4.83 (m, 6H), 4.76 (d, $J = 7.7$ Hz, 1H), 4.56–3.26 (m, 28H), 3.79 (s, 3H), 3.00–2.97 (m, 2H), 2.91–2.87 (m, 1H), 2.80 (t, $J = 8.8$ Hz, 1H), 2.67–2.55 (m, 4H), 2.17 (s, 3H), 2.14 (s, 3H), 2.10 (s, 3H), 2.00 (s, 6H), 1.99 (s, 6H), 1.86 (t, $J = 12.6$ Hz, 1H), 1.43–1.40 (m, 2H), 1.10 ppm (br s, 6H); HRMS (MALDI): *m/z* calcd for $C_{128}H_{135}N_3O_{43}Cl_6Na$: 2634.6498 $[M+Na]^+$; found: 2634.6716.

39a: Compound **38a** (40 mg, 0.015 mmol) was dissolved in DMF (1 mL), and hydrazine acetate (4 mg, 0.046 mmol) was added. After stirring for 8 h, the mixture was diluted with EtOAc, and the organic phase was washed with 10% citric acid and brine, dried over Na_2SO_4, filtered, and concentrated. The crude product was dissolved in AcOH (2 mL), and Zn/Cu couple (400 mg) was added. After stirring for 2 days at 45 °C, the mixture was cooled to room temperature, filtered through celite, and concentrated. The residue was redissolved in pyridine (3 mL), and Ac_2O (1.5 mL) was added. After stirring for 13 h, the mixture was concentrated and coevaporated with toluene. The precipitate was dissolved again in EtOAc and washed with 10% citric acid, H_2O, aqueous $NaHCO_3$, and brine. After drying over Na_2SO_4, filtration, and concentration, purification by preparative TLC (toluene/EtOAc = 1:6) gave benzyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2-deoxy-6-*O*-benzyl-3-*O*-acetyl-2-acetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**39a**; 18 mg, 0.008 mmol, 55%).

1a: Compound **39a** (18 mg, 0.008 mmol) was dissolved in sodium methoxide in methanol (0.05 M, 3 mL). After stirring for 1 day at room temperature under an atmosphere of nitrogen, water (0.3 mL) was added, and the mixture was stirred for another 16 h. Next, the mixture was neutralized with Amberlite IR-120 resin and filtered to remove the resin. The filtrate was concentrated and dried under reduced pressure. The crude residue was dissolved in methanol (1.5 mL) and water (0.5 mL) before the addition of 20% $Pd(OH)_2$/C (9 mg) and a few drops of acetic acid. The mixture was stirred for 1 day at room temperature under an atmosphere of hydrogen. The catalyst was removed by filtration, and the filtrate was concentrated. Purification by size-exclusion chromatography (Sephadex G-15, H_2O) with a SepPak C-18 cartridge (MeOH/H_2O = 0:100–10:90) yielded aminohexyl (3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2- nonulopyranosylonate)-(2→6)-β-D-galactopyranosyl-(1→4)-2-deoxy-2-acetamidyl-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (**1a**; 4 mg, 0.004 mmol, 45%). $[\alpha]_D^{23} = -15$ ($c = 0.16$, H_2O); ^1H NMR (300 MHz, D_2O): $\delta = 4.80$ (1H, overlapped with HOD), 4.48 (d, $J = 8.1$ Hz, 1H), 4.46 (d, $J = 8.1$ Hz, 1H), 4.43 (d, $J = 7.8$ Hz, 1H), 4.16 (d, $J = 3.1$ Hz, 1H), 4.03–3.50 (m, 24H), 3.34–3.30 (m, 1H), 2.98 (t, $J = 7.5$ Hz, 2H), 2.66 (dd, $J = 4.4$, 12.5 Hz, 1H), 2.05 (s, 3H), 2.03 (s, 3H), 1.72 (t, $J = 12.1$ Hz, 1H), 1.66–1.64 (m, 4H), 1.46–1.41 ppm (m, 4H); HRMS (ESI): *m/z* calcd for $C_{43}H_{75}N_3O_{29}Na$: 1120.4379 $[M+Na]^+$; found: 1120.4391.

37b: TMSOTf (1.0 μL, 5.2 μmol) was added to a solution of **4** (55 mg, 0.034 mmol) and **7** (67 mg, 0.053 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C, and the mixture was stirred for 1 h at 0 °C under argon atmosphere. Next, the reaction mixture was diluted with CH_2Cl_2 and washed with aqueous $NaHCO_3$ before the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (toluene/EtOAc = 3:1–3:2) gave allyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4,6-di-*O*-acetyl-2-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2-deoxy-6-*O*-benzyl-3-*O*-levulinoyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**37b**; 78 mg, 0.030 mmol, 89%). $[\alpha]_D^{22} = +11$ ($c = 0.39$, chloroform); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 8.26–8.24$ (m, 2H), 8.07–7.79 (m, 7H), 7.62–7.10 (m, 32H), 6.32 (d, $J = 9.0$ Hz, 1H), 5.92–5.90 (m, 1H), 5.71–5.69 (m, 1H), 5.51 (t, $J = 10.0$ Hz, 1H), 5.37–5.16 (m, 5H), 5.02 (t, $J = 7.2$ Hz, 1H), 4.99–4.76 (m, 4H), 4.61–3.23 (m, H), 3.78 (s, 3H), 2.98–2.96 (m, 2H), 2.87–2.82 (m, 1H), 2.80 (t, $J = 8.5$ Hz, 1H), 2.76–2.46 (m, 4H), 2.12–1.84 (m, 22H), 1.44 (br s, 2H), 1.26 ppm (br s, 6H); HRMS (MALDI): *m/z* calcd for $C_{132}H_{139}N_3O_{44}Cl_6Na$: 2702.7 $[M+Na]^+$; found: 2702.6.

38b: Toluenesulfinic acid sodium salt (4 mg, 0.024 mmol) and $[Pd(PPh_3)_4]$ (1 mg, 9.5 μmol) were added to a solution of **37b** (33 mg, 0.013 mmol) in degassed THF/MeOH (2:1, 1.5 mL), and the mixture was stirred for 1 h at room temperature under argon atmosphere. After deprotection, CbzOSu (10 mg, 0.04 mmol) and Et_3N (11 μL, 0.08 mmol) were added. The mixture was stirred for another 3 h and concentrated. Purification with preparative TLC (toluene/EtOAc = 3:2) gave benzyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4,6-di-*O*-acetyl-2-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2-deoxy-3-*O*-acetyl-6-*O*-benzyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**38b**; 28 mg, 0.011 mmol, 85%). $[\alpha]_D^{23} = -7.3$ ($c = 0.43$, chloroform); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.92–7.80$ (m, 7H), 7.60–7.10 (m, 32H), 6.36 (d, $J = 9.3$ Hz, 1H), 5.91–5.89 (m, 1H), 5.62–5.60 (m, 1H), 5.53 (t, $J = 9.7$ Hz, 1H), 5.42–5.15 (m, 7H), 5.10 (dd, $J = 7.8$, 10.3 Hz, 1H), 4.94–4.75 (m, 5H), 4.69 (d, $J = 7.8$ Hz, 1H), 4.57–3.28 (m, overlapped), 3.65 (s, 3H), 2.98–2.96 (m, 2H), 2.85–2.84 (m, 2H), 2.66 (dd, $J = 4.7$, 12.8 Hz, 1H), 2.52–2.31 (m, 4H), 2.12 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.91 (s, 3H), 1.79 (t, $J = 10.9$ Hz, 1H), 1.41 (br s, 2H), 1.11 ppm (br s, 6H); HRMS (MALDI): *m/z* calcd for $C_{127}H_{141}Cl_6N_3O_{42}Na$: 2616.7017 $[M+Na]^+$; found: 2616.7101.

39b: Compound **38b** (28 mg, 0.011 mmol) was dissolved in DMF (1 mL), and hydrazine acetate (3 mg, 0.027 mmol) was added. After stirring for 8 h, the mixture was diluted with EtOAc, and the organic phase was washed with 10% citric acid and brine, dried over Na_2SO_4, filtered, and concentrated. The crude product was dissolved in AcOH (2 mL), and Zn/Cu couple (280 mg) was added. After stirring for 2 days at 45 °C, the mixture was cooled to room temperature, filtered through celite, and concentrated. The residue was redissolved in pyridine (3 mL), and Ac_2O (2 mL) was added. The mixture was stirred for 13 h, concentrated, and coevaporated with toluene. The precipitate was dissolved again in EtOAc and washed with 10% citric acid, brine, aqueous $NaHCO_3$, and brine. After drying over Na_2SO_4, filtration, and concentration, purification with preparative TLC (toluene/EtOAc = 1:6) gave benzyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4,6-di-*O*-acetyl-2-*O*-benzoyl-β-D-galactopyranosyl-(1→4)-2-deoxy-3-*O*-acetyl-6-*O*-benzyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**39b**; 12 mg, 0.0051 mmol, 40%).

1b: Compound **39b** (12 mg, 0.0051 mmol) was dissolved in a solution of sodium methoxide in methanol (0.05 M, 3 mL). After stirring for 1 day at

room temperature under nitrogen atmosphere, water (0.3 mL) was added, and the mixture was stirred for another 16 h. Next, the mixture was neutralized with Amberlite IR-120 resin and filtered to remove the resin. The filtrate was concentrated and dried under reduced pressure. The deacylated pellet was dissolved in methanol and water (1.5 mL/0.5 mL) before $Pd(OH)_2$/C (7 mg) and a few drops of AcOH were added. The mixture was stirred for 1 day at room temperature under an atmosphere of hydrogen. The catalyst was then removed by filtration, and the filtrate was concentrated. Purification by size-exclusion chromatography (Sephadex G-15, H_2O) with a SepPak C-18 cartridge (MeOH/H_2O = 0:100–10:90) furnished aminohexyl (3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-β-D-galactopyranosyl-(1→4)-2-deoxy-2-acetamidyl-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (**1b**; 3 mg, 58%). $[\alpha]_D^{23} = -9.2$ ($c = 0.16$, chloroform); ^{1}H NMR (300 MHz, D_2O): $\delta = 4.68$ (d, $J = 8.4$ Hz, 1H), 4.54 (d, $J = 7.8$ Hz, 1H), 4.46 (d, $J = 8.1$ Hz, 1H), 4.41 (d, $J = 7.8$ Hz, 1H), 4.13 (d, $J = 2.8$ Hz, 1H), 4.09 (dd, $J = 3.1$, 9.7 Hz, 1H), 3.98–3.51 (m, 23H), 3.29–3.27 (m, 1H), 2.94 (t, $J = 7.2$ Hz, 2H), 2.01 (s, 6H), 1.78 (t, $J = 12.5$ Hz, 1H), 1.65–1.62 (m, 4H), 1.40–1.38 ppm (m, 4H); HRMS (ESI): m/z calcd for $C_{43}H_{75}N_3O_{29}Na$: 1120.4379 $[M+Na]^+$; found: 1120.4387.

40a: TMSOTf (1 μL, 5.2 μmol) was added to a solution of **4** (48 mg, 0.031 mmol) and **6** (49 mg, 0.041 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C, and the mixture was stirred for 1 h at 0 °C under argon atmosphere. After dilution with CH_2Cl_2 and washing with aqueous $NaHCO_3$, the aqueous phase was extracted with CH_2Cl_2, and the combined organic layers were washed with brine, dried over Na_2SO_4, filtered, concentrated, and purified by flash silica-gel column chromatography (hexanes/EtOAc = 3:2–1:1) to give allyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-deoxy-4-*O*-acetyl-6-*O*-benzyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**40a**; 75 mg, 0.028 mmol, 94%). $[\alpha]_D^{22} = +2.1$ ($c = 0.62$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.92$–7.76 (m, 9H), 7.60–7.07 (m, 36H), 6.75 (d, $J = 6.8$ Hz, 1H), 5.92–5.90 (m, 1H), 5.53–5.46 (m, 3H), 5.40–5.16 (m, 8H), 4.95–4.60 (m, 6H), 4.58–3.17 (m, 42H), 3.71 (s, 3H), 2.96 (br s, 2H), 2.73 (t, $J = 9.0$ Hz, 1H), 2.60 (dd, $J = 4.7$, 13.1 Hz, 1H), 2.20–1.95 (m, 18H), 1.70–1.40 ppm (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.5$, 170.1, 169.7, 169.5, 169.3, 167.5, 165.3, 165.0, 164.3, 161.3, 153.8, 138.9, 137.9, 137.5, 132.9–132.2, 129.5–127.1, 117.4, 100.8, 99.1, 98.7, 95.4, 91.9, 77.2, 74.4–71.6, 69.5–67.1, 65.4, 62.2, 59.4, 53.0, 51.6, 40.8, 29.7, 29.2, 26.3, 25.5, 21.0–20.6 ppm; HRMS (MALDI): m/z calcd for $C_{124}H_{133}N_3O_{43}Cl_6Na$: 2586.6336 $[M+Na]^+$; found: 2586.6301.

41a: Toluenesulfinic acid sodium salt (12.5 mg, 0.0702 mmol) and [Pd(PPh_3)$_4$] (2.4 mg, 21 μmol) were added to a solution of **40a** (62 mg, 0.025 mmol) in degassed THF/MeOH (2:1, 1.5 mL), and the mixture was stirred for 1 h at room temperature under argon atmosphere. After deprotection, CbzOSu (18.1 mg, 0.073 mmol) and Et_3N (22 μL, 0.13 mmol) were added. The mixture was stirred for another 3 h and concentrated. Purification with preparative TLC (toluene/EtOAc = 3:2) gave benzyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-deoxy-4-*O*-acetyl-6-*O*-benzyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-O-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**41a**; 59.2 mg, 0.0226 mmol, 74%). $[\alpha]_D^{23} = +2.5$ ($c = 0.37$, chloroform); ^{1}H NMR (300 MHz) 7.95–7.50 (m, 10H), 7.55–7.10 (m, 40H), 6.73 (d, $J = 6.8$ Hz, 1H), 5.55–5.52 (m, 1H), 5.49 (t, $J = 8.4$ Hz, 1H), 5.39–5.24 (m, 4H), 5.18 (dd, $J = 3.4$, 10.5 Hz, 1H), 5.09–4.84 (m, 7H), 4.78 (d, $J = 8.1$ Hz, 1H), 4.71–3.26 (m, 30H), 3.71 (s, 3H), 2.96 (br s, 4H), 2.73 (t, $J = 8.7$ Hz, 1H), 2.63–2.54 (m, 2H), 2.16 (s, 3H), 2.08 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.40 (br s, 2H), 1.01 ppm (br s, 6H); HRMS (MALDI): m/z calcd for $C_{128}H_{135}Cl_6N_3O_{43}Na$: 2634.6498 $[M+Na]^+$; found: 2639.6578.

42a: Compound **41a** (46 mg, 0.015 mmol) was dissolved in AcOH (2 mL), and Zn/Cu couple (460 mg) was added. After stirring for 2 days at 45 °C, the mixture was cooled to room temperature, filtered through celite, and concentrated. The residue was redissolved in pyridine (3 mL), and Ac_2O (2 mL) was added. The mixture was stirred for 13 h, concentrated, and coevaporated with toluene. The precipitate was dissolved in EtOAc and washed with 10% citric acid, brine, aqueous $NaHCO_3$, and brine. After drying over Na_2SO_4, filtration, and concentration, purification with preparative TLC (toluene/EtOAc = 1:6) gave benzyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-deoxy-4-*O*-acetyl-6-*O*-benzyl-2-acetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-O-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**42a**; 21 mg, 0.009 mmol, 59%).

2a: Compound **41a** (21 mg, 0.009 mmol) was dissolved in a solution of sodium methoxide in methanol (0.05 M, 3 mL). After stirring for 1 day at room temperature under an atmosphere of nitrogen, water (0.3 mL) was added, and the mixture was stirred for another 16 h. The mixture was neutralized with Amberlite IR-120 resin and filtered to remove the resin. The filtrate was concentrated and dried under reduced pressure. The crude residue was dissolved in methanol (1.5 mL) and water (0.5 mL) before addition of $Pd(OH)_2$/C (10 mg) and a few drops of AcOH. The mixture was stirred for 1 day at room temperature under an atmosphere of hydrogen. The catalyst was removed by filtration, and the filtrate was concentrated. Purification by size-exclusion chromatography (Sephadex G-15, H_2O) with a SepPak C-18 cartridge (MeOH/H_2O = 0:100–10:90) gave aminohexyl (3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→6)-β-D-galactopyranosyl-(1→3)-2-deoxy-2-acetamidyl-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (**2a**; 6 mg, 0.006 mmol, 64%). $[\alpha]_D^{23} = +3.8$ ($c = 0.4$, chloroform); ^{1}H NMR (300 MHz, D_2O): $\delta = 4.72$ (d, $J = 8.7$ Hz, 1H), 4.46 (d, $J = 8.1$ Hz, 1H), 4.42 (d, $J = 8.1$ Hz, 1H), 4.36 (d, $J = 7.8$ Hz, 1H), 4.14 (d, $J = 2.8$ Hz, 1H), 3.98–3.43 (m, 24H), 3.30–3.28 (m, 1H), 2.97 (t, $J = 7.2$ Hz, 1H), 2.68 (dd, $J = 4.1$, 12.1 Hz, 1H), 2.07 (s, 6H), 1.68 (t, $J = 12.6$ Hz, 1H), 1.66–1.65 (m, 4H), 1.42–1.39 ppm (m, 4H); HRMS (ESI): m/z calcd for $C_{43}H_{75}N_3O_{29}Na$: 1120.4379 $[M+Na]^+$; found: 1120.4363.

40b: TMSOTf (1 μL, 5.2 μmol) was added to a solution of **5** (48 mg, 0.031 mmol) and **7** (53 mg, 0.0416 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C, and the mixture was stirred for 1 h at 0 °C under argon atmosphere. After dilution with CH_2Cl_2 and aqueous $NaHCO_3$, the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, filtered, and concentrated. Purification by flash silica-gel column chromatography (hexane/EtOAc = 2:1–2:3) gave allyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-deoxy-4-*O*-acetyl-6-*O*-benzyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**40b**; 74 mg, 0.294 mmol, 94%). $[\alpha]_D^{22} = +6.8$ ($c = 1.13$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.03$–8.01 (m, 2H), 7.91–7.83 (m, 6H), 7.57–7.09 (m, 34H), 6.48 (d, $J = 6.8$ Hz, 1H), 5.92–5.89 (m, 1H), 5.51 (t, $J = 9.7$ Hz, 1H), 5.43–5.41 (m, 1H), 5.31–5.26 (m, 5H), 5.12 (dd, $J = 7.5$, 10.0 Hz, 1H), 5.00–3.25 (m, 42H), 3.78 (s, 3H), 2.93–2.92 (m, 4H), 2.73 (t, $J = 8.7$ Hz, 2H), 2.52 (dd, $J = 4.7$, 12.5 Hz, 1H), 2.10 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.04 (s, 3H), 2.01 (s, 3H), 1.92 (s, 3H), 1.79 (s, 3H), 1.47 (br s, 3H), 1.10 ppm (br s, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.6$, 170.4, 170.1, 170.0, 169.7, 165.1, 165.1, 164.8, 164.4, 161.3, 153.9, 139.0, 137.9, 137.8, 137.5, 133.4, 132.9, 132.3, 130.4–127.1, 117.4, 100.8, 100.6, 99.0, 98.6, 96.4, 95.1, 91.5, 78.4, 77.1, 76.2, 74.3, 73.6, 73.22, 73.20, 72.9, 72.6, 71.8, 71.7, 71.31, 71.30, 70.9, 70.2, 69.6, 69.2, 68.7, 67.2, 67.1, 66.8, 66.4, 65.2, 61.9, 61.5, 59.6, 53.1, 50.9, 40.7, 37.6, 29.5–20.2 ppm; HRMS (MALDI): m/z calcd for $C_{119}H_{131}Cl_6N_3O_{43}Na$: 2522.6180 $[M+Na]^+$; found: 2522.6230.

41b: Toluenesulfinic acid sodium salt (4 mg, 0.024 mmol) and [Pd(PPh_3)$_4$] (1 mg, 9.5 μmol) were added to a solution of **40b** (50 mg, 0.019 mmol) in degassed THF/MeOH (2:1, 1.5 mL), and the mixture was stirred for 1 h at room temperature under argon atmosphere. After deprotection, CbzOSu (10 mg, 0.041 mmol) and Et_3N (11 μL, 0.079 mmol) were added. The mixture was stirred for another 3 h and concentrated. Purification with preparative TLC (toluene/EtOAc = 3:2) gave benzyloxycarbonyl-

aminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-trichloroethoxycarbonylamino-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-deoxy-4-*O*-acetyl-6-*O*-benzyl-2-trichloroacetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**41b**; 41 mg, 0.0172 mmol, 81 %). $[\alpha]_D^{23} = +3.3$ ($c = 0.55$, chloroform); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 8.12$–8.09 (m, 2H), 7.91–7.83 (m, 6H), 7.57–7.09 (m, 39H), 6.50 (d, $J = 6.9$ Hz, 1H), 5.51 (t, $J = 9.7$ Hz, 1H), 5.43–5.41 (m, 1H), 5.28–5.26 (m, 3H), 5.11 (dd, $J = 7.5$, 10.4 Hz, 1H), 5.00 (s, 2H), 4.99 (d, $J = 8.1$ Hz, 1H), 4.95 (d, $J = 3.4$ Hz, 1H), 4.90–4.87 (m, 1H), 4.82 (d, $J = 11.8$ Hz, 1H), 4.78 (dd, $J = 6.5$, 9.0 Hz, 1H), 4.73–4.19 (m, 18H), 4.10–3.90 (m, 3H), 3.82–3.57 (m, 5H), 3.78 (s, 3H), 3.51–3.25 (m, 6H), 2.98–2.96 (m, 2H), 2.91 (t, $J = 4.1$ Hz, 1H), 2.75–2.73 (m, 2H), 2.53 (dd, $J = 5.0$, 12.8 Hz, 1H), 2.11 (s, 3H), 2.08 (s, 3H), 2.05 (br s, 6H), 2.02 (s, 3H), 1.92 (s, 3H), 1.40 (br s, 2H), 1.10 ppm (br s, 6H); HRMS (MALDI): *m/z* calcd for $C_{123}H_{133}Cl_6N_3O_{43}Na$: 2572.6342 $[M+Na]^+$; found: 2572.6416.

42b: Compound **41b** (39 mg, 0.0167 mmol) was dissolved in AcOH (2 mL), and Zn/Cu couple (460 mg) was added. After stirring for 2 days at 45 °C, the mixture was cooled to room temperature, filtered through celite, and concentrated. The residue was redissolved in pyridine (3 mL), and Ac_2O (2 mL) was added. Next, the mixture was stirred for 13 h, concentrated, and coevaporated with toluene. The precipitate was dissolved in EtOAc and washed with 10 % citric acid, brine, aqueous $NaHCO_3$, and brine. After drying over Na_2SO_4, filtration, and concentration, purification with preparative TLC (toluene/EtOAc = 1:6) gave benzyloxycarbonylaminohexyl (methyl 4,7,8,9-tetra-*O*-acetyl-3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-4-*O*-acetyl-2,3-di-*O*-benzoyl-β-D-galactopyranosyl-(1→3)-2-deoxy-4-*O*-acetyl-6-*O*-benzyl-2-acetamidyl-β-D-glucopyranosyl-(1→3)-2-*O*-benzoyl-4,6-di-*O*-benzyl-β-D-galactopyranosyl-(1→4)-2,3-di-*O*-benzoyl-6-*O*-benzyl-β-D-glucopyranoside (**41b**; 25 mg, 0.0106 mmol, 62 %).

2b: Compound **41b** (25 mg, 0.0106 mmol) was dissolved in a solution of sodium methoxide in methanol (0.05 M, 3 mL). After stirring for 1 day at room temperature under an atmosphere of nitrogen, water (0.3 mL) was added, and the mixture was stirred for another 16 h. Next, the mixture was neutralized with Amberlite IR-120 resin and filtered to remove the resin. The filtrate was concentrated and dried under reduced pressure. The crude residue was dissolved in MeOH (1.5 mL) and H_2O (0.5 mL) before addition of $Pd(OH)_2$/C (10 mg) and a few drops of AcOH. The mixture was stirred for 1 day at room temperature under an atmosphere of hydrogen. The catalyst was then removed by filtration, and the filtrate was concentrated. Purification by size-exclusion chromatography (Sephadex G-15, H_2O) with a SepPak C-18 cartridge (MeOH/H_2O = 0:100–10:90) gave aminohexyl (3,5-dideoxy-5-acetamidyl-D-glycero-α-D-galacto-2-nonulopyranosylonate)-(2→3)-β-D-galactopyranosyl-(1→3)-2-deoxy-2-acetamidyl-β-D-glucopyranosyl-(1→3)-β-D-galactopyranosyl-(1→4)-β-D-glucopyranoside (**2b**; 6 mg, 0.0056 mmol, 52 %). $[\alpha]_D^{23} = -11$ ($c = 0.2$, H_2O); ^{1}H NMR (300 MHz, D_2O): $\delta = 4.71$ (d, $J = 8.1$ Hz, 1H), 4.49 (d, $J = 7.8$ Hz, 1H), 4.46 (d, $J = 7.8$ Hz, 1H), 4.42 (d, $J = 7.8$ Hz, 1H), 4.13 (d, $J = 3.1$ Hz, 1H), 4.06 (dd, $J = 3.1$, 9.6 Hz, 1H), 3.98–3.43 (m, 23H), 3.30–3.28 (m, 1H), 2.97 (t, $J = 7.5$ Hz, 2H), 2.74 (dd, $J = 4.7$, 12.8 Hz, 1H), 2.01 (s, 6H), 1.76 (t, $J = 12.1$ Hz, 1H), 1.65–1.60 (m, 4H), 1.42–1.39 ppm (m, 4H); HRMS (ESI): *m/z* calcd for $C_{43}H_{75}N_3O_{29}Na$: 1120.4379 $[M+Na]^+$; found: 1120.4398.

Acknowledgements

This work was supported by the Swiss National Science Foundation (SNF grant 200020–109555), ETH Zürich, and JSPS Postdoctoral Fellowships for Research Abroad (for S.H.). We thank Dr. Yukishige Ito (RIKEN, Japan) for providing sialic acid.

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Received: December 21, 2006
Revised: August 19, 2007

