JOC*Article*

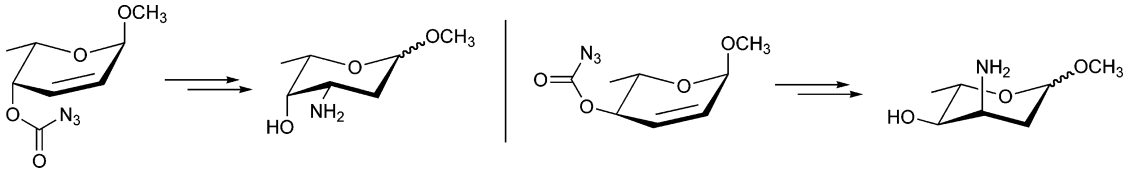
Synthesis of L-Daunosamine and L-Ristosamine Glycosides via Photoinduced Aziridination. Conversion to Thioglycosides for Use in Glycosylation Reactions

Matthew T. Mendlik, Peng Tao, Christopher M. Hadad, Robert S. Coleman,* and Todd L. Lowary*,†

Department of Chemistry, The Ohio State University, 100 West 18th Avenue, Columbus, Ohio 43210

tlowary@ualberta.ca; coleman@chemistry.ohio-state.edu

Received June 7, 2006



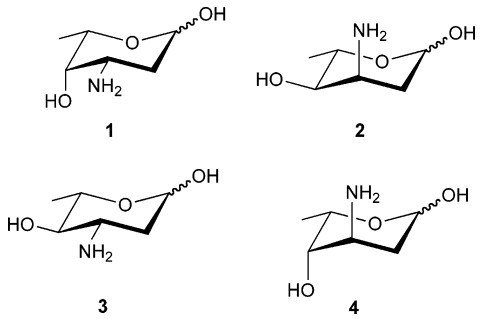
Application of photoinduced acylnitrene aziridination to the syntheses of L-daunosamine and L-ristosamine glycosides is reported. Photoreaction of methyl 4-*O*-azidocarbonyl-2,3,6-trideoxy-L-hex-2-enopyranosides, followed by aziridine opening, leads to 3-amino-3-*N*-,4-*O*-carbonyl-2,3,6-trideoxy precursors to the aminosugar methyl glycosides. Conversion of these precursors to their thioglycoside analogues followed by N-acetylation of the carbamate moiety permits high yielding and, in some cases, stereoselective glycosylations using the 1-benzenesulfinylpiperidine-triflic anhydride activation method developed by Crich and co-workers. Glycosylations involving activation with *N*-iodosuccinimide and silver triflate were also successful, but the stereoselectivities of these reactions in general were lower.

Introduction

2,6-Dideoxysugars are widespread in nature as components of many natural products.[1] Among the most prevalent are the 2,3,6-trideoxy-3-amino-hexopyranoses, e.g., L-daunosamine (**1**, Chart 1) and L-ristosamine (**2**). L-Daunosamine and related analogues are present in the carbohydrate moieties of the anthracycline family of antitumor antibiotics.[2] L-Ristosamine is part of the carbohydrate appended to the ristomycins, members of the vancomycin antibiotic family that cause platelet aggregation and that are used to diagnose variants of von Willebrand disease.[3]

Considerable attention has been devoted to the syntheses of these monosaccharides, utilizing both carbohydrate[4,5] and non-carbohydrate[6] starting materials. Of those syntheses that begin with carbohydrates, many involve stereoselective delivery of nitrogen to C3 via an imidate ester.[5] Another route to these monosaccharides, recently reported by Renneberg and co-workers, involves the addition of azide ion to a hex-2-enopyranoside derivative prepared from L-rhamnose as the key step.[7] Both **1** and **2** were produced by this method, together with acosamine (**3**) and 3-*epi*-daunosamine (**4**).

CHART 1



In considering stereocontrolled routes to **1** and **2**, we thought to combine elements from earlier syntheses with work[8] by Bergmeier and Stanchina (Figure 1), in which allylic alcohols were efficiently converted to amino alcohols via a two-step process involving an intramolecular acylnitrene aziridination followed by nucleophilic opening of the aziridine ring. We reasoned that installation of an acyl azide on the appropriate

† Current address: Alberta Ingenuity Centre for Carbohydrate Science and Department of Chemistry, The University of Alberta, Gunning-Lemieux Chemistry Centre, Edmonton, AB T6G 2G2, Canada.

(1) Johnson, D. A.; Liu, H.-W. *Comp. Nat. Prod. Chem.* **1999**, *3*, 311−365.

(2) Arcamone, F.; Cassinelli, G. *Curr. Med. Chem.* **1998**, *5*, 391−419.

(3) (a) Sweeney, J. D.; Hoernig, L. A.; Fitzpatrick, J. E. *Am. J. Hematol.* **1989**, *32*, 190−193. (b) Zhou, L.; Schmaier, A. H. *Am. J. Clin. Pathol.* **2005**, *123*, 172−183.

10.1021/jo061167z CCC: $33.50
Published on Web 09/09/2006

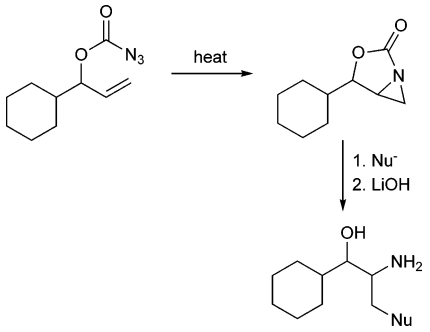


FIGURE 1. Bergmeier−Stanchina route to amino alcohols from allylic alcohols.[8]

hex-2-enopyranoside (e.g., **5**, Figure 2), followed by cyclization to the aziridine and reductive ring opening would yield the carbamate-protected L-daunosamine derivative **6**. Diastereofacial selectivity would be determined by the absolute configuration at C-4, thereby making the synthesis stereospecific. Subsequent carbamate deprotection would afford the L-daunosamine methyl glycoside **7**. Alternatively, conversion of **6** into the corresponding thioglycoside **8** would allow the efficient preparation of other glycosides containing this aminosugar. A similar series of transformations starting from hex-2-enopyranoside **9** would afford, via **10**, either the L-ristosamine methyl glycoside **11** or thioglycoside **12**. We report the successful execution of these synthetic routes to daunosamine and ristosamine and the use of the corresponding thioglycosides in glycosylation reactions. The utility of glycosyl donors containing fused cyclic carbonate or oxazolidinone rings has been previously studied by a number of other groups;[9] however, these investigations have not employed species that would lead directly to 2-deoxy sugar glycosides.

Results and Discussion

Syntheses of Methyl Glycosides 7 and 11. The preparation of L-daunosamine methyl glycoside **7** started from the known L-*threo*-hex-2-enopyranoside derivative **13** (Scheme 1), which was prepared in six steps from commercially available L-rhamnose.[5a] A modification of the method reported by Bergmeier and Stanchina[8] was used to access acyl azide **5**: reaction of **13** with *N*,*N*′-carbonyldiimidazole in pyridine and benzene, followed by displacement of the resulting acyl imidazole derivative with sodium azide in DMF afforded **5** in 98% yield. The published workup for similar reactions involves acidification with HCl in DMF; with our substrates, however, better yields were obtained when the acidification was carried out first by the addition of acetic acid in DMF, followed by HCl. After several unsuccessful attempts to effect aziridination using heat and pressure,[8] we succeeded in converting **5** into **14** through photochemical generation of a presumed acylnitrene intermediate upon exposure to UV light (254 nm).[10] The yield for this process was high (79%) when the concentration of starting material was kept below 0.01 M; at higher concentrations, the yield was reduced. For example, when a concentration of 0.023 M was used, only a 64% yield of the product was obtained, whereas at a concentration of 0.082 M, the reaction did not proceed. Compound **14** has been reported[11] once previously in the literature but was synthesized via a route different than that reported here and data were not provided to support its structure. In the ^{1}H NMR spectrum of **14**, the resonance for the hydrogen on C-2 appeared at 2.80 ppm and was coupled to hydrogens at C-1 (5.08 ppm, $J = 0.5$ Hz) and C-3 (3.51 ppm, $J = 4.7$ Hz). Using an HMQC NMR experiment, the signals for the C-2 and C-3 hydrogens could be correlated with carbon resonances at 43.2 and 41.3 ppm, respectively. The chemical shift of these carbons is indicative of their attachment to nitrogen and supports the proposed structure. Further evidence for the structure of **14** was obtained when, in a subsequent step, a crystalline compound was obtained (see below).

We were pleased to find that the aziridine ring in **14** could then be opened regioselectively and in excellent yield (95%) by hydrogenation over palladium on carbon to give the 3,4-carbamate-protected methyl glycoside of daunosamine (**6**). The regioselectivity of the opening could be readily established from a ^{1}H−^{1}H COSY experiment, which showed correlations between the protons on C1 ($\delta = 4.84$ ppm) and C2 ($\delta = 1.75$ and 2.08 ppm). In one large-scale reaction, we observed the formation of trace amounts of the isomeric 2,4-carbamate derivative, resulting from hydrogenation of the C3−N bond. Compound **6** was crystalline, and its structure was further confirmed by X-ray crystallographic analysis.[12] Perhaps not surprisingly, the carbamate ring induces significant conformational bias to the pyranoside ring, forcing it into a twist-boat (^2S_O) conformation, which places both the methyl group at C-5 and the anomeric methoxy group in pseudoequatorial orientations. Deprotection of the

(4) Selected methods: (a) Gurjar, M. K.; Pawar, S. M.; Mainkar, P. S. *J. Carbohydr. Chem.* **1989**, *8*, 785−791. (b) Monneret, C.; Gagnet, R.; Florent, J.-C. *J. Carbohydr. Chem.* **1987**, *6*, 221−229. (c) Grethe, G.; Mitt, T.; Williams, T. H.; Uskokovic. M. R. *J. Org. Chem.* **1983**, *48*, 5309−5315. (d) Boivin, J.; Pais, M.; Monneret, C. *Carbohydr. Res.* **1978**, *64*, 271−278. (e) Cheung, T.-M.; Horton, D.; Sorenson, R. J.; Weckerle, W. *Carbohydr. Res.* **1978**, *63*, 77−89.

(5) (a) Szechner, B.; Achmatowicz, O; Badowska-Roslonek, K. *Pol. J. Chem.* **1999**, *73*, 1133−1141. (b) Pauls, H. W.; Fraser-Reid, B. *Carbohydr. Res.* **1986**, *150*, 111−119. (c) Cardillo, G.; Orena, M.; Sandri, S.; Tomasini, C. *J. Org. Chem.* **1984**, *49*, 3951−3953.

(6) Selected methods: (a) Hayman, C. M.; Larsen, D. S.; Simpson, J.; Bailey, K. B.; Gill, G. S. *Org. Biomol. Chem.* **2006**, *4*, 2794−2800. (b) Ginesta, X.; Pastó, M.; Pericàs, M. A.; Riera, A. *Org. Lett.* **2003**, *5*, 3001−3004. (c) Davies, S. G.; Smyth, G. D.; Chippindale. A. M. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3089−3104. (d) Sibi, M. P.; Lu, J.; Edwards, J. *J. Org. Chem.* **1997**, *62*, 5864−5872. (e) Banfi, L.; Cardani, S.; Potenza, D.; Scolastico, C. *Tetrahedron* **1987**, *43*, 2317−2322. (f) Po, S.-Y.; Uang, B.-J. *Tetrahedron: Asymmetry* **1994**, *5*, 1869−1872. (g) Jurczak, J.; Kocak. J.; Golebiowski, A. *Tetrahedron* **1992**, *48*, 4231−4238. (h) Sammes, P. G.; Thetford, D. *J. Chem. Soc., Perkin Trans. 1* **1988**, 111−123. (i) Tietze, L. F.; Voss, E. *Tetrahedron Lett.* **1986**, *27*, 6181−6184. (j) Warm, A.; Vogel, P. *J. Org. Chem.* **1986**, *51*, 5348−5353. (k) Wovkulich, P. M.; Uskokovi. M. R. *Tetrahedron* **1985**, *41*, 3455−3462. (l) Heathcock, C. H.; Montgomery, S. H. T*etrahedron Lett.* **1983**, *24*, 4637−4640. (m) Grethe, G.; Sereno, J.; Williams, T. H.; Uskokovic. M. R. *J. Org. Chem.* **1983**, *48*, 5315−5317.

(7) Renneberg, B.; Li, Y.-M.; Laatsch, H.; Fiebig, H.-H. *Carbohydr. Res.* **2000**, *329*, 861−872.

(8) (a) Bergmeier, S. C.; Stanchina, D. *J. Org. Chem.* **1999**, *64*, 2852−2859. (b) Bergmeier, S. C.; Stanchina, D. *J. Org. Chem.* **1997**, *62*, 4449−4456.

(9) (a) Benakli, K.; Zha, C.; Kerns, R. J. *J. Am. Chem. Soc.* **2001**, *123*, 9461−9462. (b) Crich, D.; Vinod, A. U.; Picione, J. *J. Org. Chem.* **2003**, *68*, 8453−8458. (c) Kerns, R. J.; Zha, C.; Benakli, K.; Liang, Y.-Z. *Tetrahedron Lett.* **2003**, *44*, 8069−8072. (d) Crich, D.; Jayalath. P. *J. Org. Chem.* **2005**, *70*, 7252−7259. (e) Wei, P.; Kerns, R. J. *J. Org. Chem.* **2005**, *70*, 4195−4198. (f) Boysen, M.; Gemma, E.; Lahmann, M.; Oscarson, S. *Chem. Commun.* **2005**, *24*, 3044−3046. (g) Tanaka, H.; Nishiura, Y.; Takahashi, T. *J. Am. Chem. Soc.* **2006**, *128*, 7124−7125. (h) Manabe, S.; Ishii, K.; Ito, Y. *J. Am. Chem. Soc.* **2006**, *128*, 10666−10667.

(10) Lwowski, W. Acyl azides and nitrenes. In *Azides and Nitrenes: Reactivity and Utility*; Scriven, E. F. V., Ed.; Academic Press: Orlando, FL, 1984; pp 205−246.

(11) Baer, H. H.; Mateo, F. H.; Siemsen, L. *Carbohydr. Res.* **1990**, *195*, 225−245.

(12) Mendlik, M. T.; Coleman, R. S.; Qi, G.; Lowary, T. L.; McDonald, R. *Acta Crystallogr., Sect. E* **2006**, *62*, o2490−o2492.

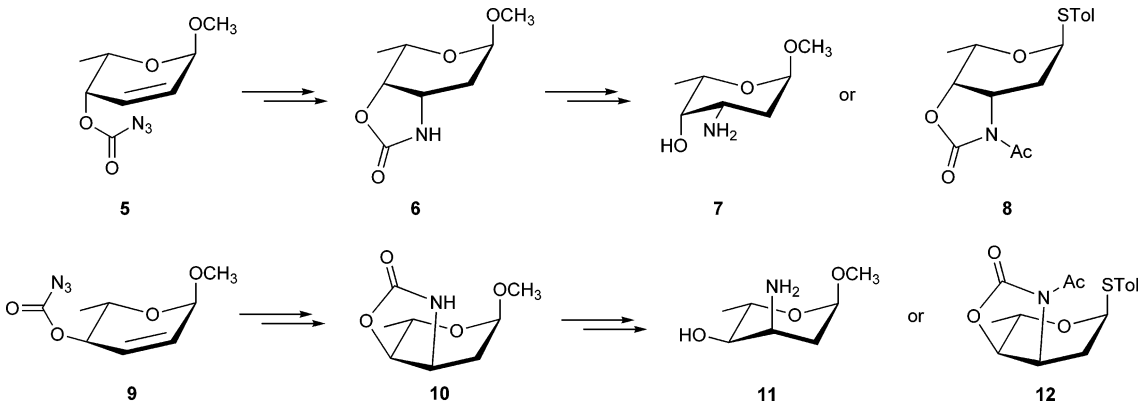
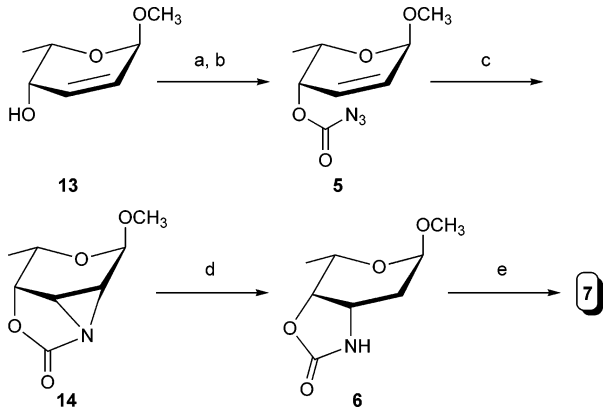


FIGURE 2. Proposed routes to methyl glycoside and thioglycoside derivatives of L-daunosamine (**7** and **8**) or L-ristosamine (**11** and **12**).

SCHEME 1 [a]



[a] Reagents and conditions: (a) *N*,*N*′-Carbonyldiimidazole, pyridine, benzene, rt, 2 h; (b) NaN_3, HOAc, HCl, DMF, rt, 98%; (c) 254 nm light, CH_2Cl_2, rt, 1 h, 79%; (d) Pd/C, H_2, EtOH/EtOAc 5:1, rt, 3 h, 95%; (e) $Ba(OH)_2 \cdot 8H_2O$ (70 equiv), H_2O, 125 °C, 1 h, then CO_2(s), rt, 100%.

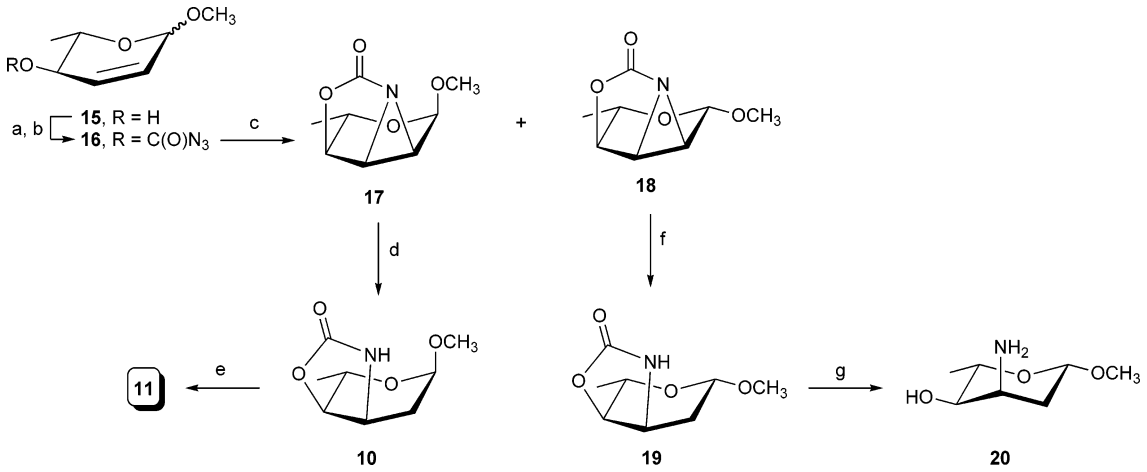
carbamate was achieved by reaction with barium hydroxide in water,[13] affording in quantitative yield the deprotected methyl glycoside **7**, which had NMR spectral data identical to that reported previously.[6g,14]

The synthesis of **11** was achieved via an analogous series of reactions that started with L-*erythro*-hex-2-enopyranoside derivative **15** (Scheme 2).[15] Like its counterpart **13**, alkene **15** was prepared from L-rhamnose. A 2:1 α:*β* mixture was obtained, which could not be easily separated, nor could the mixture of acyl azides that were prepared in 67% yield upon treatment of **15** with *N*,*N*′-carbonyldiimidazole and then sodium azide. However, upon irradiation (254 nm) of **16** in dichloromethane, the resulting mixture of **17** and **18**, produced together in 91% yield, was separable by chromatography. Both **17** and **18** were crystalline, and analysis by X-ray crystallography established their structures.[16,17] Despite the tricyclic system, the pyranoside ring in **18** appears to be relatively unstrained and adopts an envelope conformation in which C5 is below the plane of the other five ring atoms (E_5). Subsequent hydrogenolysis of **17** afforded **10** (92%), which was deprotected with barium hydroxide to provide **11**[6g] (95%). The same two reactions were used to convert **18**, via **19**, to the corresponding *β*-glycoside, **20**,[6g] in 72% overall yield.

Synthesis of Thioglycoside Donors. In the interest of using this methodology as part of a larger project on the synthesis of 3-amino-2,3,6-trideoxysugar glycosides, it was necessary to convert the carbamate-protected methyl glycosides shown in Schemes 1 and 2 into potential glycosyl donors. For this purpose, we synthesized the corresponding thioglycosides (Scheme 3) of **6** and **10**. For **6**, this conversion could be readily achieved upon treatment with *p*-thiocresol and boron trifluoride etherate, which provided the thioglycoside **21** in excellent (99%) yield. This reaction was highly α-selective, with less than 5% of the *β*-anomer being isolated. Single-crystal X-ray analysis of **21** showed that, like its methyl glycoside counterpart **6**, the pyranoside ring adopts a ^2S_O twist-boat conformation, with the α-thiocresyl moiety being oriented in a pseudoequatorial orientation.[18] Acetylation of the carbamate nitrogen under standard conditions gave the expected product **22**, also in high yield; this step facilitated purification of the carbamate-protected sugars and was later found to be necessary for certain glycosylation protocols. An analogous series of reactions was used to convert a mixture of **10** and **19** into thioglycosides **24** and **25** (82% yield over two steps via **23**) as a 1.8:1 α:*β* mixture of anomers. A mixture of **10** and **19** was used in this sequence of reactions as treatment of either of these (pure) compounds with *p*-thiocresol and $BF_3 \cdot Et_2O$ led to the same ratio of thioglycosides **23** (data not shown). In addition, although the anomers of **23** were separated for the purposes of characterization, in large-scale preparations they were carried through to the acetylation step as a mixture. Thioglycosides **24** and **25** were used as a mixture in the glycosylation reactions because their separation by chromatography was difficult and the stereoselectivity of the glycosylations was shown not to depend on the stereochemistry at the anomeric center in the donor (see below). However, via careful chromatography, it was possible to obtain these compounds pure, and NOE studies were used to establish the stereochemistry of the major and minor isomers in the mixture. The major isomer (**24**) showed no NOE between the hydrogens on

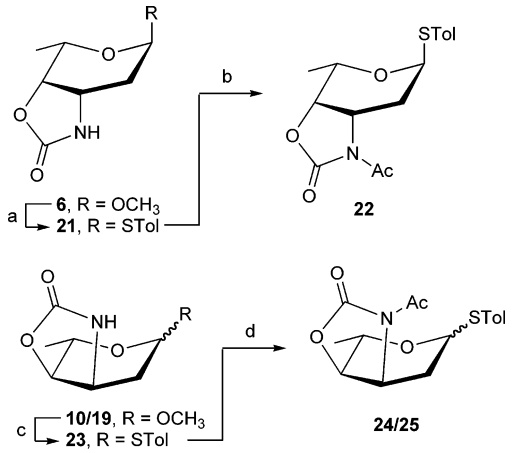
(13) Horton, D.; Weckerle, W. *Carbohydr. Res.* **1975**, *44*, 227−240.
(14) Barthwal, R.; Mujeeb, A.; Srivastava, N.; Sharma, U. *Chem. Biol. Interact.* **1996**, *100*, 125−139.
(15) Brimacombe, J. S.; Doner, L. W.; Rollins, A. J. *J. Chem. Soc., Perkin Trans. 1* **1972**, 2977−2979.
(16) Mendlik, M. T.; Coleman, R. S.; Qi, G.; Lowary, T. L.; McDonald, R. *Acta Crystallogr., Sect. E* **2006**, *62*, o2573−o2575.
(17) Mendlik, M. T.; Coleman, R. S.; Qi, G.; Lowary, T. L.; Ferguson, M. J. *Acta Crystallogr., Sect. E* **2006**, *62*, o2576−o2577.
(18) Mendlik, M. T.; Coleman, R. S.; Qi, G.; Lowary, T. L.; Ferguson, M. J. *Acta Crystallogr., Sect. E* **2006**, *62*, o2788−o2790.

SCHEME 2 [a]



[a] Reagents and conditions: (a) *N*,*N*′-Carbonyldiimidazole, pyridine, benzene, rt, 2 h; (b) NaN_3, HOAc, HCl, DMF, rt, 67%; (c) 254 nm light, CH_2Cl_2, rt, 1 h, 92%; (d) Pd/C, H_2, EtOH/EtOAc 5:1, rt, 3 h, 95%; (e) $Ba(OH)_2 \cdot 8H_2O$ (70 equiv), H_2O, 125 °C, 1 h, then CO_2(s), rt, 100%; (f) Pd/C, H_2, EtOH/EtOAc 5:1, rt, 3 h, 83%; (g) $Ba(OH)_2 \cdot 8H_2O$ (70 equiv), H_2O, 125 °C, 1 h, then CO_2(s), rt, 87%.

SCHEME 3 [a]



[a] Reagents and conditions: (a) *p*-thiocresol, $BF_3 \cdot OEt_2$, CH_2Cl_2, rt, 2 h, 99%; (b) Ac_2O, DMAP, pyridine, rt, 2 h, 99%; (c) *p*-thiocresol, $BF_3 \cdot OEt_2$, CH_2Cl_2, rt, 2 h, 85%, 1.8:1 α:*β*; (d) Ac_2O, DMAP, pyridine, rt, 2 h, 96%.

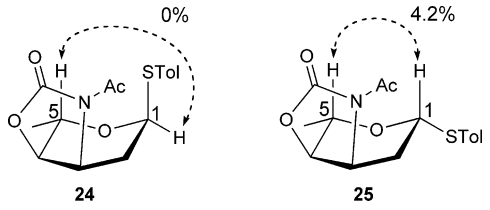
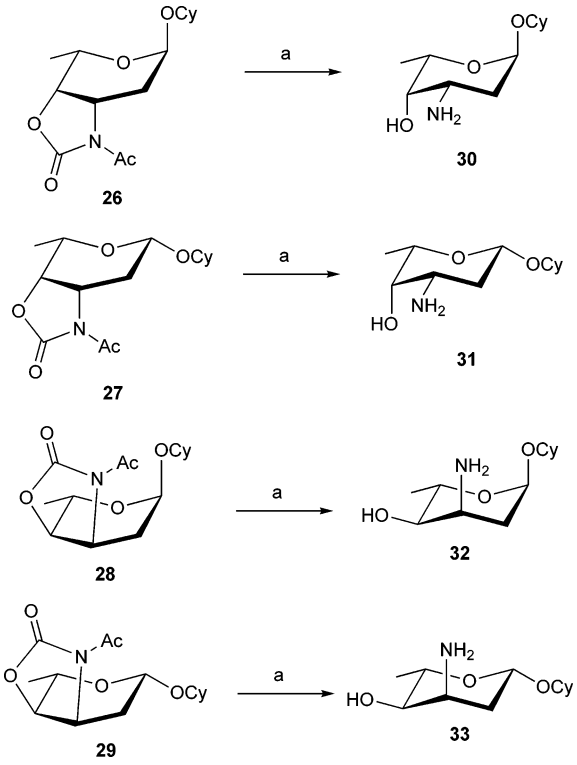


FIGURE 3. NOEs in thioglycosides **24** and **25** that were used to establish anomeric stereochemistry. Experiments were carried out by irradiation of the anomeric hydrogen.

C1 and C5, whereas in the minor isomer (**25**) a 4.2% NOE was observed between these two hydrogens (Figure 3).

Determination of Glycoside Stereochemistry in Carbamate-Protected Glycosides. It was clear from the crystal structures of **6** and **21** that the presence of the carbamate protecting group in these species substantially alters the conformation of the pyranoside ring. We therefore expected that it would be non-

SCHEME 4 [a]



[a] Reagents and conditions: (a) $Ba(OH)_2 \cdot 8H_2O$, H_2O, 125 °C, 1 h, then CO_2(s), rt, 85% (for **26**); 86% (for **27**); 87% (for **28**); 87% (for **29**).

trivial to unambiguously assign the anomeric stereochemistry in these glycosides as obtained from coupling of the thioglycosides with different alcohols. Although we could rely on NOE measurements (e.g., Figure 3), we sought a more direct method. To this end, both **22** and **25** were converted to the corresponding α/*β* mixture of cyclohexyl glycosides as described below. For both ring systems, the anomers could be separated, and all four compounds (**26**−**29**, Scheme 4) were fully characterized before being individually deprotected to aminosugars **30**−**33**. The pyranoside rings of **30**−**33** adopt the canonical chair conformer;

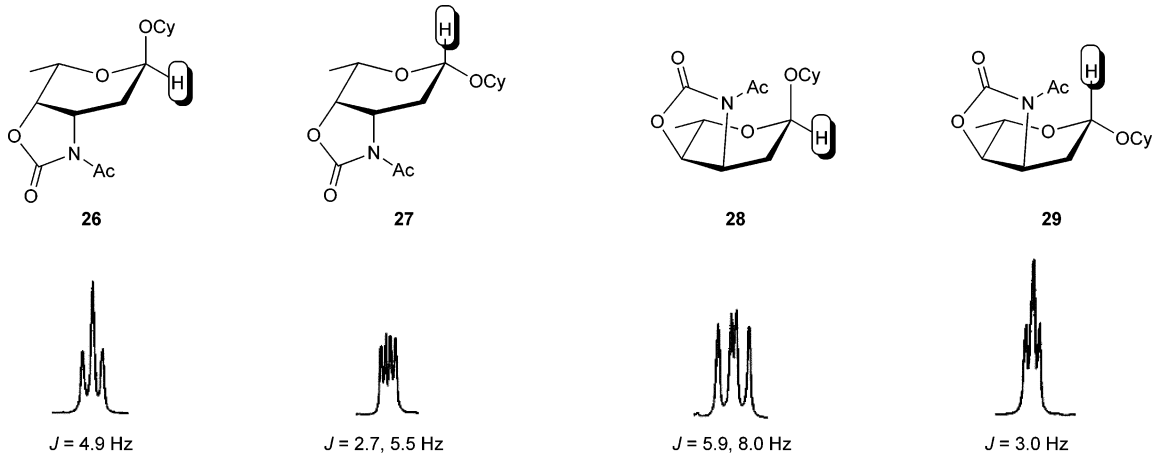


FIGURE 4. Multiplicity of anomeric hydrogen resonances in **26**−**29**.

determination of the C1 stereochemistry using NMR spectroscopy was consequently straightforward. Thus, the resonance for the anomeric hydrogen of **30** and **32** appeared as an apparent triplet with $J = 3.7$ and 2.5 Hz, respectively, as expected given the axial orientation of the aglycone. For **31** and **33**, in which the cyclohexyloxy group is equatorial, the multiplicity of anomeric hydrogen resonance is a doublet of doublets with $J =$ 2.2 and 9.6 (**31**) or 2.5 and 8.4 Hz (**33**), in line with predictions made from the Karplus relationship.[19] After unambiguously determining the structures of **30**−**33**, it was possible to assign C1 stereochemistry in the precursors **26**−**29** from the multiplicity of the anomeric hydrogen resonance. As depicted in Figure 4, for the isomers in which the carbamate and aglycone are trans, the C1-H resonance appears as an apparent triplet with $J = 4.9$ Hz (**26**) or 3.0 Hz (**29**). For the other two isomers, **27** and **28** (cis carbamate and aglycone), the anomeric hydrogen resonance appears as a doublet of doublets ($J = 2.7$ and 5.5 Hz for **27**; 5.9 and 8.0 Hz for **28**). Therefore, inspection of the multiplicity of the anomeric hydrogen resonance in the ^{1}H NMR spectra of these carbamate-protected aminosugars enabled rapid determination of the anomeric configuration. Further support for this trend was achieved by N-acylation of the previously prepared methyl glycosides **6**, **10**, and **19** (see Figure S1 in Supporting Information). In addition, we investigated the use of NOE measurements between the hydrogens on C1 and C5 for differentiating the glycoside anomers in **26**−**29**. As illustrated in Figure S2 of Supporting Information, the NOE between these hydrogens was substantially different in **26** and **27** (0.2 vs 1.7), but for **28** and **29**, the difference was significantly less (0.3 vs 0.7).

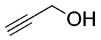
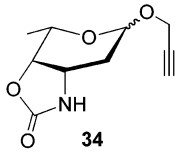
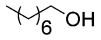
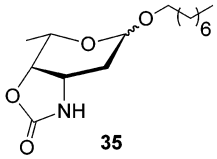
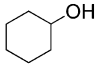
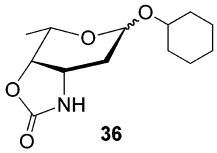
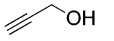
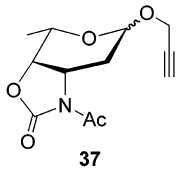
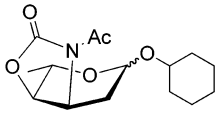
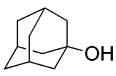
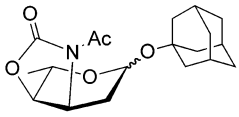
Glycosylations with Thioglycosides. With a method in place for differentiating anomeric stereochemistry, we explored the potential of these thioglycosides as glycosylating agents by first treating thioglycoside **21**, **22** or **24**/**25** with various alcohols and *N*-iodosuccinimide (NIS) and silver triflate[20] in dichloromethane (Table 1). Although the yields of these reactions were good to excellent, the stereoselectivities were highly variable, ranging from excellent with propargyl alcohol to poor with *n*-octanol. (Glycosylation reactions with pure **24** or **25** afforded the same product ratios as those involving the mixture of **24** and **25**.) In all cases, the isomeric glycosides could be separated, and the NMR parameters discussed above were used to prove anomeric stereochemistry. Given these modest results, we chose to abandon the use of this activation method.

As an alternate promoter system for these glycosylations, we examined the 1-benzenesulfinyl piperidine/triflic anhydride (BSP/Tf_2O) system recently developed by Crich and coworkers.[21] This method has been demonstrated to afford high glycosylation yields and excellent stereoselectivity through the formation of glycosyl triflate intermediates. We envisioned that glycosylations with these thioglycosides might lead to a single glycosyl triflate intermediate that, in turn, would react in a stereospecific manner (via an "exploded" S_N2-transition state[22]) affording glycosides with high stereoselectivity.

To probe the feasibility of this hypothesis, we carried out density functional theory calculations of the four possible triflate intermediates (**39**−**42**, Chart 2) that would be produced from the *N*-acylated thioglycosides **22** and **24**/**25**. Each of the four structures was initially optimized at the B3LYP/6-31G* level of theory[23] in the gas phase, and then single-point energies were calculated at the B3LYP/6-311+G(3df,3pd) level of theory. These triflate intermediates, if formed in the course of these reactions, would be present in a relatively nonpolar reaction medium (CH_2Cl_2), and therefore the energy differences between a given pair of glycosyl triflates in the gas phase should be representative of their relative energies in the reaction solvent. Following zero-point vibrational energy (ZPE), thermal and entropic corrections at 298 K, ΔG_{298}, and ΔH_{298} values for each isomer were determined as shown in Table 2. As can be seen from the values for each pair of diastereomers, the isomer in which the triflate moiety is trans to the oxazolidinone ring is the most stable, although for the ristosamine precursors, the energy difference between the two species is relatively small. If the intermediate triflates are the species that react with glycosyl acceptor alcohols, it would be anticipated that application of the BSP/Tf_2O approach to thioglycoside **22** would lead

(19) Tvaroska. I.; Taravel, F. R. *Adv. Carbohydr. Chem. Biochem.* **1995**, *51*, 15−61.
(20) Konradsson, P.; Udodong, E. U.; Fraser-Reid, B. *Tetrahedron Lett.* **1990**, *31*, 4313−4316.
(21) Crich, D.; Smith, M. *J. Am. Chem. Soc.* **2001**, *123*, 9015−9020.
(22) Crich, D.; Chandrasekera, N. S. *Angew. Chem. Int. Ed.* **2004**, *43*, 5386−5389.
(23) (a) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098−3100. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648−5652. (c) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785−789.

TABLE 1. Glycosidation of 21, 22, and 24/25 Using NIS/AgOTf Activation[a]

Donor	Acceptor	Product	Yield (%)[b] Anomeric Ratio (α:β)[c]
21		 **34**	75 (>10:1)
21		 **35**	94 (1.5:1)
21		 **36**	99 (2:1)
22		 **37**	99 (3.6:1)
24/25		 **28/29**	97 (1.3:1)
24/25		 **38**	97 (2.3:1)

[a] Thioglycoside **21** (0.33 mmol) and the alcohol (0.98 mmol) were dissolved in CH_2Cl_2 (10 mL). Molecular sieves (4 Å, 250 mg) were added, and the solution was cooled to 0 °C before NIS (0.36 mmol) and AgOTf (0.07 mmol) were added. The reaction was allowed to warm to room temperature over 1 h and then quenched by the addition of a saturated aqueous solution of $NaHCO_3$. [b] Isolated yield. [c] Ratio of anomers determined by ^1H NMR spectroscopy, by integration of resonances for the anomeric hydrogens.

ultimately to β-glycosides of daunosamine, whereas donors **24**/**25** would give α-ristosamine glycosides.

Our initial attempts to use the BSP/Tf_2O activation method with thioglycosides **21** and **23** led to extensive decomposition of the donor. Fortunately, clean reactions were observed for the N-acetylated derivatives **22** and **24**/**25**. Using the reported protocol,[21] thioglycoside **22** was treated with BSP, tri-*tert*-butylpyrimidine and molecular sieves in dichloromethane at −60 °C, followed by addition of the Tf_2O and a solution of the glycosyl acceptor in dichloromethane. A range of alcohols was cleanly glycosylated by **22** under these conditions (Table 3). The yields of these reactions were generally lower than those promoted by NIS/AgOTf, but the stereoselectivities were higher in all cases, and with the α-glycoside being the favored product. In the case of adamantol, only trace amounts of the β-glycoside were detected in ^1H NMR spectrum of the crude product, and none could be isolated. In all cases the mixture of glycosides could be separated by chromatography.

CHART 2

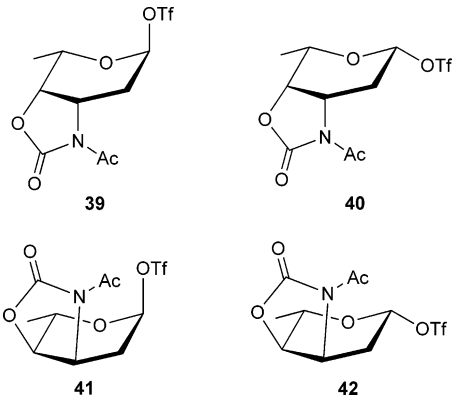


TABLE 2. Relative Gas-Phase Energies (kcal/mol) of Triflates 39−42[a]

	compound			
	daunosamine glycoside precursors		ristosamine glycoside precursors	
	39	**40**	**41**	**42**
ΔE_{BW}[b]	0	3.1	0.3	0
ΔH_{298}[c]	0	3.1	0.4	0
ΔG_{298}[d]	0	3.1	1.3	0

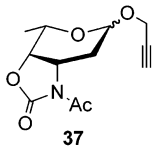
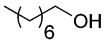
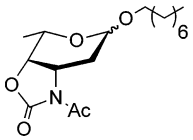
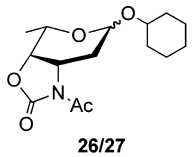
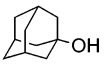
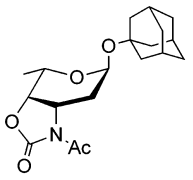
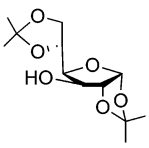
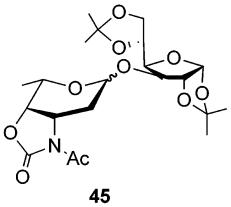
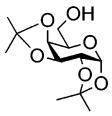
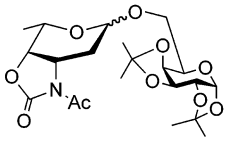
[a] Lowest energy species of a given triflate pair set to 0 kcal/mol. [b] Relative bottom-of the well energies (kcal/mol) without ZPE, thermal, or entropic corrections. [c] Relative enthalpies (kcal/mol) with (scaled) ZPE and thermal corrections at 298 K. [d] Relative Gibbs free energies (kcal/mol) at 298 K.

When the same protocol was applied to glycosylations using thioglycosides **24**/**25**, only low yields of the desired glycosides were obtained, and the reaction was accompanied by decomposition of the donor. This problem was overcome by a slight procedural modification in which the CH_2Cl_2 solution of the acceptor was added immediately following the addition of the Tf_2O. Under these conditions, the same panel of acceptors was glycosylated in good to excellent yields (Table 4).[24] In comparing the glycosylations with donors possessing the daunosamine and ristosamine stereochemistry, **22** and **24**/**25**, respectively, there was an inverse relationship between yield and stereoselectivity. The daunosamine donor **22** generally gave lower product yields but higher stereoselectivity, whereas **24**/**25**, which possess the ristosamine stereochemistry, gave lower selectivities but higher yields. In a separate series of experiments (data not shown), it was demonstrated that the stereochemistry at the anomeric center of the donor had no effect on reaction stereoselectivity and yield, i.e., **24** and **25** gave identical results.

In rationalizing the stereoselectivities of the glycosylations with the BSP/Tf_2O activation method, it is interesting to note that the major product formed from both donors is the α-glycoside. This result suggests that the species that undergoes reaction with the alcohols is not a glycosyl triflate intermediate but rather an oxacarbenium ion. In such a regime (Figure 5) where an oxacarbenium ion (e.g., **51**) is in equilibrium with

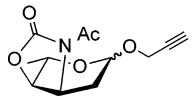
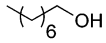
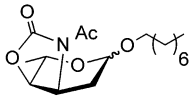
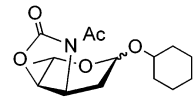
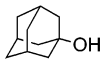
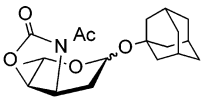
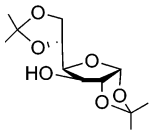
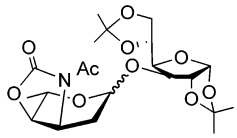
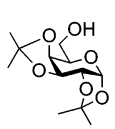
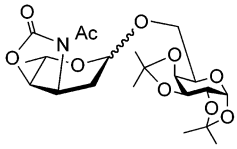
(24) Application of this modified procedure to the daunosamine series (thioglycoside **22**) did not lead to results significantly different from those obtained previously.

TABLE 3. Glycosylations with 22 Using BSP/Tf_2O Activation[a]

Acceptor	Product	Yield (%)[b] Anomeric Ratio (α:β)[c]
	 **37**	83 (2.7:1)
	 **43**	80 (4:1)
	 **26/27**	92 (6.8:1)
	 **44**	78 (1:0)[d]
	 **45**	71 (5.6:1)
	 **46**	73 (5:1)

[a] Thioglycoside **22** (0.33 mmol), 4 Å molecular sieves (250 mg), BSP (0.33 mmol), and TTBP (0.66 mmol) were suspended in CH_2Cl_2 (5 mL) and cooled to −60 °C before Tf_2O (0.36 mmol) was added. After 2 min of stirring, a solution of the acceptor (0.49 mmol) in CH_2Cl_2 (2 mL) was added. After 5 min, the mixture was warmed to room temperature and stirred until complete by TLC. [b] Isolated yield. [c] Ratio of anomers determined by weight after separation by chromatography. [d] The β-anomer of **44** constituted less than 5% of the reaction yield (from NMR spectrum of the crude reaction mixture) and could not be isolated.

TABLE 4. Glycosylations with 24/25 Using BSP/Tf_2O Activation[a]

Acceptor	Product	Yield (%)[b] Anomeric Ratio (α:β)[c]
	 **47**	90 (2.7:1)
	 **48**	95 (2:1)
	 **28/29**	81 (2:1)
	 **38**	86 (3.5:1)
	 **49**	99 (2.5:1)
	 **50**	84 (1:1)

[a] Thioglycoside **24/25** (0.33 mmol), 4 Å molecular sieves (250 mg), BSP (0.33 mmol), and TTBP (0.33 mmol) were suspended in CH_2Cl_2 (5 mL) and cooled to −60 °C before Tf_2O (0.36 mmol) was added, followed immediately by a solution of the acceptor (0.49 mmol) in CH_2Cl_2 (2 mL). After 5 min, the mixture was warmed to room temperature and stirred until complete by TLC. [b] Isolated yield. [c] Ratio of anomers determined by weight after separation by chromatography, except for **48** and **49**, which were inseparable. In these cases, the ratios were obtained by ^1H NMR spectroscopy through integration of resonances for the anomeric hydrogens of the aminosugar moiety.

the corresponding glycosyl triflate intermediates (e.g., **39** and **40**), it would be expected that the flattening of the pyranose ring induced by the carbamate moiety would reduce the barrier to formation of the charge-separated species from the covalent triflate. This, in turn, would be expected to lead to a higher concentration of the more reactive oxacarbenium ion in the reaction mixture. If one assumes that the glycosidic bond is formed in these reactions via the attack of an alcohol on a species such as **51**, the stereoselectivity of the reaction can be easily rationalized. In the case of **22**, formation of the α-glycoside would be favored as this product would result from attack of the alcohol on the least hindered side of the molecule, anti to the carbamate moiety. Furthermore, the α-glycoside would be the product favored by the kinetic anomeric effect;[25] in the X-ray crystal structure of **6**, the glycosidic bond is oriented antiperiplanar to the position occupied by one of the lone pairs on the pyran oxygen. The erosion of stereocontrol in the ristosamine system is presumably due to steric effects of the carbamate ring. In an analogous oxacarbenium ion formed from **24**/**25**, formation of the α-glycoside would be disfavored as it would result from

(25) Juaristi, E.; Cuevas, G. The Kinetic Anomeric Effect. *The Anomeric Effect*; CRC Press: Boca Raton, 1995; pp 183−194.

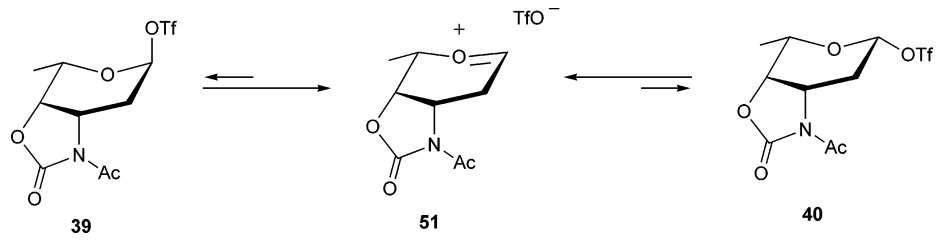


FIGURE 5. Equilibrium between the oxacarbenium ion (**51**) and glycosyl triflate intermediates (**39** and **40**) produced from treatment of thioglycoside **22** with BSP and Tf_2O. The flattening of the pyranose ring induced by the carbamate moiety would be expected to reduce the torsional barrier leading to **51**.

attack of the alcohol syn to the carbamate. That there is still a preponderance of the α-glycoside suggests that there is also a stereoelectronic bias leading to α-glycoside formation or some participation of direct displacement of the triflate leaving group. We note that increased α-selectivity in glycosyl donors possessing fused rings that in turn flatten the pyranose ring have previously been reported by Crich and co-workers for 2,3-carbonate protected systems with the D-*manno* and L-*rhamno* stereochemistry.[9b,26]

In summary, we report here a new and stereospecific synthesis of methyl glycoside derivatives of the 2,3,6-trideoxy-3-amino-hexopyranoses with the L-*xylo* (daunosamine, **7**) and L-*lyxo* (ristosamine, **11** and **20**) stereochemistry. The key steps in the synthesis are a photochemically induced acylnitrene aziridination reaction followed by a regioselecitve hydrogenolytic cleavage of the aziridine. Appropriately protected thioglycoside derivatives of these sugars have also been synthesized, and their utility as glycosylating agents was studied using two promoter systems (NIS/AgOTf and BSP/Tf_2O). Of the two, the BSP/Tf_2O method provides glycosides with the best stereoselectivity, although stereocontrol is not high in all cases. For the promoter systems reported, it appears that these thioglycosides are of modest utility in the stereocontrolled synthesis of ristosamine and duanosamine glycosides.

Experimental Section

General Procedures for Glycosylations. Method A, NIS/AgOTf. Thioglycoside (0.327 mmol) and the glycosyl acceptor (0.980 mmol) were stirred in dichloromethane (10 mL) with activated 4 Å molecular sieves for 30 min. The reaction mixture was cooled in an ice bath at 0 °C, and NIS (0.359 mmol) and AgOTf (0.065 mmol) were added. The reaction mixture was stirred 1 h and was diluted with dichloromethane (10 mL). The reaction mixture was filtered, washed with saturated $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$. The organic layer was dried ($MgSO_4$) and concentrated. The glycoside products were purified by column chromatography.

Method B, BSP/Tf_2O Glycosylation Reactions with Daunosamine Derivatives. Thioglycoside (0.327 mmol), BSP (0.327 mmol) and TTBP (0.653 mmol) were stirred in dichloromethane (5 mL) with activated 4 Å molecular sieves for 30 min. The reaction mixture was cooled in a dry ice/acetone bath at −60 °C, and triflic anhydride (0.359 mmol) was added. The reaction mixture was stirred for 2 min, and a solution of the glycosyl acceptor (0.490 mmol) in dichloromethane (2 mL) was added. After 5 min, the mixture was warmed to room temperature and was diluted with dichloromethane (10 mL). The reaction mixture was filtered and washed with saturated $NaHCO_3$, 1 N HCl, and saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and concentrated. The glycoside products were purified by column chromatography.

Method C, BSP/Tf_2O Glycosylation Reactions with Ristosamine Derivatives. Thioglycoside (0.327 mmol), BSP (0.327 mmol), and TTBP (0.653 mmol) were stirred in dichloromethane (5 mL) with activated 4 Å molecular sieves for 30 min. The mixture was cooled in a dry ice/acetone bath at −60 °C, and triflic anhydride (0.359 mmol) was added, followed immediately by a solution of the glycosyl acceptor (0.490 mmol) in dichloromethane (2 mL). After 5 min the mixture was warmed to room temperature and was diluted with dichloromethane (10 mL). The reaction mixture was filtered and washed with saturated $NaHCO_3$, 1 N HCl, and saturated aqueous NaCl. The organic layer was dried ($MgSO_4$) and concentrated. The glycosides were purified by column chromatography.

Methyl 4-*O*-Azidocarbonyl-2,3,6-trideoxy-α-L-*threo*-hex-2-enopyranoside (5). Alcohol **13**[5a] (820 mg, 5.75 mmol), 1,1′-carbonyldiimidazole (1.40 g, 8.64 mmol), and pyridine (1.40 mL, 17.3 mmol) were dissolved in benzene (20 mL) and stirred for 2 h at room temperature. The reaction mixture was diluted with ethyl acetate (20 mL) and washed with saturated aqueous NaCl (50 mL). The organic layer was dried ($MgSO_4$) and concentrated. The residue was dissolved in DMF (20 mL), and sodium azide (1.87 g, 28.8 mmol) was suspended in the reaction mixture. This mixture was acidified with glacial HOAc (10 mL) until conversion to the acyl azide no longer proceeded, at which point concentrated HCl (5 mL) was added to effect completion. The reaction mixture was poured onto a saturated aqueous solution of $NaHCO_3$, and the layers were separated. The organic layer was washed with $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated. The crystalline solid obtained (**5**, 1.21 g, 98%) was used without further purification: R_f 0.70 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ −265.0 (*c* 1.9, $CHCl_3$); mp 70−73 °C; IR 2988, 2194, 2154, 1724, 1266, 1241, 1108 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.12 (dd, 1 H, *J* = 5.0, 10.0 Hz, C3-H), 6.07 (dd, 1 H, *J* = 2.7, 10.0 Hz, C2-H), 4.91 (d, 1 H, *J* = 2.7 Hz, C1-H), 4.84 (dd, 1 H, *J* = 2.4, 5.0 Hz, C4-H), 4.24 (dq, 1 H, *J* = 2.4, 6.6 Hz, C5-H), 3.43 (s, 3 H, OCH_3), 1.28 (d, 3 H, *J* = 6.6 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5 (C═O), 131.6, 124.5 (C-2, C-3), 95.4 (C-1), 69.4 (C-4), 64.3 (C-5), 55.7 (OCH_3), 15.9 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{11}N_3O_4$ + Na 236.0647, found 236.0647.

Methyl 3-Amino-3-*N*-,4-*O*-carbonyl-2,3,6-trideoxy-α-L-*lyxo*-hexopyranoside (6). Aziridine **14** (460 mg, 2.48 mmol) and 10% palladium on carbon (400 mg, 0.62 mmol Pd) were dissolved in ethyl acetate (20 mL). The reaction vessel was charged with a balloon of hydrogen gas, and the reaction mixture was stirred at room temperature for 3 h, when it was filtered through Celite. The filtrate was concentrated, and the residue was filtered through silica (1 × 3 cm, 5:1 chloroform/methanol) to afford **6** as white crystalline plates (440 mg, 95%): R_f 0.49 (6:1 chloroform/methanol); $[\alpha]^{23}_D$ −47.1 (*c* 0.4, $CHCl_3$); mp 115−120 °C; IR 2936, 2253, 1757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 1 H, NH), 4.84 (app t, 1 H, *J* = 6.0 Hz, C1-H), 4.46 (dd, 1 H, *J* = 1.7, 8.8 Hz, C4-H), 4.19 (app dt, 1 H, *J* = 4.3, 8.8 Hz, C3-H), 3.99 (dq, 1 H, *J* = 1.7, 6.6 Hz, C5-H), 2.08 (app dt, 1 H, *J* = 4.9, 15.0 Hz, C2-H_β), 1.75 (ddd,

(26) Crich, D.; Vinod, A. U.; Picione, J.; Wink, D. J. *ARKIVOC* **2005**, 339−344.

1 H, J = 4.3, 6.0, 15.0 Hz, C2-H$_\alpha$), 1.31 (d, 3 H, J = 6.6 Hz C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (C=O), 96.8 (C-1), 76.2 (C-4), 63.3 (C-5), 54.8 (OCH_3), 47.8 (C-3), 30.0 (C-2), 15.6 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{13}NO_4$ + Na 210.0742, found 210.0736.

Methyl 3-Amino-3-*N*-,4-*O*-carbonyl-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (10). Aziridine **17** (860 mg, 4.64 mmol) and 10% palladium on carbon (1.24 g, 1.16 mmol Pd) were dissolved in a 5:1 solution of ethyl alcohol/ethyl acetate (42 mL). The reaction vessel was charged with a balloon of hydrogen gas. The reaction mixture was stirred at room temperature for 3 h and filtered through Celite with a 10:1 solution of chloroform/methanol (50 mL). The filtrate was concentrated, and the residue was purified by column chromatography (5 × 10 cm silica, 20:1 chloroform/methanol) to afford **10** as a crystalline, granular solid (800 mg, 92%): R_f 0.61 (10:1 chloroform/methanol); $[\alpha]^{23}_D$ −202.0 (*c* 0.3, $CHCl_3$); mp 136−138 °C; IR 3280, 2935, 1760, 1047 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.57 (s, 1 H, NH), 4.71−4.68 (m, 1 H, C1-H), 4.25 (app t, 1 H, J = 8.9 Hz, C4-H), 3.97 (dq, 1 H, J = 6.2, 8.9 Hz, C5-H), 3.96−3.92 (m, 1 H, C3-H), 3.37 (s, 3 H, OCH_3), 2.20 (app dt, 1 H, J = 5.6 14.4 Hz, C2-H$_\beta$), 1.83 (ddd, 1 H, J = 6.8, 9.5, 14.4 Hz, C2-H$_\alpha$), 1.34 (d, 3 H, J = 6.2 Hz, C6-H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 159.5 (C=O), 97.0 (C-1), 78.2 (C-4), 63.7 (C-5), 54.9 (OCH_3), 47.9 (C-3), 31.9 (C-2), 18.7 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{13}NO_4$ + Na 210.0737, found 210.0738.

Methyl 2,3-Diamino-3-*N*-,4-*O*-carbonyl-2,3-*N*-cyclo-2,3,6-trideoxy-α-L-talopyranoside (14). Acyl azide **5** (1.46 g, 6.85 mmol) was dissolved in dichloromethane (685 mL, 0.01 M). In 150-mL portions, the reaction mixture was exposed to 254 nm light at room temperature in quartz vessels for 1 h. The reaction mixture was concentrated, and the brown residue was purified by column chromatography (6 × 12 cm silica, 2:1 hexane/ethyl acetate) to afford **14** as a slightly yellow oil (929 mg, 79%): R_f 0.25 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ −68.0 (*c* 0.3, $CHCl_3$); IR 2938, 2254, 1784, 1340, 1259, 1118 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.08 (br. s, 1 H, C1-H), 4.57 (d, 1 H, J = 6.3 Hz, C4-H), 3.95 (q, 1 H, J = 6.6 Hz, C5-H), 3.52−3.50 (m, 4 H, C3-H, OCH_3), 2.80 (dd, 1 H, J = 0.5, 4.7 Hz, C2-H), 1.21 (d, 3 H, J = 6.6 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9 (C=O), 93.9 (C-1), 72.8 (C-4), 62.6 (C-5), 55.8 (OCH_3), 43.2 (C-2), 41.3 (C-3), 16.3 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{11}NO_4$ + Na 208.0580, found 208.0578.

Methyl 4-*O*-Azidocarbonyl-2,3,6-trideoxy-α/β-L-*erythro*-hex-2-enopyranoside (16). Alcohol **15**[15] (2:1 α:β mixture, 1.50 g, 10.41 mmol), 1,1′-carbonyldiimidazole (2.53 g, 15.61 mmol), and pyridine (2.52 mL, 31.2 mmol) were dissolved in benzene (50 mL) and stirred for 2 h at room temperature. The reaction mixture was diluted with ethyl acetate (40 mL) and washed with saturated aqueous NaCl (100 mL). The organic layer was dried ($MgSO_4$) and concentrated. The crude residue was then dissolved in DMF (40 mL), and sodium azide (3.38 g, 52.0 mmol) was added. This mixture was then acidified with a 1:2 solution of HCl/DMF to pH ∼4. When conversion was complete, the reaction mixture was diluted with ethyl acetate (40 mL) and washed with water (3 × 100 mL) and a saturated aqueous solution of $NaHCO_3$. The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (6 × 12 cm silica, 6:1 hexane/ethyl acetate) to afford **16** as a clear oil (1.65 g, 2:1 α/β, 67%): R_f 0.56 (1:1 hexane/ethyl acetate); IR 2181, 2139, 1730, 1244, 1056 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99−5.83 (m, 2 H, C2-H, C3-H, β/α), 5.05−5.04 (m, 0.9 H, C1-H β), 5.01−4.99 (m, 1 H, C4-H β/α), 4.86 (br. s, 0.1 H, C1-H α), 3.97 (dq, 0.1 H, J = 2.9, 6.2 Hz, C5-H α), 3.90 (app p, 0.9 H, J = 6.5 Hz, C5-H β), 3.48 (s, 2.7 H, OCH_3 β), 3.43 (s, 0.3 H, OCH_3 α), 1.35 (d, 2.7 H, J = 6.5 Hz, C6-H β), 1.27 (d, 0.3 H, J = 6.2 Hz, C6-H α); ^{13}C NMR (100 MHz, $CDCl_3$) δ (β): 157.1 (C=O), 131.3, 126.3 (C-2, C-3) 96.7, (C-1), 73.7 (C-4), 70.6 (C-5), 55.0 (OCH_3), 18.3 (C-6); (α): 157.1 (C=O), 128.6, 128.1 (C-2, C-3) 95.2, (C-1), 75.0 (C-4), 64.2 (C-5), 55.7 (OCH_3), 17.7 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{11}N_3O_4$ + Na 236.0647, found 236.0643.

Methyl 2,3-Diamino-3-*N*-,4-*O*-carbonyl-2,3-*N*-cyclo-2,3,6-trideoxy-α/β-L-allopyranoside (17, 18). Acyl azide **16** (1.50 g, 7.02 mmol, 2:1 α/β) was dissolved in dichloromethane (702 mL, 0.01 M). In 150-mL portions, the reaction mixture was exposed to 254 nm light at room temperature in quartz vessels for 1 h. The reaction mixture was concentrated, and the brown residue was purified by column chromatography (6 × 12 cm silica, 0.9 L of 2:1 hexane/ethyl acetate followed by 1.5 L 1:2 hexane/ethyl acetate) to afford **17** (788 mg, 61%) and **18** (394 mg, 30%) as white solids. Data for **17**: R_f 0.10 (1:1 hexane/ethyl acetate); mp 143−145 °C; IR 1787, 1136, 1110, 1077 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.29 (d, 1 H, J = 2.6 Hz, C1-H), 4.60 (dd, 1 H, J = 1.8, 6.0 Hz, C4-H), 4.16 (dq, 1 H, J = 1.8, 7.0 Hz, C5-H), 3.50 (s, 3 H, OCH_3), 3.46 (dd, 1 H, J = 4.9, 6.0 Hz, C3-H), 3.04 (dd, 1 H, J = 2.6, 4.9 Hz, C2-H), 1.32 (d, 3 H, J = 7.0 Hz, C6-H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.7 (C=O), 93.5 (C-1), 72.9 (C-4), 70.9 (C-5), 56.5 (OCH_3), 43.3 (C-2), 40.3 (C-3), 14.6 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{11}NO_4$ + Na 208.0580, found 208.0572. Data for **18**: R_f 0.25 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ +139.7 (*c* 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.00 (s, 1 H, C1-H), 4.72 (dd, 1 H, J = 2.1, 6.3 Hz, C4-H), 3.94 (dq, 1 H, J = 2.1, 7.2 Hz, C5-H), 3.52 (s, 3 H, OCH_3), 3.51−3.48 (m, 1 H, C3-H), 2.91 (d, 1 H, J = 4.8 Hz, C2-H), 1.37 (d, 3 H, J = 7.2 Hz, C6-H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 163.1 (C=O), 92.6 (C-1), 73.0 (C-4), 66.8 (C-5), 55.9 (OCH_3), 42.2 (C-2), 37.9 (C-3), 15.7 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{11}NO_4$ + Na 208.0580, found 208.0571.

Methyl 3-Amino-3-*N*-,4-*O*-carbonyl-2,3,6-trideoxy-β-L-*ribo*-hexopyranoside (19). Aziridine **18** (380 mg, 2.05 mmol) and 10% palladium on carbon (546 mg, 0.513 mmol Pd) were dissolved in a 5:1 solution of ethyl alcohol/ethyl acetate (20 mL). The reaction vessel was charged with a balloon of hydrogen gas. The reaction mixture was stirred at room temperature for 3 h and filtered through Celite with a 6:1 solution of chloroform/methanol (35 mL). The filtrate was concentrated, and the residue was purified by column chromatography (5 × 10 cm silica, 20:1 chloroform/methanol) to afford **19** as a clear, colorless oil (319 mg, 83%): R_f 0.08 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ +10.7 (*c* 0.2, $CHCl_3$); IR 1761, 1522, 1420 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.49 (s, 1 H, NH), 4.71 (dd, 1 H, J = 2.5, 7.1, C1-H), 4.30−4.25 (m, 1 H, C3-H), 4.20 (app t, 1 H, J = 8.9 Hz, C4-H), 3.73 (dq, 1 H, J = 6.2, 8.9 Hz, C5-H), 3.45 (s, 3 H, OCH_3), 2.07 (ddd, 1 H, J = 2.5, 4.3, 14.4 Hz, C2-H$_\beta$), 1.94 (ddd, 1 H, J = 5.5, 7.1, 14.4 Hz, C2-H$_\alpha$), 1.36 (d, 3 H, J = 6.2 Hz, C6-H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 159.7 (C=O), 98.5 (C-1), 76.8 (C-4), 69.3 (C-5), 55.9 (OCH_3), 49.6 (C-3), 32.1 (C-2), 18.7 (C-6); HRMS (ESI) *m*/*z* calcd for $C_8H_{13}NO_4$ + Na 210.0737, found 210.0738.

***p*-Tolyl 3-Amino-3-*N*-,4-*O*-carbonyl-1,2,3,6-tetradeoxy-1-thio-α-L-*lyxo*-hexopyranoside (21).** Methyl glycoside **6** (890 mg, 4.75 mmol) and 4-methylbenzenethiol (709 mg, 5.71 mmol) were dissolved in dichloromethane (40 mL). Boron trifluoride diethyl etherate (1.51 mL, 11.9 mmol) was added dropwise at room temperature, and the solution was stirred for 2 h. The reaction mixture was poured onto a saturated solution of $NaHCO_3$ (60 mL), and the layers were separated. The aqueous layer was back-extracted with dichloromethane (3 × 10 mL), and the organic layers were combined, dried ($MgSO_4$), and concentrated. The resulting solid was purified by column chromatography (6 × 15 cm silica, 1:1 toluene/ethyl acetate) to afford **21** as white crystalline plates (1.31 g, 99%, >10:1 α/β mixture): R_f 0.59 (6:1 chloroform/methanol); mp 155−159 °C; IR 2986, 2305, 1759, 1421, 1265 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, 2 H, J = 8.1 Hz, ArH), 7.10 (d, 2 H, J = 7.9 Hz, ArH), 6.39 (s 1 H, NH), 5.48 (dd, 1 H, J = 6.2, 9.1 Hz, C1-H), 4.48 (dd, 1 H, J = 1.7, 9.1 Hz, C4-H), 4.23 (app dt, 1 H, J = 4.0, 9.1 Hz, C3-H), 4.17 (dq, 1 H, J = 1.7, 6.5 Hz, C5-H), 2.32 (s, 3 H, $ArCH_3$), 2.22 (ddd, 1 H, J = 4.0, 6.2, 15.2 Hz, C2-H$_\beta$), 1.87 (ddd, 1 H, J = 4.0, 9.1, 15.2 Hz, C2-H$_\alpha$), 1.30 (d, 3 H, J = 6.5 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6 (C=O), 137.5 (aryl C), 132.6 (2 C, aryl), 130.0 (aryl C), 129.7 (2 C, aryl), 81.0 (C-1), 76.2 (C-4), 64.3 (C-5), 48.5 (C-3), 29.9 (C-2), 21.1

($ArCH_3$), 15.8 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{14}H_{17}NO_3S$ + Na 302.0821, found 302.0810.

***p*-Tolyl 3-Acetamido-3-*N*-,4-*O*-carbonyl-1,2,3,6-tetradeoxy-1-thio-α-L-*lyxo*-hexopyranoside (22).** Thioglycoside **21** (1.27 g, 4.55 mmol), acetic anhydride (1.29 mL, 13.6 mmol), and DMAP (55 mg, 0.454 mmol) were dissolved in pyridine (25 mL). The reaction mixture was stirred for 2 h at room temperature, cooled in an ice bath, and quenched by the slow addition of methanol (10 mL). The solution was diluted with dichloromethane (50 mL) and was washed with a saturated aqueous solution of $NaHCO_3$ (100 mL) followed by 2 N HCl (200 mL). The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified by column chromatography (6 × 15 cm silica, 3:1 hexane/ethyl acetate) to afford **22** as white crystalline plates (1.45 g, 99%): R_f 0.46 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ −45.9 (*c* 1.0, $CHCl_3$); mp 115−117 °C; IR 2934, 1785, 1706, 1493, 1375 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.39−7.37 (m, 2 H, ArH), 7.12 (d, 2 H, J = 7.8 Hz, ArH), 5.33 (dd, 1 H, J = 6.0, 8.5 Hz, C1-H), 4.68 (app dt 1 H, J = 4.5, 8.5 Hz, C3-H), 4.44 (dd, 1 H, J = 1.7, 8.5 Hz, C4-H), 4.31 (dq, 1 H, J = 1.7, 6.6 Hz, C5-H), 2.67 (ddd, 1 H, J = 5.1, 6.0, 15.2 Hz, C2-H_β), 2.51 (s, 3 H, $C(O)CH_3$), 2.33 (s, 3 H, $ArCH_3$), 2.04 (ddd, 1 H, J = 4.5, 8.5, 15.2 Hz, C2-H_α), 1.34 (d, 3 H, J = 6.6 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8 (*C*(O)CH_3), 153.3 (C═O), 138.1 (aryl C), 132.7 (2 C, aryl), 129.82 (aryl C), 129.78 (2 C, aryl), 81.4 (C-1), 73.9 (C-4), 63.8 (C-5), 50.9 (C-3), 27.9 (C-2), 24.0 (C(O)*C*H_3), 21.1 ($ArCH_3$), 15.7 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{16}H_{19}NO_4S$ + Na 344.0932, found 344.0932.

***p*-Tolyl 3-Amino-3-*N*-,4-*O*-carbonyl-1,2,3,6-tetra-deoxy-1-thio-α/β-L-*ribo*-hexopyranoside (23).** A mixture of methyl glycosides **10** and **19** (1.10 g, 5.88 mmol) and 4-methylbenzenethiol (876 mg, 7.05 mmol) were dissolved in dichloromethane (55 mL). Boron trifluoride diethyl etherate (1.86 mL, 14.7 mmol) was added dropwise at room temperature. The reaction mixture was stirred for 2 h and poured onto a saturated aqueous solution of $NaHCO_3$ (80 mL). The aqueous layer was back-extracted with dichloromethane (3 × 10 mL), and the organic layers were combined, dried ($MgSO_4$), and concentrated. The resulting solids were purified by column chromatography (5 × 15 cm silica, 2:1 toluene/ethyl acetate) to afford both anomers as white crystalline plates (1.40 g, 85%, 1.8:1 α:β). Data for **23**, α: R_f 0.30 (1:1 toluene/ethyl acetate); $[\alpha]^{23}_D$ −256.4 (*c* 0.3, $CHCl_3$); mp 195−198 °C; IR 3682, 3619, 2400, 1763, 1521, 1476, 1423 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39−7.37 (m, 2 H, ArH), 7.12 (d, 2 H, J = 7.9 Hz, ArH), 5.99 (s, 1 H, NH), 5.31 (dd, 1 H, J = 6.5, 9.4 Hz, C1-H), 4.32 (app t, 1 H, J = 8.9 Hz, C4-H), 4.20 (dq, 1 H, J = 6.1, 8.9 Hz, C5-H), 4.02−3.98 (m, 1 H, C3-H) 2.39 (ddd, 1 H, J = 5.5, 6.5, 14.3 Hz, C2-H_β), 2.33 (s, 3 H, $ArCH_3$), 1.99 (app dt, 1 H, J = 9.4, 14.3 Hz, C2-H_α), 1.35 (d, 3 H, J = 6.1 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1 (C═O), 138.0 (aryl C), 132.7 (2 C, aryl), 130.3 (aryl C), 129.7 (2 C, aryl), 81.8 (C-1), 78.5 (C-5), 64.8 (C-4), 49.1 (C-3), 32.7 (C-2), 21.1 ($ArCH_3$), 18.8 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{14}H_{17}NO_3S$ + Na 302.0827, found 302.0817. Data for **23**, β: R_f 0.40 (1:1 toluene/ethyl acetate); $[\alpha]^{23}_D$ −22.0 (*c* 0.2, $CHCl_3$); mp 140−142 °C; IR 3684, 3620, 2400, 1764, 1520, 1423 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.39−7.36 (m, 2 H, ArH), 7.11 (d, 2 H, J = 7.9 Hz, ArH), 6.17 (s, 1 H, NH), 4.96 (dd, 1 H, J = 2.5, 11.4 Hz, C1-H), 4.25−4.22 (m, 1 H, C3-H), 4.10 (dd, 1 H, J = 7.1, 8.9 Hz, C4-H), 3.64 (dq, 1 H, J = 6.2, 9.0 Hz, C5-H), 2.33 (s, 3 H, $ArCH_3$), 2.21 (app dt, 1 H, J = 2.5, 14.9 Hz, C2-H_β), 1.98 (ddd, 1 H, J = 4.7, 11.4, 14.9 Hz, C2-H_α), 1.36 (d, 3 H, J = 6.2 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8 (C═O), 137.9 (aryl C), 132.2 (2 C, aryl), 129.6 (2 C, aryl), 129.3 (aryl C), 80.4 (C-1), 76.1 (C-5), 73.2 (C-4), 51.1 (C-3), 32.2 (C-2), 21.0 ($ArCH_3$), 19.0 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{14}H_{17}NO_3S$ + Na 302.0827, found 302.0827.

***p*-Tolyl 3-Acetamido-3-*N*-,4-*O*-carbonyl-1,2,3,6-tetradeoxy-1-thio-α/β-L-*ribo*-hexopyranoside (24, 25).** Thioglycosides **23** (1.27 g, 4.55 mmol) were dissolved in pyridine (35 mL), followed by addition of acetic anhydride (1.74 mL, 18.5 mmol) and DMAP (57 mg, 0.462 mmol). The reaction mixture was stirred for 2 h, cooled in an ice bath, and quenched with the slow addition of methanol (10 mL). The mixture was diluted with dichloromethane (100 mL) and poured into a saturated aqueous solution of $NaHCO_3$ (100 mL). The organic layer was washed with 2 N HCl (3 × 100 mL), dried ($MgSO_4$), and concentrated. The residue was purified by column chromatography (4 × 15 cm silica, 4:1 hexane/ethyl acetate) to afford white crystalline plates (1.53 g, 96%, 1.8:1 **24**:**25**). Data for **24**: R_f 0.92 (6:1 chloroform/methanol); $[\alpha]^{23}_D$ −322.5 (*c* 0.2, $CHCl_3$); mp 156−159 °C; IR 1786, 1707, 1375, 1353, 1300, 1210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.38 (m, 2 H, ArH), 7.12 (d, 2 H, J = 8.0 Hz, ArH), 5.33 (dd, 1 H, J = 6.2, 11.3 Hz, C1-H), 4.49 (ddd 1 H, J = 5.3, 8.6, 11.3 Hz, C3-H), 4.28 (app t, 1 H, J = 8.6 Hz, C4-H), 4.11 (dq, 1 H, J = 6.1, 8.6 Hz, C5-H), 2.85 (app dt, 1 H, J = 5.3, 14.0 Hz, C2-H_β), 2.51 (s, 3 H, C(O)-CH_3), 2.33 (s, 3 H, $ArCH_3$), 1.76 (app dt, 1 H, J = 11.3, 14.0 Hz, C2-H_α), 1.36 (d, 3 H, J = 6.1 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1 (*C*(O)CH_3), 153.0 (C═O), 138.1 (aryl C), 133.1 (2 C, aryl), 129.7 (2 C, aryl), 129.6 (aryl C), 81.9 (C-1), 76.4 (C-5), 66.0 (C-4), 51.4 (C-3), 29.5 (C-2), 23.6 (C(O)*C*H_3), 21.1 ($ArCH_3$), 18.8 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{16}H_{19}NO_4S$ + Na 344.0927, found 344.0928. Data for **25**: R_f 0.90 (6:1 chloroform/methanol); $[\alpha]^{23}_D$ −34.2 (*c* 0.23, $CHCl_3$); mp 107−109 °C; IR 1786, 1711, 1370, 1294 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.42−7.39 (m, 2 H, ArH), 7.13 (d, 2 H, J = 7.9 Hz, ArH), 5.06 (dd, 1 H, J = 4.1, 7.5 Hz, C1-H), 4.58 (app dt, 1 H, J = 5.7, 8.5, Hz, C3-H), 4.27 (app t, 1 H, J = 8.5 Hz, C4-H), 3.67 (dq, 1 H, J = 6.2, 8.5 Hz, C5-H), 2.65 (ddd, 1 H, J = 4.1, 5.7, 15.2 Hz, C2-H_β), 2.51 (s, 3 H, $C(O)CH_3$), 2.35 (ddd, 1 H, J = 5.7, 7.5, 15.2 Hz, C2-H_α), 2.34 (s, 3 H, $ArCH_3$), 1.39 (d, 3 H, J = 6.2 Hz, C6-H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3 (*C*(O)CH_3), 153.5 (C═O), 138.2 (aryl C), 133.0 (2 C, aryl), 129.7 (2 C, aryl), 129.0 (aryl C), 80.9 (C-1), 74.1 (C-5), 71.7 (C-4), 52.0 (C-3), 29.9 (C-2), 24.3 (C(O)*C*H_3), 21.1 ($ArCH_3$), 19.0 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{16}H_{19}NO_4S$ + Na 344.0927, found 344.0938.

Cyclohexyl 3-Acetamido-3-*N*-,4-*O*-carbonyl-2,3,6-trideoxy-α/β-L-*lyxo*-hexopyranoside (26, 27). These compounds were synthesized from **22** and cyclohexanol via glycosylation method B, yielding a 4:1 α:β mixture of anomers that was purified by column chromatography (2 × 15 cm silica, 3:1 hexane/ethyl acetate) to afford the α anomer as white crystals and the β anomer as white crystals in 80% combined yield. Data for **26**: R_f 0.63 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ +22.6 (*c* 1.0, $CHCl_3$); mp 135−138 °C; IR 2936, 2858, 1783, 1705, 1376 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.99 (app t, 1 H, J = 4.9 Hz, C1-H), 4.68 (ddd, 1 H, J = 5.6, 6.5, 7.8 Hz, C3-H), 4.35 (dd, 1 H, J = 2.0, 7.8 Hz, C4-H), 4.13 (dq, 1 H, J = 2.0, 6.7 Hz, C5-H), 3.59−3.53 (m, 1 H, cyclohexyl OCH), 2.51 (s, 3 H, $C(O)CH_3$), 2.16 (ddd, 1 H, J = 4.9, 6.5, 14.7 Hz, C2-H_β), 2.04 (app dt, 1 H, J = 5.6, 14.7 Hz, C2-H_α), 1.86−1.84 (m, 2 H, cyclohexyl CH_2), 1.74−1.71 (m, 2 H, cyclohexyl CH_2), 1.54−1.51 (m, 1 H, cyclohexyl CH_2), 1.39−1.18 (m, 5 H, cyclohexyl CH_2), 1.33 (d, 3 H, J = 6.7 Hz, C6-H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.4 (*C*(O)CH_3), 153.4 (C═O), 93.6 (C-1), 75.2 (cyclohexyl OCH), 74.1 (C-4), 62.4 (C-5), 50.2 (C-3), 33.6, 31.6 (cyclohexyl CH_2), 29.2 (C-2), 25.5, 24.1, 23.9 (cyclohexyl CH_2), 23.8 (C(O)*C*H_3), 15.8 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{15}H_{23}NO_5$ + Na 320.1474, found 320.1475. Data for **27**: R_f 0.40 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ +147.1 (*c* 1.0, $CHCl_3$); mp 132−135 °C; IR 2935, 2858, 1786, 1702, 1377 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 4.88 (dd, 1 H, J = 2.7, 5.5 Hz, C1-H), 4.63 (app dt, 1 H, J = 6.1, 8.1 Hz, C3-H), 4.33 (dd, 1 H, J = 1.6, 8.1 Hz, C4-H), 3.84 (dq, 1 H, J = 1.6, 6.5 Hz, C5-H), 3.65−3.61 (m, 1 H, OCH), 2.49 (s, 3 H, $C(O)CH_3$), 2.18 (ddd, 1 H, J = 2.7, 6.1, 14.5 Hz, C2-H_α), 1.94 (app dt, 1 H, J = 5.5, 14.5 Hz, C2-H_β), 1.93−1.90 (m, 1 H, cyclohexyl H), 1.79 (br. s, 1 H, cyclohexyl H), 1.72−1.68 (m, 2 H, cyclohexyl H), 1.50−1.47 (m, 1 H, cyclohexyl H), 1.40, (d, 3 H, J = 6.5 Hz, C6-H), 1.38−1.18 (m, 5 H, cyclohexyl H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.2 (*C*(O)CH_3), 153.3 (C═O), 95.2 (C-1), 75.5 (cyclohexyl OCH), 73.5 (C-4), 67.2 (C-5), 50.3 (C-3), 33.4, 31.4 (cyclohexyl CH_2), 30.1 (C-2), 25.6, 24.0,

23.9 (cyclohexyl CH_2), 23.7 (C(O)CH_3), 17.1 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{15}H_{23}NO_5$ + Na 320.1474, found 320.1477.

Cyclohexyl 3-Acetamido-3-*N*-,4-*O*-carbonyl-2,3,6-trideoxy-α/β-L-*ribo*-hexopyranoside (28, 29). These compounds were synthesized from **24/25** and cyclohexanol via glycosylation methods A and C. Products from both methods were purified by column chromatography (2 × 15 cm silica, 4:1 hexane/ethyl acetate). Method A afforded the products in a 1.3:1 ratio of **28**:**29** in 97% combined yield. Method C afforded the products in a 2:1 ratio of **28**:**29** in 81% combined yield. Compound **28** was isolated as white crystals and **29** as a clear oil. Data for **28**: R_f 0.53 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ −230.7 (*c* 0.9, $CHCl_3$); mp 87−90 °C; IR 2937, 2861, 2355, 1784, 1706, 1374, 1297, 1213 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.00 (dd, 1 H, *J* = 5.9, 8.0 Hz, C1-H), 4.41 (ddd, 1 H, *J* = 5.3, 8.3, 11.7 Hz, C3-H), 4.21 (dd, 1 H, *J* = 8.3, 8.6 Hz, C4-H), 4.43 (dq, 1 H, *J* = 6.2, 8.6 Hz, C5-H), 3.62−3.58 (m, 1 H, OCH), 2.63 (app dt, 1 H, *J* = 5.6, 14.1 Hz, C2-H_β), 2.50 (s, 3 H, C(O)CH_3), 1.85−1.81 (m, 2 H, cyclohexyl H), 1.73−1.66 (m, 2 H, cyclohexyl H), 1.70 (ddd, 1 H, *J* = 8.0, 11.7, 14.1 Hz, C2-H_α), 1.53−1.51 (m, 1 H, cyclohexyl H), 1.43−1.19 (m, 5 H, cyclohexyl H), 1.35 (d, 3 H, *J* = 6.2 Hz, C6-H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 170.2 (*C*(O)CH_3), 153.3 (C═O), 94.1 (C-1), 76.4 (C-4), 75.2 (OCH), 64.1 (C-5), 50.4 (C-3), 33.7, 31.8 (cyclohexyl C), 29.9 (C-2), 25.6, 24.0, 23.9 (cyclohexyl C), 23.6 (C(O)*C*H_3), 18.9 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{15}H_{23}NO_5$ + Na 320.1474, found 320.1467. Data for **29**: R_f 0.73 (1:1 hexane/ethyl acetate); $[\alpha]^{23}_D$ −31.4 (*c* 1.0, $CHCl_3$); IR 2936, 2861, 2355, 1784, 1708, 1368, 1295, 1223 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 5.05 (dd, 1 H, *J* = 2.6, 3.4 Hz, C1-H), 4.69 (ddd, 1 H, *J* = 6.5, 8.6, 8.8 Hz, C3-H), 4.41 (dd, 1 H, *J* = 8.6, 9.4 Hz, C4-H), 3.71 (dq, 1 H, *J* = 6.1, 9.4 Hz, C5-H), 3.63−3.60 (m, 1 H, OCH), 2.63 (ddd, 1 H, *J* = 3.4, 6.5, 14.1 Hz, C2-H_β), 2.52 (s, 3 H, C(O)CH_3), 1.98 (ddd, 1 H, *J* = 2.6, 8.8, 14.1 Hz, C2-H_α), 1.84−1.81 (m, 2 H, cyclohexyl H), 1.72−1.66 (m, 2 H, cyclohexyl H), 1.53−1.50 (m, 1 H, cyclohexyl H), 1.39−1.19 (m, 5 H, cyclohexyl H), 1.35 (d, 3 H, *J* = 6.1 Hz, C6-H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 171.0 (*C*(O)CH_3), 153.6 (C═O), 94.3 (C-1), 75.0 (C-4), 74.9 (OCH), 67.7 (C-5), 50.1 (C-3), 33.8, 31.7 (cyclohexyl C), 31.0 (C-2), 25.6, 24.1, 24.0 (cyclohexyl C), 23.8 (C(O)*C*H_3), 19.0 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{15}H_{23}NO_5$ + Na 320.1474, found 320.1463.

Cyclohexyl 3-Amino-2,3,6-trideoxy-α-L-*lyxo*-hexopyranoside (30). Cyclohexyl glycoside **26** (20 mg, 0.067 mmol), barium hydroxide octahydrate (1.49 g, 4.71 mmol), and water (3 mL) were heated in an oil bath at 125 °C for 1 h, cooled slightly, diluted with water (5 mL), and cooled to 25 °C. The reaction mixture was filtered, and dry ice was added to the filtrate to precipitate $BaCO_3$. This mixture was filtered and concentrated, and the residue was dissolved in methanol, filtered, and concentrated. The product was purified by column chromatography (1 × 2 cm silica, 4:1 chloroform/methanol) to afford **30** as a colorless oil (13 mg, 85%): R_f 0.02 (6:1 chloroform/methanol); $[\alpha]_D$ −125.9 (*c* 1.0, CH_3OH); IR 3594, 2356, 1665, 1578 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.01 (app d, 1 H, *J* = 3.7 Hz, C1-H), 3.95 (app q, 1 H, *J* = 6.6 Hz, C5-H), 3.59−3.52 (m, 1 H, cyclohexyl OCH), 3.50 (br. s, 1 H, C4-H) 3.34−3.30 (m, 1 H, C3-H), 1.88−1.79 (m, 2 H, cyclohexyl CH_2), 1.83 (app dt, 1 H, *J* = 3.7, 12.6 Hz, C2-H_β), 1.74−1.65 (m, 3 H, cyclohexyl CH_2, C2-H_α), 1.54−1.51 (m, 1 H, cyclohexyl H), 1.41−1.21 (m, 5 H, cyclohexyl CH_2), 1.18 (d, 3 H, *J* = 6.6 Hz, C6-H); ^{13}C NMR (100 MHz, CD_3OD) δ 95.9 (C-1), 75.8 (cyclohexyl OCH), 70.3 (C-4), 67.7 (C-5), 48.2 (C-3), 34.5, 32.6 (cyclohexyl CH_2), 32.4 (C-2), 26.8, 25.2, 25.0 (cyclohexyl CH_2), 17.1 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{12}H_{23}NO_3$ + Na 252.1576, found 252.1576.

Cyclohexyl 3-Amino-2,3,6-trideoxy-β-L-*lyxo*-hexopyranoside (31). Cyclohexyl glycoside **27** was deprotected as described for the synthesis of **30** to afford **31** in 86% yield: R_f 0.02 (6:1 chloroform/methanol); $[\alpha]_D$ +31.0 (*c* 0.9, CH_3OH); IR 3533, 3127, 1666, 1170 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 4.60 (dd, 1 H, *J* = 2.2, 9.6 Hz, C1-H), 3.69−3.66 (m, 1 H, cyclohexyl OCH), 3.53 (dq, 1 H, *J* = 0.9, 6.5 Hz, C5-H), 3.36 (app d, 1 H, *J* = 3.0 Hz, C4-H) 2.93 (ddd, 1 H, *J* = 3.0, 4.5, 12.6 Hz, C3-H), 1.95−1.88 (m, 2 H, cyclohexyl CH_2), 1.74−1.70 (m, 3 H, cyclohexyl CH_2, C2-H_α), 1.53 (ddd, 1 H, *J* = 9.6, 12.6, 12.6 Hz, C2-H_β), 1.56−1.50 (m, 1 H, cyclohexyl CH_2), 1.34−1.22 (m, 5 H, cyclohexyl CH_2), 1.24 (d, 3 H, *J* = 6.5 Hz, C6-H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 99.6 (C-1), 77.4 (cyclohexyl OCH), 73.1 (C-5), 70.5 (C-4), 51.6 (C-3), 35.4 (C-2), 34.7, 33.0, 26.8, 25.2, 25.1 (cyclohexyl CH_2), 17.2 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{12}H_{23}NO_3$ + H 230.1756, found 230.1759.

Cyclohexyl 3-Amino-2,3,6-trideoxy-α-L-*ribo*-hexopyranoside (32). Cyclohexyl glycoside **28** was deprotected as described for the synthesis of **30** to afford **32** in 87% yield: R_f 0.10 (6:1 chloroform/methanol); $[\alpha]^{23}_D$ −131.6 (*c* 1.0, CH_3OH); IR 3582, 2672, 2356, 1666, 1579 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 5.01 (app t, 1 H, *J* = 2.5 Hz, C1-H), 3.84 (dq, 1 H, *J* = 6.2, 9.1 Hz, C5-H), 3.61−3.57 (m, 1 H, cyclohexyl OCH), 3.42−3.34 (m, 2 H, C3-H, C4-H) 2.03−2.01 (m, 2 H, C2-H), 1.94−1.87 (m, 2 H, cyclohexyl CH_2), 1.77−1.71 (m, 2 H, cyclohexyl CH_2), 1.56−1.53 (m, 1 H, cyclohexyl CH_2), 1.46−1.41 (m, 1 H, cyclohexyl CH_2), 1.38−1.26 (m, 4 H, cyclohexyl CH_2), 1.24 (d, 3 H, *J* = 6.2 Hz, C6-H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 95.6 (C-1), 77.1 (cyclohexyl OCH), 70.9 (C-4), 64.9 (C-5), 50.5 (C-3), 34.5, 33.7 (cyclohexyl CH_2), 32.5 (C-2), 26.7, 25.2, 25.0 (cyclohexyl CH_2), 18.1 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{12}H_{23}NO_3$ + Na 252.1576, found 252.1582.

Cyclohexyl 3-Amino-2,3,6-trideoxy-β-L-*ribo*-hexopyranoside (33). Cyclohexyl glycoside **29** was deprotected as described for the synthesis of **30** to afford to afford **33** in 87% yield: R_f 0.10 (6:1 chloroform/methanol); $[\alpha]^{23}_D$ +41.5 (*c* 1.2, CH_3OH); IR 3546, 3111, 2692, 2146, 1662, 1578 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 4.98 (dd, 1 H, *J* = 2.5, 8.4 Hz, C1-H), 3.71 (dq, 1 H, *J* = 6.4, 8.1 Hz, C5-H), 3.69−3.64 (m, 1 H, cyclohexyl OCH), 3.49 (app q, 1 H, *J* = 4.5 Hz, C3-H) 3.40 (dd, 1 H, *J* = 4.5, 8.1 Hz, C4-H), 1.98 (ddd, 1 H, *J* = 2.5, 4.5, 14.1 Hz, C2-H_α), 1.89−1.87 (m, 2 H, cyclohexyl CH_2), 1.80 (ddd, 1 H, *J* = 4.5, 8.4, 14.1 Hz, C2-H_β), 1.74−1.71 (m, 2 H, cyclohexyl CH_2), 1.55−1.52 (m, 1 H, cyclohexyl CH_2), 1.38−1.18 (m, 5 H, cyclohexyl CH_2), 1.27 (d, 3 H, *J* = 6.4 Hz, C6-H); ^{13}C NMR (125.7 MHz, CD_3OD) δ 95.8 (C-1), 77.1 (cyclohexyl OCH), 71.6, 71.4 (C-5, C-4), 50.1 (C-3), 35.9 (C-2), 34.6, 32.8, 26.8, 25.1, 25.0 (cyclohexyl CH_2), 19.0 (C-6); HRMS (ESI) *m*/*z* calcd for $C_{12}H_{23}NO_3$ + Na 252.1576, found 252.1578.

Computational Methods

Initial structures of **39**−**42** were fully optimized at the B3LYP/6-31G* level of theory in the gas phase.[22] Each stationary point was confirmed to be a minimum on the potential energy surface by calculation of the vibrational frequencies (second derivatives of the energy vs coordinate), and all vibrational modes of each optimized structure possessed only real vibrational frequencies. A scaling factor of 0.9806 was used for the zero-point vibrational

(27) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502−16513.
(28) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Pettersson, G. A.; Nakatsuji, H; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Lui, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. *Gaussian 03*, Revision C.02; Gaussian, Inc.: Wallingford, CT, 2004.

energy (ZPE) correction.[27] After optimization, a single-point energy of each optimized structure was calculated at the B3LYP/6-311+G-(3df,3pd) level of theory. All of the calculations for structures **39**−**42** were performed with Gaussian03.[28]

Acknowledgment. The National Institutes of Health supported this work through grant AI44045. Computational resources from the Ohio Supercomputer Center are gratefully acknowledged.

Supporting Information Available: Additional data supporting anomeric stereochemistry from glycosylation reactions; Cartesian coordinates, vibrational frequencies and absolute energies of **39**−**42**; data for additional new compounds not included above; ^{1}H and ^{13}C NMR spectra of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

JO061167Z