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N-Hydroxyethyl-piperidine and -Pyrrolidine Homoazasugars: Preparation and Evaluation of Glycosidase Inhibitory Activity

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Abstract—An efficient and practical strategy for the synthesis of *N*-hydroxyethyl-1-deoxy-homonojirimycins **4** and **5** and *N*-hydroxyethyl-pyrrolidine homoazasugars **6** and **7** with full stereocontrol is being reported. The key step involved is the intermolecular Michael addition of benzylamine to D-glucose derived α,β-unsaturated ester **8** followed by *N*-alkylation with ethyl bromoacetate. Reduction with LAH, acetylation, hydrogenation and protection with -Cbz group afforded compounds **14a** and **14b**. Removal of 1,2-acetonide functionality, hydrogenation and deacetylation afforded *N*-hydroxyethyl-D-gluco-1-deoxyhomonojirimycin (**4**) and *N*-hydroxyethyl-L-ido-1-deoxyhomonojirimycin (**5**), respectively. Compounds **14a** and **14b** on acetylation followed by removal of 1,2-acetonide functionality, sodium metaperiodate oxidation, hydrogenation and deacetylation gave 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-D-arabino-hexitol (**6**) and 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-L-xylo-hexitol (**7**), respectively. The glycosidase inhibition activity of compounds **4**, **5**, **6**, **7**, **16a** and **16b** was evaluated using sweet almond seed as a rich source of different glycosidases.

Introduction

The discovery of polyhydroxylated piperidine[1] and pyrrolidine[2] alkaloids such as nojirimycin **1**, 1-deoxy-nojirimycin (DNJ) **1a** and 2,5-dihydroxymethyl-3,4-dihydroxy-pyrrolidine (DMDP) **3** (Fig. 1) manifests the spectacular development of azasugars (or imino-sugars) and has opened a dynamic research field at the interface between glycobiology and organic chemistry due to their action as glycosidases inhibitors. In recent years, the scope of biological activities has been extended to the inhibition of glycosyltransferases,[3] of glycogen[3] and nucleoside[4] phosphorylases and of sugar nucleotide mutase (UDP-Gal*p* mutase).[5] These properties led to a new generation of azasugar-based medicines in a wide range of diseases such as viral infections,[6] diabetes,[7] and tumor metastasis.[8] In this respect, *N*-alkylated aza-sugars were demonstrated to be stronger glycosidase inhibitors than the corresponding non-alkylated derivatives.[9] For example, *N*-alkylation of DNJ induces a shift in specific inhibition of purified glucosidases from α-glucosidase II to α-glucosidase I and may be useful against hepatitis B virus (HBV).[10] In cell culture, *N*-alkylated derivatives are also more effective inhibitors of glucosidase I than is the parent compound **1a**.[11] More therapeutic applications of *N*-alkylated DNJ are being uncovered. For example, *N*-butyl-1-deoxy-

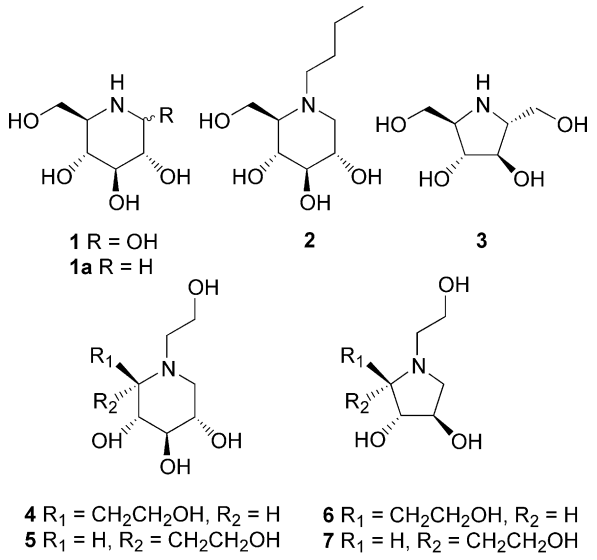

Figure 1.

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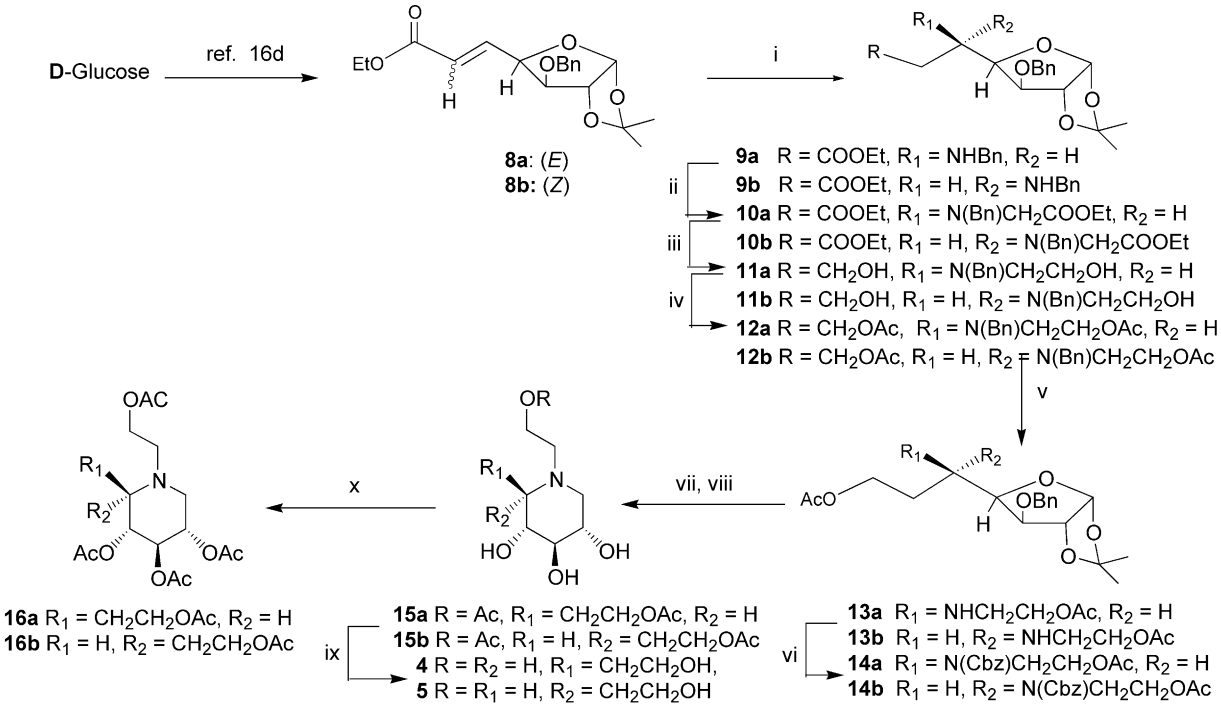
nojirimycin **2** (Fig. 1) was identified as the most active anti-HIV agent without significant cytotoxicity[12] and also active against Gaucher disease, a severe lysosomal storage disorder.[13] Amongst *N*-alkylated derivatives, *N*-hydroxyethyl-1-deoxynojirimycin was found to be a potent sucrase inhibitor.[14] In general, the synthetic routes to *N*-alkylated derivatives make use of azasugar itself as a substrate and reductive amination with a suitable alkyl aldehyde using sodium cyanoborohydride or catalytic hydrogenation or sodium bicarbonate in methanol-dioxane.[9,15] In view of the high potential of *N*-alkylated azasugars and as a part of our continuing interest in the synthesis of azasugars,[16] we report herein a practical approach for the synthesis of hitherto unknown *N*-hydroxyethyl-D-gluco-1-deoxyhomonojirimycin (**4**), *N*-hydroxyethyl-L-ido-1-deoxy-homonojirimycin (**5**) and pyrrolidine alkaloids such as 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-D-arabino-hexitol (**6**) and 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-L-xylo-hexitol (**7**).

Results and Discussion

Synthesis of *N*-hydroxyethyl-D-gluco-1-deoxyhomonojirimycin 4 and *N*-hydroxyethyl-L-ido-1-deoxyhomonojirimycin 5

D-Glucose was converted to a geometrical mixture (*E* and *Z*) of α,β-unsaturated esters **8a** and **8b**, respectively, by our earlier procedure.[16c,d] The conjugate addition of *N*-benzylamine with **8** at 25 °C afforded a diastereomeric mixture of β-amino esters **9a** (D-gluco) and **9b** (L-ido) in the ratio 3:7. The stereocontrolled formation of prochiral C-5 centre was achieved by the reaction of lithium *N*-benzylamide with a mixture (*E*+*Z*) of **8** in THF at −40 °C for 2 h, which afforded **9b** (L-ido) as the only isolable diastereomer in 85% yield.[17] Having both the sugar β-amino esters in hand, we have attempted the *N*-alkylation with ethyl bromoacetate using different bases like NaH, KO^{t}Bu, pyridine under a variety of reaction conditions. However, better result was obtained by the reaction of **9a** with ethyl bromoacetate, in the presence of potassium carbonate in DMF at room temperature for 30 h, to give **10a** in 71% yield (Scheme 1). Reduction of both the carbethoxy groups in **10a** by LAH gave the β-amino alcohol **11a,** which on acetylation afforded the diacetate **12a** in good yield. Removal of *N*- and *O*-benzyl groups in **12a** by hydrogenolysis (10% Pd/C, methanol) gave **13a**, that on selective *N*-benzyloxycarbonyl protection gave the *N*-Cbz derivative **14a**.[18,19] Opening of the 1,2-*O*-isopropylidene functionality in **14a** with TFA-water gave hemiacetal which was directly treated with 10% Pd/C and ammonium formate in methanol under reflux to afford diacetate **15a**, wherein removal of *N*-Cbz group produce primary amine that concomitantly undergoes cyclic imine formation and gets reduced to afford piperidine ring skeleton. Deacetylation of **15a** with sodium methoxide in methanol at 0 °C afforded the *N*-hydroxyethyl-D-gluco-1-deoxyhomonojirimycin **4**. Compound **4** on reaction with acetic anhydride in pyridine at room temperature gave pentaacetate derivative **16a**. The ^{1}H and ^{13}C NMR data was in accordance with the structures **4** and **16a**.

The same sequence of reactions was repeated with **9b** and compounds **10b**, **11b**, **12b**, **13b** and **14b** were isolated in good yield. Treatment of **14b** with TFA–water

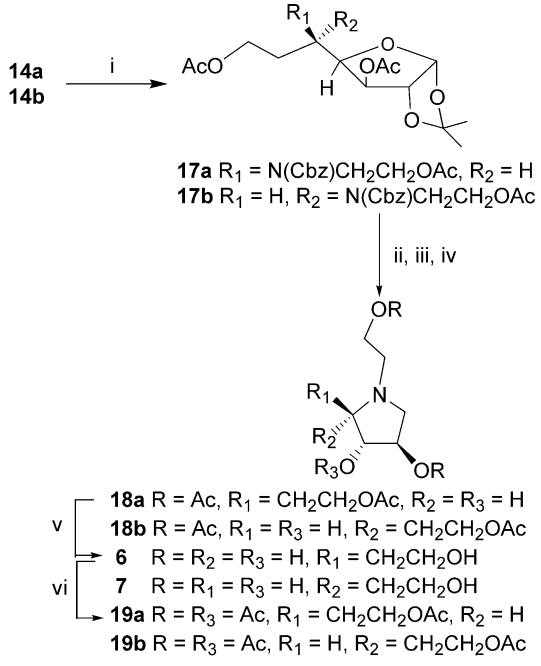


Scheme 1. *Reagents and conditions:* (i) $BnNH_2$, rt 20 h; (ii) $BrCH_2COOEt$, K_2CO_3, DMF, rt, 24–30 h; (iii) LAH, THF, 0 °C, 2 h; (iv) Ac_2O, Py, 0–25 °C, 40 h; (v) 10% Pd/C, H_2, 80 psi, MeOH, 12 h; (vi) CbzCl, $NaHCO_3$, EtOH–H_2O (8:2), 0 °C–rt, 4 h; (vii) TFA–H_2O (3:2), 0–30 °C, 3 h; (viii) 10% Pd/C, $HCOONH_4$, MeOH, reflux, 45 min; (xi) NaOMe, MeOH, 0–30 °C, 2 h; (x) Ac_2O, Py, 0–30 °C, 12 h.

and hydrogenation with 10% Pd/C, ammonium formate gave diacetate **15b** which on deacetylation afforded the *N*-hydroxyethyl-L-ido-1-deoxyhomonojirimycin **5**. The structure **5** was confirmed by converting it into pentaacetate derivative **16b**, which was characterized by spectral and analytical methods.

Synthesis of 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-D-arabino-hexitol (6) and 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-L-xylo-hexitol (7)

The compounds **14a** and **14b** were found to be promising intermediates for the synthesis of five member pyrrolidine homoazasugars **6** and **7**. Thus, acetylation of 3-OH in **14a** with acetic anhydride in pyridine afforded triacetate **17a** as semi solid in 94% yield (Scheme 2). Deprotection of the acetonide functionality in **17a** with TFA-water followed by sodium metaperiodate oxidation gave amino-aldehyde (with one carbon atom less), which was directly subjected to hydrogenation with 10% Pd/C and ammonium formate in methanol to give triacetylated pyrrolidine derivative **18a**. Deacetylation of **18a** with sodium methoxide in methanol afforded 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-D-arabino-hexitol (**6**). Similarly, **14b** on acetylation gave the triacetate **17b**, which on treatment with TFA-water, sodium metaperiodate and hydrogenation yielded pyrrolidine derivative **18b**. Deacetylation of **18b** with sodium methoxide in methanol gave 1,4,5-trideoxy-1,4-imino-*N*-hydroxyethyl-L-xylo-hexitol (**7**). The structures **6** and **7** were confirmed by converting them into tetraacetate derivatives **19a** and **19b,** respectively, which were characterized by spectral and analytical methods.



Scheme 2. *Reagents and conditions:* (i) Ac_2O, Py, 0–25 °C, 3 h; (ii) TFA–H_2O (3:2), 30 °C, 3 h; (iii) $NaIO_4$, acetone–H_2O, 0 °C–rt, 3 h; (iv) 10% Pd/C, $HCOONH_4$, MeOH, reflux, 45 min; (v) NaOMe, MeOH, 0–30 °C, 1.5 h; (vi) Ac_2O, Py, 0–30 °C, 12 h.

Conformational assignment of 4 and 5

Nojirimycin **1** and 1-deoxynojirimycin **1a** are known to exist in $^4C_1$ conformation. However, in case of compounds **4** and **5** the presence of $-CH_2CH_2OH$ groups, on adjacent atoms, increases the bulk in the molecule. Therefore, it was thought to derive the conformations of **4** and **5** using ^1H NMR spectral data. The coupling constants determined from the 300 MHz ^1H NMR spectra and decoupling experiments in D_2O of **4** and **5** are shown in Table 1. In case of **4**, appearance of two distinct doublet of doublets for 1-Ha at δ 2.20 ($J_{1a,1e}=11.8$ and $J_{1a,2}=9.7$ Hz) and for 1-He at δ 2.94 ($J_{1e,1a}=11.8$ and $J_{1e,2}=4.4$ Hz) were informative. The large coupling constant ($J_{1a,2}=9.7$ Hz) for the 1-H axial proton requires *trans*-diaxial relationship with 2-H proton. This clearly requires 2-H proton to be axial. In one step earlier compound **14a**, the relative stereochemistry of the substituents at C-2, C-3 and C-3, C-4 is *trans* and the same stereochemistry is retained in the product formation. In addition, the *trans* diaxial disposition of 4-H and 5-H protons was evident from the larger coupling constant ($J_{4,5}=9.2$ Hz). This confirms that compound **4** exists in $^4C_1$ conformation with C-5 substituent ($-CH_2CH_2OH$) equatorially oriented [(5*R*) configuration].

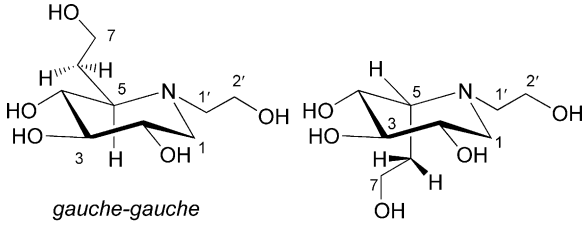
Since the ^1H NMR spectrum of **5** is very different from **4**, it was thought that **5** could exist in different conformation. However, the appearance of one triplet at δ 3.24 for 3-H with large coupling constants ($J_{3,4}=J_{2,3}=9.1$ Hz) indicated *trans*-diaxial relationship with adjacent protons. In addition, 1-Ha appeared as doublet of doublet at δ 2.34 ($J_{1a,1e}=12.2$ and $J_{1a,2}=9.9$ Hz), wherein the large coupling constant $J_{1a,2}=9.9$ Hz requires *trans*-diaxial relation with 2-H proton. This is clear indicative of the fact that compound **5** exist in $^4C_1$ conformation. The small coupling constant between 4-H and 5-H ($J_{4,5}=4.9$ Hz) clearly requires 5-H proton to be equatorial and suggestive of the fact that $-CH_2CH_2OH$ substituent at C-5 is axial with (5*S*) configuration.

In case of *N*-butyl-1-deoxynojirimycin (**2**) various rotamer populations about C-5–C-6 bond were proposed,[9a,b,20] which were estimated by the $J_{5,6a}$ and $J_{5,6b}$ coupling constants. In compounds **4** and **5**, where hydroxyethyl group is present instead of hydroxymethyl group at the C-5 position, the coupling constants $J_{5,6a}=J_{5,6b}=\sim 2.6$ Hz suggest a large population of the *gauche–gauche* rotamer for **4** as shown in Figure 2. This could be explained on the basis of possible hydrogen bonding between –OH of $-CH_2CH_2OH$ at C-5 and the ring nitrogen atom (the basicity of nitrogen is increased due to the presence of alkyl chain). Formation of such hydrogen bonding requires the 6-Ha and 6-Hb to be *gauche* to 5-H resulting in low J (~2.6 Hz) value with both of these hydrogens. On the other hand, in compound **5**, one of the staggered conformers about the C-5–C-6 bond is destabilized due to the large steric interactions of $-CH_2CH_2OH$ (at C-5) with axial hydrogen at C-1 and C-3 (ring protons). Hence, the two other staggered conformations about this bond would result in one hydrogen (6-Ha) being *anti* and other (6-Hb) *gauche* to C-5 hydrogen. The rotation around C-5–C-6 would

Table 1. Coupling constants for *N*-hydroxyethyl-1-deoxy-homonojirimycin derivatives **4**, **16a**, **5**, **16b** and *N*-hydroxyethyl-pyrrolidine analogues **6**, **19a**, **7** and **19b**

Compd	Coupling constants (Hz)												
	$J_{1a,1b}$	$J_{1a,2}$	$J_{1b,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5a}$	$J_{4,5b}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{1'\alpha a,1'\alpha b}$	$J_{1'\alpha a,2'\alpha}$	$J_{1'\alpha b,2'\alpha}$
4	11.8	9.7[a]	4.4					9.2[a]	2.8[a]	2.8[a]	13.5	5.7	6.6
16a	12.6	10.0[a]	4	9.5	9.5						14	5.3	5.7
5	12.2[a]	9.9	5.2	9.1	9.1			4.9[a]	6.1[a]	6.1[a]	12.4[a]		
16b	13.2	10.7	5.5	9.6	10.2	7.1[a]	8.2[a]	5.5					
6	11.3	6.3	5.5	1.5	3.0[a]	7.1	12.1				13.2	5.3	
19a	11.3	5.3	1.5	1.8[a]	5.3	9	9				12.6	5.7	6.8
7	11	5.2	6.1	2.5	5.1	5	8				13.2	5.7	6.6
19b	11	5.2	6.6	2.5	5.5								

[a]This value was determined by decoupling experiments.



4 **5**

Figure 2.

lead to 6-Ha *gauche* and 6-Hb *anti*. These two staggered conformational rotamers will be in equilibrium and would result in increased coupling constants for these hydrogens (6-Ha and 6-Hb) with C-5 hydrogen which was indeed observed ($J_{5,6a} = J_{5,6b} = 6.1$ Hz). In the case of pyrrolidine analogues, the magnitude of the vicinal coupling constants within the five membered ring of D-arabino-hexitol **6** was considerably different from that of L-xylo-hexitol (**7**) (Table 1). In particular, 1-Ha, 1-Hb, 3-H and 4-H signals of **6** significantly differed from those of the L-xylo-hexitol **7**. However, as in another furanose analogue DMDP (**3**), it is impossible to obtain conformational information from NMR experiments.

Biological Activity

Glycosidases particularly β-glucosidase (E.C. 3.2.1.21), α-galactosidase (E.C 3.2.1.22), β-galactosidase (E.C. 3.2.1.23) and α-mannosidase (E.C. 3.2.1.24) are abundantly present in sweet almonds. Therefore inhibitory potency of homoazasugars **4**, **5**, **6**, **7**, **16a** and **16b** was evaluated using glycosidases extracted from sweet almonds. The IC_{50} values obtained for the above mentioned compounds are summarized in Table 2.

1-Deoxynojirimycin (**1a**) is reported to be a potent inhibitor of all types of mammalian α-glucosidases and is also a moderate to weak inhibitor of β-glucosidase, β-galactosidase and α-mannosidase.[1d] From the IC_{50} obtained for *N*-hydroxyethyl compounds **4** and **5**, it can be observed that they are potent β-galactosidase, β-glucosidase and α-mannosidase inhibitors, but do not inhibit α-galactosidase. Thus, the introduction of *N*-hydroxyethyl and C-5 hydroxyethyl functionality (instead of C-5 hydroxymethyl group as in **1a**) makes

Table 2. Concentration of *N*-hydroxyethyl-1-deoxyhomonojirimycin and *N*-hydroxyethyl-pyrrolidine derivatives (μM) giving 50% inhibition of glycosidases

Compd	IC_{50} (μM)			
	β-Glucosidase	β-Galactosidase	α-Galactosidase	α-Mannosidase
4	4.25	9.04	NI	NI
5	2.11	1.29	NI	3.52
16a	NI	NI	NI	NI
16b	2.32	6.96	NI	NI
6	NI	23.5	3.27	6.54
7	NI	3.40	3.11	4.20

NI, inhibition not observed under assay condition.
All above values are an average obtained from three sets of assay performed.

them more potent against β-glycosidases as compared to α-glycosidases. Comparison of IC_{50} values between **4** and **5** suggests that the replacement of C-5 position with α-oriented $-CH_2CH_2OH$ functionality in **5** resulted in increased potency towards β-galactosidases. Inhibitory effectiveness of both azasugars (**4** and **5**) is more than that of their pentaacetate forms (**16a** and **16b**). The *N*-hydroxyethyl pyrrolidine **6** and **7** were found to be moderate to weak glycosidase inhibitors.

Conclusion

In summary, the synthetic strategy based on the 1,4-Michael addition of benzylamine to sugar derived α,β-unsaturated ester **8** followed by *N*-alkylation provides an efficient, practical and general access to *N*-(hydroxyethyl)-D-gluco- and L-ido-homo-DNJ **4** and **5**. The reaction sequence could be extended for the synthesis of different *N*-alkylated five- and six-member azasugar analogues by changing the alkylating agent. The same strategy was successfully utilized for the synthesis of *N*-hydroxyethyl-pyrrolidine homoazasugrs **6** and **7**. We have also demonstrated that the homoazasugars **4** and **5** exist in $^4C_1$ conformation in aqueous medium, although in **5** the bulky $-CH_2CH_2OH$ group at C-5 is axially oriented. The glycosidase inhibitory potency (IC_{50}) of homoazasugars **4**, **5**, **6**, **7**, **16a** and **16b** was evaluated and this showed that the presence of α-oriented $-CH_2CH_2OH$ functionality at C-5 in **5** and **16b** or C-4 in **7**, has significant effect on the glycosidase inhibition

than that of the corresponding C-5 epimers or C-4 epimers, respectively.

Experimental

Melting points were recorded with Thomas Hoover melting point apparatus and are uncorrected. IR spectra were recorded with FTIR as a thin film or in Nujol mull or using KBr pellets and are expressed in cm^{-1}. ^1H (300 MHz) and ^{13}C (75 MHz) NMR spectra were recorded using $CDCl_3$ or D_2O as a solvent. Chemical shifts were reported in δ unit (ppm) with reference to TMS as an internal standard and *J* values are given in Hz. Elemental analyses were carried out with C,H-analyzer. Optical rotations were measured using polarimeter at 25 °C. Thin-layer chromatography was performed on pre-coated plates (0.25 mm, silica gel 60 F_{254}). Column chromatography was carried out with silica gel (100–200 mesh). Resin column was performed with Dowex IR resin (H^+ form, 100–200 mesh, 50×8) with ammonia solution (25%, Merck). The reactions were carried out in oven-dried glassware under dry N_2. *N*-Benzylamine, methanol, DMF, THF were purified and dried before use. Petroleum ether (PE) that was used is a distillation fraction between 40 and 60 °C. *N*-Benzylamine, LAH, CbzCl, 10% Pd/C were purchased from Aldrich and/or Fluka. After decomposition of the reaction with water, the work-up involves: washing of combined organic layer with water, brine, drying over anhydrous sodium sulfate and evaporation of solvent at reduced pressure. Compounds **9a** and **9b** were prepared by the intermolecular Michael addition of benzyl amine to α,β-unsaturated ester **8** as per our earlier reported procedure.[16d,f]

Assay method

The substrates *p*-nitrophenyl-β-D-glucopyranoside, *p*-nitrophenyl-β-D-galactopyranoside, *p*-nitrophenyl-α-D-galactopyranoside and *p*-nitrophenyl-α-D-mannopyranoside of 2 mM concentration were prepared in 0.025 M citrate buffer with pH 4.0. An aliquot of 200 μL of test compound (5 mg/mL solution in distilled water) was preincubated with the enzyme (almond seed extract) for 1 h at 37 °C. The enzyme reaction was initiated by the addition of 100 μL substrate. Controls were run simultaneously in absence of test compound. The reaction was terminated at the end of 1.5 h by the addition of 0.05 M borate buffer (pH 9.8) and absorbance of the liberated *p*-nitrophenol was measured at 420 nm. One unit of glycosidase activity is defined as the amount of enzyme that hydrolyzed 1 μmol of *p*-nitrophenyl pyranoside per min at 25 °C.[21] IC_{50} is the amount of inhibitor in μM concentration required to decrease enzyme activity by 50% under assay conditions.

Ethyl 1,2-*O*-isopropylidene-3-*O*-benzyl-5-(*N*-benzyl, *N*-carbethoxymethylene)amino-5,6-dideoxy-α-D-gluco-heptofuranuronate (10a). To a stirred solution of **9a** (0.45 g, 0.98 mmol) and anhydrous potassium carbonate (0.68 g, 4.07 mmol) in dry DMF (3 cm^3) was added ethyl bromoacetate (0.27 g, 1.62 mmol) in dry DMF (1 cm^3). The reaction mixture was stirred at room temperature for 30 h, decomposed with cooled water (2 cm^3) and extracted with chloroform (10 cm^3×3). Work-up followed by chromatography (*n*-hexane/ethyl acetate = 96/4) gave **10a** (0.38 g, 71%) as a thick syrup (Found: C, 66.75; H, 7.36. $C_{30}H_{39}NO_8$ requires C, 66.53; H, 7.26%); R_f = 0.64 (*n*-hexane/ethyl acetate = 4/1); $[\alpha]_D$ −26.67 (*c* 0.15 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1754; δ_H (300 MHz, $CDCl_3$) 1.17 (3H, t, *J* = 7.0, CH_3), 1.24 (3H, t, *J* = 7.0, CH_3), 1.30 (3H, s, CH_3), 1.45 (3H, s, CH_3), 2.67–2.82 (2H, m, 6-Ha and Hb), 3.36 (2H, AB quartet, *J* = 17.3, *N*-CH_2CO), 3.81–4.28 (9H, m, 3-H, 4-H, 5-H, *N*-CH_2Ph, 2 *O*-CH_2CH_3), 4.51 (1H, d, *J* = 11.7, *O*-CH_2Ph), 4.54 (1H, d, *J* = 3.8, 2-H), 4.64 (1H, d, *J* = 11.7, *O*-CH_2Ph), 5.84 (1H, d, *J* = 3.8, 1-H), 7.12–7.29 (10H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 14.0, 14.1, 26.2, 26.6 (CH_3), 34.5 (*C*-6), 52.6, 54.9 (*N*-CH_2Ph/*N*-CH_2CO), 57.9 (*C*-5), 60.0, 67.9 (*O*-CH_2), 71.4 (*O*-CH_2Ph), 79.9, 81.5, 82.4 (*C*-2/*C*-3/*C*-4), 104.6 (c-1), 111.1 (O-*C*-O), 126.8, 127.3, 127.5, 127.9, 128.1, 128.6, 137.2, 138.7 (Ar-*C*), 171.8, 172.5 (*C*O).

Ethyl 1,2-*O*-isopropylidene-3-*O*-benzyl-5-(*N*-benzyl, *N*-carbethoxymethylene)amino-5,6-dideoxy-β-L-ido-heptofuranuronate (10b). The reaction of **9b** (0.67 g, 1.47 mmol), anhydrous potassium carbonate (1.0 g, 7.30 mmol) and ethyl bromoacetate (0.30 g, 1.80 mmol) in dry DMF (10 cm^3) as stated for **9a** after 20 h and column chromatographic purification (*n*-hexane/ethyl acetate = 94/6) yielded compound **10b** (0.74 g, 93%) as a thick syrup (Found: C, 66.71; H, 7.34. $C_{30}H_{39}NO_8$ requires C, 66.53; H, 7.26%); R_f = 0.49 (*n*-hexane/ethyl acetate = 4/1); $[\alpha]_D$ −3.6 (*c* 0.25 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1745 and 1734; δ_H (300 MHz, $CDCl_3$) 1.16 (3H, t, *J* = 7.1, CH_3), 1.23 (3H, t, *J* = 7.1, CH_3), 1.35 (3H, s, CH_3), 1.52 (3H, s, CH_3), 2.08 (1H, dd, *J* = 3.5 and 14.2, 6-Ha), 2.36 (1H, dd, *J* = 10.7 and 14.2, 6-Hb), 3.37 (1H, d, *J* = 16.8, *N*-CH_2Ph), 3.54 (1H, d, *J* = 16.8, *N*-CH_2Ph), 3.77 (1H, d, *J* = 3.3, 3-H), 3.84 (1H, ddd, *J* = 3.1, 3.5 and 10.7, 5-H), 3.86 (1H, d, *J* = 13.8, *N*-CH_2CO), 3.99 (2H, q, *J* = 7.1, CH_2CH_3), 4.00–4.24 (3H, m, *N*-CH_2CO, CH_2CH_3), 4.29 (1H, dd, *J* = 3.1 and 9.9, 4-H), 4.42 (1H, d, *J* = 11.8, *O*-CH_2Ph), 4.64 (1H, d, *J* = 3.9, 2-H), 4.70 (1H, d, *J* = 11.8, *O*-CH_2Ph), 5.98 (1H, d, *J* = 3.9, 1-H), 7.18–7.42 (10H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 14.0, 14.1, 26.2, 26.7 (CH_3), 35.9 (C-6), 53.3, 55.2 (*N*-CH_2CO/*N*-CH_2Ph), 57.7 (*C*-5), 59.9, 60.3 (*O*-CH_2CH_3), 71.3 (*O*-CH_2Ph), 80.6, 81.2, 81.7 (*C*-2/*C*-3/*C*-4), 104.8 (*C*-1), 111.4 (O-*C*-O), 126.7, 127.8, 127.9, 128.0, 128.3, 129.1, 136.8, 139.5 (Ar-*C*), 171.1, 172.0 (*C*O).

1,2-*O*-Isopropylidene-3-*O*-benzyl-5-(*N*-benzyl, *N*-hydroxyethyl)amino-5,6-dideoxy-α-D-gluco-heptofuranose (11a). To an ice cooled suspension of LAH (0.35 g, 9.23 mmol) in dry THF (8 cm^3) was added a solution of **10a** (1.0 g, 1.85 mmol) in dry THF (7 cm^3) over a period of 10 min. The reaction mixture was warmed to room temperature and stirred for 2 h. Ethyl acetate (10 cm^3) was added at 0 °C, stirred for 10 min and quenched with saturated solution of NH_4Cl (2 cm^3). The solution was filtered, the residue washed with ethyl acetate (3 cm^3×3) and worked-up. The organic layer was evaporated and purified by column chromatography (*n*-hexane/ethyl acetate = 3/2) to give **11a** (0.69 g, 82%) as a thick liquid

(Found: C, 68.44; H, 7.88. $C_{26}H_{35}NO_6$ requires C, 68.25; H, 7.71%); R_f = 0.30 (*n*-hexane/ethyl acetate = 2/3); $[\alpha]_D$ −20 (*c* 0.2 in $CHCl_3$); ν_{max} (nujol)/cm^{-1} 3450–3100 (br band); δ_H (300 MHz, $CDCl_3 + D_2O$) 1.32 (3H, s, C*H*$_3$), 1.49 (3H, s, C*H*$_3$), 1.49–2.10 (2H, m, 6-Ha and Hb), 2.51–2.60 (1H, m, *N*-C*H*$_2$CH$_2$), 2.83–2.94 (1H, m, *N*-C*H*$_2$CH$_2$), 3.34 (1H, dt, *J* = 4.4 and 8.8, 5-H), 3.40–3.60 (3H, m, C*H*$_2$OH and *N*-C*H*$_2$Ph), 3.60–3.68 (1H, m, C*H*$_2$OH), 3.71–3.80 (1H, m, C*H*$_2$OH), 3.84 (1H, d, *J* = 13.8, *N*-C*H*$_2$Ph), 3.89 (1H, d, *J* = 3.5, 3-H), 4.32 (1H, dd, *J* = 3.5 and 4.4, 4-H), 4.41 (1H, d, *J* = 11.8, *O*-C*H*$_2$Ph) 4.58 (1H, d, *J* = 3.8, 2-H), 4.63 (1H, d, *J* = 11.8, *O*-C*H*$_2$Ph), 5.89 (1H, d, *J* = 3.8, 1-H), 7.20–7.34 (10H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 26.3, 26.9 (*C*H$_3$), 30.0 (*C*-6), 52.3 (*N*-*C*H$_2$CH$_2$), 55.3 (*N*-*C*H$_2$Ph), 57.0 (*C*-5), 59.9, 62.2 (*C*H$_2$OH), 71.6 (*O*-*C*H$_2$Ph), 76.6, 81.4, 83.4 (*C*-2/*C*-3/*C*-4), 104.5 (*C*-1), 111.4 (O-*C*-O), 127.1, 127.6, 127.9, 128.3, 128.4, 128.8, 136.9, 138.8 (Ar-*C*).

1,2-*O*-Isopropylidene-3-*O*-benzyl-5-(*N*-benzyl, *N*-hydroxyethyl)amino-5,6-dideoxy-β-L-ido-heptofuranose (11b). The reaction of **10b** (0.5 g, 0.92 mmol) and LAH (0.18 g, 4.74 mmol) in dry THF (8 cm^3) for 2 h as described for **10a** and column chromatography (*n*-hexane/ethyl acetate = 3/2) gave **11b** (0.34 g, 83%) as a thick liquid (Found: C, 68.41; H, 7.84. $C_{26}H_{35}NO_6$ requires C, 68.25; H, 7.71%); R_f = 0.49 (*n*-hexane/ethyl acetate = 2/3); $[\alpha]_D$ −80 (*c* 0.25 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3440-3200 (br band); δ_H (300 MHz, $CDCl_3 + D_2O$) 0.85–1.05 (1H, m, 6-Ha), 1.35 (3H, s, C*H*$_3$), 1.50 (3H, s, C*H*$_3$), 1.50–1.66 (1H, m, 6-Hb), 2.84–3.00 (2H, m, *N*-C*H*$_2$CH$_2$), 3.42-3.70 (5H, m, 5-H, 2 C*H*$_2$OH), 3.77 (1H, d, *J* = 3.0, 3-H), 3.88 (2H, AB quartet, *J* = 12.7, *N*-C*H*$_2$Ph), 4.25 (1H, dd, *J* = 3.0 and 10.2, 4-H), 4.37 (1H, d, *J* = 11.8, *O*-C*H*$_2$Ph), 4.62 (1H, d, *J* = 3.8, 2-H), 4.69 (1H, d, *J* = 11.8, *O*-C*H*$_2$Ph), 6.00 (1H, d, *J* = 3.8, 1-H), 7.22–7.38 (10H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 26.2, 26.8 (*C*H$_3$), 30.2 (*C*-6), 52.8 (*N*-*C*H$_2$CH$_2$), 55.4 (*N*-*C*H$_2$Ph), 57.0 (c-5), 60.4, 61.9 (2*C*H$_2$OH), 71.5 (*O*-*C*H$_2$Ph), 81.2, 81.4, 82.0 (*C*-2/*C*-3/*C*-4), 104.9 (*C*-1), 111.5 (O-*C*-O), 127.1, 127.9, 128.1, 128.4, 128.5, 129.5, 137.0, 139.6 (Ar-*C*).

1,2-*O*-Isopropylidene-3-*O*-benzyl-5-(*N*-β-acetoxyethyl, *N*-benzyl)amino-7-*O*-acetyl-5,6-dideoxy-α-D-gluco-heptofuranose (12a). To a cooled (0 °C) solution of diol **11a** (0.72 g, 1.57 mmol) in dry pyridine (1.5 cm^3) was added acetic anhydride (2.65 g, 25.95 mmol). After stirring the reaction mixture for 4 h at 25 °C, ice water was added and extracted with chloroform (3×15 cm^3). Usual work-up and chromatography (*n*-hexane/ethyl acetate = 9/1) provided the diacetate **12a** (0.72 g, 84%) as syrup (Found: C, 66.67; H, 7.35. $C_{30}H_{39}NO_8$ requires C, 66.53; H, 7.26%); R_f = 0.54 (*n*-hexane/ethyl acetate = 2/1); $[\alpha]_D$ −16 (*c* 0.25 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1738; δ_H (300 MHz, $CDCl_3$) 1.31 (3H, s, C*H*$_3$), 1.49 (3H, s, C*H*$_3$), 1.90 (3H, s, C*H*$_3$), 1.99 (3H, s, C*H*$_3$), 1.90–2.15 (2H, m, 6-Ha and Hb), 2.68 (1H, dt, *J* = 5.6 and 14.0, *N*-C*H*$_2$CH$_2$), 2.88 (1H, dt, *J* = 6.4 and 14.0, *N*-C*H*$_2$CH$_2$), 3.25 (1H, ddd, *J* = 3.5, 5.0 and 8.8, 5-H), 3.55(1H, d, *J* = 13.7, *N*-C*H*$_2$Ph), 3.68 (1H, dd, *J* = 3.0 and 3.5, 4-H), 3.77 (1H, d, *J* = 13.7, *N*-C*H*$_2$Ph), 3.89 (1H, d, *J* = 3.0, 3-H), 3.92–4.08 (2H, m, C*H*$_2$OAc), 4.10–4.30 (2H, m, C*H*$_2$OAc), 4.40 (1H, d, *J* = 11.8, *O*-C*H*$_2$Ph), 4.54 (1H, d, *J* = 3.8, 2-H), 4.60 (1H, d, *J* = 11.8, *O*-C*H*$_2$Ph), 5.87 (1H, d, *J* = 3.8, 1-H), 7.19–7.28 (10H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 20.9, 21.0, 26.3, 26.9 (*C*H$_3$), 27.3 (C-6), 49.0 (*N*-*C*H$_2$CH$_2$), 54.3 (*N*-*C*H$_2$Ph), 55.8 (*C*-5), 62.7, 62.8 (*C*H$_2$OAc), 71.4 (*O*-*C*H$_2$Ph), 78.8, 81.5, 83.0 (*C*-2/*C*-3/*C*-4), 104.7 (*C*-1), 111.3 (O-*C*-O), 126.9, 127.3, 127.7, 128.1, 128.3, 128.6, 137.2, 139.5 (Ar-*C*), 170.7, 170.9 (CO).

1,2-*O*-Isopropylidene-3-*O*-benzyl-5-(*N*-β-acetoxyethyl, *N*-benzyl)amino-7-*O*-acetyl-5,6-dideoxy-β-L-ido-heptofuranose (12b). Acetylation of diol **11b** (0.21 g, 0.46 mmol) with acetic anhydride (0.84 g, 8.28 mmol) in dry pyridine (1 cm^3) at 0 °C to room temperature for 4 h, as stated for **11a**, gave diacetate **12b** (0.21 g, 82%) as syrup (Found: C, 66.71; H, 7.34. $C_{30}H_{39}NO_8$ requires C, 66.53; H, 7.26%); R_f = 0.50 (*n*-hexane/ethyl acetate = 2/1); $[\alpha]_D$ −66.67 (*c* 0.33 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1736; δ_H (300 MHz, $CDCl_3$) (1.24–1.54 (2H, m, 6-Ha and Hb), 1.35 (3H, s, C*H*$_3$), 1.52 (3H, s, C*H*$_3$), 1.83 (3H, s, C*H*$_3$), 1.98 (3H, s, C*H*$_3$), 2.82–2.92 (1H, m, *N*-C*H*$_2$CH$_2$), 3.01 (1H, dt, *J* = 4.6 and 14.0, *N*-C*H*$_2$CH$_2$), 3.35 (1H, ddd, *J* = 3.0, 10.2 and 11.3, 5-H), 3.97 (1H, d, *J* = 3.0, 3-H), 3.85 (2H, AB quartet, *J* = 13.5, *N*-C*H*$_2$Ph), 3.92–4.08 (2H, m, C*H*$_2$OAc), 4.12–4.23 (2H, m, C*H*$_2$OAc), 4.27 (1H, dd, *J* = 3.0 and 10.2, 4-H), 4.43 (1H, d, *J* = 11.5, *O*-C*H*$_2$Ph), 4.62 (1H, d, *J* = 3.8, 2-H), 4.67 (1H, d, *J* = 11.5, *O*-C*H*$_2$Ph), 5.99 (1H, d, *J* = 3.8, 1-H), 7.21–7.34 (10H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 20.7, 20.8, 26.2, 26.9 (*C*H$_3$), 28.2 (*C*-6), 49.1 (*N*-*C*H$_2$CH$_2$), 53.8 (*N*-*C*H$_2$Ph), 55.2 (*C*-5), 61.6, 63.1 (*C*H$_2$OAc), 71.5 (*O*-*C*H$_2$Ph), 81.2, 81.7, 82.2 (*C*-2/*C*-3/*C*-4), 104.9 (*C*-1), 111.4 (O-*C*-O), 126.7, 127.6, 127.9, 128.0, 128.4, 129.1, 137.1, 140.4 (Ar-*C*), 171.1 (strong, 2×cO).

1,2-*O*-Isopropylidene-5-(*N*-β-acetoxyethyl)amino-7-*O*-acetyl-5,6-dideoxy-α-D-gluco-heptofuranose (13a). A solution of **12a** (0.64 g, 0.67 mmol) and 10% Pd/C (0.13 g) in methanol (7 cm^3) was hydrogenolyzed at room temperature at 80 psi for 12 h. The catalyst was filtered through Celite and washed with methanol. Methanol was evaporated off in vacuo and the residue was purified by column chromatography (*n*-hexane/ethyl acetate = 3/1) to yield **13a** (0.38 g, 89%) as thick oil (Found: C, 53.24; H, 7.69. $C_{16}H_{27}NO_8$ requires C, 53.18; H, 7.53%); R_f = 0.44 (*n*-hexane/ethyl acetate = 1/9); $[\alpha]_D$ −26 (*c* 1.0 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3450–3100 and 1735; δ_H (300 MHz, $CDCl_3$) 1.30 (3H, s, C*H*$_3$), 1.46 (3H, s, C*H*$_3$), 1.89–1.98 (2H, m, 6-Ha and Hb), 2.05 (6H, s, 2×COC*H*$_3$), 2.82–3.04 (2H, m, *N*-C*H*$_2$CH$_2$), 3.35 (1H, dt, *J* = 3.0 and 6.6, 5-H), 3.41-3.55 (2H, br s, exchange with D_2O, NH and OH), 4.01 (1H, t, *J* = 3.0, 4-H), 4.07–4.22 (4H, m, 2×C*H*$_2$OAc), 4.25 (1H, d, *J* = 3.0, 3-H), 4.47 (1H, d, *J* = 3.6, 2-H), 5.94 (1H, d, *J* = 3.6, 1-H); δ_C (75 MHz, $CDCl_3$) 20.8, 20.9, 26.1, 26.8 (*C*H$_3$), 30.2 (C-6), 47.0 (*N*-*C*H$_2$CH$_2$), 55.3 (C-5), 61.4, 63.2 (*C*H$_2$OAc), 76.0, 80.3, 85.4 (*C*-2/*C*-3/*C*-4/), 104.6 (*C*-1), 111.4 (O-*C*-O), 170.5, 170.7 (*C*O).

1,2-*O*-Isopropylidene-5-(*N*-β-acetoxyethyl)amino-7-*O*-acetyl-5,6-dideoxy-β-L-ido-heptofuranose (13b). Hydrogenolysis of **12b** (0.74 g, 1.37 mmol) in dry methanol (5

cm^3) as described for **12a** followed by chromatography (*n*-hexane/ethyl acetate = 3/1) afforded **13b** (0.35 g, 71%) as a thick oil (Found: C, 53.25; H, 7.58. $C_{16}H_{27}NO_8$ requires C, 53.18; H, 7.53%); R_f = 0.58 (*n*-hexane/ethyl acetate = 1/9); $[\alpha]_D$ +14 (*c* 2.0 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3460–3100 and 1736; δ_H (300 MHz, $CDCl_3$) 0.90–1.80 (4H, m, NH, OH, 6-Ha and 6-Hb, on D_2O exchange integrated for 2H), 1.31 (3H, s, CH_3), 1.48 (3H, s, CH_3), 2.08 (6H, s, 2×COCH_3), 2.68–2.90 (1H, m, *N*-CH_2CH_2), 3.05–3.20 (2H, m, 5-*H*, *N*-CH_2CH_2), 4.04–4.27 (6H, m, 3-H, 4-H, 2 CH_2OAc), 4.52 (1H, d, *J* = 3.3, 2-H), 5.94 (1H, d, *J* = 3.3, 1-H); δ_C (75 MHz, $CDCl_3$) 20.8, 20.9, 26.1, 26.9 (CH_3), 30.4 (*C*-6), 44.7 (*N*-*C*H_2CH_2), 54.7 (*C*-5), 61.2, 63.3 (*C*H_2OAc), 77.4, 77.6, 85.8 (*C*-2/*C*-3/*C*-4), 104.8 (*C*-1), 111.5 (O-*C*-O), 171.0, 171.1 (*C*O).

1,2-*O*-Isopropylidene-5-(*N*-β-acetoxyethyl, *N*-benzoxycarbonyl)amino-7-*O*-acetyl-5,6-dideoxy-α-D-gluco-heptofuranose (14a). To a stirred solution of **13a** (0.46 g, 1.28 mmol) and $NaHCO_3$ (0.3 g, 3.60 mmol) in ethanol/water (2 cm^3, 1:1,) at 0 °C, was added benzyl chloroformate (0.33 g, 1.93 mmol). The mixture was stirred at room temperature for 4 h, quenched with water and extracted with chloroform (3×10 cm^3). Work-up and chromatography (*n*-hexane/ethyl acetate = 9/1) provided **14a** (0.56 g, 88%) as a thick liquid[19] (Found: C, 58.25; H, 6.83. $C_{24}H_{33}NO_{10}$ requires C, 58.17; H, 6.71%); R_f = 0.50 (*n*-hexane/ethyl acetate = 3/2); $[\alpha]_D$ +42.86 (*c* 0.14 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3430, 1736 and 1680; δ_H (300 MHz, $CDCl_3$) 1.20–2.00 (2H, br m, 6-Ha and H-b), 1.31 (3H, s, CH_3), 1.50 (3H, s, CH_3), 1.98 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.26–2.38 (1H, m, *N*-CH_2CH_2), 3.24–3.36 (1H, m, *N*-CH_2CH_2), 3.56 (1H, dt, *J* = 5.1 and 14.8, 5-H), 3.94–4.24 (6H, m, 3-H, 4-H and 2×CH_2OAc), 4.37–4.52 (1H, br m, OH, exchange with D_2O), 4.53 (1H, d, *J* = 3.6, 2-H), 5.08–5.26 (2H, AB quartet, *J* = 12.1, *O*-CH_2Ph), 5.92 (1H, d, *J* = 3.6, 1-H), 7.31–7.39 (5H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 20.9 (strong), 26.0, 26.8 (*C*H_3), 28.2 (C-6), 42.0 (*N*-*C*H_2CH_2), 153.1 (C-5), 61.2, 62.4 (*C*H_2OAc), 68.6 (*O*-*C*H_2Ph), 73.9, 81.2, 84.4 (*C*-2/*C*-3/*C*-4), 105.0 (*C*-1), 111.4 (O-*C*-O), 128.0, 128.5, 128.6, 135.3 (Ar-*C*), 156.2, 170.6, 170.8 (*C*O).

1,2-*O*-Isopropylidene-5-(*N*-β-acetoxyethyl, *N*-benzoxycarbonyl)amino-7-*O*-acetyl-5,6-dideoxy-β-L-ido-heptofuranose (14b). A reaction of **13b** (0.35 g, 0.97 mmol), $NaHCO_3$ (0.23 g, 2.71 mmol) and benzyl chloroformate (0.25 g, 1.45 mmol) in ethanol/water (3 cm^3, 1:1) at 0 °C for 3 h as described for **13a** and chromatography (hexane/ethyl acetate = 3/1) yielded **14b** (0.43 g, 90%) as white solid,[19] mp 108–109 °C (Found: C, 58.20; H, 6.85. $C_{24}H_{33}NO_{10}$ requires C, 58.46; H, 7.00%); R_f = 0.50 (*n*-hexane/ethyl acetate = 1/1); $[\alpha]_D$ −44.19 (*c* 0.86 in $CHCl_3$); ν_{max} (nujol)/cm^{-1} 3451, 1736 and 1683; δ_H (300 MHz, $CDCl_3$) 1.29 (3H, s, CH_3), 1.47 (3H, s, CH_3), 1.70–2.00 (2H, m, 6-Ha and Hb), 1.98 (3H, s, CH_3), 2.00 (3H, s, CH_3), 2.82–2.98 (1H, br s, exchange with D_2O), 3.37–3.56 (3H, m, 5-H and *N*-CH_2CH_2), 3.98–4.30 (6H, m, 3-H, 4-H and 2×CH_2OAc), 4.51 (1H, d, *J* = 3.0, 2-H), 5.13 (2H, s, *O*-CH_2Ph), 5.88 (1H, d, *J* = 3.0, 1-H), 7.26–7.34 (5H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 20.8, 20.9, 26.3, 26.7 (*C*H_3), 27.5 (*C*-6), 41.8 (*N*-*C*H_2CH_2), 52.1 (*C*-5), 61.4, 62.0 (*C*H_2OAc), 67.3 (*O*-*C*H_2Ph), 74.7, 79.5, 85.5 (*C*-2/*C*-3/*C*-4), 104.1 (*C*-1), 111.6 (O-*C*-O), 127.5, 127.9, 128.4, 136.2 (Ar-*C*), 156.4, 170.7, 170.9 (*C*O).

1,5,6-Trideoxy-1,5-imino-*N*-(β-acetoxyethyl)-7-*O*-acetyl-D-gluco-heptitol (15a). To a solution of TFA/water (2 cm^3, 3:2), cooled at 0 °C, was added **14a** (0.5 g, 1.01 mmol) and stirred for 30 min. The solution was allowed to warm to 30 °C and stirred for 2 h. TFA-water was co-evaporated with toluene under high vacuum to provide an anomeric mixture of hemiacetal which was directly used in the next reaction. To a solution of hemiacetal in dry methanol (6 cm^3) was added 10% Pd/C (0.09 g) and ammonium formate (0.38 g, 6.06 mmol). The reaction mixture was refluxed for 45 min and filtered through Celite, washed with methanol and concentrated. The concentrated thick liquid was purified by IR resin column (H^+ form, 100-200 mesh, Dowex 50×8) using $CHCl_3$/MeOH/NH_3 (25% solution) = 80/18/2 as an eluant to yield **15a** (0.28 g, 89%) as a thick oil (Found: C, 51.24; H, 7.75. $C_{13}H_{23}NO_7$ requires C, 51.14; H, 7.59%); R_f = 0.64 ($CHCl_3$/MeOH = 4/1); $[\alpha]_D$ −24 (*c* 1.0 in $CHCl_3$); ν_{max} (nujol)/cm^{-1} 3500–3300 (br band) and 1728; δ_H (300 MHz, D_2O) 1.90–2.20 (2H, br m, 6-Ha and Hb), 2.10 (6H, br s, 2×CH_3), 2.40–4.60 (12H, br m, 2-H, 3-H, 4-H, 5-H, 2×*N*-CH_2 and 2×CH_2OAc); δ_C (75 MHz, $CDCl_3$) 21.0, 21.1 (*C*H_3), 26.9 (*C*-6), 49.6, 56.5 (*C*-1/*C*-1′), 61.2 (strong, *C*-7/*C*-2′), 62.3 (*C*-5), 69.1, 72.6, 79.1 (*C*-2/*C*-3/*C*-4), 171.1, 171.4 (*C*O).

1,5,6-Trideoxy-1,5-imino-*N*-(β-acetoxyethyl)-7-*O*-acetyl-L-ido-heptitol (15b). A reaction of (0.4 g, 0.80 mmol) with TFA/water (2 cm^3, 3:2) followed by hydrogenolysis in dry methanol (5 cm^3) with 10% Pd/C (0.08 g) and ammonium formate (0.3 g, 4.84 mmol) as stated for **14a** gave **15b** (0.18 g, 88%) as a thick syrup (Found: C, 51.19; H, 7.68. $C_{13}H_{23}NO_7$ requires C, 51.19; H, 7.56%); R_f = 0.32 ($CHCl_3$/MeOH = 4/1); $[\alpha]_D$ +4.35 (*c* 0.46 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3500–3300 (br band) and 1730; δ_H (300 MHz, $CDCl_3$ + D_2O) 1.60–2.15 (2H, br m, 6-Ha and Hb), 2.05 (6H, s, 2×CH_3), 2.20–3.30 (5H, m, 2×*N*-CH_2 and 5-H), 3.36–3.95 (3H, m, 2-H, 3-H and 4-H), 4.02–4.20 (4H, m, 2×CH_2OAc); δ_C (75 MHz, $CDCl_3$) 21.0, 21.1 (*C*H_3), 23.0 (*C*-6), 51.1, 52.8 (*C*-1/*C*-1′), 59.2 (*C*-5), 62.0, 63.2 (*C*-7/*C*-2′), 69.6, 70.9, 76.6 (*C*-2/*C*-3/*C*-4), 171.2, 171.4 (*C*O).

1,5,6-Trideoxy-1,5-imino-*N*-hydroxyethyl-D-gluco-heptitol (4). To a cooled solution (0 °C) of dry MeOH (3 cm^3) a piece of Na (0.005 g) was added followed by **15a** (0.25 g, 0.82 mmol) in dry MeOH (1 cm^3). Reaction mixture was allowed to warm to 30 °C and stirred for 2 h. IR resin (H^+ form, 100–200 mesh, Dowex 50×8) was added to the reaction mixture till neutral pH, filtered and methanol was concentrated. The residue thus obtained was purified by IR resin (H^+ form) column ($CHCl_3$/MeOH/NH_3 = 50/48/2) to afford pentaol **4** (0.154 g, 88%) as a hygroscopic syrup (Found: C, 48.70; H, 8.73. $C_9H_{19}NO_5$ requires C, 48.86; H, 8.65%); R_f = 0.15 ($CHCl_3$/MeOH = 1/1); $[\alpha]_D$ −22.5 (*c* 0.8 in MeOH); ν_{max} (neat)/cm^{-1} 3450-3200 (br band); δ_H

(300 MHz, D_2O) 1.73–1.89 (2H, br m, 6-Ha and Hb), 2.12 (1H, dd, $J=9.2$ and 11.8, 1-Ha), 2.15–2.24 (1H, m, 5-H), 2.44 (1H, dt, $J=5.7$ and 13.5, 1′-Ha), 2.73 (1H, dt, $J=6.6$ and 13.5, 1′-Hb), 2.94 (1H, dd, $J=4.4$ and 11.8, 1-He), 3.04–3.14 (2H, m, 3-H and 4-H), 3.33–3.64 (5H, m, 2-H and 2×CH_2OH); δ_C (75 MHz, D_2O) 31.0 (*C*-6), 52.4, 56.0 (*C*-1/*C*-1′), 58.3 (*C*-5), 59.0, 62.5 (*C*-7/*C*-2′), 68.3, 72.8, 78.3 (*C*-2/*C*-3/*C*-4).

1,5,6-Trideoxy-1,5-imino-*N*-hydroxyethyl-L-ido-heptitol (5). A reaction of **15b** (0.27 g, 0.88 mmol) with sodium methoxide in dry MeOH (1 cm^3) for 2 h as described for **15a** followed by purification with IR resin column using $CHCl_3$/MeOH/NH_3 = 50/48/2 as an eluant gave pure **5** (0.19 g, 95%) as hygroscopic syrup (Found: C, 48.72; H, 8.54. $C_9H_{19}NO_5$ requires C, 48.86; H, 8.65%); R_f = 0.25 ($CHCl_3$/EtOH = 3/1); $[\alpha]_D$ −14.29 (*c* 2.1 in MeOH); ν_{max} (neat)/cm^{-1} 3450–3250 (br band); δ_H (300 MHz, D_2O) 1.51–1.60 (2H, m [apparent quartet with $J=6.1$], 6-Ha and Hb), 2.34 (1H, dd, $J=9.9$ and 12.2, 1-Ha), 2.51–2.62 (2H, m, *N*-CH_2CH_2), 2.62 (1H, dd, $J=5.2$ and 12.2, 1-He), 2.82–2.90 (1H, m, 5-H), 3.24 (1H, t, $J=9.1$, 3-H), 3.34–3.59 (6H, m, 2-H, 4-H and 2×CH_2OH); δ_C (75 MHz, D_2O) 25.0 (*C*-6), 50.3, 55.2 (*C*-1/*C*-1′), 59.2 (*C*-5), 60.1, 61.5 (*C*-7/*C*-2′), 69.3, 70.4, 74.5 (*C*-2/*C*-3/*C*-4).

1,5,6-Trideoxy-1,5-imino-2,3,4,7-tetra-*O*-acetyl-*N*-(β-acetoxyethyl)-D-gluco-heptitol (16a). To an ice cold solution of **4** (0.12 g, 0.54 mmol) in pyridine (0.8 cm^3) was added acetic anhydride (0.99 g, 9.72 mmol). The reaction mixture was allowed to warm and stirred at 30 °C for 12 h. Toluene (5 cm^3) was added and evaporated at reduced pressure (three times). The residue obtained on chromatography (hexane/ethyl acetate = 5/5) gave **16a** (0.23 g, 98%) as a thick syrup (Found: C, 52.97; H, 6.89. $C_{19}H_{29}NO_{10}$ requires C, 52.89; H, 6.77%); R_f = 0.59 ($CHCl_3$/MeOH = 9.5/0.5); $[\alpha]_D$ +15 (*c* 1.2 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1738 (br); δ_H (300 MHz, $CDCl_3$) 1.74–1.90 (1H, m, 6-Ha), 1.99 (3H, s, CH_3), 2.01 (3H, s, CH_3), 2.02 (3H, s, CH_3), 2.03–2.10 (1H, m, 6-Hb), 2.04 (3H, s, CH_3), 2.05 (3H, s, CH_3), 2.42–2.52 (1H, m, 5-H), 2.74–2.88 (2H, m, 1-Ha and 1′-Ha), 2.97 (1H, dt, $J=5.3$ and 14.0, 1′-Hb), 3.27 (1H, dd, $J=4.0$ and 12.6, 1-He), 4.02–4.27 (4H, m, 2×CH_2OAc), 4.92 (1H, t, $J=9.5$, 3-H), 4.92–5.06 (2H, m, 2-H and 4-H); δ_C (75 MHz, $CDCl_3$) 20.7 (strong), 20.8, 20.9, 21.0 (*C*H_3), 26.7 (*C*-6), 47.3 (*C*-1), 52.4 (*C*-1′), 59.7 (*C*-5), 60.5, 61.6 (*C*-7/*C*-2′), 68.1, 70.9, 74.7 (*C*-2/*C*-3/*C*-4), 169.7, 169.8, 170.1, 170.7, 170.8 (*C*O).

1,5,6-Trideoxy-1,5-imino-2,3,4,7-tetra-*O*-acetyl-*N*-(β-acetoxyethyl)-L-ido-heptitol (16b). Acetylation of **5** (0.15 g, 0.68 mmol) with acetic anhydride (1.25 g, 12.24 mmol) in pyridine (1 cm^3) for 12 h as stated for **4** and purification by column chromatography provided **16b** (0.28 g, 97%) as a thick syrup (Found: C, 52.95; H, 6.83. $C_{19}H_{29}NO_{10}$ requires C, 52.89; H, 6.77%); R_f = 0.45 ($CHCl_3$/EtOH = 9/1); $[\alpha]_D$ −12 (*c* 0.1 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1740 (br); δ_H (300 MHz, $CDCl_3$) 1.81–1.92 (1H, m, 6-Ha), 2.02 (3H, s, CH_3), 2.03 (3H, s, CH_3), 2.04 (3H, s, CH_3), 2.05 (3H, s, CH_3), 2.07 (3H, s, CH_3), 2.06–2.16 (1H, m, 6-Hb), 2.69 (1H, dd, $J=10.7$ and 13.2, 1-Ha), 2.84–3.08 (3H, m, 1-He and *N*-CH_2CH_2), 3.18–3.29 (1H, m, 5-H), 3.98–4.22 (4H, m, 2×CH_2OAc), 4.95 (1H, ddd, $J=5.5$, 9.6 and 10.7, 2-H), 5.05 (1H, dd, $J=5.5$ and 10.2, 4-H), 5.23 (1H, dd, $J=9.6$ and 10.2, 3-H); δ_C (75 MHz, $CDCl_3$) 21.1, 21.2 (strong), 21.3 (*C*H_3), 24.1 (*C*-6), 47.3 (*C*-1), 53.4 (*C*-1′), 56.7 (*C*-5), 62.1, 63.2 (*C*-7/*C*-2′), 69.4, 70.3, 71.2 (*C*-2/*C*-3/*C*-4), 170.0, 170.2, 170.3, 171.0, 171.1 (*C*O).

1,2-*O*-Isopropylidene-3,7-di-*O*-acetyl-5-(*N*-β-acetoxyethyl, *N*-benzoxycarbonyl)amino-5,6-dideoxy-α-D-gluco-hepto-furanose (17a). To a stirred solution of diacetate **14a** (1.0 g, 2.018 mmol) in pyridine (3 cm^3 mmol) was added acetic anhydride (3.70 g, 36.32 mmol) at 0 °C. The mixture was stirred at room temperature for 3 h and quenched with water. Usual workup and purification by column chromatography (*n*-hexane/ethyl acetate = 9/1) provided **17a** (1.02 g, 94%) as a semi solid[19] (Found: C, 58.25; H, 6.80. $C_{26}H_{35}NO_{11}$ requires C, 58.09; H, 6.56%); R_f = 0.41 (*n*-hexane/ethyl acetate = 3/1); $[\alpha]_D$ +8.6 (*c* 0.93 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1743 and 1703; δ_H (300 MHz, $CDCl_3$) 1.30 (3H, s, CH_3), 1.52 (3H, s, CH_3), 1.54–2.20 (2H, m, 6-Ha and Hb), 1.98 (3H, s, CH_3), 2.06 (3H, s, CH_3), 2.07 (3H, s, CH_3), 3.18–3.29 (1H, m, NCH_2CH_2), 3.38–3.52 (1H, m, 5-H), 3.98–4.36 (6H, m, 4-H, NCH_2CH_2 and 2×CH_2OAc), 4.96–5.18 (1H, d, $J=3.7$, 2-H), 5.08 (2H, s, *O*-Ch_2Ph), 5.34 (1H, br s, 3-H), 5.91 (1H, d, $J=3.7$, 1-H), 7.21–7.38 (5H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 20.7 (strong), 20.9, 25.9, 26.5 (*C*H_3), 28.8 (*C*-6), 42.6 (*N*-*C*H_2CH_2), 51.7 (*C*-5), 61.4, 62.7 (*C*H_2OAc), 67.5 (*O*-*C*H_2Ph), 74.5, 79.7, 83.2 (*C*-2/*C*-3/*C*-4), 104.4 (*C*-1), 111.7 (O-*C*-O), 127.5, 127.8, 128.3, 135.8 (Ar-*C*), 155.9, 169.1, 169.4, 170.5 (*C*O).

1,2-*O*-Isopropylidene-3,7-di-*O*-acetyl-5-(*N*-β-acetoxyethyl, *N*-benzoxycarbonyl)amino-5,6-dideoxy-β-L-ido-heptofuranose (17b). Acetylation of **14b** (1.2 g, 2.42 mmol) with acetic anhydride (4.45 g, 43.56 mmol) in pyridine (3 cm^3) for 3 h as stated for **14a** afforded **17b** (1.26 g, 77%) as a white solid[19] mp 83–84 °C; (Found: C, 58.00; H, 6.55. $C_{26}H_{35}NO_{11}$ requires C, 58.09; H, 6.56%); R_f = 0.50 (*n*-hexane/ethyl acetate = 1/1); $[\alpha]_D$ −17.5 (*c* 0.8 in $CHCl_3$); ν_{max} (nujol)/cm^{-1} 1744 and 1701; δ_H (300 MHz, $CDCl_3$) 1.29 (3H, s, CH_3), 1.50 (3H, s, CH_3), 1.49–2.30 (2H, m, 6-Ha and Hb), 1.98 (3H, s, CH_3), 2.02 (3H, s, CH_3), 2.08 (3H, s, CH_3), 2.35–3.09 (2H, m, 5-H and NCH_2CH_2), 3.92–4.30 (6H, m, 4-H, NCH_2CH_2 and 2×CH_2OAc), 4.48 (1H, d, $J=3.3$, 2-H), 5.10–5.19 (3H, m, 3-H and *O*-CH_2Ph), 5.86 (1H, d, $J=3.3$, 1-H), 7.25–7.33 (5H, m, Ar-*H*); δ_C (75 MHz, $CDCl_3$) 20.6, 20.8, 26.1, 26.3, 26.5 (*C*H_3), 27.2 (*C*-6), 41.1 (*N*-*C*H_2CH_2), 50.9 (*C*-5), 60.6, 61.7 (*C*H_2OAc), 67.1 (*O*-*C*H_2Ph), 75.8, 77.7, 83.4 (*C*-2/*C*-3/*C*-4), 104.1 (*C*-1), 111.9 (O-*C*-O), 127.4, 127.8, 128.3, 136.2 (Ar-*C*), 156.3, 169.4, 170.4, 170.5 (*C*O).

1,4,5-Trideoxy-1,4-imino-2,6-di-*O*-acetyl-*N*-(β-acetoxyethyl)-D-arabino-hexitol (18a). A solution of **17a** (0.85 g, 0.74 mmol) in TFA/water (5 cm^3, 3:2) was stirred at 30 °C for 3 h. Toluene (5 cm^3) was added and evaporated at reduced pressure to give a hemiacetal as a thick oil. To a mixture of hemiacetal in acetone/water (4 cm^3, 2:1) at 0 °C sodium metaperiodate (0.51 g, 2.37 mmol)

was added and stirred for 3 h. Ethylene glycol (0.3 cm^3) was added to the reaction mixture and extracted with dichloromethane (5 cm^3 × 3). The organic layer was dried, concentrated and the residue was purified by column chromatography (hexane/ethyl acetate = 3/1) to afford a semi-solid (0.78 g). To a solution of the semi-solid in dry methanol (5 cm^3) was added 10% Pd/C (0.15 g) and ammonium formate (0.6 g, 9.51 mmol). The reaction mixture was refluxed for 45 min and the solution was filtered through Celite, washed with methanol and concentrated. The residue was passed through silica column [hexane/ethyl acetate/ammonia solution (25%) = 64/35/1] to afford **18a** (0.38 g, 76%) as a thick oil (Found: C, 53.22; H, 7.52. $C_{14}H_{23}NO_7$ requires C, 52.99; H, 7.30%); R_f = 0.45 (hexane/ethyl acetate = 1/4); $[\alpha]_D$ −12.86 (*c* 1.4 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3400–3150 (br band) and 1734; δ_H (300 MHz, $CDCl_3 + D_2O$) 1.74–1.86 (1H, m, 5-Ha), 2.00–2.15 (1H, m, 5-Hb), 2.05 (3H, s, C*H*$_3$), 2.06 (3H, s, C*H*$_3$), 2.10 (3H, s, C*H*$_3$), 2.34–2.48 (2H, m, *N*-C*H*$_2$CH$_2$), 2.75 (1H, dd, *J* = 7.5 and 11.3, 1-Ha), 3.04 (1H, ddd, *J* = 5.5, 6.8 and 12.6, 4-H), 3.21 (1H, dd, *J* = 1.8 and 11.3, 1-Hb), 3.87 (1H, dd, *J* = 2.7 and 6.8, 3-H), 4.07–4.24 (4H, m, 2×C*H*$_2$OAc), 4.73 (1H, ddd, *J* = 1.8, 2.7 and 8.0, 2-H); δ_C (75 MHz, D_2O) 21.0, 21.1, 21.2 (*C*H$_3$), 29.9 (*C*-5), 51.7, 57.3 (*C*-1/*C*-1′), 61.3 (*C*-4), 62.5, 67.3 (*C*-2/*C*-6), 81.1 (*C*-2), 81.7 (*C*-3), 170.7, 170.9, 172.3 (*C*O).

1,4,5-Trideoxy-1,4-imino-2,6-di-*O*-acetyl-*N*-(β-acetoxyethyl)-L-xylo-hexitol (18b). A reaction of **17b** (1.0 g, 1.86 mmol) with TFA/water (6 cm^3, 3:2) for 3 h followed by sodium metaperiodate oxidation, hydrogenation as described for **17a** and purification by chromatography (*n*-hexane/ethyl acetate/ammonia = 70/28/2) gave **18b** as a thick oil (0.53 g, 90%) (Found: C, 53.24; H, 7.55. $C_{14}H_{23}NO_7$ requires C, 52.99; H, 7.30%); R_f = 0.35 (*n*-hexane/ethyl acetate = 1/4); $[\alpha]_D$ +40 (*c* 0.5 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 3450–3150 (br band) and 1736; δ_H (300 MHz, $CDCl_3 + D_2O$) 1.88–2.21 (2H, m, 5-H), 2.06 (6H, strong s, 2×C*H*$_3$), 2.08 (3H, s, C*H*$_3$), 2.34 (1H, dd, *J* = 5.7 and 10.7, 1-Ha), 2.53 (1H, dt, *J* = 5.7 and 13.2, *N*-C*H*$_2$CH$_2$), 2.69 (1H, ddd, *J* = 4.4, 4.7 and 9.6, 4-H), 3.05 (1H, dt, *J* = 5.7 and 13.2, *N*-C*H*$_2$CH$_2$), 3.65 (1H, dd, *J* = 6.6 and 10.7, 1-Hb), 4.02 (1H, dd, *J* = 1.7 and 4.7, 3-H), 4.08–4.25 (4H, m, 2×C*H*$_2$OAc), 4.88 (1H, ddd, *J* = 1.7, 5.2 and 6.6, 2-H); δ_C (75 MHz, $CDCl_3$) 21.0 (s), 21.1 (*C*H$_3$), 26.2 (*C*-5), 51.7, 57.2 (*C*-1/*C*-1′), 62.1 (C-4), 62.5, 64.3 (*C*H$_2$OAc), 75.9 (*C*-3), 79.6 (*C*-2), 170.7, 170.8, 170.9 (*C*O).

1,4,5-Trideoxy-1,4-imino-*N*-hydroxyethyl-D-arabino-hexitol (6). To a cooled (0 °C) solution of dry MeOH (2 cm^3) a piece of sodium (0.005 g) was added with stirring followed by **18a** (0.22 g, 0.69 mmol) in dry MeOH (1 cm^3). Reaction mixture was allowed to warm to 30 °C and stirred for 1.5 h. IR resin was added to the reaction mixture until pH became neutral, filtered and concentrated. The residue thus obtained was washed with dry dichloromethane, concentrated in vacuo and purified by IR resin column using $CHCl_3$/MeOH/NH_3 = 50/48/2 as eluant to afford tetraol **6** (0.13 g, 95%) as hygroscopic oil (Found: C, 49.98; H, 8.66. $C_8H_{17}NO_4$ requires C, 50.25; H, 8.36%); R_f = 0.20 ($CHCl_3$/MeOH = 1/1); $[\alpha]_D$ −13.04 (*c* 0.46 in MeOH); ν_{max} (nujol)/cm^{-1} 3450–3200 (br band); δ_H (300 MHz, D_2O) 1.58–1.73 (1H, m, 5-Ha), 1.85–1.98 (1H, m, 5-Hb), 2.28–2.42 (2H, m, *N*-C*H*$_2$CH$_2$), 2.68 (1H, dd, *J* = 6.3 and 11.3, 1-Ha), 2.85–3.00 (2H, m, 1-Hb and 4-H), 3.55–3.80 (5H, m, H-3 and 2×C*H*$_2$OH), 4.00 (1H, ddd, *J* = 1.5, 5.5 and 6.3, 2-H); δ_C (75 MHz, D_2O) 33.9 (*C*-5), 55.9, 59.1 (*C*-1/*C*-1′), 59.5 (strong, CH_2OH), 69.3 (*C*-4), 75.9 (*C*-3), 82.6 (*C*-2).

1,4,5-Trideoxy-1,4-imino-*N*-hydroxyethyl-L-xylo-hexitol (7). A reaction of **18b** (0.4 g, 1.26 mmol) with sodium methoxide in dry methanol (3 cm^3) for 1.5 h as described for **18a** followed by purification with IR resin column chromatography ($CHCl_3$/MeOH/NH_3 = 50/48/2) gave **7** as syrup (0.23 g, 96%) as a oil (Found: C, 50.41; H, 8.22. $C_8H_{17}NO_4$ requires C, 50.25; H, 8.36%); R_f = 0.19 ($CHCl_3$/MeOH = 1/2); $[\alpha]_D$ +40 (*c* 0.35 in MeOH); ν_{max} (nujol)/cm^{-1} 3460–3100 (br band); δ_H (300 MHz, D_2O) 1.71–1.82 (2H, m, 5-H), 2.26 (1H, dd, *J* = 5.2 and 11.0, 1-Ha), 2.41 (1H, dt, *J* = 5.7 and 12.6, *N*-C*H*$_2$CH$_2$), 2.77 (1H, dt, *J* = 5.1 and 9.0, 4-H), 2.91 (1H, dt, *J* = 6.8 and 12.6, *N*-C*H*$_2$CH$_2$), 3.38 (1H, dd, *J* = 6.1 and 11.0, 1-Hb), 3.60–3.68 (4H, m, 2×C*H*$_2$OH), 3.97 (1H, dd, *J* = 2.5 and 5.0, 3-H), 4.04–4.09 (1H, m, 2-H); δ_C (75 MHz, D_2O) 29.6 (*C*-5), 56.2, 58.8 (*C*-1/*C*-1′), 59.5, 59.6 (CH_2OH), 64.6 (*C*-4), 76.2 (*C*-3), 77.2 (*C*-2).

1,4,5-Trideoxy-1,4-imino-2,3,6-tri-*O*-acetyl-*N*-(β-acetoxyethyl)-D-arabino-hexitol (19a). To an ice-cold solution of **6** (0.10 g, 0.52 mmol) in pyridine (0.8 cm^3) was added acetic anhydride (0.1 g, 9.36 mmol). The reaction mixture was allowed to warm and stirred at 30 °C for 12 h. Toluene (4 cm^3) was added and evaporated at reduced pressure (three times). The residue thus obtained on chromatography (hexane/ethyl acetate/ammonia solution = 70/29/1)) gave tetra-acetate **19a** (0.17 g, 93%) as a thick oil (Found: C, 53.69; H, 7.32%. $C_{16}H_{25}NO_8$ requires C, 53.47; H, 7.01%); R_f = 0.46 (hexane/ethyl acetate = 1/1; $[\alpha]_D$ −46.80 (*c* 0.47 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1740 (br); δ_H (300 MHz, $CDCl_3$) 1.80–2.08 (2H, m, 5-H), 2.05 (3H, s, C*H*$_3$), 2.06 (6H, s, 2×C*H*$_3$), 2.09 (3H, s, C*H*$_3$), 2.50 (1H, dt, *J* = 5.3 and 13.2, *N*-C*H*$_2$CH$_2$), 2.62–2.68 (1H, m, *N*-C*H*$_2$CH$_2$), 2.78 (1H, dd, *J* = 5.3 and 11.3, 1-Ha), 3.01 (1H, ddd, *J* = 5.3, 7.1 and 12.1, 4-H), 3.17 (1H, dd, *J* = 1.5 and 11.3, 1-Hb), 4.05–4.26 (4H, m, 2×C*H*$_2$OAc), 5.01 (2H, br d, *J* = 5.3, 2-H and 3-H); δ_C (75 MHz, $CDCl_3$) 21.0 (strong), 21.1 (strong, *C*H$_3$), 29.7 (*C*-5), 52.2, 57.9 (*C*-1/*C*-1), 61.0 (*C*-4), 62.5, 66.3 (*C*H$_2$OAc), 76.6 (*C*-2), 80.7 (*C*-3), 169.7, 170.2, 170.6, 170.8 (*C*O).

1,4,5-Trideoxy-1,4-imino-2,3,6-tri-*O*-acetyl-*N*-(β-acetoxyethyl)-L-xylo-hexitol (19b). Acetylation of **7** (0.15 g, 0.78 mmol) with acetic anhydride (1.43 g, 14.04 mmol) in pyridine (1 cm^3) for 12 h as described for **6** and chromatographic purification (*n*-hexane/ethyl acetate/ammonia solution = 70/29/1) gave **19b** (0.27 g, 97%) as a thick syrup (Found: C, 53.69; H, 7.17. $C_{16}H_{25}NO_8$ requires C, 53.47; H, 7.01%); R_f = 0.41 (*n*-hexane/ethyl acetate = 2/3); $[\alpha]_D$ +28.0 (*c* 0.5 in $CHCl_3$); ν_{max} (neat)/cm^{-1} 1738 (br); δ_H (300 MHz, $CDCl_3$) 1.78–1.94 (2H,

m, 5-H), 2.04 (3H, s, CH_3), 2.07 (3H, s, CH_3), 2.08 (3H, s, CH_3), 2.12 (3H, s, CH_3), 2.33 (1H, dd, $J=5.2$ and 11.0, 1-Ha), 2.57 (1H, dt, $J=5.7$ and 13.2, N-CH_2CH_2), 2.89 (1H, ddd, $J=5.0$, 5.5 and 8.0, 4-H), 3.03 (1H, dt, $J=6.6$ and 13.2, N-CH_2CH_2), 3.65 (1H, dd, $J=6.6$ and 11.0, 1-Hb), 4.07–4.22 (4H, m, 2×CH_2OAc), 5.00 (1H, ddd, $J=2.5$, 5.2 and 6.6, 2-H), 5.22 (1H, dd, $J=2.5$ and 5.5, 3-H); δ_C (75 MHz, $CDCl_3$) 21.0 (strong, CH_3), 26.7 (*C*-5), 52.3, 57.6 (*C*-1/*C*-1′), 61.8 (*C*-4), 62.6, 62.9 (CH_2OAc), 76.5, 77.2 (*C*-2/*C*-3), 169.8, 169.9, 170.6, 170.7 (*C*O).

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17. The assignment of the relative stereochemistry at C-5 of the β-aminoester **9a** and **9b** was made earlier by ^{1}H NMR spectroscopy and by the conversion of **9a** and **9b** to compounds of known configuration (see ref 16d,f).

18. In this step, unprotected primary OH also react with CbzCl. So, we used diacetate compounds **12a** and **12b** for debenzylation and Cbz protection.

19. Compounds containing *N*-Cbz functionality showed doubling of signals in ^{1}H and ^{13}C NMR due to restricted rotation around C–N bond. The prominent

signals from the spectra were identified and assigned. In the ^{13}C NMR spectra of **14a**, **14b**, **17a** and **17b** C-5 and N-CH_2CH_2 carbons appeared with weak intensity signals.

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