JOC Article

Investigations of Glycosylation Reactions with 2-*N*-Acetyl-2*N*,3*O*-oxazolidinone-Protected Glucosamine Donors

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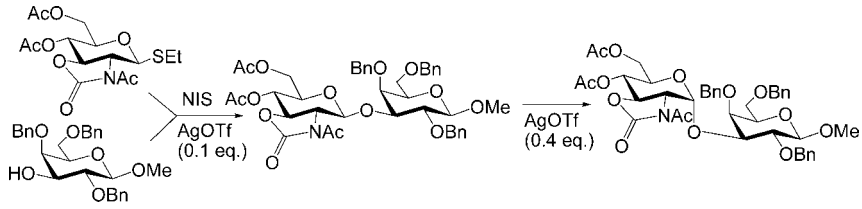

NIS/AgOTf-promoted glycosylations with ethyl 2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-glucopyranoside donors can be performed with either α- or β-selectivity by tuning the reaction conditions. Small amounts of AgOTf (0.1 equiv) and short reaction times give β-selectivity, whereas 0.4 equiv of AgOTf and prolonged reaction times afford α-linked products. NMR-monitored glycosylation and anomerization experiments show initial formation of exclusively the β-linkage, which anomerizes, through an intramolecular mechanism involving an endocyclic C−O bond cleavage, to the α-linkage.

Introduction

Synthesis of 2-acetamido-2-deoxyglycosides is still a challenge, especially, as with other glycosides, the stereoselective synthesis of 1,2-*cis*-glycosides.[1,2] In this context, 2*N*,3*O*-oxazolidinone derivatives of 2-amino-2-deoxyglycopyranosides have aroused a lot of interest recently, both as glycosyl donors and glycosyl acceptors.[3] Thus, Crich and Vinod advocated them as good 4-OH acceptors, avoiding the low reactivity of the corresponding GlcNAc acceptors.[4,5] Kerns and co-workers investigated their properties as glycosyl donors. Initially, they employed a non-*N*-acylated thiophenyl donor using phenylsulfenyl triflate as promoter to get high yields of disaccharides and with excellent α-selectivity.[6] With the *N*-acetylated tolyl thioglycoside donor and BSP-Tf_2O as promoter, they reported a correlation between the α/β-selectivity and the reactivity of the acceptor. β-Selectivity was obtained with reactive acceptors, and α/β-mixtures were produced with acceptors of intermediate reactivity, and unreactive acceptors gave mainly α-glycosides.[7] Recently, Ito and co-workers used *N*-benzylated thiophenyl donors and phenylsulfenyl triflate or *N*-(phenylthio)-ϵ-caprolactam-Tf_2O as promoter, to obtain disaccharides with high α-selectivity.[8] We tried the thioethyl *N*-acetylated donor employing NIS/AgOTf as promoter system and found that the stereochemical outcome of the reaction was highly dependent on the amount of AgOTf used; a catalytic amount gave β-selectivity, whereas the use of 0.4 molar equiv and prolonged reaction time provided α-selectivity.[9] We suggested that these results were due to an efficient anomerization of the initially formed β-glycoside when more acidic conditions were used. During the preparation and revision of this paper, Geng et al. published results on glycosylations using a preactivation protocol with similar outcome; that is, the presence of a base gave the β-product, whereas more acidic conditions (no base present) gave the α-linked product.[10,11] We herein report a more detailed investigation of our donor-promoter system and its reaction mechanism.

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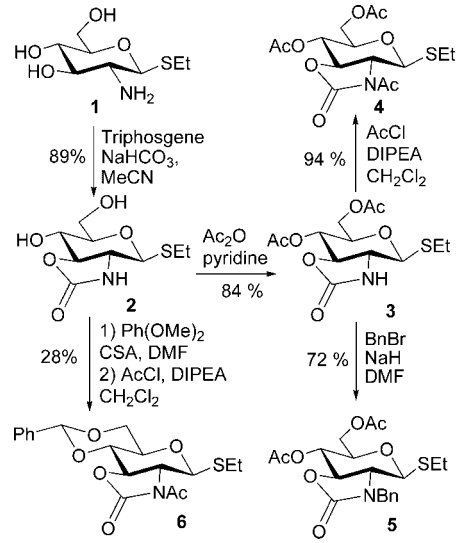
SCHEME 1. Synthesis of Glycosyl Donors



Results and Discussion

Synthesis of Glycosyl Donors. In our earlier communication, the 4,6-di-*O*-benzylated-protected oxazolidinone donor was used.[9] Shorter pathways to this donor as well as to other donors with different 4,6-*O*-protecting groups were investigated (Scheme 1). Ethyl 2-amino-2-deoxy-1-thio-β-D-glucopyranoside[12] (**1**) was treated with triphosgene[13] to regioselectively give the 2,3-cyclic carbamate **2** in high yield (89%). Unfortunately, attempts to selectively *O*-benzylate this compound were not successful, only the 2*N*,4,6-di-*O*-tribenzylated compound was isolated. However, selective *O*-acetylation was achieved using Ac_2O and pyridine to give compound **3** (84%), which could then be *N*-acetylated with AcCl and DIPEA (→ **4**, 94%) or *N*-benzylated using BnBr/NaH/DMF (→ **5**, 72%). Treatment of compound **2** with benzaldehyde dimethylacetal under acidic conditions afforded the 4,6-*O*-benzylidenated derivative (53%), which was *N*-acetylated using AcCl and DIPEA to give **6** (53%).

Glycosylation Results. The new compounds **4**−**6** were investigated for their donor properties using various acceptors, galactopyranosides **7**[14] and **8**,[15] mannopyranoside **15**,[16] rhamnopyranoside **16**,[17] and the glycosylation conditions (Method A or B) developed earlier (Table 1). The 4,6-*O*-benzylidene derivative **6** was found to be inert to activation by NIS/AgOTf, while the 4,6-*O*-acetylated derivative **4** gave very similar results to the corresponding 4,6-*O*-benzylated donor tried earlier.[9] Once again, the stereochemical outcome could be controlled by the amount of AgOTf used in the glycosylation and the reaction time; 0.1 equiv of AgOTf and reaction time of around 10 min gave the β-linked product, whereas 0.4 equiv and around 40 min produced the α-disaccharide with excellent stereoselectivity (entries *i, ii, iv, v, ix*, *x*, *xii*, and *xiii*, Table 1). The *N*-benzylated donor **5**, too, gave exclusively the α-linked products when 0.4 equiv of AgOTf was added (entries *vii* and *viii*). However, with this donor, also Method A afforded only the α-disaccharides, but in slightly lower yields.

With some donors (compare entries *i* and *xii*), glycosylations using Method A conditions and donor **4** resulted in an α/β mixture. Considering the mechanistic suggestion, this was thought to be due to unwanted anomerization of the initially formed β-product. A solution to this problem should be to use a promoter that allows buffering with a base to completely prevent anomerization. Therefore, DMTST was tried as promoter in the presence of DTBMP and was found to give complete β-selectivity and good to excellent yields (entries *iii*, *vi*, *xi*, and *xiv*) with all acceptors. The low yield with acceptor **9** (entry *iii*) was due to substantial decomposition of the donor not experienced in glycosylations with other acceptors. If DMTST was used without the addition of base, an anomerization of the originally obtained β-glycoside disaccharide was found; however, this anomerization was much slower and less efficient than with the NIS/AgOTf promoter system.

Mechanistic Studies. As mentioned, to explain the stereochemical outcome of the glycosylations using the *N*-acetylated donors, we anticipated an initial formation of the β-saccharide followed by a subsequent anomerization, aided by the presence of the oxazolidinone group, to the α-glycoside, which was most efficient under more acidic conditions. To verify this assumption, the glycosylation between donor **4** and acceptor **7**, using 0.1 molar equiv of AgOTf, was performed in the NMR tube (Figure 1). The relative amounts of α- and β-products at various times were estimated by integration over specific signals in the proton spectra (see Experimental Section). As predicted, the β-glycoside **9** was formed exclusively in the beginning, still after 20 min only the β-disaccharide could be detected. However, even with this small amount of AgOTf, the anomerization process was found to take place, and within 4 h, **9** was converted completely to the α-glycoside **10**. It is known that the *N*-acetyloxazolidinone group facilitates anomerization,[5,8,9] and, as expected, the methyl glycoside did not anomerize under these conditions.

The anomerization reaction was also studied in the NMR tube (Figure 2). Compound **9** (>95% β) was treated with a catalytic amount of AgOTf. Once more an efficient anomerization was observed giving the α-linked disaccharide **10** almost exclusively and efficiently (>90% yield) after 4 h.

This selective and high-yielding anomerization, with no or negligible hydrolysis, suggested to us that the mechanism is probably via an activation of the ring oxygen and a consecutive endocyclic C−O bond cleavage in preference over an exocyclic cleavage.[18] Since the endocyclic mechanism entails an intramolecular pathway (the "glycosidic" bond is not cleaved see Scheme 4 below), that would explain the high yields observed. To try to confirm this mechanism, the anomerization reaction was performed in the presence of an excess of methanol (Figure 3), which in the case of an exocyclic intermolecular pathway would be expected to give substantial amount of methanolysis product. However, no such monosaccharide products were detected; only the α-linked disaccharide was again formed and once more in high yield (80%), which strongly corroborates the endocyclic pathway. Attempts to trap the ring-opened intermediate by hydride reducing reagents were performed but were unsuccessful.

Oligosaccharide Synthesis. To further investigate the scope of this type of donors, the synthesis of an oligosaccharide

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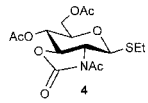
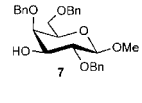
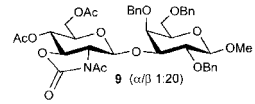
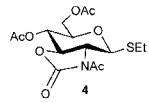
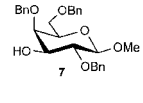
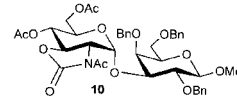
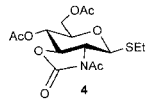
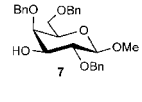
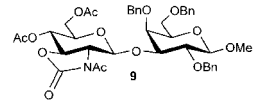
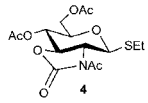
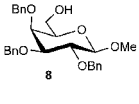
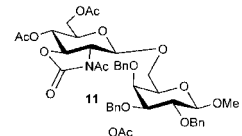
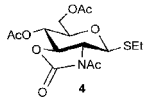
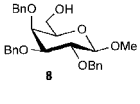
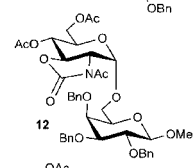
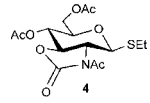
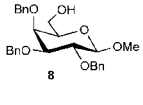
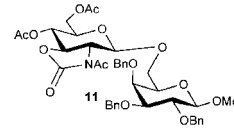
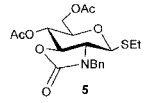
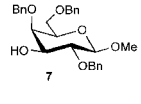
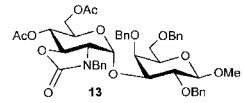
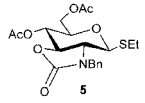
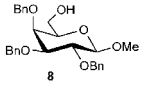
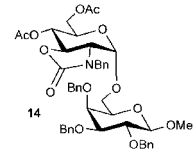
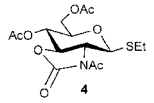
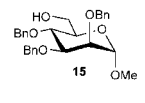
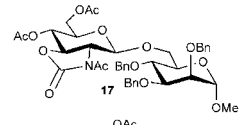
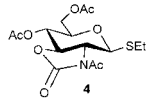
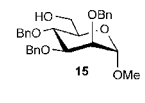
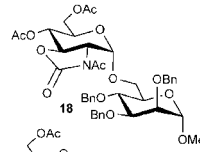
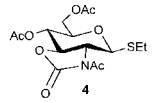
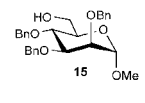
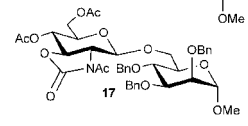
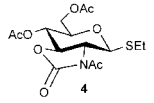
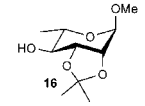
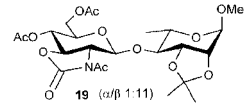
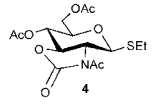
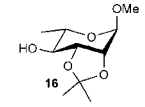
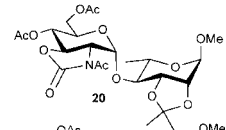
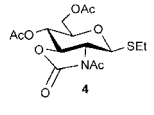
(18) Lindberg, B. *Acta Chem. Scand.* **1949**, *3*, 1153.

TABLE 1. Glycosylation Reactions

Entry	Donor	Acceptor	Method	Product	Yield
i			A		67 %
ii			B		82 %
iii			C		33 %
iv			A		76 %
v			B		68 %
vi			C		64 %
vii			B		65 %
viii			B		68 %
ix			A		58 %
x			B		66 %
xi			C		94 %
xii			A		82 %
xiii			B		62 %
xiv			C		91 %

Method A: Acceptor (1 equiv), donor (1.2−1.5 equiv), CH_2Cl_2, 4 Å molecular sieves, NIS (2 equiv), AgOTf (0.1 equiv.), rt, 10−20 min. Method B: Acceptor (1 equiv), donor (1.2−1.5 equiv), CH_2Cl_2, 4 Å molecular sieves, NIS (2 equiv), AgOTf (0.4 equiv), rt, 25−45 min. Method C: Acceptor (1 equiv), donor (1.2−1.5 equiv), CH_2Cl_2, 4 Å molecular sieves, DMTST (2 equiv), DTBMP (2.7 equiv), 0 to 20 °C, 30 min.

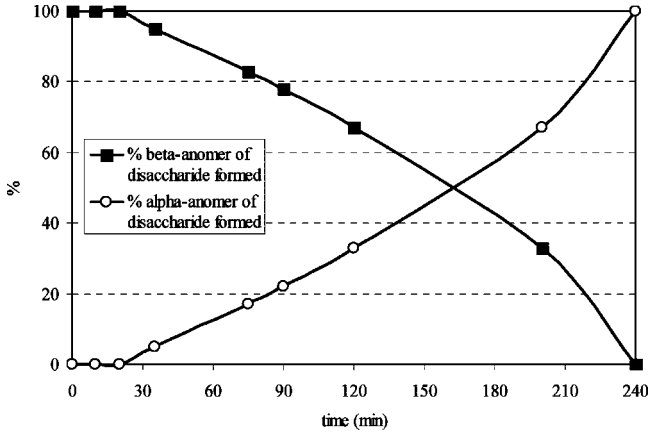


FIGURE 1. Relative amounts of β- and α-product disaccharides (**9** and **10**) versus time in NIS/AgOTf (0.1 equiv)-promoted glycosylation between donor **4** and acceptor **7** as estimated by NMR.

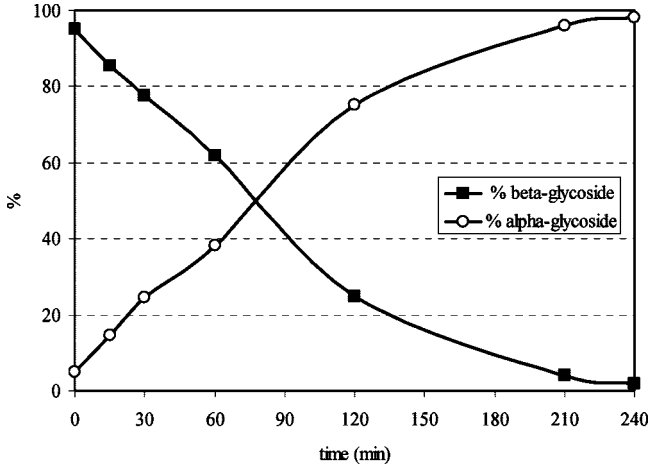


FIGURE 2. Relative amounts of β- and α-disaccharides (**9** and **10**) versus time in AgOTf (0.1 equiv)-promoted anomerization of compound **9** as estimated by NMR.

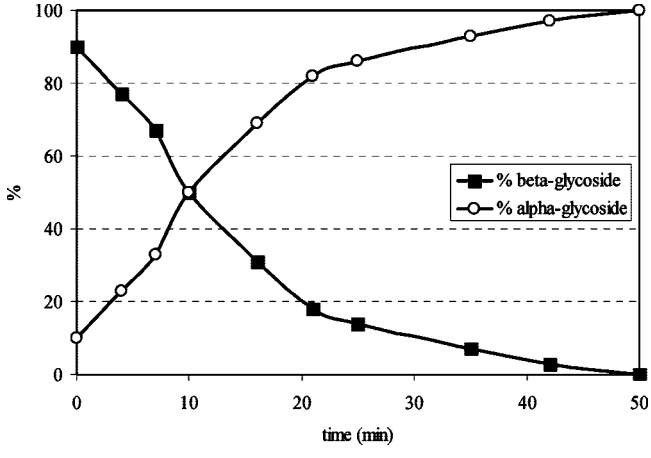
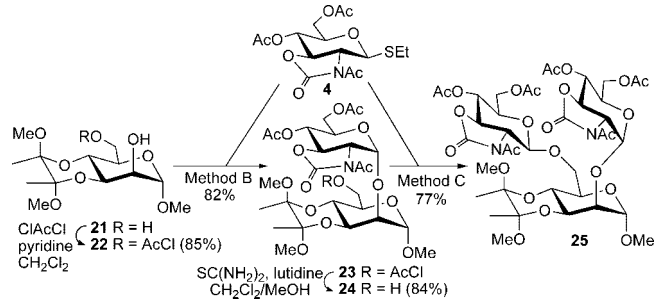


FIGURE 3. Relative amount of β- and α-disaccharides (**9** and **10**) versus time in AgOTf (excess)-promoted anomerization of compound **9** in the presence of MeOH (8 equiv) as estimated by NMR.

containing both α- and β-linked glucosamine residues was attempted (Scheme 2). As the target structure, an α-(1→2)-analogue of the branched trisaccharide β-D-GlcNAc*p*-(1→2)-[β-D-GlcNAc*p*-(1→6)]-α-D-Man*p* found in the complex form of *N*-glycans was selected. In line with the suggested mechanism, the α-linked GlcNAc moiety had to be introduced first.

SCHEME 2. Synthesis of Trisaccharide 25



Glycosylation of acceptor **22** (obtained by regioselective chloroacetylation of compound **21**[19]) using Method B (Table 1) condition and 1.4 equiv of donor **4** afforded the expected α-linked disaccharide **23** in 46% yield, a yield that was improved to 82% when 1.8 donor equiv was used. Treatment with thiourea removed the chloroacetyl group to afford the 6-OH acceptor **24** (84%). The subsequent β-glycosylation of acceptor **24** with donor **4** was tried using both Method A and Method C conditions. DMTST/DTBMP was found to be the best promoter system, affording target trisaccharide **25** in 77% yield.

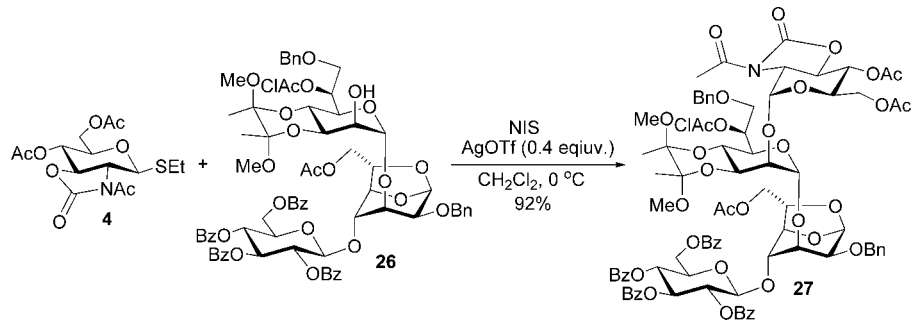
In the synthesis of a tetrasaccharide corresponding to a *Neisseria meningitidis* inner core LPS structure,[20] problems were encountered during the introduction of an α-linked GlcNAc moiety to the acceptor **26**[21] (Scheme 3). 2-Azido-2-deoxyglucopyranose donors gave high yields but low stereoselectivity (at the best α/β 1.5:1) in the couplings. Therefore, donor **4** was tried using the conditions (Method B) that were shown to give α-selectivity. Most satisfactorily, this approach gave exclusively the α-linked [H-1‴ δ 5.81 (d, J = 2.5 Hz)] tetrasaccharide **27** in 92% yield, proving the application of the methodology also to complex oligosaccharide synthesis.

Discussion and Conclusions

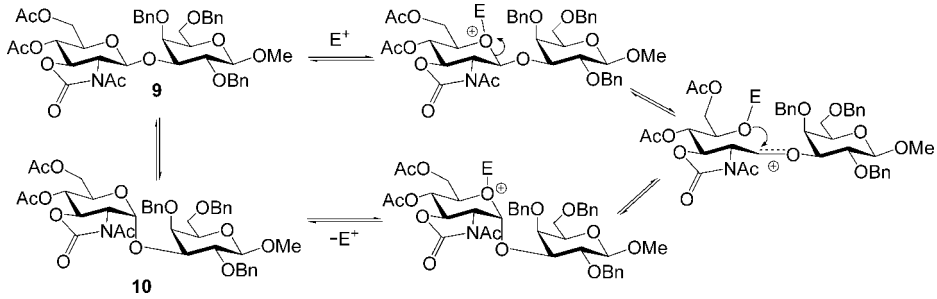
We have found that in glycosylation reactions with *N*-acetylated 2*N*,3*O*-oxazolidinone thioglycoside donors using NIS/AgOTf as promoter the stereochemical outcome of glycosylation reactions is determined by the reaction conditions used. Exclusively the β- or the α-glycoside product can be obtained from the same donor by tuning the reaction conditions. NMR-monitored glycosylation reactions show that the β-glycoside is initially formed and can be isolated if short reaction time and low acidity conditions are used. If longer time and/or more acidic conditions are employed, an efficient anomerization to give exclusively the corresponding α-glycoside takes place. These results and selectivities have also been found to be valid in more complex cases, such as the synthesis of tri- and tetrasaccharides. NMR-monitored anomerization experiments strongly suggest that the anomerization is an intramolecular reaction proceeding via an endocyclic C−O bond cleavage (Scheme 4). Both the *N*-acetyl and the oxazolidinone group as well as AgOTf were found to be important for an effective anomerization. The rationale behind the initial formation of the β-product has not been studied. However, the crystal structure of donor **4** has been elucidated (Figure 4) showing the *N*-acetyl group on the β-side of the molecule in a position where it can not act as a

(19) Montchamp, J.-L.; Tian, F.; Hart, M. E.; Frost, J. W. *J. Org. Chem.* **1996**, *61*, 3897.
(20) Raetz, C. R. H.; Whitfield, C. *Annu. Rev. Biochem.* **2002**, *71*, 635.
(21) Segerstedt, E.; Mannerstedt, K.; Johansson, M.; Oscarson, S. *J. Carbohydr. Chem.* **2004**, *23*, 443.

SCHEME 3. Synthesis of Tetrasaccharide 27



SCHEME 4. Proposed Mechanism for the Anomerization Reaction of Compound 9



participating group, findings that are corroborated by molecular modeling performed by Wei and Kerns.[7]

If the α-selective properties of the *N*-benzylated donor **5** are due to the same mechanism as for donor **4**, but with an even faster anomerization rate, or if in this case the α-linked disaccharide is the initial product has not yet been established.

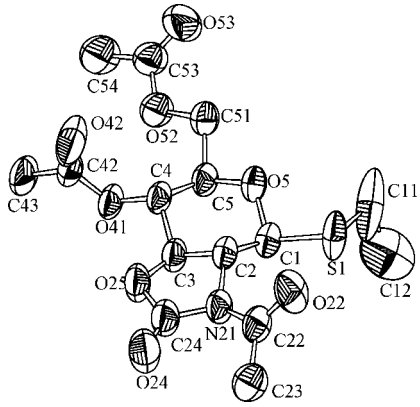


FIGURE 4. X-ray structure of compound **4**.

Experimental Section

Ethyl-2,3-*N*,*O*-Carbonyl-2-deoxy-1-thio-β-D-glucopyranoside (2). Ethyl 2-amino-2-deoxy-1-thio-β-D-glycopyranoside (0.487 g, 2.18 mmol) was dissolved in MeCN (20 mL), and $NaHCO_3$ (sat. aq, 10 mL) was added. The mixture was cooled to 0 °C, and triphosgene (0.259 g, 0.872 mmol) was added to the vigorously stirred mixture. After 30 min, EtOAc (30 mL) containing ethylenediamine (0.408 mL, 6.107 mmol) was added and the stirring was continued for 5 min. Normal workup gave **2** (0.484 g,1.94 mmol, 89%) as an analytically pure white solid: R_f 0.60 ($CHCl_3$/CH_3OH 5:1); $[\alpha]_D$ −54 (*c* 1.0, CH_3OH); ^{13}C NMR (75.4 MHz, CD_3OD) δ 15.5, 25.0, 60.6, 62.0, 68.5, 83.7, 83.9, 86.3, 162.2; ^1H NMR (300 MHz, CD_3OD) δ 1.30 (t, 3H, J = 7.5 Hz), 2.77 (m, 2H), 3.41 (m, 1H), 3.42 (dd, 1H, J = 9.6, 11.1 Hz), 3.74 (dd, 1H, J = 5.1, 12.0 Hz), 3.84−3.90 (m, 2H), 4.12 (dd, 1H, J = 10.2, 11.1 Hz), 4.74 (d, 1H, J = 9.6 Hz); EI-HRMS calcd for $C_9H_{15}NO_5S$ $[M + Na]^+$ 272.0569, found 272.0585.

Ethyl 4,6-Di-*O*-acetyl-2,3-N,O-carbonyl-2-deoxy-1-thio-β-D-glucopyranoside (3). Compound **2** (0.484 g, 1.94 mmol) was dissolved in pyridine/Ac_2O (3:2, 10 mL) at 0 °C. After 2 h, the mixture was coevaporated with toluene (3 × 15 mL). FC (toluene/EtOAc 2:1) afforded **3** (0.543 g, 1.63 mmol, 84%) as a white foam: R_f 0.53 (toluene/EtOAc 1:1); $[\alpha]_D$ −29 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 15.4, 20.7, 20.8, 25.0, 59.2, 62.3, 67.6, 77.4, 82.0, 83.2, 158.5, 169.3, 170.7; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (t, 3H, J = 7.5 Hz), 2.08 (s, 3H), 2.11 (s, 3H), 2.73 (m, 2H), 3.58 (ddd, 1H, J_{12} = 9.6, J_{23} = 9.6, J = 1.2 Hz), 3.74 (ddd, 1H, J = 9.0, J = 2.7, J = 5.1 Hz), 4.16 − 4.27 (m, 3H), 4.62 (d, 1H, J = 9.6 Hz), 5.30 (dd, 1H, J_{34} = 10.2, J = 9.0, Hz), 5.37 (br s, 1H); EI-HRMS calcd for $C_{13}H_{19}NO_7S$ $[M + Na]^+$ 356.0780, found 356.0766.

Ethyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-glucopyranoside (4). Compound **3** (0.126 g, 0.378 mmol) was dissolved in dry CH_2Cl_2 (3 mL), and DIPEA (0.33 mL, 1.89 mmol) and AcCl (0.134 mL, 1.89 mmol) were added at 0 °C. After 20 min, the mixture was diluted with CH_2Cl_2 (12 mL), washed with $NaHCO_3$ (sat. aq, 15 mL), 1 M HCl (15 mL), and subjected to normal workup. FC (toluene/EtOAc 6:1→ 3:1) followed by crystallization from Et_2O/pentane gave **4** (0.134 g, 0.357 mmol, 94%) as white crystals: R_f 0.67 (toluene/EtOAc 1:1); mp 52−53 °C; $[\alpha]_D$ −23 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.3, 20.7, 20.8, 24.8, 25.6, 60.1, 62.3, 67.8, 77.4, 79.5, 85.2, 153.5, 169.2, 170.6, 172.7; ^1H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, 3H, J = 7.5 Hz), 2.06 (s, 3H), 2.11 (s, 3H), 2.50 (s, 3H), 2.64 (m, 2H), 3.76 (m, 1H), 4.06 (dd, 1H, J = 8.4, J = 11.1 Hz), 4.20 − 4.27 (m, 3H), 4. 76 (d, 1H, J = 8.4 Hz), 5.28 (dd, 1H, J = 10.2, J = 9.0, Hz); EI-HRMS calcd for $C_{15}H_{21}NO_8S$ $[M + Na]^+$ 398.0886, found 398.0867.

Ethyl 4,6-Di-*O*-acetyl-2-*N*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-glucopyranoside (5). Compound **3** (0.086 g, 0.258 mmol) was dissolved in dry DMF (2 mL), and benzyl bromide (0.046 mL, 0.387 mmol) was added. This solution was added dropwise to a cooled (0 °C) slurry of NaH (0.008 g, 0.335 mmol) in DMF (1 mL). After 30 min, MeOH (0.5 mL) was added and the mixture was diluted with H_20 (40 mL) and toluene (50 mL). The organic phase was separated and subjected to normal workup, followed by

FC (toluene/EtOAc 6:1) to give **5** (0.079 g, 0.187 mmol, 72%): R_f 0.53 (toluene/EtOAc 2:1); $[\alpha]_D$ −70 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.8, 20.6, 20.7, 25.2, 47.3, 60.0, 62.3, 67.5, 77.2, 80.0, 83.8, 127.8, 128.4 (2C), 128.7 (2C), 135.7, 158.6, 169.2, 170.6; ^1H NMR (300 MHz, $CDCl_3$) δ 1.19 (t, 3H, J = 7.5 Hz), 2.02 (s, 3H), 2.08 (s, 3H), 2.53 (m, 2H), 3.40 (dd, 1H, J = 9.6, J = 11.1 Hz), 3.72 (m, 1H), 4.10−4.22 (m, 3H), 4.58 (benzylic d, 1H, J_{gem} = 16.3 Hz), 4.63 (d, 1H, J = 9.6 Hz), 4.73 (benzylic d, 1H, J_{gem} = 16.3 Hz), 5.21 (dd, 1H, J = 10.2, J = 9.3 Hz), 7.27 − 7.34 (m, 5H, Ar−H); EI-HRMS calcd for $C_{20}H_{25}NO_7S$: $[M + Na]^+$ 446.1244, found 446.1234.

Ethyl 2-Acetamido-4,6-*O*-benzylidene-2,3-*N*,*O*-carbonyl-2-deoxy-1-thio-β-D-glucopyranoside (6). $PhCH(OMe)_2$ (0.31 mL, 2.046 mmol) and CSA (0.024 g, 0.102 mmol) were added to a solution of compound **2** (0.255 g, 1.023 mmol) in DMF (10 mL). After stirring at 50 °C for 18 h, the solution was diluted with EtOAc (50 mL), washed with $NaHCO_3$ (sat. aq, 80 mL), and subjected to normal workup. FC (toluene/EtOAc 3:1) gave the 4,6-*O*-benzylidene derivative (0.183 g, 0.542 mmol, 53%) as a white solid. This derivative (0.176 g, 0.521 mmol) was dissolved in dry CH_2Cl_2 (5 mL), and DIPEA (0.27 mL, 1.57 mmol) and AcCl (0.111 mL, 1.57 mmol) were added at 0 °C. After 30 min, the mixture was diluted with CH_2Cl_2 (15 mL), washed with $NaHCO_3$ (sat. aq, 20 mL), 1 M HCl (20 mL), and subjected to normal workup. FC (toluene/EtOAc 6:1) followed by crystallization from EtOAc/light petroleum (65−75) gave **5** (0.183 g, 0.542 mmol, 53%) as a white solid: R_f 0.78 (toluene/EtOAc 2:1); mp 194−196 °C; $[\alpha]_D$ −44 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 14.3, 25.0, 25.7, 61.1, 68.4, 73.3, 78.6, 78.9, 86.2, 101.6, 126.2 (2C), 128.5 (2C), 129.5, 136.4, 153.8, 173.3; ^1H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, 3H, J = 7.5 Hz), 2.54 (s, 3H), 2.67 (m, 2H), 3.63 (ddd, 1H, J = 4.5, 8.7, 9.9 Hz), 3.94 (dd, 1H, J = 10.2, 10.2 Hz), 4.03−4.10 (m, 2H), 4.33−4.42 (m, 2H), 4.83 (d, 1H, J = 8.7 Hz), 5.62 (s, 1H), 7.36−7.50 (m, 5H, Ar−H); EI-HRMS calcd for $C_{18}H_{21}NO_6S$ [M + Na]$^+$ 402.0987, found 402.1000.

General Methods for the Glycosylation Reactions. Method A: The glycosyl acceptor **7** or **8** (approximately 0.10 mmol, 1 equiv) and a slight excess of the glycosyl donor **4** or **5** (1.2−1.5 equiv) were dissolved in dry CH_2Cl_2 (1 mL); 4 Å molecular sieves were added, and the mixture was stirred for 10−15 min under an argon atmosphere. NIS (2.0 equiv) and AgOTf (approximately 0.1 equiv) were added, and the mixture was stirred for an additional 10−20 min. Et_3N was added, and the mixture was applied to a silica gel column. FC (toluene → toluene/EtOAc 19:1→ 9:1 → 6:1→ 3:1) gave the desired disaccharide.

Method B: The glycosyl acceptor **7** or **8** (approximately 0.10 mmol, 1 equiv) and a slight excess of the glycosyl donor **4** or **5** (1.2−1.5 equiv) were dissolved in dry CH_2Cl_2 (1 mL); 4 Å molecular sieves were added, and the mixture was stirred for 5−15 min under an argon atmosphere. NIS (2.0 equiv) and AgOTf (0.4 equiv) were added, and the mixture was stirred for an additional 25−45 min and then applied to a silica gel column. FC (toluene → toluene/EtOAc 19:1→ 9:1 → 6:1→ 3:1) gave the desired disaccharide.

Method C: The glycosyl acceptor **15** or **16** (approximately 0.05 mmol, 1 equiv), a slight excess of the glycosyl donor **4** (1.5 equiv), and DTBMP (2.7 equiv) were dissolved in dry CH_2Cl_2 (1 mL); 4 Å molecular sieves were added, and the mixture was stirred for 20 min under an argon atmosphere. The mixture was cooled to 0 °C, and DMTST (2.0 equiv) was added. The reaction was brought to 20 °C over 30 min and then quenched with Et_3N. The mixture was filtered through Celite, the solvent evaporated, and the residue applied to a silica gel column. FC (toluene/EtOAc 9:1 → 6:1 → 3:1) gave the desired disaccharide.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-β-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside (9). Yield 67% (Method A) and 33% (Method C); R_f 0.79 (toluene/EtOAc 1:1); $[\alpha]_D$ −2 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.7, 20.8, 24.7, 57.0, 60.6, 63.0, 68.8 (2C), 73.7 (2C), 74.5, 74.7, 75.6, 75.8, 75.9, 79.8, 80.1, 102.2, 105.2, 127.0 (2C), 127.6 (2C), 128.0, 128.1 (2C), 128.2 (2C), 128.5 (2C), 128.6 (2C), 128.8 (2C), 138.0, 139.0, 139.3, 153.6, 169.5, 170.5, 170.6; ^1H NMR (300 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.12 (s, 3H), 2.28 (s, 3H), 3.51 (s, 3H), 3.63−3.59 (m, 3H), 3.94−3.80 (m, 5H), 4.03 (dd, 1H, J = 9.9, 12.3 Hz), 4.12 (dd, 1H, J = 6.6, 12.3 Hz), 4.26 (d, 1H, J = 6.9 Hz), 4.34 (dd, 1H, J = 3.3, 12.0 Hz), 4.42 (benzylic d, 1H, J_{gem} = 12.0 Hz), 4.47 (benzylic d, 1H, J_{gem} = 10.8), 4.51 (benzylic d, 1H, J_{gem} = 11.4 Hz), 4.62 (benzylic d, 1H, J_{gem} = 11.4 Hz), 4.99 (benzylic d, 1H, J_{gem} = 11.4 Hz), 5.01 (benzylic d, 1H, J_{gem} = 11.4 Hz), 5.12 (dd, 1H, J = 6.9, 9.9 Hz), 5.35 (d, 1H, J = 6.9 Hz), 7.23−7.42 (m, 15H); EI-HRMS calcd for $C_{41}H_{47}NO_{14}$ [M + Na]$^+$ 800.2894, found 800.2906.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside (10). Yield 82%; R_f 0.79 (toluene/EtOAc 1:1); $[\alpha]_D$ +61 (*c* 2.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.8, 20.8, 23.3, 57.3, 60.1, 61.1, 68.0, 68.3, 69.7, 73.3, 73.7, 73.8, 73.9, 74.6, 75.2, 76.8, 77.7, 93.0, 105.5, 127.0 (2C), 127.6, 128.0, 128.0, 128.1 (2C), 128.3 (2C), 128.5 (2C), 128.5 (2C), 128.6 (2C), 137.8, 138.3, 138.9, 152.6, 169.2, 170.6, 172.2; ^1H NMR (300 MHz, $CDCl_3$) δ 2.03 (s, 3H), 2.04 (s, 3H), 2.05 (s, 3H), 3.55 (s, 3H), 3.60 (m, 3H), 3.78−3.91 (m, 5H), 3.94 (dd, 1H, J = 2.4, 12.6 Hz), 4.23−4.30 (m, 2H), 4.42 (benzylic d, 1H, J_{gem} = 11.7 Hz), 4.58−4.48 (m, 4H), 4.65 (benzylic d, 1H, J_{gem} = 11.1 Hz), 4.96 (benzylic d, 1H, J_{gem} = 10.8 Hz), 5.22 (t, 1H, J = 9.9 Hz), 5.87 (d, 1H, J = 2.7 Hz), 7.23−7.39 (m, 15H); EI-HRMS calcd for $C_{41}H_{47}NO_{14}$ [M + Na]$^+$ 800.2894, found 800.2853.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-β-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-β-D-galactopyranoside (11). Yield 76% (Method A) and 64% (Method C); R_f 0.72 (toluene/EtOAc 1:1); $[\alpha]_D$ −20 (*c* 0.8, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.8, 20.9, 24.7, 57.1, 60.8, 63.7, 67.7, 69.7, 73.1, 73.4, 73.8, 74.5, 75.2, 75.4, 77.0, 79.6, 82.1, 100.4, 105.1, 127.6−128.5 (15C), 138.6, 138.7, 139.0, 153.3, 169.6, 170.4, 170.6; ^1H NMR (300 MHz, $CDCl_3$) δ 2.02 (s, 3H), 2.13 (s, 3H), 2.47 (s, 3H), 3.51 (s, 3H), 3.58 (dd, 1H, J = 2.7, 9.9 Hz), 3.64−3.90 (m, 5H), 3.94−4.01 (m, 2H), 4.12−4.25 (m, 2H), 4.29 (d, 1H, J = 7.2 Hz), 4.42 (dd, 1H, J = 4.8, 11.7 Hz), 4.63 (benzylic d, 1H, J_{gem} = 11.7 Hz), 4.75−4.78 (m, 3H), 4.89 (benzylic d, 1H, J_{gem} = 11.1 Hz), 4.98 (benzylic d, 1H, J_{gem} = 11.7 Hz), 5.11 (dd, 1H, J = 4.2, 9.6 Hz), 5.14 (d, 1H, J = 6.9 Hz), 7.24−7.38 (m, 15H); EI-HRMS calcd for $C_{41}H_{47}NO_{14}$ [M + Na]$^+$ 800.2894, found 800.2853.

Methyl 2-Acetamido-4,6-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-β-D-galactopyranoside (12). Yield 68%; R_f 0.83 (toluene/EtOAc 1:1); $[\alpha]_D$ +40 (*c* 0.4, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.7, 20.8, 23.9, 57.1, 60.1, 61.6, 68.0, 70.1, 73.0, 73.5, 73.9, 74.4, 74.4, 75.3, 79.6, 82.1, 95.3, 105.1, 127.7, 127.8 (2C), 127.9, 128.0, 128.2 (2C), 128.4 (4C), 128.5 (2C), 128.6 (2C), 138.3, 138.5, 138.8, 152.8, 169.2, 170.7, 171.1 (Note: one ^{13}C signal overlaps with solvent peaks); ^1H NMR (300 MHz, $CDCl_3$) δ 2.06 (s, 3H), 2.11 (s, 3H), 2.46 (s, 3H), 3.44−3.53 (m, 3H), 3.54 (s, 3H), 3.67 (d, 1H, J = 2.7 Hz), 3.77−3.95 (m, 4H), 4.13 (dd, 1H, J = 2.1, 12.3 Hz), 4.21−4.28 (m, 2 H), 4.55−4.62 (m, 2H), 4.73 (benzylic d, 1H, J_{gem} = 12.0 Hz), 4.76 (benzylic d, 1H, J_{gem} = 10.8 Hz), 4.82 (benzylic d, 1H, J_{gem} = 12.0 Hz), 4.91 (benzylic d, 1H, J_{gem} = 10.5 Hz), 4.94 (benzylic d, 1H, J_{gem} = 11.1 Hz), 5.29 (t, 1H, J = 9.9 Hz), 5.64 (d, 1H, J = 2.7 Hz), 7.28−7.38 (m, 15H); EI-HRMS calcd for $C_{41}H_{47}NO_{14}$ [M + Na]$^+$ 800.2894, found 800.2853.

Methyl 4,6-Di-*O*-acetyl-2-*N*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranosyl-(1→3)-2,4,6-tri-*O*-benzyl-β-D-galactopyranoside (13). Yield 65%; R_f 0.60 (toluene/EtOAc 2:1); $[\alpha]_D$ +28 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.8 (2C), 48.3, 57.3, 60.7, 61.6, 68.6, 68.4, 70.6, 73.1, 73.6, 73.8, 74.3, 74.6, 75.2, 77.9, 78.8, 93.4, 105.3, 127.4 (2C), 127.9 (2C), 128.1 (2C), 128.1, 128.2 (2C), 128.5, 128.5 (3C), 128.7 (2C), 128.8 (2C), 129.3 (2C), 134.9, 137.9, 138.1, 138.5, 158.6, 169.3, 170.6; ^1H NMR (300 MHz, $CDCl_3$) δ 1.98 (s, 3H), 2.02 (s, 3H), 3.30 (dd, 1H, J = 2.7, 11.7 Hz), 3.37 (dd, 1H, J = 3.0, 9.6 Hz), 3.53 (s, 3H), 3.55 (m, 1H),

3.66−3.69 (m, 2H), 3.73 (dd, 1H, J = 7.2, 9.6 Hz), 3.79 (d, 1H, J = 2.1 Hz), 3.89−3.91 (m, 2H), 4.02 (benzylic d, 1H, J_{gem} = 15.0 Hz), 4.08 (m, 1H), 4.22 (d, 1H, J = 7.2 Hz), 4.37−4.51 (m, 2H), 4.49 (benzylic d, 1H, J_{gem} = 11.4 Hz), 4.56 (benzylic d, 1H, J_{gem} = 11.7 Hz), 4.62 (benzylic d, 1H, J_{gem} = 11.4 Hz), 4.65 (benzylic d, 1H, J_{gem} = 10.5 Hz), 4.79 (benzylic d, 1H, J_{gem} = 11.4 Hz), 4.91 (benzylic d, 1H, J_{gem} = 10.5 Hz), 5.13 (t, 1H, J = 9.9 Hz), 5.26 (d, 1H, J = 2.7 Hz), 7.17−7.38 (m, 20H, Ar−H); EI-HRMS calcd for $C_{46}H_{51}NO_{13}$ [M + K]$^+$ 864.2992, found 864.2949.

Methyl 4,6-Di-*O*-acetyl-2-*N*-benzyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-β-D-galactopyranoside (14). Yield 68%; R_f 0.56 (toluene/EtOAc 2:1); [α]$_D$ +18 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 20.7, 20.8, 48.7, 57.1, 61.2, 61.6, 68.4 (2C), 70.5, 73.3, 73.7, 73.8, 74.0, 74.2, 75.3, 79.7, 82.0, 95.0, 105.1, 127.8, 127.9 (2C), 128.0, 128.0, 128.2 (2C), 128.4 (3C), 128.5 (2C), 128.5 (2C), 128.6 (2C), 128.9 (2C), 128.9 (2C), 135.2, 138.3, 138.5, 138.8, 158.4, 169.3, 170.6; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.01 (s, 3H), 2.08 (s, 3H), 3.29−3.35 (m, 2H), 3.48−3.56 (m, 2H), 3.54 (s, 3H), 3.64 (dd, 1H, J = 7.5, 9.9 Hz), 3.78 (dd, 1H, J = 7.5, 9.6 Hz), 3.84 (m, 1H), 4.04 (dd, 1H, J = 3.5, 12.3 Hz), 4.19 (dd, 1H, J = 4.5, 12.3 Hz), 4.25 (d, 1H, J = 7.8 Hz), 4.32 (s, 2H), 4.50 (dd, 1H, J = 10.2, 12.0 Hz), 4.58 (d, 1H, J = 2.7 Hz), 4.59 (benzylic d, 1H, J_{gem} = 12.0 Hz), 4.75 (benzylic d, 1H, J_{gem} = 12.0 Hz), 4.76 (benzylic d, 1H, J_{gem} = 11.1 Hz), 4.86 (benzylic d, 1H, J_{gem} = 12.0 Hz), 4.92 (benzylic d, 1H, J_{gem} = 11.1 Hz), 4.97 (benzylic d, 1H, J_{gem} = 12.0 Hz), 5.20 (dd, 1H, J = 10.2, 10.2 Hz), 7.17−7.39 (m, 20H, Ar−H); EI-HRMS calcd for $C_{46}H_{51}NO_{13}$ [M + Na]$^+$ 848.3253, found 848.3216.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-β-D-glycopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-β-D-mannopyranoside (17). Yield 58% (Method A) and 94% (Method C); R_f 0.76 (toluene/EtOAc 1:1); [α]$_D$ +1 (*c* 1.0, $CHCl_3$); ^{13}C NMR (124.6 MHz, 30 °C, $CDCl_3$) δ 20.7, 20.8, 24.5, 54.8, 60.5, 63.9, 68.2, 70.0, 71.4, 72.0, 72.5, 74.5, 74.7, 74.8, 75.3, 77.2, 80.2, 98.9, 100.5, 127.5, 127.5, 127.6 (3C), 127.8 (2C), 127.9 (2C), 128.3 (2C), 128.3 (2C), 128.3, 138.4, 138.5, 138.9, 153.2, 169.4, 169.9, 170.5; ^{1}H NMR (500 MHz, 30 °C, $CDCl_3$) δ 2.00 (s, 3H), 2.11 (s, 3H), 2.46 (s, 3H), 3.30 (s, 3H), 3.72−3.77 (m, 2H), 3.87−3.99 (m, 4H), 4.04 (dd, 1H, J = 1.5, 11.0 Hz), 4.22 (dd, 1H, J = 10.0, 12.5 Hz), 4.33 (dd, 1H, J = 6.0, 12.0 Hz), 4.41 (dd, 1H, J = 6.0, 12.0 Hz), 4.61 (s, 2H), 4.70−4.73 (m, 4H), 4.93 (benzylic d, 1H, J_{gem} = 10.5 Hz), 5.10 (d, 1H, J = 6.5 Hz), 5.14 (dd, 1H, J = 4.5, 10.0 Hz), 7.27−7.37 (m, 15H, Ar−H); EI-HRMS calcd for $C_{41}H_{47}NO_{14}$ [M + Na]$^+$ 800.2894, found 800.2921.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glycopyranosyl-(1→6)-2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (18). Yield 66%; R_f 0.66 (toluene/EtOAc 2:1); [α]$_D$ +60 (*c* 1.0, $CHCl_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.9, 20.9, 24.6, 54.9, 60.6, 64.0, 68.3, 70.1, 71.5, 72.1, 72.6, 74.5, 74.8, 74.9, 75.4, 77.3, 80.3, 99.0, 100.6, 127.6−128.5 (Ar−C), 138.6, 138.7, 139.0, 153.4, 169.6, 170.1, 170.7; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.01 (s, 3H), 2.12 (s, 3H), 2.47 (s, 3H), 3.31 (s, 3H), 3.71−3.78 (m, 2H), 3.86−4.01 (m, 5H), 4.04 (dd, 1H, J = 1.5, 10.5 Hz), 4.22 (dd, 1H, J = 9.6, 12.6 Hz), 4.33 (dd, 1H, J = 6.0, 12.0 Hz), 4.41 (dd, 1H, J = 6.0, 12.0 Hz), 4.61 (s, 2H), 4.67−4.74 (m, 4H), 4.93 (benzylic d, 1H, J_{gem} = 11.1 Hz), 5.10 (d, 1H, J = 6.9 Hz), 5.14 (dd, 1H, J = 4.2, 9.6 Hz), 7.27−7.39 (m, 15H, Ar−H); EI-HRMS calcd for $C_{41}H_{47}NO_{14}$ [M + Na]$^+$ 800.2894, found 800.2906.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-β-D-glycopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (19). Yield 82% (Method A) and 91% (Method C); R_f 0.64 (toluene/EtOAc 1:1); [α]$_D$ −48 (*c* 1.0, $CHCl_3$); ^{13}C NMR (124.6 MHz, 30 °C, $CDCl_3$) δ 17.6, 20.6, 20.7, 24.7, 26.4, 28.0, 54.8, 60.8, 63.5, 63.8, 69.1, 76.0, 76.1 (2C), 77.3, 78.7, 97.9, 98.9, 109.2, 153.3, 169.3, 170.5, 170.6; ^{1}H NMR (500 MHz, 30 °C, $CDCl_3$) δ 1.27 (d, 3H, J = 6.0 Hz), 1.33 (s, 3H), 1.52 (s, 3H), 2.08 (s, 3H), 2.12 (s, 3H), 2.51 (s,3H), 3.36 (s, 3H), 3.65 (dd, 1H, J = 7.5, 9.5 Hz), 3.70 (dd, 1H, J = 6.0, 10.0 Hz), 3.90−3.95 (m, 2H), 4.09 (d, 1H, J = 6.0 Hz), 4.19 (dd, 1H, J = 6.0, 12.0 Hz), 4.24 (dd, 1H, J = 10.0, 12.0 Hz), 4.33−4.41 (m, 2H), 5.08 (s, 1H), 5.18 (dd, 1H, J = 5.0, 10.0 Hz), 5.55 (d, 1H, J = 7.5 Hz); EI-HRMS calcd for $C_{23}H_{33}NO_{13}$ [M + H]$^+$ 532.2030, found 532.2019.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glycopyranosyl-(1→4)-2,3-*O*-isopropylidene-α-L-rhamnopyranoside (20). Yield 62%; R_f 0.48 (toluene/EtOAc 2:1); [α]$_D$ +96 (*c* 1.0, $CHCl_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.5, 20.9, 20.9, 23.9, 26.5, 28.3, 55.1, 60.4, 61.4, 64.4, 68.1, 70.1, 74.2, 76.1, 77.1, 81.3, 96.0, 97.9, 109.6, 152.9, 169.4, 170.9, 171.7; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.21 (d, 3H, J = 6.4 Hz), 1.34 (s, 3H), 1.52 (s, 3H), 2.09 (s, 3H), 2.12 (s, 3H), 2.50 (s, 3H), 3.35 (s, 3H), 3.44 (dd, 1H, J = 6.0, 10.0 Hz), 3.59 (dd, 1H, J = 6.0, 10.0 Hz), 3.89 (dd, 1H, J = 2.8, 12.0 Hz), 4.07−4.12 (m, 3H), 4.34 (m, 1H), 4.33 (dd, 1H, J = 2.8, 12.0 Hz), 4.65 (dd, 1H, J = 2.8, 12.0 Hz), 4.84 (s, 1H), 5.37 (dd, 1H, J = 10.0, 10.0 Hz), 5.83 (d, 1H, J = 2.8 Hz); EI-HRMS calcd for $C_{23}H_{33}NO_{13}$ [M + Na]$^+$ 554.1844, found 554.1838.

Methyl 6-*O*-Chloroacetyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-mannopyranoside (22). Compound **21**[19] (0.612 g, 1.98 mmol) was dissolved in CH_2Cl_2/pyridine (14:1, 15 mL), and the solution was cooled to −70 °C. Chloroacetyl chloride (0.173 mL, 2.18 mmol) was added dropwise, and the mixture was slowly brought to −20 °C over 90 min and the reaction was then quenched with MeOH (3 mL). The mixture was diluted with CH_2Cl_2 (10 mL), washed with 1 M HCl (50 mL), and subjected to normal workup. FC (toluene/EtOAc 3:1→ 1:1) gave **22** (0.648 g, 1.68 mmol, 85%) as a white foam: R_f 0.71 (toluene/EtOAc 1:3); [α]$_D$ +183 (*c* 1.0, $CHCl_3$); ^{13}C NMR (125.6 MHz, 30 °C, $CDCl_3$) δ 17.8, 17.9, 40.9, 48.2, 48.3, 55.2, 63.3, 64.5, 68.4, 68.5, 69.8, 100.2, 100.6, 101.3, 167.4; ^{1}H NMR (500 MHz, 30 °C, $CDCl_3$) δ 1.28 (s, 3H), 1.32 (s, 3H), 3.23 (s, 3H), 3.27 (s, 3H), 3.38 (s, 3H), 3.92−4.10 (m, 6H), 4.33 (dd, 1H, J = 6.0, 12.0 Hz), 4.52 (d, J = 12.0 Hz), 4.73 (s, 1H); EI-HRMS calcd for $C_{15}H_{25}ClO_9$ [M + Na]$^+$ 407.1085, found 407.1078.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glycopyranosyl-(1→2)-6-*O*-chloroacetyl-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-mannopyranoside (23). Acceptor **22** (0.126 g, 0.327 mmol) and donor **4** (0.225 g, 0.599 mmol) were dissolved in dry CH_2Cl_2 (5 mL) containing crushed 4 Å molecular sieves. After stirring for 30 min under argon, the mixture was cooled to 0 °C. NIS (0.162 g, 0.719 mmol) and AgOTf (0.042 g, 0.164 mmol) were added, and the mixture was stirred for an additional 30 min. The reaction was quenched with Et_3N (0.300 mL) and the mixture filtered through Celite, washed with $Na_2S_2O_3$ (10% aq, 20 mL), and subjected to normal workup. FC (toluene/EtOAc 19:1 → 6:1 → 3:1) afforded **23** (0.188 g, 0.269 mmol, 82%): R_f 0.65 (toluene/EtOAc 1:1); [α]$_D$ +115 (*c* 1.0, $CHCl_3$); ^{13}C NMR (125.6 MHz, 30 °C, $CDCl_3$) δ 17.8, 17.9, 20.8, 20.9, 23.7, 40.8, 48.2, 48.3, 55.3, 60.1, 62.2, 63.1, 64.0, 67.0, 68.6, 68.7, 71.0, 74.1, 77.4, 97.0, 100.2, 100.3, 100.4, 153.1, 167.2, 169.4, 170.6, 170.9; ^{1}H NMR (500 MHz, 30 °C, $CDCl_3$) δ 1.24 (s, 3H), 1.25 (s, 3H), 2.08 (s, 3H), 2.14 (s, 3H), 2.49 (s, 3H), 3.19 (s, 3H), 3.23 (s, 3H), 3.37 (s, 3H), 3.85−4.00 (m, 6H), 4.11 (s, 2H), 4.14 (dd, 1H, J = 5.0, 12.0 Hz), 4.23 (dd, 1H, J = 2.0, 12.0 Hz), 4.35 (dd, 1H, J = 4.5, 12.0 Hz), 4.48 (dd, 1H, J = 2.0, 12.0 Hz), 4.69 (dd, 1H, J = 10.5, 10.5 Hz), 4.76 (s, 1H), 5.27 (dd, 1H, J = 10.0, 10.0 Hz), 5.81 (d, 1H, J = 2.5 Hz); EI-HRMS calcd for $C_{28}H_{40}ClNO_{17}$ [M + Na]$^+$ 720.1874, found 720.1882.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glycopyranosyl-(1→2)-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-mannopyranoside (24). Thiourea (0.043 g, 0.572 mmol) was added to a stirred solution of **23** (0.057 g, 0.082 mmol) and 2,6-lutidine (0.038 mL, 0.328 mmol) in CH_2Cl_2/MeOH (1:1, 4 mL), and the resulting solution was heated to 35 °C. After stirring for 40 h, the mixture was diluted with CH_2Cl_2 (8 mL), washed consecutively with 1 M HCl (25 mL) and H_2O (25 mL), and subjected to normal workup. FC (toluene/EtOAc 3:1 → 1:1) gave **22** (0.043 g, 0.069 mmol, 84%): R_f 0.40 (toluene/EtOAc 1:3); [α]$_D$ +123 (*c* 1.0, $CHCl_3$); ^{13}C NMR (125.6 MHz, 30 °C, $CDCl_3$) δ 17.7, 17.8, 20.7, 20.9, 23.5, 47.9, 48.0, 55.0, 60.0, 61.3, 62.4, 63.1,

66.8, 68.6, 70.5, 70.9, 73.9, 77.1, 96.6, 99.8, 100.0, 100.2, 152.9, 169.4, 170.7, 171.0; ^{1}H NMR (500 MHz, 30 °C, $CDCl_3$) δ 1.24 (s, 3H), 1.25 (s, 3H), 2.10 (s, 3H), 2.14 (s, 3H), 2.49 (s, 3H), 3.22 (s, 3H), 3.23 (s, 3H), 3.36 (s, 3H), 3.69 (m, 1H), 3.75−3.87 (m, 4H), 3.95−4.05 (m, 3H), 4.12 (dd, 1H, J = 6.0, 12.0 Hz), 4.25 (d, 1H, J = 12.0 Hz), 4.68 (dd, 1H, J = 11.5, 11.5 Hz), 4.75 (s, 1H), 5.23 (dd, 1H, J = 10.0, 10.0 Hz), 5.82 (d, 1H, J = 2.0 Hz); EI-HRMS calcd for $C_{26}H_{39}NO_{16}$ $[M + Na]^+$ 644.2167, found 644.2187.

Methyl 2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glycopyranosyl-(1→2)-[2-acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-β-D-glycopyranosyl-(1→6)]-3,4-*O*-(2,3-dimethoxybutane-2,3-diyl)-α-D-mannopyranoside (25). DTBMP (0.022 g, 0.107 mmol), **4** (0.022 g, 0.059 mmol), and **24** (0.022 g, 0.035 mmol) were dissolved in dry CH_2Cl_2 (3 mL). After stirring for 20 min in the presence of 4 Å molecular sieves under an Ar atmosphere, the mixture was cooled to 0 °C and DMTST (0.022 g, 0.085 mmol) was added. The reaction was brought to 20 °C over 20 min and was then quenched with Et_3N (0.150 mL). The mixture was filtered through Celite and subjected to normal workup. FC (toluene/EtOAc 3:1 → 2:1) yielded **23** (0.026 g, 0.028 mmol, 77%): R_f 0.45 (toluene/EtOAc 1:1); $[\alpha]_D$ +73 (*c* 1.0, $CHCl_3$); ^{13}C NMR (125.6 MHz, 30 °C, $CDCl_3$) δ 17.6, 17.8, 20.6 (3C), 20.7, 23.4, 24.5, 47.8, 47.9, 54.9, 59.9, 60.6, 61.9, 63.6 (2C), 67.0, 67.6, 68.5, 69.7, 70.1, 70.6, 73.4, 75.2, 76.7, 76.9, 96.8, 99.8, 99.9, 100.1, 101.0, 153.1, 153.1, 169.2, 169.4, 170.1, 170.5, 170.5, 170.7; ^{1}H NMR (500 MHz, 30 °C, $CDCl_3$) δ 1.23 (s, 3H), 1.25 (s, 3H), 2.09 (s, 3H), 2.10 (s, 3H), 2.13 (s, 3H), 2.13 (s,3H), 2.49 (s, 3H), 2.51 (s, 3H), 3.12 (s, 3H), 3.22 (s, 3H), 3.37 (s, 3H), 3.74 (dd, 1H, J = 6.5, 10.5 Hz), 3.78−3.88 (m, 4H), 3.96−4.06 (m, 4H), 4.09 (dd, 1H, J = 2.0, 10.5 Hz), 4.19−4.20 (m, 2H), 4.24−4.30 (m, 2H), 4.45 (dd, 1H, J = 5.5, 12.5 Hz), 4.71 (s, 1H), 4.81 (dd, 1H, J = 10.0, 12.0 Hz), 5.09 (d, 1H, J = 7.0 Hz), 5.15 (dd, 1H, J = 5.0, 10.0 Hz), 5.28 (dd, 1H, J = 10.0, 10.0 Hz), 5.81 (d, J = 3.0 Hz); EI-HRMS calcd for $C_{39}H_{54}N_2O_{24}$ $[M + Na]^+$ 957.2964, found 957.2974.

2-Acetamido-4,6-di-*O*-acetyl-2,3-*N*,*O*-carbonyl-2-deoxy-α-D-glucopyranosyl-(1→2)-7-*O*-benzyl-6-*O*-chloroacetyl-3,4-*O*-(2′,3′-dimethoxybutane-2′,3′-diyl)-L-glycero-α-D-mannoheptapyranosyl-(1→3)-[2,3,4,6-tetra-*O*-benzoyl-β-D-glucopyranosyl-(1→4)]-7-*O*-acetyl-1,6-anhydro-2-*O*-benzyl-L-glycero-α-D-mannoheptapyranose (27). Acceptor **26**[20] (0.016 g, 0.012 mmol) and donor **4** (0.018 g, 0.048 mmol) were dissolved in dry CH_2Cl_2 (1.5 mL). After stirring for 30 min in presence of 4 Å molecular sieves under argon, the mixture was cooled to 0 °C. NIS (0.011 g, 0.050 mmol) and AgOTf (0.002 g, 0.008 mmol) were added, and the mixture was stirred for additional 30 min. Et_3N (0.10 mL) was added, and the mixture was then filtered through Celite, washed with $Na_2S_2O_3$ (10% aq, 8 mL), and subjected to normal workup. FC (toluene/EtOAc 6:1 → 3:1 → 1:1) gave **27** (0.018 g, 0.011 mmol, 92%): R_f 0.63 (toluene/EtOAc 1:1); ^{1}H NMR (500 MHz, 30 °C, $CDCl_3$) δ 1.20 (s, 3H), 1.25 (s, 3H), 2.05 (s, 3H), 2.06 (s, 3H), 2.07 (s, 3H), 2.47 (s,3H), 3.09 (s, 3H), 3.15 (s, 3H), 3.31 (dd, 1H, J = 5.5, 10.5 Hz), 3.38 (dd, 1H, J = 2.0, 5.5 Hz), 3.51 (dd, 1H, J = 8.0, 10.0 Hz), 3.79−3.83 (m, 3H), 3.90 (dd, 1H, J = 10.0, 10.0 Hz), 3.94−3.97 (m, 2H), 4.06− 4.33 (m, 16H), 4.54 (dd, 1H, J = 4.5, 12.5 Hz), 4.67−4.71 (m, 2H), 5.11 (d, 1H, J = 7.5 Hz), 5.23 (benzylic d, 2H, J_{gem} = 12.0 Hz), 5.29−5.33 (m, 2H), 5.55 (dd, 1H, J = 8.0, 9.5 Hz), 5.76 (dd, 1H, J = 9.5, 9.5 Hz), 5.81 (d, 1H, J = 2.5 Hz), 5.94 (dd, 1H, J = 9.5, 9.5 Hz), 7.17−7.53 (m, 22H, Ar−H), 7.83 (d, 2H, J = 7.0 Hz), 7.88 (d, 2H, J = 7.5 Hz), 7.94 (d, 2H, J = 7.0 Hz), 7.98 (d, 2H, J = 7.5 Hz).

NMR Experiments. Experiment 1: Glycosylation. Solutions of **4** (6.0 mg, 16.0 μmol, in 0.4 mL of CH_2Cl_2) and **7** (5.5 mg, 11.8 μmol, in 0.4 mL of CH_2Cl_2) were added to a NMR tube; the solvent was evaporated, and the NMR tube was dried under vacuum overnight. CD_2Cl_2 (0.4 mL) was added, and a reference spectrum was recorded. NIS (4.8 mg, 21.2 μmol) and AgOTf (~0.3 mg, 1.2 μmol) were added, and the NMR tube was sealed under an argon atmosphere. The reaction was followed by integration of signals corresponding to the acetyl singlets, and ^{1}H NMR spectra were recorded during 360 min. Selected peaks: **9** (β-1→3-linkage, 300 MHz, CD_2Cl_2): δ 1.97, 2.11, 2.26; **10** (α-1→3-linkage, 300 MHz, CD_2Cl_2): δ 2.00, 2.04, 2.06.

Experiment 2: Anomerization. Compound **9** (5.0 mg, 6.4 μmol) was dissolved in CD_2Cl_2 (0.4 mL), and a reference spectrum was recorded. A catalytic amount of AgOTf was added, and the NMR tube was sealed under an argon atmosphere. The reaction was followed by integration of signals corresponding to the acetyl singlets, and ^{1}H NMR spectra were recorded during 240 min. Selected peaks: **9** (β-1→3-linkage, 300 MHz, CD_2Cl_2): δ 1.97, 2.11, 2.26; **10** (α-1→3-linkage, 300 MHz, CD_2Cl_2): δ 2.00, 2.04, 2.06.

Experiment 3: Anomerization in the Presence of CH_3OH. Compound **9** (5.0 mg, 6.4 μmol) was dissolved in CD_2Cl_2 (0.4 mL), and a reference spectrum was recorded. CH_3OH (2.0 μL, 51.0 μmol, 8.0 equiv) and an excess of AgOTf were added, and the NMR tube was sealed under an argon atmosphere. The reaction was followed by integration of signals corresponding to the acetyl singlets, and ^{1}H NMR spectra were recorded under 60 min, whereafter the solution was evaporated and FC (toluene/EtOAc 19:1→ 9:1 → 6:1) gave **7** (4.0 mg, 5.1 μmol, 80%). Selected peaks: **9** (β-1→3-linkage, 300 MHz, CD_2Cl_2): δ 1.97, 2.11, 2.26; **10** (α-1→3-linkage, 300 MHz, CD_2Cl_2): δ 2.00, 2.04, 2.06.

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Supporting Information Available: General experimental procedures, copies of spectra of compounds **2**−**6**, **9**−**14**, **17**−**25**, and **27**, and X-ray crystallographic data (CIF file) for compound **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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