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α-*N*-Acetylmannosamine (ManNAc) Synthesis via Rhodium(II)-Catalyzed Oxidative Cyclization of Glucal 3-Carbamates†

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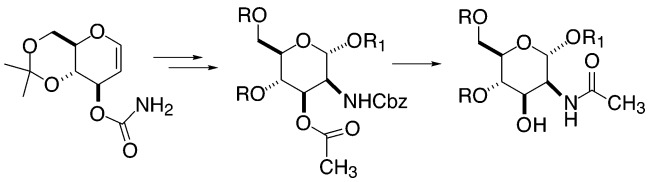

Glucal 3-carbamates **1** and **7** underwent oxidative cyclization with iodobenzene diacetate or iodosobenzene in the presence of $Rh_2(OAc)_4$, providing mannosamine 2-*N*,3-*O*-oxazolidinones. With iodosobenzene, incorporation of 4-penten-1-ol provided a readily separable anomeric mixture of *n*-pentenyl glycosides, with the anomers exhibiting pronounced differences in reactivity as glycosyl donors. N-acylation of the sugar oxazolidinones led to α-selective glycosyl donors for the elaboration of various 2-mannosamine frameworks. Alternatively, the anomeric *n*-pentenyl glycosides of *N*-Cbz 2-mannosamine oxazolidinones were converted separately to oxazolidinone-opened derivatives **28**α and **28***β*. These served as stereoconvergent glycosyl donors, and the α-linked products were readily advanced to a variety of *N*-acetylmannosamine (ManNAc) frameworks, using an intramolecular O→N acetyl transfer as the final step.

Introduction

N-Acetylmannosamine (ManNAc) is the biosynthetic precursor of the nine-carbon α-keto acid *N*-acetylneuraminic acid, the progenitor of the structurally diverse family of sialic acids.[1] Chemically modified ManNAc units can be incorporated in vivo into the sialic acid termini of cell-surface glycans, a valuable tool for probing the biochemistry of cell-surface recognition processes.[2] The biological significance and utility of ManNAc structures provide powerful incentives for the development of new synthetic routes to these building blocks. Classical methods for synthesis of the 2-mannosamine framework include epimerization at the N-bearing carbon,[3] stereoselective reduction of C2 oxime derivatives,[4] and, most commonly, C2 inversion via nucleophilic displacement, both inter-[5] and intramolecular.[6]

Amidation of glucal derivatives, meanwhile, offers unique opportunities for 2-amino-2-deoxy-mannopyranoside synthesis but presents the challenge of incorporating the C2 nitrogen cis to the C3 oxygen substituent (or vice versa).[7] In addition to stereocontrol at the nitrogen-bearing center, glucal amidation methodology should also permit stereoselective incorporation of anomeric substituents and streamlined elaboration to ManNAc-type products. Using a strategy for intramolecular nitrogen

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(1) Angata, T.; Varki, A. *Chem. Rev.* **2002**, *102*, 439−469.

(2) (a) Prescher, J. A.; Dube, D. H.; Bertozzi, C. R. *Nature* **2004**, *430*, 873−877. (b) Luchansky, S. J.; Goon, S.; Bertozzi, C. R. *ChemBioChem* **2004**, *5*, 371−374.

(3) (a) Kuhn, R.; Jochims, J. C. *Liebigs Ann. Chem.* **1959**, *628*, 172−186. (b) Spivak, C. T.; Roseman, S. *J. Am. Chem. Soc.* **1959**, *81*, 2403−2404. (c) Mack, H.; Basabe, J. V.; Brossmer, R. *Carbohydr. Res.* **1988**, *175*, 311−316.

(4) (a) Tsuda, Y.; Okuno, Y.; Iwaki, M.; Kanemitsu, K. *Chem. Pharm. Bull.* **1989**, *37*, 2673−2678. (b) Kaji, E.; Osa, Y.; Takahashi, K.; Hirooka, M.; Zen, S.; Lichtenthaler, F. W. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 1130−1140.

(5) (a) Kiso, M.; Ishida, H.; Kawaide, A.; Hasegawa, A. *Carbohydr. Res.* **1984**, *127*, 129−135. (b) Sato, K.; Yoshitomo, A. *Chem. Lett.* **1995**, 39−40. (c) Sato, K.; Yoshitomo, A.; Takai, Y. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 885−890. (d) Stolz, F.; Reiner, M.; Blume, A.; Reutter, W.; Schmidt, R. R. *J. Org. Chem.* **2004**, *69*, 665−679.

(6) (a) Cerny, M.; Vecerková, H.; Cerny, I.; Pacák, J. *Collect. Czech. Chem. Commun.* **1980**, *45*, 1837−1844. (b) Cerny, I.; Trnka, T.; Cerny, M. *Collect. Czech. Chem. Commun.* **1983**, *48*, 2386-2394. (c) Knapp, S.; Kukkola, P. J.; Sharma, S.; Dhar, T. G. M.; Naughton, A. B. J. *J. Org. Chem.* **1990**, *55*, 5700−5710. (d) Knapp, S. *Chem. Soc. Rev.* **1999**, *28*, 61−72.

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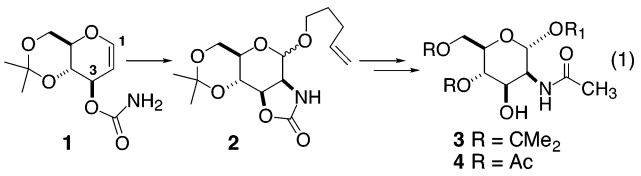
atom delivery that we first applied to allal amidoglycosylation,[8] we have now found that glucal 3-carbamates such as **1**, with iodine(III) oxidation and Rh(II) catalysis,[9] provide β-face C2−N bond formation[10] and in situ addition of an alcohol nucleophile at C1 (eq 1).

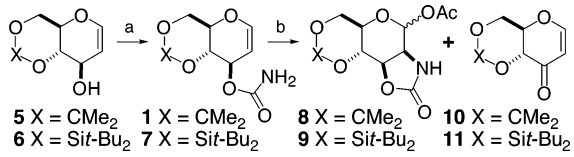


In contrast to our results in the allal series,[8] amidoglycosylation of glucal 3-carbamates **1** and **7** provided anomeric mixtures, making direct incorporation of the final acceptor impractical. Instead, we introduced an *n*-pentenyl glycoside (NPG) (**1** → **2**), expecting that either anomer could act as a stereoselective glycosyl donor after appropriate modification of the mannosamine scaffold, including N-acylation. As described in this article, we have successfully implemented such a strategy as a new route to α-linked ManNAc derivatives from glucal starting materials. We show that the NPGs **2** can be advanced to ManNAc products **3** and **4**, and we have utilized an intramolecular O→N acetyl transfer to install the acetamide function, while selectively revealing the C3 hydroxyl of the ManNAc framework.

Results and Discussion

Glucal 3-carbamates **1** and **7** were readily available from D-glucal via the known alcohols **5**[11] and **6**,[12] using the method of Kocovsky[13] (Scheme 1). Treatment of acetonide-protected **1** with iodobenzene diacetate in the presence of $Rh_2(OAc)_4$ provided 2-amidomannosyl acetates **8** as a chromatographically separable 2.6:1 mixture of anomers. The less polar, major anomer had a C1−H singlet (δ 6.13) in the ^{1}H NMR spectrum (300 MHz, $CDCl_3$), while the more polar, minor diastereomer showed

SCHEME 1[a]



[a] Key: (a) trichloroacetyl isocyanate, CH_2Cl_2, 0 °C, 30 min, then K_2CO_3, MeOH, 23 °C, 71% of **1**, 90% of **7**; (b) $PhI(OAc)_2$, $Rh_2(OAc)_4$ (0.1 equiv), MgO, CH_2Cl_2, 40 °C, 18 h, 51% of **8** (**8**α:**8**β = 2.6:1, **8**:**10** = 3.1:1 by ^{1}H NMR of crude product), 34% of **9** (**9**α:**9**β = 2.1:1, **9**:**11** = 2.0:1 by ^{1}H NMR of crude product).

a C1−H doublet (δ 6.09, J = 3.0 Hz). Single-crystal X-ray analysis[14] identified the major anomer as the α-acetate **8**α (see Figures S1 and S2 in the Supporting Information), correlating the ^{1}H NMR data with C1 stereochemistry.[15]

We obtained analogous results, including ^{1}H NMR behavior of the anomers, using the silylene-protected carbamate **7**, although reaction was sluggish compared with that of **1**, resulting in incomplete conversion. Dihydro-4-pyranones **10**[16] and **11** were byproducts in these reactions, while control experiments verified that $Rh_2(OAc)_4$ was required for formation of amidoacetoxylation products **8** and **9** as well as the C3-oxidized byproducts.[17] We also examined alternative dirhodium(II) carboxylate catalysts in the amidoacetoxylation reaction. However, $Rh_2(OAc)_4$ provided higher yields of **8** and **9** than $Rh_2[OC(O)CPh_3]_4$, Rh_2(octanoate)$_4$, or $Rh_2[OC(O)CF_3]_4$. Neither were the alternative catalysts effective in suppressing the formation of dihydropyranones **10** and **11**. In view of these results, further studies utilized the rhodium(II) acetate dimer as the catalyst. Recently, tethered dirhodium(II) carboxylates have been developed to minimize catalyst decomposition via ligand dissociation in C−H amidation reactions,[18] and these novel catalysts may offer additional opportunities in our glycal carbamate systems.

We next investigated in situ glycosylation with iodosobenzene as the oxidant in the presence of an alcohol acceptor. Whereas allal 3-carbamates (differing in C3 stereochemistry from the glucal series) provided highly trans-selective glycosylation relative to the new C2−N bond,[8] we found that stereocontrol was limited using glucal carbamates **1** and **7**. In the allal series, we

(7) (a) Liu, J.; Di Bussolo, V.; Gin, D. Y. *Tetrahedron Lett.* **2003**, *44*, 4015−4018. (b) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L., Vega, J. A. *Angew. Chem., Int. Ed.* **2000**, *39*, 2525−2529. (c) Nicolaou, K. C.; Baran, P. S.; Zhong, Y.-L.; Barluenga, S.; Hunt, K. W.; Kranich, R.; Vega, J. A. *J. Am. Chem. Soc.* **2002**, *124*, 2233−2244. (d) Takeda, K.; Kaji, E.; Nakamura, H.; Akiyama, A.; Konda, Y.; Mizuno, Y.; Takayanagi, H.; Harigaya, Y. *Synthesis* **1996**, 341−348. (e) Takeda, K.; Kaji, E.; Konda, Y.; Sato, N.; Nakamura, H.; Miya, N.; Morizane, A.; Yanagisawa, Y.; Akiyama, A.; Zen, S.; Harigaya, Y. *Tetrahedron Lett.* **1992**, *33*, 7145−7148. (f) Paulsen, H.; Lorentzen, J. P. *Carbohydr. Res.* **1984**, *133*, C1−C4. (g) Baer, H. H.; Siemsen, L.; Defaye, J.; Burak, K. *Carbohydr. Res.* **1984**, *134*, 49−61. (h) Dyong, I.; Lam-Chi, Q.; Schulte, G.; Fraser-Reid, B.; Primeau, J. L. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 553−554. (i) Heyns, K.; Feldmann, J. *Tetrahedron Lett.* **1977**, 2789−2792. (j) Lemieux, R. U.; Nagabhushan, T. L. *Can. J. Chem.* **1968**, *46*, 401−403.

(8) Levites-Agababa, E.; Menhaji, E.; Perlson, L. N.; Rojas, C. M. *Org. Lett.* **2002**, *4*, 863−865.

(9) Development for intramolecular C−H insertion using carbamates: (a) Espino, C. G.; Du Bois, J. *Angew. Chem., Int. Ed.* **2001**, *40*, 598−600. Application to intramolecular aziridination using carbamates: (b) Padwa, A.; Flick, A. C.; Leverett, C. A.; Stengel, T. *J. Org. Chem.* **2004**, *69*, 6377−6386. (c) Padwa, A.; Stengel, T. *Org. Lett.* **2002**, *4*, 2137−2139. (d) Liang, J.-L.; Yuan, S.-X.; Chan, P. W. H.; Che, C.-M. *Tetrahedron Lett.* **2003**, *44*, 5917−5920.

(10) Review of iminoiodinanes in C−N bond formation: Dauban, P.; Dodd, R. H. *Synlett* **2003**, 1571−1586.

(11) Kjølberg, O.; Neumann, K. *Acta Chem. Scand.* **1993**, *47*, 843−845.

(12) Hoberg, J. O. *Carbohydr. Res.* **1997**, *300*, 365−367.

(13) Kocovsky, P. *Tetrahedron Lett.* **1986**, 27, 5521−5524.

(14) Crystallographic data (excluding structure factors) for **8**α have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-254675. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.; fax +44 1223 336033; e-mail deposit@ccdc.cam.ac.uk).

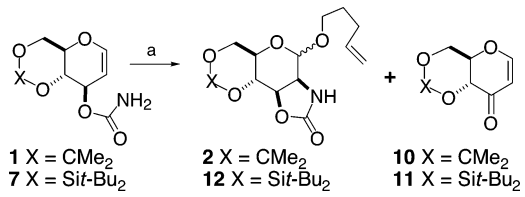
(15) Very similar $J_{H1,H2}$ couplings (0 Hz for the α-anomers, 3 Hz for the β-anomers) are observed in the conformationally analogous 2,3-*O*-carbonates of manno- and rhamnopyranosides: (a) Günther, W.; Kunz, H. *Carbohydr. Res.* **1992**, *228*, 217−241. (b) Crich, D.; Cai, W.; Dai, Z. *J. Org. Chem.* **2000**, *65*, 1291−1297. (c) Crich, D.; Vinod, A. U.; Picione, J. *J. Org. Chem.* **2003**, *68*, 8453−8458.

(16) (a) Fraser-Reid, B.; Walker, D. L.; Tam, S. Y.-K.; Holder, N. L. *Can. J. Chem.* **1973**, *51*, 3950−3954. (b) Fetizon, M.; Khac, D. D.; Tho, N. D. *Tetrahedron Lett.* **1986**, *26*, 1777−1780.

(17) We are investigating mechanistic possibilities for dihydro-4-pyranone production, including initial iodonium formation at the glycal C=C and elimination of a proton from C3 or C3 hydride transfer to the carbonyl oxygen of a metallanitrene intermediate. Compare: (a) Kirschning, A. *Eur. J. Org. Chem.* **1998**, 2267−2274. (b) Doyle, M. P.; Dyatkin, A. B.; Autry, C. L. *J. Chem. Soc., Perkin Trans. 1* **1995**, 619−622.

(18) Espino, C. G.; Fiori, K. W.; Kim, M.; Du Bois, J. *J. Am. Chem. Soc.* **2004**, *126*, 15378−15379.

SCHEME 2[a]



[a] Key: (a) 4-penten-1-ol (5 equiv), PhIO, $Rh_2(OAc)_4$ (0.06−0.10 equiv), 4 Å molecular sieves, CH_2Cl_2, 23 °C, 61% of **2** (**2**α:**2**β = 1.3:1, **2**:**10** = 3.1:1 by ^{1}H NMR of crude product), 53% of **12** (**12**α:**12**β = 2.2:1, **12**:**11** = 3.2:1 by ^{1}H NMR of crude product).

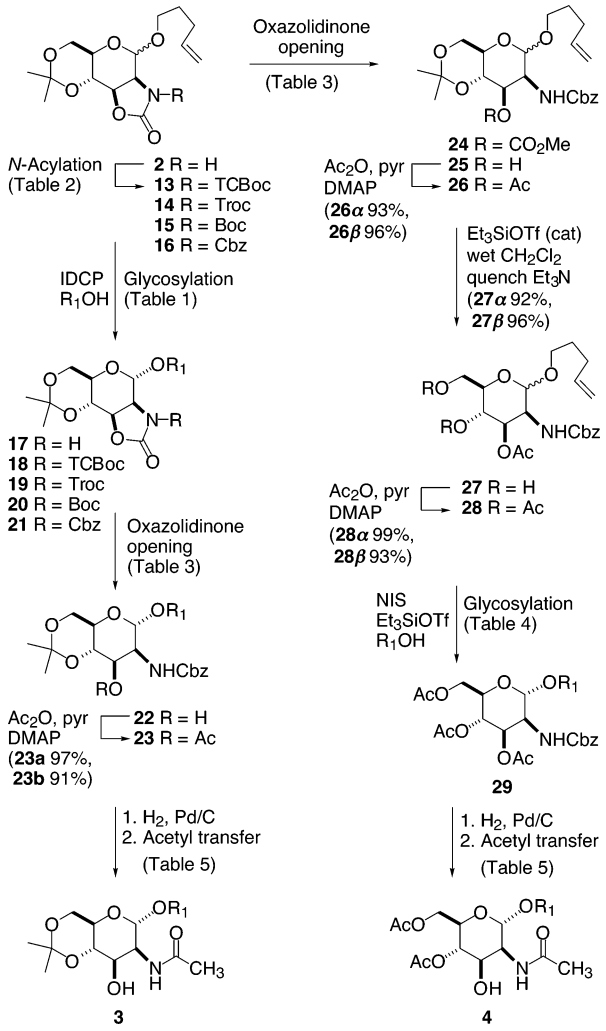
attributed the high level of anomeric stereocontrol to the intermediacy of a glycosyl aziridine or possibly a metallacycle that would offer anchimeric assistance from the C2 substituent during the nucleophilic addition at C1.[8] While we did not observe such an intermediate directly, we noted in another study that the glycosyl chlorides of an allosamine 2*N*,3*O*-oxazolidinone gave low stereoselectivity as donors under ionizing conditions with silver(I) salts.[19] This suggested that an open oxocarbenium intermediate could not account for the high anomeric stereoselectivity in the rhodium-promoted amidoglycosylation reactions of *allal* carbamates.

On the other hand, in our current studies with *glucal* carbamates **1** and **7**, it appears that amidoglycosylation proceeds via an intermediate with greater C1-oxocarbenium character and with little participation from the C2 nitrogen. In related reactions of indole carbamates, Padwa proposed metal-free zwitterionic intermediates and suggested that the anionic nitrogen might assist in cis addition of alcohol nucleophiles by helping deprotonate the incoming hydroxyl group.[9b,c] In our case, such a phenomenon could be responsible for the increased levels of cis amidoglycosylation products when starting from glucal carbamates **1** and **7**.

Because of the lack of C1 stereoselectivity in the amidoglycosylation process using **1** or **7**, we opted to incorporate a latent anomeric activating group that could be replaced later in the synthesis with high levels of stereocontrol. Inclusion of 4-penten-1-ol in the reaction for nitrogen insertion in **1** provided NPGs **2** as a 1.3:1 anomeric mixture, along with byproduct **10** (Scheme 2). A similar result, but with lower efficiency, was obtained by starting from **7**. The anomeric distributions were similar for **2** and **12**, with the α-NPG as the major product in each case, as determined by ^{1}H NMR comparison of the C1−H resonances (singlets for the major anomers, doublets for the minor anomers). In addition to the difference in yields, the anomers of **2** were readily separable,[20] while those of **12** were not, leading to the selection of the acetonide-protected system **2** for further elaboration.

We investigated two complementary strategies, differing in the order of the glycosylation and oxazolidinone-opening steps, for the stereoconvergent advancement of NPGs **2** to α-linked ManNAc derivatives **3** and **4** (Scheme 3). In the path toward products **3**, NPGs **2** or N-acylated

SCHEME 3. Complementary Strategies for Elaborating NPGs 2 to ManNAc Frameworks 3 and 4



derivatives **13**−**16** were first used as stereoselective glycosyl donors, providing α-glycosides **17**−**21**. Oxazolidinone opening of the *N*-Cbz compounds **21** then provided **23** after 3-O-acetylation. In the alternative route, initial oxazolidinone opening of *N*-Cbz derivatives **16** led to NPGs **28**, following manipulation of the hydroxyl protecting groups. Subsequent glycosylation using either anomer of **28** provided α-linked derivatives **29** with complete stereocontrol. Along both routes, the final step (**23** → **3** or **29** → **4**) was an intramolecular acetyl transfer that occurred upon removal of the N protection. Detailed below are the results of our studies to develop these two complementary strategies. Because the anomers of **2** were readily separable, we were able to advance them individually, providing insights into their differing reactivities.

We began by examining the efficacy of NPGs **2** as donors in iodonium-promoted glycosylations.[21] Using iodonium di-*sym*-collidine perchlorate (IDCP)[22] activation

(19) Churchill, D. G.; Rojas, C. M. *Tetrahedron Lett.* **2002**, *43*, 7225−7228.

(20) The anomer **2**α elutes with **10** on silica gel chromatography. The byproduct can be removed by brief treatment in basic methanol (Cs_2CO_3) or after N-acylation of **2**α.

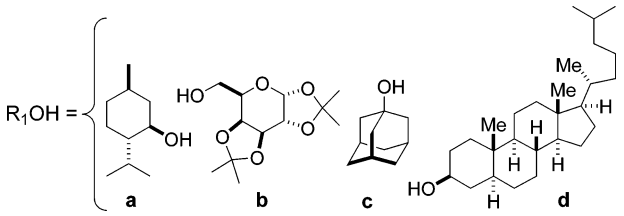
(21) (a) Fraser-Reid, B.; Udodong, U. E.; Wu, Z.; Ottosson, H.; Merritt, J. R.; Rao, C. S.; Roberts, C.; Madsen, R. *Synlett* **1992**, 927−942. (b) Fraser-Reid, B.; Madsen, R. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, 1997; pp 339−356.

TABLE 1. Glycosylation Using Oxazolidinone-Protected NPGs 2 and 13−16[a,b]

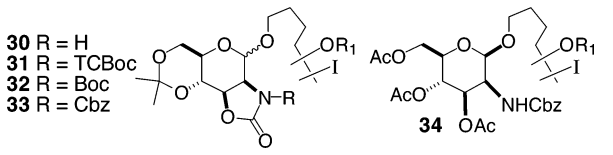
entry	starting material	R_1OH	product (% yield[c])	α:β
1	**2**α	**a**	**17a** (53[d,e])	4:1
2	**2**β	**a**	**17a** (24[d,e])	5:1
3	**13**α	**a**	**18a** (41[f])	α only
4	**14**α	**a**	**19a** (50[f])	α only
5	**15**α	**a**	**20a** (63[f])	α only
6	**16**α	**a**	**21a** (71[f])	α only
7	**16**α	**b**	**21b** (64[f])	α only
8	**16**α	**c**	**21c** (73[f])	α only
9	**16**α	**d**	**21d** (35[f,g])	α only
10	**16**β	**a**	**21a** (4[f,h])	α only

[a] See Scheme 3. [b] Conditions: R_1OH (2 equiv), IDCP = iodonium di-*sym*-collidine perchlorate (2−4 equiv), 4 Å molecular sieves, CH_2Cl_2, 23 °C, 18−24 h. [c] Isolated yield after silica gel chromatography. [d] Using 2 equiv of IDCP. [e] Combined yield of both anomers. [f] Using 4 equiv of IDCP. [g] 42% of the acceptor recovered as the corresponding ketone. [h] 51% recovered starting material and 15% of iodoetherification byproduct **33a**β isolated after 21 h.

and (−)-menthol (**a** series) as the acceptor, both **2**α and **2**β provided glycosylated product **17a** with modest ano-



meric selectivity (Table 1, entries 1 and 2). We also detected the regio- and stereoisomeric byproducts **30a** from direct iodoetherification of the *n*-pentenyl alkene.[23]



We noted that, under a common set of conditions, more of the byproducts formed and a lower yield of desired product was obtained starting from **2**β (Table 1, entry 2) compared to **2**α (Table 1, entry 1). Although NPGs **2**α and **2**β serve as stereoconvergent donors, ionization of **2**α occurs more readily, possibly for stereoelectronic reasons.[24] In fact, the X-ray structure of model system **8**α (see Figure S1 in the Supporting Information) shows a rigid tricyclic framework with the exocyclic anomeric C−O bond well positioned for cleavage with participation by the antiperiplanar ring-oxygen lone pair.

TABLE 2. Preparation of N-Acyl Oxazolidinones 13−16[a,b]

entry	starting material	acyl−X[c]	product[d] (% yield[e])
1	**2**α	A	**13**α (65)
2	**2**α	B	**14**α (62)
3	**2**α	C	**15**α (80)
4	**2**α	D	**16**α (92)
5	**2**β	D	**16**β (77)

[a] See Scheme 3. [b] Conditions: acyl−X, Et_3N, DMAP, THF, 23 °C. [c] Acyl-X: (A) 2,2,2-trichloro-1,1-dimethylethyl chloroformate; (B) 2,2,2-trichloroethyl chloroformate; (C) di-*tert*-butyl dicarbonate; (D) benzyl chloroformate. [d] TCBoc = (2,2,2-trichloro-1,1-dimethylethoxy)carbonyl, Troc = (2,2,2-trichloroethoxy)carbonyl, Boc = *tert*-butoxycarbonyl, Cbz = (benzyloxy)carbonyl. [e] Isolated yield after silica gel chromatography.

To enhance anomeric stereocontrol and yields, we sought to introduce a suitable group at the oxazolidinone nitrogen. In systematizing the use of protecting groups for differential activation of glycosyl donors, Wong has noted dramatic effects with carbamate-protected 2-amino sugars.[25] We prepared the series of carbamate derivatives **13**−**16** (Scheme 3 and Table 2) for comparison with **2** in glycosylations using IDCP and (−)-menthol (Table 1, entries 3−6). N-acylation allowed complete stereocontrol, as only the α-anomers of products **18**−**21** formed, along with some (9−22%) of the iodoetherification byproducts (e.g., **31**−**33**).[23] However, N-acyl donors **13**−**16** were deactivated, requiring 4 equiv of IDCP for adequate conversion of starting material. We did not observe the dramatic activating effect for the *N*-Troc group that was evident in Wong's studies using *p*-methylphenyl thioglycoside donors[25] and that has also been applied with a glycosyl bromide donor[26] but obtained best results with the Cbz-protected **16**α (Table 1, entry 6).

The donor **16**α was also effective for glycosylation of a C6−OH galactopyranoside (**b** series, Table 1, entry 7), 1-adamantanol (**c** series, Table 1, entry 8), and 3β-dihydrocholesterol (**d** series, Table 1, entry 9), although the yield in this last case was depressed by competing oxidation of the dihydrocholesterol acceptor to ketone under the IDCP conditions. There was a dramatic dependence of donor ability on anomeric configuration, with *N*-Cbz diastereomer **16**β providing only a trace of product **21a** under identical conditions (Table 1, entry 10).[27] This effect may be stereoelectronic (vide supra) or simply steric, with cyclization of the exo-anomeric oxygen onto the iodonium intermediate[21] inhibited by β-face congestion when starting from **16**β.

Suspecting that conformational restraints in the oxazolidinone-containing[28] systems might be responsible for the differing reactivities of the NPG anomers, we next examined ring opening prior to NPG activation as a strategy for conversion of **2** to ManNAc structures. Kerns has reported that 2-glucosamine N−H oxazolidinones are readily ring-opened by addition of cesium alkoxides to the oxazolidinone carbonyl.[28b] However, those conditions, using methanol or 2,2,2-trichloroethanol, were ineffective

(22) Lemieux, R. U.; Morgan, A. R. *Can. J. Chem.* **1965**, *43*, 2190−2198.

(23) Characterization data and isolated yields for the iodoetherification byproducts **30**−**34** are included in the Supporting Information.

(24) (a) Andrews, C. W.; Fraser-Reid, B.; Bowen, J. P. In *The Anomeric Effect and Associated Stereoelectronic Effects*; Thatcher, G. R. J., Ed.; ACS Symposium Series 539; American Chemical Society: Washington, DC, 1993; pp 114−125, and references therein. (b) Li, S.; Kirby, A. J.; Deslongchamps, P. *Tetrahedron Lett.* **1993**, *34*, 7757−7758. (c) Andrews, C. W.; Rodebaugh, R.; Fraser-Reid, B. *J. Org. Chem.* **1996**, *61*, 5280−5289. (d) Deslongchamps, P.; Li, S.; Dory, Y. L. *Org. Lett.* **2004**, *6*, 505−508. (e) Deslongchamps, P.; Dory, Y. L.; Li, S. *Can. J. Chem.* **1994**, *72*, 2021−2027.

(25) Zhang, Z.; Ollmann, I. R.; Ye, X.-S.; Wischnat, R.; Baasov, T.; Wong, C.-H. *J. Am. Chem. Soc.* **1999**, *121*, 734−753.

(26) Saha, S. L.; Van Nieuwenhze, M. S.; Hornback, W. J.; Aikins, J. A.; Blaszczak, L. C. *Org. Lett.* **2001**, *3*, 3575−3577.

(27) For another report of differential NPG anomer reactivity: Svarovsky, S. A.; Barchi, J. J., Jr. *Carbohydr. Res.* **2003**, *338*, 1925−1935.

TABLE 3. Ring Opening of *N*-Cbz Oxazolidinones 16 and 21[a]

entry	starting material	conditions[b]	products (% yield[c])
1	**16**α	A	**25**α + **2**α (1:5[d])
2	**16**α	B	**24**α (47) + **2**α (30)
3	**16**α	C	**25**α (70) + **2**α (26)
4	**16**β	C	**25**β (36) + **2**β (59)
5	**16**β	D	**24**β (45) + **2**β (40)
6	**16**β	A	**25**β (48) + **2**β (31)
7	**21a**	C	**22a** (47) + **17a** (42)
8	**21b**	C	**22b** (61) + **17b** (27)

[a] See Scheme 3. [b] Conditions: (A) LiOH, THF/H_2O (3/1), 0 → 23 °C; (B) Cs_2CO_3, MeOH, −15 → 0 °C, 10 min; (C) NaH, MeOH, PhMe, −70 → −15 °C, 45 min; (D) $BnMe_3NOH$ (40% w/w in MeOH), PhMe, −70 → −20 °C, 2 h. [c] Isolated yield after silica gel chromatography. [d] Ratio from ^1H NMR analysis of the crude product; yields not determined.

for our N−H oxazolidinone **2**α, returning only starting material, even at prolonged reaction times and temperatures up to 80 °C. Evidently, the cis-fused 2-mannosamine oxazolidinone is considerably more stable toward alcoholysis than its trans-fused 2-glucosamine counterpart.

As an alternative, we explored ring opening of the N-acyl oxazolidinones to β-hydroxy carbamates such as **25** (Scheme 3 and Table 3). With an *N*-Boc group, selective reaction at the internal carbonyl is typical,[29] and we have used the method in previous studies in the 2-allosamine series.[30] However, the more synthetically useful[31] *N*-Cbz compounds were far more challenging in terms of site selectivity. With **16**α, simple hydrolysis (Table 3, entry 1) gave predominant cleavage of the *N*-Cbz group, returning oxazolidinone **2**α. Methoxide addition in methanol solution was more selective (Table 3, entry 2), with carbonate **24**α obtained as the major product after a brief reaction time. Inspired by a report from Rivier,[32] we obtained best results for substrate **16**α using an in situ prepared dispersion of sodium methoxide in cold toluene (Table 3, entry 3). Careful temperature control was necessary to ensure complete conversion of the methyl carbonate intermediate **24**α to the desired β-hydroxy carbamate product **25**α, while avoiding cyclization of the **25**α alkoxide back to N−H oxazolidinone **2**α.[33]

Interestingly, under the same conditions, the oxazolidinone-opening behavior of diastereomer **16**β was quite different (Table 3, entry 4), with **2**β as the major product.[34] However, switching to the hydrolytic conditions that were ineffective for **16**α (cf. Table 3, entry 1) gave predominantly the desired ring-opened material **25**β when applied to oxazolidinone **16**β (Table 3, entry 6).

The substrate dependence of ring-opening selectivity was also evident in reactions to advance oxazolidinones **21a** and **21b** (Scheme 3 and Table 3, entries 7 and 8). Nevertheless, the desired β-hydroxy carbamates **22** were obtained as the predominant products, overall material recovery was high, and the N−H oxazolidinone byproducts were amenable to recycling via high-yielding N-acylation reactions. The C3 alcohols **22a** and **22b** were converted in high yield to acetates **23** (Scheme 3) in preparation for final acetyl transfer (vide infra).

Meanwhile, with access to NPGs **25**, we were poised to study glycosylation after oxazolidinone opening. Acetylation of **25** (Scheme 3) provided derivatives **26**, whereupon we noted that the 3-*O*-acetyl NPG **26**α was *not* a competent donor under the same IDCP-mediated conditions that had provided complete conversion of the *N*-Cbz oxazolidinone NPG **16**α (cf. Table 1, entries 6−9). The systems were comparable in terms of the inductive influence of the C2 and C3 substituents, but **26**α lacked the conformational restriction of the oxazolidinone cis fusion. Crich has observed a similar "torsional arming" effect with stereochemically analogous 2,3-*O*-carbonate-protected rhamnosyl bromide donors.[15c]

To overcome the lower reactivity of NPGs **26**, we applied more vigorous (and acidic) conditions, using *N*-iodosuccinimide with triethylsilyl triflate.[21] Due to incompatibility of the acetonide with these glycosylation conditions, each anomer **26** was first converted in high yield to the corresponding triacetate **28** via acetonide cleavage to diol **27**, followed by bis acetylation (Scheme 3).

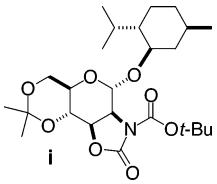
Both NPG anomers **28** provided smooth glycosylation of several acceptors (Scheme 3 and Table 4), stereoconvergently providing products **29** as single anomers. Evidently, neighboring group participation by the *N*-Cbz group engendered anomeric stereocontrol.[35] The slighly lower yields starting from **28**β were due to small quantities (6−11% isolated yields) of alkene iodoetherification byproducts **34** that formed in the reactions of **28**β, but not when **28**α was used.[23] Thus, we have established the alternative strategy of postponing glycosylation of our ManNAc building blocks until after opening of the

(28) For other synthetic applications of sugar oxazolidinones: (a) Kerns, R. J.; Zha, C.; Benakli, K.; Liang, Y.-Z. *Tetrahedron Lett.* **2003**, *44*, 8069−8072. (b) Benakli, K.; Zha, C.; Kerns, R. J. *J. Am. Chem. Soc.* **2001**, *123*, 9461−9462. (c) Crich, D.; Vinod, A. U. *Org. Lett.* **2003**, *5*, 1297−1300. (d) Georges, M.; MacKay, D.; Fraser-Reid, B. *Carbohydr. Res.* **1984**, *130*, 115−124. (e) Kusumoto, S.; Imaoka, S.; Kambayashi, Y.; Shiba, T. *Tetrahedron Lett.* **1982**, *23*, 2961−2964. (f) Pauls, H. W.; Fraser-Reid, B. *J. Am. Chem. Soc.* **1980**, *102*, 3956−3957. (g) Kuzuhara, H.; Emoto, S. *Tetrahedron Lett.* **1975**, 1853−1856. (h) Miyai, K.; Zimmerman, H. K.; Gross, P. H. *J. Org. Chem.* **1969**, *34*, 1635−1637. (i) Miyai, K.; Gross, P. H. *J. Org. Chem.* **1969**, *34*, 1638−1642. (j) Gross, P. H.; Brendel, K.; Zimmerman, H. K. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 379−380. (k) Gross, P. H.; Brendel, K.; Zimmerman, H. K., Jr. *Liebigs Ann. Chem.* **1964**, *680*, 159−162.

(29) Ishizuka, T.; Kunieda, T. *Tetrahedron Lett.* **1987**, *28*, 4185−4188.

(30) Kan, C.; Long, C. M.; Paul, M.; Ring, C. M.; Tully, S. E.; Rojas, C. M. *Org. Lett.* **2001**, *3*, 381−384.

(31) The *N*-Boc derivative **i** did undergo selective hydrolysis (LiOH, THF/H_2O) at the internal carbonyl, revealing the C3 hydroxyl. However, the nonorthogonality of the Boc and acetonide protecting groups complicated subsequent manipulations. In NPG-containing systems, the Boc group also precluded anomeric activation using Lewis acidic conditions (NIS, Et_3SiOTf).



i

(32) Sypniewski, M.; Penke, B.; Simon, L.; Rivier, J. *J. Org. Chem.* **2000**, *65*, 6595−6600.

(33) The latter pathway was demonstrated by isolation of the intermediate carbonate **24**α and resubjection to the reaction conditions, warming above −15 °C, to give **25**α along with cyclized **2**α.

(34) Monitoring by TLC as well as experiments with **16**β in MeOH/Cs_2CO_3 suggested that the altered ratio was due to differing carbonyl site selectivities between the anomers rather than more facile recyclization of the initially formed **25**β alkoxide.

(35) Boullanger, P.; Jouineau, M.; Bouammali, B.; Lafont, D.; Descotes, G. *Carbohydr. Res.* **1990**, *202*, 151−164.

TABLE 4. Stereoconvergent Glycosylation with NPG Anomers 28α and 28*β*[a,b]

entry	starting material	R_1OH	product (% yield[c])
1	**28**α	**a**	**29a** (63)
2	**28***β*	**a**	**29a** (60)
3	**28**α	**c**	**29c** (66)
4	**28***β*	**c**	**29c** (60)
5	**28**α	**d**	**29d** (68)
6	**28***β*	**d**	**29d** (63)

[a] See Scheme 3. [b] Conditions: R_1OH (2 equiv), *N*-iodosuccinimide, Et_3SiOTf, CH_2Cl_2, 23 °C, 20 min, then Et_3N quench. [c] Isolated yield after silica gel chromatography.

TABLE 5. Completion of ManNAc Derivatives via Hydrogenation and Acetyl Transfer of 23 and 29[a,b]

entry	starting material	acetyl transfer conditions[c]	product (% yield[d])
1	**23a**	A	**3a** (77)
2	**23b**	B	**3b** (93)
3	**23b**	C	**3b** (84)
4	**29a**	B	**4a** (77)
5	**29c**	B	**4c** (82)
6	**29c**	D	**4c** (76)

[a] See Scheme 3. [b] Hydrogenation conditions: H_2 (1 atm), 10% Pd/C, 1/1 MeOH/EtOAc, 23 °C. [c] Acetyl transfer conditions: (A) pyr, CH_2Cl_2, 23 °C, 96 h; (B) adsorb on SiO_2, 18−23 h; (C) 2-pyridone (0.5 equiv), pyr-d_5, 75 °C, 96 h; (D) pyr-d_5, 75 °C. [d] Isolated yield (two steps, from **23** or **29**) after silica gel chromatography.

oxazolidinone ring, permitting the use of either NPG anomer. Our study also adds to the limited examples of 2-aza NPG derivatives used as glycosyl donors.[27,36]

To complete the ManNAc arrays **3** and **4**, we applied acetyl migration after N-deprotection of substrates **23** and **29** (Scheme 3 and Table 5). Despite the thermodynamic tendency toward amide products and the proximity of the reacting groups in the intermediate *β*-acetoxy amines, acetyl transfer was sluggish upon hydrogenolysis of the *N*-Cbz compounds, even in the polar, protic (MeOH/EtOAc) reaction mixture.[37] The crude material after hydrogenation of **23a** was converted cleanly to acetamide **3a** upon protracted stirring in the presence of pyridine (Table 5, entry 1). We also found that adsorbing the *β*-acetoxy amines onto silica gel promoted acetyl transfer, providing products **3** and **4** in good yield after chromatographic purification (Table 5, entries 2, 4, and 5).

While even the potentially acid-sensitive tris(acetonide) **23b** was amenable to the SiO_2-mediated procedure, we also explored a complementary route by warming the crude hydrogenation product in pyridine solution (Table 5, entries 3 and 6). With the slower reacting substrate derived from **23b** (Table 5, entry 3, half-life for acetyl transfer >48 h at 75 °C in pyr-d_5), the bifunctional ester-aminolysis catalyst 2-pyridone (0.5 equiv) was added to accelerate the process.[38] The *N*-acetyl mannosamines **3b** and **4c**, bearing free C3 hydroxyls, were isolated in good yields. It is noteworthy that in triacetates **29** it would otherwise be difficult to reveal a single hydroxyl group.

Conclusions

Starting from glucal 3-carbamates **1** and **7**, readily available in gram quantities from D-glucal, we have developed novel synthetic routes to α-linked 2-mannosamine derivatives,[39] including ManNAc frameworks **3** and **4**. Intramolecular nitrogen insertion provided stereocontrolled introduction of the C2−N bond, with concomitant NPG formation. Using appropriate N-acylation, the α-NPG oxazolidinones served as highly stereoselective donors, while the *β*-anomer **16***β* was nearly inert. However, regioselective *N*-Cbz oxazolidinone ring opening prior to glycosylation permitted elaboration of either NPG anomer to the desired ManNAc products. Finally, we utilized an intramolecular O→N acetyl transfer to complete the acetamide functionality. Further studies to develop and apply these concepts in synthesis are under way.

Experimental Section

3-*O*-Carbamoyl-4,6-*O*-isopropylidene-D-glucal (1). To a solution of glucal acetonide **5**[11] (2.207 g, 11.9 mmol) in CH_2Cl_2 (20 mL) was added trichloroacetyl isocyanate (2.11 mL, 17.8 mmol). The solution was stirred at 0 °C for 10 min and then at 23 °C for 1.5 h. MeOH (20 mL) was added, followed by K_2CO_3 (5.03 g, 36.4 mmol). After 30 min at 0 °C and 5 h at 23 °C, the reaction was quenched with NH_4Cl and enough water was added to solubilize all salts. The mixture was extracted with CH_2Cl_2 (3 × 20 mL), dried ($MgSO_4$), filtered, and concentrated. The crude product was recrystallized from EtOAc/hexanes (2/1), providing glucal 3-carbamate **1** as a fluffy white solid (1.938 g, 71%). A higher yield (78%) was obtained on a smaller scale when the product was chromatographed (70% EtOAc/hexanes, SiO_2), but recrystallization was far more convenient on a larger scale due to the limited solubility of the carbamate product in EtOAc/hexanes or CH_2Cl_2. $R_f = 0.36$ (50% EtOAc/hexanes). Mp: 218−219 °C. IR (thin film): 3441, 3339, 3282, 3191, 1717, 1675, 1648, 1626, 1610 cm^{-1}. ^1H NMR (300 MHz, DMSO-d_6): δ 6.90−6.10 (br, 2H), 6.45 (dd, $J = 6.1$, 1.3 Hz, 1H), 5.06 (ddd, $J = 7.9$, 1.6, 1.6 Hz, 1H), 4.69 (dd, $J =$ 6.1, 1.9 Hz, 1H), 3.98 (dd, $J = 9.8$, 8.1 Hz, 1H), 3.93−3.68 (m, 3H), 1.47 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 156.3, 144.7, 101.8, 99.3, 69.5, 69.3, 68.4, 60.6, 28.8, 19.0. HRMS (FAB): *m/z* calcd for $C_{10}H_{16}NO_5$ $(M + H)^+$ 230.1028, found 230.1026.

1-*O*-Acetyl-2-amino-2-*N*,3-*O*-carbonyl-2-deoxy-4,6-*O*-isopropylidene-D-mannopyranosides (8) and the Byproduct 1,2-Dideoxy-4,6-*O*-isopropylidene-D-*erythro*-hex-1-enopyran-3-ulose (10).[16] The glucal 3-carbamate **1** (40 mg, 0.18 mmol), activated MgO (35 mg, 0.88 mmol), $PhI(OAc)_2$ (84 mg, 0.26 mmol), and $Rh_2(OAc)_4$ (8.8 mg, 0.020 mmol) were stirred in CH_2Cl_2 (3.0 mL) at 40 °C in a resealable pressure tube for 18 h. After it was cooled to ambient temperature, the mixture was filtered through Celite and the filtrate was concentrated. The crude material was analyzed by ^1H NMR and chromatographed (50% → 60% → 70% → 80% EtOAc/hexanes, 15 mL of SiO_2), providing pure α-acetate **8**α (15.2 mg, 30%), a mixture of α- and *β*-acetates **8**α and **8***β* (10.3 mg,

(36) (a) Nair, L. G.; Fraser-Reid, B.; Szardenings, A. K. *Org. Lett.* **2001**, *3*, 317−319. (b) Fraser-Reid, B.; Anilkumar, G.; Nair, L. G.; Olsson, L.; Martin, M. G.; Daniels, J. K. *Isr. J. Chem.* **2000**, *40*, 255−262. (c) Anilkumar, G.; Nair, L. G.; Olsson, L.; Daniels, J. K.; Fraser-Reid, B. *Tetrahedron Lett.* **2000**, *41*, 7605−7608. (d) Olsson, L.; Jia, Z. J.; Fraser-Reid, B. *J. Org. Chem.* **1998**, *63*, 3790−3792. (e) Debenham, J. S.; Debenham, S. D.; Fraser-Reid, B. *Bioorg. Med. Chem.* **1996**, *4*, 1909−1918. (f) Mootoo, D. R.; Fraser-Reid, B. *Tetrahedron Lett.* **1989**, *30*, 2363−2366.

(37) For an example of a 3-*O*-acetyl-2-mannosamine isolated without acetyl transfer, see: Yeung, B. K. S.; Adamski-Werner, S. L.; Bernard, J. B.; Poulenat, G.; Petillo, P. A. *Org. Lett.* **2000**, *2*, 3135−3138.

(38) (a) Rony, P. R. *J. Am. Chem. Soc.* **1969**, *91*, 6090−6096. (b) Su, C.-W.; Watson, J. W. *J. Am. Chem. Soc.* **1974**, *96*, 1854−1857.

(39) For a promising example of de novo 2-mannosamine synthesis: Northrup, A. B.; MacMillan, D. W. C. *Science* **2004**, *305*, 1752−1755.

21%), and the byproduct dihydropyranone **10**[16] (6.7 mg, 20%). The pure α-acetate was recrystallized from EtOAc/hexanes (1/1, slow evaporation through Parafilm), providing crystals for X-ray analysis.[14] Data for **8**α: $R_f = 0.35$ (80% EtOAc/hexanes). Mp: 168−170 °C. IR (thin film): 3326, 1766, cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.34 (br s, 1H), 6.14 (s, 1H), 4.66 (dd, *J* = 7.8, 7.8 Hz, 1H), 4.11 (d, *J* = 7.8 Hz, 1H), 4.02−3.88 (m, 2H), 3.84−3.62 (m, 2H), 2.14 (s, 3H), 1.54 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 158.3, 100.5, 90.9, 75.2, 71.5, 63.1, 61.9, 55.8, 29.1, 21.1, 19.2. HRMS (FAB): *m/z* calcd for $C_{12}H_{18}NO_7$ $(M + H)^+$ 288.1083, found 288.1092. Data for **8**β: $R_f = 0.28$ (80% EtOAc/hexanes). Mp: 199−203 °C. IR (thin film): 3306, 1755 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.09 (d, *J* = 3.0 Hz, 1H), 5.91 (br s, 1H), 4.69 (dd, *J* = 7.8, 7.8 Hz, 1H), 4.30 (dd, *J* = 10.7, 7.2 Hz, 1H), 4.22 (dd, *J* = 8.4, 3.0 Hz, 1H), 3.97 (dd, *J* = 11.0, 5.4 Hz, 1H), 3.74 (dd, *J* = 10.5, 10.5 Hz, 1H), 3.50 (ddd, *J* = 10.4, 10.4, 5.4 Hz, 1H), 2.17 (s, 3H), 1.54 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.5, 158.8, 100.3, 90.0, 76.1, 70.8, 65.9, 62.7, 52.8, 29.0, 21.3, 19.1. HRMS (FAB): *m/z* calcd for $C_{12}H_{18}NO_7$ $(M + H)^+$ 288.1083, found 288.1086. Data for **10**: $R_f = 0.18$ (40% EtOAc/hexanes). IR (thin film): 1701, 1591 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.28 (dd, *J* = 6.0, 0.6 Hz, 1H), 5.44 (d, *J* = 6.0 Hz, 1H), 4.49 (d, *J* = 13.1 Hz, 1H), 4.27 (m, 1H), 4.13−4.00 (m, 2H), 1.56 (s, 3H), 1.52 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 189.7, 161.3, 106.2, 100.8, 73.9, 71.0, 61.2, 28.6, 18.6. HRMS (FAB): *m/z* calcd for $C_9H_{13}O_4$ $(M + H)^+$ 185.0814, found 185.0817.

4-Pentenyl 2-Amino-2-*N*,3-*O*-carbonyl-2-deoxy-4,6-*O*-isopropylidene-D-mannopyranosides (2). The glucal 3-carbamate **1** (1.012 g, 4.42 mmol), activated 4 Å molecular sieves (2.01 g), PhIO (1.950 g, 8.86 mmol), $Rh_2(OAc)_4$ (110 mg, 0.250 mmol), and 4-penten-1-ol (1.80 mL, 17.7 mmol) were stirred in CH_2Cl_2 (40 mL) at 23 °C for 25 h. The mixture was filtered through Celite and washed with EtOAc, and the filtrate was concentrated. The crude material was analyzed by ^1H NMR and chromatographed (40% → 50% → 60% EtOAc/hexanes, 300 mL of SiO_2), providing the α-NPG **2**α (552 mg, 40%), together with the byproduct dihydropyranone **10** (89.5 mg, 21%) and the β-NPG **2**β (284 mg, 21%). The yields of the α-NPG **2**α and the byproduct dihydropyranone **10** were calculated on the basis of the integration data from the ^1H NMR spectrum of the chromatographed material. Data for **2**α: R_f = 0.31 (60% EtOAc/hexanes). Mp: 120−122 °C. IR (thin film): 3293, 1755 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.28 (br s, 1H), 5.80 (dddd, *J* = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.10−4.93 (m, 2H), 4.84 (s, 1H), 4.62 (dd, *J* = 8.0, 8.0 Hz, 1H), 4.10 (d, *J* = 7.8 Hz, 1H), 3.90 (m, 2H), 3.78 (dd, *J* = 10.4, 10.4 Hz, 1H), 3.65 (m, 2H), 3.38 (ddd, *J* = 9.6, 6.5, 6.5 Hz, 1H), 2.12 (m, 2H), 1.68 (m, 2H), 1.52 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.5, 137.7, 115.2, 100.1, 97.0, 75.7, 71.8, 67.3, 62.0, 60.3, 56.5, 30.1, 29.0, 28.4, 19.0. HRMS (FAB): *m/z* calcd for $C_{15}H_{24}NO_6$ $(M + H)^+$ 314.1604, found 314.1598. Data for **2**β: R_f = 0.20 (60% EtOAc/hexanes). IR (thin film): 3305, 1760 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.80 (dddd, *J* = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.40 (br s, 1H), 5.07−4.97 (m, 2H), 4.70 (d, *J* = 2.7 Hz, 1H), 4.57 (dd, *J* = 7.6, 7.6 Hz, 1H), 4.14 (dd, *J* = 7.3, 3.2 Hz, 1H), 4.10 (dd, *J* = 10.3, 7.3 Hz, 1H), 3.98−3.87 (m, 2H), 3.79 (dd, *J* = 10.5, 10.5 Hz, 1H), 3.52 (ddd, *J* = 9.5, 6.6, 6.6 Hz, 1H), 3.27 (ddd, *J* = 10.2, 5.5, 5.5 Hz, 1H), 2.13 (m, 2H), 1.71 (m, 2H), 1.51 (s, 3H), 1.42 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.6, 137.7, 115.1, 100.0, 97.5, 76.3, 71.4, 69.1, 65.0, 62.3, 54.5, 30.0, 28.9, 28.6, 18.9. HRMS (FAB): *m/z* calcd for $C_{15}H_{24}NO_6$ $(M + H)^+$ 314.1604, found 314.1602.

4-Pentenyl 2-Amino-2-*N*-((benzyloxy)carbonyl)-2-*N*,3-*O*-carbonyl-2-deoxy-4,6-*O*-isopropylidene-α-D-mannopyranoside (16α). To a solution of oxazolidinone **2**α (77.8 mg, 0.249 mmol) in THF (3.5 mL) were added Et_3N (95 μL, 0.69 mmol) and DMAP (4.0 mg, 0.33 mmol), followed by benzyl chloroformate (85 μL, 0.60 mmol). The cloudy mixture was stirred at 23 °C during 4 h, with additional portions of reagents added at 1 h intervals: Et_3N (3 × 95 μL) and benzyl chloroformate (3 × 85 μL). The reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic extract was washed with brine (×1), dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed (20% EtOAc/hexanes, 70 mL SiO_2), affording Cbz-protected oxazolidinone **16**α (103 mg, 92%) as a clear oil that solidified on standing in the freezer at −20 °C. $R_f = 0.51$ (40% EtOAc/hexanes). Mp: 89−91 °C. IR (thin film): 1832, 1805, 1733 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.48−7.30 (m, 5H), 5.78 (dddd, *J* = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.32 (AB, J_{AB} = 12.3 Hz, $\Delta\nu_{AB}$ = 23.6 Hz, 2H), 5.31 (s, 1H), 5.08−4.97 (m, 2H), 4.60 (dd, *J* = 7.9, 7.9 Hz, 1H), 4.36 (d, *J* = 4.4 Hz, 1H), 3.90−3.85 (m, 1H), 3.78−3.67 (m, 3H), 3.61 (ddd, *J* = 9.6, 6.6, 6.6 Hz, 1H), 3.35 (ddd, *J* = 9.6, 6.5, 6.5 Hz, 1H), 2.10 (m, 2H), 1.65 (m, 2H), 1.48 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.6, 151.4, 137.6, 134.3, 128.7, 128.2, 115.2, 100.2, 95.3, 72.6, 72.0, 69.2, 67.4, 61.9, 59.9, 58.6, 30.0, 28.9, 28.3, 18.9. HRMS (FAB): *m/z* calcd for $C_{23}H_{30}NO_8$ $(M + H)^+$ 448.1971, found 448.1956.

(−)-Menthyl 2-Amino-2-*N*-((benzyloxy)carbonyl)-2-*N*,3-*O*-carbonyl-2-deoxy-4,6-*O*-isopropylidene-α-D-mannopyranoside (21a). The NPG **16**α (27.1 mg, 0.0605 mmol), activated 4 Å molecular sieves (104 mg), and (−)-menthol (19.0 mg, 0.122 mmol) were stirred in CH_2Cl_2 (3.0 mL), and IDCP (115 mg, 0.245 mmol) was added. After the mixture was stirred in the dark at 23 °C for 17 h, 10% w/w aqueous $Na_2S_2O_3$ (6 mL) was added with vigorous stirring, discharging the yellow-orange color of the reaction mixture. The mixture was filtered through a pad of Celite, rinsing with CH_2Cl_2 and water. The filtrate was transferred to a separatory funnel, and the layers were shaken and separated. The organic layer was washed with saturated aqueous $CuSO_4$ (×1) and saturated aqueous $NaHCO_3$ (×1), dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed (10% → 15% → 20% EtOAc/hexanes, 15 mL of SiO_2), affording the glycosylated product **21a** (22.3 mg, 71%) and iodoetherification byproduct **33a**α (4.8 mg, 11%).[23] Data for **21a**: $R_f = 0.38$ (30% EtOAc/hexanes). IR (thin film): 1833, 1805, 1733 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.50−7.31 (m, 5H), 5.46 (s, 1H), 5.34 (s, 2H), 4.62 (dd, *J* = 7.9, 7.9 Hz, 1H), 4.39 (d, *J* = 7.9 Hz, 1H), 3.90−3.80 (m, 2H), 3.78−3.66 (m, 2H), 3.32 (ddd, *J* = 10.6, 10.6, 4.4 Hz, 1H), 2.16 (qqd, *J* = 6.9, 6.9, 2.5 Hz, 1H), 1.98 (m, 1H), 1.64 (m, 2H), 1.50 (s, 3H), 1.44 (s, 3H), 1.40−0.80 (m, 5H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.4 Hz, 3H), 0.77 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 151.9 (s), 151.5 (s), 134.5 (s), 128.7 (o), 128.6 (o), 128.2 (o), 100.3 (o), 96.9 (o), 82.2 (o), 72.8 (o), 72.1 (o), 69.2 (t), 61.8 (t), 60.0 (o), 58.98 (o), 48.5 (o), 43.0 (t), 34.1 (t), 31.6 (o), 30.0 (o), 25.6 (o), 23.0 (t), 22.3 (o), 21.1 (o), 18.9 (o), 16.0 (o). HRMS (FAB): *m/z* calcd for $C_{28}H_{40}NO_8$ $(M + H)^+$ 518.2754, found 518.2769.

4-Pentenyl 2-Amino-2-*N*-((benzyloxy)carbonyl)-2-deoxy-4,6-*O*-isopropylidene-3-*O*-methoxycarbonyl-α-D-mannopyranoside (24α). Using conditions B (Table 3): a solution of *N*-Cbz oxazolidinone **16**α (77.3 mg, 0.173 mmol) in MeOH (4.0 mL) was cooled to −15 °C (bath temperature), giving a white suspension. Cesium carbonate (61.5 mg, 0.189 mmol) was added, and the −15 °C bath was replaced with a 0 °C bath, giving a homogeneous solution. After 10 min saturated aqueous NH_4Cl (5 mL) was added, followed by enough water to solubilize all salts. The mixture was extracted with EtOAc (×1), and the organic layer was dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed (20% → 30% → 40% → 50% → 60% EtOAc/hexanes, 40 mL of SiO_2), providing the desired methyl carbonate **24**α (38.7 mg, 47%) and the N−H oxazolidinone byproduct **2**α (23.3 mg, 30%). Data for **24**α: $R_f = 0.41$ (30% EtOAc/hexanes). IR (thin film): 3338, 1754, 1726 cm^{-1}; a minor rotamer was evident in the carbonate methyl resonance of the ^1H NMR spectrum. ^1H NMR (300 MHz, $CDCl_3$): δ 7.43−7.29 (m, 5H), 5.80 (dddd, *J* = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.20−4.85 (m, 6H), 4.76 (s, 1H), 4.48 (dd, *J* = 8.8, 4.1 Hz, 1H), 3.90−3.70 (m, 6.5H), 3.65 (ddd, *J* = 9.5, 6.6, 6.6 Hz, 1H), 3.48 (br s, 0.5H), 3.39 (ddd, *J* = 9.5, 6.5, 6.5 Hz, 1H), 2.14 (apparent q, *J* = 7.1 Hz, 2H), 1.71 (apparent pentet,

J = 6.6 Hz, 2H), 1.49 (s, 3H), 1.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9, 154.5, 137.8, 135.9, 128.5, 128.3, 115.2, 100.2, 100.1, 72.8, 69.2, 67.4, 67.3, 64.2, 62.2, 55.0, 52.4, 30.1, 29.0, 28.3, 19.1.

4-Pentenyl 2-Amino-2-*N*-((benzyloxy)carbonyl)-2-deoxy-4,6-*O*-isopropylidene-3-*O*-methoxycarbonyl-β-D-mannopyranoside (24β). Using conditions D (Table 3): a solution of the *N*-Cbz oxazolidinone **16**β (18.9 mg, 0.0422 mmol) in toluene (2.5 mL) was cooled to −65 °C (bath temperature), and $BnMe_3NOH$ (90 μL of a 40% w/w solution in MeOH, 0.198 mmol) was added. The reaction mixture was warmed gradually to −20 °C over 2 h and then was recooled to −65 °C. Saturated aqueous NH_4Cl (5 mL) was added, the mixture was warmed to 23 °C, and enough water was added to solubilize all salts. The mixture was extracted with EtOAc (×2), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed (30% → 60% EtOAc/hexanes, 15 mL of SiO_2), providing methyl carbonate **24**β (9.2 mg, 45%) and the N−H oxazolidinone byproduct **2**β (5.3 mg, 40%). Data for **24**β: R_f = 0.65 (80% Et_2O (with 2% EtOH stabilizer)/20% *n*-pentane). IR (thin film): 3359, 1750, 1726 cm^{-1}; a minor rotamer was evident in the carbonate methyl resonance of the ^{1}H NMR spectrum. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42−7.28 (m, 5H), 5.78 (dddd, J = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.20−4.88 (m, 5H), 4.70 (dd, J = 10.0, 3.8 Hz, 1H), 4.64 (s, 1H), 4.57 (m, 1H), 3.91 (dd, J = 10.8, 5.2 Hz, 1H), 3.87−3.68 (m, 3H), 3.82 (s, 2.6H), 3.52 (ddd, J = 9.5, 6.6, 6.6 Hz, 1H), 3.41 (s, 0.4H), 3.28 (ddd, J = 9.9, 9.9, 5.2 Hz, 1H), 2.08 (m, 2H), 1.66 (apparent pentet, J = 7.0 Hz, 2H), 1.48 (s, 3H), 1.40 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.9, 154.8, 137.8, 136.3, 128.5, 128.1, 115.0, 100.2, 99.6, 75.3, 69.1, 68.9, 68.3, 67.1, 62.0, 55.0, 52.9, 30.0, 29.7, 29.0, 28.6, 19.1. HRMS (FAB): *m/z* calcd for $C_{24}H_{34}NO_9$ (M + H)$^+$ 480.2234, found 480.2224.

4-Pentenyl 2-Amino-2-*N*-((benzyloxy)carbonyl)-2-deoxy-4,6-*O*-isopropylidene-α-D-mannopyranoside (25α). Using conditions C (Table 3): sodium hydride (97.1 mg of a 60% w/w dispersion in oil, 2.43 mmol) was triturated with *n*-pentane (4 × 1.5 mL), dried under a gentle stream of Ar, and suspended in toluene (3.0 mL) with efficient stirring. The suspension was cooled to 0 °C, and MeOH (0.60 mL, 15 mmol) was added. Once H_2 evolution subsided, the mixture was warmed to 23 °C for 5 min and then cooled to −70 °C (bath temperature), maintaining good stirring throughout. A solution of *N*-Cbz oxazolidinone **16**α (106 mg, 0.236 mmol) in toluene (1.5 mL) was added dropwise to the cold methoxide suspension, rinsing with additional toluene (2 × 0.8 mL). The total addition time was 15 min. The mixture was warmed gradually to −15 °C (bath temperature) over 45 min and then was recooled to −70 °C and quenched with saturated aqueous NH_4Cl (12 mL). The frozen mass was warmed to 23 °C, and enough water was added to dissolve all salts. The mixture was extracted with EtOAc (×2), and the combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed (30% → 35% EtOAc/hexanes, 80 mL of SiO_2), affording the desired ring-opened product **25**α (69.3 mg, 70%) and the N−H oxazolidinone byproduct **2**α (19.1 mg, 26%). Data for **25**α: R_f = 0.38 (40% EtOAc/hexanes). IR (thin film): 3409, 3334, 1709 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42−7.28 (m, 5H), 5.80 (dddd, J = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.21 (br d, J = 6.6 Hz, 1H), 5.16−4.86 (m, 4H), 4.84 (s, 1H), 4.15 (m, 2H), 3.88−3.55 (m, 5H), 3.38 (m, 1H), 2.70 (br s, 1H), 2.13 (apparent q, J = 7.1 Hz, 2H), 1.69 (apparent pentet, J = 7.0 Hz, 2H), 1.50 (s, 3H), 1.43 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 156.8, 137.8, 135.9, 128.6, 128.3, 115.1, 100.2, 99.7, 72.0, 67.4, 67.3, 67.2, 63.7, 62.2, 54.9, 30.2, 29.1, 28.4, 19.2. HRMS (FAB): *m/z* calcd for $C_{22}H_{32}NO_7$ (M + H)$^+$ 422.2179, found 422.2196.

4-Pentenyl 3-*O*-Acetyl-2-amino-2-*N*-((benzyloxy)carbonyl)-2-deoxy-4,6-*O*-isopropylidene-β-D-mannopyranoside (26β). A solution of alcohol **25**β (83.0 mg, 0.196 mmol) in CH_2Cl_2 (7.5 mL) was cooled to 0 °C, and pyridine (98 μL, 1.2 mmol) was added, followed by acetic anhydride (55 μL, 0.59 mmol) and 4-(dimethylamino)pyridine (1.6 mg, 0.0098 mmol). The cooling bath was removed, and the solution was warmed to 23 °C. After 3 h the reaction mixture was poured into saturated aqueous $NaHCO_3$ (20 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by chromatography (30% EtOAc/hexanes, 45 mL SiO_2), affording acetate **26**β (88.0 mg, 96%). R_f = 0.30 (30% EtOAc/hexanes). IR (thin film): 3350, 1726 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45−7.28 (m, 5H), 5.77 (dddd, J = 17.0, 10.3, 6.6, 6.6 Hz, 1H), 5.12 (AB, J_{AB} = 12.1 Hz, $\Delta\nu_{AB}$ = 11.6 Hz, 2H), 5.10 (m, 1H), 4.99−4.93 (m, 2H), 4.84 (dd, J = 10.1, 3.7 Hz, 1H), 4.64 (s, 1H), 4.45 (dd, J = 8.3, 2.4 Hz, 1H), 3.90 (dd, J = 10.8, 5.2 Hz, 1H), 3.83−3.70 (m, 3H), 3.51 (ddd, J = 9.4, 6.6, 6.6 Hz, 1H), 3.27 (ddd, J = 9.9, 9.9, 5.2 Hz, 1H), 2.07 (apparent q, J = 7.1 Hz, 2H), 2.02 (s, 3H), 1.65 (apparent pentet, J = 7.0 Hz, 2H), 1.49 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 156.8, 137.8, 136.4, 128.5, 128.1, 128.0, 115.0, 100.1, 99.6, 71.6, 69.1, 68.8, 68.5, 66.9, 62.0, 52.9, 30.0, 29.0, 28.5, 21.0, 19.1. HRMS (FAB): *m/z* calcd for $C_{24}H_{34}NO_8$ (M + H)$^+$ 464.2284, found 464.2271.

4-Pentenyl 3-*O*-Acetyl-2-amino-2-*N*-((benzyloxy)carbonyl)-2-deoxy-β-D-mannopyranoside (27β). Methylene chloride (10 mL) and water (20 mL) were shaken in a separatory funnel, and the wet organic layer was used as solvent. Acetonide **26**β (144.5 mg, 0.311 mmol) was dissolved in the wet CH_2Cl_2 (10 mL) at 23 °C, and Et_3SiOTf (7 μL, 0.031 mmol) was added, giving a cloudy mixture. After 5 min, triethylamine (43 μL, 0.31 mmol) was added, giving a clear solution. The mixture was diluted with CH_2Cl_2, dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by chromatography (80% EtOAc/hexanes, 80 mL of SiO_2), affording the diol **27**β as an oil (126.2 mg, 96%). R_f = 0.36 (80% EtOAc/hexanes). IR (thin film): 3359, 1721 cm^{-1}. Two rotamers were evident in the ^{1}H and ^{13}C NMR spectra. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45−7.20 (m, 5H), 6.19 (br d, J = 9.1 Hz, 0.3 H), 5.78 (dddd, J = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.47 (br d, J = 8.9 Hz, 0.7H), 5.20−4.88 (m, 4H), 4.76 (m, 1H), 4.58 (s, 0.7H), 4.49 (s, 0.3H), 4.44−4.25 (m, 1.3H), 3.94 (br s, 0.3H), 4.10−3.68 (m, 3H), 3.77 (ddd, J = 9.5, 6.6, 6.6 Hz, 1H), 3.56−3.40 (m, 1H), 3.31 (m, 1H), 3.23 (s, 0.7H), 2.89 (s, 0.7H), 2.20−1.90 (m, 2H), 2.03 (s, 2.1H), 1.72 (s, 0.9H), 1.65 (apparent pentet, J = 7.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.0, 156.8, 137.8, 136.5, 128.5, 128.1, 128.0, 115.0, 99.1, 76.0, 74.9, 69.0, 66.8, 65.3, 61.7, 52.4, 29.9, 28.5, 20.9; additional ^{13}C NMR resonances from minor rotamer δ 170.5, 157.5, 135.9, 74.5, 67.2, 63.6, 60.7, 53.2, 20.4. HRMS (FAB): *m/z* calcd for $C_{21}H_{30}NO_8$ (M + H)$^+$ 424.1971, found 424.1982.

4-Pentenyl 3,4,6-Tri-*O*-acetyl-2-amino-2-*N*-((benzyloxy)-carbonyl)-2-deoxy-β-D-mannopyranoside (28β). To a solution of diol **27**β (117.3 mg, 0.278 mmol) in CH_2Cl_2 (10 mL) at 23 °C was added pyridine (0.24 mL, 2.98 mmol) and 4-(dimethylamino)pyridine (3.4 mg, 0.028 mmol), followed by acetic anhydride (0.17 mL, 1.7 mmol). After 3 h, the reaction mixture was poured into saturated aqueous $NaHCO_3$ (20 mL) and the mixture was extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated. The crude material was purified by chromatography (80% EtOAc/hexanes, 80 mL SiO_2), giving triacetate **28**β (130.6 mg, 93%). R_f = 0.33 (50% EtOAc/hexanes). IR (thin film): 3360, 1744 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.45−7.25 (m, 5H), 5.78 (dddd, J = 17.0, 10.3, 6.7, 6.7 Hz, 1H), 5.25−5.05 (m, 4H), 5.05−4.88 (m, 3H), 4.65 (d, J = 1.0 Hz, 1H), 4.43 (ddd, J = 8.5, 2.4, 1.0 Hz, 1H), 4.25 (dd, J = 12.2, 5.1 Hz, 1H), 4.11 (dd, J = 12.2, 2.7 Hz, 1H), 3.82 (ddd, J = 9.4, 6.6, 6.6 Hz, 1H), 3.63 (ddd, J = 8.6, 5.4, 2.7 Hz, 1H), 3.51 (ddd, J = 9.4, 6.7, 6.7 Hz, 1H), 2.20−1.90 (m, 2H), 2.08 (s, 3H), 2.05 (s, 3H), 1.98 (s, 3H), 1.68 (apparent pentet, J = 6.9 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.4, 169.5, 156.7, 137.8, 136.3, 128.5, 128.1, 127.9, 115.0, 98.9, 72.3, 71.9, 69.1, 66.9, 65.9, 62.3, 52.1, 29.9,

28.4, 20.68, 20.62. HRMS (FAB): *m/z* calcd for $C_{25}H_{34}NO_{10}$ $(M + H)^+$ 508.2183, found 508.2179.

3*β*-Dihydrocholesteryl 3,4,6-Tri-*O*-acetyl-2-amino-2-*N*-((benzyloxy)carbonyl)-2-deoxy-α-D-mannopyranoside (29d). The NPG **28**α (29.1 mg, 0.0573 mmol) and 3*β*-dihydrocholesterol (45.4 mg, 0.177 mmol) were dried separately under vacuum (0.5 mmHg, 15 h), combined, and dissolved in CH_2Cl_2 (3.0 mL) at 23 °C. *N*-Iodosuccinimide (21.8 mg, 0.0969 mmol) was added, followed by Et_3SiOTf (15 *μ*L, 0.064 mmol), providing a violet solution that became deep purple. After 20 min, Et_3N (55 *μ*L, 0.40 mmol) was added, discharging the purple color. The mixture was poured into 10% w/w saturated aqueous $Na_2S_2O_3$ (10 mL) and extracted with CH_2Cl_2 (×2). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (×1), back extracting with CH_2Cl_2 (×1). The organic phases were combined and dried ($MgSO_4$), filtered, and concentrated. The residue was chromatographed (20% → 23% EtOAc/hexanes, 20 mL of SiO_2), affording the glycosylated product **29d** (31.6 mg, 68%). $R_f = 0.49$ (40% EtOAc/hexanes). IR (thin film): 3349, 1750, 1736 (sh), 1727 (sh) cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.43−7.28 (m, 5H), 5.31 (dd, $J = 10.1$, 4.3 Hz, 1H), 5.18−5.01 (m, 4H), 4.94 (d, $J = 1.1$ Hz, 1H), 4.28 (dd, $J = 9.2$, 3.5 Hz, 1H), 4.20 (dd, $J = 12.7$, 5.5 Hz, 1H), 4.12−3.98 (m, 2H), 3.52 (dddd, $J = 10.6$, 10.6, 5.3, 5.3 Hz, 1H), 2.13−0.52 (m, 31H), 2.09 (s, 3H), 2.04 (s, 3H). 1.95 (s, 3H), 0.90 (d, $J = 6.5$ Hz, 3H), 0.86 (d, $J = 6.6$ Hz, 3H), 0.86 (d, $J = 6.6$ Hz, 3H), 0.80 (s, 3H), 0.65 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.6, 170.0, 169.8, 155.9, 136.1, 128.6, 128.3, 128.2, 97.6, 78.1, 69.6, 68.0, 67.1, 66.1, 62.5, 56.4, 56.3, 54.3, 52.6, 45.0, 42.6, 40.0, 39.5, 36.7, 36.1, 35.8, 35.7, 35.5, 35.4, 32.0, 28.8, 28.0, 27.8, 27.6, 24.1, 23.8, 22.8, 22.5, 21.2, 20.77, 20.74, 20.66, 18.6, 12.2, 12.0. HRMS (FAB): *m/z* calcd for $C_{47}H_{72}NO_{10}$ $(M + H)^+$ 810.5156, found 810.5137.

6-*O*-(2-Acetamido-2-deoxy-4,6-*O*-isopropylidene-α-D-mannopyranosyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (3b). Benzyl carbamate **23b** (9.2 mg, 0.014 mmol) was dissolved in MeOH/EtOAc (1.5 mL/1.5 mL), and 10% Pd/C (27 mg) was added. The mixture was stirred under a gentle stream of H_2 for 10 min and then under a static H_2 atmosphere (balloon) for 1 h. The reaction flask was flushed with Ar during 10 min, the reaction mixture was filtered through a pad of Celite, rinsing with MeOH/EtOAc (50 mL/50 mL), and the filtrate was concentrated. Using conditions B (Table 5) for acetyl transfer: the crude *β*-acetoxy amine from the above hydrogenation was dissolved in EtOAc (2 mL), silica gel (103 mg) was added, and the solvent was removed on the rotary evaporator. After standing at 23 °C under air for 4 h, the silica was suspended in EtOAc, whereupon TLC indicated some remaining *β*-acetoxy amine. Additional SiO_2 (50 mg) was added and the suspension rotavapped to dryness. After standing an additional 19 h, the silica gel was stirred in MeOH/EtOAc (1/10) and filtered, rinsing with the same solvent. The filtrate was concentrated and the residue chromatographed (3% → 4% → 5% MeOH/EtOAc, 10 mL of SiO_2), affording acetamide **3b** (6.8 mg, 93%) as a clear oil. Using conditions C (Table 5) for acetyl transfer: starting with benzyl carbamate **23b** (8.8 mg, 0.014 mmol), hydrogenation was carried out as described above. The crude *β*-acetoxy amine was transferred to an NMR tube with pyridine-d_5 (0.75 mL), and the solution was heated at 75 °C (oil bath) under Ar for 48 h. ^1H NMR indicated that less than half of the material had undergone O→N acetyl transfer. 2-Pyridone (0.6 mg, 0.006 mmol, 0.5 equiv) was added, and heating was resumed at 75 °C under Ar, leading to smooth acetyl transfer over 96 h, as monitored by ^1H NMR every 24 h. The final acetamide:acetate ratio was >20:1 by ^1H NMR analysis. The reaction mixture was concentrated, rotavapping the residue several times with CH_2Cl_2 to remove pyridine, and the crude material was chromatographed (3% → 4% MeOH/EtOAc, 10 mL of SiO_2), providing acetamide **3b** (5.9 mg, 84%). $R_f = 0.21$ (10% MeOH/CH_2Cl_2). IR (thin film): 3368, 1651 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 5.81 (br d, $J = 7.4$ Hz, 1H), 5.52 (d, $J = 5.0$ Hz, 1H), 4.84 (s, 1H), 4.62 (dd, $J = 7.9$, 2.4 Hz, 1H), 4.46 (dd, $J = 6.5$, 5.0 Hz, 1H), 4.32 (dd, $J = 5.0$, 2.4 Hz, 1H), 4.25 (dd, $J = 7.9$, 1.8 Hz, 1H), 4.17 (dd, $J = 9.6$, 4.7 Hz, 1H), 3.96 (ddd, $J = 6.2$, 6.2, 1.7 Hz, 1H), 3.90−3.55 (m, 6H), 3.30−2.30 (vbr, 1H), 2.08 (s, 3H), 1.56 (s, 3H), 1.54 (s, 3H), 1.44 (s, 3H), 1.44 (s, 3H), 1.34 (s, 3H), 1.34 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 171.6, 109.4, 108.7, 100.1, 99.9, 96.3, 72.0, 70.9, 70.57, 70.55, 67.6, 66.8, 66.4, 63.8, 62.1, 53.5, 29.1, 26.1, 25.9, 24.9, 24.4, 23.4, 19.4. HRMS (FAB): *m/z* calcd for $C_{23}H_{38}NO_{11}$ $(M + H)^+$ 504.2445, found 504.2460.

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Supporting Information Available: Text, tables, and figures giving general experimental conditions, characterization data for all other compounds, including iodoetherification byproducts **30**−**34**, copies of ^1H NMR spectra for all compounds, and copies of ^{13}C NMR spectra for compounds **1**, **2**α, **2***β*, **3b**, **4c**, **8**α, **10**, **11**, **16**α, **16***β*, **18a**, **21a**, **21c**, **25**α, **25***β*, **26**α, **26***β*, **28**α, **28***β*, and **29d** and an ORTEP drawing and CIF file for the X-ray structure determination of **8**α. This material is available free of charge via the Internet at http://pubs.acs.org.

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