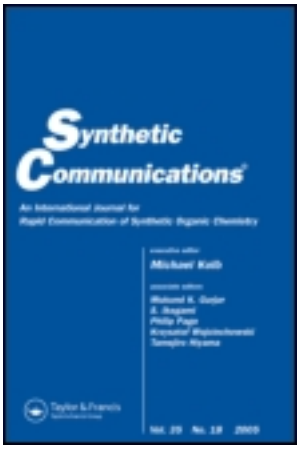

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A Convenient Synthesis of Novel Glycosyl Azetidines Under Mitsunobu Reaction Conditions

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A CONVENIENT SYNTHESIS OF NOVEL GLYCOSYL AZETIDINES UNDER MITSUNOBU REACTION CONDITIONS

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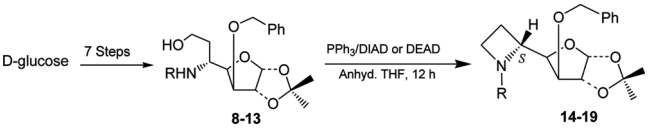
GRAPHICAL ABSTRACT



Abstract *A facile, simple, and high-yielding protocol for synthesis of novel glycosyl azetidines was developed from glycosyl* β*-amino alcohols* via *intramolecular cyclization under Mitsunobu reaction conditions.*

Keywords DIAD/PPh_3; glycosyl amino alcohol; glycosyl amino ester; glycosyl azetidines; Mitsunobu reaction

INTRODUCTION

Azetidines, the saturated four-membered monocyclic aza-heterocycles, have a special place in organic chemistry because of their occurrence in numerous biologically active natural products.[1] Apart from 2-azetidinone (β-lactams), they form a core skeleton to carbapenem antibiotics, mugineic acid, penaresidin/penazetidine, peptidyl polyoxins, and sphingosine classes of compounds obtained from numerous marine organisms.[2] These four-membered monocyclic aza-heterocycles have found diffuse applications in medicinal chemistry as pharmacological tools, in peptidomimetics as unnatural amino acids, and also in numerous natural products. The ability of azetidines to undergo various transformations such as cycloaddition,[3,4] ring expansion,[5] and ring opening[6] makes them highly valuable in organic synthesis. In comparison to the chemistry of β-lactams, the chemistry of azetidines has not

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This article is dedicated to V.K.T.'s doctoral mentor, Dr. R. P. Tripathi, Senior Scientist at Central Drug Research Institute, Lucknow, India.

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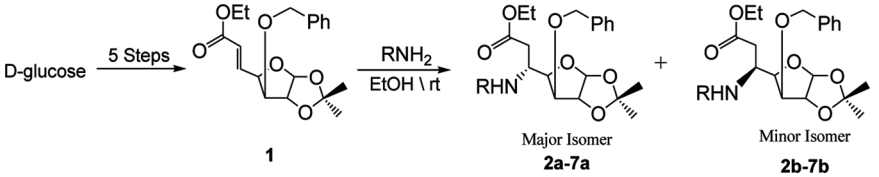
been much investigated and many of the efforts involving the azetidine nucleus have been directed toward its synthesis only.[7,8]

The most important and easy synthetic protocol to obtain azetidines involves the ring closure of amino alcohols (obtained by asymmetric reduction of β-amino ketones or β-amino acids) induced by transformation of the hydroxyl moiety into a good leaving group. Other important methods employed include the base-induced intramolecular cyclization of *N*-alkylamino oxiranes,[9] stereospecific ring opening of aziridines and subsequent ring closure with dimethyl sulfoxide,[10] metal-catalyzed intramolecular *N*H-insertion of diazo compounds,[11] electroreductive intramolecular cross coupling of imines with alkoxycarbonyl compounds, Pd-catalyzed coupling–cyclizations of allenes with phenyliodonium salts[12] or organic halides,[13] cycloaddition reactions of imines and alkenes,[14] rearrangement of four-membered or larger rings,[15] and reduction of azetidin-2-ones.[16a,b] However, these methods have not been well investigated in the area of carbohydrate chemistry.

The reports on carbohydrate derivatives with azetidine rings are scarce.[16c] In continuation of our efforts on development of carbohydrate-based potential chemotherapeutic agents,[17–19] the present communication introduces azetidines in the area of carbohydrate research and discloses a facile, simple, and high-yielding protocol for the synthesis of some novel glycosyl azetidines starting from glycosyl β-amino alcohols via intramolecular cyclization under Mitsunobu reaction conditions.

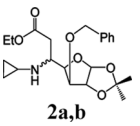
RESULTS AND DISCUSSION

The synthetic strategy starts from cheap and readily available D-glucose, which after processing through a number of high-yielding steps such as isopropylidene protection, 3-*O*-benzyl protection, selective 5,6-isopropylidene deprotection, $NaIO_4$ oxidation, and finally the Horner–Wadsworth–Emmons modification affords the glycosyl olefinic ester (1*R*,2*R*,3*S*,4*R*)-ethyl (3-*O*-benzyl-1,2-*O*-isopropylidene-1,4-pentofuranose-4-yl)-hept-5-enoate (**1**).[17a] The 1,4-conjugate addition of cyclopropyl amine to olefinic ester (**1**) afforded (1*R*,2*R*,3*S*,4*R*)-ethyl [3-*O*-benzyl-5-cyclopropyl-amino-5,6-dideoxy-1,2-*O*-isopropylidene]-α-D-gluco- and β-L-ido-hepto-furanuronate (**2a** and **2b**) as a diastereomeric mixture (73:27) in good yield (Scheme 1).[17a–c] The diastereoselectivity was determined by comparing the signals in ^{1}H NMR spectrum of crude product **2** obtained after conjugate addition reaction. In the majority of the cases the major isomer of glycosyl amino esters (**2a–7a**) were separated in pure form using column chromatography (SiO_2), whereas the minor isomer was contaminated with the major isomer. We tried with some known suitable catalyst to achieve the better diastereoselectivity, where unfortunately the $InCl_3$ or amidine bases such as 1,8-diazabicyclo [5.4.0]undec-7-ene (DBU) or 1,4-diazabicyclo[2.2.2]octane (DABCO) could not result in better selectivity. The $InCl_3$-catalyzed



Scheme 1. Synthesis of glycosylated amino ester (**2–7**).

Table 1. Conjugate addition of cyclopropyl amine to glycosyl olefinic ester **1**

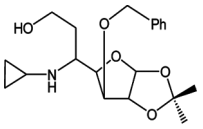
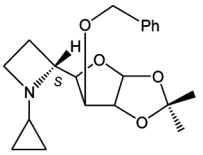
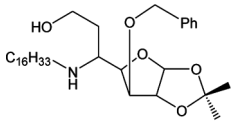
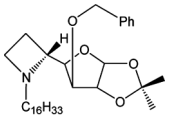
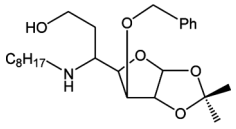
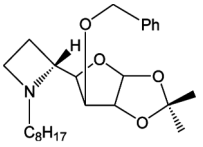
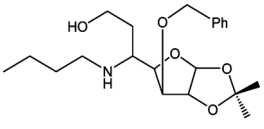
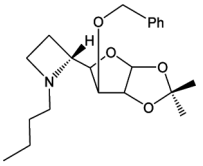
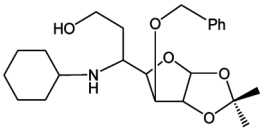
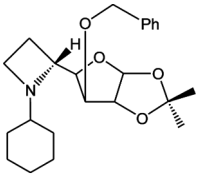
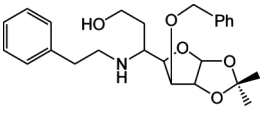
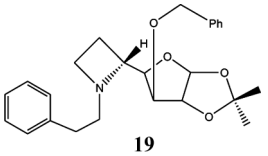
Glycosyl β-amino ester	Catalyst	Yield (%)	Time (h)	Diastereo selectivity (major/minor isomer)
 **2a,b**	—	80	40	73:27
	$InCl_3$ (5 mm %)	90	16	75:25
	$InCl_3$ (10 mm %)	90	16	75:25
	DBU	92	30	71:29
	DABCO	88	32	77:23

conjugate addition of cyclopropyl amine to olefinic ester **1** afforded compound **2a** with almost similar selectivity; however, yield was improved and reaction time was also reduced to 16 h (Table 1).

Thus, the predominant diastereoselectivity is only because of the presence of the alkene–arene π stacking effect as described earlier on the basis of Felkin–Anh-like transition-state model.[17a,b] Similarly, 1,4-conjugate addition of compound **1** with other aliphatic amines (viz, hexadecyl, *n*-octyl, *n*-butyl, cyclohexyl, and phenylethyl amine) led to the formation of corresponding glycosyl β-amino esters (**3–7**) in excellent yield.

Although the configuration at the newly formed stereogenic center at C-5 in compounds **2–7** was difficult to assign at this stage because in the majority of the cases the -OCH_2 (q) peak was merged with *H*-4 (dd) signal and complicated to determine the $J_{4,5}$ value. However, the configuration at C-5 was determined successfully after lithium aluminum hydride (LAH) reduction of specific major or minor isomers to the corresponding glycosyl amino alcohol (**9–13**), where $J = 9.6$ Hz was calculated for amino alcohol reduced from the major isomer while $J = 5.7$ Hz for the minor isomer and thus relative configuration was assigned as *S* and *R* for major (threo-) and minor (erythro-) isomers, respectively. As the C-5 stereocenter is not involved in the reduction process, the stereochemistry at this center would be the same as in the glycosyl amino esters already established. The LAH reduction of glycosyl β-amino ester **2a** affords the corresponding glycosyl β-amino alcohol (1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-benzyl-5-cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-1,4-pentofuranos-4-yl]-β-L-ido-heptanol (**8**) in 90% yield. ^{1}H NMR spectrum of compound **8** exhibited signals corresponding to 15 proton resonances. An aromatic multiplet integrated to five protons appeared at δ 7.33 was identified for the phenyl group whereas a doublet observed at δ 5.95 (1H, $J = 3.9$ Hz) was evidenced for *H*-1. The two doublets of one proton each were observed at δ 4.72 ($J = 11.8$ Hz) and 4.41 ($J = 11.8$ Hz) were assigned for benzylic protons -OCH_APh and -OCH_BPh, respectively. A doublet appearing at δ 4.65 (1H, $J = 3.9$ Hz) was identified for *H*-2 while a double doublet integrated to one proton observed at δ 4.17 ($J = 9.6$, 3.3 Hz) was evidenced for *H*-4. A doublet appearing at δ 3.82 (1H, $J = 3.3$ Hz) was assigned for *H*-3 whereas a two-proton multiplet observed at δ 3.73 was identified for hydroxyl methylene protons (*H*-7). Similarly, multiplets of one proton each observed at δ 3.31 and δ 2.43 were evidenced for *H*-5 and -NC*H*, respectively. A multiplet integrated to eight protons appearing at δ 1.43–1.33 was assigned for corresponding two methyl resonances of isopropylidene unit and methylene protons *H*-6 whereas four methylene protons of the cyclopropyl ring

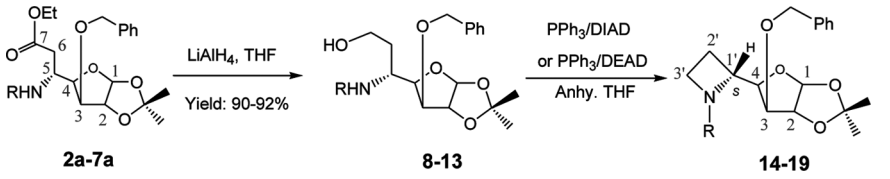
Table 2. Glycosyl azetidines **(14–19)** synthesized from β-amino alcohols **(8–13)** via Scheme 2

Entry	Glycosyl amino alcohol **(8–13)**[a]	Reaction conditions	Glycosyl azetidines **(14–19)**	Yields (%)[b]
1	 **8**	PPh_3/DEAD (1.2 eq)	 **14**	45[c]
2	**8**	PPh_3/DEAD (1.5 eq)	**14**	48
3	**8**	PPh_3/DIAD (1.2 eq)	**14**	58
4	**8**	PPh_3/DIAD (1.5 eq)	**14**	63
5	 **9**	PPh_3/DIAD (1.5 eq)	 **15**	65
6	 **10**	PPh_3/DIAD (1.5 eq)	 **16**	62
7	 **11**	PPh_3/DIAD (1.5 eq)	 **17**	60
8	 **12**	PPh_3/DIAD (1.5 eq)	 **18**	60
9	 **13**	PPh_3/DIAD (1.5 eq)	 **19**	64

[a]Diastereoselectivity of conjugate additions was determined by comparative signal in ^{1}H NMR spectrum of crude glycosyl β-amino ester (**2–7**), where $InCl_3$ or DBU/DABCO could not result in better selectivity and the configuration was determined by $J_{4,5}$ in ^{1}H NMR spectrum of corresponding alcohols.

[b]Yield refers the isolated product. All intramolecular cyclization reactions were carried out in anhydrous THF for 12 h.

[c]Intermolecular cyclization of compound **8** using PPh_3/DEAD results in comparatively poor yield of compound **14**.



Scheme 2. Synthesis of *N*-substituted glycosyl azetidines (**14–19**).

resonated as a multiplet at δ 0.46–0.39. Compound **8** exhibited a broad absorption band at 3730 cm^{-1} corresponding to OH group, and 20 carbon resonances appearing in ^{13}C NMR in addition to the molecular ion peak $(M+H)^+$ observed at m/z 364 in the mass spectrum finally confirmed the structure. Similar LAH reduction of glycosyl β-amino esters (**3a–7a**) results in the formation of corresponding glycosyl β-amino alcohols (**9–13**) in excellent yield.

The esters and related compounds can be easily prepared by reaction of alcohol and carboxylic acids under Mitsunobu reaction condition using azodicarboxylate (DEAD) and triphenylphosphine (PPh_3). To achieve the practical and easy synthesis of novel glycosyl azetidines, we turned our attention to a related chemistry. The intramolecular cyclization of **8** with PPh_3 in the presence of DEAD in anhydrous tetrahydrofuran(THF) afforded 2-(3-*O*-benzyl-5,6-dideoxy-6-hydroxymethyl-1,2-*O*-isopropylidene-β-L-ido-furanose)-1-cyclopropyl azetidine (**14**) in poor yield (Table 2).

However, intramolecular cyclization of glycosyl β-amino alcohols **(8–13)** using DIAD not just increases the product yield significantly but also avoids various hazards associated with the use of DEAD (e.g., toxic, shock sensitive, thermally unstable, etc). Because the involved alcohols are of primary nature, inversion of configuration under Mitsunobu reaction condition is not a problem. Based on the same methodology, various glycosyl β-amino alcohols (**8–13**) were prepared from glycosyl amino esters (**2–7**) having *S* stereochemistry at C-5 (major compound) and were cyclized intramolecularly to afford corresponding glycosyl azetidines **(14–19)** in good yield under Mitsunobu reaction condition using PPh_3 and DIAD (Scheme 2). In ^1H NMR spectrum, proton resonances of glycosyl azetidines **(14–19)** resembled closely those observed in glycosyl β-amino alcohols (**8–13**) with no significant difference except the multiplets corresponding to hydroxyl methylene protons were now shifted upfield while the signal corresponding to –NC*H* disappeared. In addition to all the sugar carbon signals, the peaks appeared at δ 64.42 (C-1′), 54.59 (C-3′), and 37.69 (C-2′) in ^{13}C NMR of compound **14** corresponding to azetidine ring and the mass spectra(MS) at m/z 346 (M + H) with supported elemental analysis finally confirms the structure of synthesized glycosyl azetidine (**14**). All the synthesized glycosyl amino esters (**2–7**), glycosyl β-amino alcohols (**8–13**), and glycosyl azetidines (**14–19**) were purified by column chromatography using silica gel and characterized through spectroscopic techniques including IR, ^1H NMR, ^{13}C NMR, MS, and elemental analysis.

CONCLUSION

In conclusion, the novel glycosyl azetidines with different substitution patterns on *N*-atoms have been synthesized through a simple, facile, and high-yielding protocol via intramolecular cyclization of glycosyl β-amino alcohols under Mitsunobu

reaction condition. The azetidine ring formation under the Mitsunobu reaction offers several advantages including (a) the mild reaction conditions, (b) simple workup procedure, and (c) good yields of the desired products. To the best of our knowledge all the synthesized glycosyl azetidiens (**14–19**) are novel. Moreover, the use of DIAD has also been disclosed for the first time in the construction of an azetidine ring. The developed glycosyl azetidine may be useful in the development of well-defined natural and synthetic imino sugar, where the work on this direction is in progress in our laboratory.

EXPERIMENTAL

Glassware was dried over an open flame before use in connection with an inert atmosphere (N_2), and solvents were evaporated under reduced pressure at <55 °C. Unless otherwise stated, all materials were obtained from commercial suppliers (Sigma Aldrich Company, SRL, and Spectrochem Pvt. Ltd.) and were used without further purification. Silica gel (230–400 mesh) from commercial supplier Spectrochem Pvt. Ltd. was used for column chromatography. The thin-layer chromatographic(TLC) spots were visualized by spraying Liebermann–Burchard reagent and iodine (I_2) developer wherever applicable. IR spectra were recorded as KBr pellets on a Perkin-Elemer RX-1 spectrometer. Elemental analyses were performed on a Perkin-Elmer 2400 C, H, N analyzer, and results were found to be within ±0.4% of the calculated values. NMR spectra for the compounds were obtained on a Jeol AL300 FT-NMR spectrometer (300 MHz for ^{1}H, 75 MHz for ^{13}C NMR) in $CDCl_3$. Chemical shifts are given in parts per million(ppm) downfield from internal tetramethylsilane(TMS); *J* values are given in hertz(Hz). The mass spectra were recorded on a Jeol JMS D 300 spectrometer with accelerating potential of 3 kV and an ionization potential of 30 eV or on a Jeol SX-102(EI/CI/FAB) mass spectrometer.

Syntheses of Glycosyl β-Amino Esters (2–7)

(1*R*,2*R*,3*S*,4*R*)-Ethyl [3-*O*-benzyl-5-cyclopropyl-amino-5,6-dideoxy-1,2-*O*-isopropylidene]-α-D-gluco and β-L-ido-heptofuranuronate (2). A solution of glycosyl olefinic ester **1** (3.48 g, 10.0 mmol) dissolved in EtOH (15 mL) was stirred with cyclopropylamine (1.16 mL, 10.8 mmol) at room temperature (25 °C). On completion of the reaction (monitored through TLC), the solvent was evaporated under reduced pressure and the syrup thus obtained was dissolved in ethyl acetate (100 mL) and washed with H_2O (2 × 25 mL). The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to obtain a crude product, which on silica-gel column chromatography using *n*-hexane–EtOAc (80:20) as eluant afforded compound **2** as a colorless solid in diastereomeric ratio 73:27 (yield: 80%); $[\alpha]_D = -60.0$ (*c*, 0.30, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 3350 (NH), 2956 and 2918 (CH_3 and CH_2 stretching), 1730 (>C=O); MS (FAB): 406 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (m, 5 H, Ar-H), 5.94 (d, *J* = 3.7 Hz, 1 H, H-1), 4.72 (d, *J* = 12 Hz, 1 H, -OCH$_A$Ph), 4.64 (d, *J* = 3.7 Hz, 1 H, H-2), 4.46 (d, *J* = 12 Hz, 1 H, -OCH$_B$Ph), 4.22–4.07 (m, 3 H, H-4 and -OC*H*$_2$), 3.91 (d, *J* = 2.7 Hz, 1 H, H-3), 3.58 (m, 1 H, H-5), 3.36–2.16 (m, 3 H, -NC*H* and H-6), 1.63 (bs, 1 H, NH), 1.48 and 1.32 [each s, each 3 H, 2 × >C(C*H*$_3$)$_2$], 1.24 (t, *J* = 7.1 Hz, 3 H, -OCH$_2$C*H*$_3$), 0.39–0.35 (m, 4

H, CH_2's) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 171.79$ (>C=O), 136.99, 128.47, 128.09, 127.99 (Ar-C), 111.57 [$2\times > C(CH_3)_2$], 104.78 (C-1), 81.82 (C-2), 81.74 (C-4), 81.49 (C-3), 71.49 (OCH_2Ph), 60.28 (OCH_2), 54.24 (C-5), 36.26 (C-6), 28.06 (NCH), 26.72 and 26.28 [$2\times > C(CH_3)_2$], 14.20 (OCH_2CH_3), 7.31 and 5.68 ($2\times$ CH_2's) ppm. Similar conjugate addition of cyclopropyl amine to olefinic acid **1** in presence of catalytic amount of $InCl_3$ results in the glycosyl amino ester **2** in the same selectivity; however, the reaction time was reduced to 16 h.

(1*R*,2*R*,3*S*,4*R*)-Ethyl [3-*O*-benzyl-5,6-dideoxy-5-(hexadec-1-yl-amino)-1,2-*O*-isopropylidene]-α-D-gluco and β-L-ido-heptofuranuronate (3). Reaction of olefinic ester **1** with hexadecylamine and workup as described previously gave compound **3** as a colorless solid in diastereomeric ratio 65:35 (yield: 92%); $[\alpha]_D = -32.0$ (*c*, 0.15, $CHCl_3$); IR (KBr): ν_{max} cm^{-1} 3332 (NH), 2921 and 2852 (CH_3 and CH_2 stretching), 1730 (>C=O); MS (FAB): 591 $[M+2]^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.32$ (m, 5 H, Ar-H), 5.91 (d, $J = 3.7$ Hz, 1 H, H-1), 4.67 (d, $J = 11.8$ Hz, Hz, 1 H, -OCH_APh), 4.64 (d, $J = 3.7$ Hz, 1 H, H-2), 4.47 (d, $J = 11.8$ Hz, 1 H, OCH_BPh), 4.09–4.11 (m, 3 H, H-4 and OCH_2), 3.92 (d, $J = 2.7$ Hz, 1 H, H-3), 3.44 (m, 1 H, H-5), 2.50 and 2.36 (m, 4 H, H-6 and NHCH_2), 1.58 (bs, 1 H, NH), 1.47 and 1.31 [each s, each 3 H, $2\times > C(CH_3)_2$], 1.24 (m, 31 H, CH_2's and -OCH_2CH_3), 0.87 (t, $J = 6.6$ Hz, 3 H, CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 171.83$ (>C=O), 137.09, 128.47, 128.03 and 127.86 (Ar-C), 111.59 [$>C(CH_3)_2$], 104.80 (C-1), 82.11 (C-2), 81.82 (C-4), 81.72 (C-3), 71.47 (-OCH_2Ph), 60.32 (OCH_2CH_3), 54.05 (C-5), 47.36 (NHCH_2), 36.35 (C-6), 32.32, 30.83, 30.09, 27.75 and 23.08 (CH_2's), 26.74 and 26.31 [$2\times > C(CH_3)_2$], 14.18 and 14.10 (OCH_2CH_3 and CH_2CH_3) ppm.

(1*R*,2*R*,3*S*,4*R*)-Ethyl [3-*O*-benzyl-5-octylamino-5,6-dideoxy-1,2-*O*-isopropylidene]-α-D-gluco- and β-L-ido-heptofuranuronate (4). The reaction of olefinic ester **1** with octylamine and workup as described previously gave a diastereomeric mixture of compound **4** as a colorless oil (yield: 94%); $[\alpha]_D = -24.2$ (*c*, 0.28, $CHCl_3$); IR: ν_{max} cm^{-1} 3350 (NH), 3040, 2990, 2880 (CH_3 and CH_2 stretching), 1730 (>C=O); MS (FAB): 478 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33 (m, 5 H, Ar-H), 5.89 (d, $J = 3.7$ Hz, 1 H, H-1), 4.71 (d, $J = 12.0$ Hz, 1 H, -OCH_APh), 4.64 (d, $J = 3.7$ Hz, 1 H, H-2, major isomer), 4.51 (d, $J = 12.0$ Hz, 1 H, -OCH_BPh), 4.25–4.08 (m, 3 H, H-4 and -OCH_2CH_3), 3.97 (d, $J = 3.1$ Hz, 1 H, H-3), 3.39 (m, 1 H, H-5), 2.75–2.30 (m, 4 H, -NHCH_2, H-6_A and H-6_B), 1.54 [bs, 1 H, -NH(CH_2)$_7CH_3$], 1.49–1.27 [m, 18 H, $2\times > C(CH_3)_2$ and CH_2's], 1.25 (t, $J = 7.1$ Hz, Hz, 3 H, -OCH_2CH_3), 0.87 [t, $J = 6.9$ Hz, 3 H, -NH(CH_2)$_7CH_3$] ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.54$ (>C=O), 137.59, 128.49, 128.45 and 127.84 (Ar-C), 111.90 [$>C(CH_3)_2$], 105.00 (C-1), 82.80 (C-2), 82.20 (C-4), 81.63 (C-3), 72.22 (-O-CH_2Ph), 60.41 (-OCH_2CH_3), 52.66 (C-5), 47.00 (-NHCH$_2$), 35.81 (C-6), 31.83, 30.69, 29.52, 26.80, 26.19, 22.65 (CH_2's), 27.33 and 26.35 [$2\times > C(CH_3)_2$], 14.24 (-OCH_2CH_3), 14.10 [-NH(CH_2)$_7CH_3$] ppm. Anal. calcd. for $C_{27}H_{43}NO_6$: C, 67.88; H, 9.08; N, 2.93. Found: C, 67.96; H, 9.13; N, 2.88.

(1*R*,2*R*,3*S*,4*R*)-Ethyl [3-*O*-benzyl-5-butylamino-5,6-dideoxy-1,2-*O*-isopropylidene]-α-D-gluco- and β-L-ido-heptofuranuronate (5). Reaction of olefinic ester **1** with *n*-butyl amine and workup as described previously gave a

diastereomeric mixture of compound **5** as a colorless oil; 90%); $[\alpha]_D = -42.3$ (*c*, 0.18, $CHCl_3$); IR: ν_{max} cm^{-1} 3350 (NH), 3040, 2990, 2880 (CH_3 and CH_2 stretching), 1730 (>C=O); MS (FAB): 422 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): δ 7.32 (m, 5 H, Ar-H), 6.10 (d, $J = 3.7$ Hz, 1 H, H-1, major isomer), 4.84 (d, $J = 12$ Hz, 1 H, -OCH_APh), 4.69 (d, $J = 3.7$ Hz, 1 H, H-2, major isomer), 4.58 (d, $J = 12$ Hz, 1 H, -OCH_BPh), 4.17–4.10 (m, 3 H, H-4 and -OCH_2CH_3), 3.22–3.20 (m, 2 H, H-5 and H-3), 2.65 (m, 2 H, -$NHCH_2$), 2.38 and 2.32 (dd, $J = 15.6$ Hz and 4.7 Hz, 1 H, H-6_A), 2.25 and 2.19 (dd, $J = 15.6$ Hz and 6.6 Hz, 1 H, H-6_B), 1.59 [bs, 1 H, -$NH(CH_2)_3CH_3$], 1.40–1.27 [m, 11 H, $2 \times > C(CH_3)_2$, $NHCH_2CH_2CH_2$ and OCH_2CH_3], 0.88 [t, $J = 7.2$ Hz, 3 H, -$NH(CH_2)_3CH_3$] ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.20 (>C=O), 137.51, 129.10, 128.42 and 128.14 (each Ar-C), 111.90 [$>C(CH_3)_2$], 105.21 (C-1), 82.63 (C-2), 82.26 (C-4), 82.12 (C-3), 71.88 (-O-CH_2Ph), 60.68 (OCH_2CH_3), 54.44 (C-5), 47.34 ($NHCH_2$), 36.74 (C-6), 32.90 ($NHCH_2CH_2$), 27.14 and 26.73 [$2 \times > C(CH_3)_2$], 20.81 [$NH(CH_2)_2CH_2CH_3$], 14.57 (OCH_2CH_3), 14.36 [$NH(CH_2)_3CH_3$] ppm.

(1*R*,2*R*,3*S*,4*R*)-Ethyl [3-*O*-benzyl-5-cyclohexylamino-5,6-dideoxy-1,2-*O*-isopropylidene]-α-D-gluco- and β-L-ido-heptofuranuronate (6). Reaction of olefinic ester **1** with cyclohexylamine and workup as described previously gave a diastereomeric mixture of compound **6** as colorless oil; $[\alpha]_D = -22.6$ (*c*, 0.18, $CHCl_3$); IR: ν_{max} cm^{-1} 3350 (NH), 3040, 2990, 2880 (CH_3 and CH_2 stretching), 1730 (>C=O); MS (FAB): 448 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): δ 7.33 (m, 5 H, Ar-H), 5.93 (d, $J = 3.7$ Hz, 1 H, H-1, major isomer), 4.70 (d, $J = 12$ Hz, 1 H, -OCH_APh), 4.64 (d, $J = 3.7$ Hz, 1 H, H-2, major isomer), 4.45 (d, $J = 12$ Hz, 1 H, -OCH_BPh), 4.12–4.07 (m, 3 H, H-4 and OCH_2CH_3), 3.93 (d, $J = 3.1$ Hz, 1 H, H-3), 3.40 (m, 1 H, H-5), 2.65 (m, 1 H, -NHC*H*), 2.38 and 2.32 (dd, $J = 15.6$ Hz and 4.7 Hz, 1 H, H-6_A), 2.65 and 2.49 (dd, $J = 15.6$ Hz and 6.6 Hz, 1 H, H-6_B), 2.35 (m, 1 H, NHC*H*), 2.12–2.09 (m, 2H, $2 \times CH_2$), 1.70 (bs, 1 H, -N*H*), 1.48–1.23 [s, 12 H, $2 \times CH_3$ and cyclohexyl ring] ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.20 (>C=O), 137.51, 129.10, 128.42 and 128.14 (Ar-C), 111.90 [$>C(CH_3)_2$], 105.21 (C-1), 82.63 (C-2), 82.26 (C-4), 82.12 (C-3), 71.88 (-O*C*H_2Ph), 60.68 (-O-*C*H_2CH_3), 54.44 (C-5), 47.34 (-NHCH), 36.74, 33.4, 29.9, 25.6, and 25.5 (CH_2's), 27.14 and 26.73 [$2 \times > C(CH_3)_2$], 14.57 (-OCH_2CH_3) ppm. Anal. calcd. for $C_{25}H_{37}NO_6$: C, 67.07; H, 8.34; N, 3.13. Found: C, 67.12; H, 8.41; N, 3.16.

(1*R*,2*R*,3*S*,4*R*)-Ethyl [3-*O*-benzyl-5-phenylethylamino-5,6-dideoxy-1,2-*O*-isopropyl-idene]-α-D-gluco- and β-L-ido-heptofuranuronate (7). Conjugate addition of phenylethylamine to olefinic ester **1** and workup as described previously gave a diastereomeric mixture of compound **7** as a colorless oil; $[\alpha]_D = -18.0$ (*c*, 0.11, $CHCl_3$); IR: ν_{max} cm^{-1} 3350 (-NH), 3020, 2980, 2920 (CH_3 and CH_2 stretching), 1710, (>C=O); MS (FAB): 470 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): δ = 7.30 (m, 10 H, Ar-H), 5.93 (d, $J = 3.9$ Hz, 1 H, H-1), 4.68 (d, $J = 12$ Hz, 1 H, -OCH_APh), 4.62 (d, $J = 3.9$ Hz, 1 H, H-2), 4.43 (d, $J = 12$ Hz, 1 H, -OCH_BPh), 4.19 and 4.16 (dd, $J = 9.0$ Hz and 3.3 Hz, 1 H, H-4), 4.10 (q, $J = 7.14$ Hz, 2 H, -OCH_2CH_3), 3.90 (d, $J = 3.19$ Hz, 1 H, H-3), 3.48 (m, 1 H, H-5), 2.92 (t, 2 H, -$NHCH_2CH_2$Ph), 2.76 (t, 2 H, -$NHCH_2CH_2$Ph), 2.41 and 2.36 (dd, $J = 15.6$ Hz and 4.8 Hz, 1 H, H-6_A), 2.29 and 2.25 (dd, $J = 15.6$ Hz and 6.6 Hz, 1 H, H-6_B), 1.70 (bs, 1 H, -N*H*), 1.47 and, 1.31 [each s, each 3 H, $2 \times > C(CH_3)_2$], 1.20 (t, $J = 7.14$ Hz, 3 H, -OCH_2CH_3)

ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 172.80 (>C=O), 141.07, 137.97, 128.86, 128.69, 128.42, 128.26, 128.12 and 127.27 (Ar-C), 111.98 [>*C*$(CH_3)_2$], 105.20 (C-1), 82.60 (C-2), 82.40 (C-4), 82.22 (C-3), 71.37 (-O*C*H_2Ph), 60.26 (-O*C*H_2CH_3), 53.79 (C-5), 48.63 (*C*H_2), 36.73 (C-6), 36.25 (N*C*H_2), 26.68 and 26.24 [2 × > C(*C*$H_3)_2$], 14.10 (-OCH_2*C*H_3) ppm. Anal. calcd. for $C_{27}H_{35}NO_6$: C, 69.05; H, 7.52; N, 2.98. Found: C, 68.95; H, 7.57; N, 2.94.

Syntheses of Glycosyl β-Amino Alcohols (8–13)

(1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-Benzyl-5-cyclopropyl amino-5,6-dideoxy-1,2-*O*-isopropylidene-1,4-pento-furanos-4-yl]-β-L-ido-heptanol (8). A solution of major glycosyl amino ester **2a** (0.5 g, 1.52 mmol) in anhydrous THF (5.0 ml) was added drop-wise to the stirring slurry of $LiAlH_4$ (0.058 g, 1.52 mmol) in anhydrous THF (5.0 ml) at 0 °C under a nitrogen atmosphere. The reaction mixture was stirred for 30 min at 0 °C followed by stirring for further 3 h at ambient temperature. On completion of reaction, excess reducing agent was quenched by adding saturated aqueous Na_2SO_4 solution and the reaction mixture was filtered. The solid cake was washed with THF, and the filtrate was concentrated under reduced pressure followed by extraction with chloroform (2 × 25 ml) and water (12 ml). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to give a crude mass, which on silica-gel column chromatography using chloroform–methanol (98:2) as eluent afforded glycosyl β-amino alcohol **8** as a colorless oil (yield: 90%); $[\alpha]_D = -88.6$ (*c*, 0.43, $CHCl_3$); IR: ν_{max} cm^{-1} 3730 (OH), 3350 (NH), 2970 and 2910 (CH_2 and CH_3 stretching); MS (FAB): 364 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33 (m, 5 H, Ar-H), 5.95 (d, *J* = 3.9 Hz, 1 H, H-1), 4.72 (d, *J* = 11.8 Hz, 1 H, -OCH_APh), 4.65 (d, *J* = 3.9 Hz, 1 H, H-2), 4.41 (d, *J* = 11.8 Hz, Hz, 1 H, -OCH_BPh), 4.17 (dd, *J* = 9.6 and 3.3 Hz, 1 H, H-4), 3.82 (d, *J* = 3.3 Hz, 1 H, H-3), 3.73 (m, 2 H, H-7), 3.31 (m, 1 H, H-5), 2.43 (m, 1 H, NCH), 1.43–1.33 [m, 8 H, >C$(CH_3)_2$ and H-6], 0.46–0.39 (m, 4 H, cyclopropyl ring CH_2's) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.80, 128.52, 128.26 and 128.15 (Ar-C), 111.54 [>*C*$(CH_3)_2$],], 104.70 (C-1), 82.74 (C-2), 81.68 (C-4), 81.26 (C-3), 71.65 (O*C*H_2Ph), 62.69 (C-7), 57.82 (C-5), 30.2 (C-6), 28.51 (CH), 26.65 and 26.14 [2 × > C(*C*$H_3)_2$], 6.44 and 6.42 (2 × CH_2) ppm.

(1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-Benzyl-5,6-dideoxy-5-hexadecylamino-1,2-*O*-isopropylidene-1,4-pentofu-ranos-4-yl]-β-L-ido-heptanol (9). Reduction of glycosyl β-amino ester **3a** (major isomer) with $LiAlH_4$ and workup as described previously gave corresponding glycosyl β-amino alcohol **9** as a colorless oil (yield 90%), $[\alpha]_D = -27.0$ (*c*, 0.50, $CHCl_3$); IR: ν_{max} cm^{-1} 3740 (OH), 3346 (NH), 2927 and 2856 (CH_3 and CH_2 stretching); MS (FAB): 548 $(M+H)^+$; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.29 (m, 5 H, Ar-H), 5.93 (d, *J* = 3.7 Hz, 1 H, H-1), 4.71 (d, *J* = 11.6 Hz, 1 H, -O*C*H_APh), 4.65 (d, *J* = 3.7 Hz, 1 H, H-2), 4.41 (d, *J* = 11.6 Hz, Hz, 1 H, –O*C*H_BPh), 4.21 (dd, *J* = 9.4 and 3.0 Hz, 1 H, H-4), 3.83 (d, *J* = 3.0 Hz, 1 H, H-3), 3.76 (m, 2 H, H-7), 3.26 (m, 1H, H-5), 2.70 (m, 2 H, N*C*H_2), 1.53–1.25 (m, 36 H, 2 × > C(C$H_3)_2$, H-6, 14 × CH_2's), 0.87 (t, *J* = 6.6 Hz, 3 H, -CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ = 136.5, 128.55, 128.33 and 128.04 (Ar-C), 111.64 [>*C*$(CH_3)_2$], 104.64 (C-1), 81.81 (C-2), 81.22 (C-4), 81.09 (C-3), 71.70 (–O*C*H_2Ph),

62.31 (C-7), 57.12 (C-5), 46.11 (NCH_2), 32.2, 30.0, 29.9, 29.8, 29.7, 29.4, 27.44 and 26.71 (CH_2's), 27.20 and 26.19 [$2 \times >C(CH_3)_2$], 14.11 (CH_2CH_3) ppm.

(1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-Benzyl-5,6-dideoxy-5-octylamino-1,2-*O*-isopropylidene-1,4-pentofuranos-4-yl]-β-L-ido-heptanol-(10). Reduction of glycosyl β-amino ester **4a** (major isomer) with $LiAlH_4$ and workup as described previously gave corresponding glycosyl β-amino alcohol **10** as colorless oil (yield 92%); $[\alpha]_D = -18.2$ (*c*, 0.2, $CHCl_3$); IR: ν_{max} cm^{-1} 3330 (NH), 2929 and 2857 (CH_3 and CH_2 stretching); MS (FAB): 436 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$ (m, 5 H, Ar-H), 5.93 (d, $J = 3.8$ Hz, 1 H, H-1), 4.70 (d, $J = 11.7$ Hz, 1 H, -OCH_APh), 4.65 (d, $J = 3.8$ Hz, 1 H, H-2), 4.41 (d, $J = 11.7$ Hz, 1 H, -OCH_BPh), 4.21 (dd, $J = 9.6$ and 3.0 Hz, 1 H, H-4), 3.82 (d, $J = 3.0$ Hz, 1 H, H-3), 3.24 (m, 3 H, H-5 and NCH_2), 1.50 (bs, 1 H, -NH), 3.69 (m, 2 H, H-7), 1.41–1.25 [m, 20 H, $>C(CH_3)_2$, H-6 and $6 \times CH_2$'s] and 0.87 (t, $J = 6.9$ Hz, 3 H, CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 136.85$, 128.51, 128.18 and 128.00 (Ar-C), 111.59 [$>C(CH_3)_2$], 104.63 (C-1), 81.84 (C-2), 81.22 (C-4), 81.18 (C-3), 71.68 (OCH2Ar), 62.39 (C-7), 57.10 (C-5), 46.09 (NCH_2), 31.78, 30.38, 29.19, 28.76, 27.19, 22.61 (CH_2's), 26.69 and 26.18 [$>C(CH_3)_2$], 14.05 (CH_2CH_3) ppm. Anal. calcd. for $C_{25}H_{41}NO_5$: C, 68.93; H, 9.49; N, 3.22. Found: C, 68.97; H, 9.46; N, 3.25.

(1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-Benzyl-5,6-dideoxy-5-butylamino-1,2-*O*-isopropylidene-1,4-pentofuranos-4-yl]-β-L-ido-heptanol (11). Reduction of glycosyl β-amino ester **5a** (major isomer) with $LiAlH_4$ and workup as described previously gave corresponding glycosyl β-amino alcohol **11** as a colorless oil (yield 90%); $[\alpha]_D = -43.3$ (*c*, 0.15, $CHCl_3$); IR: ν_{max} cm^{-1} 3346, 2927 and 2856 (CH_3 and CH_2 stretching); MS (FAB): 380 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.32$ (m, 5 H, Ar-H), 5.94 (d, $J = 3.6$ Hz, 1 H, H-1), 4.69 (d, $J = 11.6$ Hz, 1 H, -OCH_APh), 4.64 (d, $J = 3.7$ Hz, 1 H, H-2), 4.40 (d, $J = 11.6$ Hz, 1 H, -OCH_BPh), 4.20 (dd, $J = 9.4$ and 3.0 Hz, 1 H, H-4), 3.83 (d, $J = 3.0$ Hz, 1 H, H-3), 3.72 (m, 2 H, H-7), 3.24 (m, 1 H, H-5), 2.75 (m, 2 H, NCH_2), 1.53–1.25 (m, 12 H, $>C(CH_3)_2$, H-6 and $2 \times CH_2$'s), 0.87 (t, $J = 6.9$ Hz, 3 H, -CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 136.5$, 129.1, 128.9 and 128.78 (Ar-C), 113.0 [$>C(CH_3)_2$], 105.4 (C-1), 82.2 (C-2), 81.4 (C-4), 79.72 (C-3), 72.3 (-OCH_2Ph), 59.9 (C-7), 58.4 (C-5), 47.3 (NCH_2), 32.2, 30.0, 29.9, 29.4, and 27.2 (CH_2's), 27.44 and 27.0 [$2 \times >C(CH_3)_2$], 14.4 (CH_2CH_3) ppm.

(1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-Benzyl-5,6-dideoxy-5-cyclohexylamino-1,2-*O*-isopropylidene-1,4-pento-furanos-4-yl]-β-L-ido-heptanol (12). Reduction of glycosyl β-amino ester **6a** (major isomer) with $LiAlH_4$ and workup as described previously gave the corresponding glycosyl β-amino alcohol **12** as a colorless oil (yield 90%); $[\alpha]_D = -14.9$ (*c*, 0.23, $CHCl_3$); IR: ν_{max} cm^{-1} 3350 (NH), 2970 and 2910 (CH_3 and CH_2 stretching); MS (FAB): 406 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.34$ (m, 5 H, Ar-H), 5.92 (d, $J = 3.9$ Hz, 1 H, H-1), 4.69 (d, $J = 11.8$ Hz, Hz, 1 H, -OCH_APh), 4.62 (d, $J = 3.9$ Hz, 1 H, H-2), 4.53 (d, $J = 11.8$ Hz, 1 H, -OCH_BPh), 4.10 (dd, $J = 9.6$ and 3.0 Hz, 1 H, H-4), 3.84 (m, 1 H, H-3), 3.40 (m, 1 H, H-7 and 1 H, H-5), 2.72 (m, 1 H, NCH), 1.64 (bs, 1 H, NH), 1.49–1.33 [m, 7 H, $>C(CH_3)_2$ and H-6], 1.25–1.05 (m, 6 H, cyclohexyl ring protons) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 136.66$, 128.31, 127.86 and 127.61 (Ar-C), 111.31

[$>C(CH_3)_2$], 104.27 (C-1), 82.30 (C-2), 81.34 (C-4), 81.16 (C-3), 71.47 (OCH_2Ph), 62.25 (C-7), 54.35 (C-5), 33.70 (NCH), 32.22, 25.67, 24.83 and 24.47 (CH_2's), 26.47 and 25.67 [$>C(CH_3)_2$] ppm. Anal. calcd. for $C_{23}H_{35}NO_5$: C, 68.12; H, 8.70; N, 3.45; Found: C, 68.09; H, 8.73; N, 3.41.

(1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-Benzyl-5,6-dideoxy-5-phenylethylamino-1,2-*O*-isopropylidene-1,4-pento-uranos-4-yl]-β-L-ido-heptanol (13). Reduction of glycosyl β-amino ester **7a** (major isomer) with $LiAlH_4$ and workup as described previously gave corresponding glycosyl β-amino alcohol **13** as colourless oil (yield 92%); $[\alpha]_D = -27.0$ (*c*, 0.16, $CHCl_3$); IR: ν_{max} cm^{-1} 3330 (NH), 2929 and 2857 (CH_3 and CH_2 stretching); MS (FAB): 428 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.29$–7.15 (m, 10 H, Ar-H), 5.91 (d, $J = 3.8$ Hz, 1 H, H-1), 4.47 (d, $J = 11.7$ Hz, 1H, -OCH_APh), 4.24 (d, $J = 3.9$ Hz, 1 H, H-2), 4.14 (d, $J = 11.7$ Hz, 1 H, -OCH_BPh), 3.67 (m, 2 H, H-4 and H-3), 3.26 (m, 2 H, H-7 and H-5), 2.83–2.70 (m, 4 H, NCH_2 and PhCH_2), 1.50–1.25 [m, 8H, $>C(CH_3)_2$ and H-6] ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.3$, 128.9, 128.5 and 128.4 (Ar-C), 111.70 [$>C(CH_3)_2$], 104.89 (C-1), 82.3 (C-2), 81.7 (C-4), 81.6 (C-3), 72.1 (OCH_2Ar), 58.58 (C-7), 54.81 (PhCH_2), 47.38 (C-5), 36.55 (NCH_2), 26.90 and 26.20 [$>C(CH_3)_2$] ppm. Anal. calcd. for $C_{25}H_{33}NO_5$: C, 70.23; H, 7.78; N, 3.28; Found: C, 70.20; H, 7.74; N, 3.24.

Synthesis of Glycosyl Azetidines (14–19)

3-*O*-Benzyl-4-*N*-cyclopropyl azetidine-1,2-*O*-isopropylidene-β-L-ido-furanose (14). A solution of (1*R*,2*R*,3*S*,4*R*,5*S*)-[3-*O*-benzyl-5-cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-1,4-pentofuranos-4-yl]-β-L-ido-heptanol (**8**, 0.5 g, 1.38 mmol) and DIAD (0.42 g, 2.07 mmol, 1.5 eq) in dry THF was stirred for 20 min at 0 °C under anhydrous condition followed by dropwise addition of a freshly prepared solution of PPh_3 (0.54 g, 2.07 mmol) in dry THF. After complete addition of PPh_3, the reaction mixture was further stirred for 8–10 h at room temperature. The reaction was monitored on TLC, which after completion was concentrated under reduced pressure followed by extraction with chloroform (2×25 ml) and water (12.5 ml). The organic layer was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure to afford a crude mass, which on silica-gel column chromatography and elution with chloroform–methanol (98:2) afforded glycosyl azetidine **14** as a colorless oil (yield 63%); $[\alpha]_D = -28.6$ (*c*, 0.13, $CHCl_3$); MS (FAB): 346 $(M+H)^+$, ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.34$ (m, 5 H, Ar-H), 5.92 (d, $J = 3.9$ Hz, 1 H, H-1), 4.66 (d, $J = 11.8$ Hz, 1 H, -OCH_APh), 4.64 (d, $J = 3.9$ Hz, Hz, 1 H, H-2), 4.48 (d, $J = 11.8$ Hz, 1 H, -OCH_BPh), 4.20 (dd, $J = 9.6$ and 3.1 Hz, 1 H, H-4), 3.88 (d, $J = 3.1$ Hz, 1 H, H-3), 3.57 (m, 1 H, H-1′), 3.11 (m, 1 H, NCH), 1.80 (m, 2 H, H-3′), 1.48–1.22 [m, 8 H, $>C(CH_3)_2$ and H-2′], 0.42 (m, 4 H, cyclopropyl ring CH_2's) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.20$, 128.48, 128.32 and 127.85 (Ar-C), 111.21 [$>C(CH_3)_2$], 105.43 (C-1), 82.04 (C-2), 81.76 (C-4), 81.44 (C-3), 71.67 (OCH_2Ph), 64.42 (C-1′), 54.59 (C-3′), 47.50 (NCH), 37.69 (C-2′), 26.57 and 26.15 [$>C(CH_3)_2$], 6.95 and 6.89 (cyclopropyl ring CH_2) ppm. Anal. calcd. for $C_{20}H_{27}NO_4$: C, 69.54; H, 7.88; N, 4.05; Found: C, 69.86; H, 8.01; N, 3.98.

3-*O*-Benzyl-4-*N*-hexadecyl azetidine-1,2-*O*-isopropylidene-β-L-ido-furanose (15). Intramolecular cyclization of glycosyl β-amino alcohol **9** using PPh_3/

DIAD and workup as described previously gave the corresponding glycosyl azetidene **15** as a colorless oil (yield 65%); $[\alpha]_D = -19.3$ (*c*, 0.17, $CHCl_3$); MS (FAB): 530 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.34$ (m, 5 H, Ar-H), 5.95 (d, $J = 3.7$ Hz, 1 H, H-1), 4.65 (d, $J = 11.6$ Hz, 1 H, -OCH_APh), 4.56 (d, $J = 3.7$ Hz, 1 H, H-2), 4.41 (d, $J = 11.6$ Hz, 1 H, -OCH_BPh), 4.21 (dd, $J = 9.4$ and 2.9 Hz, 1 H, H-4), 3.86 (d, $J = 2.9$ Hz, 1 H, H-3), 3.40 (m, 1 H, H-1′), 2.76 (m, 2 H, NC*H*), 1.86 (m, 2 H, H-3′), 1.53–1.25 [m, 34 H, $>C(CH_3)_2$, H-2′, $14 \times CH_2$'s], 0.87 (t, $J = 6.7$ Hz, 3 H, CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 136.2$, 128.12, 128.03 and 127.64 (Ar-C), 111.60 [$>C(CH_3)_2$], 104.14 (C-1), 81.81 (C-2), 81.22 (C-4), 81.09 (C-3), 71.70 (-OCH_2Ph), 56.12 (C-1′), 50.6 (C-3′), 46.11 (NCH_2), 31.30, 30.00, 29.91, 29.8, 29.7, 29.4, 27.44 and 27.2 (CH_2'S), 26.71 and 26.19 [$2 \times >C(CH_3)_2$], 14.11 (CH_2CH_3) ppm. Anal. calcd. for $C_{33}H_{55}NO_4$: C, 74.80; H, 10.47; N, 2.65. Found: C, 74.58; H, 9.98; N, 2.71.

3-*O*-Benzyl-4-*N*-octyl azetidine-1,2-*O*-isopropylidene-β-L-ido-furanose (16). Intramolecular cyclization of glycosyl β-amino alcohol **10** using PPh_3/DIAD and workup as described previously gave the corresponding glycosyl azetidene **16** as colorless oil (yield 62%); $[\alpha]_D = -21.6$ (*c*, 0.14, $CHCl_3$); MS (FAB): 418 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$ (m, 5 H, Ar-H), 5.95 (d, $J = 3.8$ Hz, 1 H, H-1), 4.65 (d, $J = 11.7$ Hz, 1 H, -OCH_APh), 4.60 (d, $J = 3.8$ Hz, 1 H, H-2), 4.41 (d, $J = 11.7$ Hz, 1 H, -OCH_BPh), 4.20 (dd, $J = 9.6$ and 3.0 Hz, 1 H, H-4), 3.82 (d, $J = 3.0$ Hz, 1 H, H-3), 3.24 (m, 2 H, H-3′), 3.69 (m, 1 H, H-1′ and 2 H, NCH_2), 1.41–1.25 [m, 20 H, $>C(CH_3)_2$, H-2′ and $6 \times CH_2$'s], 0.87 (t, $J = 6.9$ Hz, 3 H, CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.27$, 128.42, 128.17 and 127.81 (Ar-C), 111.64 [$>C(CH_3)_2$], 105.47 (C-1), 84.92 (C-2), 81.85 (C-4), 81.50 (C-3), 71.75 (OCH_2Ph), 65.03 (C-1′), 59.42 (C-3′), 51.89 (NCH_2), 31.79, 30.34, 29.52, 29.24, 27.37 and 22.67 (CH_2's), 27.44 and 26.28 [$>C(CH_3)_2$], 14.06 (CH_2CH_3) ppm. Anal. calcd. for $C_{25}H_{39}NO_4$: C, 71.91; H, 9.41; N, 3.35. Found: C, 71.67; H, 9.40; N, 3.63.

3-*O*-Benzyl-4-*N*-butyl azetidine-1,2-*O*-isopropylidene-β-L-ido-furanose (17). Intramolecular cyclization of glycosyl β-amino alcohol **11** using PPh_3/DIAD and workup as described previously gave corresponding glycosyl azetidene **17** as a colorless oil (yield 60%); $[\alpha]_D = -20.1$ (*c*, 0.21, $CHCl_3$); MS (FAB): 362 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$ (m, 5 H, Ar-H), 5.88 (d, $J = 3.6$ Hz, 1 H, H-1), 4.67 (d, $J = 11.6$ Hz, 1 H, -OCH_APh), 4.62 (d, $J = 3.6$ Hz, 1 H, H-2), 4.42 (d, $J = 11.6$ Hz, 1 H, -OCH_BPh), 4.11 (dd, $J = 9.4$ and 3.0 Hz, 1 H, H-4), 3.87 (d, $J = 3.0$ Hz, 1 H, H-3), 3.23 (m, 2 H, H-3′), 3.14 (m, 1 H, H-1′), 2.75 (m, 2 H, NCH_2), 1.53–1.25 [m, 12 H, $>C(CH_3)_2$, H-2′, $2 \times CH_2$'s], 0.87 (t, $J = 6.7$ Hz, 3 H, -CH_2CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 136.5$, 129.1, 128.9 and 128.78 (Ar-C), 113.0 [$>C(CH_3)_2$], 105.4 (C-1), 82.2 (C-2), 81.4 (C-4), 79.72 (C-3), 72.3 (–OCH_2Ph), 60.09 (C-1′), 58.44 (C-3′), 49.30 (NCH_2), 32.14, 30.10, 29.22, 29.13, and 27.12 (CH_2's), 27.44 and 27.03 [$2 \times >C(CH_3)_2$], 14.02(CH_2CH_3) ppm. Anal. calcd. for $C_{21}H_{31}NO_4$: C, 69.78; H, 8.64; N, 3.87. Found: C, 69.42; H, 9.07; N, 3.65.

3-*O*-Benzyl-4-*N*-cyclohexyl azetidine-1,2-*O*-isopropylidene-β-L-ido-furanose (18). Intramolecular cyclization of glycosyl β-amino alcohol **12** using PPh_3/DIAD and workup as described previously gave the corresponding glycosyl

azetidene **18** as a colorless oil (yield 60%); $[\alpha]_D = -17.0$ (*c*, 0.15, $CHCl_3$); MS (FAB): 388 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$ (m, 5 H, Ar-H), 5.92 (d, $J = 3.9$ Hz, 1 H, H-1), 4.68 (d, $J = 11.8$ Hz, 1 H, -OCH_APh), 4.64 (d, $J = 3.9$ Hz, 1 H, H-2), 4.48 (d, $J = 11.8$ Hz, 1 H, -OCH_BPh), 4.22 (dd, $J = 9.6$ and 3.1 Hz, 1 H, H-4), 3.86 (m, 1 H, H-3), 3.56 (m, 1 H, H-1′), 3.15 (m, 1 H, NCH), 2.25 (m, 2 H, H-3′), 1.45–1.24 [m, 8 H, $>C(CH_3)_2$ and H-2′], 1.22–1.05 (m, 6 H, cyclohexyl ring protons) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 136.66$, 128.31, 127.86 and 127.61 (Ar-C), 111.58 [$>C(CH_3)_2$], 105.07 (C-1), 82.03 (C-2), 81.43 (C-4), 81.06 (C-3), 72.24 (OCH_2Ph), 64.25 (C-1′), 53.35 (C-3′), 33.70 (NCH), 32.11, 25.56, 24.33 and 24.02 (CH_2's), 26.47 and 26.06 ($>C(CH_3)_2$) ppm. Anal. calcd. for $C_{23}H_{33}NO_4$: C, 71.29; H, 8.58; N, 3.61. Found: C, 71.08; H, 9.12; N, 3.39.

3-*O*-Benzyl-4-*N*-phenylethyl azetidine-1,2-*O*-isopropylidene-β-L-idofuranose (19). Intramolecular cyclization of glycosyl β-amino alcohol **13** using PPh_3/DIAD and workup as described previously gave the corresponding glycosyl azetidene **19** as a colorless oil (yield 64%); $[\alpha]_D = -19.6$ (*c*, 0.23, $CHCl_3$); MS (FAB): 410 $(M+H)^+$; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.31$–7.12 (m, 10 H, Ar-H), 5.91 (d, $J = 3.9$ Hz, 1 H, H-1), 4.64 (d, $J = 11.7$ Hz, 1 H, -OCH_APh), 4.51 (d, $J = 3.9$ Hz, 1 H, H-2), 4.39 (d, $J = 11.7$ Hz, 1 H, -OCH_BPh), 4.20 (m, 1 H, H-4), 3.89 (m, 1 H, H-3), 3.48 (m, 1 H, H-1′), 3.03–2.62 (m, 4 H, NCH_2 and $PhCH_2$), 1.60 (m, 2 H, H-3′), 1.50–1.25 [m, 8 H, $>C(CH_3)_2$ and H-2′]; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 137.3$, 128.9, 128.5 and 128.4 (Ar-C), 111.58 [$>C(CH_3)_2$], 104.84 (C-1), 82.03 (C-2), 81.74 (C-4), 81.45 (C-3), 71.65 (OCH_2Ar), 63.33 (C-1′), 52.39 ($PhCH_2$), 36.78 (NCH_2), 33.98 (C-3′), 26.80 and 26.16 [$>C(CH_3)_2$] ppm. Anal. calcd. for $C_{25}H_{31}NO_4$: C, 73.32; H, 7.63; N, 3.42. Found: C, 73.95; H, 7.52; N, 3.49.

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