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Concise and Efficient Synthesis of 2-Acetamido-2-deoxy-β-D-hexopyranosides of Diverse Aminosugars from 2-Acetamido-2-deoxy-β-D-glucose

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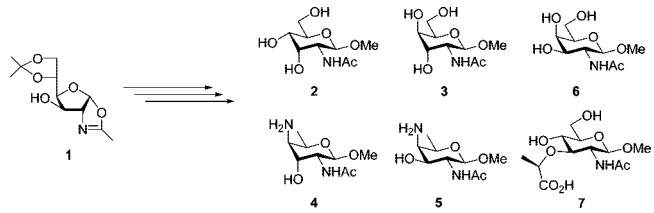

The furanose acetonide derivative **1** is readily prepared from 2-acetamido-2-deoxy-D-glucose on a large scale without the need for chromatography. Mesylation of **1** provides an efficient, concise, synthetic route to rare 2-acetamido-2-deoxy-β-D-hexopyranosides (**2** and **3**) via the corresponding methyl 2-acetamido-2-deoxy-3-*O*-methanesulfonyl-β-D-glucopyranoside and subsequent inversion of configuration by direct displacement or formation of a 3,4-epoxide. Opening of this epoxide by azide provided a direct route to methyl 2-acetamido-4-amino-2,4,6-trideoxy-β-D-gulopyranoside **4**. Benzylation of **1** followed by ring expansion to the glucopyranoside, deoxygenation at C-6, and subsequent displacement of a C-4 triflate permitted the synthesis of methyl 2-acetamido-4-amino-2,4,6-trideoxy-β-D-galactopyranoside **5**. Methyl 2-acetamido-2-deoxy-β-D-glucopyranoside available from **1** in quantitative yield was readily converted to methyl 2-acetamido-2-deoxy-β-D-galactopyranoside **6** (>60%) by inversion of configuration at C-4. Introduction of a lactyl substituent at C-3 of oxazoline **1** also provides a facile synthesis of the biologically important muramic acid β-glycoside **7**. An interesting reaction to convert 2-acetamido-2-deoxyhexopyranosides to the corresponding 2-deoxy-2-tetrazole is also reported.

Introduction

2-Amino-2-deoxyhexoses are among the most important modified sugars found in nature.[1] 2-Acetamido-2-deoxy-D-glucose (D-GlcNAc) is the most abundant 2-amino-2-deoxyhexose found in nature, and together with 2-acetamido-2-deoxy-D-galactose (D-GalNAc), both constitute essential building blocks of bioactive oligosaccharides and glycoconjugates that include glycoproteins, glycopeptides, glycolipids, peptidoglycan, and glycosaminoglycans.[1,2] Other rare aminosugars[3] such as 2-acetamido-2-deoxy-D-allosamine (D-AllNAc) and 2-acetamido-2-deoxy-D-gulosamine (D-GulNAc), are also found in nature. For example, D-AllNAc exists as a component of allosamidin, a selective and powerful chitinase inhibitor,[4] and D-GulNAc was isolated from the antibiotic streptothricin F and streptolidin B (Figure 1).[5] The L-counterpart of D-GulNAc constitutes another important nucleoside antibiotic, adenomycin.[6] Bacterial glycoconjugates are a source of an even wider number of aminosugars; two important examples are 2,4-diamino-2,4,6-trideoxyhexoses[7−10] and *N*-acetylmuramic acid (MurNAc).[11] 2,4-

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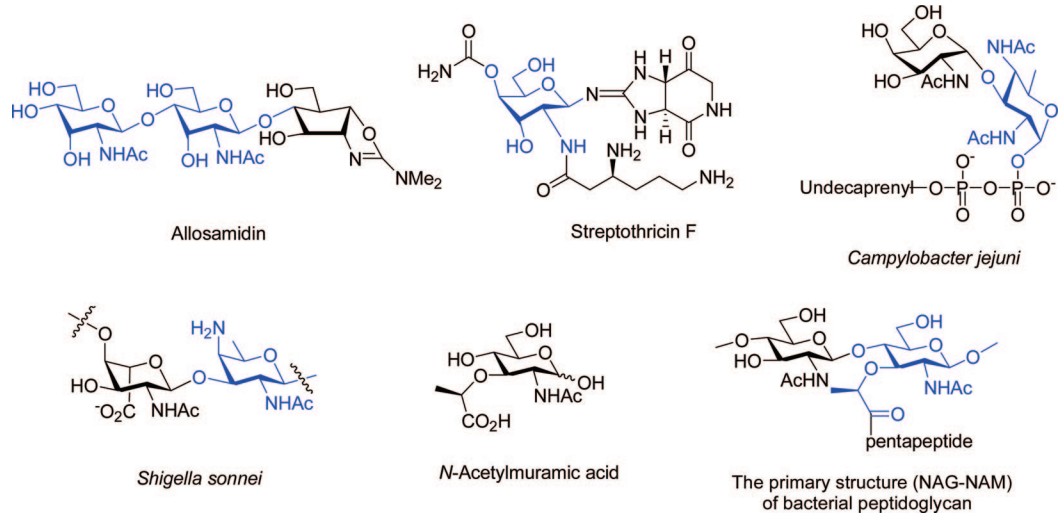

FIGURE 1. Some naturally occurring 2-amino-2-deoxyhexoses.

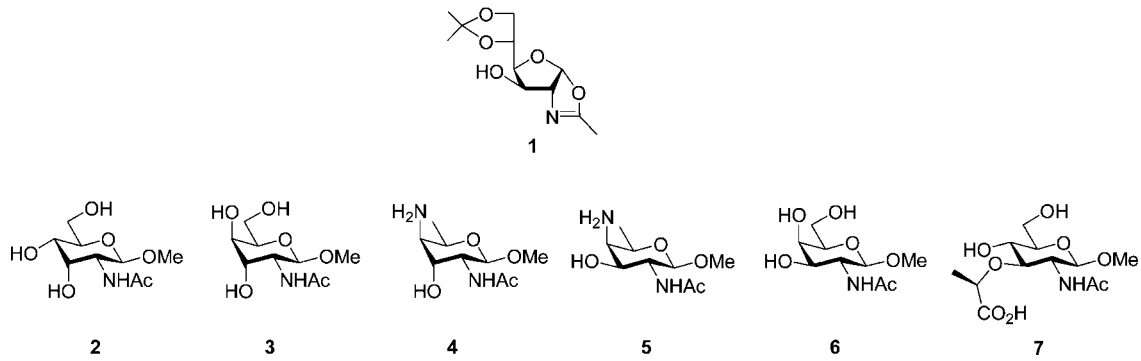

FIGURE 2. Amino sugars readily prepared from **1**.

Diamino-2,4,6-trideoxyhexoses are frequently found in bacterial polysaccharides. For instance, 2,4-diamino-2,4,6-trideoxy-D-glucose (bacillosamine) has been isolated from *Bacillus subtilis* polysaccharide[7] and from the *N*-linked glycoprotein of *Campylobacter jejuni*.[8] 2,4-Diamino-2,4,6-trideoxy-D-galactose is a constituent of the capsular polysaccharides of *Streptococcus pneuoniae*[9] and *Shigella sonnei*,[9] while 2,4-diamino-2,4,6-trideoxy-D-gulose occurs as a component of the O-antigen of *Pseudomonas aeruginosa*.[10] Muramic acid (MurNAc) is universally present in bacterial peptidoglycans as the repeating disaccharide element β-D-GlcNAc-(1→4)-β-D-MurNAc (Figure 1)[11] and is an important component of Freund's complete adjuvant.[12,13] A facile synthesis of a muramic acid glycoside would provide a convenient route to muramylpeptides. *N*-Acetylmuramyl-L-alanyl-D-isoglutamine is one of the smallest immunoadjuvants capable of replacing whole mycobacteria of Freund's adjuvant. Recently, UDP-MurNAc was found to be a potent inhibitor for MurA enzyme, which plays an important role in the biosynthesis of bacterial peptidoglycan, an important target for developing new antibiotics to fight microbial resistance.[14,15]

Despite their broad existence in nature, most of the 2-amino-2-deoxyhexoses are not commercially available. The only exception is D-GlcNAc, which is inexpensive and can be purchased in large quantities. The commercial sources of D-GalNAc are limited and expensive. Conversion of D-GlcNAc to other 2-amino-2-dexoyhexoses is thus an attractive and economically viable strategy. However, most of the reported routes require either tedious transformation or harsh conditions.[16−18] The development of concise syntheses of unusual aminosugars is therefore of practical interest. Here, we extend our recent report[19] of a facile and efficient two-step synthesis of 2-acetamido-2-deoxy-β-D-glucopyranosides from commercial D-GlcNAc via the 5,6-*O*-isopropylidene furanose derivative **1** to the synthesis of the aminosugars (**2**−**7**) (Figure 2).

Results and Discussion

Oxazoline **1** was prepared from D-GlcNAc[20] in one step and in 30 g quantities without the need for chromatography. In our

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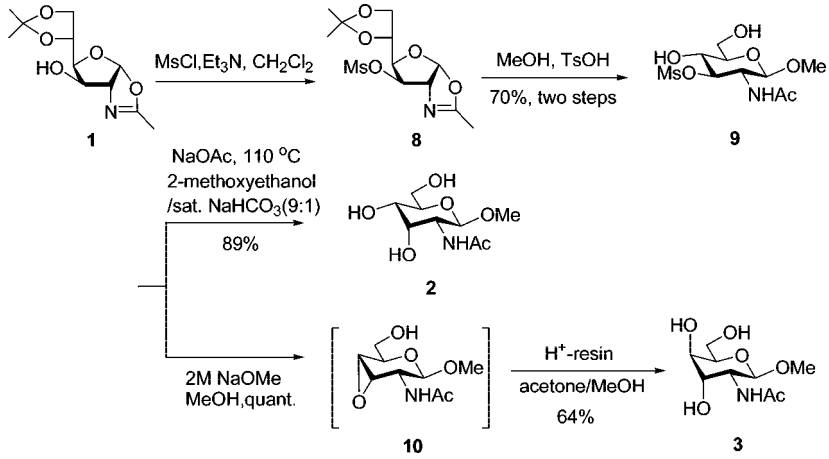
SCHEME 1. Synthesis of Methyl 2-Acetamido-2-deoxy-β-D-allo- and β-D-gulopyranosides 2 and 3



previous report, we discovered that furanose **1** can be cleanly and conveniently converted to the corresponding β-pyranoside in quantitative yield on a 20 g scale by reacting **1** with an alcohol solution under sulfonic acid catalysis.[19] Here, we take advantage of the presence of a single hydroxyl group at C-3 of oxazoline **1** by introducing a protecting group at C-3 prior to the acid-catalyzed furanose to pyranose ring expansion. We anticipated that the introduction of groups at C-3 would not interfere with the rearrangement to give conveniently derivatized β-pyranosides in high stereoselectivity and in high yield. Manipulation of methanesulfonyl, benzyl, and lactyl derivatives of **1** provide access to the β-glycosides **2**−**6** and the muramic acid glycoside **7**.

Scheme 1 shows the routes to the β-pyranosides of D-AllNAc **2** and D-GulNAc **3**. Mesylation of oxazoline **1** was carried out on a 17 g scale and preceded smoothly in almost quantitative yield as judged by TLC. Purification of crude mesylate **8** was unnecessary, and subsequent treatment of **8** with methanol in the presence of 0.1 equiv of *p*-toluenesulfonic acid afforded the desired β-pyranoside **9** in 70% yield over two steps. Mesylate **9** was readily converted to the target methyl 2-acetamido-2-deoxy-β-D-allopyranoside **2** in 89% yield under reflux in a mixture of 2-methoxyethanol, sodium acetate, and saturated sodium bicarbonate solution.[21] The *allo*-configuration of **2** was unambiguously established by ^{1}H NMR and the diagnostic $J_{2,3}$ (2.8 Hz) and $J_{3,4}$ (2.9 Hz) coupling constants.

The probable mechanism for the inversion of configuration at C-3 involves the participation by the neighboring acetamido group leading to a protonated oxazoline which could be deprotonated by acetate anion followed by subsequent hydrolysis of the intermediate oxazoline to afford the target compound **2** (Figure 3).

When mesylate **9** was treated with 2 M NaOMe in methanol at room temperature, the 3,4-epoxide **10** was obtained in almost quantitative yield on a 10 g scale (Scheme 2). The 3,4-epoxide **10** underwent acid-catalyzed diaxial ring opening with Amberlite IR-120 (H^+) to the gulopyranoside **3** in 64% yield. The *gulo*-configuration was confirmed by the characteristic ^{1}H NMR coupling constants $J_{2,3}$ (3.2 Hz), $J_{4,5}$ (1.4 Hz), and $J_{3,4}$ (3.5 Hz).

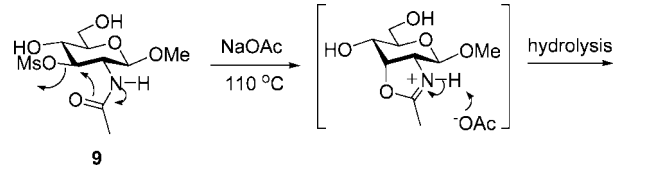
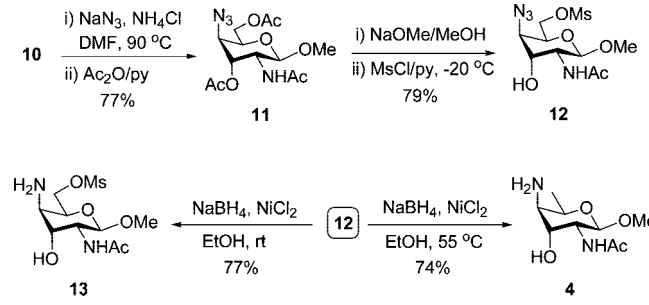


FIGURE 3. Intramolecular displacement of **9** by treatment with NaOAc.

SCHEME 2. Synthesis of Methyl 2-Acetamido-4-amino-2,4,6-trideoxy-β-D-gulopyranoside 4 from Epoxide 10



Adaptation of the ring expansion of 3-*O*-substituted derivatives of **1** provides an attractive route to methyl 2-acetamido-4-amino-2,4,6-trideoxy-β-hexopyranosides **4** and **5**. Previously, syntheses of the corresponding α-glycoside[17] and a L-sugar analogue[17] have been achieved. Our improved synthesis of 3,4-epoxide **10** allowed us to synthesize the β-glycoside **4** in an efficient manner, and benzylation of **1** provided a convenient route to **5**. As shown in Scheme 2, treatment of epoxide **10** with NaN_3 in the presence of NH_4Cl in dry DMF at 90 °C followed by acetylation gave the target **11** as the major

(16) For examples of the synthesis of D-galactosamine, D-allosamine, and D-gulosamine derivatives, see: McGeary, R. P.; Wright, K.; Toth, I. *J. Org. Chem.* **2001**, *66*, 5102–5105. Jäger, V.; Schröter, D. *Synthesis* **1990**, 556–560. Suami, T.; Tadano, K.; Iimura, Y.; Tanabe, H. *Carbohydr. Res.* **1985**, *135*, 319–323. Rochepeau-Jobron, L.; Jacquinet, J. C. *Carbohydr. Res.* **1998**, *305*, 181–191.

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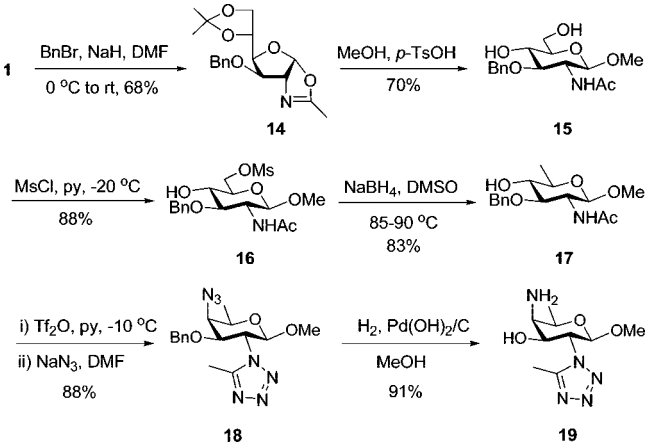
compound (77% yield). Acetylation was necessary in order to obtain the desired D-*gulo*-isomer in pure form by removing an unidentified minor compound, presumably the D-*gluco*-isomer. With pure **11** in hand, deacetylation and selective 6-mesylation gave **12** in 79% yield. Reduction of mesylate of **12** with $NaBH_4$ in DMSO was unsuccessful even at elevated temperature. $NaBH_4/NiCl_2$ in EtOH[22] only reduced the azido group to afford the amino compound **13** in 77% yield. Simultaneous reduction of the azido and mesylate groups was finally achieved using the same reagent at 50−60 °C, providing the target compound **4** in 74% yield. The D-*gulo* configuration of **4** was confirmed by three small $J_{2,3}$, $J_{3,4}$, and $J_{4,5}$ coupling constants (3.2 Hz, 3.2 Hz, 1.8 Hz).

SCHEME 3. Synthesis of 6-Deoxy Derivative 19 from Oxazoline 1



The synthesis of methyl 2-acetamido-4-amino-2,4,6-trideoxy-β-D-galactopyranoside **5** was accomplished via the 3-benzylated oxazoline **14** (Schemes 3 and 4). *p*-Toluenesulfonic acid catalyzed methanolysis yielded the desired 3-*O*-benzyl-β-D-glucopyranoside **15** in 70% yield. Selective 6-mesylation gave compound **16** in 88% yield, and the 6-mesylate was smoothly reduced by $NaBH_4$ in dry DMSO at elevated temperature to furnish compound **17** in 83% yield. Compound **17** was converted to the corresponding triflate using conditions similar to those employed by Imperialli et al.[23] Treatment of alcohol **17** with 2 equiv of triflic anhydride in pyridine at 0 °C afforded an intermediate which was immediately reacted with NaN_3 in DMF. To our surprise, although we successfully inverted the configuration at the C-4 position with an azido group, compound **18** also contained a tetrazole functionality at C-2 and was isolated in 88% yield. The same outcome was observed even when the temperature was lowered to −30 °C during the triflation step. The presence of a tetrazole moiety in **18** was unambiguously confirmed by high resolution mass spectrometry (HRMS) and elemental analysis. NMR experiments were also consistent with the proposed structure. The ^1H NMR revealed the absence of a N−H signal, while the ^{13}C NMR spectrum had a signal at 154.2 ppm correlating with that of a typical tetrazole carbon (150−160 ppm).[24]

(22) For examples of $NaBH_4/NiCl_2$ reduction, see: Thiem, J.; Meyer, B. *Chem. Ber.* **1980**, *113*, 3067. Paulsen, H.; Schnell, D. *Chem. Ber.* **1981**, *114*, 333–345. Weigel, T. M.; Liu, H.-W. *Tetrahedron Lett.* **1988**, *34*, 4221–4224.

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The formation of the tetrazole functionality (Figure 4) presumably arose from an excess of triflic anhydride (2 equiv), which activates the acetamido group to form a triflate imidate intermediate. This subsequently reacts with excess NaN_3 not only inverting the C-4 position but also converting the activated imidate to the tetrazole ring. This finding could be used as a general methodology to synthesize 2-deoxy-2-tetrazole derivatives from 2-acetamido-2-deoxyglycosides. Subsequent hydrogenation of **18** gave compound **19** in 91% yield without affecting the 2-tetrazole moiety.

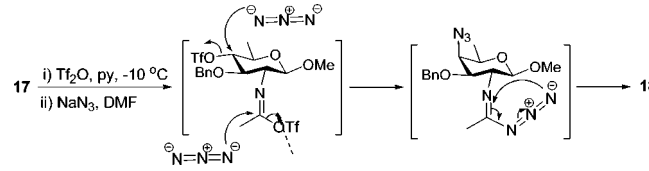
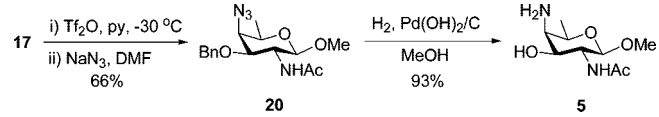


FIGURE 4. Synthesis of tetrazole-containing derivative **18** via a proposed triflate imidate.

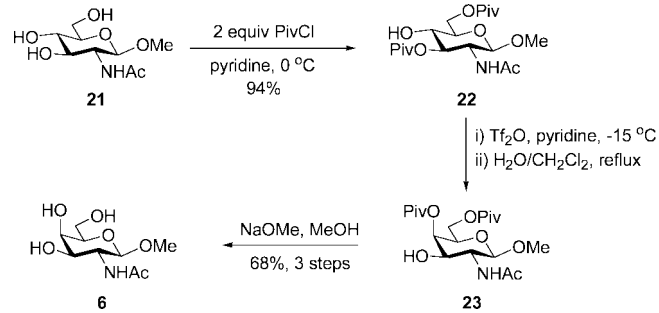
To avoid the activation of the acetamido group (Scheme 4), compound **17** was treated with triflic anhydride (1.1 equiv). The desired product **20** was then obtained in 66% yield. Hydrogenation of **20** over palladium hydroxide afforded the target compound **5** in excellent yield (93%). Our seven-step route to **5** starting from D-GlcNAc compares favorably with the previously published 17-step synthesis of **5**.[17]

SCHEME 4. Synthesis of Target Compound 5 from 17



The ease of large-scale synthesis of methyl 2-acetamido-2-deoxy-β-D-glucopyranoside **21** in near-quantitative yield from **1**[19] renders its conversion to methyl 2-acetamido-2-deoxy-β-D-galactopyranoside **6** an attractive prospect for the facile synthesis of this otherwise expensive compound (Scheme 5). Selective pivaloylation[16] gave the 3,6-diester **22** in 94% yield followed by activation at O-4 by triflate and subsequent in situ displacement of the triflate yielded **23**. The reaction mechanism might follow an intramolecular attack of the intermediate 4-triflate by the 3-*O*-pivaloyl group to form a cyclic orthoester which subsequently undergoes hydrolysis to give the 4,6-di-*O*-pivalolated **23**. Transesterification furnished the desired galactopyranoside **6** in 68% overall yield from **22**.

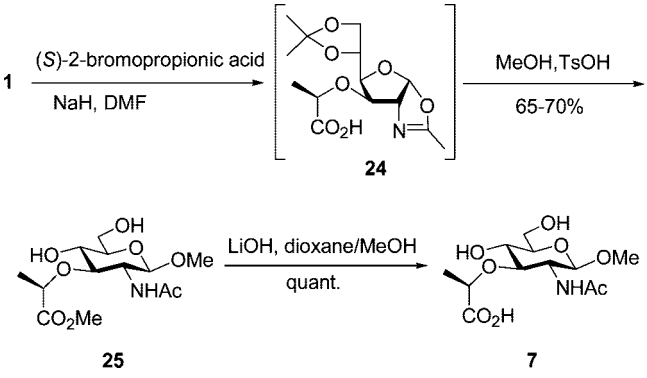
SCHEME 5. Synthesis of Methyl 2-Acetamido-2-deoxy-β-D-galactopyranoside 6



The biological significance of muramic acid prompted us to apply our methodology to the synthesis of muramic glycosides.[18]

The use of oxazoline **1** to synthesize muramic acid has been reported by Brossmer's group[25] by reacting oxazoline **1** with (*S*)-2-chloropropionic acid; the obtained 3-*O*-lactyl furanose was not isolated but subjected to an acid-catalyzed hydrolysis to give a mixture of anomeric hemiacetals; the reported yield was 73% for two steps. In order to prepare the glycosides of muramic acid, 4,6-*O*-protected *N*-acetyl-D-glucosamine glycosides were usually prepared via multiple steps prior to the introduction of a lactate moiety at C-3. We describe here an extension of Brossmer's methodology that achieves the synthesis of β-glycosides of muramic acid in just two steps from furanosyl oxazoline **1** (three steps from commercial D-GlcNAc, Scheme 6). Oxazoline **1** was reacted with (*S*)-2-bromopropionic acid in the presence of NaH in dry DMF, and crude intermediate **24** was then directly subjected to acid-catalyzed methanolysis using *p*-toluenesulfonic acid to furnish the β-glycoside of muramic acid **25** in 67% overall yield; the carboxylic acid was simultaneously esterified. Hydrolysis of methyl ester **25** using 1.0 M lithium hydroxide gave MurNAc methyl β-glycopyranoside **7** in almost quantitative yield. No racemization was observed. It is noteworthy that we successfully scaled the synthesis to approximately 3 g.

SCHEME 6. Synthesis of Methyl B-Glycoside of MurNAc 7



Large-scale synthesis of **7** prompted us to synthesize the biologically active *N*-acetyl-β-D-glycopyranosyl-(1→4)-*N*-acetyl-β-D-muramic acid (NAG-NAM) disaccharide repeating unit of bacterial cell wall peptidoglycans.[26] The synthesis of the NAG-NAM disaccharide is challenging due to problems associated with MurNAc chemistry.[26] The presence of a lactic acid residue at *O*-3 not only introduces steric crowding but also complicates the chemistry through the potential for lactone formation with the 4-hydroxyl group. Literature methods to form the β-(1→4) glycosydic linkage have employed several kinds of donors including oxazoline,[26] glycosyl halides,[26] and glycosyl imidate[18,26] and with nitrogen protecting groups such as phthalimido,[26] Troc,[26] and dimethylmaleoyl (DMM).[18,26] In order to minimize intramolecular lactonization, the lactate residue has to be orthogonally protected by groups such as phenylsufonylethyl[26] or by an alanine residue.[15] Thus, MurNAc acceptor **25** was first selectively protected with 1.1 equiv of pivaloyl chloride in pyridine at 0 °C to afford the desired acceptor **26** in excellent yield (82%). We decided to re-examine direct glycosylation using a glycosyl halide donor such as the bromide **27**[27] (Scheme 7). Glycosylation of **26** with **27** was performed using AgOTf as a promoter, but unfortunately, a complicated mixture was obtained most likely due to intramolecular lactonization.[26] However, when we carried out the reaction at −60 °C, we found that the side reactions could be effectively suppressed and the desired disaccharide **28** was obtained in satisfactory yield (70%). No lactonized product was isolated. The presence of the β-(1→4) linkage in **28** was established by two large anomeric coupling constants ($J_{1,2}$ = 7.8 Hz, $J_{1',2'}$ = 8.4 Hz). This glycosylation was successfully scaled to 1 g. Disaccharide **28** was subsequently treated with dilute hydrazine in EtOH at 35 °C to cleave the phthalimido group[26,28] without affecting the methyl ester group of the lactate; this could be explained by the unusual crowding of the methyl ester of the lactate in the molecule making the nucleophilic attack by hydrazine less accessible. However, TLC has indeed revealed some partial de-*O*-acetylations. After reacetylations with excess acetic anhydride and pyridine, the desired compound **29** was isolated in 87% yield over two steps. The methyl ester of **29** was finally selectively removed by treatment of **29** with lithium iodide in dry pyridine at 100 °C to provide the target disaccharide **30** in 85% yield. Compound **30** could be used directly in the synthesis of bacterial cell wall peptidoglycan by coupling with suitably protected peptides (not reported here).

In summary, the acid-catalyzed alcoholysis of the furanose acetonide **1** of D-GlcNAc is an efficient method to synthesize the β-pyranosides of a variety of amino sugar derivatives. By introducing leaving groups or protecting groups at the *O*-3 position of **1**, we have successfully and efficiently synthesized several biological important amino sugars in large quantities. The success in applying this methodology to muramic acid chemistry should provide abundant opportunities to expand and apply the method for preparation of challenging carbohydrate targets related to bacterial cell wall research.

Experimental Section

2-Methyl-(3-*O*-methanesulfonyl-1,2-dideoxy-5,6-*O*-isopropylidene-α-D-glucofurano)-[2,1-*d*]-2-oxazoline (8). Mesyl chloride (12 mL, 140 mmol) was added to a solution of oxazoline **1**[19,20] (17 g, 70 mmol) and Et_3N (25 mL) in anhydrous dichloromethane (240 mL) at 0 °C. The mixture was stirred at 0 °C for 2 h and quenched with water. The resulting mixture was extracted several times with dichloromethane. The combined organic layers were washed with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated to afford a yellow oily residue that was used directly in the next glycosylation step without chromatography. A small amount (258 mg) of the mixture was purified by silica gel chromatography (1:1 toluene−EtOAc) to give the desired product **8** as a white amorphous solid (196 mg): R_f = 0.49 (1:3 toluene−EtOAc); $[\alpha]_D$ +49.6 (*c* 0.73, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.18 (d, 1H, $J_{1,2}$ = 5.0 Hz, H-1), 5.10 (d, 1H, $J_{3,4}$ = 2.9 Hz, H-3), 4.80 (dd, 1H, $J_{2,3}$ = 1.6 Hz, H-2), 4.25 (ddd, 1H, $J_{5,6a}$ = 6.0 Hz, $J_{5,6b}$ = 4.2 Hz, H-5), 4.15 (dd, 1H, $J_{6a,6b}$ = 9.0 Hz, H-6a), 4.03 (dd, 1H, H-6b), 3.85 (dd, 1H, $J_{4,5}$ = 8.5 Hz, H-4), 3.11 (s, 3H, SCH_3), 2.08 (s, 3H, $N=CCH_3$), 1.42, 1.32 (2 × s, 2 × 3H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 109.7, 106.9, 82.4, 80.4, 72.1, 67.3, 38.0, 26.9, 25.1, 14.1; ESI HRMS *m/z* calcd for $C_{12}H_{20}NO_7S$ ($M + H^+$) 322.0955, found 322.0956. Anal. Calcd for $C_{12}H_{19}NO_7S$: C, 44.85; H, 5.96; N, 4.36. Found: C, 45.24; H, 5.96; N, 4.60.

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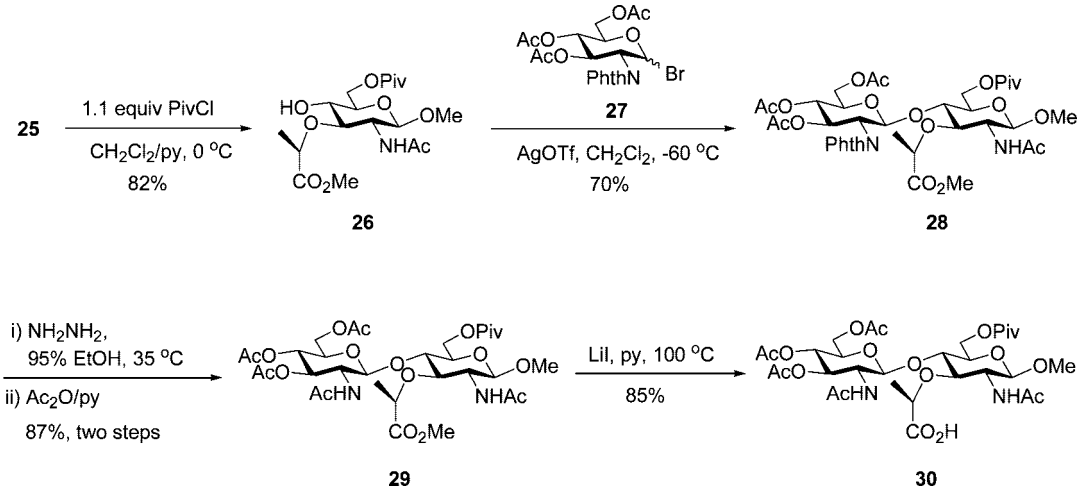
SCHEME 7. Synthesis of a Peptidoglycan Disaccharide Unit 30 from 25



Methyl 2-Acetamido-2-deoxy-3-*O*-methanesulfonyl-β-D-glucopyranoside (9). The above crude **8** (22 g, 68.5 mmol) was dissolved in dry methanol (250 mL), and *p*-TsOH (1.42 g, 7.5 mmol) was added. The mixture was stirred at room temperature for 18 h and quenched by adding the Amberlite IRA-400 basic resin (OH^-) to pH 7. After filtration, the solvent was evaporated, and the residue was purified by silica gel chromatography (15:1 $CH_2Cl_2-CH_3OH$) to afford the desired product **9** as a pale yellow oil (15.3 g, 48.8 mmol, 70% over two steps): R_f = 0.26 (10:1 $CH_2Cl_2-CH_3OH$); $[\alpha]_D$ −78.9 (*c* 0.92, CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.57 (dd, 1H, $J_{3,4}$ = 9.1 Hz, H-3), 4.47 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 3.88 (dd, 1H, $J_{6a,6b}$ = 12.0 Hz, H-6a), 3.77 (dd, 1H, $J_{2,3}$ = 10.3 Hz, H-2), 3.72 (dd, 1H, H-6b), 3.57 (dd, 1H, $J_{4,5}$ = 9.6 Hz, H-4), 3.47 (s, 3H, SCH_3), 3.35 (ddd, 1H, $J_{5,6b}$ = 5.4 Hz, $J_{5,6a}$ = 2.6 Hz, H-5), 3.11 (s, 3H, OCH_3), 1.95 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.7, 102.8, 85.7, 77.6, 69.9, 62.3, 75.2, 55.7, 39.1, 23.0; ESI HRMS *m*/*z* calcd for $C_{10}H_{19}NO_8SNa$ ($M + Na^+$) 336.0723, found 336.0721. Anal. Calcd for $C_{10}H_{19}NO_8S$: C, 38.33; H, 6.11; N, 4.47. Found: C, 37.97; H, 6.43; N, 4.14.

Methyl 2-Acetamido-2-deoxy-β-D-allopyranoside (2). Compound **9** (15.1 g, 48.2 mmol) was dissolved in a mixture of 2-methoxyethanol and satd $NaHCO_3$ (250 mL, 9:1, v/v), and NaOAc (20 g, 244 mmol) was added. The mixture was refluxed for 18 h. After concentration and filtration, the filtrate was concentrated and applied to a silica gel column (15% $CH_3OH-CH_2Cl_2$) to afford the desired product **2** as a white solid (10.1 g, 43.0 mmol, 89%): mp 156−158 °C; R_f = 0.40 (5:1 $CH_2Cl_2-CH_3OH$); $[\alpha]_D$ −99.7 (*c* 0.77, CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ 4.59 (d, 1H, $J_{1,2}$ = 8.6 Hz, H-1), 3.96 (dd, 1H, $J_{3,4}$ = 2.9 Hz, H-3), 3.85 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, H-6a), 3.76 (dd, 1H, $J_{2,3}$ = 2.8 Hz, H-2), 3.72 (ddd, 1H, $J_{5,6b}$ = 5.6 Hz, $J_{5,6a}$ = 2.2 Hz, H-5), 3.67 (dd, 1H, H-6b), 3.52 (dd, 1H, $J_{4,5}$ = 9.6 Hz, H-4), 3.45 (s, 3H, OCH_3), 1.97 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.0, 101.2, 75.6, 71.4, 68.7, 63.2, 56.9, 54.8, 22.7; ESI HRMS *m*/*z* calcd for $C_9H_{17}NO_6Na$ ($M + Na^+$) 258.0948, found 258.0950. Anal. Calcd for $C_9H_{17}NO_6$: C, 45.95; H, 7.28; N, 5.95. Found: C, 45.72; H, 7.35; N, 5.81.

Methyl 2-Acetamido-3,4-anhydro-2-deoxy-β-D-allopyranoside (10). Compound **9** (11.5 g, 3.7 mmol) was dissolved in dry methanol (90 mL), and a solution of 2 M sodium methoxide in methanol (30 mL) was added. The mixture was stirred at room temperature for 18 h, and a white precipitate was formed. The reaction was quenched with Amberlite IR-120 resin (H^+) to adjust the pH to 7. The solution was concentrated to afford a crude product as a solid in quantitative yield. The product could be used directly in the next step. A small amount of crude product (764 mg) was further purified by silica gel chromatography using 5% MeOH in CH_2Cl_2 as eluent to give the desired product **10** (738 mg) as a white solid: mp 171−173 °C; R_f = 0.38 (10:1 $CH_2Cl_2-CH_3OH$); $[\alpha]_D$ −183.5 (*c* 0.93, CH_3OH); ^{1}H NMR (600 MHz, CD_3OD) δ 4.31 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.13 (dd, 1H, $J_{2,3}$ = 2.0 Hz, H-2), 3.92 (dd, 1H, $J_{3,4}$ = $J_{4,5}$ = 5.4 Hz, H-4), 3.78 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, $J_{5,6a}$ = 5.1 Hz, H-6a), 3.75 (dd, 1H, $J_{5,6b}$ = 5.6 Hz, H-6b), 3.38−3.42 (m, 2H, H-3 and H-5), 3.39 (s, 3H, OCH_3), 1.98 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.5, 100.8, 76.2, 63.5, 57.0, 56.7, 56.0, 51.2, 22.5; ESI HRMS *m*/*z* calcd for $C_9H_{15}NO_5Na$ ($M + Na^+$) 240.0842, found 240.0842. Anal. Calcd for $C_9H_{15}NO_5$: C, 49.76; H, 6.96; N, 6.45. Found: C, 49.65; H, 7.01; N, 6.26.

Methyl 2-Acetamido-2-deoxy-β-D-gulopyranoside (3). Crude epoxide **10** (4 g, 18 mmol) was dissolved in a mixture of acetone and water (200 mL, 1:1, v/v), and Amberlite IR-120 resin (H^+) (35 g) was added. The mixture was stirred at room temperature until all of the starting material was consumed or stirred at 70 °C for 3 h. After filtration, the filtrate was concentrated and chromatographed on silica gel using 10% MeOH in CH_2Cl_2 as eluent to yield the target compound **3** as a white amorphous solid (2.7 g, 11.5 mmol, 64%): R_f = 0.25 (5:1 $CH_2Cl_2-CH_3OH$); $[\alpha]_D$ −108.3 (*c* 0.66, CH_3OH); ^{1}H NMR (600 MHz, CD_3OD) δ 4.57 (d, 1H, $J_{1,2}$ = 8.8 Hz, H-1), 4.10 (dd, 1H, $J_{2,3}$ = 3.2 Hz, H-2), 3.92 (ddd, 1H, $J_{5,6a}$ = 6.7 Hz, $J_{5,6b}$ = 5.3 Hz, H-5), 3.88 (dd, 1H, $J_{3,4}$ = 3.5 Hz, H-3), 3.75 (dd, 1H, $J_{6a,6b}$ = 11.4 Hz, H-6a), 3.71 (dd, 1H, H-6b), 3.63 (dd, 1H, $J_{4,5}$ = 1.4 Hz, H-4), 3.45 (s, 3H, OCH_3), 1.96 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.2, 101.8, 75.1, 71.9, 70.6, 62.8, 56.7, 49.5, 22.8; ESI HRMS *m*/*z* calcd for $C_9H_{17}NO_6Na$ ($M + Na^+$) 258.0948, found 258.0950. Anal. Calcd for $C_9H_{17}NO_6$: C, 45.95; H, 7.28; N, 5.95. Found: C, 45.55; H, 7.53; N, 5.62.

Methyl 2-Acetamido-3,6-di-*O*-acetyl-4-azido-2,4-dideoxy-β-D-gulopyranoside (11). Epoxide **10** (1.09 g, 5 mmol) was dissolved in dry DMF, and NaN_3 (1 g, 15.4 mmol) and NH_4Cl (1 g, 18.7 mmol) were added. The resulting mixture was stirred at 90 °C for 18 h. The solvent was removed under high vacuum, and the residue was extracted with methanol; the solid residue was removed by filtration. The filtrates were combined and evaporated under reduced pressure to afford a colorless oil. Anhydrous pyridine (50 mL) and acetic anhydride (5 mL) were added at 0 °C, and the mixture was stirred at room temperature for 18 h. After concentration, the resulting mixture was separated by silica gel chromatography using a gradient eluent of toluene and ethyl acetate (1:1 to 1:2) to provide the pure compound **11** (1.32 g, 3.8 mmol, 77%): R_f = 0.27 (1:6 toluene−EtOAc); $[\alpha]_D$ −84.9 (*c* 0.94, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.64 (d, 1H, $J_{NH,H-2}$ = 8.2 Hz, NH), 5.33 (dd, 1H, $J_{3,4}$ = 3.6 Hz, H-3), 4.54 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 4.38 (ddd, 1H, $J_{2,3}$ = 3.3 Hz, H-2), 4.34 (dd, 1H, $J_{6a,6b}$ = 11.5 Hz, H-6a), 4.20 (dd, 1H, H-6b), 4.06 (ddd, 1H, $J_{5,6a}$ = $J_{5,6b}$ = 6.6 Hz, H-5), 3.74 (dd, 1H, $J_{4,5}$ = 2.0 Hz, H-4), 3.47 (s, 3H, OCH_3), 2.16 (s, 3H, $COCH_3$), 2.10 (s, 3H, $COCH_3$), 2.01 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, $CDCl_3$)

δ 170.5, 169.7, 169.3, 100.0, 70.9, 70.2, 62.7, 58.4, 55.9, 47.9, 23.3, 20.9, 20.8; ESI HRMS *m/z* calcd for $C_{13}H_{20}N_4O_7Na$ (M + Na^+) 367.1224, found 367.1223. Anal. Calcd for $C_{13}H_{20}N_4O_7$: C, 45.35; H, 5.85; N, 16.27. Found: C, 44.93; H, 5.86; N, 16.47.

Methyl 2-Acetamido-4-azido-2,4-dideoxy-6-*O*-methanesulfonyl-β-D-gulopyranoside (12). Compound **11** (0.99 g, 2.6 mmol) was dissolved in anhydrous methanol (50 mL), and a solution of 2 M sodium methoxide in methanol (0.5 mL) was added. The mixture was stirred at room temperature for 18 h and quenched with Amberlite IR-120 resin (H^+). After filtration, the organic mixture was concentrated to give a solid residue. The residue was redissolved in anhydrous pyridine (15 mL), and the mixture was cooled to −20 °C; mesyl chloride (0.2 mL, 2.6 mmol) was added, and the mixture was stirred at −20 °C for 18 h. After concentration, the residue was purified by silica gel chromatography using 5% MeOH in CH_2Cl_2 as eluent to yield the desired product **12** as a white amorphous solid (695 mg, 2.05 mmol, 79%): R_f = 0.43 (10:1 CH_2Cl_2−CH_3OH); $[\alpha]_D$ −123 (*c* 0.88, CH_3OH); ^1H NMR (600 MHz, CD_3OD) δ 4.63 (d, 1H, $J_{1,2}$ = 8.7 Hz, H-1), 4.34−4.38 (m, 2H, H-6a and H-6b), 4.30 (d, 1H, $J_{5,6a}$ = $J_{5,6b}$ = 6.3 Hz, H-5), 4.11 (dd, 1H, $J_{3,4}$ = 3.3 Hz, H-3), 4.02 (dd, 1H, $J_{2,3}$ = 3.1 Hz, H-2), 3.70 (dd, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 3.44 (s, 3H, SCH_3), 3.12 (s, 3H, OCH_3), 1.97 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.2, 101.5, 71.2, 70.0, 69.4, 62.9, 56.9, 51.3, 37.3, 22.7; ESI HRMS *m/z* calcd for $C_{10}H_{18}N_4O_7SNa$ (M + Na^+) 361.0788, found 361.0788. Anal. Calcd for $C_{10}H_{18}N_4O_7S$: C, 35.50; H, 5.36; N, 16.56. Found: C, 35.15; H, 5.27; N, 16.00.

Methyl 2-Acetamido-4-amino-2,4-dideoxy-6-*O*-methanesulfonyl-β-D-gulopyranoside (13). To a solution of compound **12** (20 mg, 0.06 mmol) in ethanol (5 mL) was successively added $NaBH_4$ (15 mg, 0.4 mmol) and a solution of 0.16 M $NiCl_2$ in EtOH (0.2 mL). The mixture was stirred at room temperature for 18 h and quenched with acetic acid (1 mL). The mixture was concentrated and purified by silica gel chromatography (100:10:1 CH_2Cl_2−CH_3OH−NH_4OH) to provide the compound **13** as a colorless oil (14.5 mg, 0.046 mmol, 77%): R_f = 0.30 (5:1 CH_2Cl_2−CH_3OH); $[\alpha]_D$ −72.8 (*c* 0.28, CH_3OH); ^1H NMR (500 MHz, CD_3OD) δ 4.57 (d, 1H, $J_{1,2}$ = 8.7 Hz, H-1), 4.40 (dd, 1H, $J_{6a,6b}$ = 11.1 Hz, H-6a), 4.34 (dd, 1H, H-6b), 4.25 (ddd, 1H, $J_{5,6a}$ = 7.9 Hz, $J_{5,6b}$ = 4.1 Hz, H-5), 4.02 (dd, 1H, $J_{2,3}$ = 3.1 Hz, H-2), 3.84 (dd, 1H, $J_{3,4}$ = 3.3 Hz, H-3), 3.43 (s, 3H, SCH_3), 3.11 (s, 3H, OCH_3), 2.87 (dd, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 1.97 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.1, 102.2, 72.9, 72.4, 71.2, 56.9, 54.0, 50.9, 37.3, 22.7; ESI HRMS *m/z* calcd for $C_{10}H_{20}N_2O_7SNa$ (M + Na^+) 335.0889, found 335.0885.

Methyl 2-Acetamido-4-amino-2,4,6-trideoxy-β-D-gulopyranoside (4). To a solution of compound **12** (110 mg, 0.32 mmol) in ethanol (10 mL) were added $NaBH_4$ (100 mg, 2.64 mmol) and 0.16 M $NiCl_2$ in ethanol (0.2 mL). The mixture was then stirred at 50−60 °C for 18 h and quenched by acetic acid (1 mL). The mixture was concentrated and purified by silica gel chromatography (100:10:1 CH_2Cl_2−CH_3OH−NH_4OH) to afford the desired product **4** as a colorless oil (52 mg, 0.24 mmol, 74%): R_f = 0.17 (5:1 CH_2Cl_2/CH_3OH); $[\alpha]_D$ −93.8 (*c* 0.88, CH_3OH); ^1H NMR (600 MHz, D_2O) δ 4.72 (d, 1H, $J_{1,2}$ = 8.8 Hz, H-1), 4.39 (qd, $J_{5,6}$ = 6.6 Hz, H-5), 4.22 (dd, 1H, $J_{3,4}$ = 3.3 Hz, H-3), 3.87 (dd, 1H, $J_{2,3}$ = 3.2 Hz, H-2), 3.51 (s, 3H, OCH_3), 3.40 (dd, 1H, $J_{4,5}$ = 1.8 Hz, H-4), 1.96 (s, 3H, $NHCOCH_3$), 1.30 (d, 3H, H-6 CH_3); ^{13}C NMR (125 MHz, CD_3OD) δ 173.1, 102.1, 72.9, 69.6, 56.7, 56.6, 50.9, 22.7, 16.7; ESI HRMS *m/z* calcd for $C_9H_{18}N_2O_4Na$ (M + Na^+) 241.1159, found 241.1156.

2-Methyl-(3-*O*-benzyl-1,2-dideoxy-5,6-*O*-isopropylidene-α-D-glucofurano)-[2,1-*d*]-2-oxazoline (14). Oxazoline **1** (6 g, 24.7 mmol) was dissolved in dry DMF (150 mL), and sodium hydride (60% dispersion of in mineral oil, 5 g) was added. After the mixture was stirred for 30 min at room temperature, benzyl bromide (5 mL) was added dropwise at 0 °C. The mixture was stirred for 18 h at room temperature. The reaction was quenched with methanol (30 mL) and concentrated. Water (100 mL) was added, and the mixture was extracted several times with dichloromethane. The combined extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in dichloromethane and passed through a short silica gel pad. Further purification by silica gel chromatography (1:1 hexane−ethyl acetate containing 1% Et_3N) afforded compound **14** as a pale yellow oil (5.56 g, 17.1 mmol, 68%): R_f = 0.47 (1:3 hexane−EtOAc); $[\alpha]_D$ −27.6 (*c* 0.92, $CHCl_3$) [lit.[25] $[\alpha]_D$ −36 (*c* 1.2, $CHCl_3$)]; ^1H NMR (600 MHz, $CDCl_3$) δ 7.34−7.38 (m, 4H, ArH), 7.28−7.32 (m, 1H, ArH), 6.13 (d, 1H, $J_{1,2}$ = 5.1 Hz, H-1), 4.73 (d, 1H, *J* = 11.8 Hz, $PhCH_2$), 4.66 (d, 1H, *J* = 11.8 Hz, $PhCH_2$), 4.53 (dd, 1H, $J_{2,3}$ = 1.2 Hz, H-2), 4.38 (dd, 1H, $J_{5,6a}$ = $J_{5,6b}$ = 5.9 Hz, H-5), 4.10 (dd, 1H, $J_{6a,6b}$ = 8.6 Hz, H-6a), 4.20 (dd, 1H, H-6b), 4.11 (d, 1H, $J_{3,4}$ = 3.2 Hz, H-3), 3.85 (dd, 1H, $J_{4,5}$ = 7.1 Hz, H-4), 2.02 (s, 3H, *N*-CCH_3), 1.42, 1.37 (2 × s, 2 × 3H, $C(CH_3)_2$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.0, 137.6, 128.4, 127.8, 127.8, 127.8, 127.8, 127.7, 109.0, 107.1, 81.6, 75.4, 72.6, 72.2, 67.0, 26.7, 25.3, 14.2; ESI HRMS *m/z* calcd for $C_{18}H_{24}NO_5Na$ (M + Na^+) 334.1649, found 334.1646.

Methyl 2-Acetamido-3-*O*-benzyl-2-deoxy-β-D-glucopyranoside (15). Compound **14** (5.48 g, 16.4 mmol) was dissolved in dry methanol (150 mL), and camphor-10-sulfonic acid (1.04 g, 4.5 mmol) was added. The mixture was stirred at room temperature for 36 h. The acid was removed by adding Amberlite IRA-400 resin (OH^-). After filtration, the filtrate was concentrated and the residue was purified by silica gel chromatography using 5% MeOH in CH_2Cl_2 as eluent to afford the desired compound **15** as a white amorphous solid (3.73 g, 11.5 mmol, 70%): R_f = 0.29 (10:1 CH_2Cl_2−CH_3OH); $[\alpha]_D$ −26.6 (*c* 0.74, CH_3OH); ^1H NMR (500 MHz, CD_3OD) δ 7.20−7.32 (m, 5H, ArH), 4.86 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 4.64 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 4.34 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 3.89 (dd, 1H, $J_{6a,6b}$ = 11.9 Hz, H-6a), 3.74 (dd, 1H, $J_{2,3}$ = 9.8 Hz, H-2), 3.70 (dd, 1H, H-6b), 3.47−3.52 (m, 2H, H-4 and H-3), 3.28 (dd, 1H, $J_{5,6b}$ = 6.0 Hz, $J_{5,6a}$ = 2.4 Hz, H-5), 3.45 (s, 3H, OCH_3), 1.86 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.3, 140.3, 129.2, 128.8, 128.5, 103.5, 84.2, 78.0, 75.6, 72.1, 62.7, 57.0, 56.2, 23.0; ESI HRMS *m/z* calcd for $C_{16}H_{23}NO_6Na$ (M + Na^+) 348.1417, found 348.1411. Anal. Calcd for $C_{16}H_{23}NO_6$: C, 59.06; H, 7.13; N, 4.31. Found: C, 58.85; H, 7.14; N, 4.36.

Methyl 2-Acetamido-3-*O*-benzyl-2-deoxy-6-*O*-methanesulfonyl-β-D-glucopyranoside (16). Compound **15** (1.2 g, 3.7 mmol) was dissolved in dry pyridine (30 mL), and the solution was cooled to −15 °C. Mesyl chloride (1.05 equiv, 0.31 mL, 4 mmol) was added dropwise, and the mixture was stirred for 4 h until all starting material was consumed. Methanol (1 mL) was added to quench the reaction. The solvent was evaporated under reduced pressure, and the resulting residue was purified by silica gel chromatography using 2.5% MeOH in CH_2Cl_2 as eluent to afford the desired compound **16** as a white amorphous solid (1.32 g, 3.27 mmol, 88%): R_f = 0.53 (10:1 CH_2Cl_2−CH_3OH); $[\alpha]_D$ +1.8 (*c* 2.09, CH_3OH); ^1H NMR (500 MHz, CD_3OD) δ 7.22−7.34 (m, 5H, ArH), 4.87 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 4.65 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 4.55 (dd, 1H, $J_{6a,6b}$ = 11.2 Hz, H-6a), 4.41 (dd, 1H, $J_{6b,5}$ = 5.0 Hz, H-6b), 4.39 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 3.73 (dd, 1H, $J_{2,3}$ = 8.7 Hz, H-2), 3.48−3.55 (m, 3H, H-3, H-4 and H-5), 3.44 (s, 3H, SCH_3), 3.11 (s, 3H, OCH_3), 1.86 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 173.4, 140.1, 129.3, 128.8, 128.6, 103.4, 83.8, 75.8, 75.3, 71.5, 70.4, 57.1, 56.1, 37.5, 23.0; ESI HRMS *m/z* calcd for $C_{17}H_{25}NO_8SNa$ (M + Na^+) 426.1193, found 426.1196. Anal. Calcd for $C_{17}H_{25}NO_8S$: C, 50.61; H, 6.25; N, 3.47. Found: C, 50.60; H, 6.22; N, 3.54.

Methyl 2-Acetamido-3-*O*-benzyl-2,6-dideoxy-β-D-glucopyranoside (17). Compound **16** (1.1 g, 2.7 mmol) was dissolved in dry DMSO (20 mL), and $NaBH_4$ (1.0 g, 26.4 mmol) was added. The mixture was heated at 85−90 °C for 18 h. The reaction was quenched by adding a 5% acetic acid solution (2 mL) at 0 °C until it became a clear solution. Next, the solution was diluted with more H_2O and extracted several times with ethyl acetate. The combined extracts were evaporated under reduced pressure to yield a residue,

which was chromatographed on silica gel using toluene/ethyl acetate (1:2) as eluent providing the title compound **17** as a white amorphous solid (0.69 g, 2.23 mmol, 83%): R_f = 0.28 (1:10 hexane−EtOAc); $[\alpha]_D$ −9.6 (*c* 0.75, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.30−7.40 (m, 5H, ArH), 5.60 (d, 1H, $J_{NH,H\text{-}2}$ = 7.3 Hz, NH), 4.76 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 4.75 (d, 1H, *J* = 12.4 Hz, $PhCH_2$), 4.70 (d, 1H, *J* = 11.7 Hz, $PhCH_2$), 3.99 (dd, 1H, $J_{3,4}$ = 8.8 Hz, H-3), 3.48 (s, 3H, OCH_3), 3.42 (qd, 1H, $J_{5,6}$ = 6.2 Hz, H-5), 3.30 (ddd, 1H, $J_{2,3}$ = 10.3 Hz, H-2), 3.27 (dd, 1H, $J_{4,5}$ = 9.1 Hz, H-4), 1.96 (s, 3H, $NHCOCH_3$), 1.33 (d, 3H, *J* = 6.3 Hz, H-6 CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6, 138.3, 128.7, 128.1, 128.0, 128.0, 100.5, 80.7, 76.1, 74.1, 71.4, 57.7, 56.7, 23.7, 17.7; ESI HRMS *m*/*z* calcd for $C_{16}H_{23}NO_5Na$ (M + Na^+) 332.1468, found 332.1465. Anal. Calcd for $C_{16}H_{23}NO_5$: C, 62.12; H, 7.49; N, 4.53. Found: C, 61.98; H, 7.20; N, 4.50.

Methyl 4-Azido-3-*O*-benzyl-2,4,6-trideoxy-2-(1*H*-5-methyltetrazol-1-yl)-β-D-galactopyranoside (18). To a solution of compound **17** (430 mg, 1.4 mmol) in anhydrous dichloromethane (30 mL) and pyridine (3 mL) was added dropwise trifluoromethanesulfonic anhydride (0.48 mL, 2.8 mmol) at −10 °C under argon. The mixture was stirred at −10 °C for 3 h. Dichloromethane (20 mL) was added, and the mixture was washed successively with 1 M HCl, satd $NaHCO_3$, and water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure (<20 °C bath) to afford a yellow oil. This residue was redissolved in dry DMF (5 mL)d and NaN_3 (450 mg, 7 mmol) was added. The mixture was stirred for 18 h at room temperature. After concentration, the residue was dissolved in dichloromethane, washed with water and brine, and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed, and the crude residue was purified by silica gel chromatography (10:1 toluene−ethyl acetate) to afford **18** as a white solid (438 mg, 1.22 mmol, 87%): mp 104−105 °C; R_f = 0.37 (4:1 toluene−EtOAc); $[\alpha]_D$ −1.8 (*c* 1.13, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28−7.32 (m, 3H, ArH), 7.20−7.25 (m, 2H, ArH), 4.70 (d, 1H, $J_{1,2}$ = 8.1 Hz, H-1), 4.45 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 4.39 (dd, 1H, $J_{3,4}$ = 3.5 Hz, H-3), 4.33 (d, 1H, *J* = 11.2 Hz, $PhCH_2$), 3.78 (qd, 1H, $J_{5,6}$ = 6.3 Hz, H-5), 3.76 (dd, 1H, $J_{4,5}$ = 1.3 Hz, H-4), 3.34 (s, 3H, OCH_3), 2.54 (s, 3H, tetrazole CH_3), 1.41 (d, 3H, H-6 CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 154.2, 136.1, 128.7, 128.5, 128.1, 101.6, 78.6, 72.8, 69.4, 62.5, 59.5, 57.2, 17.5, 8.9; ESI HRMS *m*/*z* calcd for $C_{16}H_{21}N_7O_3Na$ (M + Na^+) 382.1598, found 382.1598. Anal. Calcd for $C_{16}H_{21}N_7O_3$: C, 53.47; H, 5.89; N, 27.28. Found: C, 53.38; H, 5.81; N, 26.89.

Methyl 4-Amino-2,4,6-trideoxy-2-(1*H*-5-methyltetrazol-1-yl)-β-D-galactopyranoside (19). To a solution of compound **18** (68 mg, 0.19 mmol) in dry methanol (2 mL) and acetic acid (0.2 mL) was added 10% palladium on carbon (100 mg). The mixture was stirred under a hydrogen atmosphere for 18 h at room temperature. After filtration, the mixture was concentrated, and the crude residue was purified by silica gel chromatography using 5% methanol in dichloromethane as eluent to afford **19** as a white solid (42 mg, 0.17 mmol, 91%): mp 202−204 °C; R_f = 0.39 (5:1 CH_2Cl_2−CH_3OH); $[\alpha]_D$ +12.8 (*c* 0.69, CH_3OH); ^{1}H NMR (400 MHz, CD_3OD): δ 4.78 (d, 1H $J_{1,2}$ = 8.1 Hz, H-1), 4.30−3.36 (m, 2H, *J* = 10.6 Hz, 8.8 Hz, 2.8 Hz, H-3 and H-2), 3.94 (qt, 1H, $J_{5,6}$ = 6.5 Hz, H-5), 3.34 (s, 3H, OCH_3), 3.02 (dd, 1H, $J_{4,3}$ = 3.4 Hz, $J_{4,5}$ = 1.7 Hz, H-4), 2.57 (s, 3H, tetrazole CH_3), 1.36 (d, 3H, H-6 CH_3); ^{13}C NMR (125 MHz, CD_3OD) δ 155.8 (tet-C), 103.2(C-1), 71.9, 71.4, 61.9, 57.2, 56.2, 17.1, 8.7 (CH_3−CN); ESI HRMS *m*/*z* calcd for $C_9H_{18}N_5O_3$ (M + H^+) 244.1404, found 244.1404.

Methyl 2-Acetamido-4-azido-3-*O*-benzyl-2,4,6-trideoxy-β-D-galactopyranoside (20). Compound **17** (300 mg, 0.97 mmol) was dissolved in anhydrous dichloromethane (10 mL) and pyridine (1 mL) under argon. After the solution was cooled −30 °C, trifluoromethanesulfonic anhydride (0.19 mL, 1.1 mmol) was added dropwise over approximately 1 min. The mixture was stirred at −30 °C for 3 h. The reaction was diluted with dichloromethane (20 mL) and washed successively with 1 M HCl, satd $NaHCO_3$, and water. The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure (<20 °C) to afford an oil. This residue was redissolved in dry DMF (5 mL), and NaN_3 (325 mg, 5 mmol) was added. After being stirred at room temperature for 18 h, the mixture was concentrated. The residue was dissolved in dichloromethane, washed with water and brine, and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed. The residue was purified by silica gel chromatography (1:1 toluene−ethyl acetate) to yield compound **20** as a white amorphous solid (213 mg, 0.64 mmol, 66%): R_f = 0.20 (1:2 toluene−EtOAc); $[\alpha]_D$ +44.5 (*c* 0.53, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.40 (m, 5H, ArH), 5.68 (d, 1H, $J_{NH,H\text{-}2}$ = 7.8 Hz, NH), 4.91 (d, 1H, $J_{1,2}$ = 8.4 Hz, H-1), 4.70 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 4.62 (dd, 1H, $J_{3,4}$ = 3.6 Hz, H-3), 4.56 (d, 1H, *J* = 11.4 Hz, $PhCH_2$), 3.72 (dd, 1H, $J_{4,5}$ = 0.9 Hz, H-4), 3.68 (t, 1H, $J_{5,6}$ = 6.5 Hz, H-5), 3.20 (ddd, 1H, $J_{2,3}$ = 10.6 Hz, H-2), 3.47 (s, 3H, OCH_3), 1.94 (s, 3H, $NHCOCH_3$), 1.33 (d, 3H, H-6 CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 137.5, 128.6, 128.2, 128.2, 99.9, 76.4, 72.6, 68.8, 63.4, 56.7, 55.5, 23.8, 17.6; ESI HRMS *m*/*z* calcd for $C_{16}H_{22}N_4O_4Na$ (M + Na^+) 357.1533, found 357.1534. A satisfactory elemental analyses could not be obtained.

Methyl 2-Acetamido-4-amino-2,4,6-trideoxy-β-D-galactopyranoside (5). Compound **20** (150 mg, 0.45 mmol) was dissolved in anhydrous methanol (5 mL), and 20% palladium hydroxide on carbon (100 mg) was added. The mixture was stirred under a hydrogen atmosphere for 18 h at room temperature. After filtration, the solution was concentrated under reduced pressure followed by silica gel chromatography using dichloromethane/methanol/ammonium hydroxide (100:10:1) as eluent to afford the target compound **5** as a white amorphous solid (91 mg, 0.42 mmol, 93%): R_f = 0.33 (100:20:1 CH_2Cl_2−CH_3OH−NH_4OH); $[\alpha]_D$ −10.8 (*c* 0.91, CH_3OH) [lit.[17] $[\alpha]_D$ −8.7 (*c* 1.0, CH_3OH)]; ^{1}H NMR (600 MHz, D_2O) δ 4.43 (d, 1H, $J_{1,2}$ = 8.7 Hz, H-1), 4.02−4.07 (m, 2H, *J* = 10.7 Hz, *J* = 4.5 Hz, H-3 and H-5), 3.75 (dd, 1H, $J_{2,3}$ = 10.9 Hz, H-2), 3.59 (d, 1H, *J* = 4.6 Hz, H-4), 3.50 (s, 3H, OCH_3), 2.04 (s, 3H, $NHCOCH_3$), 1.34 (d, 3H, $J_{6,5}$ = 6.7 Hz, H-6 CH_3); ^{13}C NMR (125 MHz, D_2O) δ 176.0, 103.3, 68.8, 68.5, 58.3, 55.7, 52.9, 23.1, 16.5; ESI HRMS *m*/*z* calcd for $C_9H_{19}N_2O_4$ (M + H^+) 219.1339, found 219.1336.

Methyl 2-Acetamido-2-deoxy-3,6-di-*O*-pivoyl-β-D-glucopyranoside (22). Pivaloyl chloride (13.6 mL, 112 mmol) was added dropwise to a solution of methyl 2-acetamido-2-deoxy-β-D-glucopyranoside **21**[19] (9.4 g, 40 mmol) in a mixture of anhydrous CH_2Cl_2 (70 mL) and pyridine (170 mL) at 0 °C. The mixture was stirred at 0 °C for 3 h (after 30 min the solution became cloudy). CH_2Cl_2 (300 mL) was added, and the mixture was washed with satd $NaHCO_3$, water, and brine and dried over anhydrous Na_2SO_4. After concentration, the residue was purified by silica gel chromatography (50% AcOEt−hexane) to afford **22** as a white foam (15.2 g, 37.7 mmol, 94%): R_f = 0.20 (1:1 hexane−EtOAc); $[\alpha]_D$ −45.2 (*c* 0.69, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 5.65 (d, 1H, $J_{NH,2}$ = 9.3 Hz, NH), 5.04 (dd, 1H, $J_{3,4}$ = 8.5 Hz, H-3), 4.42 (dd, 1H, $J_{6a,6b}$ = 12.1 Hz, H-6a), 4.40 (d, 1H, $J_{1,2}$ = 8.2 Hz, H-1), 4.37 (dd, 1H, H-6b), 3.98 (ddd, 1H, $J_{2,3}$ = 10.6 Hz, H-2), 3.55 (ddd, 1H, $J_{5,6a}$ = $J_{5,6b}$ = 2.4 Hz, H-5), 3.51 (ddd, 1H, $J_{4,5}$ = 9.7 Hz, $J_{4,OH}$ = 5.1 Hz, H-4), 3.47 (s, 3H, OCH_3), 3.01 (d, 1H, OH at C-4), 1.94 (s, 3H, $NHCOCH_3$), 1.24 (s, 9H, $C(CH_3)_3$), 1.21 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ 179.8, 179.2, 170.0, 102.0, 74.9, 74.3, 69.4, 63.1, 56.4, 53.7, 39.0, 39.0, 27.2, 27.0, 23.3; ESI HRMS *m*/*z* Calcd for $C_{19}H_{33}NO_8Na$ (M + Na^+) 426.2098, found 426.2102.

Methyl 2-Acetamido-2-deoxy-β-D-galactopyranoside (6). Trifluoromethanesulfonic anhydride (2.9 mL, 17 mmol) was added dropwise to a solution of compound **22** (6 g, 14.9 mmol) in anhydrous CH_2Cl_2 (75 mL) and pyridine (7 mL) at −15 °C under an atmosphere of argon. The mixture was stirred for several hours at this temperature until all starting material was consumed (monitored by TLC) before warming to room temperature. Water (6 mL) was added, and the resulting mixture was refluxed for 5−6 h. Then the mixture was diluted with dichloromethane (100 mL), washed with satd $NaHCO_3$, water, and brine, and dried over

anhydrous Na_2SO_4. After filtration, the filtrate was concentrated. The residue was redissolved in anhydrous methanol (80 mL), a solution of 2 M sodium methoxide in methanol (5 mL) was added, and the mixture was stirred at room temperature for 18 h. After a deionizeation with Amberlite IR-120 resin (H^+), the mixture was filtered and the organic solution was concentrated. The residue was purified by silica gel chromatography (10% methanol in dichloromethane) to provide the target compound **6** as a white amorphous solid (3.13 g, 13.3 mmol, 89%): $R_f = 0.19$ (5:1 $CH_2Cl_2-CH_3OH$); $[\alpha]_D$ −10.8 (*c* 0.63, CH_3OH); ^1H NMR (600 MHz, CD_3OD) δ 4.28 (d, 1H, $J_{1,2} = 8.5$ Hz, H-1), 3.90 (dd, 1H, $J_{2,3} = 10.8$ Hz, H-2), 3.82 (dd, 1H, $J_{4,5} = 0.6$ Hz, H-4), 3.77 (dd, 1H, $J_{6a,6b} = 11.4$ Hz, H-6a), 3.73 (dd, 1H, H-6b), 3.56 (dd, 1H, $J_{3,4} = 3.3$ Hz, H-3), 3.48 (ddd, 1H, $J_{5,6a} = 6.7$ Hz, $J_{5,6b} = 5.4$ Hz, H-5), 1.97 (s, 3H, $NHCOCH_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 174.2, 103.9, 76.7, 73.5, 69.7, 62.5, 56.9, 54.2, 23.0; ESI HRMS *m*/*z* calcd for $C_9H_{17}NO_6Na$ ($M + Na^+$) 258.0948, found 258.0946. Anal. Calcd for $C_9H_{17}NO_6$: C, 45.95; H, 7.28; N, 5.95. Found: C, 45.59; H, 7.25; N, 5.93.

Methyl 2-Acetamido-2-deoxy-4,6-di-*O*-pivoyl-β-D-galactopyranoside (23). Compound **23** was prepared from **22** following the above procedure for compound **6** without carrying out the transesterification. A small amount of crude **23** was purified as a white solid by silica gel chromatography using 3% CH_2Cl_2 in MeOH as eluent: mp 80−81 °C; $R_f = 0.22$ (1:1 hexane−EtOAc); $[\alpha]_D$ −23.4 (*c* 1.07, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.84 (bs, 1H, NH), 5.30 (d, 1H, $J_{4,5} = 3.7$ Hz, H-4), 4.42 (d, 1H, $J_{1,2} = 8.2$ Hz, H-1), 4.17 (dd, 1H, $J_{6a,6b} = 11.3$ Hz, $J_{6a,5} = 7.3$ Hz, H-6a), 4.09 (dd, 1H, $J_{6b,5} = 6.1$ Hz, H-6b), 3.99 (dd, 1H, $J_{3,4} = 3.5$ Hz, H-3), 3.89 (dd, 1H, $J_{2,3} = 10.4$ Hz, H-2), 3.69 (m, 1H, H-5), 3.51 (s, 3H, OCH_3), 2.06 (s, 3H, $NHCOCH_3$), 1.26 (s, 9H, $C(CH_3)_3$), 1.19 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 178.0, 177.8, 173.1, 101.2, 72.0, 72.0, 72.0, 71.4, 68.4, 61.86, 55.7, 55.7, 39.2, 38.7, 27.2, 27.0, 23.4; ESI HRMS *m*/*z* calcd for $C_{19}H_{33}NO_8Na$ ($M + Na^+$) 426.2098, found 426.2095.

2-Methyl-(1,2-dideoxy-5,6-*O*-isopropylidene-3-*O*-[(*R*)-1-carboxyethyl]-α-D-glucofurano)-[2,1-*d*]-2-oxazoline (24). To a solution of oxazoline **1** (1.2 g, 5 mmol) in anhydrous DMF (50 mL) was added a 60% dispersion of NaH in mineral oil (4 g, 0.1 mol) that was previously washed with hexane. The mixture was stirred at 60 °C for 20−30 min. A solution of (*S*)-2-bromoproponic acid (1.35 mL, 15 mmol) in dry DMF (5 mL) was added, and then the mixture was warmed to 60 °C with stirring for 5 h. After removal of solvent, the residue was dissolved in a minimum amount of methanol, filtered through a short pad of silica gel, and eluted with 20% MeOH in CH_2Cl_2 containing 1% NH_4OH. The filtrate was concentrated under reduced pressure to give a crude residue that was used in the next step without further purification. A small amount of the residue (223 mg) was purified by chromatography on silica gel using dichloromethane/methanol/NH_4OH (100:10:1) as eluent to afford compound **24** (109 mg): $R_f = 0.22$ (100:5:0.5 dichloromethane−methanol−NH_4OH); ^1H NMR (600 MHz, $CDCl_3$) δ 6.15 (d, 1H, $J_{1,2} = 5.2$ Hz, H-1), 4.84 (dd, 1H, $J_{2,3} = 1.0$ Hz, H-2), 4.28 (ddd, 1H, $J_{5,6a} = 6.3$ Hz, $J_{5,6b} = 5.9$ Hz, H-5), 4.14 (q, 1H, $J = 6.8$ Hz, $-CH(CO_2H, CH_3)$), 4.10 (dd, 1H, $J_{6a,6b} = 8.6$ Hz, H-6a), 4.02 (d, 1H, $J_{3,4} = 3.1$ Hz, H-3), 3.95 (dd, 1H, H-6b), 3.71 (dd, 1H, $J_{4,5} = 7.9$ Hz, H-4), 1.98 (s, 3H, $N{=}CCH_3$), 1.38 (s, 3H, $-C(CH_3)_2$), 1.37 (d, 3H, $J = 6.8$ Hz, CH_3CHCO_2H)), 1.33 (s, 3H, $-C(CH_3)_2$).

Methyl 2-Acetamido-2-deoxy-3-*O*-[(*R*)-1-(methoxycarbonyl)ethyl]-β-D-glucopyranoside (25). Crude residue **24** was dissolved in anhydrous methanol (80 mL), and *p*-TsOH (0.95 g, 5 mmol) was added to adjust the solution to the pH range of 2−3. The mixture was stirred at room temperature overnight. Amberlite IRA-400 resin (OH^-) was added to the solution to quench the reaction. After filtration, the solvent was removed, and the resulting residue was purified by silica gel chromatography using 8% methanol in dichloromethane as eluent to afford the desired product **25** as a white solid (1.08 g, 3.36 mmol, 67%): mp 150−151 °C; $R_f = 0.32$ (10:1 $CH_2Cl_2-CH_3OH$); $[\alpha]_D$ −4.6 (*c* 1.69, CH_3OH); ^1H NMR (600 MHz, CD_3OD) δ 4.52 (q, 1H, $J = 6.8$ Hz, $-CH(CO_2CH_3,CH_3)$), 4.32 (d, 1H, $J_{1,2} = 8.5$ Hz, H-1), 3.85 (dd, 1H, $J_{6a,6b} = 11.9$ Hz, H-6a), 3.71 (s, 3H, CO_2CH_3), 3.66 (dd, 1H, H-6b), 3.59 (dd, 1H, $J_{2,3} = 10$ Hz, H-2), 3.44 (dd, 1H, $J_{3,4} = 8.7$ Hz, H-3), 3.44 (s, 3H, OCH_3), 3.40 (dd, 1H, $J_{4,5} = 8.7$ Hz, H-4), 3.23 (ddd, 1H, $J_{5,6b} = 5.8$ Hz, $J_{5,6a} = 2.3$ Hz, H-5), 1.97 (s, 3H, $NHCOCH_3$), 1.35 (d, 3H, $J = 6.8$ Hz, $CH_3CHCO_2CH_3$)); ^{13}C NMR (125 MHz, CD_3OD) δ 175.7, 173.7, 103.5, 83.3, 77.9, 77.0, 72.5, 62.6, 57.0, 56.1, 52.4, 23.2, 19.4; HRMS *m*/*z* calcd for $C_{13}H_{23}NO_8Na$ ($M + Na^+$) 344.1315, found 344.1313. Anal. Calcd for $C_{13}H_{23}NO_8$: C, 48.59; H, 7.21; N, 4.36. Found: C, 48.66; H, 7.22; N, 4.31.

Methyl 2-Acetamido-3-*O*-[(*R*)-1-carboxyethyl]-2-deoxy-β-D-glucopyranoside (7). To a solution of compound **25** (0.94 g, 2.9 mmol) in a mixture of dioxane and methanol (60 mL, 1:1, v/v) was added dropwise an aqueous solution of 1 M lithium hydroxide until the solution reached pH 10. The mixture was then stirred at room temperature for 10 h over which period the pH of the mixture was kept in the range 9.5−10.5 by adding more 1 M LiOH solution as needed. The mixture was neutralized with Amberlite IR-120 resin (H^+). After filtration, the solvent was removed, and the resulting residue was applied to a C18 reversed-phase column and eluted with a gradient of water−methanol (0 → 10%) to afford the desired compound **7** (0.89 g, 2.9 mmol, 99%): $[\alpha]_D$ −8.8 (*c* 1.3, CH_3OH); ^1H NMR (600 MHz, D_2O) δ 4.42 (d, 1H, $J_{1,2} = 8.5$ Hz, H-1), 4.31 (q, 1H, $J = 6.9$ Hz, CH_3CHCO_2H), 3.92 (dd, 1H, $J_{6a,6b} = 12.4$ Hz, H-6a), 3.74 (dd, 1H, H-6b), 3.70 (dd, 1H, $J_{2,3} = 10$ Hz, H-2), 3.53 (dd, 1H, $J_{3,4} = 8.6$ Hz, H-3), 3.49 (dd, 1H, $J_{4,5} = 8.6$ Hz, H-4), 3.48 (s, 3H, OCH_3), 3.45 (ddd, 1H, $J_{5,6b} = 5.7$ Hz, $J_{5,6a} = 2.2$ Hz, H-5), 2.0 (s, 3H, $NHCOCH_3$), 1.37 (d, 3H, $J = 6.9$ Hz, CH_3CHCO_2H); ^{13}C NMR (125 MHz, D_2O) δ 179.4, 175.4, 102.9, 83.0, 78.3, 76.5, 70.4, 61.6, 58.0, 55.4, 23.2, 19.5; ESI HRMS *m*/*z* calcd for $C_{12}H_{21}NO_8Na$ ($M + Na^+$) 330.1159, found 330.1157.

Methyl 2-Acetamido-2-deoxy-3-*O*-[(*R*)-1-(methoxycarbonyl)ethyl]-6-*O*-pivaloyl-β-D-glucopyranoside (26). To a solution of compound **25** (0.44 g, 1.36 mmol) in a mixture of anhydrous dichloromethane (3 mL) and pyridine (4.5 mL) was added dropwise pivaloyl chloride (0.17 mL, 1.37 mmol) at 0 °C. The mixture was stirred at 0 °C for 3 h. The mixture was diluted with dichloromethane, washed with satd $NaHCO_3$, water, and brine, and dried over anhydrous Na_2SO_4. After filtration, the solvent was removed, and the residue was chromatographed using 2.5% MeOH in CH_2Cl_2 to afford the desired compound **26** as a white amorphous solid (455 mg, 1.12 mmol, 82%): $R_f = 0.55$ (20:1 $CH_2Cl_2-CH_3OH$); $[\alpha]_D$ −20.8 (*c* 1.14, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 6.5 (d, 1H, $J_{NH,H-2} = 7.1$ Hz, NH), 4.64 (q, 1H, $J = 7.0$ Hz, $CH_3CHCO_2CH_3$)), 4.56 (dd, 1H, $J_{6a,6b} = 12.1$ Hz, H-6a), 4.43 (d, 1H, $J_{1,2} = 8.0$ Hz, H-1), 4.22 (dd, 1H, H-6b), 3.74 (s, 3H, $COOCH_3$), 3.62 (dd, 1H, $J_{3,4} = 8.2$ Hz, H-3), 3.57(dd, 1H, $J_{2,3} = 10.5$ Hz, H-2), 3.48 (s, 3H, OCH_3), 3.39 (ddd, 1H, $J_{5,6a} = 4.0$ Hz, $J_{5,6b} = 2.4$ Hz, H-5), 3.35 (dd, 1H, $J_{4,5} = 9.6$ Hz, H-4), 2.03 (s, 3H, $NHCOCH_3$), 1.39 (d, 3H, $J = 7.0$ Hz, $CH_3CHCO_2CH_3$), 1.22 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 179.9, 175.4, 171.6, 102.6, 79.7, 74.4, 74.3, 71.4, 63.2, 56.6, 54.9, 52.1, 39.0, 27.2, 23.6, 19.1; HRMS *m*/*z* calcd for $C_{18}H_{31}NO_9Na$ ($M + Na^+$) 428.1891, found 428.1893. Anal. Calcd for $C_{18}H_{31}NO_9$: C, 53.32; H, 7.71; N, 3.45. Found: C, 53.00; H, 7.55; N, 3.44.

Methyl 2-Acetamido-4-*O*-(3,4,6-tri-*O*-acetyl-2-deoxy-2-phthalimido-β-D-glucopyranosyl)-2-deoxy-3-*O*-[(*R*)-1-(methoxycarbonyl)-ethyl]-6-*O*-pivaloyl-β-D-glucopyranoside (28). To a solution of compound **26** (0.55 g, 1.36 mmol) and glycosyl donor **27**[27] (2.6 g, 5.4 mmol) in dry dichloromethane (14 mL) were added 4 Å molecular sieves (3 g), and the mixture was stirred at room temperature for 10 min before cooling to −60 °C. Silver triflate (1.41 g, 5.4 mmol) was added at −60 °C under argon, and the mixture was stirred at this temperature for 18 h. The reaction was slowly warmed to room temperature over 2 h. The solution was washed with satd $NaHCO_3$, water, and brine and dried over anhydrous Na_2SO_4. Upon concentration of the filtrate, the residue was purified by silica gel chromatography using a gradient of MeOH

in CH_2Cl_2 (1 → 2%) to yield the target compound **28** as a white amorphous solid (0.78 g, 0.95 mmol, 70%): R_f = 0.32 (20:1 CH_2Cl_2−CH_3OH); $[\alpha]_D$ −22.8 (*c* 0.18, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 (bs, 2H, ArH), 7.76 (m, 2H, ArH), 6.87 (d, 1H, $J_{NH,H\text{-}2}$ = 7.1 Hz, NH), 5.82 (dd, 1H, $J_{3',4'}$ = 9.0 Hz, H-3′), 5.42 (d, 1H, $J_{1',2'}$ = 8.4 Hz, H-1′), 5.18 (dd, 1H, $J_{4',5'}$ = 10.0 Hz, H-4′), 4.68 (q, 1H, *J* = 6.9 Hz, $CH_3CHCO_2CH_3$)), 4.46 (dd, 1H, $J_{6a',6b'}$ = 12.4 Hz, H-6a′), 4.36 (dd, 1H, $J_{6a,6b}$ = 12.2 Hz, H-6a), 4.26 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, H-2′), 4.17 (d, 1H, $J_{1,2}$ = 7.8 Hz, H-1), 4.13 (dd, 1H, H-6b′), 3.89 (dd, 1H, $J_{4,5}$ = 8.8 Hz, H-4), 3.86 (ddd, $J_{5',6a'}$ = 4.6 Hz, $J_{5',6b'}$ = 2.2 Hz, H-5′), 3.77 (s, 3H, $COOCH_3$), 3.67 (ddd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.61 (dd, 1H, H-6b), 3.47 (dd, 1H, $J_{3,4}$ = 8.5 Hz, H-3), 3.40 (s, 3H, OCH_3), 3.24 (ddd, 1H, $J_{5,6b}$ = 4.5 Hz, $J_{5,6a}$ = 2.1 Hz, H-5), 2.08 (s, 3H, $COCH_3$), 2.04 (s, 3H, $COCH_3$), 2.02 (s, 3H, $COCH_3$), 1.85 (s, 3H, $COCH_3$), 1.44 (d, 3H, *J* = 6.9 Hz, $CH_3CHCO_2CH_3$)), 1.20 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$) δ 177.3, 171.6, 170.4, 169.9, 169.5, 134.5, 134.4, 131.3, 131.2, 124.0, 123.7, 102.7, 97.3, 74.9, 72.8, 72.0, 70.5, 68.6, 61.9, 61.6, 56.2, 55.1, 54.5, 52.1, 38.8, 27.1, 23.5, 20.6, 20.6, 20.4, 18.6; ESI HRMS *m*/*z* calcd for $C_{38}H_{50}N_2O_{18}Na$ (M + Na^+) 845.2951, found 845.2957.

Methyl 2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-2-deoxy-3-*O*-[(*R*)-1-(methoxycarbonyl)ethyl]-6-*O*-pivaloyl-β-D-glucopyranoside (29). To a solution of compound **28** (250 mg, 0.3 mmol) in 95% ethanol (15.5 mL) was added hydrazine (115 μL), and the mixture was stirred at 35 °C for 2 days. The reaction was quenched with several drops of acetic acid and evaporated. This residue was dissolved in a mixture of anhydrous pyridine (3 mL) and acetic anhydride (1 mL) and stirred at room temperature for several hours. The mixture was diluted with dichloromethane, washed with water and brine, and dried over anhydrous Na_2SO_4. Filtration and concentration of the filtrate gave a residue, which was purified by silica gel chromatography (2.5% MeOH in CH_2Cl_2) to provide the target product **29** as a white amorphous solid (194 mg, 0.26 mmol, 87%): R_f = 0.28 (20:1 CH_2Cl_2−CH_3OH); $[\alpha]_D$ −36.4 (*c* 0.11, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$/CD_3OD) δ 5.16 (dd, 1H, $J_{3',4'}$ = 9.2 Hz, H-3′), 5.02 (dd, 1H, $J_{4',5'}$ = 9.8 Hz, H-4′), 4.63 (q, 1H, *J* = 7.0 Hz, $CH_3CHCO_2CH_3$)), 4.56 (d, 1H, $J_{1',2'}$ = 8.4 Hz, H-1′), 4.50 (dd, 1H, $J_{6a,6b}$ = 11.9 Hz, H-6a), 4.37 (dd, 1H, $J_{6a',6b'}$ = 12.5 Hz, H-6a′), 4.24 (d, 1H, $J_{1,2}$ = 7.9 Hz, H-1), 4.06 (dd, 1H, H-6b′), 4.02 (dd, 1H, H-6b), 3.92 (dd, 1H, $J_{2',3'}$ = 10.5 Hz, H-2′), 3.75 (dd, 1H, $J_{4,5}$ = 8.7 Hz, H-4), 3.72 (s, 3H, $COOCH_3$), 3.69 (ddd, 1H, $J_{5',6a'}$ = 4.3 Hz, $J_{5',6b'}$ = 2.3 Hz, H-5′), 3.66 (dd, 1H, $J_{2,3}$ = 10.1 Hz, H-2), 3.54 (dd, 1H, $J_{3,4}$ = 8.4 Hz, H-3), 3.48 (ddd, 1H, $J_{5,6b}$ = 6.0 Hz, $J_{5,6a}$ = 2.3 Hz, H-5), 3.38 (s, 3H, OCH_3), 2.02 (s, 3H, $COCH_3$), 2.00 (s, 3H, $COCH_3$), 1.98 (s, 6H, $COCH_3$), 1.90 (s, 3H, $COCH_3$), 1.37 (d, 3H, *J* = 7.0 Hz, $CH_3CHCO_2CH_3$)), 1.20 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, $CDCl_3$/CD_3OD) δ 179.8, 176.3, 173.9, 173.5, 172.3, 171.9, 171.3, 103.6, 101.6, 79.5, 78.5, 76.7, 74.4, 73.8, 73.0, 70.0, 63.8, 63.8, 63.1, 40.1, 57.3, 56.0, 52.8, 52.8, 28.0, 23.7, 23.7, 23.3, 23.3, 21.3, 21.1, 19.4, 19.4; HRMS *m*/*z* calcd for $C_{32}H_{50}N_2O_{17}Na$ (M + Na^+) 757.3001, found 757.2996. Anal. Calcd for $C_{32}H_{50}N_2O_{17}$: C, 52.31; H, 6.86; N, 3.81. Found: C, 52.04; H, 6.87; N, 3.80.

Methyl 2-Acetamido-4-*O*-(2-acetamido-3,4,6-tri-*O*-acetyl-2-deoxy-β-D-glucopyranosyl)-3-*O*-[(*R*)-1-carboxyethyl]-2-deoxy-6-*O*-pivaloyl-β-D-glucopyranoside (30). Anhydrous lithium iodide (240 mg, 1.8 mmol) was added to a solution of compound **29** (120 mg, 0.16 mmol) in anhydrous pyridine (4 mL). The mixture was stirred at 100 °C for 3 days under argon and monitored by TLC. After the removal of pyridine, the residue was dissolved in a mixture of water/dichloromethane and acidified with 1 M HCl solution to pH 2. Extraction with dichloromethane and concentration of the extract gave a residue which was purified by silica gel chromatography using 5% methanol in dichloromethane containing 1% acetic acid to provide the desired compound **30** as a white amorphous solid (101 mg, 0.14 mmol, 85%): R_f = 0.36 (100:10:1 CH_2Cl_2−CH_3OH−AcOH); $[\alpha]_D$ −45.5 (*c* 0.67, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3OD) δ 5.28 (dd, 1H, $J_{3',4'}$ = 10.0 Hz, H-3′), 5.00 (dd, 1H, $J_{4',5'}$ = 9.8 Hz, H-4′), 4.74 (d, 1H, $J_{1',2'}$ = 8.4 Hz, H-1′), 4.61 (dd, 1H, $J_{6a,6b}$ = 12.0 Hz, H-6a), 4.56 (s, broad, 1H, $CH_3CHCO_2CH_3$), 4.39 (dd, 1H, $J_{6a',6b'}$ = 12.4 Hz, H-6a′), 4.28 (d, 1H, $J_{1,2}$ = 8.0 Hz, H-1), 4.12 (d, broad, H-6b′), 4.04 (dd, 1H, $J_{5,6b}$ = 6.2 Hz, H-6b), 3.81 (m, 3H, H-2′, H-2, H-4), 3.76 (ddd, 1H, $J_{5',6a'}$ = 4.0 Hz, $J_{5',6b'}$ = 2.2 Hz, H-5′), 3.61 (dd, H, $J_{2,3}$ = 9.0 Hz, H-3), 3.54 (m, 1H, H-5), 3.39 (s, 3H, OCH_3), 2.02 (s, 3H, $COCH_3$), 1.99 (s, 3H, $COCH_3$), 1.98 (s, 3H, $COCH_3$), 1.96 (s, 3H, $COCH_3$), 1.92 (s, 3H, $COCH_3$), 1.44 (d, 3H, *J* = 6.8 Hz, $CH_3CHCO_2CH_3$)), 1.23 (s, 9H, $C(CH_3)_3$); ^{13}C NMR (125 MHz, CD_3OD) δ 179.4, 173.7, 172.3, 171.8, 171.3, 103.6, 101.5, 79.9, 78.6, 74.4, 73.7, 73.0, 70.0, 63.7, 62.9, 56.9, 56.2, 56.2, 49.2, 39.9, 27.6, 23.2, 22.9, 20.7, 20.6, 20.5, 19.3; ESI HRMS *m*/*z* calcd for $C_{31}H_{48}N_2O_{17}Na$ 743.2845, found 743.2848.

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Supporting Information Available: ^{1}H and ^{13}C NMR scanned spectra are provided for compounds **2**−**30**. This material is available free of charge via the Internet at http://pubs.acs.org.

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