JOC The Journal of Organic Chemistry

Article

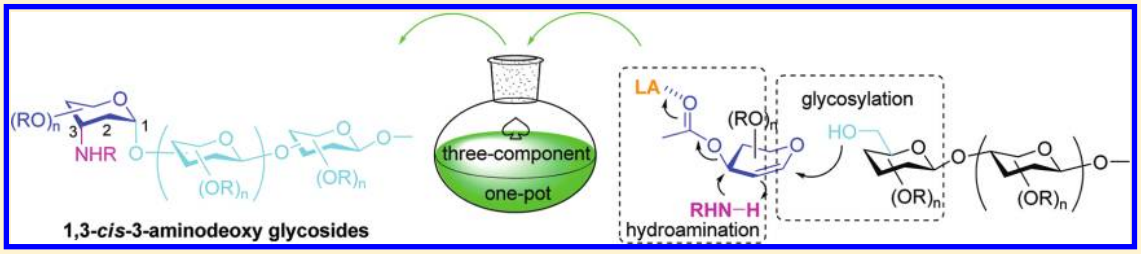
pubs.acs.org/joc

Direct and Stereoselective Synthesis of 1,3-*cis*-3-Arylsulphonaminodeoxydisaccharides and Oligosaccharides

Feiqing Ding, Ronny William, Shuting Cai, Jimei Ma, and Xue-Wei Liu*

Division of Chemistry and Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, 21 Nanyang Link, Singapore 637371

Supporting Information



ABSTRACT: The 3-aminoglycosides are ubiquitous in biologically important classes of glycoconjugates and naturally occurring oligosaccharides. Despite the rapid growth in the development of synthetic method of 3-amino glycosides, the current state-of-the art suffers from limited substrate scope, low yields, long reaction times, and anomeric mixtures. This work presents a novel direct method for the synthesis of 1,3-*cis*-3-arylsulphonaminodeoxydisaccharides and oligosaccharides via α-selective glycosylation and hydroamination of glycal in a one-pot manner. This efficient multicomponent reaction methodology provides ready access to 1,3-*cis*-3-arylsulphonaminodeoxydisaccharides and oligosaccharides and allows derivatization by variation of each component.

INTRODUCTION

2,3-Di- and 2,3,6-trideoxyaminosaccharides are key components of many biologically active natural products,[1] and their synthesis is particularly challenging.[2] Significant attention has been placed on them over the past years as they constitute important elements in many pharmacological compounds. Noteworthy, their roles in aminodeoxy di- and oligosaccharide anthracycline antibiotics such as daunosaminyl daunosamine, rubomycin, marcellomycin, and aclacinomycin has been one of the main focus in recent years (Figure 1).[3] The synthesis of 3-amino-2,3-dideoxyglycosides with linkages to other sugar residues via either 1,3-*cis*- or 1,3-*trans*-3-amino *O*-glycosidic bonds have attracted growing interest due to their broad spectrum of applications in chemistry, medicine, and pharmaceutical fields.[4]

Stereocontrolled glycosylation in the assembly of glycosidic bonds in deoxysugar derivatives is inherently difficult to achieve because of the lack of stereodirecting substituents at C2.[5] Therefore, many advances in the synthesis of 3-amino-deoxyglycosides in the past decades have predominantly focused on the stereoselective formation of glycosidic bond.[6] However, the development of reliable methods for stereoselective construction of both α- and β-deoxyglycosides remains a challenging area of research. Although the α-deoxyglycosides are relatively more accessible than the β-anomers because of the anomeric effect, glycosylation of 2-deoxyglycosides under acidic conditions frequently provides a mixture of both anomers. In addition, the routinely used methods for the synthesis of 1,3-*cis*-3-aminodeoxydisaccharides and oligosaccharides employ an indirect approach whereby the glycosyl donors possess a protected heteroatom at C2 that directs facial selectivity of the reaction, and the protecting group can be cleaved at later stage.[7]

Our interest in drug discovery motivated us to devise new methodologies for the aminosugar syntheses.[8] Recently, we derived a strategy for ready access to 3-arylsulphonamino-2,3-dideoxysugars via regio- and stereoselective tandem hydroamination/glycosylation of glycal.[9] In conjunction with our previous work, herein, we wish to report a direct and reliable synthetic approach that provides 1,3-*cis*-3-arylsulphonamino-2,3-deoxydisaccharides and oligosaccharides with not only exclusive anomeric stereoselectivity, but also a wide range of derivatization. We envisaged a straightforward synthesis of 1,3-*cis*-3-arylsulphonamino-2,3-dideoxyglycosides by a three-component reaction of the glycosyl donor, glycosyl acceptor, and sulfonamide/carbamate in a one-pot manner. This methodology involves regio- and stereoselective tandem hydroamination/glycosylation on the protected glycal scaffold (Figure 2).

RESULTS AND DISCUSSION

We first sought to examine the feasibility in constructing the *N*-protected 1,3-*cis*-3-aminodeoxydisaccharides through a one-pot three-component reaction. In our initial studies, treatment of glycosyl donor 3,4,6-tri-*O*-acetyl-D-glucal (**1a**), glucose acceptor (**2a**) and *p*-toluenesulfonamide (**3a**) with 1.1 equiv of $BF_3{\cdot}OEt_2$

Received: August 6, 2011
Published: May 31, 2012

   dx.doi.org/10.1021/jo300791v | *J. Org. Chem.* 2012, 77, 5245–5254

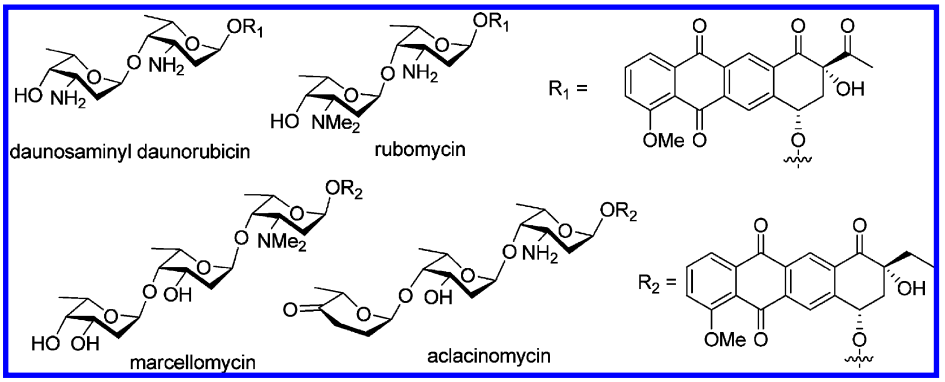


Figure 1. Anthracycline antibiotics containing 3-amino-2,3-dideoxy di- and trisaccharides.

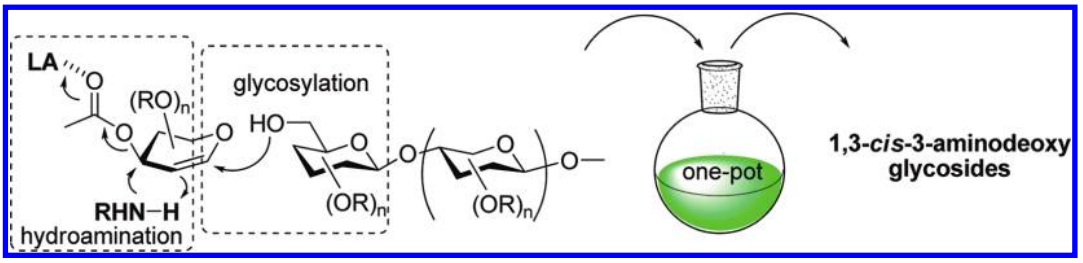
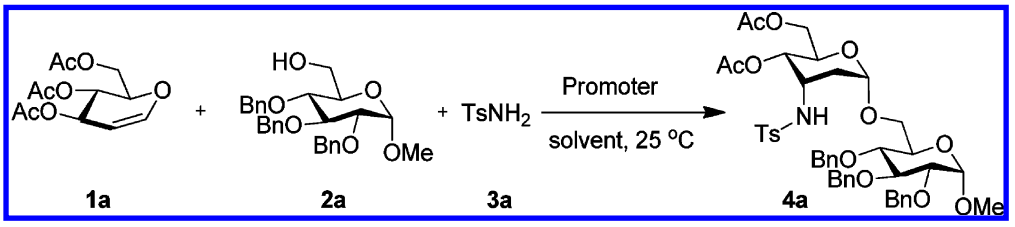


Figure 2. Quick access to 1,3-*cis*-3-arylsulphonaminodeoxyglycosides via regio- and stereoselective tandem hydroamination/glycosylation of glycols.

Table 1. Optimization of Reaction Conditions for Selective Formation of 1,3-*cis*-3-Arylsulphonaminodeoxydisaccharides[a]



entry	promoter (equiv)	solvent	yield (%)[b]
1	$BF_3{\cdot}OEt_2$ (1.1)	DCE	19
2	TMSOTf (2.2)	DCE	trace
3	$SnCl_4$ (2.2)	DCE	trace
4	TsOH (2.2)	DCE	–[c]
5	$Cu(OTf)_2$ (2.2)	DCE	–
6	$BF_3{\cdot}OEt_2$ (2.2)	DCE	68
7	$BF_3{\cdot}OEt_2$ (2.2)	toluene	61
8	$BF_3{\cdot}OEt_2$ (2.2)	THF	n.r.[d]
9	$BF_3{\cdot}OEt_2$ (2.2)	MeCN	26

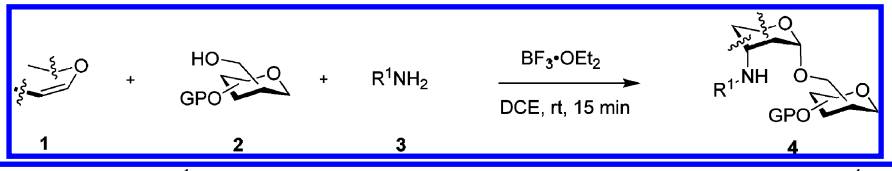
[a]Reaction conditions: donor **1a** (1 equiv), acceptor **2a** (1.1 equiv), and $TsNH_2$ **3a** (1.1 equiv) were mixed together in 2 mL/0.1 mmol of solvent under N_2 atmosphere, and finally promoter was added, 25 °C, 15 min. [b]Isolated yield. [c]Complex mixture. [d]No reaction.

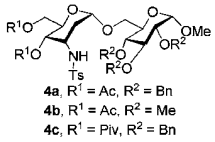
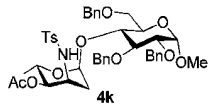
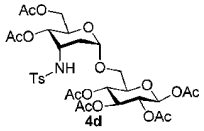
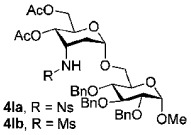
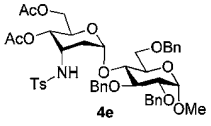
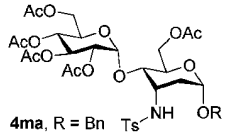
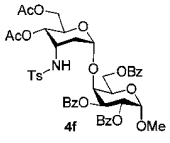
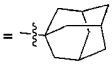
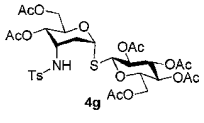
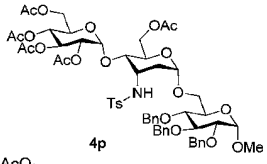
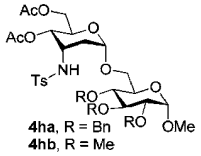
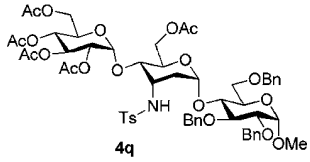
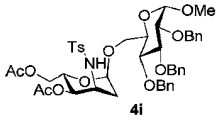
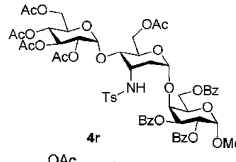
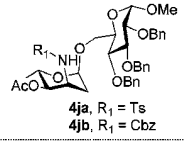
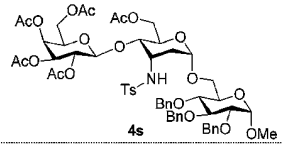
in 1,2-dichloroethane (DCE) at room temperature for 15 min provided the desired 1,3-*cis*-3-tosylaminodeoxydisaccharide **4a** in 19% yield (Table 1, entry 1). The structural and stereochemical characterization of **4a** was determined by extensive NMR studies (^1H NMR, ^{13}C NMR, COSY, HMQC, HMBC, NOESY, see the Supporting Information). Although the glycosylation reaction resulted in poor yield, the desired disaccharide **4a** was isolated with exclusive α-selectivity. Further optimization revealed that an increase in promoter loading (2.2 equiv) led to an increase in the yield of **4a** to 68% (Table 1, entry 6). In addition, trace amount of the desired disaccharide **4a** was detected when the model glycosylation reaction was conducted in the presence of stronger Lewis acids such as TMSOTf (2.2 equiv) and $SnCl_4$ (2.2 equiv). On the other hand, the use of Lewis acid $Cu(OTf)_2$ as the glycosylation promoter did not result in the desired product (Table 1, entries 2, 3, and 5). Furthermore, a complex mixture of products was obtained in the presence of 2.2 equiv of strong Brönsted acid TfOH (Table 1, entry 4). Solvent screening demonstrated that DCE was the optimal solvent for the effective assembly of glycosidic linkage via this one-pot strategy (Table 1, entries 6–9). These results indicated that the optimal condition is employing 2.2 equiv of $BF_3{\cdot}OEt_2$ with anhydrous DCE as solvent at room temperature for 15 min. It is noteworthy that the present one-pot methodology is operationally simple, and more importantly, the product in all cases was obtained as a pure diastereomer.

With the optimized condition in hand, we investigated versatility of the method by preparation of α-linked deoxyglycosides composing of various *N*-protected 2,3-dideoxy- and 2,3,6-

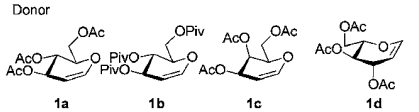
dx.doi.org/10.1021/jo300791v | J. Org. Chem. 2012, 77, 5245–5254

Table 2. Substrate Scope Studies for BF_3·OEt_2-Promoted Three-Component α-Selective Glycosylation[a]

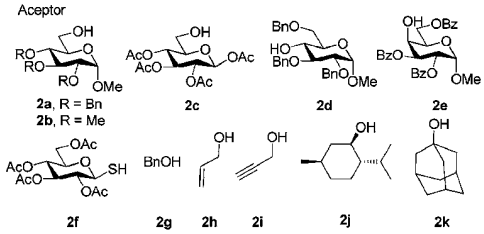


Entry	1	2	3	Product[b]	Yield(%)[c]	Entry	1	2	3	Product[b]	Yield(%)[c]
1	1a 1a 1b	2a 2b 2a	3a	 **4a**, R^1 = Ac, R^2 = Bn **4b**, R^1 = Ac, R^2 = Me **4c**, R^1 = Piv, R^2 = Bn	68 (**4a**) 69 (**4b**) 59 (**4c**)	9	1e	2d	3a	 **4k**	58
2	1a	2c	3a	 **4d**	86	10	1a	2a	3b 3c	 **4la**, R = Ns **4lb**, R = Ms	69 (**4la**) 61 (**4lb**)
3	1a	2d	3a	 **4e**	54			2g 2h		 **4ma**, R = Bn **4mb**, R = All **4mc**, R = Propargyl	71 (**4ma**) 62 (**4mb**) 67 (**4mc**)
4	1a	2e	3a	 **4f**	47	11	1f	2i 2j 2k	3a	**4n** R =  **4o** R = 	55 (**4n**) 48 (**4o**)
5	1a	2f	3a	 **4g**	53	12	1f	2a	3a	 **4p**	46
6	1c	2a 2b	3a	 **4ha**, R = Bn **4hb**, R = Me	51 (**4ha**) 56 (**4hb**)	13	1f	2d	3a	 **4q**	44
7	1d	2a	3a	 **4i**	81	14	1f	2e	3a	 **4r**	43
8	1e	2a	3a 3d	 **4ja**, R_1 = Ts **4jb**, R_1 = Cbz	75 (**4ja**) 64 (**4jb**)	15	1g	2a	3a	 **4s**	54

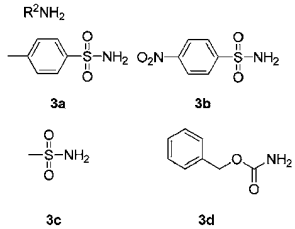
Donor



Aceptor



R^2NH_2



[a]Reaction conditions: donor **1** (1 equiv), acceptor **2** (1.1 equiv), and **3** (1.1 equiv) were mixed together in 2 mL/0.1 mmol of DCE under N_2 atmosphere, and finally BF_3·OEt_2 (2.2 equiv) was added, 25 °C, 15 min. [b]All products were characterized by ^{1}H NMR, ^{13}C NMR, IR, and HRMS. [c]Isolated yield.

trideoxy-1,3-*cis*-3- aminodisaccharides and oligosaccharides **4a**–**4s** (Table 2). We found that a combination of 2D NMR spectroscopy methods such as COSY, HMQC, HMBC, NOESY (see the Supporting Information) is critical in

dx.doi.org/10.1021/jo300791v | J. Org. Chem. 2012, 77, 5245–5254

determining the structural and stereochemical outcome of the reaction. For example, the structure of product **4b** as shown in Figure 3 was analyzed from the result of such NMR studies. On

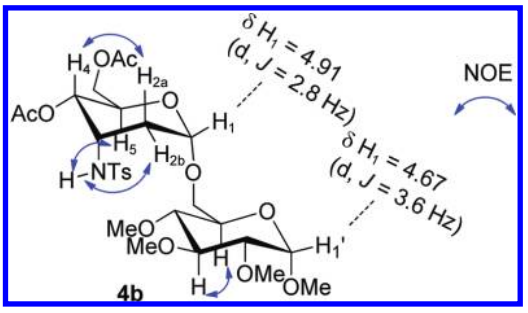
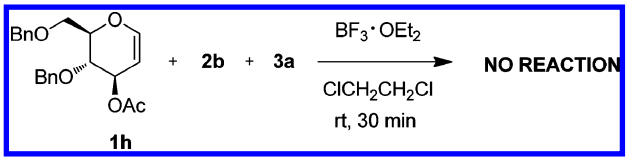


Figure 3. Selected data of ^{1}H NMR and NOESY for 1,3-*cis*-3-tosylaminodeoxydisaccharide **4b**.

the basis of the COSY spectrum, we were able to assign each individual peak to the corresponding protons of the product. Appearance of small coupling constants J_{H1-H2} of 2.8 Hz for anomeric proton H-1 signal at δ 4.91 in ^{1}H NMR is diagnostic for α-linked glycosides. NOESY experiments further confirmed the stereochemical assignment at C1 and C3 position on the basis of observed correlation for N−H/H-5 and H-2a/H-4. In contrast, no correlation was observed in the signals for H-1/N−H or H-1/H-3. These results indicated that the newly introduced sulfonamido group and glycosyl acceptor are in *cis* configuration and the α-glycosyl linkage was formed.

The glycosylation of glucosides **2b** and **2c**, which possess free hydroxyl groups at C6 position, with 3,4,6-*tri*-*O*-acetyl-D-glucal (**1a**) and *p*-toluenesulfonamide (**3a**) under the optimized condition afforded the corresponding 1,3-*cis*-3-tosylamino-2,3-deoxydisaccharides **4b** and **4c** in 69 and 86% yield, respectively (Table 2, entries 1, 2). Pivaloyl protected glycals also gave the desired product **4c** in moderate yield under standard conditions. The possibility of secondary alcohol as viable nucleophilic glycosyl acceptor was also investigated. Accordingly, glycosylation of glycosides **2d** and **2e** possessing hydroxyl groups at C4 with glucal donor (**1a**) and *p*-toluenesulfonamide provided disaccharides **4e** and **4f** as pure α-isomers in poor yields (Table 2, entries 3, 4). When glucose thiol **2f** was employed as the glycosyl acceptor, the corresponding *S*-linked deoxyglycoside **4g** was obtained in slightly lower yield (Table 2, entry 5). Importantly, the α-linked 3-arylsulphonamino-2,3-deoxydisaccharides did not decompose under the reaction conditions. In our protocol, we found that aromatic and aliphatic sulfonamides such as $TsNH_2$, $NsNH_2$, and $MsNH_2$ worked particularly well for this reaction and provided the corresponding products in good yields and are anomerically pure (Table 2, entry 10). In the same manner, the reaction with benzyl carbamate ($CbzNH_2$) proceeded smoothly to afford the corresponding 3-benzyloxycarbonylamino-2,3-dideoxydisaccharide **4t** in moderate yields (Table 2, entry 8). Hydrogenolysis of the benzyloxycarbonyl (Cbz) group in the resulting product is expected to liberate the amino group.[9b] For example, removal of the acetyl group by treating 3-benzyloxycarbonylamino-2,3-dideoxydisaccharide **4jb** with NaOMe in methanol, followed by direct removal of the Cbz group through treatment with Pd/C under H_2 provided 3-amino-2,3-deoxydisaccharide **6** in 74% with exclusive stereo- and regioselection (Scheme 1). We next examined the glycosylation of **2a** with a variety of glycosyl donors **1c**−**1e** under $BF_3{\cdot}OEt_2$-mediated conditions. All the reactions afforded the expected arylsulphonaminodeoxydisaccharides **4h**−**4k** in moderate to good yields with exclusive α-selectivity (Table 2, entries 6−9). Similarly, *N*-protected 3-amino-2,3-dideoxydisaccharides **4ma** and **4mb** were prepared by the treatment of disaccharides donor **1e** with nucleophiles **2g** and **2h** bearing primary hydroxyl moieties (Table 2, entry 11). With this expedient protocol, we synthesized L-menthol glucoside **4n** in 55% yield (Table 2, entry 11), which exemplifies a common 3-arylsulphonamino-2,3-dideoxydisaccharide motif appended to biologically important natural products. To demonstrate that the current method can be employed for oligosaccharide synthesis, a number of deoxytrisaccharides **4p**−**4s** were prepared from disaccharide donors hex-*O*-acetyl-D-maltal (**1f**), hex-*O*-acetyl-D-lactal (**1g**), and acceptors (Table 2, entries 12−15). Further exploration revealed that a more armed donor **1h** in which the hydroxyl group at C-4 and C-6 was protected by benzyl group failed to provide the desired *N*-protected 1,3-*cis*-3-aminodisaccharide (Scheme 2). To the best of our knowledge, the $BF_3{\cdot}OEt_2$-

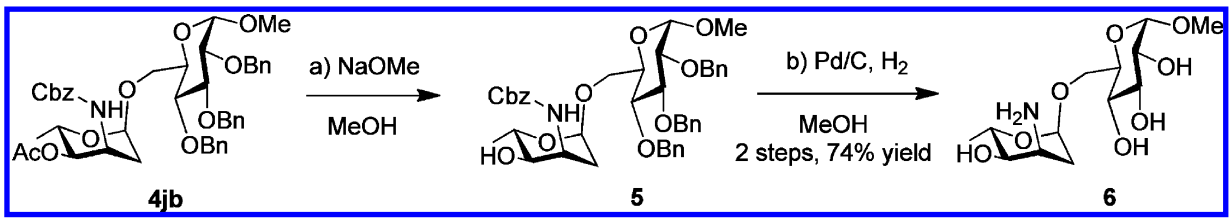
Scheme 2. Three-Component Reaction with More Armed Donor 1h



promoted one-pot α-selective tandem hydroamination/glycosylation is the first example of a direct and stereoselective synthesis of *N*-protected 2,3-dideoxy- or 2,3,6-trideoxy-1,3-*cis*-3-aminodisaccharides and oligosaccharides.

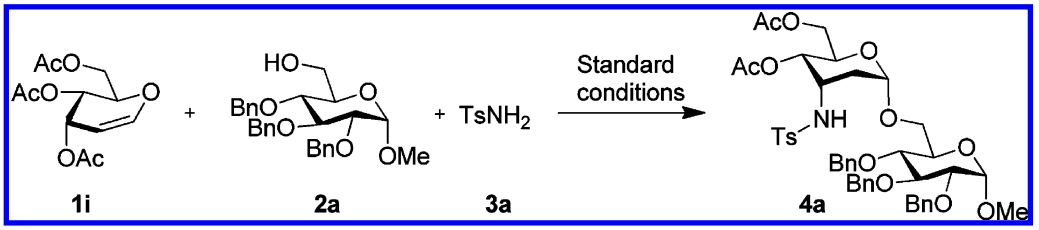
In our initial attempt to probe the reaction mechanism, we found that when C-3 epimer of 3,4,6-*tri*-*O*-acetyl-D-glucal **1i** was reacted under the same reaction conditions, the disaccharide formed was of the same configuration as that obtained from the corresponding D-glucal in 64% yield (Scheme 3). This observation implies that both acetyl protected D-glucal and its epimer led to a common reactive intermediate that eventually converged to the resulting

Scheme 1. Deprotection of 3-Benzyloxycarbonylamino-2,3-dideoxydisaccharide 4jb to Synthesize 3-Amino-2,3-dideoxydisaccharide 6

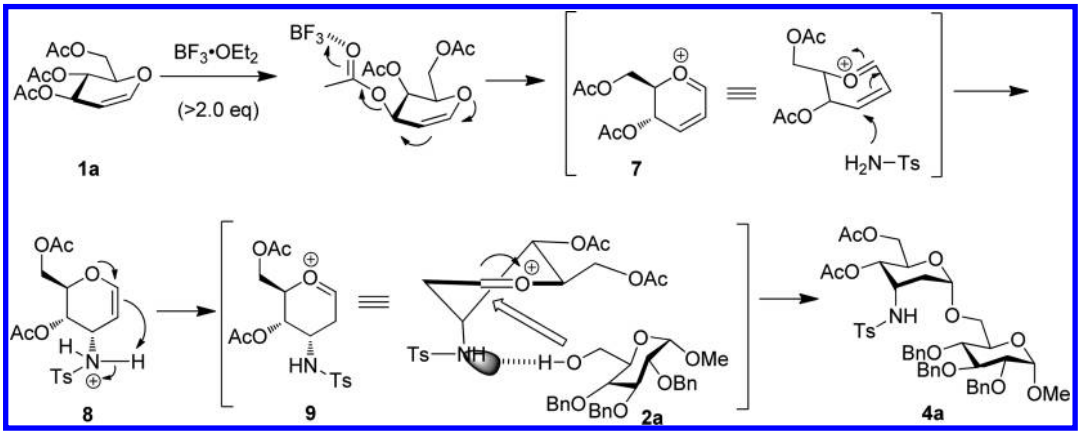


dx.doi.org/10.1021/jo300791v | J. Org. Chem. 2012, 77, 5245−5254

Scheme 3. Three-Component Reaction with More Armed Donor 1i



Scheme 4. Proposed Reaction Mechanism



disaccharide. The use of $TMSN_3$, which lacks acidic hydrogen, did not result in desired product formation. Additionally, when secondary sulfonamide ($TsNHCH_3$) was employed as one of the nucleophiles, no desired disaccharide was obtained as well.

The diastereofacial selectivities observed in the absence of a directing group at C2 position is novel and prompted us to look into the mechanistic cause. Though a detailed mechanism of the present protocol still awaits further studies, a plausible pathway is postulated (Scheme 4). One possibility is that the reaction proceeds through allyloxocarbenium ion intermediate **7**. Preferential attack of *N*-nucleophile occurs from stereoelectronically favored α face of the presumably almost planar conformation of the allyloxocarbenium intermediate to generate **8**. Rapid proton transfer follows to generate the corresponding oxocarbenium ion. Subsequently, nucleophilic addition of carbohydrate oxygen or sulfur nucleophiles to the oxonium ion proceeds readily to furnish the desired product with high stereo- and regioselectivity. The observed α-anomeric selectivity can reasonably be explained by considering addition of O-nucleophile to the stereoelectronically preferred face of the more stable conformer.[10] The facial selectivity might be further reinforced by possible effective coordination (hydrogen bonding) between the nitrogen and the incoming *O*-nucleophile (ROH) as shown in structure **9**.[9,11] In this way, the carbohydrate alcohol or thiol is directed to attack pseudoaxially from the same face of the oxocarbenium ion on the C1 carbon to furnish the thermodynamically favored 1,3-*cis* α-isomer.

CONCLUSION

In conclusion, we have described a highly efficient direct and stereoselective one-pot procedure for assembly of *N*-protected 1,3-*cis*-3-aminodeoxydisaccharides and oligosaccharides via $BF_3{\cdot}OEt_2$-promoted hydroamination and α-selective glycosylation on glycal scaffold. This multicomponent reaction protocol offers simplicity over the conventional indirect method and the exclusive stereoselectivity facilitated the purification to a great extent. Additionally, the method works with a broad range of disarmed sugars, and primary amines make derivatization possible. Because of the aforementioned advantages, the present methodology is believed to be able to find broad applications in glycochemistry.

EXPERIMENTAL SECTION

General Experimental Procedures. All solvents were distilled under nitrogen from the following drying agents immediately before use: tetrahydrofuran (THF) was distilled from sodium/benzophenone ketyl; dichloromethane and 1,2-dichloroethane were distilled from calcium hydride. $BF_3{\cdot}OEt_2$ was distilled from calcium hydride before use. The 3,4-di-*O*-acetyl-6-deoxy-L-glucal (**1a**), glycosyl acceptor **2e**, **2g**−**2k**, and *N*-containing nucleophiles **3a**−**3d** were purchased from commercial suppliers and used without further purification. Glycosyl acceptor **1b**−**1i** and glycosyl acceptor **2a**−**2d**, **2f** were prepared according to literature reported procedure.[12] The promoters were purchased from commercial suppliers and used without further purification. Analytical thin layer chromatography (TLC) was performed using precoated silica gel plate. Visualization was achieved by UV light (254 nm) and/or $KMnO_4$ stain. Flash chromatography was performed using silica gel and a gradient solvent system (EtOAc/hexane as eluent). NMR spectra were recorded at room temperature on Bruker ACF 300, Bruker DPX 400, Bruker AMX 500, and JEOL ECA 400 NMR spectrometers. Chemical shifts (ppm) were recorded with tetramethylsilane (TMS) as the internal reference standard. Multiplicities are given as follows: s (singlet), bs (broad singlet), d (doublet), t (triplet), dd (doublet of doublets), or m (multiplet). The number of protons (*n*) for a given resonance is indicated by *n*H, and coupling constants are reported in Hz. High resolution mass spectra (HRMS) were recorded on Waters Q-Tof premier mass spectrometer.

General Procedure for Synthesis of 1,3-*cis*-3-Arylsulphonaminodeoxydisaccharides and Oligosaccharides 4. To a solution of glycosyl donor **1** (0.1 mmol, 1.0 equiv) and nitrogen nucleophiles **3** (1.1 equiv) in DCE (2 mL, dry) was added glycosyl acceptor **2** (1.1 equiv) under N_2 atmosphere. $BF_3{\cdot}OEt_2$ (2.2 equiv) was then added to this mixture. The reaction mixture was stirred for 15 min at room temperature, quenched with saturated $NaHCO_3$ (3 mL) and

dx.doi.org/10.1021/jo300791v | J. Org. Chem. 2012, 77, 5245−5254

subsequently extracted with CH_2Cl_2 (3 × 5 mL). The extract was dried and concentrated. The residue was subjected to column chromatography (silica gel, hexane/EtOAc) to obtain pure 1,3-*cis*-3-arylsulphonaminodeoxydisaccharides or oligosaccharides **4**.

Characterization of 1,3-*cis*-3-Tosylaminodeoxydisaccharide (4a). Compound **4a** (gummy liquid, 57 mg, 68% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^{D}_{20}$ = +45.2 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (d, *J* = 8.4 Hz, 2H), 7.23−7.39 (m, 17H), 6.08 (d, *J* = 9.2 Hz, 1H), 5.02 (d, *J* = 11.2 Hz, 1H), 4.95 (d, *J* = 10.8 Hz, 1H), 4.77−4.84 (m, 3H), 4.69−4.74 (m,2H), 4.62 (dd, *J* = 10.4, 3.6 Hz, 1H), 4.56 (d, *J* = 11.2 Hz, 1H), 4.26 (dd, *J* = 13.6, 4.8 Hz, 1H), 4.15 (m, 2H), 4.05 (t, *J* = 9.2 Hz, 1H), 3.81−3.91 (m, 1H), 3.70−3.75 (m, 1H), 3.72 (m, *J* = 11.2, 4.4 Hz, 1H), 3.55−3.58 (m, 2H), 3.46 (s, 3H), 3.34 (t, *J* = 9.2 Hz, 1H), 2.39 (s, 3H), 2.07 (s, 3H), 2.02 (s, 3H), 1.80 (td, *J* = 10.4, 3.6 Hz, 1H), 1.52 (dd, *J* = 9.6, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 170.5, 143.3, 138.6, 138.1, 138.0, 137.9, 129.8, 128.5, 128.4, 128.3, 128.1, 128.01, 127.95, 127.92, 127.8, 127.7, 126.8, 97.9, 97.2, 81.8, 80.0, 78.6, 75.8, 75.3, 73.3, 69.3, 67.2, 66.8, 64.5, 62.6, 55.6, 47.9, 32.6, 21.5, 21.0, 20.8; IR ($CHCl_3$) 3426, 3024, 2932, 1744, 1643, 1450, 1366, 1242, 1157, 1057, 756 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{45}H_{53}NO_{13}SNa$ 870.3142, found 870.3135.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4b). Compound **4b** (gummy liquid, 43 mg, 69% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2b** (26 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^{D}_{20}$ = +46.3 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.11 (d, *J* = 8.8 Hz, 1H), 4.91 (d, *J* = 2.8 Hz, 1H), 4.87 (d, *J* = 3.6 Hz, 1H), 4.65 (dd, *J* = 10.4, 3.6 Hz, 1H), 4.21−4.33 (m, 3H), 3.90−3.93 (m, 1H), 3.79 (dd, *J* = 10.0, 6.4 Hz, 1H), 3.68−3.72 (m, 1H), 3.64 (s, 3H), 3.62−3.53 (m, 1H), 3.57 (s, 3H), 3.50−3.53 (m, 1H), 3.55 (s, 3H), 3.47 (s, 3H), 3.19 (dd, *J* = 9.6, 3.6 Hz, 1H), 2.97 (t, *J* = 9.2 Hz, 1H), 2.42 (s, 3H), 2.08 (s, 3H), 2.02 (s, 3H), 1.82 (dt, *J* = 14.8, 3.6 Hz, 1H), 1.52 (dd, *J* = 14.8, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 170.5, 143.3, 138.1, 129.8, 126.8, 97.3, 97.2, 83.3, 81.8, 80.4, 69.4, 67.0, 66.9, 64.5, 62.7, 60.9, 60.7, 59.0, 55.5, 48.0, 32.6, 21.5, 21.05, 20.8; IR ($CHCl_3$) 3426, 2947, 2839, 1744, 1643, 1342, 1242, 1157, 1096, 1049, 903, 579 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{41}NO_{13}SNa$ 642.2198, found 642.2196.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4c). Compound **4c** (gummy liquid, 54 mg, 59% yield) was prepared according to the general procedure from glycosyl donor **1b** (40 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^{D}_{20}$ = +55.2 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.65 (d, *J* = 8.0 Hz, 2H), 7.28−7.37 (m, 15H), 7.22 (d, *J* = 8.0 Hz, 2H), 5.95 (d, *J* = 9.2 Hz, 1H), 5.02 (d, *J* = 10.8 Hz, 1H), 4.95 (d, *J* = 11.2 Hz, 1H), 4.77−4.84 (m, 3H), 4.69−4.72 (m, 2H), 4.54 (d, *J* = 11.2 Hz, 1H), 3.94−3.96 (m, 1H), 3.84 (t, *J* = 8.0 Hz, 1H), 3.73 (dd, *J* = 10.4, 6.8 Hz, 1H), 3.57 (d, *J* = 10.4 Hz, 1H), 3.51 (dd, *J* = 10.0, 3.6 Hz, 1H), 3.46 (s, 3H), 3.30 (t, *J* = 9.6 Hz, 1H), 2.38 (s, 3H), 1.71 (dt, *J* = 14.8, 3.6 Hz, 1H), 1.33 (dd, *J* = 14.4, 2.4 Hz, 1H), 1.25 (s, 9H), 1.17 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 178.0, 177.6, 143.2, 138.6, 138.5, 138.0, 137.9, 129.8, 128.5, 128.4, 128.0, 127.9, 127.8, 127.7, 127.6, 127.2, 127.1, 126.7, 97.9, 97.3, 81.8, 80.0, 78.6, 75.8, 75.3, 73.3, 69.7, 67.1, 66.9, 64.7, 62.7, 55.7, 48.4, 38.9, 32.4, 27.2, 27.0, 21.5, 14.2; IR ($CHCl_3$) 3419, 2972, 1732, 1629, 1454, 1346, 1284, 1165, 1091, 981, 752, 667 cm^{-1}; HRMS (ESI) *m*/*z* [M + H]$^+$ calcd for $C_{51}H_{66}NO_{13}S$ 932.4255, found 932.4238.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4d). Compound **4d** (gummy liquid, 63 mg, 86% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2c** (39 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^{D}_{20}$ = +81.5 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 6.34 (d, *J* = 3.6 Hz, 1H), 6.07 (d, *J* = 9.6 Hz, 1H), 5.54 (d, *J* = 10.0 Hz, 1H), 5.13 (d, *J* = 9.6 Hz, 1H), 5.03 (dd, *J* = 10.4, 3.6 Hz, 1H), 4.86 (d, *J* = 3.2 Hz, 1H), 4.64 (dd, *J* = 10.4, 4.0 Hz, 1H), 4.08−4.17 (m, 4H), 3.93−3.97 (m, 1H), 3.59 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.57 (dd, *J* = 12.0, 2.0 Hz, 1H), 2.43 (s, 3H), 2.19 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 1.99 (s, 3H), 1.80 (dt, *J* = 14.8, 4.0 Hz, 1H), 1.55 (dd, *J* = 14.4, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 170.4, 170.1, 169.8, 169.6, 169.0, 143.2, 138.5, 129.7, 126.9, 97.6, 88.9, 71.0, 69.5, 69.4, 68.2, 66.9, 64.9, 64.5, 62.7, 47.9, 32.9, 21.5, 20.9, 20.85, 20.79, 20.7, 20.67, 20.5; IR ($CHCl_3$) 3317, 2947, 1751, 1435, 1373, 1219, 1157, 1041, 933, 756, 671, 601, 547 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{31}H_{41}NO_{17}SNa$ 754.1951, found 754.1954.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4e). Compound **4e** (gummy liquid, 46 mg, 54% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2d** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^{D}_{20}$ = +34.3 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, *J* = 8.8 Hz, 2H), 7.29−7.38 (m, 12H), 7.22−7.25 (m, 3H),7.02−7.04 (m, 2H), 5.89 (d, *J* = 11.2 Hz, 1H), 5.25 (d, *J* = 3.6 Hz, 1H), 4.96 (d, *J* = 11.2 Hz, 1H), 4.72 (d, *J* = 8.8 Hz, 1H), 4.69 (d, *J* = 9.2 Hz, 1H) 4.58−4.62 (m, 3H), 4.50 (dd, *J* = 8.4, 3.6 Hz, 1H), 4.26 (d, *J* = 11.2 Hz, 1H), 4.08 (dd, *J* = 12.0, 4,4 Hz, 1H), 3.98−4.02 (m, 1H), 3.77−3.89 (m, 4H), 3.56−3.69 (m, 3H), 3.50 (dd, *J* = 8.4, 3.6 Hz, 1H), 3.45 (s, 3H), 2.38 (s, 3H), 2.09 (s, 3H), 1.98 (s, 3H), 1.51 (dt, *J* = 14.8, 4.0 Hz, 1H), 1.20 (dd, *J* = 14.4, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.3, 143.4, 138.3, 138.1, 137.7, 137.6, 129.8, 128.6, 128.5, 128.4, 128.2, 128.1, 127.9, 127.8, 127.7, 127.4, 126.9, 98.7, 97.7, 82.3, 80.1, 77.2, 75.5, 73.5, 73.2, 69.7, 69.1, 67.0, 64.8, 62.7, 55.6, 47.7, 32.8, 21.5, 21.0, 20.8; IR ($CHCl_3$) 3433, 2924, 1743, 1643, 1450, 1357, 1242, 1157, 1049, 910, 740, 548 cm^{-1}; HRMS (ESI) *m*/*z* [M + Na]$^+$ calcd for $C_{45}H_{53}NO_{13}SNa$ 870.3133, found 870.3135.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4f). Compound **4f** (gummy liquid, 43 mg, 47% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2e** (56 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^{D}_{20}$ = +98.6 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.10 (d, *J* = 7.2 Hz, 2H), 8.00−8.08 (m, 4H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.33−7.46 (m, 11H), 6.03 (d, *J* = 9.2 Hz, 1H), 5.81 (dd, *J* = 11.2, 3.2 Hz, 1H), 5.61 (dd, *J* = 11.2, 3.6 Hz, 1H), 5.33 (d, *J* = 3.6 Hz, 1H), 4.95 (d, *J* = 3.2 Hz, 1H), 4.56 (d, *J* = 3.2 Hz, 1H), 4.49−4.56 (m, 2H), 4.43 (t, *J* = 6.8 Hz, 1H), 4.16−4.21 (m, 2H), 3.95−3.98 (m, 1H), 3.68 (dd, *J* = 9.2, 3.6 Hz, 1H), 3.49 (s, 3H), 3.24 (dd, *J* = 8.4, 3.0 Hz, 1H), 2.43 (s, 3H), 1.98 (s, 3H), 1.90 (s, 3H), 1.80 (dt, *J* = 14.8, 3.6 Hz, 1H), 1.62 (dd, *J* = 14.8, 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 170.2, 166.0, 165.8, 143.4, 138.4, 133.7, 133.6, 133.3, 130.0, 129.7, 129.6, 129.3, 129.2, 128.8, 128.7, 128.6, 128.5, 128.4, 127.0, 126.9, 98.0, 97.5, 73.9, 69.4, 68.8, 67.6, 66.5, 64.9, 62.3, 61.9, 55.8, 47.7, 32.7, 21.6, 20.9, 20.6; IR ($CHCl_3$) 3333, 3063, 2955, 1728, 1450, 1265, 1111, 1057, 710 cm^{-1}; HRMS (ESI) *m*/*z* [M + H]$^+$ calcd for $C_{45}H_{47}NO_{16}SNa$ 912.2505, found 912.2513.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4g). Compound **4g** (gummy liquid, 40 mg, 53% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2f** (40 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^{D}_{20}$ = −1.5 (*c* 0.5 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.0 Hz, 2H), 5.68 (d, *J* = 10.0 Hz, 1H), 5.21 (t, *J* = 9.2 Hz, 1H), 5.05 (t, *J* = 10.0 Hz, 1H), 4.96 (t, *J* = 9.2 Hz, 1H), 4.86 (td, *J* = 10.8, 2.0 Hz, 1H), 4.68−4.73 (m, 2H), 4.27 (dd, *J* = 8.4, 4.8 Hz, 1H), 4.16 (dd, *J* = 12.4, 2.0 Hz, 1H), 4.05 (dd, *J* = 12.4, 4.8 Hz, 1H), 3.78 (dd, *J* = 12.4, 2.4 Hz, 1H), 3.68 (dq, *J* = 10.0, 2.0 Hz, 1H), 3.54 (dq, *J* = 8.8, 1.6 Hz, 1H), 3.05 (td, *J* = 12.0, 4.0 Hz, 1H), 2.42 (s, 3H), 2.39−2.41 (m, 1H), 2.06 (s, 3H), 2.05 (s, 6H), 2.03 (s, 3H), 2.01 (s, 3H), 2.00 (s,3H), 1.92−1.95 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 170.5,

dx.doi.org/10.1021/jo300791v | *J. Org. Chem.* 2012, 77, 5245−5254

170.1, 169.7, 169.4, 169.2, 143.6, 138.5, 129.4, 127.2, 81.7, 81.3, 77.2, 76.0, 75.8, 73.8, 70.0, 68.3, 66.7, 62.6, 61.9, 44.5, 39.6, 21.5, 20.83, 20.76, 20.62, 20.59, 20.55; IR ($CHCl_3$) 3271, 2955, 1744, 1435, 1373, 1335, 1157, 1041, 910, 817, 756, 671, 586 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{31}H_{41}NO_{16}S_2Na$ 770.1764, found 770.1764.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4ha). Compound **4ha** (gummy liquid, 32 mg, 51% yield) was prepared according to the general procedure from glycosyl donor **1c** (27.2 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +40.9 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, J = 8.0 Hz, 2H), 7.31 (d, J = 8.0 Hz, 2H), 6.23 (d, J = 8.4 Hz, 1H), 4.96 (d, J = 2.8 Hz, 1H), 4.89 (d, J = 3.6 Hz, 1H), 4.76 (d, J = 2.4 Hz, 1H), 4.30 (t, J = 6.4 Hz, 1H), 4.04−4.07 (m, 2H), 3.72−3.80 (m, 2H), 3.65−3.64 (m, 1H), 3.63 (s, 3H), 3.59−3.56 (m, 1H), 3.57 (s, 3H), 3.54 (s, 3H), 3.53−3.50 (m, 1H), 3.49 (s, 3H), 3.22 (dd, J = 9.6, 3.6 Hz, 1H), 2.98 (t, J = 9.2 Hz, 1H), 2.42 (s, 3H), 2.07 (s, 3H), 2.03 (s, 3H), 1.99−2.03 (m, 1H), 1.52 (d, J = 14.8, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.3, 169.5, 143.4, 138.0, 129.8, 127.0, 97.4, 97.0, 83.3, 81.9, 80.6, 77.2, 69.2, 67.8, 66.9, 63.4, 62.9, 60.9, 60.6, 59.0, 55.6, 47.6, 28.5, 21.5, 20.8; IR ($CHCl_3$) 3310, 2932, 2832, 1744, 1373, 1335, 1227, 1157, 1096, 1049 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{27}H_{41}NO_{13}SNa$ 642.2195, found 642.2196.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4hb). Compound **4hb** (gummy liquid, 47 mg, 56% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2b** (26 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +29.3 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.72 (d, J = 8.4 Hz, 2H), 7.27−7.40 (m, 14H), 7.23−7.26 (m, 3H), 6.21 (d, J = 8.4 Hz, 2H), 5.02 (d, J = 10.8 Hz, 1H), 4.95 (d, J = 11.2 Hz, 1H), 4.89 (d, J = 2.8 Hz, 1H), 4.78−4.83 (m, 2H), 4.70−4.76 (m, 2H), 4.56 (d, J = 11.2 Hz, 1H), 4.24 (t, J = 6.0 Hz, 1H), 3.94−4.08 (m, 3H), 3.87 (td, J = 9.2, 3.6 Hz, 1H), 3.71 (dd, J = 10.4, 6.8 Hz, 1H), 3.56−3.64 (m, 3H), 3.48 (s, 3H), 3.32−3.37 (m, 1H), 2.40 (s, 3H), 2.06 (s, 3H), 1.96−2.01 (m, 1H), 1.92 (s, 3H), 1.50 (d, J = 14.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.4, 169.5, 143.4, 138.6, 138.04, 138.02, 137.97, 129.8, 128.51, 128.48, 128.46, 128.11, 128.05, 127.95, 127.88, 127.71, 127.68, 127.0, 97.9, 97.0, 81.8, 80.0, 78.7, 75.8, 75.2, 73.2, 69.3, 67.7, 66.9, 66.3, 62.8, 55.7, 47.6, 28.4, 21.5, 20.8, 20.7; IR ($CHCl_3$) 3317, 2916, 1744, 1405, 1427, 1366, 1227, 1157, 1087, 1049, 740, 702, 548 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{45}H_{53}NO_{13}SNa$ 870.3144, found 870.3135.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4i). Compound **4i** (gummy liquid, 69 mg, 81% yield) was prepared according to the general procedure from glycosyl donor **1d** (27.2 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +9.0 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.69 (d, J = 8.4 Hz, 2H), 7.11−7.41 (m, 17H), 6.27 (d, J = 9.6 Hz, 1H), 5.07 (d, J = 10.8 Hz, 1H), 4.84 (d, J = 3.2 Hz, 1H), 4.72−4.81 (m, 4H), 4.58 (dd, J = 10.8, 4.0 Hz, 1H), 4.50 (d, J = 11.6 Hz, 1H), 4.35 (d, J = 1.6 Hz, 1H), 4.25 (dd, J = 12.0, 3.6 Hz, 1H), 4.17 (dd, J = 12.0, 2.0 Hz, 1H), 4.01−4.07 (m, 2H), 3.90−3.94 (m, 1H), 3.83 (dd, J = 9.6, 3.2 Hz, 1H), 3.65−3.72 (m, 2H), 3.49 (t, J = 8.8 Hz, 1H), 3.40 (s, 3H), 3.83 (dd, J = 10.0, 3.6 Hz, 1H), 2.35 (s, 3H), 2.08 (s, 3H), 2.04 (s, 3H), 1.61 (td, J = 12.4, 4.0 Hz, 1H), 1.17 (dd, J = 14.4, 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 170.4, 143.0, 139.0, 138.9, 138.2, 138.1, 129.8, 128.3−128.4 (m, 5C), 128.1, 127.8, 127.7, 127.6, 126.6, 98.0, 96.1, 81.9, 80.7, 75.9, 75.5, 74.5, 73.4, 68.6, 66.9, 64.4, 63.9, 62.7, 55.4, 48.1, 32.6, 21.4, 21.0, 20.8; IR ($CHCl_3$) 3479, 3032, 2916, 1744, 1450, 1358, 1258, 1196, 1072, 1026, 741, 694 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{45}H_{53}NO_{13}SNa$ 870.3132, found 870.3135.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4ja). Compound **4ja** (gummy liquid, 59 mg, 75% yield) was prepared according to the general procedure from glycosyl donor **1e** (22 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = −5.28 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.68 (d, J = 8.0 Hz, 2H), 7.32−7.41 (m, 7H), 7.25−7.31 (m, 3H), 7.20−7.22 (m, 3H), 7.12−7.16 (m, 4H), 6.29 (d, J = 9.6 Hz, 1H), 5.07 (d, J = 10.8 Hz, 1H), 4.72−4.81 (m, 5H), 4.49 (d, J = 11.2 Hz, 1H), 4.27−4.31 (m, 2H), 4.04 (t, J = 8.8 Hz, 1H), 3.91−3.98 (m, 1H), 3.80−3.87 (m, 2H), 3.66−3.73 (m, 2H), 3.50 (t, J = 9.6 Hz, 1H), 3.41 (s, 3H), 3.30 (dd, J = 10.0, 2.0 Hz, 1H), 2.34 (s, 3H), 2.08 (s, 3H), 1.59 (dd, J = 14.4, 3.2 Hz, 1H), 1.18 (dd, J = 14.4, 2.4 Hz, 1H), 1.16 (d, J = 6.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.7, 142.9, 139.1, 138.9, 138.2, 138.1, 129.8, 128.3−128.4 (m, 5C), 128.1, 127.8, 127.7, 127.6, 126.7, 98.0, 96.1, 81.9, 80.6, 76.2, 75.6, 74.5, 73.4, 72.6, 68.8, 64.1, 62.0, 55.4, 48.1, 32.9, 21.4, 21.1, 17.4; IR ($CHCl_3$) 3302, 2932, 1736, 1450, 1342, 1234, 1157, 1064, 1026, 987, 910, 817, 748,702, 671 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{43}H_{51}NO_{11}SNa$ 812.3082, found 812.3081.

1,3-*cis*-3-Benzyloxycarbonylaminodeoxydisaccharide (4jb). Compound **4jb** (gummy liquid, 49 mg, 64% yield) was prepared according to the general procedure from glycosyl donor **1e** (22 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and benzyl carbamate **3d** (17 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = −12.2 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.25−7.34 (m, 20H), 6.32 (d, J = 9.6 Hz, 1H), 5.10 (d, J = 12.8 Hz, 1H), 4.87−4.98 (m, 3H), 4.80 (d, J = 9.6 Hz, 1H), 4.43−4.63 (m, 6H), 4.31−4.34 (m, 1H), 3.91−4.01 (m, 2H), 3.83 (dd, J = 2.0, 10.0 Hz, 1H),3.74−3.79 (m, 1H), 3.46−3.52 (m, 2H), 3.38−3.42 (m, 1H), 3.29 (s, 3H), 1.96 (dt, J = 10.8, 3.6 Hz, 1H),1.91 (s, 3H), 1.82 (dd, J = 14.4, 2.0 Hz, 1H), 1.15 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.2, 156.3, 138.7, 138.2, 138.1, 137.1, 128.5, 128.3−124 (m, 4C), 128.1, 128.0, 127.9, 127.89, 127.8, 127.7, 127.66, 98.0, 96.4, 82.1, 80.6, 75.8, 75.0, 73.2, 73.19, 69.5, 66.2, 65.1, 61.7, 55.2, 45.4, 33.4, 20.8, 17.4; IR ($CHCl_3$) 3402, 2931, 1728, 1512, 1430, 1366, 127, 1065, 910, 748 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{44}H_{51}NO_{11}Na$ 792.3356, found 792.3360.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4k). Compound **4k** (gummy liquid, 46 mg, 58% yield) was prepared according to the general procedure from glycosyl donor **1e** (22 mg, 0.1 mmol), glycosyl acceptor **2d** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = −17.8 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.69 (d, J = 7.6 Hz, 2H), 7.43 (d, J = 7.2 Hz, 2H), 7.24−7.33 (m, 15H), 5.84 (d, J = 8.8 Hz, 1H), 5.19 (d, J = 10.8 Hz, 1H), 4.73−4.78 (m, 4H), 4.60−4.63 (m, 4H), 4.35 (d, J = 12.0 Hz, 1H), 4.15 (d, J = 2.4 Hz, 2H), 3.84 (t, J = 8.0 Hz, 1H), 3.60−3.69 (m, 2H), 3.53 (dd, J = 10.8, 2.0 Hz, 1H), 3.43 (dd, J = 10.8, 2.4 Hz, 1H), 3.40 (s, 3H), 2.41 (s, 3H), 1.93 (s, 3H), 1.49 (dt, J = 14.4, 4.0 Hz, 1H), 1.28 (dd, J = 14.0, 2.8 Hz, 1H), 0.67 (d, J = 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 143.4, 138.7, 138.5, 138.0, 137.3, 129.6, 128.5, 128.4, 128.2, 128.14, 128.10, 128.0, 127.9, 127.3, 127.2, 127.0, 98.0, 96.7, 80.8, 79.6, 75.6, 74.2, 73.6, 73.3, 72.6, 70.1, 68.3, 62.2, 55.5, 48.1, 33.4, 21.5, 20.9, 16.8; IR ($CHCl_3$) 3318, 2932, 2862, 1736, 1450, 1342, 1242, 1165, 1096, 1049 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{43}H_{51}NO_{11}SNa$ 812.3073, found 812.3081.

1,3-*cis*-3-Mesylaminodeoxydisaccharide (4la). Compound **4la** (gummy liquid, 60 mg, 69% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-nitrosulfonamide **3b** (23 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +44.0 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.28 (d, J = 8.8 Hz, 2H), 7.94 (d, J = 8.8 Hz, 2H), 7.26−7.39 (m, 15H), 6.38 (d, J = 9.2 Hz, 1H), 5.01 (d, J = 11.2 Hz, 1H), 4.96 (d, J = 11.2 Hz, 1H), 4.86 (d, J = 2.8 Hz, 1H), 4.80−4.83 (m, 2H), 4.63−4.71 (m, 3H), 4.56 (d, J = 8.8 Hz, 1H), 4.25 (dd, J = 12.4, 4.4 Hz, 1H), 4.12−4.17 (m, 2H), 4.06 (t, J = 9.2 Hz, 1H), 3.97−4.00 (m, 1H), 3.83−3.87 (m, 1H), 3.75 (dd, J = 10.4, 6.4 Hz, 1H), 3.60 (dd, J = 10.0, 1.6 Hz, 1H), 3.53 (t, J = 9.6, 3.6 Hz, 1H), 3.44 (s, 3H), 3.34 (t, J = 9.6 Hz, 1H), 2.07 (s, 3H), 2.01 (s, 3H), 1.86 (dt, J = 10.8, 3.6 Hz, 1H), 1.51 (dd, J = 14.4, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.5, 170.3, 150.0, 147.1, 138.5, 138.1 137.9, 128.53, 128.51, 128.47, 128.2, 128.03, 127.96, 127.9, 127.8, 127.69,

dx.doi.org/10.1021/jo300791v | J. Org. Chem. 2012, 77, 5245−5254

124.4, 98.1, 97.1, 81.6, 80.2, 78.6, 77.2, 75.8, 75.2, 73.4, 69.4, 67.2, 66.7, 64.5, 62.5, 55.7, 48.5, 32.7, 20.9, 20.7; IR ($CHCl_3$) 3309, 2932, 1744, 1527, 1350, 1234, 1056, 856, 740, 694, 617 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{44}H_{50}N_2O_{15}SNa$ 901.2827, found 901.2835.

1,3-*cis*-3-Nosylaminodeoxydisaccharide (4lb). Compound **4lb** (gummy liquid, 47 mg, 61% yield) was prepared according to the general procedure from glycosyl donor **1a** (27.2 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and methanesulfonamide **3c** (11 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +47.3 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.26−7.38 (m, 15H), 5.95 (d, *J* = 8.8 Hz, 1H), 4.92−5.01 (m, 2H), 4.68−4.82 (m, 4H), 4.55 (d, *J* = 11.2 Hz, 1H), 4.28 (d, *J* = 12.0, 4.4 Hz, 1H), 4.09−4.16 (m, 2H), 4.03 (t, *J* = 9.2 Hz, 1H), 3.85−3.97 (m, 1H), 3.69 (dd, *J* = 10.4, 7.2 Hz, 1H), 3.62 (dd, *J* = 10.4, 2.4 Hz, 1H), 3.54 (dd, *J* = 9.6, 3.6 Hz, 1H), 3.43 (s, 3), 3.31 (t, *J* = 9.2 Hz, 1H), 2.87 (s, 3H), 2.17 (s, 3H), 2.11 (dt, *J* = 12.0, 4.4 Hz, 1H), 2.09 (s, 3H), 2.04 (s, 3H), 2.00 (dd, *J* = 14.4, 2.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.0, 138.6, 138.1, 138.0, 128.5, 128.4, 128.3, 128.04, 128.0, 127.9, 127.88, 127.7, 127.6, 97.9, 97.0, 81.8, 80.1, 78.7, 75.8, 75.1, 69.3, 67.1, 67.05, 64.5, 62.6, 55.5, 48.5, 41.6, 33.8, 30.9, 21.0, 20.7; IR ($CHCl_3$) 3332, 2924, 1744, 1450, 1365, 1334, 1234, 1149, 1056, 910, 748, 702 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{39}H_{49}NO_{13}SNa$ 794.2825, found 794.2822.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4ma). Compound **4ma** (gummy liquid, 55 mg, 71% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2g** (12 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +105.2 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.64 (d, *J* = 8.4 Hz, 2H), 7.35−7.42 (m, 3H), 7.27−7.29 (m, 4H), 5.85 (d, *J* = 10.0 Hz, 1H), 5.42−5.47 (m, 2H), 5.25 (dd, *J* = 3.6, 10.4 Hz, 1H), 5.11 (t, *J* = 9.6 Hz, 1H), 4.79 (d, *J* = 2.4 Hz, 1H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.49 (dd, *J* = 2.8, 12.0 Hz, 1H), 4.43 (d, *J* = 11.6 Hz, 1H), 4.31 (dd, *J* = 12.0, 4.0 Hz, 1H), 4.19 (dd, *J* = 11.6, 4.0 Hz, 1H), 4.09−4.17 (m, 2H), 3.90−3.97 (m, 2H), 3.75 (dd, *J* = 9.6, 4.0 Hz, 1H), 2.43 (s, 3H), 2.18 (s, 3H), 2.10 (s, 6H), 2.03 (s, 3H), 1.99 (s, 3H), 1.55 (dt, *J* = 14.8, 3.6 Hz, 1H), 1.25 (dd, *J* = 14.8, 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.4, 170.3, 169.9, 169.5, 143.5, 138.3, 136.6, 129.8, 128.7, 128.3, 127.8, 126.8, 96.2, 91.9, 70.1, 69.8, 68.7, 68.5, 68.4, 68.2, 65.8, 63.1, 61.7, 46.3, 31.6, 21.6, 20.9, 20.8, 20.7, 20.63, 20.61; IR ($CHCl_3$) 3302, 3024, 2954, 1751, 1435, 1373, 1334, 1226, 1165, 1041, 910, 756, 671 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{36}H_{45}NO_{16}SNa$ 802.2357, found 802.2359.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4mb). Compound **4mb** (gummy liquid, 45 mg, 62% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2h** (7 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +79.1 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.72 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 5.85−5.91 (m, 2H), 5.44−5.49 (m, 2H), 5.25−5.31 (m, 3H), 5.14 (t, *J* = 9.6 Hz, 1H), 4.78 (d, *J* = 2.4 Hz, 1H), 4.51 (dd, *J* = 12.0, 2.8 Hz, 1H), 4.33 (dd, *J* = 12.0, 4.4 Hz, 1H), 4.18−4.25 (m, 2H), 4.12−4.15 (m, 2H), 3.92−3.99 (m, 3H), 3.76 (dd, *J* = 9.6, 4.0 Hz, 1H), 2.45 (s, 3H), 2.22 (s, 3H), 2.13 (s, 3H), 2.11 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 1.57 (dt, *J* = 14.8, 3.6 Hz, 1H), 1.23−1.29 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.5, 170.3, 170.0, 169.6, 143.6, 138.2, 133.1, 129.9, 126.8, 117.9, 96.3, 91.6, 77.2, 70.0, 68.6, 68.5, 68.4, 68.2, 68.1, 65.5, 63.0, 61.6, 46.2, 31.6, 21.6, 21.0, 20.8, 20.7, 20.6; IR ($CHCl_3$) 3309, 2916, 1751, 1435, 1373, 1334, 1226, 1165, 1041, 910, 817, 756, 678 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{32}H_{43}NO_{16}SNa$ 752.2200, found 752.2197.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4mc). Compound **4mc** (gummy liquid, 49 mg, 67% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2i** (7 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +67.4 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 5.69 (d, *J* = 10.0 Hz, 1H), 5.42−5.46 (m, 1H), 5.24 (dd, *J* = 10.4, 2.4 Hz, 1H), 5.12 (t, *J* = 10.0 Hz, 1H), 4.93 (d, *J* = 1.6 Hz, 1H), 4.47 (dd, *J* = 12.0, 2.4 Hz, 1H), 4.19−4.33 (m, 3H), 4.09−4.17 (m, 4H), 3.95−3.98 (m, 1H), 3.75 (dd, *J* = 9.6, 4.0 Hz, 1H), 2.49 (t, *J* = 2.4 Hz, 1H), 2.43 (s, 3H), 2.20 (s, 3H), 2.11 (s, 3H), 2.09 (s, 3H), 2.04 (s, 3H), 2.00 (s, 3H), 1.61 (dt, *J* = 14.4, 3.6 Hz, 1H), 1.31 (dd, *J* = 14.8, 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.4, 170.3, 170.0, 169.6, 143.6, 138.1, 129.9, 126.8, 95.7, 92.1, 78.2, 75.4, 70.0, 68.6, 68.4, 68.1, 66.1, 62.9, 61.7, 60.4, 54.9, 46.2, 31.5, 21.5, 20.9, 20.8, 20.7, 20.6, 14.2; IR ($CHCl_3$) 3413, 1657, 1542, 1364, 1217, 1154, 1049, 687 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{32}H_{41}NO_{16}SNa$ 750.2044, found 750.2042.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4n). Compound **4n** (gummy liquid, 45 mg, 55% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2j** (18 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +83.4 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 7.6 Hz, 2H), 5.94 (d, *J* = 10.0 Hz, 1H), 5.42−5.48 (m, 2H), 5.27 (dd, *J* = 10.4, 3.6 Hz, 1H), 5.11 (t, *J* = 10.0 Hz, 1H), 4.76 (d, *J* = 2.8 Hz, 1H), 4.45 (dd, *J* = 11.6, 2.4 Hz, 1H), 4.31 (dd, *J* = 11.6, 4.8 Hz, 1H), 4.20−4.29 (m, 1H), 4.17 (d, *J* = 3.6 Hz, 1H), 4.09−4.13 (m, 1H), 3.87−3.93 (m, 2H), 3.69 (dd, *J* = 10.0, 4.0 Hz, 1H), 3.24 (td, *J* = 9.6, 4.0 Hz, 1H), 2.42 (s, 3H), 2.20 (s, 3H), 2.10 (s, 3H), 2.08 (s, 3H), 2.03 (s, 3H), 1.99 (s, 3H), 1.73−1.80 (m, 1H), 1.63−1.67 (m, 2H), 1.48 (dt, *J* = 14.4, 3.6 Hz, 1H), 1.38−1.41 (m, 1H), 1.10−1.28 (m, 4H), 0.85−0.98 (m, 8H), 0.63 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.5, 170.4, 170.0, 169.6, 143.5, 138.2, 129.7, 126.7, 99.1, 91.2, 82.3, 70.0, 68.5, 68.4, 68.1, 68.0, 65.3, 63.3, 61.7, 48.9, 46.1, 43.1, 34.0, 32.0, 31.7, 25.5, 22.8, 22.3, 21.6, 21.4, 21.0, 20.9, 20.7, 20.66, 20.6, 15.8; IR ($CHCl_3$) 3302, 2924, 2870, 1751, 1435, 1373, 1334, 1226, 1165, 1041, 910, 756, 671, 555 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{39}H_{57}NO_{16}SNa$ 850.3309, found 850.3296.

1,3-*cis*-3-Tosylaminodeoxydisaccharide (4o). Compound **4o** (gummy liquid, 40 mg, 48% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2k** (17 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +108.1 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.71 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 6.29 (d, *J* = 9.6 Hz, 1H), 5.44−5.51 (m, 2H), 5.29 (dd, *J* = 10.5, 3.9 Hz, 1H), 5.10−5.17 (m, 2H), 4.43−4.46 (m, 1H), 4.30−4.37 (m, 2H), 4.22 (dd, *J* = 12.6, 1.8 Hz, 1H), 4.11−4.15 (m, 1H), 3.88−3.97 (m, 2H), 3.71 (dd, *J* = 9.6, 3.6 Hz, 1H), 2.45 (s, 3H), 2.23 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 1.61−1.86 (m, 15H), 1.48 (dt, *J* = 14.4, 3.6 Hz, 1H), 0.96−1.05 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.5, 170.4, 170.0, 169.6, 143.4, 138.4, 129.7, 126.8, 91.2, 90.3, 75.9, 70.1, 68.4−68.5 (m, 4C), 68.0, 67.2, 65.4, 62.8, 61.7, 46.3, 42.5, 36.1, 32.3, 30.6, 21.6, 21.0, 20.8, 20.7, 20.6; IR ($CHCl_3$) 3294, 2916, 2854, 1751, 1435, 1372, 1226, 1165, 1041, 756, 678 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{39}H_{53}NO_{16}SNa$ 846.2980, found 846.2983.

1,3-*cis*-3-Tosylaminodeoxytrisaccharide (4p). Compound **4p** (gummy liquid, 52 mg, 46% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +61.6 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, *J* = 8.4 Hz, 2H), 7.28−7.39 (m, 15H), 7.23 (d, *J* = 8.0 Hz, 2H), 5.87 (d, *J* = 11.2 Hz, 1H), 5.43−5.49 (m, 2H), 5.29 (dd, *J* = 12.4, 3.6 Hz, 1H), 5.12 (t, *J* = 9.6 Hz, 1H), 5.04 (d, *J* = 11.2 Hz, 1H), 4.98 (d, *J* = 11.2 Hz, 1H), 4.78−4.86 (m, 2H), 4.70−4.74 (m, 3H), 4.57 (d, *J* = 11.2 Hz, 1H), 4.45 (dd, *J* = 12.4, 4.0 Hz, 1H), 4.19 (dd, *J* = 10.0, 2.4 Hz, 2H), 4.03−4.10 (m, 3H), 3.79−3.92 (m, 3H), 3.70−3.74 (m, 2H), 3.51−3.56 (m, 2H), 3.47 (s, 3H), 3.34 (t, *J* = 8.4 Hz, 1H), 2.39 (s, 3H), 2.17 (s, 3H), 2.10 (s, 3H), 2.03(s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 1.50−1.54 (m, 1H), 1.20−1.25 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.4, 170.2, 170.0, 169.5, 143.5, 138.7, 138.3, 138.0, 129.9, 128.6, 128.5, 128.4, 128.3,

dx.doi.org/10.1021/jo300791v | *J. Org. Chem.* 2012, 77, 5245−5254

128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 126.7, 98.0, 97.2, 91.5, 81.8, 80.1, 78.6, 75.6, 75.3, 73.3, 70.2, 69.6, 68.5, 68.4, 68.0, 67.7, 67.2, 65.4, 62.8, 61.6, 55.8, 46.1, 31.6, 30.9, 21.5, 20.9, 20.8, 20.7, 20.6; IR ($CHCl_3$) 3417, 1751, 1643, 1365, 1226, 1041, 740, 555 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{57}H_{69}NO_{21}SNa$ 1158.3986, found 1158.3981.

1,3-*cis*-3-Tosylaminodeoxytrisaccharide (4q). Compound **4q** (gummy liquid, 50 mg, 44% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2d** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +44.3 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, *J* = 6.8 Hz, 2H), 7.22−7.45 (m, 15H), 7.00 (d, *J* = 6.0 Hz, 2H), 6.21 (d, *J* = 10.0 Hz, 1H), 5.51 (t, *J* = 6.0 Hz, 1H), 5.45 (d, *J* = 4.8 Hz, 1H), 5.26−5.28 (m, 1H), 5.14 (d, *J* = 4.8 Hz, 1H), 5.12 (t, *J* = 9.2 Hz, 1H), 4.88 (d, *J* = 10.8 Hz, 1H), 4.79 (d, *J* = 12.0 Hz, 1H), 4.70 (d, *J* = 12.8 Hz, 1H), 4.57−4.65 (m, 4H), 4.02−4.17 (m, 5H), 3.88−3.91 (m, 2H), 3.37−3.77 (m, 3H), 3.49−3.59 (m, 2H), 3.46 (s, 3H), 2.39 (s, 3H), 2.12 (s, 3H), 2.09 (s, 3H), 2.05 (s, 3H), 2.00 (s, 3H), 1.95−1.98 (m, 4H), 1.11 (d, *J* = 13.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.3, 170.2, 170.0, 169.5, 143.4, 138.9, 137.7, 137.0, 129.9, 128.7, 128.6, 128.4, 128.3, 128.1, 128.2, 127.9, 127.8, 127.7, 127.6, 126.9, 97.8, 97.3, 91.2, 82.7, 79.9, 76.7, 76.5, 75.5, 73.6, 73.3, 70.2, 70.1, 69.0, 68.7, 68.5, 68.1, 68.0, 65.7, 63.0, 61.6, 55.6, 45.6, 31.6, 21.5, 20.8, 20.7, 20.6, 20.5; IR ($CHCl_3$) 3433, 2945, 1746, 1447, 1241, 1040, 765 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{57}H_{69}NO_{21}SNa$ 1158.3975, found 1158.3972.

1,3-*cis*-3-Tosylaminodeoxytrisaccharide (4r). Compound **4r** (gummy liquid, 50 mg, 43% yield) was prepared according to the general procedure from glycosyl donor **1f** (56 mg, 0.1 mmol), glycosyl acceptor **2e** (56 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +104.2 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 8.11 (d, *J* = 7.2 Hz, 2H), 7.99−8.01 (m, 4H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.70−7.72 (m, 1H), 7.45−7.60 (m, 6H), 7.34−7.38 (m, 4H), 5.92−5.96 (m, 2H), 5.55 (dd, *J* = 10.8, 3.6 Hz,1H), 5.46 (d, *J* = 2.0 Hz, 1H), 5.37 (d, *J* = 3.6 Hz, 1H), 5.28−5.30 (m, 2H), 5.08−5.11 (m, 2H), 4.84 (d, *J* = 2.4 Hz, 1H), 4.40−4.48 (m, 3H), 4.23−4.25 (m, 1H), 4.08 (dd, *J* = 10.4, 6.0 Hz, 1H), 3.98−4.02 (m, 2H), 3.72 (dt, *J* = 14.4, 2.4 Hz, 1H), 3.62 (dd, *J* = 9.6, 4.0 Hz, 1H), 3.58 (dd, *J* = 12.0, 2.0 Hz, 1H), 3.49 (s, 3H), 3.44 (dd, *J* = 12.0, 4.4 Hz, 1H), 2.45 (s, 3H), 2.30 (s, 3H), 2.07 (s, 3H), 2.05 (s, 3H), 2.02 (s, 3H), 1.88 (s, 3H), 1.54 (dt, *J* = 14.8, 3.6 Hz, 1H), 1.40 (dd, *J* = 14.4, 2.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.6, 170.5, 170.0, 169.9, 169.5, 165.9, 165.8, 165.7, 143.7, 138.3, 134.5, 133.6, 133.3, 130.1, 129.9, 129.6, 129.3, 129.2, 129.1, 128.7, 128.5, 128.4, 128.3, 127.0, 97.4, 97.3, 91.4, 73.2, 70.2, 69.2, 68.7, 68.6, 68.5, 68.4, 67.8, 67.6, 65.8, 62.3, 62.0, 61.5, 55.8, 45.8, 31.5, 21.6, 21.1, 20.71, 20.68, 20.62, 20.59; IR ($CHCl_3$) 3317, 2954, 1728, 1597, 1450, 1365, 1226, 1165, 1103, 1041, 910, 756, 709 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{57}H_{63}NO_{24}SNa$ 1200.3357, found 1200.3358.

1,3-*cis*-3-Tosylaminodeoxytrisaccharide (4s). Compound **4s** (gummy liquid, 61 mg, 54% yield) was prepared according to the general procedure from glycosyl donor **1g** (56 mg, 0.1 mmol), glycosyl acceptor **2a** (51.2 mg, 0.11 mmol), and *p*-toluenesulfonamide **3a** (18.8 mg, 0.11 mmol) and purified by column chromatography (hexane/ethyl acetate = 2:1 to 1:1): $[\alpha]^D_{20}$ = +2.38 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.71 (d, *J* = 8.0 Hz, 2H), 7.23−7.39 (m, 17H), 5.37 (d, *J* = 2.8 Hz, 1H), 5.22 (d, *J* = 6.0 Hz, 1H), 5.15 (dd, *J* = 10.4, 7.6 Hz, 1H), 4.97−5.01 (m, 2H), 4.78−4.86 (m, 3H), 4.69−4.73 (m, 2H), 4.65 (d, *J* = 3.6 Hz, 1H), 4.45 (d, *J* = 3.6 Hz, 1H), 4.43 (d, *J* = 8.0 Hz, 1H), 4.15−4.17 (m, 1H), 4.05−4.11 (m, 2H), 3.89−4.00 (m, 5H), 3.66−3.71 (m, 3H), 3.51−3.56 (m, 2H), 3.46 (t, *J* = 9.2 Hz, 1H), 3.35 (s, 3H), 2.28 (s, 3H), 2.11−2.18 (m, 4H), 2.04 (s, 3H), 2.03(s, 6H), 1.99 (s, 3H), 1.46 (dt, *J* = 13.6, 4.0 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.33, 170.27, 170.1, 170.0, 169.4, 143.7, 138.8, 138.3, 138.2, 137.4, 129.8, 128.4−128.5 (m, 6C), 128.13, 128.10, 127.9, 127.8, 127.7, 127.6, 127.1, 101.7, 98.2, 97.9, 82.0, 80.0, 75.8, 75.0, 73.3, 72.5, 71.0, 70.5, 69.7, 68.6, 67.3, 66.7, 64.1, 60.9, 55.1, 47.4, 32.3, 21.3, 20.8, 20.7, 20.6, 20.5; IR ($CHCl_3$) 3302, 2924, 1751, 1450, 1365, 1334, 1226, 1157, 1072, 910, 817, 748, 702, 601 cm^{-1}; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{57}H_{69}NO_{21}SNa$ 1158.3975, found 1158.3981.

Procedure for Deprotection of 3-Benzyloxycarbonylamino-2,3-dideoxydisaccharide 4ib to Synthesize 3-Amino-2,3-dideoxydisaccharide 6. To a solution of 3-benzyloxycarbonylamino-2,3-dideoxydisaccharide **4jb** (71.0 mg, 0.1 mmol) in MeOH (2 mL) was added NaOMe (3.0 mg, 0.03 mmol, 0.3 equiv) under N_2 atmosphere. The reaction mixture was stirred at room temperature for 5 h, filtered with silica gel, and washed with MeOH. The filtrate was concentrated. The crude product **5** was dissolved in MeOH (2 mL), and palladium on carbon (10%, 7 mg) was added. The mixture was degassed and then stirred overnight under H_2. The mixture was filtered through a pad of Celite and washed with EtOAc. The solvent was evaporated under reduced pressure, and the residue was subjected to column chromatography (silica gel, $CHCl_3$/MeOH = 1:1) to obtain 3-amino-2,3-dideoxydisaccharide **6** (two-step yield: 74%).

1,3-*cis*-3-Benzyloxycarbonylaminodeoxydisaccharide (5). Data: ^1H NMR ($CDCl_3$, 400 MHz) δ 7.24−7.33 (m, 20H), 6.42 (d, *J* = 8.0 Hz, 1H), 5.07 (q, *J* = 12.4 Hz, 2H), 5.01 (d, *J* = 12.4 Hz, 1H), 4.95 (d, *J* = 10.8 Hz, 1H), 4.79 (d, *J* = 10.8 Hz, 1H), 4.40−4.57 (m, 5H), 4.11−4.18 (m, 1H), 3.98 (t, *J* = 9.2 Hz, 1H), 3.82 (d, *J* = 10.0 Hz, 1H), 3.73−3.75 (m, 2H), 3.45−3.50 (m, 2H), 3.37−3.38 (m, 2H), 3.26 (s, 3H), 3.03−3.05 (m, 1H), 1.81−1.94 (m, 2H), 1.26 (d, *J* = 5.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.4, 138.7, 138.2, 138.13, 137.08, 136.4, 128.6, 128.49, 128.45, 128.41, 128.23, 128.15, 128.10, 128.05, 127.93, 127.86, 127.8, 127.7, 97.8, 96.1, 82.0, 80.5, 75.8, 75.0, 73.6, 73.2, 69.4, 67.0, 64.9, 64.4, 55.2, 48.7, 33.4, 17.5; HRMS (ESI) m/z $[M + Na]^+$ calcd for $C_{42}H_{49}NO_{10}Na$ 750.3254, found 750.3259.

1,3-*cis*-3-Aminodeoxydisaccharide (6). Data: $[\alpha]^D_{20}$ = 2.02 (*c* 1.0 MeOH); ^1H NMR (CD_3OD, 400 MHz) δ 4.59 (d, *J* = 3.6 Hz, 1H), 3.80 (dd, *J* = 2.4, 10.8 Hz, 1H), 3.70−3.76 (m, 1H), 3.45−3.52 (m, 1H), 3.31 (s, 3H), 3.19−3.30 (m, 4H), 3.02−3.07 (m, 1H), 1.80−1.96 (m, 2H), 1.15 (d, *J* = 6.0 Hz, 3H); ^{13}C NMR (CD_3OD, 100 MHz) δ 100.0, 96.9, 73.7, 72.1, 71.4, 70.7, 69.7, 65.8, 63.0, 54.3, 33.1, 16.9; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{13}H_{26}NO_8$ 324.1658, found 324.1653.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra of compounds **4a**−**4r**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: xuewei@ntu.edu.sg.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We gratefully acknowledge Nanyang Technological University (RG50/08) and the Ministry of Education, Singapore (MOE 2009-T2-1-030) for the financial support of this research.

■ REFERENCES

(1) (a) Boltje, T. J.; Buskas, T.; Boons, G. J. *Nat. Chem.* **2009**, *1*, 611−622. (b) He, X.; Agnihotri, G.; Liu, H. W. *Chem. Rev.* **2000**, *100*, 4615−4661. (c) Kirschning, A.; Bechthold, F. W.; Rohr, J. In *Bioorganic Chemistry: Deoxysugars, Polyketides and Related Classes: Synthesis; Biosynthesis: Enzymes*; Springer: Berlin, 1997; pp 1−84. (d) Varki, A. *Glycobiology* **1993**, *3*, 97−130.

(2) (a) Boons, G. J. *Tetrahedron* **1996**, *52*, 1095−1121. (b) Animati, F.; Arcamone, F.; Berettoni, M.; Cipollone, A.; Franciotti, M.; Lombardi, P. *J. Chem. Soc., Perkin Trans. 1* **1996**, 1327−1329. (c) Kolar, C.; Kneissl, G.; Wolf, H.; Kampchen, T. *Carbohydr. Res.* **1990**, *208*, 111−116.

(3) Wang, A. H. J. *Curr. Opin. Struct. Biol.* **1992**, *2*, 361−368.

(4) Temperini, C.; Messori, L.; Orioli, P.; Bugno, C. D.; Animati, F.; Ughetto, G. *Nucleic Acids Res.* **2003**, *31*, 1464−1469. (b) He, X. M.; Liu, H. W. *Curr. Opin. Chem. Biol.* **2002**, *6*, 590−597.
(5) (a) Varki, A.; Cummings, R.; Esko, J.; Freeze, H.; Hart, G.; Marth, J. *Essentials of Glycobiology*; Cold Spring Harbor Laboratory Press: Cold Spring Harbor, NY, 1999. For recent reviews: (b) Dwek, R. A.; Butters, T. D. *Chem. Rev.* **2002**, *102*, 283−284. (c) Bertozzi, C. R.; Kiessling, L. L. *Science* **2001**, *291*, 2357−2364. (d) Dove, A. *Nat. Biotechnol.* **2001**, *19*, 913−917. (e) Kobata, A. *Glycoconjugate J.* **2001**, *17*, 443−464. (f) Koeller, K. M.; Wong, C. H. *Nat. Biotechnol.* **2000**, *18*, 835−841.
(6) For recent syntheses of 3-aminodeoxyglycosides, see: (a) Matsushima, Y.; Kino, J. *Eur. J. Org. Chem.* **2010**, 2206−2211. (b) Shi, W.; Coleman, R. S.; Lowary, T. L. *Org. Biomol. Chem.* **2009**, *7*, 3709−3722. (c) Colinas, P. A.; Nicolás, A. N.; Bravo, R. D. *J. Carbohydr. Chem.* **2008**, *27*, 141−147. (d) Fan, E.; Shi, W.; Lowary, T. L. *J. Org. Chem.* **2007**, *72*, 2917−2928. (e) Friestad, G. K.; Jiang, T.; Mathies, A. K. *Org. Lett.* **2007**, *9*, 777−780. (f) Hayman, C. M.; Larsen, D. S.; Simpson, J.; Bailey, K. B.; Gill, G. S. *Org. Biomol. Chem.* **2006**, *4*, 2794−2800. (g) Matthew, T. M.; Peng, T.; Christopher, M. H.; Robert, S. C.; Lowary, T. L. *J. Org. Chem.* **2006**, *71*, 8059−8070. (h) Parker, K. A.; Chang, W. *Org. Lett.* **2005**, *7*, 1785−1788. (i) Trost, B. M.; Jiang, C. H.; Hammer, K. *Synthesis* **2005**, 3335−3345. (j) Parker, K. A.; Chang, W. *Org. Lett.* **2003**, *5*, 3891−3893. (k) Colinas, P. A.; Bravo, R. D. *Org. Lett.* **2003**, *5*, 4509−4511. (l) Ginesta, X.; Pasto, M.; Pericas, M. A.; Riera, A. *Org. Lett.* **2003**, *5*, 3001−3004. (m) Cutchins, W. W.; McDonald, F. E. *Org. Lett.* **2002**, *4*, 749−752. (n) Sibi, M.; Lu, J.; Edwards, J. *J. Org. Chem.* **1997**, *62*, 5864−5872 and references therein.
(7) For reviews, see: (a) Carmona, A. T.; Moreno-Vargas, A. J.; Robina, I. *Curr. Org. Synth.* **2008**, *5*, 33−60. (b) Klefel, M. J.; Itzstein, M. *Chem. Rev.* **2002**, *102*, 471−490. (c) Boons, G. J.; Demchenko, A. V. *Chem. Rev.* **2000**, *100*, 4539−4565. (d) Marzabadi, C. H.; Franck, R. W. *Tetrahedron* **2000**, *56*, 8385−8417. (e) Hallis, T. M.; Liu, H. *Acc. Chem. Res.* **1999**, *32*, 579−588. (f) Kirschning, A.; Bechtold, A. F. W.; Rohr, J. *Top. Curr. Chem.* **1997**, *188*, 1−84.
(8) (a) Lorpitthaya, R.; Xie, Z. Z.; Sophy, K. B.; Kuo, J. L.; Liu, X.-W. *Chem.—Eur. J.* **2010**, *16*, 588−594. (b) Ding, F. Q.; William, R.; Gorityala, B. K.; Ma, J. M.; Wang, S. M.; Liu, X.-W. *Tetrahedron Lett.* **2010**, *51*, 3146−3148. (c) Sudibya, H. G.; Ma, J. M.; Dong, X.; Ng, S.; Li, L.-J.; Liu, X.-W.; Chen, P. *Angew. Chem., Int. Ed.* **2009**, *48*, 2723−2726. (d) Yang, R. L.; Pasunooti, K. K.; Li, F.; Liu, X.-W.; Liu, C.-F. *J. Am. Chem. Soc.* **2009**, *131*, 13592−13593.
(9) (a) Ding, F. Q.; William, R.; Wang, S. M.; Gorityala, B. K.; Liu, X.-W. *Org. Biomol. Chem.* **2011**, *9*, 3929−3939. (b) Ding, F. Q.; William, R.; Wang, F.; Ma, J. M.; Ji, L.; Liu, X.-W. *Org. Lett.* **2011**, *13*, 652−655.
(10) Krumper, J. R.; Salamant, W. A.; Woerpel, K. A. *J. Org. Chem.* **2009**, *74*, 8039−8050.
(11) (a) Bussolo, V. D.; Romano, M. R.; Pineschi, M.; Crotti, P. *Org. Lett.* **2005**, *7*, 1299−1302. (b) Bussolo, V. D.; Caselli, M.; Romano, M. R.; Pineschi, M.; Crotti, P. *J. Org. Chem.* **2004**, *69*, 7383−7386.
(12) (a) Adriano, A. M.; Dasciana, S. R.; Marco, F.; Roberto, F. L.; Jose, M. G.; Jose, M. P. *Tetrahedron* **2008**, *64*, 10721. (b) Nobuo, T.; Izumi, O.; Shigeki, Y.; Junzo, N. *Carbohydr. Res.* **2008**, *343*, 2675. (c) Wallach, L.; Latifeh, N.; Scott, D. T. *Carbohydr. Res.* **2005**, *340*, 1213. (d) Crich, D.; Li, H. *J. Org. Chem.* **2000**, *65*, 801. (e) Shull, B. K.; Wu, Z.; Koreeda, M. *J. Carbohydr. Chem.* **1996**, *15*, 955.