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Selective Protection of 2-Azido-lactose and in Situ Ferrier Rearrangement during Glycosylation: Synthesis of a Dimeric Lewis X Fragment

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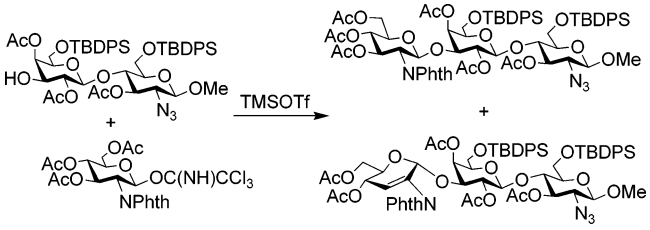
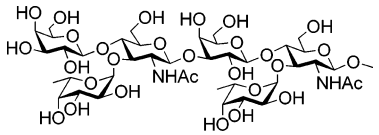
Received December 12, 2006



In our efforts to design new anti-cancer vaccines based on the tumor associated carbohydrate antigen dimeric Le^x, we have synthesized the fragment GlcNAc-β-(1→3)-Gal-β-(1→4)-GlcNAc-β-(1→O)-Me. Although it is notoriously difficult to chemically protect the primary OH groups in β-lactoside derivatives, a 6,6′-disilylated intermediate was prepared in 82% yield. It was converted to a glycosyl acceptor free at O-3′ that was glycosylated with a 2-deoxy-2-phthalimido trichloroacetimidate glucosyl donor. This glycosylation required large amounts of TMSOTf to proceed. Such conditions led to the formation of a Ferrier rearrangement glycosylation product. Despite these hurdles, the desired trisaccharide was isolated in 53% yield and easily deprotected in four steps.

Aberrant glycosylation in human cancer was first suggested in the mid-1960s when several papers reported the accumulation of fucose-containing glycolipids in adenocarcinomas.[1] Since these early reports, the structures and occurrence of tumor associated carbohydrates antigens (TACAs) have been reviewed several times,[2] and extensive work has been performed on glycoconjugates as potential anti-cancer vaccines.[3] Within our research program aimed at designing a safe anti-cancer vaccine based on the TACA[4] dimLe^x (**1**), we have prepared the trisaccharide fragment **2**. Since methyl 2-azido-2-deoxy-lactoside



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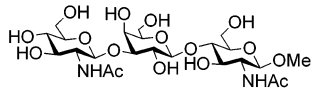

2

(**3**) is easily available from lactose via the azido-nitration of peracetylated lactal,[5] it was chosen as a precursor to make a disaccharide acceptor free at O-3′, which could then be glycosylated with a glucosamine glycosyl donor. Lactoside derivatives can be selectively protected at the 3′,4′-hydroxyl groups of the galactose residue through the formation of thermodynamically more stable 3′,4′-*O*-isopropylidenes[6] or orthoacetates.[7] In contrast, it has been shown that such reactions are more difficult to achieve on 2-azido-lactosides[8] because they often lead to considerable amounts of the kinetic 4′,6′-protected isomers. To prevent the formation of a 4′,6′-orthoester when preparing a 3′,4′-orthoacetate intermediate, we have investigated the selective protection of the primary hydroxyl groups in disaccharide **3** with pivaloyl and *tert*-butyldiphenylsilyl groups. A silylated intermediate could then be easily converted in excellent yields to an acceptor free at O-3′ via the intermediate formation of a 3′,4′-orthoacetate. We also report the unusual isolation of a Ferrier rearrangement glycosylation product while coupling this acceptor with a trichloroacetimidate glycosyl donor under high concentration of TMSOTf.

Our results confirmed[9] that the reactivity at O-3 of a galactose residue is similar to that of its primary hydroxyl group, whether it is a monosaccharide[9a] or the non-reducing end unit of a disaccharide in lactose[9a] or in *N*-acetyllactosamine.[9b] Indeed, the selective pivaloylation of disaccharide **3** at O-6 and O-6′ could not be accomplished. When the reaction was carried out using less than 4 equiv of pivaloyl chloride (PivCl) or at temperatures below 40 °C, only complex mixtures of inseparable mono-, di-, and tripivaloylated disaccharides were obtained. In contrast and similarly to the results described[9b] for the pivaloylation of *N*-acetyllactosamine, the tripivaloylated disaccharide **4** was obtained in excellent yields (90%) when the reaction was allowed to proceed at 40 °C in the presence of 4.0 equiv of PivCl. The structure of the tripivaloate **4** was determined using NMR spectroscopy. The ^{1}H NMR spectrum showed the pres-

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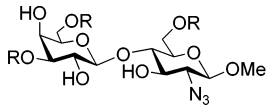
10.1021/jo062541y CCC: $37.00
Published on Web 03/28/2007

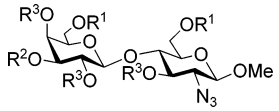


3 R = H
4 R = Piv

ence of three pivaloyl groups giving signals at ~1.2 ppm (27 hydrogens). Three exchangeable OH signals were found to correlate in the COSY spectrum with H-3, H-2′, and H-4′, supporting that O-3, O-2′, and O-4′ were not pivaloylated. Pivaloylation at O-6 and O-6′ was supported by the downfield chemical shift observed for the primary hydrogens of glucose (H-6a′, H-6b′ at ~4.15/4.62 ppm) and galactose (H-6a′, H-6b′ at 4.25 /~4.4 ppm) when compared to the same signals in disaccharide **3** (~3.7 and ~3.7, 3.87 ppm, respectively). Similarly the presence of a pivaloate at C-3′ was supported by the downfield chemical shift measured for H-3′ found at 4.84 ppm, while it was found at ~3.55 ppm in disaccharide **3**.

We thus attempted to introduce selectively on the primary hydroxyl groups more bulky *tert*-butyldiphenylsilyl protecting groups. Selective silylation was first attempted using *tert*-butyldiphenylsilyl chloride (TBDPSCl) in the presence of equimolar amounts of silver nitrate.[10] As shown in Table 1 (entries 1−4), different amounts of silylating reagents resulted in different product distributions. When 3.0 equiv of TBDPSCl was used, the desired disilylated disaccharide **5** was only isolated in 20% yield with no other product being formed. However, increasing the amount of TBDPSCl to 3.3 equiv led to the formation of the trisilylated disaccharide **6** in 32% yield (entry 4). The highest yield of the desired disilylated disaccharide **5** was obtained when using 3.2 equiv of TBDPSCl (entry 3). It is interesting to notice that small variations in reagent concentrations led to drastic differences in product distribution. In a second attempt to selectively[11] silylate disaccharide **3**, it was treated with 3.2 equiv of TBDPSCl in the presence of 6.0 equiv of imidazole in DMF (Table 1, entry 5). Although this reaction proved to proceed slowly, it also proved to be more selective. Indeed, the desired disilylated disaccharide **5** was obtained in 82% yield, and the trisilylated disaccharide **6** was isolated in only 7% yield. The structure of the disilylated disaccharide **5** was confirmed by NMR spectroscopy. The presence of two silyl groups was supported by signals in the ^{1}H NMR spectrum corresponding to 4 phenyl rings (7.4−7.8 ppm) and two *tert*-butyl groups (~1.1 ppm). Silylation of O-6 and O-6′ did not greatly affect the chemical shift of the primary hydrogens in disaccharide **5**. However, the presence of four exchangeable hydrogens that, in the COSY spectrum, correlated with H-3, H-2′, H-3′, and H-4′ allowed us to conclude that O-3, O-2′, O-3′, and O-4′ were not protected while O-6 and O-6′ were indeed silylated. Analysis of the trisilylated disaccharide **6** proved to be more difficult. Again, the presence of three silyl groups was confirmed by the occurrence in the ^{1}H NMR spectrum of signals corresponding to six phenyl rings and three *tert*-butyl groups. Exchangeable hydrogens were found at 4.39 and 2.15 ppm that correlated with H-3 and H-2′, respectively, supporting that O-3 and O-2′ were not silylated. A third exchangeable hydrogen was identified and seen to correlate to either the galactosyl H-3′ or H-4′ signals that overlapped in the ^{1}H NMR spectrum. Thus, we concluded that two of the three silyl groups were carried by the primary O-6 and O-6′ positions while the third one was carried by either O-3′ or O-4′. To determine which of O-3′ or O-4′ was silylated, disaccharide **6** was acetylated (Ac_2O/pyridine/DMAP, 40 °C) to give the triacetate **7**, which was analyzed by NMR. Whereas H-4′ in disaccharide **7** was found to shift downfield to 5.18 ppm from ~3.6 ppm in disaccharide **6**, the chemical shift of H-3′ in **7** (3.91 ppm) remained similar to that of the same hydrogen in disaccharide **6** (~3.6 ppm). These results clearly indicated that disaccharide **6** was trisilylated at O-6, O-6′, and O-3′ similarly to disaccharide **4** that was pivaloylated on the same three positions.

TABLE 1. Selective Silylation Conditions

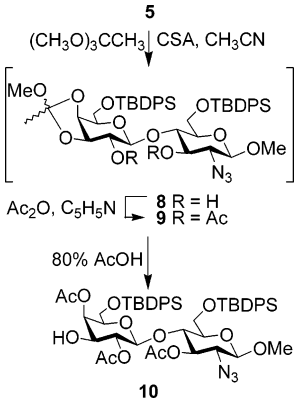


5 R^1= TBDPS; R^2, R^3 = H
6 R^1, R^2 = TBDPS; R^3 = H
7 R^1, R^2 = TBDPS; R^3 = Ac

entry	TBDPSCl (equiv)	time (h)	**5** (%)	**6** (%)
1	3.0[a]	0.5	20	0
2	3.1[a]	0.5	44	2
3	3.2[a]	0.5	70	18
4	3.3[a]	0.5	44	32
5	3.2[b]	48	82	7

[a] TBDPSCl/$AgONO_2$. [b] TBDPSCl/imidazole.

SCHEME 1



The disilylated disaccharide **5** was, in turn, converted in three steps to the disaccharide acceptor **10** (Scheme 1). Reaction of disaccharide **5** with trimethylorthoacetate in the presence of camphorsulfonic acid gave the 3′,4′-orthoacetate **8** as a 1/1 mixture of the endo and exo stereoisomers. After workup, the crude orthester **8** was acetylated (Ac_2O/pyridine), and the orthoacetate in disaccharide **9** was subsequently opened regioselectively on O-4′ by treatment with 80% AcOH. The yield obtained over these three steps proved to be difficult to control and varied between 60% and 80% as a result of the unwanted partial opening of the orthoester ring in **8** during the workup carried out after the first step. To circumvent this problem, the acetylation of disaccharide **8** was carried out in situ by adding pyridine and Ac_2O directly to the reaction mixture once it was observed by TLC that **5** had been fully converted to the orthoacetate **8**. Although the acetylation step required higher temperature (50 °C) to proceed, the desired acceptor **10** was obtained reproductively in 81% yield after workup, treatment of the crude disaccharide **9** with 80% AcOH, and flash chromatography.

Acceptor **10** was then submitted to glycosylation with the known[12] trichloroacetimidate *N*-phtalimido glucosyl donor **11**

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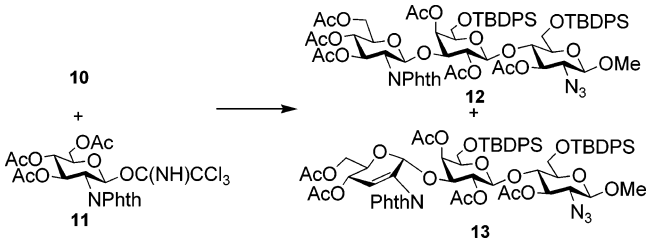
(Table 2). All of the reactions were carried out in anhydrous CH_2Cl_2 containing freshly activated powdered molecular sieves (4 Å) and under TMSOTf activation. Although reactions performed at −70 °C with up to 0.8 equiv (entry 1) of TMSOTf did not lead to efficient activation of the glycosyl donor, a reaction carried out at −15 °C with 0.8 equiv of TMSOTf (entry 2) led to rapid degradation of the donor **11** prior to its reaction with acceptor **10**. Reducing the amount of molecular sieves and carrying the reaction at −30 °C with 3.0 equiv of donor **11** and 0.6 equiv of activator TMSOTf (entry 3) allowed formation and isolation of trisaccharide **12** in 44% yield after RP-HPLC purification. Because during this reaction 23% of the acceptor **10** was also recovered, we attempted to increase the concentration of TMSOTf to promote glycosylation. When the concentration of TMSOTf was raised to 1.0 equiv, a 2:1 mixture (estimated by NMR) of the desired trisaccharide **12** and the unsaturated trisaccharide **13** was obtained in 79% yield upon flash chromatography. Interestingly, when the concentration of TMSOTf was further increased to 3.0 equiv (entry 5), the two products were isolated in 72% yield, but in this case the ratio **12** to **13** decreased to 1:1 (estimated by NMR).

The trisaccharide **13** was purified by reverse phase HPLC and its structure was established by NMR and HRMS. ^{1}H NMR showed that compound **13** carried only five acetyl groups. The HSQC spectrum showed typical signals corresponding to the CH of an olefin: a carbon signal at 128 ppm correlating to a hydrogen giving a broad singlet at 6.07 ppm. In addition, the HSQC also showed that the methylene C-6, C-6′, and C-6″ correlated as expected with two hydrogens. Integration of the proton spectrum showed only 14 instead of 15 ring hydrogens, confirming that the double bond was intracyclic. While H-1 and H-1′ were found as doublets with chemical shifts virtually identical to those of the same signals in disaccharide **10**, H-1″ appeared as a singlet that showed no correlation to other hydrogens in the COSY spectrum, suggesting that there was no hydrogen at C-2″. Finally, the HMBC spectrum showed long-range correlations between the olefin hydrogen and C-1″, C-2″, and C-4″, permitting us to conclude that this hydrogen was carried by C-3″ and that the double bond was between C-2″ and C-3″. Therefore the unsaturated trisaccharide **13** was identified as a Ferrier rearrangement adduct.[13] Because there is no hydrogen atom at C-2″, no $J_{H-1'',H-2''}$ coupling constant can be used to assign the configuration of the newly formed glycosidic bond. Therefore, the configuration of this glycosidic bond was assigned relying on the "allylic effect" defined by Ferrier[14] and the coupling constant between H-4″ and H-5″. Based on this "allylic effect" and as illustrated in Figure 1, steric hindrance between the vinylic phthalimido substituent at C-2″ and the aglycon in the α-glycoside **13** forces this ring to adopt the $^{O}H_5$ rather than the $^{5}H_O$ half-chair conformation in which these substituents would be quasi-eclipsed. In contrast, it is expected that a *β*-glycosidic bond such as that shown in trisaccharide **14** (Figure 1) would result in this ring adopting the $^{5}H_O$ conformation rather than the $^{O}H_5$ conformation. Thus, as can be seen in Figure 1, an α-glycosidic bond in such Ferrier rearrangement product leads to a conformation in which H-4″ and H-5″ assume a trans di-axial orientation, whereas a *β*-glycosidic bond leads to a conformation in which these hydrogens assume a trans di-equatorial orientation. In the case of our isolated byproduct, ^{1}H NMR gave a $J_{H-4'',H-5''}$ of 9.6 Hz, consistent with a trans di-axial relationship between these hydrogens and therefore supporting a $^{O}H_5$ conformation and an α configuration for the newly formed glycosidic bond in trisaccharide **13**. This value is in good agreement with that reported by Silva et al.[15] ($J_{H-4,H-5}$ = 10 Hz) for the 2′,3′ unsaturated disaccharide **17** having an α configuration (Scheme 2). Interestingly this compound was obtained by Ferrier rearrangement glycosidation of the 2-deoxy-2-phthalimido-D-glucal derivative **15** with the acceptor **16** under BF_3/Et_2O catalysis. It is known[16] that 2-deoxy-2-phthalimido glycosyl donors may undergo elimination during glycosylation reactions and lead to isolable quantities of 2-deoxy-2-phthalimido-D-glucal derivatives such as **15**. Thus, we propose that large concentrations of

TABLE 2. Glycosylation and Formation of Ferrier Rearrangement Trisaccharide 13



entry	**11** (equiv)	MS 4Å (mg/mL)	TMSOTf (equiv)	temp (°C)	**10** (%)	**12** (%)	**13** (%)
1	1.5−3.0	100	0.2−0.8	−70	*a*	*b*	*b*
2	1.6	100	0.8	−15	*a*	*b*	*b*
3	3.0	50	0.6	−30 to −24	23	44	*b*
4	3.0	50	1.0	−30 to −24	*c*	53[d]	26[d]
5	3.0	50	3.0	−30 to −24	*c*	36[d]	36[d]

[a] Seen unreacted by TLC but not recovered. [b] Not observed by TLC. [c] Full disappearance as assessed by TLC. [d] Yields were estimated by ^{1}H NMR on the isolated mixture of **12** and **13.**

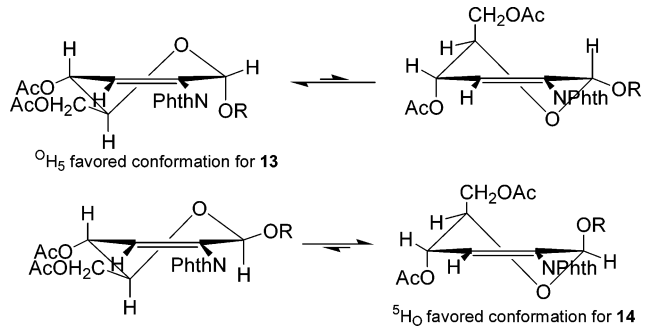
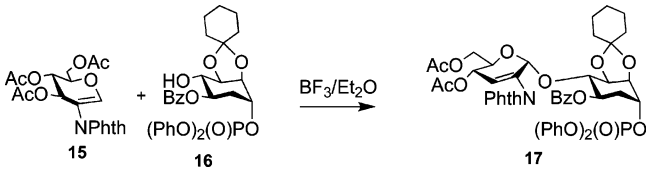


FIGURE 1. Conformations and allylic effects[14] in Ferrier rearranged adducts provide evidence of the α-glycosidic bond in trisaccharide **13**.

SCHEME 2. Ferrier Rearrangement Glycosidation by Silva et al.[16]



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TMSOTf (Table 2, entries 4 and 5) led to the conversion of trichloroacetimidate **11** to the glucal **15** that, in turn, underwent Ferrier-type glycosidation by the acceptor **10** to give trisaccharide **13**. Although Ferrier rearrangement reactions with 2-phthalimido-D-glucal have been described[15] and such glucals have been isolated during glycosylation reactions,[16] this is, to our knowledge, the first report of the formation of a Ferrier rearrangement product during the glycosylation of a saccharide acceptor with a 2-deoxy-2-phthalimido-glucosyl donor.

Although the formation of trisaccharide **13** decreased the yield of the desired trisaccharide **12**, we were able to isolate sufficient amounts of **12** to proceed with its deprotection to obtain trisaccharide **2**. Thus trisaccharide **12** was treated with fluoride ions to remove the silyl groups, and the resulting diol was submitted to Zemplén deacetylation. The phthalimido group was removed with ethylene diamine, and the resulting trisaccharide still carrying an azido group at C-2 was reduced (H_2, Pd/C in MeOH) and selectively *N*-acetylated in situ at both amino groups with acetic anhydride. The final trisaccharide **2** was purified by flash silica gel and Biogel P2 chromatography successively and was obtained in a 47% yield over the four steps of deprotection.

The dimLe^x trisaccharide fragment GlcNAc-β-(1→3)-Gal-β-(1→4)-GlcNAc-β-(1→O)-Me (**2**) was synthesized. A key intermediate to our synthesis was the selectively disilylated 2-deoxy-2-azido lactose derivative **5**. Although the selective enzymatic acetylation of OH-6 and OH-6′ on a similar disaccharide has been reported,[17] we are describing here, to the best of our knowledge, the first selective chemical protection of the primary hydroxyl groups in a 2-azido β-lactoside. Indeed, as we and others[9] have observed, the reactivity of the galactosyl OH-3′ in lactose derivatives often leads to the concomitant protection of O-6, O-6′, and O-3′. It is also interesting to point out that although silylation at O-6 and O-6′ of an α-benzyl glycoside of *N*-acetyllactosamine has been reported[11c] in good yields (82%), only mediocre (42%) yields have been reported[11b] for a similar reaction carried out on the analogous β-allyl glycoside. We also report that using high concentration of TMSOTf to catalyze a glycosylation employing a 2-deoxy-2-phthalimido glucosyl donor may lead to the formation of a Ferrier rearrangement oligosaccharide. However, the desired trisaccharide fragment **2** could be prepared in sufficient quantities to be used in NMR studies to assess its conformational behavior as well to be employed as competing antigen in immunological binding experiments. These further studies are ongoing on our laboratory.

Experimental Section

Methyl 2-Azido-6-*O*-*tert*-butyldiphenylsilyl-4-*O*-(6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranosyl)-2-deoxy-β-D-glucopyranoside (5). TBDPSCl (37 μL, 2.2 equiv) was added to a solution of disaccharide **3** (25 mg, 66 μmol) in DMF (2 mL) containing imidazole (27 mg, 6.0 equiv) and stirred under N_2. The reaction mixture was stirred at room temperature for 1 h, more TBDPSCl (17 μL, 1.0 equiv) was added, and the reaction was allowed to proceed for 2 days at room temperature. The solvent was evaporated, and the residue was co-concentrated with toluene (3 × 5 mL). Flash chromatography of the residue (EtOAc/hexanes, 1:9 to 3:7 to 7:3) gave first the trisilylated product **6** (5 mg, 7%) and then the disilylated product **5** (46 mg, 82%). $[\alpha]_D = -13°$ (*c* 3.8, $CHCl_3$). Selected ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.45 (d, 1 H, J = 8.0 Hz, H-1′), 4.26 (s, 1 H, OH-3), 4.10 (d, 1 H, J = 8.0 Hz, H-1), 4.03 (dd, 1 H, J = 12.0, 3.2 Hz, H-6a), 3.99 (m, 1 H, H-4′), 3.93−3.88 (m, 2 H, H-6b, H-6b′), 3.83 (dd, 1 H, J = 10.5, 6.0 Hz, H-6a′), 3.74 (t, 1 H, $J \approx$ 9 Hz, H-4), 3.64 (m, 1 H, H-2′), 3.58 (m, 1 H, H-5′), 3.56−3.49 (m, 2 H, H-3, H-3′), 3.52 (s, 3 H, CH_3O), 3.33−3.30 (m, 1 H, H-5), 3.27 (dd, 1 H, J = 9.6, 8.0 Hz, H-2), 2.97 (d, 1 H, J = 6.0 Hz, OH-3′), 2.81 (d, 1 H, J = 2.0 Hz, OH-2′), 2.71 (d, 1 H, J = 3.6 Hz, OH-4′). HRESIMS calcd for $C_{45}H_{59}O_{10}N_3Si_2$ $[M + NH_4]^+$ 875.4083, found 875.4047.

Methyl 3-*O*-Acetyl-4-*O*-[2,4-di-*O*-acetyl-6-*O*-*tert*-butyldiphenylsilyl-3-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-*N*-phthalimido-β-D-glucopyranosyl)-β-D-galactopyranosyl]-2-azido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (12) and Methyl 3-*O*-Acetyl-4-*O*-[2,4-di-*O*-acetyl-3-*O*-(4,6-di-*O*-acetyl-2,3-dideoxy-2-*N*-phthalimido-α-D-*erythro*-hex-2-eno-pyranosyl)-6-*O*-*tert*-butyldiphenylsilyl-β-D-galactopyranosyl]-2-azido-6-*O*-*tert*-butyldiphenylsilyl-2-deoxy-β-D-glucopyranoside (13). The disaccharide acceptor **10** (97 mg, 0.1 mmol) and the donor **11** (171 mg, 3.0 equiv) were dissolved in anhydrous CH_2Cl_2 (10 mL) and predried with MS 4 Å (500 mg, 50 mg/mL) for 2 h under N_2. The mixture was cooled down to −30 °C, and freshly distilled TMSOTf (54 μL, 3.0 equiv) was added. The reaction mixture was kept at −24 °C overnight, triethylamine was added, and the molecular sieves were filtered off through glass wool. The solids were washed with CH_2Cl_2 (5 mL), and the combined filtrate and washings were concentrated. Flash chromatography (EtOAc/hexanes, 1:1) of the residue and further purification with centrifugal chromatography (EtOAc/hexanes, 1:1) gave a mixture of trisaccharides **12** and **13** (100 mg, **12**/**13** = 1:1 by NMR integration, 72%). Further purification by reverse phase HPLC (H_2O/CH_3CN, 20:80 to 0:100) gave the pure trisaccharides **12** (28 mg, 20%) and **13** (33 mg, 25%). **Analytical data for 12:** $[\alpha]_D = 3°$ (*c* 1.5, $CHCl_3$). Selected ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.83 (dd, 1 H, J = 10.0, 9.2 Hz, H-3″), 5.48 (d, 1 H, J = 3.6 Hz, H-4′), 5.40 (d, 1 H, J = 8 Hz, H-1″), 5.18 (t, 1 H, $J \approx$ 9.5 Hz, H-4″), 4.84 (t, 1 H, $J \approx$ 10.0 Hz, H-3), 4.77 (dd, 1 H, J = 10.0, 8.0 Hz, H-2′), 4.64 (d, 1 H, J = 8 Hz, H-1′), 4.29 (dd, 1 H, J = 12.4, 2.8 Hz, H-6″), 4.23−2.20 (m, 1 H, H-6b″), 4.21−4.18 (m, 1 H, H-2″), 4.15 (d, 1 H, J = 8 Hz, H-1), 3.96 (t, 1 H, J = ∼9.5 Hz, H-4), 3.90−3.84 (m, 3 H, H-6a, H-6b, H-5″), 3.69 (dd, 1 H, J = 10.0, 3.6 Hz, H-3′), 3.63−3.56 (m, 3 H, H-5′, H-6a′, H-6b′), 3.54 (s, 3 H, CH_3O), 3.34 (dd, 1 H, J = 10.0, 8.0 Hz, H-2), 3.17 (d, 1 H, J = 9.6 Hz, H-5). HRESIMS calcd for $C_{71}H_{84}O_{22}N_4Si_2$ $[M + Na]^+$ 1423.5013, found 1423.4960. **Analytical data for 13:** $[\alpha]_D = 39°$ (*c* 1.1, $CHCl_3$). Selected ^{1}H NMR (300 MHz, $CDCl_3$): 6.07 (s, 1 H, H-3″), 5.83 (s, 1 H, H-1″), 5.58 (d, 1 H, J = 9.6 Hz, H-4″), 5.28 (d, 1 H, J = 2.7 Hz, H-4′), 4.98−4.89 (m, 2 H, H-3, H-2′), 4.62 (d, 1 H, J = 8.0 Hz, H-1′), 4.39 (dd, 1 H, J = 12.3, 1.8 Hz, H-6a″), 4.22−4.16 (m, 2 H, H-1, H-6b″), 4.10−4.02 (m, 1 H, C-5″), 4.05−3.95 (m, 1 H, H-4), 4.02−3.88 (m, 2 H, H-6a, H-6b), 3.94−3.83 (m, 1 H, H-3′), 3.68−3.58 (m, 1 H, H-6a′), 3.60−3.52 (m, 1 H, H-5′), 3.53 (s, 3 H, CH_3O), 3.48−3.40 (m, 1 H, H-6b′), 3.42−3.33 (m, 1 H, H-2), 3.38−3.28 (m, 1 H, H-5). Selected ^{13}C NMR (75 MHz, $CDCl_3$): δ 129.4 (C-2″), ∼128.0 (C-3″), 102.5 (C-1), 100.3 (C-1′), 92.7 (C-1″). HRESIMS calcd for $C_{69}H_{80}O_{20}N_4Si_2$ $[M + NH_4]^+$ 1358.5248, found 1358.5237.

Acknowledgment. We thank the National Science and Engineering Research Council of Canada, the Canada Foundation for Innovation, and the Ontario Innovation Trust for financial support of this work. F.-I. A. is also grateful to the Ontario Ministry of Research and Innovation for a Premier's Research Excellence Award.

Supporting Information Available: General experimental procedures and preparation of compounds **4**, **5**, and **6** (TBDPSCl/DMF $AgNO_3$), **7**, **10**, **12**, and **2**. Additional listing of ^{1}H and ^{13}C NMR data for **5**, **12**, and **13**. ^{1}H, and Jmod spectra for **2** in D_2O and **4**−**7**, **10, 12**, **13** in $CDCl_3$. This material is available free of charge via the Internet at http://pubs.acs.org.

JO062541Y

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