Exploration of Modalities in Building α-O-Linked Systems through Glycal Assembly: A Total Synthesis of the Mucin-Related F1α Antigen

Xiao-Tao Chen,[†] Dalibor Sames,[‡] and Samuel J. Danishefsky*[,†,‡]

Contribution from the Department of Chemistry, Columbia University, New York, New York 10027; and Laboratory for Bioorganic Chemistry, Memorial Sloan-Kettering Cancer Center, 1275 York Avenue, New York, New York 10021

Received March 4, 1998

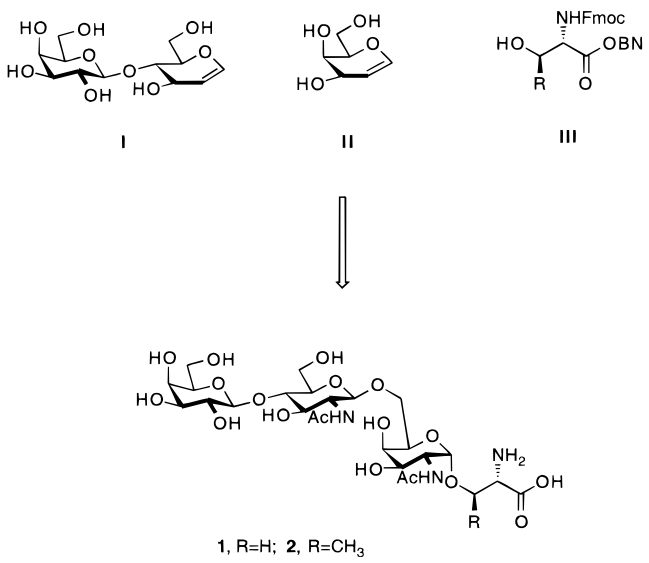
Abstract: The total synthesis of the F1α antigen, a member of the tumor-associated O-linked mucin glycopeptides, was achieved via two alternative routes. In the first approach, an α-O-linkage between serine/threonine and GalNAc (2-deoxy-2-*N*-acetylamino-D-galactose) was fashioned first. This prebuilt cassette was then linked to a lactosamine unit. Alternatively, assembly of the trisaccharide glycal preceded activation of the glycal double bond and the construction of the glycopeptide linkage. Both strategies lead to the desired glycosyl amino acid derivatives. During our investigation, we uncovered remarkable effects of even remote protecting groups on the reactivity and stereoselectivity of glycosidations.

Introduction

As part of a program directed toward synthetically derived mimics of the surfaces of tumor tissues, we have focused on the mucin family of glycoproteins.[1] Due to their high expression on epithelial cell surfaces and the high content of clustered O-linked carbohydrates, mucins constitute important targets for antitumor immunological studies. Mucins on epithelial tumors often carry aberrant α-O-linked carbohydrates.[2] The recently identified F1α antigens **1** and **2** represent examples of aberrant carbohydrate epitopes found on mucins associated with gastric adenocarcinomas (Scheme 1).[3] With this fact well in mind, we set out to construct the F1α epitope through synthesis.[4]

In light of the strategy of glycal assembly,[5] it seemed likely that the F1α structure could be constructed from the three principal building units **I**−**III** (Scheme 1). Such a general plan invites two alternative modes of implementation. First, a GalNAc-serine/threonine construct might be assembled in the initial phase. This would be followed by the extension at the "nonreducing end" (**II** + **III**, then **I**). Alternatively, the entire glycodomain could be assembled first in a form of trisaccharide glycal (**I** + **II**). This milestone would be followed by coupling of the resultant trisaccharide donor to a serine or threonine amino acid residue (cf. **III**). In this paper we report our studies of both of these strategies and show, at least in the case at hand, the advantages of the former.

Scheme 1



[†] Columbia University.

[‡] Memorial Sloan-Kettering Cancer Center.

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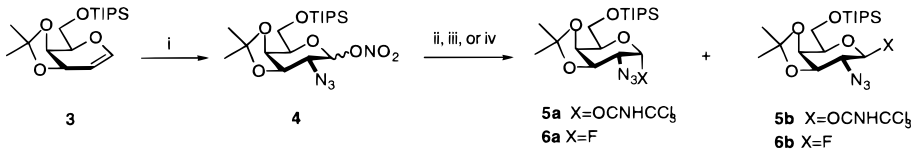
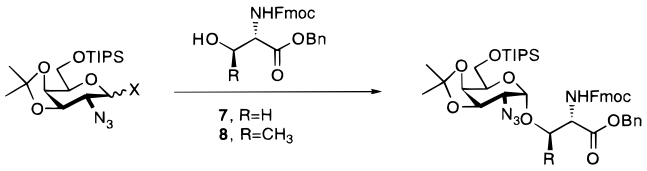
Published on Web 07/23/1998

Scheme 2[a]



[a] Conditions: (i) NaN_3, CAN, CH_3CN, −20 °C, overnight, 40%, α (**4a**):*β* (**4b**) 1:1; (ii) PhSH, EtN(*i*-Pr)$_2$, CH_3CN, 0 °C, 1 h, 99.8%; (iii) K_2CO_3, CCl_3CN, CH_2Cl_2, rt, 5 h, 84%, **5a**:**5b** 1:5; (iv) DAST, CH_2Cl_2, 0 °C, 1 h, 93%, **6a**:**6b** 1:1.

Table 1



x	catalyst/promotor	R = H (**9**) α:*β* (%)	R = CH_3 (**10**) α:*β* (%)
O(CNH)CCl_3 (**5b**)	TMSOTf (0.1 equiv), CH_2Cl_2/Hex	7:3 (100)	7:1 (33)
O(CNH)CCl_3 (**5b**)	TMSOTf (0.5 equiv), THF	1:0 (86)	1:0 (15)
O(CNH)CCl_3 (**5a**)	TMSOTf (0.5 equiv), THF	1:0 (66)	
F (**6a**)	Cp_2ZrCl_2/$AgClO_4$ (2 equiv), CH_2Cl_2	2:1 (89)	6:1 (87)
F (**6b**)	Cp_2ZrCl_2/$AgClO_4$ (2 equiv), CH_2Cl_2	2:1 (91)	6:1 (82)

Discussion and Results

The first synthetic approach that we explored commenced with preparation of monosaccharide donors **5a/b** and **6a/b** (Scheme 2). The protecting groups of the galactal (cf. **II**) were carefully chosen to fulfill several requirements. They must be stable to the reagents and conditions in the azidonitration protocol (vide infra). Also, the protecting functions must not undermine the coupling step leading to the glycosyl amino acid. After some initial experimentation, galactal **3** became the starting material of choice. The azidonitration protocol (NaN_3, CAN, CH_3CN, −20 °C) provided a 40% yield of a 1:1 mixture of **4a** and **4b**.[6] Both anomers were hydrolyzed and then converted to a 1:5 mixture of trichloroacetimidates **5a** and **5b** in good yield (84%).[7] Alternatively, hydrolysis of nitrate **4** followed by use of the DAST reagent[8] yielded a 1:1 mixture of fluoride donors **6a** and **6b**. In both cases the α/*β* anomers were separable, thus allowing the subsequent investigation of their behavior in the coupling event. The best results obtained from the coupling of donors **5** and **6** to serine or threonine acceptors bearing the free side-chain alcohol, with protected carboxy and amino moieties, are summarized in Table 1.

The trichloroacetimidate donor type **5** provided excellent yields in coupling reactions with the serine-derived alcohol **7**. After optimization, donor **5b** in the presence of TMSOTf in THF (entry 2, Table 1) provided 86% yield of pure α-product **9**. Interestingly, donor **5a** also provided α-glycoside **9** exclusively. The coupling of donor **5b** to threonine, though stereoselective, was low yielding. In this instance, fluoride donors **6a** and **6b**, promoted by Cp_2ZrCl_2/$AgClO_4$, provided the desired glycosyl threonine **10** in excellent yield (82−87%) though with somewhat reduced selectivity (6:1, α:*β*).[9] Thus, both sets of donors proved complementary to one another, and glycosyl serine **9** and glycosyl threonine **10** were in hand in high yield and with excellent margins of stereoselectivity. It was found that the configurations at the anomeric centers of these donors had no practical effect on the stereochemical outcome of their coupling steps. This result differs from the finding with the commonly used 2-deoxy-2-azido-tri-*O*-acetylgalactose-1-*O*-trichloroacetimidate.[10] In that case, each anomer yields a different ratio of α/*β* products (see discussion below).

The TIPS group at position 6 was quantitatively removed with TBAF and AcOH to give acceptors **11** and **12** (Scheme 3). The final coupling to lactosamine donor **13** was performed in the presence of BF_3·OEt_2 in THF. The crude products from this apparently stereoselective coupling step were converted to compounds **14** and **15**, respectively, with thiolacetic acid.[11] These glycosyl amino acids represent suitable units for the glycopeptide assembly. To confirm their structure, we executed global deprotection. This was accomplished in five steps yielding free F1α antigens **1** and **2** in 70% and 73% yields, respectively (Scheme 3). Fortunately, the glycosidic linkages had not been compromised under the conditions of the acidic and basic deprotection protocols.

Encouraged by our success in a previous study,[12] we also pursued a direct coupling of trisaccharide donors, synthesized through glycal assembly[5] to suitably protected serine or threonine amino acids. This logic was discussed earlier under the formalism **I** + **II** followed by coupling with **III**. Trisaccharide donors **23**−**27** were prepared as outlined in Scheme 4. Readily available lactal **16**[13] was converted to the thio donor **17** via a sequence of iodo-sulfonamidation and subsequent rearrangements with ethanethiol in the presence of LiHMDS.[14] The MeOTf-promoted coupling to galactals **18** and **19** provided trisaccharide glycals **20** and **21** in excellent yield and stereo-

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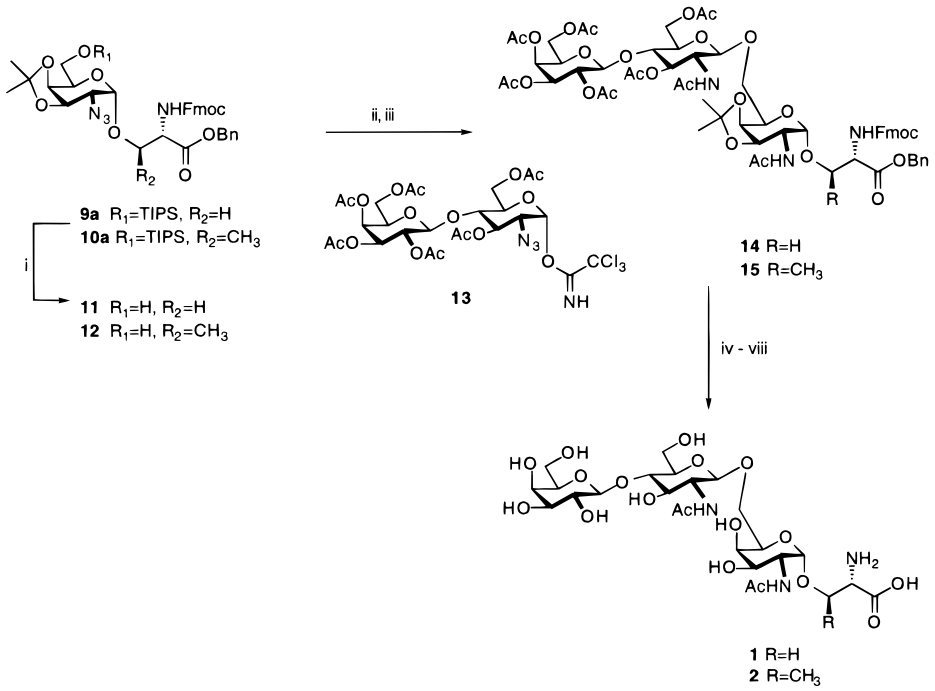
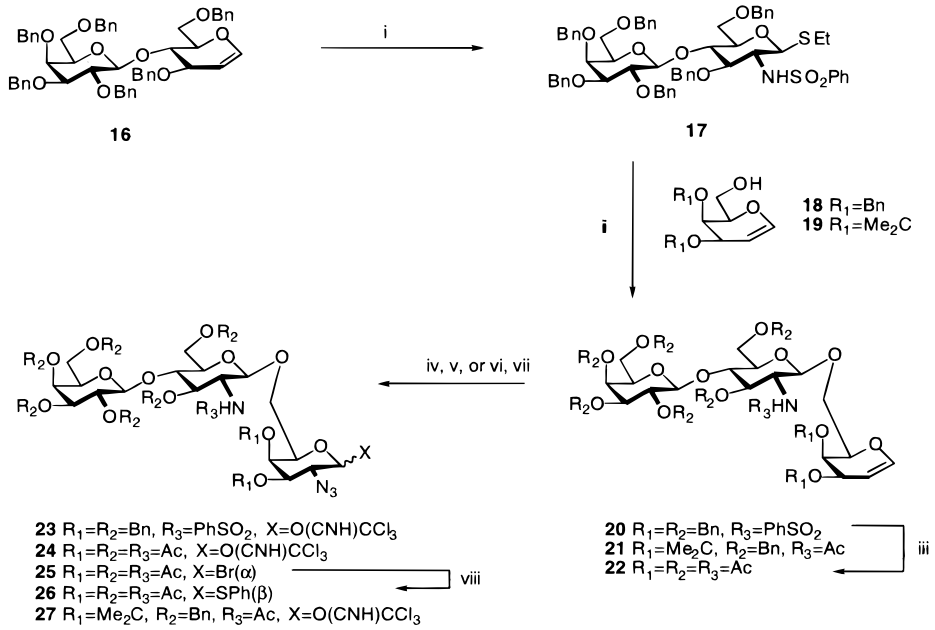
Scheme 3[a]



[a] Conditions: (i) TBAF, HOAc, THF, rt, 3 d, 100% yield for **9**, 94% yield for **10**; (ii) **11**, $BF_3{\cdot}Et_2O$, −30 °C, overnight; (iii) AcSH, pyridine, rt, overnight, 72% yield based on 50% conversion of **11**, 58% yield based on 48% conversion of **12** (two steps); (iv) 80% aq HOAc, overnight, rt−40 °C; (v) Ac_2O, pyridine, rt, overnight; (vi) 10% Pd/C, H_2, MeOH−H_2O, rt, 4 h; (vii) morpholine, DMF, rt, overnight; (viii) NaOMe, MeOH−THF, rt, overnight, 64% yield for **1**, 72% yield for **2** (five steps).

Scheme 4[a]

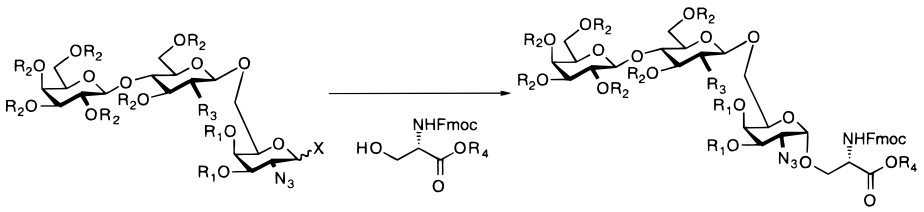


[a] Conditions: (i) I(*sym*-collidine)$_2$ClO$_4$, $PhSO_2NH_2$, 0 °C; LiHMDS, EtSH, −40 °C−rt, 88% yield in two steps; (ii) MeOTf, DTBP, 0 °C, 86% yield for **20** plus 8% yield of the α isomer; 85% yield for **21** plus 6% yield of the α isomer; (iii) Na, NH_3, −78 °C; Ac_2O, Py, rt, 59% yield for **22** in two steps; (iv) NaN_3, CAN, CH_3CN, −20 °C; (v) PhSH, EtN(*i*-Pr)$_2$; CCl_3CN, K_2CO_3, for **23**, 17% yield of 2:7, α:*β* in three steps; for **24**, 30% yield of 3:1, α:*β* in three steps; (vi) LiBr, CH_3CN, for **25**, 46% yield, α only; (vii) Ac_2O, Py; Na-Hg, Na_2HPO_4, 94% yield in two steps; NaN_3, CAN, 26% yield; PhSH, EtN(*i*-Pr)$_2$, K_2CO_3, CCl_3CN, 53% yield in two steps (**27**); (viii) LiSPh, THF, 60% yield, *β* only (**26**).

selectivity. Reductive deprotection of the benzyl groups and the sulfonamide in **20** and subsequent uniform acetylation of the crude product yielded glycal **22**. The azidonitration of glycals **20**−**22** provided intermediate azidonitrates, which were converted to the corresponding donors **23**−**27**.

The results of the couplings of these trisaccharide donors with suitable serine/threonine derived acceptors are summarized in Table 2. The protection pattern again had a profound effect on the reactivity and stereoselectivity of the coupling. Despite the seemingly large distance from the hydroxyl and other functional groups of the lactose domain to the anomeric center, the character of these substituents strongly affects the stereochemical outcome. As a qualitative guideline, uniform protection of functionality with electron-donating groups (cf. benzyl) leads

Table 2



R_1	R_2	R_3	X	R_4	catalyst/promotor	α:β (%)
Bn	Bn	$PhSO_2HN$	X = $O(CNH)CCl_3$ (**23**β)	Me	TMSOTf (0.5 equiv), THF	10:1 (90) **29**
Ac	Ac	AcHN	X = $O(CNH)CCl_3$ (**24**α/β, 3:1)	Bn	TMSOTf (1.0 equiv), THF	2:1 (22) **30**
Ac	Ac	AcHN	X= Br (**25**α)	Bn	$AgClO_4$ (1.5 equiv), CH_2Cl_2	3.5:1 (56) **30**
Ac	Ac	AcHN	X = SPh (**26**β)	Bn	NIS/TfOH, CH_2Cl_2	2:1 (40) **30**
Me_2C	Bn	AcHN	X = $O(CNH)CCl_3$ (**27**α)	Bn	TMSOTf (0.3 equiv), THF	1:0 (50) **31**
Me_2C	Ac	N_3	X = $O(CNH)CCl_3$ (**28**α/β, 1:1)	Bn	$BF_3{\cdot}Et_2O$ (0.5 equiv), THF	0:1 (67) **32**
Me_2C	Ac	N_3	X = $O(CNH)CCl_3$ (**28**β)	Bn	$BF_3{\cdot}Et_2O$ (1.5 equiv), THF	0:1 (35) **32**

to a very reactive donor by virtue of stabilization of the presumed oxonium cation. By contrast, electron-withdrawing protecting groups tend to deactivate the donor in the coupling step.[15] Such deactivation may also confer upon a donor some stereochemical memory in terms of the sensitivity of coupling to the original stereochemistry of the donor function at the anomeric center. As shown in Table 2, per-*O*-benzyl-protected donor **23** was highly reactive at −78 °C, providing product **29** in 90% yield with high stereoselectivity (10:1, first entry, Table 2). A dramatic difference was seen upon changing the overall protection from per-*O*-benzyl to per-*O*-acetyl groups, as demonstrated in the case of donor **24**. The yield and stereoselectivity of the coupling step were diminished. Comparable results were obtained with donors **25** and **26**.

In the case of compounds **27** and **28**, where the galactosamine ring was conformationally restricted by engaging the 3 and 4 positions in the cyclic acetonide, an even more surprising finding was registered. Donor **27**α with a per-*O*-benzyl-protected lactosamine disaccharide afforded only the desired α anomer **31**. However, a mixture of trichloroacetimidates, as well as the pure β anomer of **28**, yielded the undesired β anomer **32** exclusively. Thus, a modification of the protection pattern at a relatively distant site, on the second and third carbohydrate unit from the ring containing the donor function, exerted a profound reversing effect on the stereoselectivity of glycosidation. To explain our findings, in particular entries 5−7 in Table 2, would require a careful study encompassing many permutations in the coupling processes. Clearly, conformational limitations imposed on a ring within the donor ensemble by cyclic protecting groups can influence donor reactivity, as judged by rates of hydrolysis.[16] However, there is a significant gap in our understanding of the interrelationships between reactivity and stereodetermining factors in glycosidation reactions. Protecting groups, via their electronic, steric, and conformational influences, coupled with solvation effects, can strongly modulate the characteristics of glycosyl donors. Thus, at the present time, predictions as to longer range effects in the glycosidation of serine and threonine side-chain hydroxyls cannot be registered with confidence.

Given this situation, there is much to be said for the cassette approach wherein prebuilt, stereospecifically synthesized α-O-linked serine or threonine glycosides (cf. **9** and **10**) are employed to complete the saccharide assembly.

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Experimental Section

General Methods. Infrared spectra were recorded on a Perkin-Elmer FT-IR Paragon 1000 spectrometer. ^{1}H NMR spectra were obtained on a Bruker 300 (300 MHz) and are reported in parts per million (δ) relative to either tetramethylsilane (0.00 ppm) or $CHCl_3$ (7.24 ppm) for spectra run in $CDCl_3$. Coupling constants (*J*) are reported in hertz. ^{13}C NMR spectra were obtained on a Varian 300 (300 MHz) and are reported in δ relative to $CDCl_3$ (77.00 ppm) as internal reference. High-resolution mass spectra were recorded on a JEOL-DX-303 HF mass spectrometer. Optical rotations were recorded on a Jasco DIP-1000 polarimeter using a 1-dm cell at the reported temperatures and concentrations. Chemicals used were reagent grade and were used as supplied except where noted. Tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl under N_2. Dichloromethane (CH_2Cl_2) was distilled from calcium hydride under N_2. Analytical thin-layer chromatography was performed on E. Merck silica gel 60 F254 plates (0.25 mm). Compounds were visualized by dipping the plates in a cerium sulfate−ammonium molybdate solution followed by heating. Liquid column chromatography was performed using a forced flow of a hexane−ethyl acetate mixture on E. Merck silica gel 60 (40−63 nm).

Preparation of Azidonitrates 4. To a solution of protected galactal **3** (4.14 g, 12.1 mmol) in 60 mL of anhydrous CH_3CN at −20 °C was added a mixture of NaN_3 (1.18 g, 18.1 mmol) and CAN (19.8 g, 36.2 mmol). The reaction mixture was vigorously stirred at −20 °C overnight. The reaction mixture was then diluted with diethyl ether and washed with cold water and brine. Finally, the solution was dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel. A mixture of α and β isomers (**4**) (2.17 g, 40% yield) was obtained. The ratio of α isomer to β isomer was almost 1:1 based on ^{1}H NMR results. **4a**: $[\alpha]^{20}_D$ 94.5° (*c* 1.14, $CHCl_3$); FT-IR (film) 2940, 2862, 2106, 1661, 1460, 1381, 1278 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.34 (d, *J* = 3.9 Hz, 1H), 4.34 (m, 2H), 4.21 (t, *J* = 6.4 Hz, 1H), 3.95 (dd, *J* = 9.6, 7.2 Hz, 1H), 3.85 (dd, *J* = 9.6, 6.4 Hz, 1H), 3.78 (m, 1H), 1.52 (s, 3H), 1.35 (s, 3H), 1.04 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.29, 97.02, 73.36, 71.89, 71.23, 61.95, 59.57, 28.18, 25.96, 17.86, 11.91; HRMS (FAB) calcd for $C_{18}H_{34}N_4O_7SiK$ [M + K$^+$] 485.1833, found 485.1821.

4b: $[\alpha]^{20}_D$ 27.9° (*c* 1.28, $CHCl_3$); FT-IR (film) 2940, 2862, 2106, 1666, 1459, 1376, 1283 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.50 (d, *J* = 8.9 Hz, 1H), 4.30 (dd, *J* = 4.3, 1.5 Hz, 1H), 4.15 (dd, *J* = 6.2, 4.3 Hz, 1H), 3.89−4.03 (m, 3H), 3.56 (dd, *J* = 8.9, 7.3 Hz, 1H), 1.58 (s, 3H), 1.38 (s, 3H), 1.08 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.90, 98.09, 77.53, 74.58, 71.99, 61.82, 61.68, 28.06, 25.97, 17.85, 11.89; HRMS (FAB) calcd for $C_{18}H_{34}N_4O_7SiK$ [M + K$^+$] 485.1833, found 485.1857.

Preparation of Trichloroacetimidates 5a and 5b. To a solution of a mixture of azidonitrates (**4**) (1.36 g, 3.04 mmol) in 10 mL of anhydrous CH_3CN at 0 °C were slowly added Et(*i*-Pr)$_2$N (0.53 mL, 3.05 mmol) and PhSH (0.94 mL, 9.13 mmol). The reaction mixture was stirred at 0 °C for 1 h, and then the solvent was evaporated at

room temperature in vacuo. The residue was separated by chromatography on silica gel to give the hemiacetal (1.22 g, 99.8% yield). To a solution of this hemiacetal (603 mg, 1.50 mmol) in 15 mL of anhydrous CH_2Cl_2 at 0 °C were added K_2CO_3 (1.04 g, 7.50 mmol) and CCl_3CN (1.50 mL, 15.02 mmol). The reaction mixture was stirred from 0 °C to room temperature for 5 h. The suspension was filtered through a pad of Celite and washed with CH_2Cl_2. The filtrate was evaporated, and the residue was separated by chromatography on silica gel to give α-trichloroacetimidate **5a** (118 mg, 14% yield), β-trichloroacetimidate **5b** (572 mg, 70% yield), and the recovered hemiacetal (72 mg). **5a**: $[\alpha]^{20}_D$ 84.0° (c 1.02, $CHCl_3$); FT-IR (film) 2942, 2867, 2111, 1675, 1461, 1381, 1244 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.69 (s, 1H), 6.29 (d, J = 3.3 Hz, 1H), 4.47 (dd, J = 8.0, 5.3 Hz, 1H), 4.39 (dd, J = 5.3, 2.4 Hz, 1H), 4.25 (m, 1H), 3.97 (dd, J = 9.5, 7.8 Hz, 1H), 3.87 (dd, J = 9.5, 6.0 Hz, 1H), 3.67 (dd, J = 8.0, 3.3 Hz, 1H), 1.53 (s, 3H), 1.36 (s, 3H), 1.04 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.67, 109.98, 94.72, 77.20, 73.35, 72.11, 70.83, 62.01, 60.80, 28.29, 26.09, 17.88, 11.88; HRMS (FAB) calcd for $C_{20}H_{35}N_4O_5SiKCl_3$ [M + K^+] 583.1080, found 583.1071.

5b: $[\alpha]^{20}_D$ 30.6° (c 1.12, $CHCl_3$); FT-IR (film) 2941, 2110, 1677, 1219 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 8.71 (s, 1H), 5.57 (d, J = 9.0 Hz, 1H), 4.27 (d, J = 5.2 Hz, 1H), 3.95−4.02 (m, 4H), 3.63 (t, J = 9.0 Hz, 1H), 1.57 (s, 3H), 1.34 (s, 3H), 1.04 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.94, 110.55, 96.47, 77.20, 74.58, 72.21, 64.84, 61.89, 28.29, 26.07, 17.87, 11.90; HRMS (FAB) calcd for $C_{20}H_{35}N_4O_5SiKCl_3$ [M + K^+] 583.1080, found 583.1073.

Preparation of Glycosyl Fluorides 6a and 6b. To a solution of the hemiacetal prepared previously (68.0 mg, 0.169 mmol) in 3 mL of anhydrous CH_2Cl_2 at 0 °C was slowly added DAST (134 μL, 1.02 mmol). The reaction mixture was stirred at 0 °C for 1 h. The mixture was then diluted with EtOAc and washed with saturated $NaHCO_3$ and brine subsequently. Finally, the solution was dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give α-fluoride **6a** (30.2 mg, 44% yield) and β-fluoride **6b** (33.7 mg, 49% yield). **6a**: $[\alpha]^{20}_D$ 689.5° (c 1.47, $CHCl_3$); FT-IR (film) 2944, 2867, 2115, 1462, 1381 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.59 (dd, J = 53.0, 2.6 Hz, 1H), 4.34−4.40 (m, 2H), 4.26 (m, 1H), 3.96 (t, J = 9.3 Hz, 1H), 3.88 (dd, J = 9.3, 6.0 Hz, 1H), 3.48 (ddd, J = 25.5, 7.0, 2.6 Hz, 1H), 1.50 (s, 3H), 1.34 (s, 3H), 1.05 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.03, 107.45, 104.46, 77.21, 76.38, 73.21, 71.79, 70.48, 61.88, 61.23, 60.91, 28.17, 26.03, 17.09, 11.92; HRMS (FAB) calcd for $C_{18}H_{35}N_3O_4SiF$ [M + H^+] 404.2378, found 404.2369.

6b: $[\alpha]^{20}_D$ 153.8° (c 1.65, $CHCl_3$); FT-IR (film) 2943, 2867, 2116, 1456, 1382, 1246 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.05 (dd, J = 52.6, 7.4 Hz, 1H), 4.27 (dt, J = 5.5, 2.0 Hz, 1H), 3.89−4.05 (m, 4H), 3.70 (dt, J = 12.3, 5.1 Hz, 1H), 1.53 (s, 3H), 1.32 (s, 3H), 1.04 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 110.64, 109.09, 106.24, 76.27, 76.16, 73.42, 71.63, 64.80, 64.52, 61.77, 27.80, 25.78, 17.03, 11.86; HRMS (FAB) calcd for $C_{18}H_{35}N_3O_4SiF$ [M + H^+] 404.2378, found 404.2373.

Coupling of β-Trichloroacetimidate 5b with Protected Serine Derivative 7 for the Synthesis of 9a and 9b. To a suspension of β-trichloroacetimidate **5b** (52.3 mg, 0.096 mmol), serine derivative **7** (44.0 mg, 0.105 mmol), and 200 mg of 4 Å molecular sieves in a mixture of 2 mL of anhydrous CH_2Cl_2 and 2 mL of anhydrous hexane at −78 °C was added a solution of TMSOTf (1.91 μL, 0.01 mmol) in 36 μL of CH_2Cl_2. The reaction mixture was stirred at −78 °C for 30 min and then warmed to room temperature for 3 h. The reaction was quenched with Et_3N. The suspension was filtered through a pad of Celite and washed with EtOAc. The filtrate was washed with H_2O and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give α product **9a** (55 mg, 71% yield) and β product **9b** (22 mg, 29% yield). **9a**: $[\alpha]^{20}_D$ 70.5° (c 2.0, $CHCl_3$); FT-IR (film) 3433, 3348, 2943, 2867, 2109, 1730, 1504, 1453, 1381, 1336 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.74 (d, J = 7.5 Hz, 2H), 7.57 (d, J = 7.5 Hz, 2H), 7.25−7.40 (m, 9H), 5.73 (d, J = 8.4 Hz, 1H), 5.24 (d, J = 12.1 Hz, 1H), 5.17 (d, J = 12.1, 1H), 4.73 (d, J = 3.2 Hz, 1H), 4.60 (m, 1H), 4.41 (dd, J = 10.2, 7.2 Hz, 1H), 4.20−4.31 (m, 4H), 3.82−3.98 (m, 5H), 3.23 (dd, J = 8.0, 3.2 Hz, 1H), 1.47 (s, 3H), 1.31 (s, 3H), 1.02 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.65, 155.88, 143.81, 143.73, 141.27, 135.04, 128.63, 128.54, 127.71, 127.60, 125.18, 125.11, 109.67, 98.71, 77.23, 72.88, 72.39, 68.95, 68.79, 67.73, 67.36, 62.28, 61.10, 54.39, 47.08, 28.26, 26.10, 17.91, 11.90; HRMS (FAB) calcd for $C_{43}H_{56}N_4O_9SiK$ [M + K^+] 839.3453, found 839.3466.

9b: $[\alpha]^{20}_D$ 20.6° (c 1.05, $CHCl_3$); FT-IR (film) 3433, 2943, 2866, 2114, 1729, 1515, 1453, 1382 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, J = 7.4 Hz, 2H), 7.63 (t, J = 7.4 Hz, 2H), 7.30−7.44 (m, 9H), 5.91 (d, J = 8.4 Hz, 1H), 5.30 (d, J = 12.4 Hz, 1H), 5.26 (d, J = 12.4 Hz, 1H), 4.65 (m, 1H), 4.48 (dd, J = 10.0, 2.6 Hz, 1H), 4.39 (t, J = 7.4 Hz, 2H), 4.23−4.28 (m, 3H), 3.89−4.04 (m, 3H), 3.85 (dd, J = 10.0, 3.1 Hz, 1H), 3.78 (m, 1H), 3.41 (t, J = 8.2 Hz, 1H), 1.58 (s, 3H), 1.36 (s, 3H), 1.08 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.37, 155.92, 143.90, 143.69, 141.25, 135.27, 128.55, 128.27, 127.94, 127.68, 127.07, 125.27, 125.21, 119.94, 110.37, 102.30, 76.87, 73.78, 72.19, 69.68, 67.40, 67.33, 65.44, 61.99, 54.20, 47.06, 28.32, 26.10, 17.89, 11.88; HRMS (FAB) calcd for $C_{43}H_{56}N_4O_9SiK$ [M + K^+] 839.3453, found 839.3466.

Coupling of β-Trichloroacetimidate 5b with Protected Serine Derivative 7 in THF Promoted by TMSOTf (0.5 equiv). To a suspension of trichloroacetimidate **5b** (14.4 mg, 0.027 mmol), serine derivative **7** (16.7 mg, 0.040 mmol), and 50 mg of 4 Å molecular sieves in 0.2 mL of anhydrous THF at −78 °C was added a solution of TMSOTf (2.7 μL, 0.013 mmol) in 50 μL of THF. The reaction was stirred at −78 °C for 2 h and neutralized with Et_3N. The reaction mixture was filtered through a pad of Celite and washed with EtOAc. The filtrate was washed with H_2O and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the α product **9a** (18.5 mg, 86% yield).

Coupling of α-Trichloroacetimidate 5a with Protected Serine Derivative 7 in THF Promoted by TMSOTf (0.5 equiv). To a suspension of trichloroacetimidate **5a** (12.3 mg, 0.023 mmol), serine derivative **7** (14.1 mg, 0.034 mmol), and 50 mg of 4 Å molecular sieves in 0.2 mL of anhydrous THF at −78 °C was added a solution of TMSOTf (2.2 μL, 0.011 mmol) in 45 μL of THF. The reaction was stirred at −78 °C for 4 h and neutralized with Et_3N. The reaction mixture was filtered through a pad of Celite and washed with EtOAc. The filtrate was washed with H_2O and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the α product **9a** (11.8 mg, 66% yield).

Coupling of β-Trichloroacetimidate 5b with Protected Threonine Derivative 8 for the Synthesis of 10a and 10b. To a suspension of β-trichloroacetimidate **5b** (50.6 mg, 0.093 mmol), threonine derivative **8** (44.0 mg, 0.102 mmol), and 200 mg of 4 Å molecular sieves in a mixture of 2 mL of anhydrous CH_2Cl_2 and 2 mL of anhydrous hexane at −78 °C was added a solution of TMSOTf (1.85 μL, 0.009 mmol) in 35 μL of CH_2Cl_2. The reaction mixture was stirred at −78 °C for 30 min and then warmed to room temperature for 4 h. The reaction was quenched with Et_3N. The suspension was filtered through a pad of Celite and washed with EtOAc. The filtrate was washed with H_2O and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give recovered threonine derivative **7** (28.0 mg), the α product **10a** (22.0 mg, 29% yield), and the β product **10b** (3.0 mg, 4% yield). **10a**: $[\alpha]^{20}_D$ 55.2° (c 0.88, $CHCl_3$); FT-IR (film) 3430, 2941, 2866, 2109, 1730, 1510, 1452, 1380 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 7.5 Hz, 2H), 7.59 (d, J = 7.5 Hz, 2H), 7.26−7.41 (m, 9H), 5.62 (d, J = 9.4 Hz, 1H), 5.22 (d, J = 12.3 Hz, 1H), 5.18 (d, J = 12.3 Hz, 1H), 4.73 (d, J = 3.6 Hz, 1H), 4.36−4.47 (m, 3H), 4.19−4.32 (m, 4H), 4.09 (m, 1H), 3.91 (dd, J = 9.8, 6.6 Hz, 1H), 3.83 (dd, J = 9.8, 5.5 Hz, 1H), 3.24 (dd, J = 8.1, 3.6 Hz, 1H), 1.49 (s, 3H), 1.33 (s, 3H), 1.32 (d, J = 6.0 Hz, 3H), 1.05 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.12, 156.74, 143.94, 143.69, 141.29, 135.00, 128.65, 128.59, 127.70, 127.10, 125.19, 119.96, 109.78, 99.09, 77.22, 73.16, 72.53, 69.03, 67.71, 67.40, 62.54, 61.61, 58.84, 47.15, 28.32, 26.17, 18.76, 17.94, 11.92; HRMS (FAB) calcd for $C_{44}H_{58}N_4O_9SiK$ [M + K^+] 853.3608, found 853.3588.

10b: $[\alpha]^{20}_D$ 92.4° (c 0.47, CH_2Cl_2); FT-IR (film) 3434, 3351, 2940, 2865, 2111, 1728, 1515, 1455 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ

7.74 (d, J = 7.5 Hz, 2H), 7.59 (t, J = 7.5 Hz, 2H). 7.25−7.40 (m, 9H), 5.68 (d, J = 9.3 Hz, 1H), 5.20 (d, J = 12.4 Hz, 1H), 5.17 (d, J = 12.4 Hz, 1H), 4.58 (m, 1H), 4.47 (dd, J = 9.3, 3.4 Hz, 1H), 4.34 (d, J = 7.8 Hz, 2H), 4.18−4.29 (m, 3H), 3.96 (t, J = 8.9 Hz, 1H), 3.84 (dd, J = 10.0, 5.2 Hz, 1H), 3.81 (dd, J = 8.2, 5.2 Hz, 1H), 3.65 (m, 1H), 3.34 (t, J = 8.1 Hz, 1H), 1.55 (s, 3H), 1.32 (s, 3H), 1.30 (d, J = 6.4 Hz, 3H), 1.02 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.89, 156.73, 143.96, 143.73, 141.27, 135.38, 128.61, 128.27, 127.93, 127.67, 127.08, 125.26, 119.93, 110.26, 99.32, 77.91, 77.82, 74.03, 73.55, 72.01, 67.42, 67.25, 65.32, 61.66, 58.61, 47.12, 28.36, 26.08, 17.88, 16.52, 11.87; HRMS (FAB) calcd for $C_{44}H_{58}N_4O_9SiNa$ [M + Na^+] 837.3869, found 837.3887.

Coupling of α-Glycosyl Fluoride 6a with Protected Threonine Derivative 8 in CH_2Cl_2 Promoted by $(Cp)_2ZrCl_2$−$AgClO_4$. To a suspension of $AgClO_4$ (25.1 mg, 0.121 mmol), $(Cp)_2ZrCl_2$ (17.8 mg, 0.06 mmol), and 150 mg of 4 Å molecular sieves in 1 mL of anhydrous CH_2Cl_2 at −30 °C was slowly added a solution of α-glycosyl fluoride **6a** (16.3 mg, 0.04 mmol) and threonine derivative **8** (19.2 mg, 0.045 mmol) in 4.0 mL of anhydrous CH_2Cl_2. The reaction was stirred at −30 °C for 6 h and quenched with saturated $NaHCO_3$. The solution was filtered through a pad of Celite and washed with EtOAc. The filtrate was washed with saturated $NaHCO_3$ and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the α product **10a** (24.8 mg, 75% yield) and the β product **10b** (3.9 mg, 12% yield).

Coupling of β-Glycosyl Fluoride 6b with Protected Threonine Derivative 8 in CH_2Cl_2 Promoted by $(Cp)_2ZrCl_2$−$AgClO_4$. To a suspension of $AgClO_4$ (24.4 mg, 0.118 mmol), $(Cp)_2ZrCl_2$ (17.2 mg, 0.059 mmol), and 200 mg of 4 Å molecular sieves in 1 mL of anhydrous CH_2Cl_2 at −30 °C was slowly added a solution of β-glycosyl fluoride **6b** (15.8 mg, 0.03918 mmol) and threonine derivative **8** (20.3 mg, 0.04702 mmol) in 4.0 mL of anhydrous CH_2Cl_2. The reaction was stirred at −30 °C for 10 h and quenched with saturated $NaHCO_3$. The solution was filtered through a pad of Celite and washed with EtOAc. The filtrate was washed with saturated $NaHCO_3$ and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the α product **10a** (22.3 mg, 70% yield) and the β product **10b** (3.9 mg, 12% yield).

Deprotection of the Silyl Group of 9a. To a solution of the α product **9a** (15.0 mg, 0.01873 mmol) in 2 mL of THF at 0 °C were added HOAc (56 μL, 0.978 mmol) and 1 M TBAF (240 μL, 0.240 mmol). The reaction was run at 0 °C for 1 h and then warmed to room temperature for 3 days. The mixture was diluted with EtOAc, washed with H_2O and brine, and finally dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the desired product **11** (12.4 mg, 100%). **11**: $[\alpha]^{20}_D$ 78.3° (*c* 0.67, CH_2Cl_2); FT-IR (film) 3432, 3349, 2987, 2938, 2109, 1729, 1517, 1452, 1382 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 7.5 Hz, 2H), 7.59 (d, J = 7.5 Hz, 2H), 7.27−7.41 (m, 9H), 6.01 (d, J = 9.2 Hz, 1H), 5.21 (d, J = 12.4 Hz, 1H), 5.18 (d, J = 12.4 Hz, 1H), 4.74 (d, J = 3.3 Hz, 1H), 4.58 (m, 1H), 4.41 (d, J = 7.0 Hz, 2H), 4.14−4.23 (m, 3H), 4.02 (dd, J = 5.4, 2.4 Hz, 1H), 3.91−3.97 (m, 2H), 3.68−3.85 (m, 2H), 3.27 (dd, J = 8.2, 3.3 Hz, 1H), 1.48 (s, 3H), 1.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.71, 155.85, 143.78, 143.71, 141.32, 135.03, 128.59, 127.72, 127.08, 125.08, 119.99, 110.20, 99.12, 77.20, 73.35, 73.11, 70.22, 68.54, 67.76, 67.04, 62.48, 60.73, 54.66, 47.12, 28.10, 26.14; HRMS (FAB) calcd for $C_{34}H_{37}N_4O_9$ [M + H^+] 645.2560, found 645.2549.

Deprotection of the Silyl Group of 10a. To a solution of the α product **10a** (16.0 mg, 0.02 mmol) in 3 mL of THF at 0 °C were added HOAc (67 μL, 1.18 mmol) and 1 M TBAF (300 μL, 0.3000 mmol). The reaction was run at 0 °C for 1 h and then warmed to room temperature for 3 days. The mixture was diluted with EtOAc, washed with H_2O and brine, and finally dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the desired product **12** (12.1 mg, 94%). **12**: $[\alpha]^{20}_D$ 731.8° (*c* 0.62, CH_2Cl_2); FT-IR (film) 3430, 2986, 2936, 2109, 1728, 1515, 1451, 1382 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J = 7.4 Hz, 2H), 7.60 (d, J = 7.4 Hz, 2H), 7.25−7.41 (m, 9H), 5.67 (d, J = 9.0 Hz, 1H), 5.21 (br s, 2H), 4.82 (d, J = 3.2 Hz, 1H), 4.40−4.52 (m, 3H), 4.33−4.38 (m, 2H), 4.19−4.29 (m, 2H), 4.09 (m, 1H), 3.75−3.92 (m, 2H), 3.30 (dd, J = 8.0, 3.2 Hz, 1H), 2.04 (m, 1H), 1.50 (s, 3H), 1.35 (s, 3H), 1.30 (d, J = 6.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.13, 156.69, 143.91, 143.69, 141.30, 134.98, 128.61, 127.72, 127.10, 125.20, 119.97, 110.25, 98.39, 76.26, 73.49, 68.35, 67.75, 67.36, 62.62, 61.31, 58.69, 47.16, 28.18, 26.24, 18.54; HRMS (FAB) calcd for $C_{35}H_{39}N_4O_9$ [M + H^+] 659.2716, found 659.2727.

Preparation of Compound 14. To a suspension of trichloroacetimidate **13** (332.0 mg, 0.435 mmol), the acceptor **11** (140.2 mg, 0.218 mmol), and 1.0 g of 4 Å molecular sieves in 4 mL of anhydrous CH_2Cl_2 at −30 °C was slowly added a solution of BF_3·Et_2O (13.8 μL, 0.109 mmol) in 120 μL of anhydrous CH_2Cl_2. The reaction mixture was stirred at −30 °C overnight and then warmed to room temperature for 3 h. The reaction was quenched with Et_3N, filtered through a pad of Celite, and washed with EtOAc. The filtrate was washed with H_2O and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give crude recovered acceptor **11** which was further converted to compound **9a** (87.0 mg, 0.109 mmol) and the crude coupling product which was further reduced to compound **14** by pyridine and thiolacetic acid. The crude coupling product was dissolved in 1 mL of anhydrous pyridine and 1 mL of thiolacetic acid at 0 °C. The reaction mixture was stirred at room temperature overnight. The solvent was evaporated in vacuo at room temperature, and the residue was separated by chromatography on silica gel to give compound **14** (99.6 mg, 72% yield based on 50% conversion of acceptor **11**). **14**: $[\alpha]^{20}_D$ 267.9° (*c* 4.0, $CHCl_3$); FT-IR (film) 3361, 3018, 1751, 1672, 1543, 1452, 1372 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, J = 7.5 Hz, 2H), 7.58 (m, 2H), 7.26−7.38 (m, 9H), 6.26 (d, J = 8.2 Hz, 1H), 5.83 (d, J = 9.3 Hz, 1H), 5.59 (d, J = 9.2 Hz, 1H), 5.32 (d, J = 2.7 Hz, 1H), 5.16 (s, 2H), 5.02−5.11 (m, 2H), 4.94 (dd, J = 10.4, 3.4 Hz, 1H), 4.59 (d, J = 3.4 Hz, 1H), 4.35−4.52 (m, 6H), 3.60−4.19 (m, 16H), 2.11 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 2.00 (s, 3H), 1.93 (s, 3H), 1.91 (s, 3H), 1.83 (s, 3H), 1.48(s, 3H), 1.24 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.33, 170.23, 170.15, 170.07, 169.94, 169.85, 169.19, 155.92, 143.75, 143.64, 141.22, 135.12, 128.62, 128.39, 127.67, 127.01, 124.99, 119.93, 109.81, 101.12, 100.84, 98.14, 77.21, 75.49, 74.28, 72.61, 72.12, 70.74, 69.10, 68.80, 67.61, 67.38, 67.28, 67.09, 66.64, 62.28. 60.77, 54.25, 53.03, 50.09, 47.09, 27.76, 26.40, 23.18, 23.03, 20.71, 20.47, 20.36; HRMS (FAB) calcd for $C_{62}H_{75}N_3O_{26}Na$ [M + Na^+] 1300.4539, found 1300.4520.

Preparation of Compound 15. To a suspension of trichloroacetimidate **13** (305.0 mg, 0.3996 mmol), the acceptor **12** (131.6 mg, 0.1998 mmol), and 1.0 g of 4 Å molecular sieves in 4 mL of anhydrous CH_2Cl_2 at −30 °C was slowly added a solution of BF_3·Et_2O (12.7 μL, 0.10 mmol) in 115 μL of anhydrous CH_2Cl_2. The reaction mixture was stirred at −30 °C overnight and then warmed to room temperature for 3 h. The reaction was quenched with Et_3N, filtered through a pad of Celite, and washed with EtOAc. The filtrate was washed with H_2O and brine and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give crude recovered acceptor **12** which was further converted to compound **10a** (85.0 mg, 0.104 mmol) and the crude coupling product which was further reduced to compound **15** by pyridine and thiolacetic acid. The crude coupling product was dissolved in 1 mL of anhydrous pyridine and 1 mL of thiolacetic acid at 0 °C. The reaction mixture was stirred at room temperature overnight. The solvent was evaporated in vacuo at room temperature, and the residue was separated by chromatography on silica gel to give compound **15** (71.1 mg, 58% yield based on 48% conversion of acceptor **12**). **15**: $[\alpha]^{20}_D$ 346.8° (*c* 0.53, $CHCl_3$); FT-IR (film) 3366, 2986, 1750, 1673, 1541, 1452, 1372 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 7.4 Hz, 1H), 7.57 (d, J = 7.4 Hz, 2H), 7.27−7.45 (m, 9H), 5.83 (d, J = 9.4 Hz, 1H), 5.74 (d, J = 9.4 Hz, 1H), 5.61 (d, J = 8.9 Hz, 1H), 5.31 (d, J = 3.0 Hz, 1H), 4.91−5.16 (m, 5H), 4.62 (d, J = 3.2 Hz, 1H), 4.32−4.46 (m, 6H), 3.95−4.22 (m, 11H), 3.64−3.84 (m, 3H), 3.57 (m, 1H), 2.12 (s, 6H), 2.10 (s, 3H), 2.06 (s, 3H), 2.01 (s, 6H), 1.93 (s, 3H), 1.86 (s, 3H), 1.51 (s, 3H), 1.26 (s, 3H), 1.22 (d, J = 5.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.70, 170.38, 170.19, 169.94, 169.86, 169.74, 169.20, 156.34, 143.72, 143.59, 141.26, 134.59, 128.74, 128.37, 127.71, 127.03,

124.92, 119.94, 109.76, 101.48, 100.86, 99.48, 77.20, 76.23, 75.49, 74.41, 72.74, 72.43, 70.76, 69.26, 69.13, 67.56, 67.45, 67.13, 66.65, 62.29, 60.78, 58.47, 52.83, 50.35, 47.16, 27.86, 26.54, 23.22, 23.03, 20.72, 20.49, 20.37, 18.20; HRMS (FAB) calcd for $C_{63}H_{78}N_3O_{26}$ [M + H^+] 1292.4871, found 1292.4890.

Synthesis of Compound 1. The trisaccharide **14** (105.8 mg, 0.083 mmol) was dissolved in 5 mL of 80% aqueous HOAc at room temperature. The reaction mixture was stirred at room temperature overnight and then at 40 °C for 3 h. The solution was extracted with EtOAc, washed with saturated $NaHCO_3$, H_2O and brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the diol (93.0 mg, 91% yield). To a solution of this diol (91.5 mg, 0.074 mmol) in 10 mL of anhydrous CH_2Cl_2 at 0 °C were added catalytic DMAP (4.5 mg, 0.037 mmol), Et_3N (103 μL, 0.74 mmol), and Ac_2O (28 μL, 0.30 mmol). The reaction was run overnight at room temperature. The reaction mixture was diluted with EtOAc, washed with H_2O and brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the peracetylated compound (88.8 mg, 91% yield). To a suspension of 10% Pd/C (5.0 mg) in a mixture of 1 mL of MeOH and 0.1 mL of H_2O was added a solution of the peracetylated compound (38.5 mg, 0.03 mmol) in 4.0 mL of MeOH. The reaction was stirred under an H_2 atmosphere at room temperature for 4 h. The reaction mixture was passed through a short column of silica gel to remove the catalyst and washed with MeOH. After removal of the solvent, the residue was dissolved in 1.5 mL of DMF and to this solution was slowly added 0.5 mL of morpholine at 0 °C. The reaction was stirred at room temperature overnight. The solvent was evaporated in vacuo, and the residue was separated by chromatography on silica gel to give 29.0 mg of material which was further deacetylated under basic conditions. The material obtained previously was dissolved in 50 mL of anhydrous THF and 5 mL of anhydrous MeOH. The solution was cooled to 0 °C, and to this solution was added a solution of NaOMe (14.0 mg, 0.26 mmol) in 5 mL of anhydrous MeOH. The reaction was stirred at room temperature overnight and quenched with 50% aqueous HOAc. After evaporation of the solvent, the residue was separated by chromatography on reverse-phase silica gel to give the crude product, which was further purified by gel permeation filtration on Sephadex LH-20 to give the final product **1** (15.1 mg, 77%yield). **1**: $[\alpha]^{20}_D$ 715.6° (*c* 0.1, H_2O); ^{1}H NMR (300 MHz, $CD_3OD{\cdot}D_2O$) δ 4.85 (d, J = 3.4 Hz, 1H), 4.55 (d, J = 7.4 Hz, 1H), 4.46 (d, J = 7.0 Hz, 1H), 4.26 (dd, J = 10.9, 3.5 Hz, 1H), 3.34−4.09 (m, 20H), 2.07 (s, 3H), 2.06 (s, 3H); ^{13}C NMR (75 MHz, $CD_3OD{\cdot}D_2O$) δ 175.64, 175.36, 104.61, 102.98, 99.57, 80.35, 76.94, 76.36, 74.32, 73.88, 72.57, 71.30, 70.82, 70.16, 69.21, 62.50, 61.62, 56.64, 51.58, 51.22, 23.63, 23.40; HRMS (FAB) calcd for $C_{25}H_{44}N_3O_{18}$ [M + H^+] 674.2620, found 674.2625.

Synthesis of Compound 2. The trisaccharide **15** (70.2 mg, 0.054 mmol) was dissolved in 5 mL of 80% aqueous HOAc at room temperature. The reaction mixture was stirred at room temperature overnight and then at 40 °C for 3 h. The solution was extracted with EtOAc, washed with saturated $NaHCO_3$, H_2O, and brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the diol (67.1 mg, 99% yield). To a solution of diol (65.1 mg, 0.052 mmol) in 8 mL of anhydrous CH_2Cl_2 at 0 °C were added catalytic DMAP (3.2 mg, 0.026 mmol), Et_3N (72 μL, 0.52 mmol), and Ac_2O (20 μL, 0.21 mmol). The reaction was run overnight at room temperature. The reaction mixture was diluted with EtOAc, washed with H_2O and brine, and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the peracetylated compound (66.0 mg, 95% yield). To a suspension of 10% Pd/C (5.0 mg) in a mixture of 1 mL of MeOH and 0.1 mL of H_2O was added a solution of the peracetylated compound (22.1 mg, 0.017 mmol) in 4.0 mL of MeOH. The reaction was stirred under an H_2 atmosphere at room temperature for 4 h. The reaction mixture was passed through a short column of silica gel to remove the catalyst and washed with MeOH. After removal of the solvent, the residue was dissolved in 1.5 mL of DMF and to this solution was added 0.5 mL of morpholine at 0 °C slowly. The reaction was stirred at room temperature overnight. The solvent was evaporated in vacuo, and the residue was separated by chromatography on silica gel to give 29.0 mg of material which was further deacetylated under basic conditions. The material obtained previously was dissolved in 50 mL of anhydrous THF and 5 mL of anhydrous MeOH. The solution was cooled to 0 °C, and to this solution was added a solution of NaOMe (14.9 mg, 0.276 mmol) in 5 mL of anhydrous MeOH. The reaction was stirred at room temperature overnight and quenched with 50% aqueous HOAc. After evaporation of the solvent, the residue was separated by chromatography on reverse-phase silica gel to give the crude product, which was further purified by gel permeation filtration on Sephadex LH-20 to give the final product **2** (8.4 mg, 74% yield). **2**: $[\alpha]^{20}_D$ 418.4° (*c* 0.1, H_2O); ^{1}H NMR (300 MHz, $CD_3OD{\cdot}D_2O$) δ 4.91 (d, J = 3.3 Hz, 1H), 4.56 (d, J = 8.2 Hz, 1H), 4.46 (d, J = 7.4 Hz, 1H), 3.52−4.22 (m, 20H), 2.10 (s, 3H), 2.06 (s, 3H), 1.36 (d, J = 6.5 Hz, 3H); ^{13}C NMR (75 MHz, $CD_3OD{\cdot}D_2O$) δ 175.90, 175.48, 104.20, 103.97, 102.47, 79.75, 78.71, 76.72, 76.56, 73.92, 73.76, 70.94, 70.52, 70.10, 69.79, 68.98, 62.25, 61.28, 56.25, 51.20, 50.79, 23.51, 19.44; HRMS (FAB) calcd for $C_{26}H_{46}N_3O_{16}$ [M + H^+] 688.2776, found 688.2774.

Preparation of Thioglycoside 17. To a suspension of perbenzylated lactal **16** (420 mg, 0.49 mmol) and 600 mg of 4 Å molecular sieves in 5 mL of anhydrous CH_2Cl_2 was added benzenesulfonamide (116 mg, 0.74 mmol) at room temperature. After 10 min, the suspension was cooled to 0 °C and I(*sym*-collidine)$_2ClO_4$ was added in one portion. Fifteen minutes later, the solution was filtered through a pad of Celite and washed with EtOAc. The organic solution was washed with $Na_2S_2O_3$ and brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give 500 mg of the iodosulfonamidate derivative (90%yield). To a solution of ethanethiol (150 μL, 1.98 mmol) in 4 mL of anhydrous DMF at −40 °C was added a solution of LiHMDS (0.88 mL, 0.88 mmol). After 15 min, a solution of the iodosulfonamidate (450 mg, 0.397 mmol) in 6 mL of anhydrous DMF was slowly added at that temperature. The reaction mixture was stirred at −40 °C for 4 h and quenched with H_2O. The aqueous solution was extracted with EtOAc three times, and the combined organic layer was washed with H_2O and brine and dried over Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give the desired thioglycoside **17** (350 mg, 83% yield) and recover the iodosulfonamidate (60 mg). **17**: IR (film) 3020, 3000, 2860, 1480, 1450 cm^{-1}; ^{1} H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 7.7 Hz, 2H), 7.17−7.45 (m, 33H), 5.01 (d, J = 8.9 Hz, 1H), 4.93 (d, J = 11.4 Hz, 1H), 4.79 (s, 2H), 4.69 (m, 3H), 4.56 (d, J = 11.3 Hz, 2H), 4.30−4.50 (m, 6H), 3.95 (t, J = 5.0 Hz, 1H), 3.90 (d, J = 2.7 Hz, 1H), 3.75 (m, 3H), 3.65 (m, 2H), 3.52 (m, 2H), 3.39−3.46 (m, 3H), 2.50 (q, J = 7.4 Hz, 2H), 1.12 (t, J = 7.4 Hz, 3H); HRMS (FAB) calcd for $C_{62}H_{67}O_{11}NS_2K$ [M + K^+] 1104.3789, found 1104.3760.

Preparation of Trisaccharide 20. In a round-bottom flask were placed thioglycoside **17** (2.10 g, 1.97 mmol), acceptor **18** (964 mg, 2.95 mmol), di-*tert*-butylpyridine (2.65 mL, 11.81 mmol), and 7.0 g of 4 Å molecular sieves. The mixture was dissolved in 10 mL of anhydrous CH_2Cl_2 and 20 mL of anhydrous Et_2O. This solution was cooled to 0 °C, and then MeOTf (1.11 mL, 8.85 mmol) was added to it slowly. The reaction mixture was stirred at 0 °C overnight. After filtration through a pad of Celite, the organic layer was submitted to aqueous workup. The EtOAc extract was dried over Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give **20**α (206 mg, 8%) and **20**β (2.26 g, 86%). **20**β: IR (film) 3020, 3000, 2860, 1480, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (d, J = 7.7 Hz, 2H), 7.20−7.45 (m, 43H), 6.32 (d, J = 6.2 Hz, 1H), 4.96 (d, J = 9.2 Hz, 1H), 4.90 (d, J = 6.2 Hz, 1H), 4.80 (m, 4H), 4.72 (s, 2H), 4.54−4.68 (m, 6H), 4.28−4.48 (m, 6H), 4.07 (br s, 1H), 4.00 (t, J = 5.0 Hz, 1H), 3.90 (s, 1H), 3.74 (m, 4H), 3.35−3.61 (m, 10H); HRMS (FAB) calcd for $C_{80}H_{83}O_{15}NSK$ [M + K^+] 1368.5123, found 1368.5160.

Preparation of Trisaccharide 21. In a round-bottom flask were placed thioglycoside **17** (966 mg, 0.906 mmol), acceptor **19** (219 mg, 1.18 mmol), di-*tert*-butylpyridine (1.22 mL, 5.44 mmol), and 2.5 g of 4 Å molecular sieves. The mixture was dissolved in 5 mL of anhydrous CH_2Cl_2 and 10 mL of anhydrous Et_2O. This solution was cooled to 0 °C, and then MeOTf (0.51 mL, 4.53 mmol) was added to it slowly.

The reaction mixture was stirred at 0 °C for 5 h. After filtration through a pad of Celite, the organic layer was submitted to aqueous workup. The EtOAc extract was dried over Na_2SO_4. After evaporation of the solvent, the residue was separated by chromatography on silica gel to give **21**α (59 mg, 6%) and **21**β (910 mg, 84%). **21**α: IR (film) 3020, 3000, 2860, 1480, 1450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.83 (d, J = 7.5 Hz, 2H), 7.12−7.46 (m, 33H), 6.36 (d, J = 6.2 Hz, 1H), 5.11 (d, J = 8.9 Hz, 1H), 4.98 (d, J = 10.9 Hz, 1H), 4.93 (d, J = 11.6 Hz, 1H), 4.83 (d, J = 8.1 Hz, 1H), 4.80 (d, J = 11.6 Hz, 1H), 4.68−4.73 (m, 4H), 4.50−4.58 (m, 3H), 4.27−4.32 (m, 4H), 4.27 (d, J = 6.2 Hz, 1H), 4.05 (m, 1H), 3.97 (m, 2H), 3.83 (m, 2H), 3.70 (m, 2H), 3.58 (m, 2H), 3.24−3.49 (m, 4H), 1.52 (s, 3H), 1.41 (s, 3H); HRMS (FAB) calcd for $C_{69}H_{75}O_{15}NSNa$ [M + Na^+] 1212.4756, found 1212.4720.

21β: IR (film) 3020, 3000, 2860, 1480, 1450 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ (7.87 (d, J = 7.2 Hz, 2H), 7.19−7.45 (m, 33H), 6.35 (d, J = 6.2 Hz, 1H), 4.98 (d, J = 8.9 Hz, 1H), 4.95 (d, J = 11.6 Hz, 1H), 4.78 (m, 4H), 4.67 (m, 3H), 4.56 (m, 2H), 4.50 (d, J = 12.0 Hz, 1H), 4.43 (d, J = 6.2 Hz, 1H), 4.27−4.39 (m, 4H), 4.04 (d, J = 6.2 Hz, 1H), 3.97 (t, J = 7.2 Hz, 1H), 3.90 (d, J = 2.5 Hz, 1H), 3.73−3.82 (m, 3H), 3.48−3.66 (m, 6H), 3.35−3.42 (m, 3H), 1.43 (s, 3H), 1.30 (s, 3H); HRMS (FAB) calcd for $C_{69}H_{75}O_{15}NSNa$ [M + Na^+] 1212.4755, found 1212.4780.

Preparation of Trisaccharide 22. In a flame-dried flask was condensed 30 mL of anhydrous NH_3 at −78 °C. To this liquid NH_3 was added sodium metal (320 mg, 13.95 mmol) in one portion. After 15 min, the dry ice−ethanol bath was removed and the dark blue solution was refluxed for 20 min. It was cooled to −78 °C again, and a solution of trisaccharide **20** (619 mg, 0.47 mmol) in 6 mL of anhydrous THF was added slowly. The reaction mixture was refluxed at −30 °C for 30 min and quenched with 10 mL of MeOH. After evaporation of the NH_3, the basic solution was neutralized with Dowex resin. The organic solution was filtered and evaporated to give the crude product which was submitted to acetylation. The crude product was dissolved in 3.0 mL of pyridine and 2.0 mL of Ac_2O in the presence of 10 mg of DMAP at 0 °C. The reaction mixture was stirred from 0 °C to room temperature overnight. After aqueous workup, the organic layer was dried over Na_2SO_4. The solvent was evaporated, and the residue was separated by chromatography on silica gel to give peracetylated trisaccharide **22** (233 mg, 59%). **22**: $[\alpha]^{20}_D$ −19.77° (*c* 1.04, $CHCl_3$); IR (film) 1740, 1360 cm^{-1}, ^1H NMR (300 MHz, $CDCl_3$) δ 6.46 (dd, J = 6.2, 1.5 Hz, 1H), 5.64 (d, J = 9.1 Hz, 1H), 5.54 (d, J = 2.0 Hz, 1H), 5.40 (d, J = 4.5 Hz, 1H), 5.36 (d, J = 2.9 Hz, 1H), 5.12 (m, 2H), 4.98 (dd, J = 10.4, 3.4 Hz, 1H), 4.70 (d, J = 6.2 Hz, 1H), 4.58 (d, J = 7.3 Hz, 1H), 4.50 (m, 2H), 4.26 (t, J = 5.0 Hz, 1H), 4.12 (m, 3H), 3.89 (m, 2H), 3.78 (m, 2H), 3.64 (m, 1H), 2.16 (s, 3H), 2.13 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.06 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.29, 170.14, 169.24, 145.34, 128.20, 100.85, 100.72, 88.86, 75.58, 74.26, 72.58, 72.06, 70.71, 70.61, 68.98, 66.77, 66.55, 64.19, 63.53, 62.09, 60.70, 52.97, 23.05, 20.72, 20.56; HRMS (FAB) calcd for $C_{36}H_{49}O_{22}NNa$ [M + Na^+] 870.2645, found 870.2644.

Preparation of Trisaccharide Donor 23. To a solution of trisaccharide glycal **20** (460 mg, 0.346 mmol) in 3 mL of anhydrous CH_3CN at −25 °C were added NaN_3 (34 mg, 0.519 mmol) and CAN (569 mg, 1.4 mmol). The mixture was stirred at −25 °C for 8 h. After aqueous workup, the organic layer was dried over Na_2SO_4. The solvent was evaporated, and the residue was separated by chromatography on silica gel to give a mixture of azidonitrate derivatives (134 mg, 27%). This azidonitrate mixture was hydrolyzed under reductive conditions. The azidonitrates were dissolved in 2 mL of anhydrous CH_3CN at room temperature. $EtN(i\text{-}Pr)_2$ (16 μL, 0.091 mmol) and PhSH (28 μL, 0.272 mmol) were added. After 15 min, the reaction was complete and the solvent was evaporated at room temperature. The hemiacetal derivative (103 mg, 74%) was obtained after chromatography on silica gel. This hemiacetal (95 mg, 0.068 mmol) was dissolved in 2 mL of anhydrous CH_2Cl_2. To this solution were added 1 mL of CCl_3CN and 0.5 g of K_2CO_3 at room temperature. The reaction was run overnight. After filtration through a pad of Celite, the organic solvent was evaporated and the residue was separated by chromatography on silica gel to give **23**α (18 mg, 17%) and **23**β (70 mg, 67%). **23**α: FT-IR (film) 3322, 3025, 2867, 2113, 1670, 1452 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.67 (s, 1H), 7.78 (d, J = 7.4 Hz, 2H), 7.15−7.42 (m, 43H), 6.26 (d, J = 3.3 Hz, 1H), 4.91−4.93 (m, 2H), 4.83 (d, J = 11.0 Hz, 1H), 4.73−4.80 (m, 3H), 4.65−4.70 (m, 5H), 4.53 (d, J = 11.5 Hz, 1H), 4.47 (d, J = 11.2 Hz, 1H), 4.27−4.42 (m, 6H), 4.10−4.14 (m, 2H), 3.96 (m, 2H), 3.86−3.90 (m, 2H), 3.69−3.79 (m, 3H), 3.33−3.56 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 141.7, 138.8, 138.5, 138.3, 138.2, 138.1, 138.0, 137.2, 132.1, 128.5, 128.4, 128.3, 128.2, 128.0, 127.9, 127.7, 127.6, 127.5, 127.4, 127.1, 103.0, 101.5, 95.9, 91.0, 82.2, 79.7, 79.0, 75.8, 75.4, 74.8, 74.6, 73.4, 73.2, 73.0, 72.6, 72.3, 71.8, 68.4, 68.1, 66.4, 59.0, 58.1; HRMS (FAB) calcd for $C_{82}H_{84}O_{16}N_5Cl_3SK$ [M + K^+] 1570.4336, found 1570.4399.

23β: FT-IR (film) 3303, 3025, 2867, 2113, 1670, 1447 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.32 (s, 1H), 7.86 (d, J = 7.5 Hz, 2H), 7.10−7.44 (m, 43H), 6.10 (d, J = 9.3 Hz, 1H), 5.25 (d, J = 8.3 Hz, 1H), 4.92 (d, J = 11.5 Hz, 1H), 4.86 (d, J = 11.5 Hz, 1H), 4.66−4.82 (m, 8H), 4.61 (d, J = 11.5 Hz, 1H), 4.51−4.55 (m, 2H), 4.41 (d, J = 8.5 Hz, 1H), 4.32−4.37 (m, 3H), 4.25 (d, J = 11.8 Hz, 1H), 3.98−4.04 (m, 2H), 3.78−3.87 (m, 3H), 3.71 (dd, J = 9.6, 7.8 Hz, 1H), 3.59−3.64 (m, 2H), 3.55 (d, J = 2.3 Hz, 1H), 3.40−3.45 (m, 2H), 3.27−3.35 (m, 4H), 3.18 (m, 1H), 3.12 (dd, J = 9.5, 8.5 Hz, 1H), 3.07 (d, J = 6.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 143.3, 139.0, 138.5, 138.4, 138.1, 138.0, 137.4, 137.2, 131.6, 128.6, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.6, 127.5, 127.4, 127.2, 102.6, 102.1, 97.7, 90.4, 82.2, 80.0, 79.7, 76.2, 75.1, 74.5, 74.3, 73.3, 73.0, 72.7, 72.4, 72.0, 68.9, 68.0, 62.7, 58.9; HRMS (FAB) calcd for $C_{82}H_{84}O_{16}N_5Cl_3SK$ [M + K^+] 1570.4336, found 1570.4298.

Preparation of Trisaccharide Donor 24. To a solution of trisaccharide glycal **22** (225 mg, 0.264 mmol) in 2 mL of anhydrous CH_3CN at −15 °C were added NaN_3 (26 mg, 0.40 mmol) and CAN (436 mg, 0.794 mmol). The mixture was stirred at −15 °C overnight. After aqueous workup, the organic layer was dried over Na_2SO_4. The solvent was evaporated, and the residue was separated by chromatography on silica gel to give a mixture of azidonitrate derivatives (130 mg, 51%). This azidonitrate mixture was hydrolyzed under reductive conditions. The azidonitrates (125 mg, 0.129 mmol) were dissolved in 5 mL of anhydrous CH_3CN at room temperature. $EtN(i\text{-}Pr)_2$ (25 μL, 0.147 mmol) and PhSH (45 μL, 0.441 mmol) were added. After 15 min, the reaction was complete and the solvent was evaporated at room temperature. The hemiacetal derivative (92 mg, 77%) was obtained after chromatography on silica gel. This hemiacetal (80 mg, 0.087 mmol) was dissolved in 5 mL of anhydrous CH_2Cl_2. To this solution were added 0.9 mL of CCl_3CN and 0.12 g of K_2CO_3 at room temperature. The reaction was run overnight. After filtration through a pad of Celite, the organic solvent was evaporated and the residue was separated by chromatography on silica gel to give a mixture of the α and β isomers of **24** (71 mg, 77%, α:β 3:1). **24**: ^1H NMR (300 MHz, $CDCl_3$) δ 9.55 (s, 1H, NH of β isomer), 8.71 (s, 1H, NH of α isomer), 6.54 (d, J = 3.6 Hz, amomeric H of α isomer). Compound **24** decomposes quickly at room temperature.

Preparation of Trisaccharide Donor 25. The azidonitrate derivatives (100 mg, 0.103 mmol) from peracetylated trisaccharide **22** were dissolved in 0.5 mL of anhydrous CH_3CN at room temperature. To this solution was added anhydrous LiBr (45 mg, 0.52 mmol). The mixture was stirred for 3 h. After aqueous workup, the solvent was evaporated and the residue was separated by chromatography on silica gel to give compound **25** (91 mg, 90%). **25**: ^1H NMR (300 MHz, $CDCl_3$) δ 6.04 (d, J = 3.6 Hz, 1H, anomeric H). The low stability of this compound prevented further characterization.

Preparation of Trisaccharide Donor 26. The trisaccharide donor **25** (91 mg, 0.093 mmol) was dissolved in 2 mL of anhydrous THF at 0 °C. To this solution was added LiSPh (100 mL, 0.103 mmol). The reaction was run at 0 °C for 30 min. The solvent was removed, and the residue was separated by chromatography on silica gel to give compound **26** (61 mg, 66%). **26**: IR (film) 3000, 2100, 1750, 1680, 1500 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.61 (m, 2H), 7.39 (m, 3H), 5.50 (d, J = 9.1 Hz, 1H), 5.35 (m, 2H), 5.11 (m, 2H), 4.96 (dt, J = 10.5, 3.5 Hz, 1H), 4.84 (dd, J = 10.2, 3.0 Hz, 1H), 4.50 (m, 4H), 4.16 (m, 3H), 3.59−3.90 (m, 8H), 2.15 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.06 (s, 6H), 2.05 (s, 3H), 2.04 (s, 3H), 1.97 (s, 3H), 1.87 (s, 3H). HRMS (FAB) calcd for $C_{42}H_{54}N_4O_{22}SNa$ [M + Na^+] 1021.8620, found 1021.8612.

Preparation of Trisaccharide Donor 27. The trisaccharide **21** (860 mg, 0.722 mmol) was dissolved in 2 mL of pyridine and 1 mL of Ac_2O in the presence of 10 mg of DMAP. The reaction was run at 0 °C to room temperature overnight. After aqueous workup, the solvent was removed and the residue was dissolved in 10 mL of MeOH and 5 mL of EtOAc at room temperature. To this solution were added Na_2HPO_4 (410 mg, 2.89 mmol) and 20% Na−Hg (1.0 g, 4.35 mmol). The reaction was run for 2 h, and aqueous workup followed. After removal of the organic solvent, the residue was separated by chromatography on silica gel to give *N*-acetyl trisaccharide glycal (740 mg, 94%). The trisaccharide glycal (624 mg, 0.571 mmol) was dissolved in 3 mL of anhydrous CH_3CN at −40 °C. To the solution were added NaN_3 (56 mg, 0.86 mmol) and CAN (939 mg, 1.71 mmol). The mixture was stirred at −40 °C for 4 h. After aqueous workup, the organic solvent was removed and the residue was separated by chromatography on silica gel to give a mixture of α and *β* azidonitrate anomers (191 mg, 27%). This mixture of anomers (172 mg, 0.137 mmol) was dissolved in 1 mL of CH_3CN at room temperature. To the solution were added EtN-(*i*-Pr)$_2$ (24 *μ*L, 0.137 mmol) and PhSH (42 *μ*L, 0.410 mmol). The reaction was complete in 30 min, and the solvent was blown off. Column separation afforded the desired hemiacetal (170 mg). This hemiacetal was dissolved in 1 mL of CH_2Cl_2 at room temperature. To the solution were added 1 mL of CCl_3CN and 500 mg of K_2CO_3. The reaction was run at room temperature overnight. After filtration through a pad of Celite, the organic solvent was removed and the residue was separated by chromatography on silica gel to give the desired α-trichloroacetimidate **27** (70 mg, 42%). **27**: IR (film) 3000, 2120, 1670, 1490, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 8.62 (s, 1H), 7.06−7.48 (m, 30H), 6.44 (d, *J* = 3.0 Hz, 1H), 5.21 (d, *J* = 11.4 Hz, 1H), 5.03 (m, 2H), 4.89 (d, *J* = 11.0 Hz, 1H), 4.80 (d, *J* = 11.3 Hz, 1H), 4.69 (d, *J* = 11.1 Hz, 1H), 4.64 (d, *J* = 7.8 Hz, 1H), 4.44−4.58 (m, 5H), 4.18−4.36 (m, 7H), 3.96−4.08 (m, 3H), 3.72−3.81 (m, 3H), 3.38−3.62 (m, 6H), 3.31 (dd, *J* = 7.0, 2.7 Hz, 1H), 1.59 (s, 3H), 1.31 (s, 3H), 1.14 (s, 3H); HRMS (FAB) calcd for $C_{68}H_{74}O_{15}N_5Cl_3Na$ [M + Na$^+$] 1316.4145, found 1316.4110.

Coupling of Trisaccharide Donor 23*β* with Methyl *N*-Fmoc Serinate. To a solution of trisaccharide donor **23***β* (70 mg, 0.046 mmol), methyl *N*-Fmoc serinate (23.4 mg, 0.068 mmol), and 300 mg of 4 Å molecular sieves in 0.5 mL of THF at −78 °C was added TMSOTf (4.6 *μ*L, 0.023 mmol). The reaction was stirred at −35 °C overnight. The reaction was quenched with Et_3N, and the solution was filtered through a pad of Celite. The filtrate was evaporated, and the residue was separated by chromatography on silica gel to give **29**α (70 mg, 90%) and **29***β* (7.0 mg, 9.0%). **29**α: FT-IR (film) 3341, 3024, 2866, 2112, 1726, 1698, 1493, 1450 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.80 (d, *J* = 7.8 Hz, 5/8 × 2H), 7.75 (d, *J* = 7.8 Hz, 3/8 × 2H), 7.70 (d, *J* = 7.5 Hz, 2H), 7.54 (t, *J* = 6.4 Hz, 3/8 × 2H), 7.47 (d, *J* = 7.2 Hz, 5/8 × 2H), 6.99−7.45 (m, ∼46H), 6.91 (d, *J* = 7.4 Hz, 5/8 × 2H), 6.68 (d, *J* = 8.6 Hz, 5/8 × 1H), 5.98 (d, *J* = 8.4 Hz, 3/8 × 1H), 5.16 (d, *J* = 7.8 Hz, 3/8 × 1H), 3.14−4.89 (m, ∼46H); ^{13}C NMR (75 MHz, $CDCl_3$) *δ* 170.7, 168.9, 156.2, 155.7, 143.7, 143.6, 143.5, 143.3, 142.8, 142.1, 141.4, 141.3, 141.2, 139.0, 138.9, 138.8, 138.7, 138.5, 138.4, 138.2, 138.0, 137.8, 137.6, 132.0, 131.6, 128.4, 128.3, 128.2, 128.0, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 127.0, 126.8, 126.4, 125.1, 124.4, 124.3, 120.2, 120.1, 120.0, 106.0, 102.8, 102.5, 99.7, 98.2, 82.4, 82.2, 80.8, 79.8, 79.7, 79.2, 75.5, 75.3, 75.2, 74.9, 74.4, 73.5, 73.3, 73.0, 72.8, 72.5, 72.4, 71.7, 71.2, 70.1, 69.9, 69.3, 68.1, 67.8, 67.6, 67.1, 59.4, 58.8, 58.5, 54.5, 52.9, 47.1; HRMS (FAB) calcd for $C_{99}H_{101}O_{20}N_5SK$ [M + K$^+$] 1750.6397, found 1750.6334.

29*β*: FT-IR (film) 3294, 3024, 2922, 2103, 1726, 1497, 1450 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.71−7.76 (m, 4H), 7.57 (d, *J* = 7.3 Hz, 2H), 7.03−7.58 (m, 47H), 5.84 (d, *J* = 8.0 Hz, 1H), 5.22 (d, *J* = 5.5 Hz, 1H), 4.88 (d, *J* = 11.5 Hz, 1H), 4.59−4.83 (m, 10H), 4.18−4.52 (m, 13H), 4.11 (d, *J* = 8.1 Hz, 1H), 3.96 (m, 1H), 3.88 (dd, *J* = 10.5, 3.7 Hz, 1H), 3.83 (br s, 1H), 3.29−3.76 (m, 16H), 3.20 (d, *J* = 10.3 Hz, 1H), 3.11 (t, *J* = 6.0 Hz, 1H); HRMS (FAB) calcd for $C_{99}H_{101}O_{20}N_5SK$ [M + K$^+$] 1750.6397, found 1750.6451. Note: There are two rotamers of **29**α, which become one compound when heated to 70 °C in toluene.

Coupling of Trisaccharide Donor 24 with Benzyl *N*-Fmoc Serinate. To a solution of trisaccharide donor **24** (33 mg, 0.030 mmol), benzyl *N*-Fmoc serinate (33.0 mg, 0.075 mmol), and 100 mg of 4 Å molecular sieves in 0.3 mL of THF at −78 °C was added TMSOTf (6.0 *μ*L, 0.030 mmol). The reaction was stirred from −78 °C to room temperature for 2 h. The reaction was quenched with Et_3N, and the solution was filtered through a pad of Celite. The filtrate was evaporated, and the residue was separated by chromatography on silica gel to give **30** (8.6 mg, 22%, α:*β* 2:1). **30**: IR (film) 3400, 3000, 2100, 1740, 1500 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 6.25 (d, *J* = 8.4 Hz, 2/3H), 5.90 (d, *J* = 8.6 Hz, 1/3H), 5.76 (d, *J* = 9.0 Hz, 1/3H), 5.71 (d, *J* = 9.0 Hz, 2/3); MS(CI) 1306 [M$^+$].

Coupling of Trisaccharide Donor 25α with Benzyl *N*-Fmoc Serinate. To a solution of benzyl *N*-Fmoc serinate (45 mg, 0.107 mmol), $AgClO_4$ (37.0 mg, 0.179 mmol), and 200 mg of 4 Å molecular sieves in 0.6 mL of anhydrous CH_2Cl_2 was slowly added a solution of trisaccharide donor **25**α (88 mg, 0.0893 mmol) in 0.5 mL of CH_2Cl_2. The reaction was run at room temperature overnight. After filtration through a pad of Celite, the solvent was removed and the residue was separated by chromatography on silica gel to give the coupling product **30** (66 mg, 56%, α:*β* 3.5:1).

Coupling of Trisaccharide Donor 26*β* with Benzyl *N*-Fmoc Serinate. To a solution of benzyl *N*-Fmoc serinate (45 mg, 0.107 mmol), trisaccharide donor **26***β* (23 mg, 0.023 mmol) and 50 mg of 4 Å molecular sieves in 1.0 mL of anhydrous CH_2Cl_2 at 0 °C was slowly added a solution of NIS (6.2 mg, 0.027 mmol) and TfOH (0.24 *μ*L, 0.003 mmol) in 0.5 mL of CH_2Cl_2. The reaction was run at 0 °C for 1 h. The reaction was quenched with Et_3N, and aqueous workup followed. The organic solvent was dried over Na_2SO_4. After removal of the solvent, the residue was separated by chromatography on silica gel to give the coupling product **30** (12.1 mg, 40%, α:*β* 2:1).

Coupling of Trisaccharide Donor 27α with Benzyl *N*-Fmoc Serinate. To a solution of trisaccharide donor **27**α (40.1 mg, 0.029 mmol), benzyl *N*-Fmoc serinate (18.0 mg, 0.044 mmol), and 200 mg of 4 Å molecular sieves in 2.0 mL of THF at −20 °C was added TMSOTf (1.8 *μ*L, 0.009 mmol). The reaction was stirred from −20 °C to room temperature for 3 h. The reaction was quenched with Et_3N, and aqueous workup followed. After it was dried over Na_2SO_4, the filtrate was evaporated and the residue was separated by chromatography on silica gel to give **31** (24 mg, 51%). **31**: IR (film) 3000, 2920, 2860, 2100, 1720, 1665, 1500, 1480, 1450 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.78 (m, 2H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.20−7.42 (m, 39 H), 6.18 (d, *J* = 7.8 Hz, 1H), 6.05 (d, *J* = 7.3 Hz, 1H), 5.23 (s, 2H), 4.95−5.02 (m, 3H), 4.80 (s, 2H), 4.78 (d, *J* = 2.8 Hz, 1H, anomeric H), 4.72 (s, 2H), 4.58 (m, 4H), 4.37−4.52 (m, 6H), 4.24−4.31 (m, 2H), 4.20 (m, 1H), 4.08 (m, 2H), 3.92−4.02 (m, 5H), 3.78−3.85 (m, 5H), 3.65 (m, 1H), 3.58 (t, *J* = 6.2 Hz, 1H), 3.36−3.46 (m, 5H), 3.26 (dd, *J* = 7.5, 2.8 Hz, 1H), 1.85 (s, 3H), 1.48 (s, 3H), 1.34 (s, 3H); HRMS (FAB) calcd for $C_{90}H_{95}O_{19}N_5Na$ [M + Na$^+$] 1572.6520, found 1572.6550.

Coupling of Trisaccharide Donor 28 with Benzyl *N*-Fmoc Serinate. To a solution of trisaccharide donor **28** (α:*β* 1:1)(162 mg, 0.163 mmol), benzyl *N*-Fmoc serinate (48.0 mg, 0.097 mmol) and 300 mg of 4 Å molecular sieves in 2.0 mL of THF at −78 °C was added BF_3·Et_2O (0.5 equiv, 0.082 mmol) in CH_2Cl_2. The reaction was stirred from −78 °C to room temperature for 2 h. The reaction was quenched with Et_3N, and aqueous workup followed. After it was dried over Na_2SO_4, the filtrate was evaporated and the residue was separated by chromatography on silica gel to give **32** (81 mg, 67%). **32**: IR (film) 3420, 3020, 2940, 2880, 2120, 1745, 1500, 1450 cm^{-1}, ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 7.74 (d, *J* = 7.4 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 2H), 7.20−7.39 (m, 9H), 5.85 (d, *J* = 8.4 Hz, 1H), 5.48 (d, *J* = 12.6 Hz, 1H), 5.32 (d, *J* = 3.4 Hz, 1H), 5.19 (d, *J* = 12.6 Hz, 1 H), 5.07 (d, *J* = 8.0 Hz, 1H), 4.90 (dd, *J* = 10.3, 3.4 Hz, 1H), 4,83 (t, *J* = 10.3 Hz, 1H), 4.72 (d, *J* = 9.3 Hz, 1H), 4.67 (d, *J* = 9.6 Hz, 1H), 3.80−4.47 (m, 9H), 3.62 (t, *J* = 9.5 Hz, 1H), 3.32−3.42 (m, 2H), 2.93 (d, *J* = 7.7 Hz, 1H), 2.14 (s, 3H), 2.08 (s, 6H), 2.04 (s, 3H), 2.02 (s, 3H), 1.95 (s, 3H), 1.55 (s, 3H), 1.34 (s, 3H).

Coupling of Trisaccharide Donor 28*β* with Benzyl *N*-Fmoc Serinate. To a solution of trisaccharide donor **28***β* (12.0 mg, 0.012 mmol), benzyl *N*-Fmoc serinate (9.0 mg, 0.022 mmol), and 100 mg of 4 Å molecular sieves in 0.5 mL of THF at −40 °C was added BF_3·Et_2O (1.5 equiv, 0.018 mmol) in CH_2Cl_2. The reaction was stirred from

−40 °C to room temperature for 2 h. The reaction was quenched with Et_3N, and aqueous workup followed. After it was dried over Na_2SO_4, the filtrate was evaporated and the residue was separated by chromatography on silica gel to give **32** (5.2 mg, 35%).

Acknowledgment. This work was supported by the National Institutes of Health (Grants AI16943 and HL25848). A Graduate Fellowship is gratefully acknowledged by X.-T.C. (Kanagawa Academy of Science and Technology). A Postdoctoral Fellowship is gratefully acknowledged by D.S. (Irvington Institute for Immunological Research and M. R. Bloomberg). We are grateful to Vinka Parmakovich and Barbara Sporer of the Columbia University Mass Spectral facility.

JA980724Z