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PAPER

Stereoselective synthesis of protected 3-amino-3,6-dideoxyaminosugars†

Joaquim Nebot, Pedro Romea* and Fèlix Urpí*

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New syntheses of densely functionalized protected derivatives of 3-amino-3,6-dideoxyaminosugars have been accomplished in an efficient and straightforward manner. The key step of such approaches involves a highly stereoselective titanium-mediated aldol addition of a chiral α-bromo ketone, easily available from lactate esters, to crotonaldehyde. Further functional group transformations, including a new regioselective Staudinger–aza-Wittig reaction of an azidodiacetate, afford in a few steps and high yield the desired carbohydrates as advanced intermediates capable of participating in subsequent glycosylation reactions.

Introduction

The biological activity of a significant class of complex secondary metabolites synthesized by plants, fungi, and bacteria depends, in a large extent, on deoxyaminosugars moieties embedded in their structures.[1] This applies to well-known 14-membered-ring macrolides, such as erythromycin A, whose antibiotic properties are due to D-desosamine-ribosome hydrogen-bond interactions blocking the tunnel that channels the nascent peptides away from the peptidyl transferase center,[2] or to the vancomycin analogs containing modified deoxyaminosugars, which are specially effective against resistant bacteria because they interact directly with bacterial proteins involved in the transglycosylation step of the cell wall biosynthesis.[3] The specific character of these interactions is emphasized by the occasional presence of both enantiomers of some deoxyaminosugars in such metabolites, as occurs in the case mycosamine. Thereby, D-mycosamine is attached to the macrolactone ring of polyene macrolide antibiotics amphotericin B, nystatin, and pimaricin,[4] whereas L-mycosamine has been located in a family of antifungal macrolactams[5] (Fig. 1).

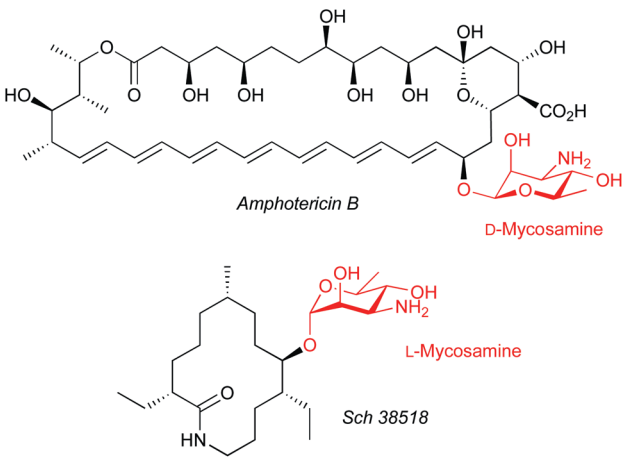

Fig. 1 Natural products containing D- and L-mycosamine

Despite the dramatic influence of the deoxyaminosugar moiety on the biological activity of these secondary metabolites,[1,6] the construction of the aglycon part and the development of increasingly efficient glycosylation methodologies have received more attention than the synthesis of the carbohydrate itself.[7] Thus, most of the synthetic approaches to suitably protected deoxyaminosugars rely on appropriate manipulations of readily available precursors like glucose.[8] These *chiron* approaches[9] have the advantage of being amenable to large scale preparations, but they often involve too many non-strategic steps and their efficiency becomes low. Instead, synthetic approaches rooted on stereoselective grounds usually improve ideality but often require more elaborate reagents and experimental conditions.[10] The synthesis of mycosamine can illustrate the pros and cons of both approaches. Indeed, Nicolaou reported the preparation of a protected mycosamine derivative from an easily available benzylideneglucopyranoside in fourteen steps and 29% overall yield,[11,12] whereas Franck–Neumann obtained a fully protected mycosamine aldehyde starting from an optically pure tricarbonyliron α-amino ketone and a chiral lactaldehyde in five steps and 54% yield.[13] Therefore, it would be highly desirable to design new synthetic sequences to gain access to such densely functionalized targets in a few steps using simple reagents and experimental procedures.[14,15]

In this context, we envisaged that stereoselective methodologies developed by our group might furnish protected L-3-amino-3,6-dideoxyaldohexoses **1** and **2** (Scheme 1) from structurally simple starting materials in a straightforward,

Departament de Química Orgànica, Universitat de Barcelona, Martí i Franqués 1–11, 08028 Barcelona, Catalonia, Spain.
E-mail: pedro.romea@ub.edu, felix.urpi@ub.edu

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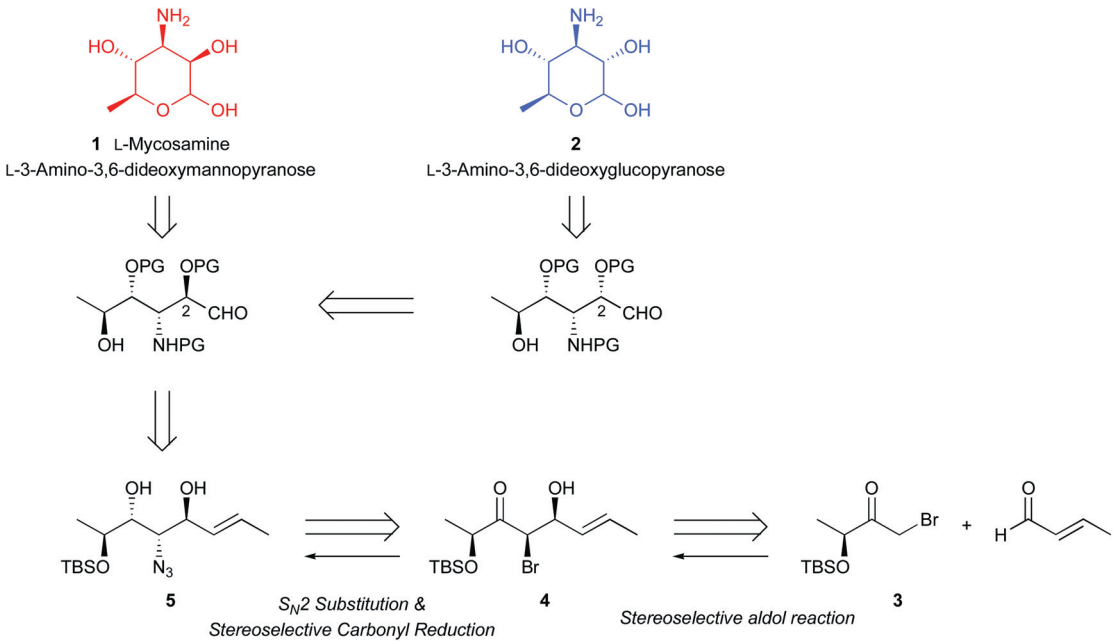


Scheme 1

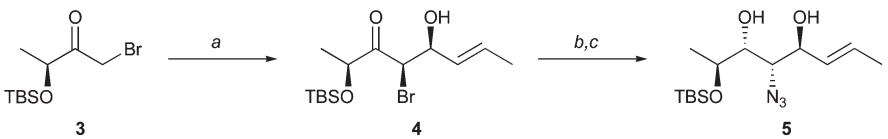
flexible, and efficient manner.[16] Our retrosynthetic analysis relies on a substrate-controlled reaction from chiral α-bromo ketone **3**, easily available in optically pure form from (*S*) lactate esters.[16b] As outlined in Scheme 1, we anticipated that highly diastereoselective titanium-mediated aldol addition of **3** to crotonaldehyde followed by displacement of bromine by a nitrogenated nucleophile and stereoselective reduction of the carbonyl group of aldol **4** would give an advanced intermediate **5** containing all the stereocenters. Then, functional group transformations and subsequent removal of silicon protecting group should render protected derivatives of L-mycosamine **1** in a straightforward manner. Moreover, this synthetic approach could also be used to prepare 3-amino-3,6-dideoxyglucopyranose **2**, a precursor of L-mycaminose,[17] provided that a suitable protecting group facilitated the epimerization of the C2 stereocenter. Herein, we describe our studies towards the stereoselective synthesis of protected L-3-amino-3,6-dideoxypyranose derivatives capable to be employed in the synthesis of metabolites possessing these deoxyaminosugars.

Results and discussion

Initial steps

Keeping in mind such an analysis, we first focused our attention on the synthesis of intermediate **5**. The key step of our approach was the substrate-controlled aldol reaction of α-bromo α′-silyloxy ketone **3** and crotonaldehyde, which would be followed by the displacement of the bromine by an azido group and the *anti*-reduction of the carbonyl group (Scheme 2). As expected, the titanium-mediated aldol addition of **3** to crotonaldehyde proceeded with a complete stereocontrol, providing *syn*-aldol **4** as a single diastereomer in 78% yield. This reaction proved to be highly reliable and afforded the desired *syn*-aldol **4** in near 80% yield at 10 mmol scale under very mild conditions. Having prepared the carbon backbone, we next assessed the introduction of an azide through displacement of the bromine atom in **4**. To our surprise, this apparently simple reaction was more complicated than expected because long reaction times or slight excesses of NaN_3 produced the epimerization of Cα in variable extents. Finally, it was found that stoichiometric amounts of NaN_3 in DMSO at room temperature furnished a mixture that could be submitted to the Evans–Chapman–Carreira conditions to afford azidopolyol **5** as a single diastereomer in 72% yield over two steps.[18] Thus, advanced intermediate **5** possessing all the stereocenters had been prepared in a straightforward manner from lactate-derived ketone **3** in three steps and 56% overall yield.

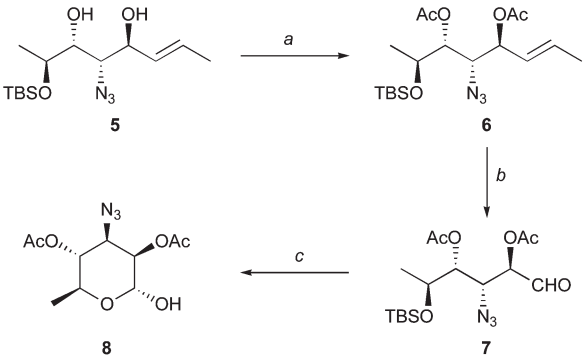
With azidopolyol **5** in hand, the conversion of the carbon–carbon double bond into the required aldehyde and the selective reduction of the azido group appeared as the most important hurdles to achieve the synthesis of the desired deoxyaminosugars. Thus, we envisioned different synthetic approaches depending on the way these reactions were orchestrated.



Scheme 2 Reagents and conditions: (*a*) (i) $TiCl_2(i\text{-}PrO)_2$, i-Pr_2NEt, CH_2Cl_2, −20 °C; (ii) Crotonaldehyde, −78 to −20 °C, 78%; (*b*) NaN_3, DMSO, rt; (*c*) $Me_4NHB(OAc)_3$, 1 : 1 CH_3CN–AcOH, −35 to −20 °C, 72% over two steps.

First approach to the synthesis of L-mycosamine

We began exploring the conversion of azidopolyol **5** into the corresponding aldehyde (Scheme 3). Initially, both hydroxyl groups in **5** were protected with acetic anhydride affording diester **6** in excellent yield. Then, the oxidation of the alkene was carried out quantitatively following the osmate-periodate procedure and the resultant sensitive aldehyde **7** was immediately treated with HF to remove the silicon protecting group, which delivered pure 2,4-di-*O*-acetyl-3-azido-3,6-dideoxy-α-L-mannopyranose **8** in 67% over two steps.[19]

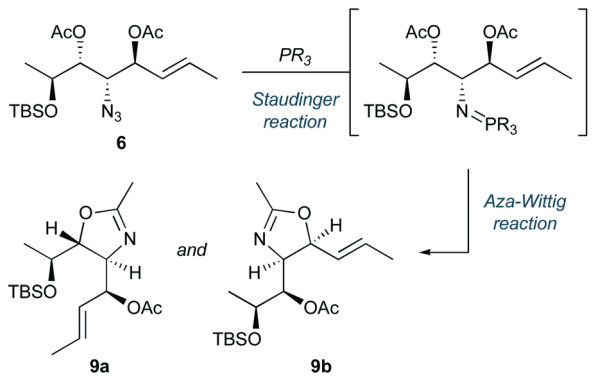


Scheme 3 Reagents and conditions: (*a*) Ac_2O, Et_3N, DMAP cat, CH_2Cl_2, rt, 97%; (*b*) $K_2OsO_4{\cdot}2H_2O$ (4 mol%), $NaIO_4$, 2,6-lutidine, 3 : 1 1,4-dioxane–H_2O, rt; (*c*) HF, CH_3CN, rt, 67% over two steps.

Thus, we had accomplished the stereoselective synthesis of the azido derivative of L-mycosamine **8** from α-bromo α′-silyloxy ketone **3** in six steps and 36% overall yield under very mild conditions. The success of this sequence led us to explore in depth the whole strategy and to assess other approaches in which the azide was reduced and protected before oxidizing the carbon–carbon double bond, as described below.

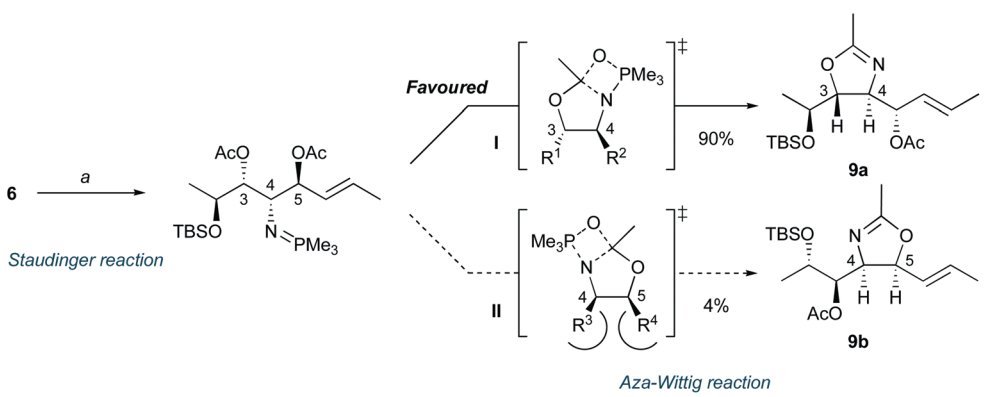
Second approach to the synthesis of L-mycosamine

Taking advantage of azidodiester **6**, we envisioned that the phosphine-mediated reduction of the azide followed by the attack of the resultant iminophosphorane to a neighboring acetate might produce an oxazoline (Scheme 4). This one-step transformation involving a Staudinger and an aza-Wittig reaction was particularly appealing because an acetate protecting group and the amino group could be masked in a single and stable heterocycle, which could deliver both functional groups at any stage of the synthetic sequence. Surprisingly, this sort of transformation is well documented for aldehydes and ketones but there are few reports involving less electrophilic esters.[20,21] We were also aware that the presence of two acetate groups flanking the azide introduced a serious problem of regioselectivity, since both esters were rather similar and the intramolecular aza-Wittig reaction could produce two oxazoline heterocycles **9a** and **9b** (Scheme 4). There were no precedents on such regioselective issues, so the lack of reactivity of the ester groups was compounded by the potential formation of two products. Nevertheless, we expected that any mixture of oxazoline isomers **9a** and **9b** could be carried ahead and furnish the desired carbohydrate.



Scheme 4

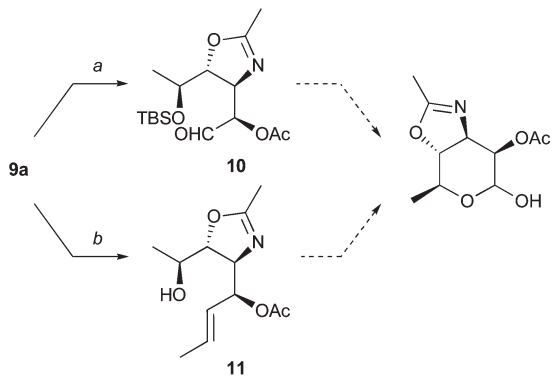
To our delight, simple treatment of **6** with PMe_3 under water-free conditions at room temperature provided oxazoline **9a** with an outstanding regioselectivity in excellent yield (Scheme 5). Indeed, ^1H NMR analysis of the reacting mixture uncovered the formation of **9a** : **9b** in a ratio greater than 20 : 1 and a further chromatographic purification afforded pure oxazolines **9a** and **9b** in 90% and 4% yield respectively. Thus, this transformation entailed the reduction of the azide and the selective addition of the putative iminophosphorane to the *syn*-acetate group at C3, likely as a result of the lower steric hindrance of eclipsed transition state **I** leading to **9a** (Scheme 5). This remarkable result not only proves that a Staudinger–aza-Wittig tandem reaction



Scheme 5 Reagents and conditions: (*a*) PMe_3, THF, rt, **9a** in 90%, **9b** in 4%.

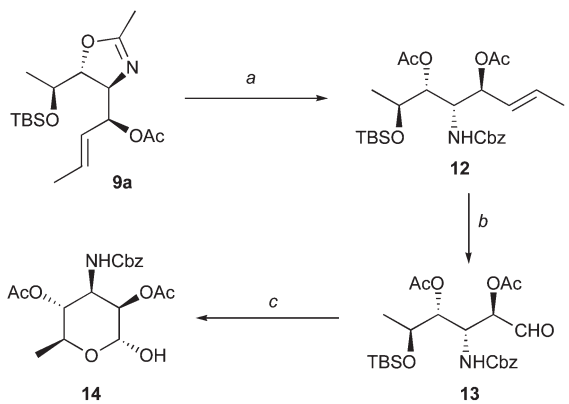
may be carried out on acyclic azidodiacetates under very mild conditions to afford the corresponding oxazolines in excellent yield but also in high regioselectivity favoring the *syn* neighboring acetate group.

With a reliable access to advanced intermediate **9a** on hand, we were ready to assess the conversion of the olefin into the aldehyde and the removal of the silicon protecting group (Scheme 6). Oxidation of the alkene using previously optimized conditions gave quantitatively aldehyde **10**, which was judged pure enough by ^{1}H NMR to be used in the next steps without further purification. Regrettably, all our attempts to remove the TBS group failed and we always obtained complex mixtures instead of the hemiacetal form of protected L-mycosamine. A change in the order of the later steps was also unsuccessful. Indeed, deprotection of silyl ether in oxazoline **9a** gave alcohol **11** in 94% yield, but further oxidation of the remaining alkene under a wide set of conditions only produced complex reaction mixtures.



Scheme 6 Reagents and conditions: (*a*) $K_2OsO_4{\cdot}2H_2O$ (4 mol%), $NaIO_4$, 2,6-lutidine, 3 : 1 1,4-dioxane–H_2O, rt, 95%; (*b*) TBAF, THF, rt, 94%.

Considering that the heterocyclic moiety might be responsible for these failures, oxazoline **9a** was opened with BnOCOCl to provide carbamate **12** in excellent yield (Scheme 7).[22] As expected, this substrate proved to be more suitable and oxidation

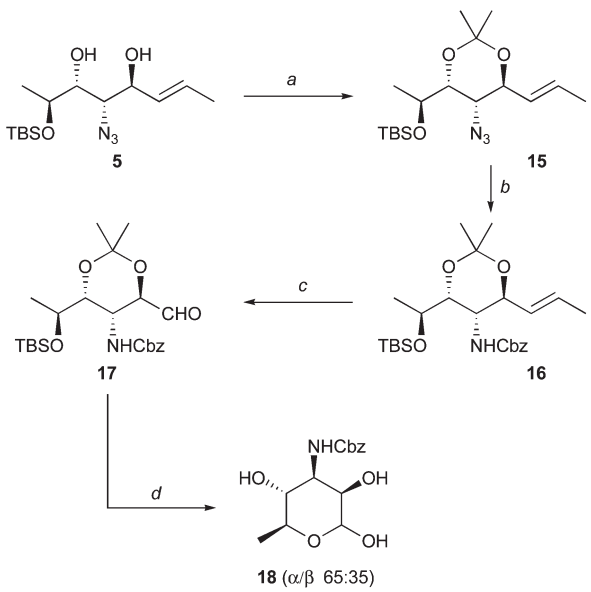


Scheme 7 Reagents and conditions: (*a*) BnOCOCl, Na_2CO_3, 1 : 1 CH_2Cl_2–H_2O, rt, 96%; (*b*) $K_2OsO_4{\cdot}2H_2O$ (4 mol%), $NaIO_4$, 2,6-lutidine, 3 : 1 1,4-dioxane–H_2O, rt; (*c*) HF, CH_3CN, rt.

of the alkene and removal of the silicon protecting group furnished fully protected L-mycosamine **14** under mild conditions. Unfortunately, ester protecting groups were not completely stable under these conditions, so both steps were not easily reproducible and the resulting deoxyaminosugar was contaminated by tiny amounts of unknown impurities.

This drawback led us to look for a more reliable protecting group strategy. Hence, isopropylidene acetal was chosen as the new protecting group for 1,3-diol **5** because it could be removed simultaneously to the TBS group avoiding undesired side reactions. Furthermore, such a cyclic protecting group might facilitate the epimerization of the C2 stereocenter and to provide the diastereomeric L-mycaminose-like deoxyaminosugar.

In accordance to this new design, azidopolyol **5** was readily converted into the isopropylidene acetal **15** (Scheme 8), which was used to confirm the relative configuration of the stereocenters embedded in the 1,3-dioxane ring by 1D and 2D NMR analyses.[18] Treatment of this azido derivative **15** with PMe_3 and hydrolysis of the resultant iminophosphorane in wet THF gave the desired primary amine, which was *in situ* protected as the corresponding Cbz carbamate **16** in 96% yield. Clean oxidation of **16** afforded aldehyde **17**, which was used in the next step without further purification. Finally, concurrent removal of the silicon and the isopropylidene protecting groups by HF provided a 65 : 35 α,β-mixture of *N*-benzyloxycarbonyl L-mycosamine **18** in 74% yield.[19]

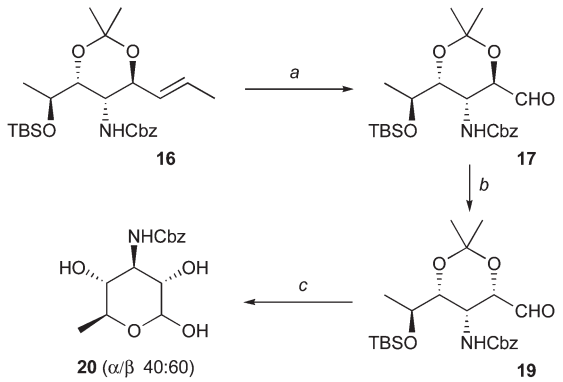


Scheme 8 Reagents and conditions: (*a*) $Me_2C(OMe)_2$, PPTS cat., CH_2Cl_2, rt, 89%; (*b*) (i) PMe_3, H_2O, THF, rt. (ii) BnOCOCl, $NaHCO_3$, MeOH, rt, 96%; (*c*) $K_2OsO_4{\cdot}2H_2O$ (4 mol%), $NaIO_4$, 2,6-lutidine, 3 : 1 1,4-dioxane–H_2O; (*d*) HF, CH_3CN, rt, 74% over two steps.

Thus, the synthetic sequence outlined in Scheme 8 represents a highly stereoselective and efficient approach to the synthesis of an *N*-protected L-mycosamine derivative from lactate-derived ketone **3** in seven steps and 36% yield. Furthermore, aldehyde **17** was a key intermediate to prepare a C2 epimer, that is a precursor of L-mycaminose.

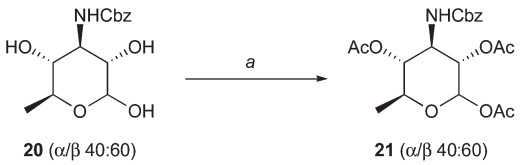
Synthesis of L-3-amino-3,6-dideoxyglucopyranose

The formyl group at 1,3-dioxane **17** adopting a twist-boat conformation was pivotal to promote the epimerization of C2 stereocenter by a mild base. Indeed, oxidation of fully protected aminopolyol **16** and simple stirring of **17** in the presence of sodium carbonate gave the more stable chairlike aldehyde **19** in 74% yield (Scheme 9). Then, simultaneous deprotection of the silyl ether and the isopropylidene acetal under the experimental conditions previously optimized afforded in 78% yield a 40 : 60 α,β-mixture of *N*-benzyloxycarbonyl L-3-amino-3,6-dideoxyglucopyranose **20**, a protected precursor of L-mycaminose.[17,19] Thus, the synthesis of deoxyaminosugar **20** has been completed in eight steps and a remarkable 28% overall yield from chiral ketone **3**. These figures together with those achieved in former cases prove that the strategy outlined in Scheme 1 is a powerful tool to synthesize 3-amino-3,6-dideoxyaminosugars in a highly stereoselective, efficient, and straightforward manner.



Scheme 9 Reagents and conditions: (*a*) $K_2OsO_4{\cdot}2H_2O$ (4 mol%), $NaIO_4$, 2,6-lutidine, 3 : 1 1,4-dioxane–H_2O; (*b*) Na_2CO_3, MeOH, rt, 74% over two steps; (*c*) HF, CH_3CN, rt, 78%.

Finally, treatment of **20** with acetic anhydride afforded polyacetylated deoxyaminosugar **21** as a 40 : 60 mixture of diastereomers (Scheme 10), whose ^1H and ^{13}C NMR peaks for the major anomer matched to the data reported in the literature for the β-1,2,4-tri-*O*-acetyl-3-amino-*N*-benzyloxycarbonyl-3,6-dideoxyglucopyranose.[23]



Scheme 10 Reagents and conditions: (*a*) Ac_2O, pyr, rt, 95%.

Conclusions

Several protected L-3-amino-3,6-dideoxyaminosugars have been prepared from an easily available lactate-derived ketone **3**. The kernel of our strategy lies on the titanium-mediated aldol reaction of such chiral ketone followed by the S_N2 substitution of the bromine and the substrate-controlled reduction of the carbonyl group. The introduction of the most important structural features by these highly reliable transformations and the appropriate orchestration of subsequent functional group modifications, including a new regioselective Staudinger–aza-Wittig reaction of an azidodiacetate, provide the aforementioned protected deoxyaminosugars in a fews steps and high overall yield. Hence, the synthesis of these carbohydrates, capable to be engaged in glysosylation reactions, has been accomplished in a highly stereoselective, efficient, and straightforward manner.

Experimental section

General methods

Specific rotations were determined at 20 °C on a Perkin-Elmer 241 MC polarimeter. IR spectra were recorded on either a Nicolet 6700 FT spectrometer and only the more representative frequencies (cm^{-1}) are reported. ^1H NMR (300 MHz) and ^{13}C NMR (75.4 MHz) spectra were recorded on a Unity-Plus 300 spectrometer. ^1H NMR (400 MHz) and ^{13}C NMR (100.6 MHz) spectra were recorded on a Varian-Mercury 400 spectrometer. ^1H NMR chemical shifts (δ) are quoted in ppm and referenced to internal TMS (δ 0) for $CDCl_3$, or referenced to solvent residual peak for CD_3OD (δ 3.31) and C_6D_6 (δ 7.16). Coupling constants (*J*) are quoted in Hz; data are reported as follows: s, singlet; d, doublet; t, triplet; q, quartet; quint, quintet; m, multiplet; br, broad. ^{13}C NMR chemical shifts (δ) are quoted in ppm and referenced to $CDCl_3$ (δ 77.0) and CD_3OD (δ 49.0). Where appropriate, 2D techniques were also used to assist in structure elucidation. High resolution mass spectra (HRMS) were obtained with a Agilent 1100 spectrometer by the Unitat d'Espectrometria de Masses, Centres Científics i Tecnològics, Universitat de Barcelona. Flash column chromatography was performed on SDS silica gel 60 (35–70 μm). Analytical thin-layer chromatography was carried out on Merck Kieselgel 60 F_{254} plates. All reactions were conducted in oven-dried glassware with anhydrous solvents. The solvents and reagents were purified and dried according to standard procedures.

(2*S*,4*R*,5*S*,6*E*)-4-Bromo-2-*tert*-butyldimethylsilyloxy-5-hydroxy-6-octen-3-one (4). Recently distilled $Ti(i\text{-}PrO)_4$ (1.66 mL, 5.6 mmol) was added to a solution of $TiCl_4$ (615 μL, 5.6 mmol) in CH_2Cl_2 (10 mL) at 0 °C under N_2. The resultant mixture was stirred for 10 min at 0 °C, diluted with CH_2Cl_2 (10 mL) and further stirred for 10 min at room temperature, which afforded an almost colorless solution. This $TiCl_2(i\text{-}PrO)_2$ solution in CH_2Cl_2 (11.2 mmol) was carefully added *via* cannula (+1 mL CH_2Cl_2) to a solution of **3** (2.87 g, 10.2 mmol) in CH_2Cl_2 (30 mL) at −78 °C under N_2, which developed a yellow-orange color. It was stirred for 3–4 min at −78 °C and i-Pr_2NEt (1.95 mL, 11.2 mmol) was added dropwise. The resultant mixture was stirred for 15 min at −78 °C and 1.5 h at −20 °C. Eventually, the color of the reaction mixture became dark orange. Then, it was cooled at −78 °C and recently distilled crotonaldehyde (1.26 mL, 15.3 mmol) was added dropwise. The mixture was stirred for 2 h at −78 °C and 1 h at −20 °C. The reaction was quenched by addition of sat NH_4Cl (50 mL). The mixture was diluted with Et_2O, washed with H_2O, sat $NaHCO_3$, and brine, and the aqueous layers were extracted with Et_2O. The organic extracts were dried and concentrated. Spectroscopic

analysis (^{1}H NMR) of the residue showed a single diastereomer of the expected aldol, which was purified by column chromatography (from hexanes–EtOAc 99 : 1 to 90 : 10) to afford 2.79 g (7.9 mmol, 78%) of **4** as a colorless oil. R_f = 0.25 (hexanes–EtOAc 90 : 10); $[\alpha]_D$ +63.2 (*c* 1.00, $CHCl_3$); IR (film): ν_{max} 3471, 2956, 2933, 2887, 2857, 1721, 1671, 1254, 1115 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (1H, dqd, *J* 15.3, *J* 6.6, *J* 1.1, CH=C*H*CH$_3$), 5.44 (1H, ddq, *J* 15.3, *J* 6.5, *J* 1.7, C*H*=CHCH$_3$), 4.82 (1H, d, *J* 6.1, C*H*Br), 4.49–4.44 (1H, m, C*H*OH), 4.31 (1H, q, *J* 6.9, C*H*OTBS), 1.71 (3H, ddd, *J* 6.6, *J* 1.7, *J* 0.9, CH=CHC*H*$_3$), 1.46 (3H, d, *J* 6.9, C*H*$_3$CHOTBS), 0.93 (9H, s, SiC(C*H*$_3$)$_3$), 0.11 (3H, s, SiC*H*$_3$), 0.09 (3H, s, SiC*H*$_3$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 206.9, 130.8, 128.2, 73.8, 71.3, 50.3, 25.7, 22.4, 18.0, 17.8, −4.6, −5.0; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{27}{}^{79}BrNaO_3Si$ $[M + Na]^+$ 373.0805, found 373.0798; calcd for $C_{14}H_{27}{}^{81}BrNaO_3Si$ $[M + Na]^+$ 375.0780, found 375.0779.

(2*S*,3*R*,4*S*,5*S*,6*E*)-4-Azido-2-*tert*-butyldimethylsilyloxy-6-octene-3,5-diol (5). A mixture of **4** (1.846 g, 5.25 mmol) and NaN_3 (358 mg, 5.5 mmol) in DMSO (20 mL) was stirred for 2 h at room temperature under N_2. It was diluted with Et_2O and washed with H_2O and brine. The aqueous layers were extracted with Et_2O and the combined organic extracts were dried and concentrated. Filtration of the residue through a short pad of silica (hexanes–EtOAc 90 : 10) afforded a yellow oil, which was used in the next step without further purification.

A solution of this oil in CH_3CN (20 + 2 mL) was carefully added to a mixture of $Me_4NHB(OAc)_3$ (11.16 g, 42.4 mmol) in 1 : 1 CH_3CN–AcOH (50 mL) at −35 °C under N_2 [the $Me_4NHB(OAc)_3$ solution had been previously stirred for 1 h at room temperature]. The stirring continued for 5 h and the reacting mixture was kept in the fridge (−20 °C) overnight. Then, it was stirred at 0 °C for 20 min, quenched by addition of 0.5 M solution of Rochelle salt (75 mL), and stirred for 1 h. It was diluted with CH_2Cl_2, washed with sat $NaHCO_3$, dried, and concentrated. The resultant residue was purified by column chromatography (from hexanes–EtOAc 98 : 2 to 80 : 20) affording 1.190 g (3.77 mmol, 72%) of **5** as a single diastereomer by ^{1}H NMR. Colorless oil. R_f = 0.25 (hexanes–EtOAc 80 : 20); $[\alpha]_D$ +41.6 (*c* 1.10, $CHCl_3$); IR (film): ν_{max} 3402, 2958, 2933, 2889, 2860, 2107, 1675, 1465, 1258, 1092 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (1H, dqd, *J* 15.3, *J* 6.5, *J* 1.1, CH=C*H*CH$_3$), 5.59 (1H, ddq, *J* 15.3, *J* 7.0, *J* 1.7, C*H*=CHCH$_3$), 4.41–4.37 (1H, m, C*H*OHCH=CH), 3.83 (1H, dq, *J* 7.0, *J* 6.1, C*H*OTBS), 3.67–3.62 (1H, m, TBSOCHC*H*OH), 3.58 (1H, dd, *J* 5.1, *J* 2.5, C*H*N$_3$), 2.53 (1H, br s, O*H*), 2.32 (1H, br s, O*H*), 1.76 (1H, br d, *J* 6.5, CH=CHC*H*$_3$), 1.23 (3H, d, *J* 6.1, C*H*$_3$CHOTBS), 0.89 (9H, s, SiC(C*H*$_3$)$_3$), 0.10 (3H, s, SiC*H*$_3$), 0.09 (3H, s, SiC*H*$_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 130.2, 129.9, 74.8, 73.7, 68.6, 64.6, 25.8, 19.7, 17.9 (×2), −4.1, −5.0; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{30}N_3O_3Si$ $[M + H]^+$ 316.2051, found 316.2048; calcd for $C_{14}H_{29}N_3NaO_3Si$ $[M + Na]^+$ 338.1870, found 338.1869.

(2*S*,3*R*,4*S*,5*S*,6*E*)-3,5-Di-*O*-acetyl-4-azido-2-*O*-*tert*-butyldimethylsilyl-6-octene-2,3,5-triol (6). A mixture of **5** (620 mg, 1.96 mmol), Ac_2O (0.75 mL, 8.0 mmol), Et_3N (2.2 mL, 15.8 mmol), and DMAP (25 mg, 0.2 mmol) in CH_2Cl_2 (30 mL) was stirred at room temperature for 45 min under N_2. It was diluted with Et_2O, washed with 1 M HCl, sat $NaHCO_3$, and brine. The organic layer was dried and concentrated and the resulting residue was purified by column chromatography (hexanes–EtOAc 90 : 10), affording 760 mg (1.90 mmol, 97%) of **6** as a colorless oil. R_f = 0.35 (hexanes–EtOAc 90 : 10); $[\alpha]_D$ +18.2 (*c* 1.00, $CHCl_3$); IR (film): ν_{max} 2932, 2858, 2103, 1753, 1372, 1232 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.95 (1H, dqd, *J* 15.3, *J* 6.6, *J* 0.7, CH=C*H*CH$_3$), 5.50 (1H, ddq, *J* 15.3, *J* 8.3, *J* 1.7, C*H*=CHCH$_3$), 5.30–5.23 (1H, m, AcOC*H*CH=CH), 4.95 (1H, dd, *J* 8.1, *J* 2.4, TBSOCH-C*H*OAc), 4.01 (1H, dq, *J* 8.1, *J* 6.2, C*H*OTBS), 3.71 (1H, dd, *J* 7.7, *J* 2.4, C*H*N$_3$), 2.07 (3H, s, C*H*$_3$CO$_2$), 2.05 (3H, s, C*H*$_3$CO$_2$), 1.75 (1H, dd, *J* 6.6, *J* 1.7, CH=CHC*H*$_3$), 1.13 (3H, d, *J* 6.2, C*H*$_3$CHOTBS), 0.90 (9H, s, SiC(C*H*$_3$)$_3$), 0.10 (6H, s, Si(C*H*$_3$)$_2$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.8, 169.7, 133.7, 125.8, 74.4, 72.9, 66.9, 61.9, 25.8, 21.1, 20.7, 20.0, 18.0, 17.9, −4.1, −5.0; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{34}N_3O_5Si$ $[M + H]^+$ 400.2262, found 400.2261.

2,4-Di-*O*-acetyl-3-azido-3,6-dideoxy-α-L-mannopyranose (8). A mixture of **6** (133 mg, 0.33 mmol), $K_2OsO_4{\cdot}2H_2O$ (5 mg, 4 mol %), $NaIO_4$ (285 mg, 1.33 mmol), and 2,6-lutidine (80 μL, 0.69 mmol) in 3 : 1 1,4-dioxane–H_2O (4 mL) was stirred at room temperature for 4 h, when a TLC analysis showed that the starting material had been consumed. It was diluted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the organic extracts were dried and concentrated.

The residue containing aldehyde **7** was treated with 0.5 M HF in CH_3CN (2.8 mL, 1.4 mmol) and the resulting brown solution was stirred for 4 h at room temperature. The reacting mixture was diluted with Et_2O, washed with sat $NaHCO_3$, and the aqueous layer was extracted with Et_2O twice. The organic extracts were dried and concentrated. The resulting brown oil was purified by column chromatography (from hexanes–EtOAc 95 : 5 to 50 : 50) to obtain 61 mg (0.22 mmol, 67% yield over two steps) of **8** as a colorless oil. R_f = 0.20 (hexanes–EtOAc 70 : 30); $[\alpha]_D$ −13.3 (*c* 0.60, $CHCl_3$); IR (film): ν_{max} 3434, 2929, 2110, 1755, 1374, 1223, 1049 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.20–5.15 (2H, m, HOC*H*C*H*OAc), 5.09 (1H, *pseudo* t, *J* ≈ 10.1, CH$_3$CHC*H*OAc), 4.07 (1H, dq, *J* 9.8, *J* 6.2, CH$_3$C*H*O), 3.86 (1H, dd, *J* 10.4, *J* 3.2, C*H*N$_3$), 3.00 (1H, br s, O*H*), 2.16 (3H, s, C*H*$_3$CO$_2$), 2.15 (3H, s, C*H*$_3$CO$_2$), 1.22 (3H, d, *J* 6.2, C*H*$_3$CHO); ^{1}H NMR (400 MHz, C_6D_6) δ 5.41 (1H, *pseudo* t, *J* ≈ 10.0, CH$_3$CHC*H*OAc), 5.21 (1H, dd, *J* 3.3, *J* 2.0, HOCHC*H*OAc), 4.86 (1H, br s, C*H*OH), 3.88 (1H, dq, *J* 9.8, *J* 6.3, CH$_3$C*H*O), 3.72 (1H, dd, *J* 10.4, *J* 3.3, C*H*N$_3$), 2.03 (1H, br s, O*H*), 1.67 (3H, s, C*H*$_3$CO$_2$), 1.61 (3H, s, C*H*$_3$CO$_2$), 1.17 (3H, d, *J* 6.3, C*H*$_3$CHO); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.1, 169.6, 91.4, 71.6, 71.4, 66.4, 58.3, 20.9, 20.8, 17.4; HRMS (ESI): *m*/*z* calcd for $C_{10}H_{15}N_3NaO_6$ $[M + Na]^+$ 296.0853, found 296.0852; calcd for $C_{10}H_{14}N_3O_5$ $[M - OH]^+$ 256.0927, found 256.0928.

(4*S*,5*R*)-4-((1*S*,2*E*)-1-Acetoxy-2-buten-1-yl)-5-((*S*)-1-*tert*-butyldimethylsilyloxyethyl)-2-methyl-2-oxazoline (9a). A 1 M solution of PMe_3 in THF (0.88 mL, 0.88 mmol) was added dropwise to a solution of **6** (321 mg, 0.80 mmol) in toluene (3 mL) at room temperature under N_2. A few minutes later, a gas began to evolve slowly and the stirring was kept for 45 min at room

temperature. The resulting mixture was diluted with CH_2Cl_2 and washed with brine. The aqueous layer was extracted with CH_2Cl_2 and the organic extracts were dried and concentrated. The resulting oil was purified by column chromatography (from hexanes–EtOAc 90 : 10 to 50 : 50) affording 257 mg (0.72 mmol, 90%) of **9a** and 11 mg (31 μmol, 4%) of a minor oxazoline isomer, **9b**.

9a: Colorless oil. R_f = 0.40 (hexanes–EtOAc 50 : 50); $[\alpha]_D$ −60.7 (*c* 0.95, $CHCl_3$); IR (film): ν_{max} 2931, 2858, 1748, 1679, 1374, 1235, 1021 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.80 (1H, dqd, *J* 15.3, *J* 6.6, *J* 0.8, CH═C*H*CH_3), 5.43 (1H, ddq, *J* 15.3, *J* 7.2, *J* 1.6, C*H*═$CHCH_3$), 5.22–5.18 (1H, m, AcOC*H*), 4.15 (1H, ddd, *J* 6.0, *J* 4.8, *J* 1.2, C*H*N), 4.06 (1H, dd, *J* 6.0, *J* 3.7, TBSOCHC*H*O), 3.92 (1H, qd, *J* 6.4, *J* 3.7, C*H*OTBS), 2.06 (3H, s, CH_3CO_2), 1.98 (3H, d, *J* 1.2, N═CCH_3), 1.72 (1H, ddd, *J* 6.6, *J* 1.6, *J* 0.4, CH═CHCH_3), 1.10 (3H, d, *J* 6.4, CH_3CHOTBS), 0.86 (9H, s, SiC(CH_3)$_3$), 0.06 (3H, s, SiCH_3), 0.04 (3H, s, SiCH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.0, 165.7, 131.4, 125.9, 84.9, 75.9, 69.4, 68.5, 25.6, 21.2, 19.1, 17.9, 17.9, 13.9, −4.5, −4.9; HRMS (ESI): *m*/*z* calcd for $C_{18}H_{34}NO_4Si$ $[M + H]^+$ 356.2252, found 356.2260; calcd for $C_{18}H_{33}NNaO_4Si$ $[M + Na]^+$ 378.2071, found 378.2070.

9b: Colorless oil. R_f = 0.45 (hexanes–EtOAc 50 : 50); $[\alpha]_D$ +64.3 (*c* 0.35, $CHCl_3$); IR (film): ν_{max} 2930, 2857, 1748, 1675, 1378, 1233, 1105 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.77 (1H, dqd, *J* 15.2, *J* 6.6, *J* 1.0, CH═C*H*CH_3), 5.41 (1H, ddq, *J* 15.2, *J* 7.9, *J* 1.7, C*H*═$CHCH_3$), 4.93–4.86 (1H, m, OC*H*CH═CH), 4.82 (1H, dd, *J* 7.9, *J* 2.8, C*H*OAc), 4.43–4.36 (1H, m, C*H*N), 4.06 (1H, dq, *J* 7.9, *J* 6.3, C*H*OTBS), 2.06 (3H, s, CH_3CO_2), 1.98 (3H, d, *J* 1.2, N═CCH_3), 1.72 (1H, ddd, *J* 6.6, *J* 1.6, *J* 0.7, CH═CHCH_3), 1.08 (3H, d, *J* 6.3, CH_3CHOTBS), 0.88 (9H, s, SiC(CH_3)$_3$), 0.10 (3H, s, SiCH_3), 0.08 (3H, s, SiCH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 170.2, 164.9, 130.9, 125.6, 82.1, 74.7, 67.8, 67.7, 25.8, 21.4, 19.9, 17.9, 17.9, 14.1, −4.3, −4.7; MS (CI): *m*/*z* (%) 356 $[M + H]^+$ (100).

(2*S*,3*R*,4*S*,5*S*,6*E*)-3,5-Di-*O*-acetyl-4-amino-*N*-benzyloxycarbonyl-2-*O*-(*tert*-butyldimethylsilyl)-6-octene-2,3,5-triol (12). A 5% Na_2CO_3 aq solution (5.2 mL, 2.5 mmol) was added to a solution of **9** (180 mg, 0.5 mmol) and BnOCOCl (120 μL, 0.8 mmol) in CH_2Cl_2 (5 mL) and the resulting mixture was stirred at room temperature overnight under N_2. It was diluted with Et_2O, washed with brine, and the aqueous layer was extracted with Et_2O. The organic extracts were dried and concentrated. The residue was purified by column chromatography (from hexanes–EtOAc 95 : 5 to 75 : 25), which furnished 248 mg (0.49 mmol, 96%) of **12** as a colorless oil. R_f = 0.35 (hexanes–EtOAc 90 : 10); $[\alpha]_D$ −3.4 (*c* 1.1, $CHCl_3$); IR (film): ν_{max} 3357, 2955, 2931, 2857, 1736, 1508, 1373, 1234, 1055 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38–7.31 (5H, m, Ar*H*), 5.78 (1H, dq, *J* 15.3, *J* 6.6, CH═C*H*CH_3), 5.48–5.40 (1H, m, C*H*═$CHCH_3$), 5.14 (1H, d, *J* 12.3, OC$H_a$$H_b$Ph), 5.12–5.02 (2H, m, AcOC*H*CH═CH and N*H*), 5.05 (1H, d, *J* 12.3, OC$H_a$$H_b$Ph), 4.97 (1H, dd, *J* 6.4, *J* 1.8, TBSOCHC*H*OAc), 4.29–4.22 (1H, m, C*H*NH), 3.91 (1H, quint, *J* 6.3, C*H*OTBS), 2.04 (3H, s, CH_3CO_2), 2.01 (3H, s, CH_3CO_2), 1.66 (1H, dd, *J* 6.6, *J* 1.2, CH═CHCH_3), 1.12 (3H, d, *J* 6.3, CH_3CHOTBS), 0.88 (9H, s, SiC(CH_3)$_3$), 0.04 (3H, s, SiCH_3), 0.03 (3H, s, SiCH_3); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 169.9, 169.5, 155.8, 136.4, 132.1, 128.5, 128.2, 125.8, 74.8, 73.6, 67.4, 66.9, 52.0, 25.7, 21.1, 20.9, 19.6, 17.9, 17.8, −4.3, −5.1; HRMS (ESI): *m*/*z* calcd for $C_{26}H_{42}NO_7Si$ $[M + H]^+$ 508.2725, found 508.2726; calcd for $C_{26}H_{41}NNaO_7Si$ $[M + Na]^+$ 530.2544, found 530.2542.

2,4-Di-*O*-acetyl-*N*-benzyloxycarbonyl-L-mycosamine (14). The same experimental procedure described for **8** was followed for this material, obtaining **14** slightly contaminated by an unknown impurity. R_f = 0.50 (hexanes–EtOAc 35 : 65); ^1H NMR (400 MHz, $CDCl_3$) δ 7.40–7.29 (5H, m, Ar*H*), 5.20 (1H, d, *J* 1.7, OC*H*OH), 5.14 (1H, d, *J* 12.3, OC$H_a$$H_b$Ph), 5.03 (1H, d, *J* 12.3, OC$H_a$$H_b$Ph), 5.00 (1H, dd, *J* 3.3, *J* 1.7, OCHOHC*H*OAc), 4.95 (1H, d, *J* 9.6, N*H*), 4.80 (1H, dd, *J* 10.6, *J* 9.9, CH_3CHC*H*OAc), 4.47–4.38 (1H, m, C*H*NH), 4.16 (1H, dq, *J* 9.7, *J* 6.2, CH_3C*H*O), 3.16 (1H, br s, O*H*), 2.14 (3H, s, CH_3CO_2), 1.94 (3H, s, CH_3CO_2), 1.18 (3H, d, *J* 6.2, CH_3CHO); ^1H NMR (75.4 MHz, $CDCl_3$) δ 171.1, 170.2, 155.7, 136.3, 128.5, 128.2, 91.0, 72.7, 72.2, 67.0, 66.2, 49.8, 21.0, 20.6, 17.5.

(2*S*,3*R*,4*S*,5*S*,6*E*)-4-Azido-2-*O*-*tert*-butyldimethylsilyl-3,5-*O*-isopropylidene-6-octene-2,3,5-triol (15). A solution of **5** (260 mg, 0.82 mmol) and a crystal of PPTS in 1 : 1 $Me_2C(OMe)_2$–CH_2Cl_2 (20 mL) was stirred at room temperature overnight under N_2. The mixture was concentrated and the resulting white solid was purified by column chromatography (CH_2Cl_2) affording 260 mg (0.73 mmol, 89%) of **15**. Colorless oil. R_f = 0.60 (CH_2Cl_2); $[\alpha]_D$ +66.5 (*c* 1.00, $CHCl_3$); IR (film): ν_{max} 2931, 2860, 2099, 1472, 1258, 1225, 1113 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.87 (1H, dqd, *J* 15.3, *J* 6.5, *J* 1.0, CH═C*H*CH_3), 5.61 (1H, ddq, *J* 15.3, *J* 7.1, *J* 1.7, C*H*═$CHCH_3$), 4.28–4.23 (1H, m, OC*H*CH═$CHCH_3$), 3.98 (1H, dq, *J* 8.8, *J* 6.0, C*H*OTBS), 3.58 (1H, dd, *J* 8.8, *J* 3.5, TBSOCHC*H*O), 3.48 (1H, dd, *J* 6.2, *J* 3.5, C*H*N_3), 1.76 (3H, ddd, *J* 6.5, *J* 1.7, *J* 0.8, CH═CHCH_3), 1.41 (3H, s, (CH_3)C(CH_3)), 1.35 (3H, s, (CH_3)C(CH_3)), 1.20 (3H, d, *J* 6.0, CH_3CHOTBS), 0.89 (9H, s, SiC(CH_3)$_3$), 0.11 (6H, s, Si(CH_3)$_2$); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ 130.1, 129.4, 101.2, 74.2, 73.8, 66.7, 62.9, 25.9, 24.5, 24.3, 20.9, 18.0, 17.9, −3.8, −5.0; HRMS (ESI): *m*/*z* calcd for $C_{17}H_{33}N_3NaO_3Si$ $[M + Na]^+$ 378.2183, found 378.2183.

(2*S*,3*R*,4*S*,5*S*,6*E*)-4-Amino-*N*-benzyloxycarbonyl-2-*O*-*tert*-butyldimethylsilyl-3,5-*O*-isopropylidene-6-octene-2,3,5-triol (16). A 1 M solution of PMe_3 in THF (0.26 mL, 0.26 mmol) was added dropwise to a solution of **15** (84 mg, 0.24 mmol) and H_2O (17 μL, 0.95 mmol) in THF (2 mL) at room temperature under N_2. The resulting mixture was stirred at room temperature for 36 h and the volatiles were removed *in vacuo* using toluene (3 × 4 mL).

Then, BnOCOCl (52 μL, 0.35 mmol) was slowly added to a mixture of the residue and $NaHCO_3$ (30 mg, 0.35 mmol) in MeOH (2.75 mL) at 0 °C under N_2. The resulting mixture was stirred at this temperature for 5 min and at room temperature for 1.5 h. It was partitioned with CH_2Cl_2 and brine and the aqueous layer was extracted with CH_2Cl_2. The organic extracts were dried and concentrated. The resulting oil was purified by column chromatography (from hexanes–EtOAc 98 : 2 to 90 : 10), to obtain 105 mg (0.23 mmol, 96%) of **16**. Colorless oil. R_f = 0.20 (hexanes–EtOAc 90 : 10); $[\alpha]_D$ −9.5 (*c* 0.60, $CHCl_3$); IR (film):

ν_{max} 3393, 3033, 2955, 2930, 2856, 1729, 1505, 1380, 1253, 1223 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36–7.30 (5H, m, Ar*H*), 5.92 (1H, d, *J* 8.4, N*H*), 5.77 (1H, dq, *J* 15.2, *J* 6.2, CH═C*H*CH_3), 5.72–5.63 (1H, m, C*H*═$CHCH_3$), 5.12 (1H, d, *J* 12.4, $PhCH_aH_bO$), 5.05 (1H, d, *J* 12.4, $PhCH_aH_bO$), 4.16–4.11 (1H, m, OC*H*CH═$CHCH_3$), 3.95–3.88 (2H, m, C*H*NH and C*H*OTBS), 3.71 (1H, dd, *J* 6.0, *J* 3.6, TBSOCHC*H*O), 1.72 (3H, d, *J* 6.2, CH═$CHCH_3$), 1.37 (3H, s, $(CH_3)C(CH_3)$), 1.36 (3H, s, $(CH_3)C(CH_3)$), 1.14 (3H, d, *J* 6.0, CH_3CHOTBS), 0.88 (9H, s, $SiC(CH_3)_3$), 0.04 (3H, s, $SiCH_3$), 0.03 (3H, s, $SiCH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 156.0, 136.7, 129.7, 128.4, 128.0, 127.9, 100.3, 76.1, 71.1, 68.2, 66.5, 51.8, 26.4, 25.8, 24.9, 20.0, 18.0, 17.9, −4.6, −5.1; HRMS (ESI): *m*/*z* calcd for $C_{25}H_{41}NNaO_5Si$ $[M + Na]^+$ 486.2646, found 486.2632.

***N*-Benzyloxycarbonyl-L-mycosamine (18).** A mixture of **16** (38 mg, 82 μmol), $K_2OsO_4{\cdot}2H_2O$ (1.5 mg, 4 mol%), $NaIO_4$ (70 mg, 0.33 mmol), and 2,6-lutidine (19 μL, 0.17 mmol) in 3 : 1 1,4-dioxane–H_2O (1 mL) was stirred at room temperature for 2 h, when a TLC analysis showed that the starting material had been consumed. It was diluted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the organic extracts were dried and concentrated. The resulting brown oil was used in the next step without further purification.

This residue was treated with 0.5 M HF in CH_3CN (1.2 mL, 0.6 mmol) and the resulting brown solution was stirred for 2.5 h at room temperature. The reacting mixture was diluted with Et_2O, washed with sat $NaHCO_3$, and the aqueous layer was extracted with EtOAc. The organic extracts were dried and concentrated. The resulting brown oil was purified by column chromatography (from CH_2Cl_2 to CH_2Cl_2–MeOH 90 : 10) to obtain 18 mg (60 μmol, 74% yield over two steps) of **18** as a 65 : 35 mixture of α- and β-anomers according to its ^1H NMR. R_f = 0.20 (CH_2Cl_2–MeOH 90 : 10); IR (KBr): ν_{max} 3440, 3320, 2966, 2912, 1689, 1544, 1264, 1076, 1048 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ for **α-18** 7.40–7.26 (5H, m, Ar*H*), 5.09 (2H, s, OCH_2Ph), 4.96 (1H, d, *J* 1.2, OC*H*OH), 3.93–3.88 (1H, m, CH_3CHO), 3.93 (1H, dd, *J* 10.4, *J* 3.2, C*H*N), 3.78–3.75 (1H, m, OCHOHC*H*OH), 3.36–3.24 (2H, m, $CH_3CHCHOH$), 1.25 (3H, d, *J* 6.4, CH_3); ^1H NMR (400 MHz, CD_3OD) δ for **β-18** 7.40–7.26 (5H, m, Ar*H*), 5.09 (2H, s, OCH_2Ph), 4.76 (1H, s, OC*H*OH), 3.78–3.75 (1H, m, OCHOHC*H*OH), 3.60 (1H, dd, *J* 10.0, *J* 3.2, C*H*N), 3.36–3.24 (2H, m, $CH_3CHCHOH$), 1.29 (3H, d, *J* 6.0, CH_3); ^{13}C NMR (75.4 MHz, CD_3OD) δ for **α-18** 158.8, 138.3, 129.4, 128.9, 95.4, 72.4, 72.0, 69.7, 67.5, 55.0, 18.3; ^{13}C NMR (75.4 MHz, CD_3OD) δ for **β-18** 95.6, 74.7, 71.8, 58.3, 54.8; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{20}NO_6$ $[M + H]^+$ 298.1285, found 298.1299; calcd for $C_{14}H_{19}NNaO_6$ $[M + Na]^+$ 320.1104, found 320.1104.

(2*S*,3*R*,4*R*,5*S*)-3-Amino-*N*-benzyloxycarbonyl-5-*O*-*tert*-butyldimethylsilyl-2,4-dihydroxy-2,4-*O*-isopropylidenehexanal (19). A mixture of **16** (230 mg, 0.5 mmol), $K_2OsO_4{\cdot}2H_2O$ (8.3 mg, 4 mol%), $NaIO_4$ (430 mg, 2.0 mmol), and 2,6-lutidine (120 μL, 1.0 mmol) in 3 : 1 1,4-dioxane–H_2O (6 mL) was stirred at room temperature for 2 h, when a TLC analysis showed that the starting material had been consumed. It was diluted with Et_2O and washed with H_2O. The aqueous layer was extracted with Et_2O and the organic extracts were dried and concentrated. The resulting brown oil was used in the next step without further purification.

A mixture of this residue and Na_2CO_3 (530 mg, 5.0 mmol) in MeOH (15 mL) was stirred at room temperature under N_2 for 36 h. The reaction mixture was partitioned with CH_2Cl_2 and brine and the aqueous layer was extracted twice with CH_2Cl_2. The organic extracts were dried and concentrated. The resultant oil was purified by column chromatography (from hexanes–EtOAc 95 : 5 to 70 : 30) affording 165 mg (0.36 mmol, 74% yield over two steps) of **19**. Colorless oil. R_f = 0.25 (hexanes–EtOAc 70 : 30); $[\alpha]_D$ +68.1 (*c* 0.65, $CHCl_3$); IR (film): ν_{max} 3366, 2955, 2930, 2896, 2856, 1741, 1724, 1506, 1471, 1259, 1207, 1122, 1097 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 9.59 (1H, s, C*H*O), 7.40–7.30 (5H, m, Ar*H*), 5.39 (1H, d, *J* 9.3, N*H*), 5.07 (1H, d, *J* 12.2, $PhCH_aH_bO$), 5.00 (1H, d, *J* 12.2, $PhCH_aH_bO$), 4.45 (1H, d, *J* 1.7, C*H*CHO), 4.37 (1H, dt, *J* 9.3, *J* 1.7, C*H*NH), 3.79 (1H, dq, *J* 7.6, *J* 6.1, C*H*OTBS), 3.66 (1H, dd, *J* 7.6, *J* 1.7, TBSOCHC*H*O), 1.51 (3H, s, $(CH_3)C(CH_3)$), 1.46 (3H, s, $(CH_3)C(CH_3)$), 1.17 (3H, d, *J* 6.1, CH_3CHOTBS), 0.88 (9H, s, $SiC(CH_3)_3$), 0.03 (3H, s, $SiCH_3$), 0.00 (3H, s, $SiCH_3$); ^{13}C NMR (75.4 MHz, $CDCl_3$) δ 196.2, 155.8, 136.1, 128.5, 128.3, 128.2, 100.2, 79.0, 75.9, 67.1, 66.6, 45.3, 29.3, 25.9, 20.2, 18.9, 17.9, −4.2, −5.1; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{38}NO_6Si$ $[M + H]^+$ 452.2463, found 452.2470.

3-Amino-*N*-benzyloxycarbonyl-3,6-dideoxy-L-glucopyranose (20). A 0.5 M solution of HF in CH_3CN (1.1 mL, 0.55 mmol) was added to **19** (35 mg, 77 μmol) and the resulting mixture was stirred for 6 h at room temperature under N_2. It was diluted with a 70 : 30 mixture of sat brine–$NaHCO_3$ (25 mL) and extracted with EtOAc (6 × 25 mL). The organic layers were dried and concentrated and the resultant oil was purified by column chromatography (from CH_2Cl_2 to CH_2Cl_2–MeOH 90 : 10), which allowed to isolate 18 mg (60 μmol, 78%) of **20** as a 40 : 60 mixture of α- and β-anomers according to its ^1H NMR. R_f = 0.20 (CH_2Cl_2–MeOH 90 : 10); IR (KBr): ν_{max} 3348, 2931, 1690, 1558, 1313, 1285, 1252, 1063 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ for **α-20** 7.40–7.25 (5H, m, Ar*H*), 5.10 (2H, s, OCH_2Ph), 5.04 (1H, d, *J* 3.7, OC*H*OH), 3.91 (1H, dq, *J* 9.5, *J* 6.3, CH_3CHO), 3.80–3.72 (1H, m, C*H*NHCbz), 3.49–3.41 (1H, m, OCHOHC*H*OH), 3.05–2.98 (1H, m, OCH(CH_3)C*H*OH), 1.21 (3H, d, *J* 6.3, CH_3); ^1H NMR (400 MHz, CD_3OD) δ for **β-20** 7.40–7.25 (5H, m, Ar*H*), 5.10 (2H, s, OCH_2Ph), 4.50 (1H, d, *J* 7.6, OC*H*OH), 3.49–3.41 (1H, m, C*H*N), 3.39 (1H, dq, *J* 9.3, *J* 6.2, CH_3CHO), 3.19 (1H, dd, *J* 10.2, *J* 7.6, OCHOHC*H*OH), 3.09–3.02 (1H, m, OCH(CH_3)C*H*OH), 1.27 (3H, d, *J* 6.2, CH_3); ^{13}C NMR (100.6 MHz, CD_3OD) δ for **α-20** 93.5, 75.8, 72.4, 68.8, 57.5; ^{13}C NMR (100.6 MHz, CD_3OD) δ for **β-20** 159.7, 159.6, 138.4, 129.4, 128.9, 98.7, 75.5, 74.7, 74.5, 67.5, 61.0, 18.3; HRMS (ESI): *m*/*z* calcd for $C_{14}H_{19}NNaO_6$ $[M + Na]^+$ 320.1104, found 320.1104.

Acylation of 20. A solution of **20** (8.0 mg, 27 μmol) and Ac_2O (105 μL, 1.1 mmol) in pyridine (18 μL, 0.22 mmol) in a small vial under N_2 was stirred at room temperature for one day. The reacting mixture was diluted with water (20 mL) and extracted with EtOAc (3 × 20 mL). The organic extracts were washed with brine, dried, and concentrated. The resultant oil was purified by column chromatography (from hexanes–EtOAc

95 : 5 to 65 : 35) affording 11.0 mg (26 μmol, 95%) of 1,2,4-tri-*O*-acetyl-3-amino-*N*-benzyloxycarbonyl-3,6-dideoxy-L-glucopyranose (**21**) as a 40 : 60 mixture of α- and β-anomers according to its ^{1}H NMR. White solid. R_f = 0.25 (hexanes–EtOAc 65 : 35); IR (KBr): ν_{max} 3351, 3035, 2984, 2940, 1747, 1705, 1537, 1376, 1224, 1048 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ for **α-21** 7.39–7.25 (5H, m, ArH), 6.19 (1H, d, *J* 3.5, OC*H*OAc), 5.20–5.00 (2H, m, OCH_2Ph), 4.94 (1H, dd, *J* 11.1, *J* 3.5, OCHOAcC*H*OAc), 4.80–4.75 (1H, m, N*H*), 4.65 (1H, t, *J* 10.2, OCH(CH_3)C*H*OAc), 4.28 (1H, *pseudo* q, *J* 10.6, C*H*N), 4.06–3.95 (1H, m, CH_3C*H*O), 2.16 (3H, s, CH_3CO_2), 1.93 (3H, s, CH_3CO_2), 1.92 (3H, s, CH_3CO_2), 1.17 (3H, d, *J* 6.3, CH_3CHO); ^{1}H NMR (400 MHz, $CDCl_3$) δ for **β-21** 7.39–7.25 (5H, m, Ar*H*), 5.70 (1H, d, *J* 8.4, OC*H*OAc), 5.20–5.00 (2H, m, OCH_2Ph), 4.90–4.82 (1H, m, N*H*), 4.89 (1H, dd, *J* 10.6, *J* 8.4, OCHOAcC*H*OAc), 4.63 (1H, t, *J* 10.0, OCH(CH_3)C*H*OAc), 4.06–3.95 (1H, m, C*H*N), 3.73 (1H, dq, *J* 9.5, *J* 6.3, CH_3C*H*O), 2.09 (3H, s, CH_3CO_2), 1.93 (6H, s, CH_3CO_2), 1.22 (3H, d, *J* 6.3, CH_3CHO); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ for **α-21** 89.0, 69.6, 68.4, 52.2, 17.4; ^{13}C NMR (100.6 MHz, $CDCl_3$) δ for **β-21** 170.4, 170.1, 169.1, 169.0, 156.3, 156.1, 136.4, 136.4, 128.5, 128.1, 128.1, 128.0, 92.0, 73.5, 73.2, 72.0, 70.7, 66.8, 55.8, 20.9, 20.8, 20.5, 20.4, 17.3; HRMS (ESI): *m*/*z* calcd for $C_{20}H_{25}NNaO_9$ $[M + Na]^+$ 446.1422, found 446.1412; calcd for $C_{20}H_{29}N_2O_9$ $[M + NH_4]^+$ 441.1867, found 441.1863.

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