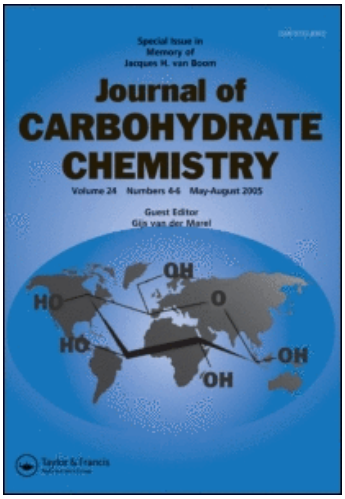

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Reductive Amination of Glycosyl Aldoses: Synthesis of *N*-Glycosylated β-Glycosyl Amino Alcohols and their Enzyme Inhibitory Effect[#]

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CONTENTS

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ABSTRACT

Reductive amination of glycosyl aldehydes (**1a–c**, **2**) with glycosyl amino esters (**3a–c**, **4**) in the presence of sodium borohydride gave diglycosylated amino esters (**5–15**) in good yield. *N*-Glycosyl-glycosylated amino esters were reduced to the respective diglycosyl amino alcohols (**16–26**) with $LiAlH_4$ in good yield. All the synthesized compounds were studied for their inhibitory effect, if any, against hepatic glucose-6-phosphatase, glycogen phosphorylase, and intestinal brush border membrane α-glucosidase; among these compounds **7, 21**, and **25** have shown marked inhibition on these enzymes, respectively.

INTRODUCTION

Apart from classical carbohydrate chemistry of *O*-glycosides[1] from many years in medicinal chemistry for the development of many therapeutics, an increase in the development of a biological or non-natural glycoside with a C–C bond or C–N bond is gaining momentum at the molecular level for the roles of carbohydrates in glycolipids and glycoproteins.[2] Identification of lead compounds from sugars for drug discovery against various diseases are being pursued by different groups, including ours,[3] because of tremendous potential of structural diversity in sugars.

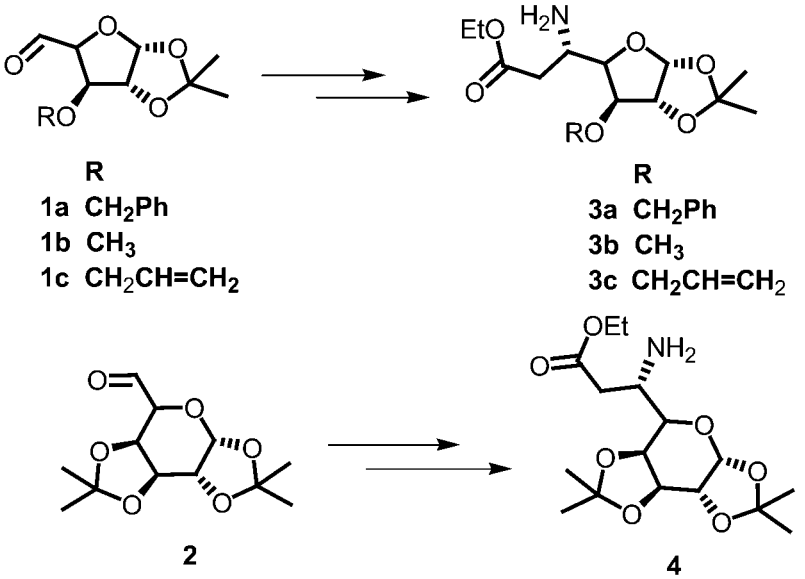
Aza disaccharides are known to inhibit various glycosyl hydrolases and glycosidases and are therefore important for drug development.[4] Polyhydroxylated pyrrolidines and piperidines are potent inhibitors of glycosidase, and few of them act as broad-spectrum enzyme inhibitors. The glycosidase enzyme inhibitory activity has been exploited in the development of many chemotherapeutics such as antiviral, anticancer, antimicrobial, antibacterial, and antiparasitic agents for the treatment of many diseases. Many compounds from natural and synthetic origins containing an aglycon moiety attached to a glycosyl cation mimetics act as selective inhibitors[5] of α-glucosidases. Disaccharide analogs linked through spacers having nitrogen atom have recently been found to bind with 16S RNA, indicating their usefulness as amino glycoside antibiotics. Moreover, certain disachharides with aminoalkyl functionality were proved to be mechanism-based inactivators of bacterial aminoglycoside 3′-phosphotransferases.[6] Dideoxyiminoalditols linked to other sugars by nonhydrolysable links have much better specificity towards glycosidases than dideoxyiminoalditols themselves; therefore, different synthetic strategies have been developed for their synthesis.[7] Nitrogen- and sulphur-linked pseudodisaccharides as relatively stable glycosidase inhibitors have been reported recently.[8] In our ongoing program to develop carbohydrates as chemotherapeutic agents, we have recently synthesized glycosyl urea and certain C-nucleoside analogs through amination of aldehydes with amino sugars as α-glucosidase inhibitors.[9] α-Glycosidase, glycogen phosphorylase, and glucose-6-phosphatase are important enzymes for the development of new drugs against many metabolic disorders, and the most important among them is diabetes. Glycogen phosphorylase breaks down glycogen to glucose-6-phosphate; this is the source of glucose in liver but not in muscles. The glucose-6-phosphatase removes phosphate from glucose and releases it in the blood. Thus, inhibitors of this enzyme may be helpful in controlling the state of hyperglycemia.

Keeping in mind the above, we were prompted to synthesize certain *aza*-linked pseudo disaccharide analogs having both pyranose and furanose sugar rings and evaluate their efficacy against the above three enzymes responsible for diabetes.

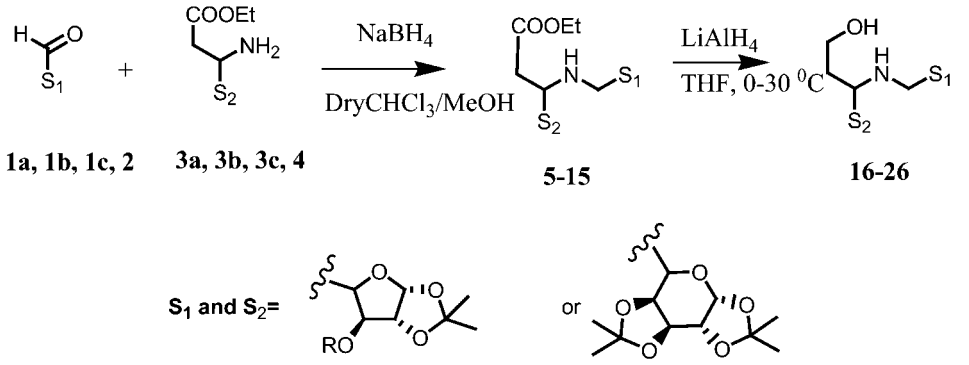
RESULTS AND DISCUSSION

Starting with the reaction of glycosyl aldehyde **(1a)** with glycosyl amino ester **(3a)**[10] (Sch. 1) resulted in the formation of an intermediate (imine), which, on subsequent *in situ* reduction with sodium borohydride, gave the disaccharide analog **5** (Sch. 2). The structure of compound **5** was determined on the basis of its spectroscopic data and analysis. IR spectrum of the compound showed an absorption band at 3753 cm^{-1} corresponding to NH-stretching, while in MS (FAB) spectrum, a peak at m/z 628 corresponded to $[M + H]^+$. In ^1H NMR spectrum of the compound **5**, the anomeric protons (H1 and H-1') of the two furanoses S_1 and S_2 were observed as *d* at δ 5.92 and 5.90 with $J = 3.9$ and 3.6 Hz, respectively. H-2 and H-2' in both S_1 and S_2 appeared as multiplet along with CH_2 protons of CH_2Ph group at δ 4.69–4.42; H-4 appeared as *m* at δ 4.26 in S_1 and while in S_2 it appeared as *m* at δ 4.16. A multiplet at δ 3.90 accounted for H-3 and H-3' of the sugar rings, while methylene protons of NCH_2 attached to S_2 appeared as *m* at δ 3.04. The protons for CH_2 and CH_3 in the carbethoxy group appeared at δ 4.04 and 1.19 as a quartet and triplet, respectively, with *J* value of 6.9 Hz besides other usual signals. In ^{13}C NMR spectrum, compound **5** showed characteristic signals for $NHCH_2$, OCH_2, and CH_3 carbons at δ 45.8, 60.7, and 14.5, respectively. Because, the stereochemistry has already been assigned to be *S* in the glycosyl amino ester (**3a**) used in this reaction, this is maintained in the final compounds as well, because C-5 is not involved in the reaction.

We have extended this work using galactopyranosyl aldehydes (**2**) and galactopyranosyl amino esters (**4**) to synthesize compounds having pyranose ring. Thus, the reaction of glycosyl amino ester **3a** with glycosyl aldehydes **2** gives *N*-galactopyranosylated



Scheme 1. Glycosyl aldehydes and amino esters.



Scheme 2. Synthesis of *N*-bridged disaccharides.

glycosyl amino ester (**8**) in good yield. IR spectrum of compound **8** showed absorption band at 3655 cm^{-1} corresponding to NH-stretching. In MS (FAB) spectrum, peak at m/z 608 corresponded to $[M + H]^+$. In ^1H NMR spectrum of this compound, the two doublets for anomeric protons (H-1 and H-1') of the furanose and pyranose sugars were observed at δ 5.96 and 5.53 with $J = 3.6$ and 5.1 Hz, respectively. The signals for protons of CH_2 and CH_3 in carbethoxy group appeared at δ 3.95 and 1.24 as a quartet ($J = 6.8$ Hz) and triplet ($J = 6.8$ Hz), respectively, besides other usual signals. In ^{13}C NMR spectrum, compound **8** showed characteristic peaks of $NHCH_2$, OCH_2, and CH_3 carbons at δ 47.1, 60.7 and 14.5, respectively, besides other usual signals of both the sugars. Similarly, reaction of galactopyranosyl amino ester **4**[11] with galactopyranosyl aldehyde (**2**) resulted in *N*-galactopyranosyl galactopyranosylated amino ester (**15**) in good yield. The structure of this compound was also established on the basis of its spectroscopic data and analysis. IR spectrum of this compound (**15**) showed absorption band at 3679 cm^{-1} corresponding to NH stretching; MS (FAB) spectrum showed a peak at m/z 588 corresponding to $[M + H]^+$. In ^1H NMR spectrum, the anomeric protons of the two sugar rings were observed as *d* at δ 5.55 and 5.50 with $J = 5.0$ Hz, besides other usual signals. In ^{13}C NMR spectrum, of **15** quaternary carbon of ester group appeared at δ 172.7 while those of isopropylidene groups were observed at δ 109.5, 109.3, 108.8, and 108.7. The anomeric carbons (C-1 and C-1') appeared at δ 97.9 and 96.7, respectively, besides other usual signals (Table 1).

Similarly, structures of all the compounds were established on the basis of spectral data and analysis. In all the compounds anomeric protons corresponding to furanose and pyranose sugars appeared at around δ 5.9 and 5.6 as *d*, with $J \approx 3.7$ and 5.0 Hz, respectively. H-2 for the furanose sugar appeared as *d* at around δ 4.6 in furanose sugar, while the same in pyranose sugar appeared as *m* merged with H-5 or as *dd* with $J \approx 5.0$ and 2.2 Hz at around δ 4.3 in the disaccharide analogs. The characteristic –NH-linkage between two sugars has been characterized both by IR (≈3650, N-H stretching) and ^1H NMR (br s at around δ 1.6). In ^{13}C NMR spectra, the characteristic signals for C-1, C-2, C-3, and C-4 in glycofuranose appeared at around δ 105, 83, 82, and 80, respectively, while in the case of glycopyranose, the signals corresponding to C-1, C-2, C-3, C-4, and C-5 appeared at around δ 97, 72, 71, 70, and 62, besides other usual signals.

Table 1. Compounds synthesized.

Entry	Compound	R^1	R^2	R^3
1	**5**	CH_2Ph	CH_2Ph	COOEt
2	**6**	CH_2Ph	CH_3	COOEt
3	**7**	CH_2Ph	$CH_2CH=CH_2$	COOEt
4	**8**	CH_2Ph	–	COOEt
5	**9**	CH_3	–	COOEt
6	**10**	$CH_2CH=CH_2$	CH_2Ph	COOEt
7	**11**	$CH_2CH=CH_2$	CH_3	COOEt
8	**12**	–	CH_2Ph	COOEt
9	**13**	–	CH_3	COOEt
10	**14**	–	$CH_2CH=CH_2$	COOEt
11	**15**	–	–	COOEt
12	**16**	CH_2Ph	CH_2Ph	CH_2OH
13	**17**	CH_2Ph	CH_3	CH_2OH
14	**18**	CH_2Ph	$CH_2CH=CH_2$	CH_2OH
15	**19**	CH_2Ph	–	CH_2OH
16	**20**	CH_3	–	CH_2OH
17	**21**	$CH_2CH=CH_2$	CH_2Ph	CH_2OH
18	**22**	$CH_2CH=CH_2$	CH_3	CH_2OH
19	**23**	–	CH_2Ph	CH_2OH
20	**24**	–	CH_3	CH_2OH
21	**25**	–	$CH_2CH=CH_2$	CH_2OH
22	**26**	–	–	CH_2OH

Lithium aluminiumhydride ($LiAlH_4$) reduction of glycosyl amino esters **5–15** was carried out at 0°C to ambient temperature, resulting in the formation of respective *N*-glycosyl glycosylated amino alcohols **16–26** in good yield (Fig. 1). The formation of alcohol from the respective amino esters was evidenced by their spectroscopic data and analysis. FAB MS of all of the above amino alcohols showed peaks corresponding to $[M+H]^+$, and in IR spectrum, appearance of a broad signal around 3400 cm^{-1} and disappearance of signal at around 1725 cm^{-1} indicated the reduction of ester functionality to the alcohol. In ^1H NMR spectrum of the diglycosyl amino alcohols, disappearance of the *q* and *t* at around δ 4.0 and 1.25 corresponds to $OCH_2$and OCH_2CH_3, respectively; and appearance of an *m* at δ 3.7 for the CH_2OH confirmed the reduction of ester to the respective alcohol. Further in the ^{13}C NMR spectrum, appearance of a peak at around δ 62.0 corresponding to CH_2OH carbon and disappearance of the signals for methylene and methyl carbons in OCH_2CH_3 at around δ 60.7, 14.5, and carbonyl carbon at around δ 172 clearly confirmed the formation of alcohol.

As evident from Table 2, out of all the compounds screened against glucose-6-phosphatase, glycogen phosphorylase, and α-glucosidase, only compounds **6**, **10**, **13**, **18**, **19**, **21**, and **25** exhibited activity against all or two of the enzymes, while other compounds did not show any significant activity. Compound **7** inhibited only α-glucosidase to the extent of 82%, while compounds **21** and **25** possessing allyl group as substituent in either of the sugar rings were found to be a good inhibitor of glycogen phosphorylase. In the present study, there were five compounds having more than 50% inhibition on

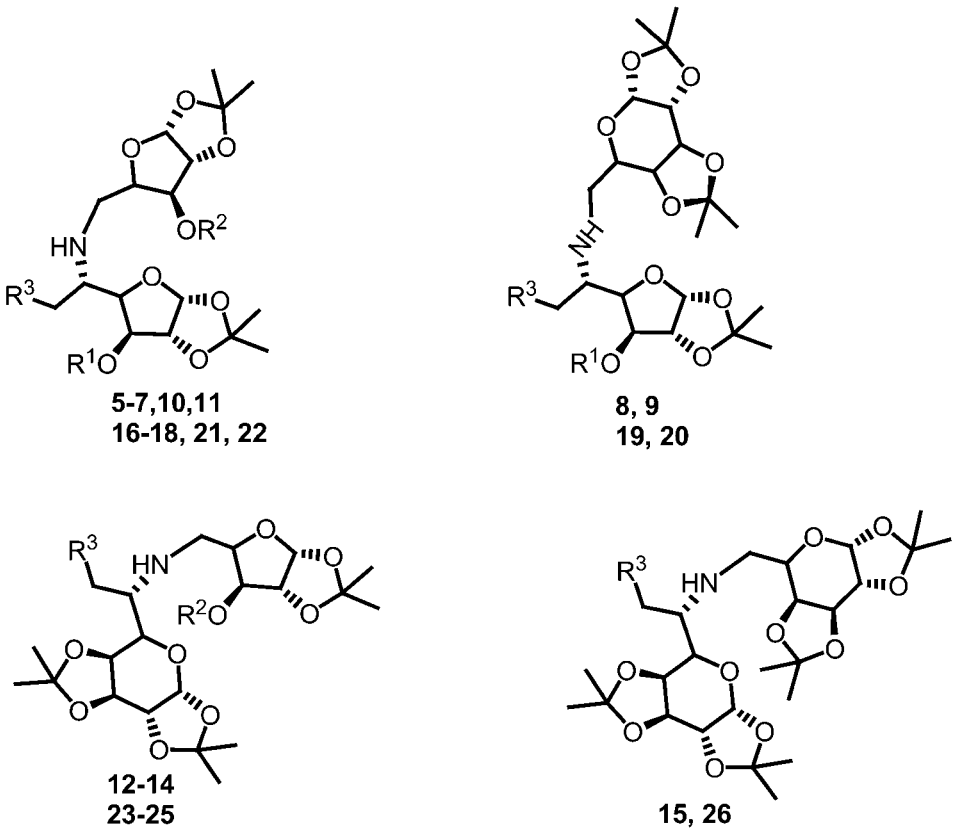


Figure 1. *N*-Glycosyl-glycosylamino ester **5–15** and alcohol **16–26** synthesized.

glucose-6-phosphatase. These molecules have the potential to be developed as antidiabetic agents, because these compounds will possibly reduce the hepatic glucose production. These agents may suppress glucose production in liver as evidenced by reduction in the activities of glucose-6-phosphatase.

EXPERIMENTAL

General Methods

Thin-layer chromatography was carried out on silica gel (Kiesel 60-F254, Merck), and spots were developed in iodine vapors and by spraying with 5% sulfuric acid in alcohol followed by heating at 100°C. Column chromatography was carried out on flash silica gel (230–400 mesh, Merck) using the indicated eluent. IR spectra were recorded as thin films on KBr plates with a Perkin Elmer 881 spectrophotometer. NMR spectra were recorded on Bruker spectrometers 200 and 300 MHz and reference used was $CDCl_3$. Chemical shifts were given as δ ppm values, and J values were given in Hertz (Hz).

Table 2. Biological activity of disaccharide analogs against different enzymes.

S. No.	Compound	% Inhibition		
		Glucose-6-phosphatase	Glycogen phosphorylase	α-Glucosidase
1	**5**	nd	nd	+1.98
2	**6**	22.5	45.9	10.1
3	**7**	31.6	NIL	**82.3**
4	**8**	nd	nd	nd
5	**9**	nd	nd	nd
6	**10**	33.8	29.7	29.8
7	**11**	nd	nd	nd
8	**12**	nd	nd	2.83
9	**13**	30.9	16.2	16.0
10	**14**	30.2	nd	3.65
11	**15**	nd	nd	3.68
12	**16**	nd	nd	+3.68
13	**17**	nd	nd	nd
14	**18**	30.9	40.5	+26.4
15	**19**	35.2	18.9	56.2
16	**20**	nd	nd	nd
17	**21**	25.3	**72.9**	+7.58
18	**22**	39.4	5.40	+1.96
19	**23**	nd	nd	+1.98
20	**24**	nd	nd	nd
21	**25**	27.4	**94.6**	nd
22	**26**	nd	nd	6.51

All the compounds were tested at the concentration of 100 μg/mL; nd = not done.

Elemental analyses were performed on a Perkin-Elmer 2400 II elemental analyzer. The optical rotations were measured in a 1.0 dm tube with Jasco dip-140 polarimeter in chloroform. The excess of the reagents or solvents were evaporated under reduced pressure at a bath temperature between the ranges 55–60°C.

General Procedure for the Preparation of the Compounds (5–15)

Ethyl 5-(5′-amino-3′-*O*-benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronate (5). To a magnetically stirred slurry of 4 Å molecular sieve (6.0 g) in dry chloroform (6.0 mL), 3-*O*-benzyl-1,2-*O*-isopropylidene-α-D-xylofuranos-5-ulose, **1a** (1.0 g, 3.59 mmol) in dry chloroform (5.0 mL), and ethyl 5-amino-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronate, **2a** (1.31, 3.59 mmol) in dry chloroform (5.0 mL) was added sequentially at 0°C, and stirring was continued for 30 min. Reaction mixture was further stirred for 6 hr at ambient temperature, until the disappearance of the aldehyde (TLC). Reaction mixture was filtered and concentrated under reduced pressure

and the residue thus obtained was dissolved in methanol (15.0 mL) and stirred magnetically at 0°C. Sodium borohydride (0.136 g, 3.70 mmol) was added to the stirring reaction mixture and reaction continued for 3 hr at ambient temperature. Saturated ammonium chloride solution was added to the reaction mixture and it was filtered. The solid cake was washed with methanol and the combined filtrate was concentrated and extracted with ethyl acetate (2 × 50 mL) and washed with water (2 × 12.5 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give a crude mass, which was chromatographed over SiO_2 column using hexane/ethyl acetate (4 : 1) as eluent to give compound **5** (2.18 g, 97.4%) as colorless oil; R_f 0.50 (hexane/ethyl acetate, 13 : 7), $[\alpha]_D^{20}$ −52.5° (*c* 0.80, chloroform); MS (FAB) = *m*/*z* 628 $(M + H)^+$; IR (Neat) $\nu_{max}\,cm^{-1}$: 3753, 1730; ^1H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 10H, Ar-H); 5.92 (d, *J* = 3.9 Hz, 1H, H-1), 5.90 (d, *J* = 3.6 Hz, 1H, H-1′), 4.69–4.42 (m, 6H, 2 × CH_2Ph, H-2, H-2′), 4.26 (m, 1H, H-4), 4.16 (m, 1H, H-4′), 4.04 (q, *J* = 6.9 Hz, 2H, OC*H2*CH_3), 3.90 (m, 2H, H-3, H-3′), 3.50 (m, 1H, H-5), 3.04 (m, 2H, CH_2NH), 2.36 (m, 2H, H-6), 1.59 (br s, exchangeable 1H, NH), 1.47, 1.25 [s, 12H, 2 × $(CH_3)_2C$], 1.19 (t, *J* = 6.9 Hz, 3H, OCH_2CH3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.0 (C═O), 138.8, 137.5, 128.4, 128.2, 128.1, 128.0 (Ar-C), 111.9, 111.8 [2 × $(CH_3)_2C$], 105.3, 105.2 (C-1, C-1′), 82.7, 82.6 (C-2, C-2′), 82.3, 82.2 (C-4, C-4′), 80.6, 80.5 (C-3, C-3′), 72.2 (-OCH_2Ph), 60.7 (OCH_2CH_3), 54.8 (C-5), 45.8 (CH_2NH), 36.7 (C-6), 27.1, 26.7 [$C(CH_3)_2$], 14.5 (CH_3).

Anal. Calcd. for $C_{34}H_{45}O_{10}N$; C, 65.07, H 7.17, N, 2.20; Found: C, 65.10, H, 7.10, N 2.17.

Ethyl 5-(5′-amino-5′-deoxy-1′,2′-*O*-isopropylidene-3′-*O*-methyl-α-D-xylofuranos-5′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronate (6). Reaction of the amino ester **3a** (1.39 g, 4.95 mmol) with the glycosyl aldehyde **1b** (1.0 g, 4.95 mmol) in presence of $NaBH_4$ (0.139 g, 3.6 mmol) as described above, followed by column chromatography of the crude product using ethyl acetate : hexane (1 : 4) as eluent gave compound **6** (2.45 g, 90.0%), as colorless oil; R_f 0.50 (hexane : ethyl acetate, 3 : 2) $[\alpha]_D^{20}$ −87.0° (*c* 0.10, chloroform); MS (FAB) = *m*/*z* 552 $(M + H)^+$; IR (Neat) $\nu_{max}\,cm^{-1}$: 3345, 1731; ^1H NMR (200 MHz, $CDCl_3$): δ 7.32–7.26 (m, 5H, Ar-H), 5.93 (d, *J* = 3.6 Hz, 1H, H-1′), 5.86 (d, *J* = 3.8 Hz, 1H, H-1), 4.66–4.48 (d, *J* = 11.8 Hz, 1H, CH_APh), 4.62 (d, *J* = 3.6 Hz, 1H, H-2′), 4.53 (d, *J* = 3.8 Hz,1H, H-2), 4.43 (d, *J* = 11.8 Hz, 1H, CH_BPh), 4.42–4.10 (m, 2H, H-4, H-4′), 4.08 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 3.91 (d, *J* = 3.2 Hz, 1H, H-3), 3.67 (d, *J* = 3.2 Hz, 1H, H-3′), 3.40 (m, 1H, H-5), 3.36 (s, 3H, OCH_3), 2.36 (m, 2H, H-6), 2.95 (d, *J* = 6.4 Hz, 2H, CH_2NH), 2.36 (m, 2H, H-6), 1.62 (br s, exchangeable 1H, -NH), 1.48, 1.30 [s, 6H, $(CH_3)_2C$], 1.25–1.19 [m, 9H, $(CH_3)2C$ and OCH_2CH_3]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.0 (C═O), 137.4, 128.9, 128.4, 128.2 (Ar-C), 111.9, 111.7 [2 × $(CH_3)2C$], 105.1, 105.2 (C-1, C-1′), 84.4, 84.3 (C-2, C-2′), 82.5, 82.3 (C-4, C-4′), 80.4, 80.3 (C-3, C-3′), 71.8 (OCH_2Ph), 60.7 (OCH_2CH_3), 58.0 (−OCH_3), 54.4 (C-5), 45.4 (CH_2 NH), 36.5 (C-6), 27.1, 26.6 [2 × $C(CH_3)_2$], 14.5 (CH_3).

Anal. Calcd. for $C_{28}H_{41}O_{10}N$: C, 60.90, H, 7.44, N, 2.50; Found: C, 60.92, H, 7.40, N, 2.54.

Ethyl 5-(3′-*O*-allyl-5′-amino-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-3-*O*-benzyl−5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronate (7). Reaction of the aldehyde **1c** (1.0 g, 4.38 mmol) with amino ester, **3b** (1.60 g, 4.38 mmol) in presence of $NaBH_4$ (0.168 g, 4.38 mmol) as described above, followed by

column chromatography gave **7** (1.9 g, 75%) as colorless oil; R_f 0.52 (hexane : ethyl acetate, 3 : 2) $[\alpha]_D^{20}$ −52.0° (0.10, chloroform); MS (FAB) = m/z 578 $(M+H)^+$; IR(Neat) $\nu_{max}\,cm^{-1}$: 3655, 1732; ^1H NMR (200 MHz, $CDCl_3$): δ 7.32–7.27 (m, 5H, Ar-H), 5.90–5.87 (m, 3H, H-1, H-1′, $CH_2CH{=}CH_2$); 5.20 (m, 2H, $OCH_2CH{=}CH_2$), 4.71–4.41 (m, 4H, OCH_2Ph, H-2, H-2′), 4.20–4.06 (m, 6H, H-4, H-4′, $OCH_2CH{=}CH_2$, OCH_2CH_3), 3.90 (d, J = 3.2 Hz, 1H, H-3′), 3.83 (d, J = 3.2, 1H, H-3), 3.30 (m, 1H, H-5), 2.90 (m, 2H, CH_2NH), 1.75 (br s, exchangeable H, NH), 1.47–1.19 [m, 15H, 2 × $(CH_3)_2C$, OCH_2CH_3], ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.1 (C=O), 138.0, 128.8 (Ar-C), 133.95 ($OCH_2CH{=}CH_2$), 118.4 ($OCH_2CH{=}CH_2$), 111.9 [$(CH_3)_2C$], 105.2, 105.1 (C-1, C-1′), 83.2, 83.1, 82.7, 82.6, 82.2 (C-2, C-2′, C-4, C-4′), 80.6, 80.5 (C-3, C-3′), 72.7 (OCH_2Ph), 71.3 ($OCH_2CH{=}CH_2$), 60.8 (OCH_2CH_3), 54.7 (C-5), 45.9 (CH_2NH), 36.7 (C-6), 27.1, 26.7 [$C(CH_3)_2$], 14.5 (CH_3).

Anal. Calcd. for $C_{30}H_{43}O_{10}N$; C, 62.40, H, 7.40, N, 2.40; Found: C, 62.45, H, 7.42, N, 2.38.

Ethyl 5-(6′-amino-6′-deoxy-1′,2′:3′,4′-di-*O*-isopropylidene-α-D-galactoctapyranos-6′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronate (8). Reaction of amino ester **3a** (2.80 g, 7.75 mmol) with the aldehyde **2** (2.09 g, 7.75 mmol) in presence of $NaBH_4$ (0.25 g, 6.61 mmol) as described above gave compound **8** (3.6 g, 85%) as colorless oil; R_f 0.50 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D^{20}$ −64.0° (c 0.10, chloroform); MS (FAB) = m/z 608 $(M+H)^+$; IR (Neat) $\nu_{max}\,cm^{-1}$: 3655, 1733; ^1H NMR (200 MHz, $CDCl_3$): δ 7.34–7.28 (m, 5H, Ar-H), 5.96 (d, J = 3.6 Hz, 1H, H-1), 5.53 (d, J = 5.1 Hz, 1H, H-1′), 4.71–4.56 (m, 3H, OCH_APh, H-2, H-3′), 4.49 (d, J = 11.7 Hz, 1H, CH_BPh), 4.30–4.20 (m, 3H, H-2′, H-4 and H-4′), 3.95 (q, J = 6.8 Hz, 2H, OCH_2), 3.80–3.70 (m, 2H, H-3, H-5′), 3.50 (m, 1H, H-5), 2.90 (m, 2H, H-6′), 2.30 (m, 2H, H-6), 1.69 (br s, exchangeable H, NH), 1.50, 1.44 [s, 12H, 2 × $(CH_3)_2C$], 1.32 [s, 6H, $(CH_3)_2C$], 1.24 (t, J = 6.8 Hz, 3H, $-OCH_2CH_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.2 (C=O), 137.6, 128.8, 128.3, 128.1 (Ar-C), 111.9, 109.4, 108.8 [3 × $(CH_3)_2C$], 105.3 (C-1), 96.7 (C-1′), 82.4, 82.2, 82.1 (C-4, C-2, and C-3), 72.0, 71.9, 71.2, 70.0 (C-2′, C-4′, C-3′, OCH_2Ph), 67.4 (C-5′), 60.7 (OCH_2CH_3), 54.0 (C-5), 47.1 (C-6′), 36.5 (C-6), 27.1, 26.4, 24.8 [3 × $C(CH_3)_2$], 14.5 (CH_3).

Anal. Calcd. for $C_{31}H_{45}O_{11}N$; C, 61.28, H, 7.41, N, 2.31; Found: C, 61.20, H, 7.46, N, 2.26.

Ethyl 5-(6′-amino-6′-deoxy-1′,2′:3′,4′-di-*O*-isopropylidene-α-D-galactoctapyranos-6′-yl)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuranuronate (9). Reaction of aldehyde, **2** (1.09 g, 3.87 mmol) with amino ester **3b** (1.13 g, 3.87 mmol) in presence of NaBH4 (0.15 g, 3.96 mmol) as described above gave compound **9** (1.54 g, 75.4%) as colorless oil; R_f 0.51 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D^{20}$ −81.3° (c 0.15, chloroform); MS (FAB) = m/z 532 $(M+H)^+$; IR(Neat) $\nu_{max}\,cm^{-1}$: 3757, 3346; ^1H NMR (200 MHz, $CDCl_3$): δ 5.90 (d, J = 4.0 Hz, 1H, H-1); 5.53 (d, J = 5.0 Hz, 1H, H-1′), 4.60–4.56 (m, 2H, H-3′, H-2), 4.31 (d, J = 5.0 Hz, 1H, H-2′), 4.21 (m, 3H, H-4′, OCH_2CH_3), 3.90 (m, 1H, H-4), 3.86–3.60 (m, 1H, H-5′), 3.60 (d, J = 2.0 Hz, 1H, H-3), 3.41 (s, 3H, OCH_3), 3.10 (m, 1H, H-5), 2.98 (m, 2H, H-6′), 1.90 (m, 2H, H-6), 1.70 (br s, exchangeable H, –NH), 1.53, 1.48, 1.43 [s, 6H, 2 × $(CH)_3C$], 1.23 [s, 6H, 2 × $(CH_3)_2C$], 1.26 (t, J = 7.2 Hz, 3H, OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 111.8, 109.6, 108.9 [3 × $(CH_3)_2C$], 104.8 (C-1), 96.7 (C-1′), 84.3 (C-2), 82.2, 81.5 (C-4, C-3), 72.2 (C-3′), 71.2, 70.9 (C-2′, C-5′), 67.9 (C-4′), 62.6 (OCH_2CH_3), 57.8 ($-OCH_3$), 47.8 (CH_2NH), 30.2 (C-6), 27.1, 26.4, 24.8 [$C(CH_3)2$], 14.5 (OCH_2CH_3).

Anal. Calcd. for $C_{25}H_{41}O_{11}N$; C,56.49, H, 7.72, N, 2.63; Found: C, 56.40, H, 7.70, N, 2.60.

Ethyl 5-(5′-amino-3′-*O*-benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-3-*O*-allyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronate (10). Reaction of aldehyde, **1a** (1.0 g, 3.59 mmol) with amino ester **3c** (1.13 g, 3.59 mmol) in presence of $NaBH_4$ (0.137 g, 3.70 mmol) as described above gave compound **10** (1.92 g, 93.8%) as colorless oil; R_f 0.50 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D^{20}$ −58.0° (*c* 0.10, chloroform); MS (FAB) = m/z 578 $(M+H)^+$; IR(Neat) ν_{max} cm^{-1}: 1730, 3630; ^1H NMR (200 MHz, $CDCl_3$): δ 7.33–7.26 (m, 5H, Ar-H), 5.92–5.81 (m, 3H, H-1, H-1′, CH_2═*CH*CH_2), 5.23 (dd, J = 19.0 and 1.4 Hz, 2H, CH_2CH═*CH*2), 4.75–4.52 (m, 4H, CH_APh, CH_BPh, H-2, H-2′), 4.21–3.89 (m, 4H, O*C*H_2CH_3, H-4, H-4′), 3.90 (d, J = 2.8 Hz, 1H, H-3), 3.83–3.76 (m, 3H, H-3′, O*C*H_2CH═CH_2), 3.20 (m, 1H, H-5), 3.06 (m, 2H, CH_2NH), 1.70 (br s, exchangeable H, –NH), 1.57, 1.31 [s, 6H, 2 × $(CH)_2C$], 1.22 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.9 (CH_2*C*H═CH_2), 133.9, 128.8, 127.9 (Ar-C), 118.5 (CH_2CH = *C*H2), 111.9 [2 × $(CH_3)_2$*C*], 105.2, 104.9 (C-1, C-1′), 82.7, 82.5, 82.3, 81.9, 80.6 (C-2, C-4, C-4′, C-2′, C-3), 80.3 (C-3′), 72.0 (OCH_2Ph), 62.3 (O*C*H_2CH═CH_2), 60.8 (O*C*H_2CH_3), 57.4(C-5), 44.4 (*C*H_2NH), 30.1 (C-6), 27.1, 26.6, 24.9 [2 × C(*C*H_3)$_2$], 14.5 (CH_3).

Anal. Calcd. for $C_{30}H_{43}O_{10}N$ C, 62.39; H, 7.45; N, 2.23; Found: C,62.30; H, 7.40; N, 2.20.

Ethyl 5-(5′-amino-5′-deoxy-1′,2′-*O*-isopropylidene-3′-*O*-methyl-α-D-xylofuranos-5′-yl)-3-*O*-allyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronate (11). Reaction of aldehyde **1b** (1.0 g, 4.95 mmol) with amino ester **3c** (1.56 g, 4.95 mmol) in presence of $NaBH_4$ (0.37 g, 5.01 mmol) as described above gave compound **11** (2.0 g, 82.2%) as colorless oil; R_f 0.48 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D^{20}$ −52.0° (*c* 0.10, chloroform); MS (FAB) = m/z 502 $(M+H)^+$; IR (Neat) ν_{max} cm^{-1}: 3788, 1780; ^1H NMR (200 MHz, $CDCl_3$): δ 5.92 (two d, J = 3.8 Hz, 2H, H-1, H-1′), 5.87 (m, 1H, OCH_2-*CH*═CH_2), 5.23 (m, 2H, O*C*H_2CH═CH_2), 4.54 (two d, 1H, J = 3.8 Hz, H-2, H-2′), 4.16 (m, 2H, C-4, C-4′), 4.14 (q, J = 6.2 Hz, 2H, O*C*H_2CH_3), 3.78 (d, J = 3.2 Hz, 1H, H-3), 3.68 (d, J = 3.2 Hz, 1H, H-3′), 3.39 (s, 3H, $-OCH_3$), 3.20 (m, 1H, H-5′), 3.04 (d, 1H, J = 6.4 Hz, 2H, H-5′), 1.70 (br s, exchangeable 1H, NH), 1.65 (m, 2H, H-6), 1.49, 1.30 [s, 12H, 2 × $(CH_3)_2C$], 1.12 (OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 133.95 (CH_2═*C*HCH_2), 118.4 (*C*H_2═$CHCH_2$), 111.9, 111.8 [2 × $(CH_3)_2$*C*], 105.1, 104.9 (C-1, C-1′), 84.5 (C-2); 82.4, 82.3, 82.2, 81.7 (C-2′, C-4, C-4′ C-3′), 80.1 (C-3), 71.1 (O*C*H_2CH═CH_2), 60.8 (-O*C*H_2CH_3) 57.9 (OCH_3), 57.0 (C-5), 44.1 (C-5′), 36.5 (C-6), 27.1, 26.3 [$C(CH_3)_2$], 14.5 (OCH_2CH_3).

Anal. Calcd. for $C_{23}H_{37}NO_{10}$: C, 56.66; H, 7.65; N, 2.87; Found: C, 56.32; H, 7.82; N, 2.77.

Ethyl 6-(5′-amino-3′-*O*-benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-6,7-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctapyranuronate (12). Reaction of aldehyde **1a** (2.0 g, 7.19 mmol) with amino ester **4** (2.50 g, 7.19 mmol) in presence of $NaBH_4$ (0.270 g, 7.10 mmol) as described above gave the compound **12** (3.60 g, 80%) as colorless oil; R_f 0.52 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D$ −40.0° (*c* 0.10, chloroform); MS (FAB) = m/z 608 $(M+H)^+$; IR(Neat)ν_{max} cm^{-1}: 3370, 1725; ^1H NMR (200 MHz, $CDCl_3$): δ 7.35–7.27 (m, 5H, Ar-H), 5.93 (d, J = 3.9 Hz, 1H, H-1′), 5.52 (d, J = 5.1 Hz, 1H, H-1), 4.63–4.54 (m, 4H, CH_APh, CH_BPh, H-3,H-2′), 4.37–4.30 (m, 3H, H-2, H-4, H-4′), 4.08 (q, J = 7.2 Hz, 2H, O*C*H_2CH_3), 3.96 (d, J = 3.0 Hz, 1H,

H-3′), 3.90 (d, $J = 7.2$ Hz, 1H, H-5), 3.40 (m, 1H, H-6), 3.0 (m, 2H, H-5′), 2.60–2.40 (m, 2H, H-7), 1.63 (br s, 1H, NH) 1.50–1.22 [m, 21H, 2 × $(CH)_3C$, CH_3]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.5 (C═O), 138.1, 128.9, 129.0, 127.9 (Ar-C), 111.9, 109.6, 108.6 [3 × $(CH_3)_2C$], 105.3 (C-1), 96.9 (C-1′), 82.7, 82.5 (C-2′,C-4′), 80.4 (C-3′), 72.3 (OCH_2Ph), 71.7, 71.4, 71.0 (C-2, C-4, C-3), 68.8 (C-5), 60.7 (OCH_2CH_3), 56.1 (C-6), 45.5 (CH_2NH), 35.9 (C-7), 27.1, 24.7 [$C(CH_3)_2$].

Anal. Calcd. for $C_{31}H_{45}NO_{11}$: C, 61.27; H, 7.46; N, 2.30; Found: C, 61.22; H, 7.40; N, 2.38.

Ethyl 6-(5′-amino-5′-deoxy-1′,2′-*O*-isopropylidene-3′-*O*-methyl-α-D-xylofuranos-5′-yl)-6,7-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctapyranuronate (13). Reaction of aldehyde, **1b** (1.50 g, 7.42 mmol) with amino ester **4** (2.70 g, 7.42 mmol) in presence of $NaBH_4$ (0.250 g, 6.61 mmol) as described above gave the above compound **13** (2.32 g, 59.2%) as colorless oil; R_f 0.54 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D^{20}$ −23.7° (*c* 0.12, chloroform); MS (FAB) = m/z 532 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3361,1726; ^1H NMR (200 MHz, $CDCl_3$): δ 5.87 (d, $J = 3.8$, 1H, H-1′), 5.50 (d, $J = 5.0$, 1H, H-1), 4.61–4.49 (m, 3H, H-2, H-2′, H-3), 4.28–4.25 (m, 2H, H-4, H-4′), 4.13 (q, $J = 6.2$ Hz, 2H, OCH_2CH_3), 3.74 (m, 2H, H-3′, H-5), 3.40 (s, 3H, OCH_3), 3.60 (m, 1H, H-6), 2.94 (m, 2H, H-5′), 2.40–2.20 (m, 2H, H-7), 1.63 (br s, exchangeable1H, -NH), 1.48–1.21 [m, 21H, (2 × $CH)_3C$, CH_3]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.0 (C═O), 111.9, 109.3, 108.8 [$(CH_3)_2C$], 105.2 (C-1′), 96.9 (C-1), 84.2 (C-2′), 82.0 (C-4′), 80.0, 79.9 (C-3, C-3′), 71.2, 70.8 (C-2, C-4), 68.7 (C-5), 60.4 (OCH_2), 58.1 (-OCH_3), 54.4 (C-6), 44.1 (CH_2NH), 34.7 (C-7), 27.1, 26.4, 24.9 [3 × $C(CH_3)_2$], 14.6 (CH_3).

Anal. Calcd. for $C_{25}H_{41}NO_{11}$:C, 56.49; H, 7.72; N, 2.63;. Found: C, 56.43; H, 7.70; N, 2.68.

Ethyl 6-(3′-*O*-allyl-5′-amino-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-6,7-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctapyranuronate (14). Reaction of aldehyde, **1c** (0.73 g, 3.30 mmol) with amino ester **4** (1.1 g, 3.30 mmol) in presence of $NaBH_4$ (0.140 g, 5.2 mmol) as described above gave the compound **14** (1.6 g, 88%) as colorless oil; R_f 0.48 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D^{20}$ −82.0° (*c* 0.10, chloroform); MS (FAB) = m/z 558 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3679, 1731; ^1H NMR (200 MHz, $CDCl_3$): δ 5.91 (d, $J = 3.6$ Hz, 1H, H-1′), 5.55 (d, $J = 5.2$ Hz, 1H, H-1), 5.25 (dd, $J = 19.0$ and 1.4 Hz, 2H, $OCH_2CH{=}CH_2$), 4.59–4.53 (m, 2H, H-3, H-2′), 4.33 (dd, $J = 5.2$ and 2.0 Hz, 1H, H-2), 4.12 (q, $J = 6.8$ Hz, 2H, OCH2), 4.00 (m, 2H, H-4, H-4′), 3.90 (m, 1H, H-3′), 3.11–3.05 (m, 3H, CH_2NH, H-5), 2.91 (m, 1H, H-6), 1.90–1.60 (m, 2H, H-7), 1.70 (br s, exchangeable H, -NH), 1.49, 1.44 [s, 12H, 2 × $(CH)_3C$], 1.31 [s, 6H, $(CH_3)_2C$], 1.25 (t, $J = 6.8$ Hz, 3H, OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.2 (*C* = O), 134.4 ($CH_2{=}CHCH_2O$), 118.2 ($OCH_2CH{=}CH_2$), 111.8, 109.6, 108.8 [3 × $(CH_3)_2C$], 105.2 (C-1′), 96.9 (C-1), 82.7, 82.1, 79.9 (C-2′,C-4′,C-3′), 71.4, 71.1, 70.9 (C-2, C-3, C-4), 68.8 (C-5), 60.7 (OCH_2CH_3), 57.7 (C-6), 43.6 (CH_2NH), 28.4 (C-7), 27.1, 26.7, 24.9 [3 × $C(CH_3)_2$], 14.5 (CH_3).

Anal. Calcd. for $C_{27}H_{43}NO_{11}$: C, 58.15; H, 7.77; N, 2.51; Found: C, 58.20; H, 7.82; N, 2.46.

Ethyl 6-(6′-amino-6′-deoxy-1′,2′:3′,4′-di-*O*-isopropylidene--α-D-galactoctapyranos-6′-yl)-6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctapyran uronate (15). Reaction of aldehyde **2** (2.0 g, 7.75 mmol) with amino ester **4** (2.70 g, 7.75 mmol) in presence of $NaBH_4$ (0.29 g, 7.86 mmol) as described above gave the compound

15 (4.10 g, 90%) as colorless oil; R_f 0.50 (hexane : ethyl acetate, 3 : 2), $[\alpha]_D^{20}$ −54.0° (*c* 0.10, chloroform); MS (FAB) = *m*/*z* 588 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3679, 1726; ^1H NMR (200 MHz, $CDCl_3$): δ 5.55, 5.50 (two d, *J* = 5.0 Hz, 2H, H-1, H-1′), 4.58 (m, 2H, H-3, H-3′), 4.37–4.26 (m, 4H, H-2, H-2′, H-4, H-4′), 4.13 (q, *J* = 6.8 Hz, 2H, OCH_2), 3.80 (d, *J* = 6.6 Hz, 2H, H-5, H-5′), 3.32 (m, 1H, H-6), 2.86–2.33 (m, 4H, H-6′, H-7), 1.85 (br s, exchangeable 1H, NH), 1.53–1.21 [m, 27H, 4 × $(CH_3)_2C$, CH_3]; ^{13}C NMR (50 MHz, $CDCl_3$): 172.7 (C═O), 109.5, 109.3, 108.8, 108.7 [$(CH_3)_2C$], 97.9, 96.7 (C-1, C-1′), 72.0, 71.8, 71.2, 71.0, 70.9, 68.6, 62.6 (C-2, C-2′ C-4, C-3, C-3′, C-5′, C-5), 60.0 (OCH_2), 55.4 (C-6), 46.5 (CH_2NH), 36.0 (C-7), 26.4, 25.3, 24.8, 24.7 [$(CH_3)_2C$]; 14.5 (CH_3).

Anal. Calcd. for $C_{28}H_{45}NO_{12}$ C, 57.23; H, 7.72; N, 2.38;. Found: C, 57.20; H, 7.76; N, 2.40.

General Procedure for the Preparation of the Compounds (16–26)

5-(5′-Amino-3′-*O*-benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptanol (16). To a magnetically stirred slurry of $LiAlH_4$ in anhydrous THF (2 mL), a solution of ethyl 5-(5′-amino-3′-*O*-benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-sopropylidene-β-L-*ido*-heptofuranuronate **5** (1.5 g, 2.39 mmol) in anhydrous THF (5.0 mL) was added drop-wise at 0°C, and stirring continued for 30 min at 0°C. The reaction mixture was further stirred magnetically for 5 hr at ambient temperature. Excess $LiAlH_4$ was quenched by adding saturated aqueous sodium sulphate solution, and the reaction mixture was filtered. The solid cake was washed with THF and the filtrate concentrated under reduced pressure. The later was extracted with chloroform (2 × 25 mL) and water (12.5 mL) and dried (Na_2SO_4). Organic layer was concentrated under reduced pressure to give a crude mass, which was chromatographed over SiO_2 column using chloroform : methanol (98 : 2) as eluent to give **16** (1.12 g, 80%) as colorless oil; R_f 0.5 (chloroform : methanol, 24 : 1); $[\alpha]_D^{20}$ −61.8° (*c* 0.22, chloroform); MS (FAB) = *m*/*z* 586 $(M + H)^+$; IR (Neat): ν_{max} cm^{-1} 3332, 3754; ^1H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 10H, Ar-H); 5.90 (two d, *J* = 3.9 and 3.6 Hz, 2H, H-1, H-1′), 4.71–4.51 (m, 6H, 2 × CH_2Ph, H-2, H-2′), 4.17 (m, 2H, H-4, H-4′), 3.90 (d, *J* = 3.2 Hz, 1H, H-3), 3.82 (d, *J* = 3.2 Hz, 1H, H-3′), 3.72 (m, 2H, H-7), 3.30 (m, 1H, H-5), 3.0 (m, 2H, H-5′), 1.91 (br s, exchangeable 1H, NH), 1.47 [s, 6H, $(CH_3)_2C$], 1.32–1.25 [m, 8H, $(CH_3)_2C$, H-6]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.9, 128.9, 128.4, 128.1 (Ar-C), 111.9, 111.8 [2 × $(CH_3)_2C$], 105.2, 105.1 (C-1, C-1′), 82.9, 82.6, 82.3, 81.9, 81.7, 82.2 (C-2, C-2′ C-4, C-4′ C-3, C-3′), 72.3 (CH_2Ph), 62.5 (C-7), 57.2 (C-5), 44.2 (CH_2NH), 30.0 (C-6), 27.1, 26.7 [$C(CH_3)_2$].

Anal. Calcd. for $C_{32}H_{43}NO_9$: C, 65.64; H, 7.35; N, 2.39; Found: C, 65.10; H, 7.25; N, 2.38.

5-(5′-Amino-5′-deoxy-1′,2′-*O*-isopropylidene-3′-*O*-methyl-α-D-xylofuranos-5′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptanol (17). Reduction of amino ester **6** (4.0 g, 7.85 mmol) with $LiAlH_4$, (0.59 g, 15.7 mmol) and work up as described above afforded glycosyl amino alcohol **17** (1.56 g, 77.5%) as colorless oil;. R_f, 0.5 (chloroform/methanol, 24 : 1); $[\alpha]_D^{20}$ −43.0° (*c* 0.10, chloroform); MS (FAB) = *m*/*z* 510 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1} 3339, 3754; ^1H NMR (200 MHz, $CDCl_3$): δ 7.33–7.26 (m, 5H, Ar-H), 5.93 and 5.87 (two d, 1H, *J* = 3.7 Hz, 2H, H-1, and H-1′), 4.66–4.63

(m, 2H, CH_APh, and H-2′), 4.55 (d, $J = 3.7$ Hz, 1H, H-2), 4.42 (d, $J = 11.6$ Hz, 1H, OCH_BPh), 4.22–4.10 (m, 2H, H-4 and H-4′), 3.81 (d, $J = 3.2$ Hz, 1H, H-3), 3.70 (m, 2H, H-7), 3.67 (d, $J = 3.2$ Hz, 1H, H-3′), 3.37 (s, 3H, OCH_3), 3.32 (m, 1H, H-5), 3.02 (m, 2H, CH_2NH), 2.70 (br s, exchangeable H, 1H, NH), 1.48 [s, 6H, $(CH_3)_2C$], 1.32–1.22 (m, 8H, $(CH_3)_2$, H-6] ^{13}C NMR (50 MHz, $CDCl_3$): 137.3, 128.9, 128.2 (Ar-*C*), 112.0, 111.8 [$(CH_3)_2C$], 105.2, 105.1 (C-1, C-1′), 84.5, 82.5, 82.2, 81.8, 81.7, 80.1 (C-2, C-2′, C-4, C-4′, C-3, C-3′), 72.1 (*CH_2Ph*), 62.5 (C-7), 57.1 (OCH_3), 43.8 (CH_2NH), 29.8 (C-6), 27.1, 26.6 [$C(CH_3)_2$].

Anal. Calcd. for $C_{26}H_{39}NO_9$: C, 61.29; H, 7.66; N, 2.75; Found: C, 61.14; H, 7.26; N, 2.30.

5-(3′-*O*-Allyl-5′-amino-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptanol (18). Reduction of amino ester **7** (1.0 g, 1.73 mmol) with $LiAlH_4$, (0.14 g, 3.46 mmol) and work up as described above afforded glycosyl amino alcohol **18** (0.32 g, 60%) as colorless oil; R_f, 0.5 (chloroform/methanol, 24 : 1); $[\alpha]_D^{20}$ −68.0° (*c* 0.10, chloroform); MS (FAB) = *m*/*z* 536 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3347, 3757; ^1H NMR (200 MHz, $CDCl_3$): δ 7.32–7.27 (m, 5H, Ar-H), 5.90, 5.87 (m, 3H, H-1, H-1′, $OCH_2CH{=}CH_2$), 5.20 (dd, $J = 19.0$ Hz, 1.4 Hz, 2H, $OCH_2CH{=}CH_2$), 4.71–4.41 (m, 4H, OCH_2Ph, H-2, H-2′), 4.20–4.06 (m, 4H, H-4, H-4′$OCH_2CH{=}CH_2$), 3.83–3.80 (m, 2H, H-3, H-3′), 3.73 (t, $J = 5.8$ Hz, 2H, H-7), 3.30 (m, 1H, H-5), 2.90 (m, 2H, CH_2NH), 1.75 (br s, exchangeable 1H, NH), 1.47 [s, 6H, $(CH_3)_2C$], 1.32–1.30 [m, 8H, $(CH_3)_2C$, H-6]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.2 (OCH_2-$CH{=}CH_2$), 134.4, 128.9, 128.5, 128.4 (Ar-C), 118.4 ($OCH_2CH{=}CH_2$), 111.9, 111.8 [$(CH_3)_2C$], 105.2, 105.0 (C-1, C-1′), 83.2, 82.6, 82.2, 82.1 81.8, 81.7 (C-2, C-2′, C-4, C-4′, C-3, C-3′), 72.7 (OCH_2Ph), 71.3 ($OCH_2CH{=}CH_2$), 62.5 (C-7), 57.1 (C-5), 45.9 (CH_2NH), 29.8 (C-6), 27.1, 26.7 [2 × $C(CH_3)_2$].

Anal. Calcd. for $C_{28}H_{41}NO_9$: C, 62.80; H, 7.66; N, 2.62; Found: C, 62.32; H, 7.26; N, 2.38.

5-(6′-Amino-6′-deoxy-1′,2′:3′,4′-di-*O*-isopropylidene-α-D-galactoctapyranos-6′-yl)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptanol (19). Reduction of amino ester **8** (1.5 g, 2.47 mmol) with $LiAlH_4$ (0.18 g, 4.49 mmol) and work up as described above afforded glycosyl amino alcohol **19** (0.55 g, 65%) as colorless oil; R_f 0.50 (chloroform : methanol, 24 : 1), $[\alpha]_D^{20}$ −76.0° (*c* 1.0, chloroform); MS (FAB) = *m*/*z* 566 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3655, 3343; ^1H NMR (200 MHz, $CDCl_3$): δ 7.35–7.32 (m, 5H, Ar-H), 5.93 (d, $J = 3.9$ Hz, 1H, H-1′), 5.53 (d, $J = 4.8$ Hz, 1H, H-1′), 4.70–4.53 (m, 3H, OCH_APh, H-2, H-3′), 4.40 (d, $J = 11.7$ Hz, 1H, CH_BPh), 4.28 (dd, $J = 4.8$ and 2.4 Hz, 1H, H-2′), 4.16 (m, 2H, H-4, H-4′), 3.80 (d, $J = 2.7$ Hz, 1H, H-3), 3.75 (m, 2H, H-7), 3.31 (m, 1H, H-5), 2.97 (m, 2H, H-6), 1.90 (br s, exchangeable 1H, NH), 1.50–1.24 [m, 20H, 3 × $(CH)_3C$, H-6]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 137, 128.9, 128.5, 128.3 (Ar-C), 111.9, 109.6, 108.9 [$(CH_3)_2C$], 105.1 (C-1), 96.7(C-1′), 82.2, 81.8 (C-2, C-4), 72.2, 72.0, 71.2, 70.8 (C-2′, C-4′, C-3′, OCH_2Ph), 66.0 (C-3), 62.7 (C-7), 57.2 (C-5), 45.7 (CH_2NH), 29.9 (C-6), 28.1, 27.1, 26.6, 26.4, 25.3, 24.9 [3 × $C(CH_3)_2$].

Anal. Calcd. for $C_{29}H_{43}NO_{10}$: C, 61.59; H, 7.61; N, 2.48; Found: C, 61.04; H, 7.26; N, 2.38.

5-(6′-Amino-6′-deoxy-1′,2′:3′,4′-di-*O*-isopropylidene-α-D-galactoctapyranos-6′-yl)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptanol (20). Reduction of amino ester **9** (0.8 g, 0.37 mmol) with $LiAlH_4$ (0.12 g, 0.74 mmol) and work up as described above afforded glycosyl amino alcohol **20** (0.23 g, 60%) as colorless oil; RF

0.50 (chloroform : methanol, 24 : 1), $[\alpha]_D^{20}$ −50.0° (*c* 0.12, chloroform); MS (FAB) = *m*/*z* 490 $(M+H)^+$; IR(Neat)ν_{max} cm^{-1}: 3757, 3357; ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.90 (d, *J* = 4.0 Hz, 1H, H-1), 5.53 (d, *J* = 5 Hz, 1H, H-1′), 4.60–4.56 (m, 2H, H-3′, H-2), 4.31 (d, *J* = 2.0 Hz, 1H, H-2′), 4.21 (m, 1H, H-4′), 3.90 (m, 1H, H-4), 3.86–3.60 (m, 3H, H-7, H-5′), 3.60 (d, *J* = 2.0 Hz, 1H, H-3), 3.41 (s, 3H, OCH_3), 3.10 (m, 1H, H-5), 2.98 (m, 2H, H-6′), 2.40 (br s, exchangeable H, 1H, -OH), 1.70 (br s, exchangeable H, 1H, −NH), 1.62–1.25 [m, 20H, 3 × $(CH)_3C$, H-6]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 111.8, 109.6, 108.9 [$(CH_3)_2C$], 104.8 (C-1), 96.7 (C-1′), 84.3 (C-2), 82.2, 81.5 (C-4, C-3), 72.2 (C-3′), 71.2, 70.9 (C-2′, C-4′), 67.9 (C-5), 62.6 (C-5′), 57.8 (−OCH_3), 47.8 (CH_2NH), 30.2(C-6), 27.1, 26.6, 26.3, 25.3, 24.9 24.8 [$C(CH_3)_2$].

Anal. Calcd. for $C_{23}H_{39}NO_{10}$: C, 56.44; H, 7.97; N, 2.86; Found: C, 56.14; H, 7.26; N, 2.38.

5-(5′-Amino-3′-*O*-benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-3-*O*-allyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptanol (21). Reduction of amino ester **10** (1.1 g, 1.90 mmol) with $LiAlH_4$ (0.14 g, 3.80 mmol) and work up as described above afforded glycosyl amino alcohol **21** (0.35 g, 60%) as colorless oil; R_f 0.50 (chloroform/methanol, 24 : 1), $[\alpha]_D^{20}$ −50.0° (*c* 0.10, chloroform); MS (FAB) = *m*/*z* 536 $(M+H)^+$; IR (Neat)ν_{max} cm^{-1}: 3368, 3678; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.33–7.26 (m, 5H, Ar-H), 5.92–5.81 (m, 3H, H-1, H-1′, $OCH_2CH{=}CH_2$), 5.23 (dd, *J* = 19.0 and 1.4 Hz, 2H, $OCH_2CH{=}CH_2$), 4.75–4.52 (m, 4H, CH_APh, CH_BPh, H-2, H-2′), 3.92–3.89 (m, 4H, H-7, H-4, H-4′), 3.83–3.76 (m, 6H, H-3, H-3′, H-7, $OCH_2CH{=}CH_2$), 3.20 (m, 1H, H-5), 3.06 (m, 2H, CH_2NH), 2.80 (br s, exchangeable 1H, −OH), 1.70 (br s, exchangeable 1H, -NH), 1.57, 1.31 [s, 6H, $(CH_3)_2C$], 1.22 [m, 8H, $(CH_3)_2C$, H-6]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 137.9 ($OCH_2CH{=}CH_2$), 133.9, 128.8, 128.1, 127.9 (Ar-C), 118.5 ($OCH_2CH{=}CH_2$), 111.9, 111.8 $(CH_3)_2C$, 105.2, 105.1 (C-1, C-1′), 82.7, 82.5, 82.3, 82.1, 81.9 (C-2, C-2′, C-4, C-4′ C-3), 80.3 (C-3′), 72.0 (OCH_2Ph), 62.3 (C-7), 62.4 ($OCH_2CH{=}CH_2$), 57.4 (C-5), 44.4 (CH_2NH), 30.1 (C-6), 32.5, 30.1, 27.1, 26.6 [$C(CH_3)_2$].

Anal. Calcd. for $C_{28}H_{41}NO_9$: C, 62.80; H, 7.66; N, 2.61; Found: C, 62.12; H, 7.66; N, 2.38.

5-(5′-Amino-5′-deoxy-1′,2′-*O*-isopropylidene-3′-*O*-methyl-α-D-xylofuranos-5′-yl)-3-*O*-allyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptanol (22). Reduction of amino ester **11** (1.3 g, 2.59 mmol) with $LiAlH_4$, (0.19 g, 5.18 mmol) and work up as described above afforded glycosyl amino alcohol **22** (0.41 g, 70%) as colorless oil; R_f 0.50 (chloroform/methanol, 24 : 1), $[\alpha]_D^{20}$ −65.0° (*c* 0.10, chloroform); MS (FAB) = *m*/*z* 460 $(M+H)^+$; IR (Neat) ν_{max} cm^{-1}: 3658, 3332; ^{1}H NMR (200 MHz, $CDCl_3$): δ 5.92 (m, 2H, H-1, H-1′), 5.87 (m, 1H, $OCH_2CH{=}CH_2$), 5.23 (dd, *J* = 19.0 and 1.2 Hz, 2H, $OCH_2CH{=}CH_2$), 4.54 (two d, *J* = 3.8 Hz, 2H, H-2, H-2′), 4.19–4.13 (m, 3H, H-4, $OCH_2CH{=}CH_2$), 3.93–3.82 (m, 4H, H-7,H-4′, H-3′), 3.78 (d, *J* = 3.2 Hz, 1H, H-3), 3.39 (s, 3H, OCH_3), 3.20 (m, 1H, H-5), 3.04 (d, *J* = 6.4 Hz, 2H, H-5′), 1.70 (br s, exchangeable 1H, NH), 1.49 [s, 6H, $(CH_3)_2C$], 1.30 [m, 8H, $(CH_3)_2$, H-6]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 133.95 ($OCH_2CH{=}CH_2$), 118.4 ($OCH_2CH{=}CH_2$), 111.9, 111.8 [2 × $(CH_3)_2C$], 105.1, 105.0 (C-1, C-1′), 84.5, 82.3, 81.9, 81.8, 81.7, 80.1 (C-4, C-4′, C-2, C-2′ C-3, C-3′), 71.1 ($OCH_2CH{=}CH_2$), 62.3 (C-7), 57.9 (OCH_3), 57.0 (C-5), 44.1 (CH_2NH), 30.1 (C-6), 27.1, 26.3 [$C(CH_3)_2$].

Anal. Calcd. for $C_{22}H_{37}NO_9$: C, 57.51; H, 8.06; N, 3.05; Found: C, 57.04; H, 8.26; N, 2.78.

6-(5′-Amino-3′-*O*-benzyl-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-6,7-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctanol (23). Reduction of amino ester **12** (2.2 g, 3.62 mmol) with $LiAlH_4$, (0.27 g, 7.24 mmol) and work up as described above afforded glycosyl amino alcohol **23** (1.22 g, 60%) as colorless oil; R_f 0.50 (chloroform/methanol, 24 : 1), $[\alpha]_D^{20}$ −67.1° (*c* 0.14, chloroform); MS (FAB) = *m*/*z* 566 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3654, 3439; ^1H NMR (200 MHz, $CDCl_3$): δ 7.34–7.26 (m, 5H, Ar-H), 5.93 (d, *J* = 4.1 Hz, 1H, H-1′), 5.49 (d, *J* = 5.2 Hz, 1H, H-1), 4.68–4.56 (m, 4H, OCH_2Ph, H-2′, H-3), 4.32–4.23 (m, 3H, H-2, H-4′, H-5′), 3.93 (d, *J* = 3.4 Hz, 1H, H-3′), 3.83–3.77 (m, 3H, H-4, H-8), 3.43–3.25 (m, 3H, H-6, CH_2NH), 2.25 (br s, 1H, -OH), 1.78 (br s, exchangeable 1H, NH), 1.46–1.26 [m, 20H, 3 × $(CH_3)_2$ C, H-7]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 138, 128.8, 128.7, 128.0 (Ar-C), 111.9, 109.8, 109.1 [3 × $(CH_3)_2C$], 105.3 (C-1′), 96.9 (C-1), 82.6, 82.5, 80.0 (C-2′, C-4′, C-3′), 72.2, 71.4, 71.2, 70.8 (C-2, C-3, C-4, OCH_2Ph), 62.4 (C-8), 57.7 (C-6), 43.7 (CH_2NH), 28.4 (C-7), 27.1, 26.4, 24.9 [3 × $C(CH_3)_2$].

Anal. Calcd. for $C_{29}H_{43}NO_{10}$: C, 61.59; H, 7.61; N, 2.48; Found: C, 61.78; H, 7.26; N, 2.38.

6-(5′-Amino-5′-deoxy-1′,2′-*O*-isopropylidene-3′-*O*-methyl-α-D-xylofuranos-5′-yl)-6,7-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctanol (24). Reduction of amino ester **13** (2.70 g, 5.1 mmol) with $LiAlH_4$ (0.38 g, 10.2 mmol) and work up as described above afforded glycosyl amino alcohol **24** (1.37 g, 55%) as colorless oil; R_f 0.50 (chloroform/methanol, 24 : 1), $[\alpha]_D^{20}$ −61.2° (*c* 0.16, chloroform); MS (FAB) = *m*/*z* 490 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3728, 3290; ^1H NMR (200 MHz, $CDCl_3$): δ 5.87 (d, *J* = 3.8 Hz, 1H, H-1′), 5.50 (d, *J* = 5.0 Hz, 1H, H-1), 4.61–4.49 (m, 3H, H-2, H-2′, H-3), 4.28–4.25 (m, 4H, H-4, H-4′, H-8), 3.74 (m, 2H, H-3′, H-5), 3.40 (s, 3H, OCH_3), 3.60 (m, 1H, H-6), 2.94 (m, 2H, CH_2NH), 1.63 (br s, exchangeable 1H, -NH), 1.43 [s, 6H, $(CH)_3C$)], 1.32–1.26 [m, 8H, $(CH_3)_2C$, H-7]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 111.9, 109.3, 108.8 [3 × $(CH_3)_2C$], 105.2 (C-1′), 96.9 (C-1), 84.2 (C-2′), 82.0 (C-4′), 80.0, 79.9 (C-3, C-3′), 71.2, 70.8 (C-2, C-4), 68.7 (C-5), 62.4 (C-8), 58.1 (OCH_3), 54.4 (C-6), 44.1 (CH_2NH), 28.7 (C-7), 27.1, 26.4, 24.9 [$C(CH_3)_2$].

Anal. Calcd. $C_{23}H_{39}NO_{10}$: C, 56.43; H, 8.03; N, 2.86; Found: C, 56.43; H, 8.03; N, 2.86.

6-(3′-*O*-Allyl-5′-amino-5′-deoxy-1′,2′-*O*-isopropylidene-α-D-xylofuranos-5′-yl)-6,7-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctanol (25). Reduction of amino ester **14** (1.2 g, 2.15 mmol) with $LiAlH_4$ (0.16 g, 4.30 mmol) and work up as described above afforded glycosyl amino alcohol **25** (0.66 g, 60%) as colorless oil; R_f 0.50 (chloroform/methanol, 24 : 1), $[\alpha]_D^{20}$ −65.0° (*c* 0.10, chloroform); MS (FAB) = *m*/*z* 516 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3650, 3346; ^1H NMR (200 MHz, $CDCl_3$): δ 5.91–5.80 (m, 2H, H-1′, $OCH_2CH{=}CH_2$), 5.55 (d, *J* = 5.2 Hz, 1H, H-1), 5.25 (dd, *J* = 19.0 and 1.4 Hz, 2H, $OCH_2CH{=}CH_2$), 4.59–4.53 (m, 2H, H-3, H-2′), 4.33 (d, *J* = 5.2 Hz, 1H, H-2), 4.21–4.10 (m, 3H, $OCH_2CH{=}CH_2$ H-4′), 3.90 (m, 1H, H-3′), 3.86 (m, 3H, H-8, H-4), 3.11–3.05 (m, 3H, CH_2NH, H-6), 2.91 (m, 1H, H-5), 2.40 (br s, exchangeable 1H, -OH), 1.70 (br s, exchangeable 1H, -NH), 1.62–1.25 [m, 20H, [3 × $(CH_3)_2$C, H-7]; ^{13}C NMR (50 MHz, $CDCl_3$): δ 134.4 $OCH_2CH{=}CH_2$), 118.2 ($OCH_2CH{=}CH_2$), 111.8, 109.6, 108.8 [3 × $(CH_3)_2C$], 105.2 (C-1′), 96.9 (C-1), 82.7, 82.1, 79.9 (C-2′, C-4′, C-3′); 71.4, 71.1, 70.9 (C-3, C-2, C-4, C-8), 68.3 (C-5), 62.4 (OCH_2-$CH{=}CH_2$), 57.7 (C-6), 43.6 (CH_2NH), 28.4 (C-7), 27.1, 26.7, 26.4, 26.3 25.3, 24.9 [3 × $C(CH_3)_2$].

Anal. Calcd. for $C_{25}H_{41}NO_{10}$: C, 58.25; H, 7.96; N, 2.48; Found: C, 58.04; H, 7.26; N, 2.38.

6-(6′-Amino-6′-deoxy-1′,2′:3′,4′-di-*O*-isopropylidene-α-D-galactoctapyranos-6′-yl)-6,7-dideoxy-1,2 : 3,4-di-*O*-isopropylidene-β-L-*glycero*-α-D-galactoctanol (26). Reduction of amino ester **15** (1.72 g, 2.93 mmol) with $LiAlH_4$ (0.22 g, 5.86 mmol) and work up as described above afforded glycosyl amino alcohol **26** (0.79 g, 50%) as colorless oil; R_f 0.50 (chloroform/methanol, 24 : 1), $[\alpha]_D^{20}$ −48.0° (*c* 0.12, chloroform), MS (FAB) = *m*/*z* 546 $(M + H)^+$; IR (Neat) ν_{max} cm^{-1}: 3679, 3445; ^1H NMR (200 MHz, $CDCl_3$): δ 5.52 (two d, *J* = 5.0 Hz, 2H, H-1, H-1′), 4.56 (two d, *J* = 6.0 Hz, 2H, H-3, H-3′), 4.33–4.28 (m, 4H, H-2, H-2′, H-8), 3.88–3.78 (m, 4H, H-4, H-4′, H-5, H-5′), 2.6 (m, 1H, H-6), 2.50–2.40 (m, 2H, CH_2NH), 1.53 (m, 2H, H-7), 1.54–1.25 [m, 20H, 4 × $[(CH_3)_2C]$; ^{13}C NMR (50 MHz, $CDCl_3$): δ 109.7, 109.0 [2 × $(CH_3)2C$], 96.8, 96.7 (C-1, C-1′), 72.5, 72.3, 71.6, 71.4, 70.9 (C-3, C-3′, C-2, C-2′, C-4, C-4′), 68.1, 67.9 (C-5, C-5′), 62.8 (C-8), 57.4 (C-6), 44.2 (CH_2NH), 28.4 (C-7), 26.4, 25.3, 24.9, 24.8 [$(CH_3)_2C$].

Anal. Calcd. for $C_{26}H_{43}NO_{11}$: C, 57.23; H, 7.94; N, 2.57; Found: C, 57.04; H, 8.26; N, 2.38.

Glucose-6-phosphatase (D-glucose-6-phosphate phosphorylase; EC 3.1.3.9) activity determination.[12] The liver of a Wistar rat that was fasted overnight was excised and a 10% homogenate was prepared in 150 mM KCl (w/v) using a Potter Elvejhem glass homogenizer fitted with Teflon pestle. The homogenate was centrifuged at 1000 × g for 15 min at 4°C, and the supernatant was decanted and used as enzyme source.

The effect of the test compound was studied by preincubating 100 μM of the compound in 1.0 mL reaction system for 10 min and then determining the residual glucose-6-phosphatase activity according to the method of Hubscher and West (1965). The assay system contained 0.3 M citrate buffer (pH6.0), 28 mM EDTA, 14 mM NaF, 200 mM glucose-6-phosphate, and appropriate amount of enzyme protein. The mixture was incubated at 37°C for 30 min, after which reaction was stopped by the addition of 1.0 mL of 10% TCA. Estimation of inorganic phosphate (Pi) in protein-free supernatant was done according to the method of Taussky and Shorr (1953). Glucose-6-phosphatase activity was defined as μM of Pi release per min per mg protein.

Glycogen phosphorylase (α-1,4 D-Glucan: Orthophosphate α- glucosyl Transferase, EC 2.4.1.1) activity determination.[13] Livers of Wistar strain of albino rats were excised. Ten percent homogenate (w/v) was prepared in 150 mM KCl using Potter Elvejhem glass homogenizer fitted with Teflon pestle. The homogenate was centrifuged at 1000 × g for 15 min at 4°C; supernatant was decanted and used as an enzyme source.

The effect of the test compound was studied by preincubating 100 μM of the compound in 1.0 mL reaction system for 10 min and then determining the residual glycogen phosphorylase activity according to the method of Rall et al. (1957). The assay mixture contained 0.2 mL mixture A (glycogen 57 mg, G-1-P 188 mg, NaF 42 mg and 5′ AMP (4 mM) in 10 mL distilled water) and 0.1 mL mixture B (enzyme protein). It was incubated at 37°C for 30 min, after which reaction was stopped by the addition of 0.1 mL of 10% TCA and then 0.4 mL sodium acetate (100 mM) was added to prevent the spontaneous hydrolysis of G-1-P present in the reaction mixture. The estimation of inorganic phosphate in the protein-free supernatant was done according to the method of Taussky and Shorr (1953). Glycogen phosphorylase activity was defined as μM of Pi release per min per mg protein.

α-Glucosidase (EC 3.2.1.20) activity determination.[14] The intestine of a male albino rat (CF strain) was excised and opened, and the mucosa was collected and

pooled. A 10% homogenate was prepared in 150 mM KCl using a Potter Elvejhem glass homogenizer fitted with Teflon pestle. The homogenate was centrifuged at 1000 × g for 15 min, and the supernatant was decanted and stored at 4°C. The supernatant was dialyzed at 4°C against 50 mM Tris–HCl buffer pH 7.0 with two or three changes of buffer. The dialyzed supernatant was saturated with ammonium sulphate to the final concentration of 30%. The sample was kept at 4°C overnight and then centrifuged to collect the supernatant and precipitate separately. Thirty percent ammonium sulphate saturated supernatant was further saturated to 60% with ammonium sulphate. Again the precipitate and supernatant were separated by centrifugation. Finally the 60% ammonium sulphate saturated supernatant was further saturated to 100% with further addition of ammonium sulphate. The precipitate and supernatant was once again separated, and all the samples were analyzed for α-glucosidase activity using p-nitrophenyl-α-D-glucopyranoid (PNPG) as substrate. The enzyme activity was found maximum in 60–100% ammonium sulphate precipitate, and this fraction was used as a source of enzyme for studying the effect of the test compounds.

Added were 100 μL of purified α-glucosidase (0.1 mg/mL) and 25 μL of glutathione (1.0 mg/mL), and the total volume was made up to 1 mL by adding 0.67 mM phosphate buffer (pH 6.8). The reaction mixture was incubated at room temperature for 10 min with the desired test compound (10 mM) dissolved in 100% DMSO. Reaction was started by the addition of 50 μL p-nitrophenyl-α-D-glucopyranoside (3 mg/mL), and increase in absorbance was recorded at 400 nm for a period of 5 min at the interval of 30 sec (Lebovitz, 1997).

Protein estimation.[15] The proteins of liver homogenate was precipitated with an equal volume of 10% TCA (w/v), washed twice with 5% TCA, dissolved in 0.1 N NaOH, and estimated according to the method of Lowry et al. (1951) using bovine serum albumin as standard.

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REFERENCES

1. (a) Pigman, W.; Horton, D., Eds., *The Carbohydrates, Chemistry and Biochemistry*, 2nd Ed.; Academic Press: New York, 1980; (b) Boons, G.J., Ed., *Carbohydrate Chemistry*; Blacie Academic and Professional: London, 1998; (c) Lehman, J. *Carbohydrate: Structure and Biology*; Theim Verlag: Stuttgart, 1998; (d) Robyt, J.F. *Essentials of Carbohydrate Chemistry*; Springer Verlag: New York, 1998.
2. (a) Varki, A. Glycobiology: Towards understanding the function of sugars. **1993**, *3*, 97; (b) Dwek, R.A. Chem. Rev. **1996**, *96*, 683; (c) Varki, A.; Cummings, R.; Esko, J.; Freeaze, H.; Hart, G.; Marth, J., Eds., *Essentials of Glycobilogy*; Cold Spring Harbor Laboratory Press: Cold Spring Harbor, New York, 1999.

3. (a) Musser, J.H. *Annual Reports in Medicinal Chemistry*; 1992; **27**(30); (b) Witczek, Z.J. *Current Medicinal Chemistry* **1995**, 392; (c) Sears, P.; Wong, C.H. Carbohydrate mimetics: A new strategy for tackling the problem of carbohydrate–mediated biological recognition. Angew. Chem. Int. Ed. Engl. **1999**, *38*, 2300–2324; (d) Danishefsky, S.J.; Allen, J.R. From the laboratory to the clinic: a retrospective on fully synthetic carbohydrate-based anticancer vaccines. Angew. Chem. Int. Ed. Engl. **2000**, *39*, 836–863.
4. Dondoni, A.; Giovanini, P.P.; Perrone, D. New synthesis of pyrrolidine homoazasugars via aminohomologation of furanoses and their use for the stereoselective synthesis of aza-*C*-disachharides. J. Org. Chem. **2002**, *67*, 7203–7214 (and references cited therein).
5. (a) Look, G.C.; Fatsch, C.H.; Wong, C.M. Enzyme-catalized organic synthesis: practical routes to aza sugars and their analogs for use as glycoprocessing inhibitors. Acc. Chem. Res. **1993**, *26*, 182–190; (b) Shilvok, J.P.; Fleet, G.W.J. The synthesis of deoxygalactostatin and 2, 6-imino-heptitol derivatives via stannane mediated hydroxymethylation of 5-azido-1,4-lactone. Synlett. **1998**, 554–556; (c) Verma, S.K.; Atanes, M.N.; Busto, J.H.; Thai, D.L.; Rapoport, H. Hydroxylated pyrrolidene. Enantiospecific synthesis of all-cis 2, 3, 4, 5-subsituted pyrrolidine derivatives from serine. J. Org. Chem. **2002**, *67*, 1314–1318.
6. (a) Wu, B.; Yang, J.; Robinson, D.; Hofstadler, S.; Griffey, R.; Swayze, E.E.; He, Y. Synthesis of linked carbohydrates and evaluation of their binding for 16 S RNA by mass spectrometry. Bioorg. Med. Chem. **2003**, *13*, 3915–3918; (b) Rostamdji, J.; Garpass, I.; Mobashery, S. Mechanism-based inactivators of bacterial aminoglycoside 3′-phosphotransferases. J. Am. Chem. Soc. **1995**, *117*, 80–84.
7. (a) Companini, L.; Dureault, A.; Depezay, J.C. One step synthesis of sulphur and nitrogen linked azadisachharide precursor from D-mannitol derived bis aziridines. Tetrahedron Lett. **1996**, *37*, 5095–5098; (b) Johnson, C.R.; Miller, M.W.; Golebiowski, A.; Sundram, H.; Ksebati, M.B. Synthesis of aza-C-disaccharides–a new class of sugar mimics. Tetrahedron Lett. **1994**, *35*, 8991–8994; (c) Wong, C.H.; Provencher, L.; Porco, J.A., Jr.; Jung, S.H.; Wang, Y.F.; Chen, L.; Wang, R.; Steensma, D.H. Synthesis and evaluation of homoazasugars as glycosidase inhibitors. J. Org. Chem. **1995**, *60*, 1492–1501; (d) Liu, K.K.C.; Kajimoto, T.; Chen, L.; Ichikawa, Y.; Wong, C.H. Use of dihydroxyacetone phosphate dependent aldolases in the synthesis of deoxyazasugars. J. Org. Chem. **1991**, *56*, 6280–6289; (e) Leemaire, S.G.; Popowyez, F.; Garcia, E.R.; Schutz, C.; Azeno, A.T.C.; Robina, I.; Vogel, P. Synthesis of tri- and tetraamines containing 2,3-dihydroxypyrrolidine and their inhibitory activity towards α-mannosidase. ARKIVOC **2002** (xii), 23–37.
8. Laurence, C.; Annie, D.; Depezay, J.C. One step synthesis of sulphur and nitrogen linked aza-disaccharide precursors from D-mannitol derived bis- aziridines. Tetrahedron Lett. **1996**, *37* (29), 5095–5098.
9. (a) Mishra, R.C.; Tewari, N.; Arora, K.; Ahmad, R.; Tripathi, R.P.; Tiwari, V.K.; Walter, R.D.; Srivatava, A.K. DBU assisted cyclorelease elimination: combinatorial synthesis and γ-glutamyl cystein synthetase & glutathione-*S*-transeferase modulatory activity of *C*-nucleoside analogs. Combi Chem & High Through Screen **2003**, *6*, 37–51; (b) Tewari, N.; Tiwari, V.K.; Mishra, R.C.; Tripathi, R.P.; Srivastava, A.K.; Ahmad, R.; Srivastava, R.; Srivastava, B.S. Synthesis and

bioevaluation of glycosyl ureas as α-glucosidase inhibitors and their effect on mycobacterium. Bioorg. Med. Chem. **2003**, *11*, 2911–2922.
10. (a) Tripathi, R.P.; Tripathi, R.; Tiwari, V.K.; Bala, L.; Sinha, S.; Srivastava, R.; Srivastava, B.S. Synthesis of glycosylated β-amino acids as new class of antitubercular agents. Eur. J. Med. Chem. **2002**, *37*, 773–781; (b) Khan, A.R.; Tripathi, R.P.; Tiwari, V.K.; Mishra, R.C.; Reddy, V.J.M.; Saxena, J.K. Conjugate addition of amines to sugar derived olefinic esters: synthesis of glycosylated amino esters as DNA topoisomerase-II inhibitors. J. Carbohydr. Chem. **2002**, *21*, 591–604.
11. Katiyar, D.; Mishra, R.C.; Tripathi, R.P. Diastereoselective synthesis of galactopyranosyl aminoesters and their transformation into C-nucleosides. J. Carbohydr. Chem. **2004**, *23*, 49–70.
12. Suter, S.L.; Nolan, J.J.; Wallace, P.; Gumbiner, B.; Olefsky, J.M. Metabolic effects of new oral hypoglycemic agent CS-045 in NIDDM subjects. Diabetes Care **1992**, *15* (2), 193–203.
13. Treadway, J.L.; Mendys, P.; Hoover, D.J. Glycogen phosphorylase inhibitors for the treatment of type 2 diabetes mellitus. Exp. Opin. Invest. Drugs. **2001**, *10*, 439–454.
14. (a) Lebovitz, H.E. α-Glucosidase inhibitors. Endrocrinol. Metabiol. Clin. North Am. **1997**, *26*, 539–555; (b) Kiyoshi, M.; Kiyofumi, T.; Kanthi, J.M.A.; Toshiro, M. Assay of α-glucosidase inhibitory activity using flow-biosensor system. Analytica Chimica Acta **1997**, *479* (2), 135–141.
15. Lowry, O.H.; Rosebrough, N.J.; Farr, A.L.; Randall, R.J. Protein measurement with the Folin phenol reagent. J. Biol. Chem. **1992**, *193* (1), 265–275.