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Synthesis and antitubercular activities of bis-glycosylated diamino alcohols ☆

R. P. Tripathi,[a,*] V. K. Tiwari,[a] N. Tewari,[a] D. Katiyar,[a] N. Saxena,[a] S. Sinha,[b] A. Gaikwad,[b] A. Srivastava,[c] V. Chaturvedi,[c] Y. K. Manju,[c] R. Srivastava[c] and B. S. Srivastava[c]

[a]*Division of Medicinal and Process Chemistry, Central Drug Research Institute, Lucknow 226001, India*
[b]*Division of Drug Target Discovery, Central Drug Research Institute, Lucknow 226001, India*
[c]*Division of Microbiology, Central Drug Research Institute, Lucknow 226001, India*

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Abstract—Conjugate addition of diamines to glycosyl olefinic esters **1a** and **1b** followed by reduction of resulting bis-glycosyl β-amino esters (**2–7** and **14–19**) with lithium aluminium hydride led to the respective glycosyl amino alcohols (**8–13** and **20–25**) in moderate to good yields. All the compounds were evaluated for antitubercular activity against *Mycobacterium tuberculosis* $H_{37}Ra$ and $H_{37}Rv$. Few of the compounds exhibited antitubercular activity with MIC as low as 6.25–3.12 μg/mL in virulent and avirulent strains. Compound **13** was found to be active against MDR strain and showed mild protection in mice.

1. Introduction

Mycobacterium tuberculosis, which causes tuberculosis (TB), is a single infectious agent that kills roughly two million people annually throughout the world, and as per WHO report, about one third of the world's population is infected with this bacterium.[1–3] The synergy of AIDS with TB and resistance to the front-line anti-TB drugs has worsened the problem.[4,5] The incredible thickness and impermeability of the cell wall complex requires a long period of treatment with many drugs[6–8] as the cell wall prevents the effective passage of the drugs into the organism.[9] Therefore, the mycobacterial cell wall is being looked at as a unique target to develop new drugs with shorter duration of treatment. Carbohydrates present mostly as arabinogalactan and arabinomannan are the integral part of the mAGP (mycolylated arabinogalactan peptidoglycan) complex of the cell wall[6] and sugars are also known to be involved in pathogenesis of the disease.[10] The glycosyl transferases as arabinosyl- and galactofuransyl transferases and many other enzymes including galactopyranosyl mutase and epimerases involved in the biosynthesis of sugar components of the cell wall are being targeted to develop new drugs.[11–13] Many sugar-based compounds have recently been reported[14] to inhibit one or more of the above enzymes and showed in vitro antitubercular activity. Looking into the structure of these compounds we have been involved in the synthesis of certain sugar-based glycosylated amino esters and amino alcohols as potent antimycobacterial agents[15–17] and few of them exhibited activity in MDR strains also. Further, it is known that dimerization of active molecules most often leads to enhancement in the bioprofile of the parent molecules.[18–20] Keeping in view the above points, we have synthesized and evaluated the antitubercular activity of bis-glycosylated diamino esters and alcohols. The synthesis of few of the bis-glycosylated diamino esters has already been reported by us,[21] however, their antitubercular activity has been carried out during this study.

2. Results and discussion

2.1. Chemistry

The bis-xylofuranosylated amino alcohols were synthesized from the respective xylofuranosylated amino

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* Corresponding author. Tel.: +91 522 22 12411; fax: +91 522 2613405; e-mail: rpt_56@yahoo.com

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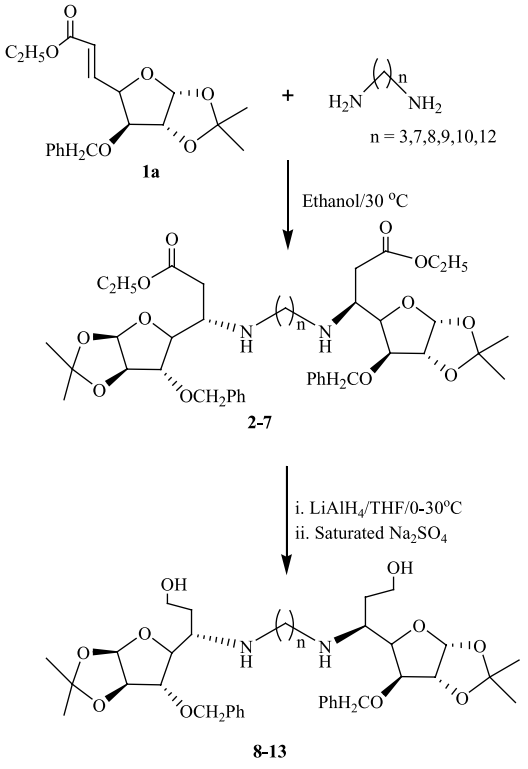
esters **2**–**7**. While the synthesis and structure elucidation of **2**, **3**, **6** and **7** have already been reported by us,[21] compounds **4** and **5** were newly prepared. The glycosyl amino esters **4** and **5** were prepared by reaction of 2 equiv of 3-*O*-benzyl glycofuranosylated olefinic ester **1a** with 1 equiv of 1,8-, and 1,9-diamino-alkanes, respectively, in ethanol at ambient temperature following the above procedure.[21] Purification of the crude products was carried out by column chromatography resulting in the isolation of diglycosylated diamino esters **4** and **5** in good yields as pure diastereoisomer with '*S*' configuration at C-5 in both the sugars. The said stereochemistry '*S*' at C-5 was determined already by us in such reactions.[15]

The structure of compound **4** was determined on the basis of its spectroscopic data and analysis. The MS FAB spectrum of this compound showed peak at *m*/*z* 841 corresponding to $[M+H]^+$. Its IR spectrum showed characteristic absorption bands at 3050, 2986, 2931, 2857 and 1728 cm^{-1} indicating the stretching frequencies of NH, CH_3, CH_2 and OC=O groups, respectively. In ^1H NMR spectrum of compound **4**, the characteristic H-1, H-2 and H-3 of the sugar ring appeared as doublet at δ 5.93 (J = 3.9 Hz), 4.62 (J = 3.9 Hz) and 3.93 (J = 3.0 Hz) respectively; while the H-4 appeared at δ 4.18 as a double doublet with J values of 8.7 and 3.1 Hz. The two geminal protons of the 3-*O*-benzyl substituent were observed as doublets at δ 4.69 and 4.44 with J values of 11.8 Hz, while the phenyl ring protons appeared as a five-proton multiplet at δ 7.32. The H-5 was observed as a multiplet at δ 3.40. The methylene protons of the carbethoxy group (OCH_2CH_3) appeared as a quartet at δ 4.12 (J = 7.0 Hz) while the carbethoxy methyl protons appeared as a multiplet at δ 2.35. A triplet at δ 1.19 (J = 7.1 Hz) and two multiplets at δ 2.60 and 1.26 each accounting for three, two and six protons, respectively, corresponded to OCH_2CH_3, NCH_2 and CH_2s, respectively. Methyl protons of the isopropylidene groups of the sugar moiety appeared as singlets at δ 1.48 and 1.31; while a broad singlet at δ 1.70 corresponded to exchangeable NH of the aminoalkyl linker. In ^{13}C NMR signals at δ 105.2, 82.3, 82.2, 82.1 and 54.4 corresponded to C-1, C-2, C-4, C-3 and C-5 of the sugar moiety, respectively, while the methylene carbon of the carbethoxy methyl substituent (CH_2COOEt) at C-5 appeared at δ 36.6. The characteristic signal for the methylene carbon of the 3-*O*-benzyl substituent of the sugar moiety was observed at δ 71.8 while the benzene ring carbons were observed at δ 137.5, 128.8, 128.4 and 128.2. The quaternary carbon of the isopropylidene moiety was observed at δ 112.0 while the two methyl carbons appeared at δ 27.1 and 26.7. A signal at δ 172.6 corresponded to the quaternary carbon of the ester group (OC=O) while the methylene and methyl carbons of the carbethoxy group were observed at δ 60.7 and 14.5, respectively. The methylene carbons of the N^1,N^8-octyl linker were observed at δ 47.6, 30.7, 29.9 and 27.6.

The spectroscopic data of compound **5** were almost similar to that of compound **4**. The only difference was the presence of one more methylene group in the diaminoalkyl linker in ^1H NMR and ^{13}C NMR spectra, and the appearance of $[M+H]^+$at 855 in FAB MS.

In the next step, reduction of the xylofuranosylated amino esters to the respective xylofuranosylated amino alcohols was carried out with lithium aluminium hydride ($LiAlH_4$) as reported earlier.[16] As a first case, the reaction of bis-xylofuranosylated amino ester **2** with $LiAlH_4$ in anhydrous terahdrofuran (TMF) at ambient temperature under nitrogen atmosphere led to the formation of bis-xylofuranosylated diamino alcohol **8** in good yield (86%) (Scheme 1). The structure of this compound could be established on the basis of spectral data and analysis. In the IR spectrum of this compound, the disappearance of stretching frequency at 1728 cm^{-1} and the appearance of an absorption band at 3328 cm^{-1} indicated the reduction of ester into alcohol. MS FAB spectrum of the compound showed $[M+H]^+$ at *m*/*z* 687. In the ^1H NMR spectrum of compound **8**, the disappearance of the signals corresponding to methylene and methyl protons of the carbethoxy group at δ 4.12 and 1.25, respectively, and the appearance of an extra signal at δ 3.74 as a multiplet, accounting for two protons for the CH_2OH, confirmed that the glycosyl amino ester was transformed into the respective alcohol. The chemical shifts and the splitting pattern of all other protons belonging to the sugar moiety and aminopropyl linker were almost similar to those of compound **2**. Further, in the ^{13}C NMR spectrum, the reduction of the two carbethoxy groups was evidenced by the disappearance of the signals at δ 172.2, 60.9 and 14.5 corresponding to quaternary carbon of the ester group and its methylene and methyl carbons. The hydroxy-

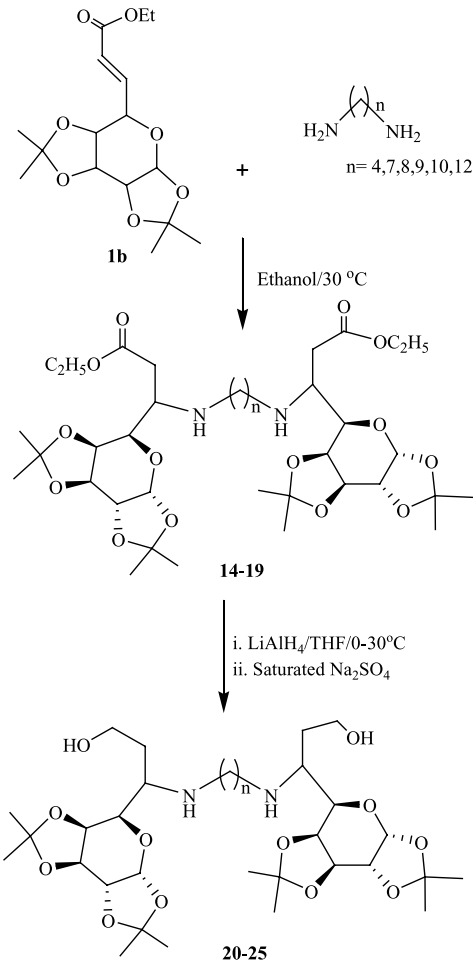


Scheme 1.

ethyl carbons were observed at δ 62.3 ($-CH_2OH$) and 30.7 (CH_2CH_2OH) while the C-6 appeared at δ 29.7. All other carbons of the sugar ring and its N^1,N^3-propyl linker were observed at their as usual chemical shifts.

Similar reduction of other xylofurnosylated amino esters **3**–**7** with $LiAlH_4$ in anhydrous THF at ambient temperature led to the formation of respective xylofuranosylated amino alcohols **9**–**13**, respectively, in good yields. The structures of all these compounds were elucidated on the basis of its spectroscopic data (IR, MS FAB, ^1H and ^{13}C NMR) and analysis as above.

In the second series of compounds, we have synthesized the N^1,N^n–bis-galactopyranosylated amino alcohols starting from respective galactopyranosylated amino esters (**14**–**19**) to see the difference of furanose and pyranose rings on the biological activity. The latter could be prepared by conjugate addition of 1 mol of diamines including 1,4-, 1,7-, 1,8-, 1,9-, 1,10- and 1,12-diamines with 2 mol of galactopyranosylated olefinic ester **1b** following our earlier reported method[22] (Scheme 2). The structures of these compounds were established on the basis of spectroscopic data and analysis. As compound **14**, like compound **2**, has C_2-symmetry, in ^1H NMR and ^{13}C NMR spectra the signals of only half of the compound were observed. In the ^1H NMR spectrum of **14** the characteristic H-1 proton of the sugar ring appeared as doublet at δ 5.54 (J = 5.1 Hz) and H-3 appeared as a double doublet at δ 4.57 (J = 7.9 and 2.0 Hz) while H-6 appeared as a multiplet at δ 3.22. The protons corresponding to carbethoxy methylene (–CH_2COOEt) and N-CH_2 appeared as a multiplet at δ 2.61. The methylene protons of the carbethoxy group (OCH_2CH_3) appeared as a quartet at δ 4.12 (J = 7.1 Hz) while NH appeared as a broad singlet at δ 1.82. Six protons of the two methyls of the isopropylidene group of the sugar moiety appeared as two singlets at δ 1.51 and 1.44, each accounting for three protons. A multiplet at δ 1.27 integrating for 11 protons was attributed to one methylene of the spacer merged with the singlet of the two isopropylidene methyls and the triplet of the three protons of the carbethoxy methyl. In the ^{13}C NMR spectrum of the above compound, signals at δ 96.9, 71.8, 71.4, 70.9 and 68.6 corresponded to sugar ring carbons C-1, C-3, C-2, C-4 and C-5, respectively. The signals corresponding to quaternary carbons of the carbonyl and two isopropylidene group appeared at δ 172.5, 109.6 and 108.9, respectively. The methylene carbons of carbethoxy, NCH_2, carbethoxy methylene and NCH_2CH_2 group appeared at δ 60.6, 47.3, 35.7 and 28.3, respectively, while signals at δ 26.3, 25.3, 24.7 and 14.5 corresponded to methyl carbons of isopropylidene and carbethoxy group. The structures of all other galactopyranosylated amino esters were in accordance with their ^1H NMR and ^{13}C NMR spectral data. It is appropriate to mention here that one of the above compounds **14** was diastereoisomerically pure and have *S*, *S* stereochemistry. However, compounds **15a** and **17a** were isolated in diastereoisomerically pure form with *R*, *S* stereochemistry at the newly created asymmetric centres while all other galactopyranosylated amino esters were isolated as a mixture of three diastereoisomers.



Scheme 2.

Galactopyranosylated amino alcohols **20**–**25** could be obtained by reduction of the respective amino esters with $LiAl_4$ in anhydrous THF at ambient temperature as above in good yields. As a first case in this series, reduction of galactopyranosylated amino ester **14** with four carbon spacer resulted in the respective galactopyranosylated amino alcohol **20** in 80% yield.

The structure of compound **20** could be established on the basis of spectral data and analysis. In the IR spectrum of this compound disappearance of stretching frequency at 1734 cm^{-1} and appearance of an absorption band at 3399 cm^{-1} indicated the reduction of ester into alcohol. The MS FAB spectrum of the compound showed $[M+H]^+$ at *m/z* 661. In the ^1H NMR spectrum, disappearance of the signals corresponding to methylene and methyl protons of the carbethoxy group at δ 4.12 and 1.27, respectively, and the appearance of a multiplet at δ 3.75, which accounted for two protons of the CH_2OH, to which the signal for H-5 merged, confirmed that the glycosyl amino ester was converted to the respective alcohol. The chemical shifts and the splitting pattern of all other protons belonging to the sugar moiety and aminobutyl linker were almost similar to those of compound **14**. Further, in the ^{13}C NMR spectrum the reduction of the two carbethoxy groups was evidenced by the disappearance of the signals at δ 172.5,

60.6 and 14.5 corresponding to quaternary carbon of the ester group and its methylene and methyl carbons. The hydroxyl ethyl carbons were observed at δ 62.4 (–CH_2CH_2OH) and 30.4 (CH_2CH_2OH) while the C-6 appeared at δ 59.3. All other carbons of the sugar ring and its N^1,N^4-butyl linker were observed at their usual chemical shifts. The structures of all other galactopyranosylated amino alcohols were in accordance with their spectral data and analysis.

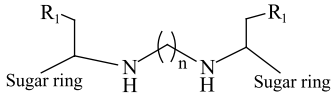
3. Biological activity

All the compounds including glycosyl amino alcohols and glycosyl amines were screened for their antitubercular efficacy using microalamar blue (MABA) method[23] against *M. tuberculosis* $H_{37}Ra$, while the agar microdilution method[24] was used for the in vitro activity determination against *M. tuberculosis* $H_{37}Rv$. Compound **13** was screened against few clinical isolates of MDR strains and also in vivo in mice model.[25] The activities of the biological screens are given in Tables 1–3.

4. Results and discussion

As is evident from Table 1 compounds **4**, **5**, **10**, **11**, **13**, **22** and **24** were found to be active as their minimum inhibitory concentrations (MIC) values were 6.25 μg/mL while other compounds have MIC values $\geqslant$12.5 μg/mL. In the bis-xylofuranosylated series, diamino ester and alcohol with eight- and nine-carbon diaminoalkane spacers were the most active compounds. It is interesting to note that compound **12** with diaminoalky spacer of 10 carbons is potent antitubercular against the avirulent strain (*M. tuberculosis* $H_{37}Ra$) while it is inactive against the virulent strain $H_{37}Rv$. Further, between compounds **7** and **13** with the same diamino alkyl spacer of 12 carbons, the alcohol is active while the ester is inactive. However, in galactopyranosyl series only the galactopyranosyl amino alcohols with 8- and 10-carbon diaminoalkyl spacers were the most active compounds while their counterparts, the amino esters **16** and **18** have MIC values of 12.5 and >25 μg/mL, respectively. No definite conclusion could be drawn for any structure–activity relationship (Fig. 1).

Table 1. Antitubercular activities of glycosylated amino esters (**2–7** and **14–19**) and corresponding alcohols (**8–13** and **20–25**)



Compound	*n*	R_1	Sugar ring	MABA MIC (μg/mL) against *M. tuberculosis* $H_{37}Ra$	Agar microdilution MIC (μg/mL) against *M. tuberculosis* $H_{37}Rv$
2	3	COOEt	Furanose	25	25
3	7	COOEt	Furanose	25	25
4	8	COOEt	Furanose	25	6.25
5	9	COOEt	Furanose	25	6.25
6	10	COOEt	Furanose	>50	>50
7	12	COOEt	Furanose	>50	>50
8	3	CH_2OH	Furanose	>50	50
9	7	CH_2OH	Furanose	>50	>50
10	8	CH_2OH	Furanose	>25	6.25
11	9	CH_2OH	Furanose	25	6.25
12	10	CH_2OH	Furanose	3.12	>50
13	12	CH_2OH	Furanose	12.5	6.25
14	4	COOEt	Pyranose	>25	>12.5
15	7	COOEt	Pyranose	>25	nd
15a	7	COOEt	Pyranose	>25	25
16	8	COOEt	Pyranose	>25	12.5
17	9	COOEt	Pyranose	25	25
17a	9	COOEt	Pyranose	nd	25
18	10	COOEt	Pyranose	nd	>25
19	12	COOEt	Pyranose	>25	>25
20	4	CH_2OH	Pyranose	>25	>12.5
21	7	CH_2OH	Pyranose	>25	12.5
22	8	CH_2OH	Pyranose	>25	6.25
22a	8	CH_2OH	Pyranose	>25	25
23	9	CH_2OH	Pyranose	>25	25
24	10	CH_2OH	Pyranose	>25	6.25
25	12	CH_2OH	Pyranose	25	12.5
INH	—	—	—	nd	0.025
Rifampicin	—	—	—	nd	0.20
Ethambutol	—	—	—	nd	2.0
Ofloxacin	—	—	—	nd	1.0

nd = not done.

Table 2. In vitro activity of compound **13** and standard drugs against MDR strains of *M. tuberculosis* H37Rv

Compound or drug	Growth of MDR strains after 6 weeks				
	BC-248[a]	BC-283[a]	VA-101[b]	BC-426[c]	BC-437[c]
Compound **13** (25 μg/mL)	–	–	–	+	–
INH (1 μg/mL)	++	++	++	++	++
Rifampicin (64 μg/mL)	++	++	++	++	++
Ethambutol (6 μg/mL)	++	++	++	–	–
No drug control	++	++	++	++	++

–, no growth; +, 1–20 growth (resistance); ++, heavy growth.
[a] Strains resistant to rifampicin, isoniazid, ofloxicin and ethambutol.
[b] Strains resistant to rifampicin, isoniazid and ethambutol.
[c] Strains resistant to rifampicin and isoniazid.

Table 3. In vivo efficacy of compound **13** in mouse model

Groups	In vivo efficacy	
	MST	Bacillary load in Lungs AFB/O/F
Compound **13** treated	21.30 ± 7.30	2.86
INH treated[a]	30.00 ± 0.00	0.30
Untreated control	19.30 ± 2.75	>300

[a] Clinical isolates were resistant to INH (1μg/mL).

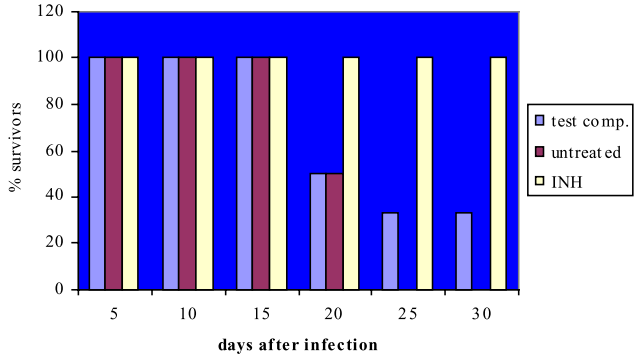


Figure 1. Efficacy evaluation of compound 13 in mouse model of tuberculosis.

Since compound **13** has the best MIC value in the series, it was also screened against five clinical MDR strains of *M. tuberculosis* isolated from TB patients. It was found to be effective against MDR strains in vitro at 25μg/mL tested while at the same concentration anti-TB drugs were ineffective (Table 2).

Compound **13**, which shows activity against MDR strains, was also screened in vivo in mouse model. As is evident from Table 3, there was only a marginal increase (5.5%) in the survival time of the mice as compared to control. Smear examination of lungs and spleen of the control and treated mice on day 22 of the treatment showed that there was 100- and 20-fold decrease of AFB/field in the lungs and spleen, respectively.

5. Conclusions

Bis-glycosylated amino esters and their respective amino alcohols could be synthesized in good yields by reaction of 2 equiv of glycosyl olefinic esters with 1 equiv of diamines followed by reduction of the intermediate amino esters with $LiAlH_4$. Many compounds displayed good activity in vitro against *M. tuberculosis* $H_{37}Rv$ and one of the compounds was found to be active against clinical isolates of resistant strain. The present study encourages further research into this series of compounds in order to find a new and novel antitubercular drug which will also be active in MDR cases.

6. Experimental

6.1. Chemistry

6.1.1. General methods. Thin-layer chromatography was carried out on silica gel (Kiesel 60-F254, Merck) and spots were developed in iodine vapours and also 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 residual proton in $CDCl_3$ was used as the reference. Chemical shifts are given as δ ppm values and '*J*' values are given in hertz (Hz). Elemental analyses were performed on a Perkin-Elmer 2400 II elemental analyzer. The optical rotations were measured in a 1.0 dm tube with a Jasco dip-140 polarimeter in chloroform. The excess of the reagents or solvents were evaporated under reduced pressure at a bath temperature between 55 and 60 °C.

6.1.2. N^1,N^8-Bis-(3-*O*-benzyl-5(*S*)-carbethoxymethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,8-diamino-octane (4). A solution of (*E*) ethyl(3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene)-α-D-1,4-heptofuranosyl-5-enoate (**1a**, 3.5 g, 10.05 mmol) and 1,8-diaminooctane (0.72 g, 5.02 mmol) in ethanol (25 mL) was magnetically stirred at ambient temperature for 18 h. The solvent was evaporated from the reaction mixture under reduced pressure and the crude product, thus obtained, was purified over SiO_2 column using chloroform:methanol (97:3) as eluent to afford the diastereochemically pure compound **4** as a colourless oil. Yield (2.80 g, 66%), $[\alpha]_D^{25} = -65.5°$ (*c* 0.10, $CHCl_3$); MS FAB *m/z*: 841

$[M+H]^+$; IR (KBr, cm^{-1}) *v*: 3450 (–NH), 2986, 2931, 2857 (CH_3 and CH_2 stretching), 1728 (OC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 7.32 (m, 5H, Ar–H), 5.93 (d, $J = 3.9$ Hz, 1H, H-1), 4.69 (d, $J = 11.8$ Hz, 1H, –OCH_APh), 4.62 (d, $J = 3.9$ Hz, 1H, H-2), 4.44 (d, $J = 11.8$ Hz, 1H, –OCH_BPh), 4.18 (dd, $J = 3.1$ and 8.7 Hz, 1H, H-4), 4.12 (q, $J = 7.0$ Hz, 2H, –OCH_2CH$_3$), 3.93 (d, $J = 3.0$ Hz, 1H, H-3), 3.40 (m, 1H, H-5), 2.60 (m, 2H, NCH_2), 2.35 (m, 1H, –CH_2COOEt), 1.70 (br s, 1H, –NH), 1.48 and 1.31 [each s, each 3H, >C(CH_3)$_2$], 1.26 (m, 6H, CH_2s), 1.19 (t, $J = 7.1$ Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.6 (OC=O), 137.5 (ArC), 128.8, 128.4, 128.2 (Ar–CH), 112.0 [>*C*(CH$_3$)$_2$], 105.2 (C-1), 82.3 (C-2), 82.2 (C-4), 82.1 (C-3), 72.5, 71.8 (–O*C* H$_2$Ph), 60.7 (–O*C*H$_2$CH$_3$), 54.4 (C-5), 47.6 (NCH$_2$), 36.6 (*C* H$_2$COOEt), 30.7, 29.9, 27.6 (CH_2s), 27.1, 26.7 [>C(*C*H$_3$)$_2$], 14.5 (–OCH$_2$*C*H$_3$). Anal. Calcd for $C_{46}H_{68}N_2O_{12}$: C, 65.71; H, 8.09; N, 3.33. Found: C, 66.54; H, 8.12; N, 3.71%.

6.1.3. N^1,N^9-Bis-(3-*O*-benzyl-5(*S*)-carbethoxymethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,9-diaminononane (5). A solution of (*E*) ethyl (3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene)-α-D-1,4-heptofuranosyl-5-enoate (**1a**, 3.20 g, 9.19 mmol) and 1,9-diaminononane (0.72 g, 4.59 mmol) was magnetically stirred as above for a period of 12 h. Column chromatography of the crude product using chloroform:methanol (98:2) as eluent afforded the compound **5** as a colourless oil. Yield (2.45 g, 62%), $[\alpha]_D^{25} = -76.8^\circ$ (*c* 0.06, $CHCl_3$); MS FAB *m*/*z*: 855 $[M+H]^+$; IR (KBr, cm^{-1}) *v*: 3430 (–NH), 2983, 2929, 2856 (CH_3 and CH_2 stretching), 1731 (OC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 7.32 (m, 5H, Ar–H), 5.93 (d, $J = 3.9$ Hz, 1H, H-1), 4.68 (d, $J = 11.8$ Hz, 1H, OCH_APh), 4.63 (d, $J = 3.9$ Hz, 1H, H-2), 4.44 (d, $J = 11.8$ Hz, 1H, OCH_BPh), 4.14 (dd, $J = 2.6$ and 9.0 Hz, 1H, H-4), 4.12 (q, $J = 7.1$ Hz, 2H, OCH_2CH$_3$), 3.93 (d, $J = 3.1$ Hz, 1H, H-3), 3.54 (m, 1H, H-5), 2.59 (m, 2H, NCH_2), 2.33 (m, 2H, CH_2COOEt), 2.00 (br s, 1H, –NH), 1.48 and 1.31 [each s, each 3H, >C(CH_3)$_2$], 1.26 (m, 6H, CH_2s), 1.22 (t, $J = 7.1$ Hz, OCH$_2$CH_3); ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.9 (OC=O), 137.4 (ArC), 128.8, 128.4, 128.2 (Ar–CH), 111.9 [>*C*(CH$_3$)$_2$], 105.2 (C-1), 82.6 (C-2), 82.4 (C-4), 82.2 (C-3), 72.4, 71.8 (O*C*H$_2$Ph), 60.7 (O*C*H$_2$CH$_3$), 54.4 (C-5), 47.7, 47.3 (NCH$_2$), 36.7 (*C* H$_2$COOEt), 31.1, 30.8, 29.9, 27.7 (CH_2s), 27.1, 26.7 [>C(*C*H$_3$)$_2$], 14.5 (OCH$_2$*C*H$_3$). Anal. Calcd for $C_{47}H_{70}N_2O_{12}$: C, 66.04; H, 8.19; N, 3.27. Found: C, 65.89; H, 8.32; N, 3.09%.

6.1.4. N^1,N^3-Bis-(3-*O*-benzyl-5(*S*)-hydroxyethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,3-diaminopropane (8). To a stirring slurry of $LiAlH_4$ (0.059 g, 1.55 mmol) in anhydrous THF (mL) under nitrogen atmosphere a solution of the above glycosyl amino ester **2** (1.20 g, 1.55 mmol) was added slowly at 0 °C during 5 min. The stirring of the reaction mixture was continued for 30 min and at 30 °C for an additional 2.5 h. The excess of the reducing agent was quenched with saturated solution of Na_2SO_4 and the reaction mixture was filtered over a celite pad and the solid cake was washed with tetrahydrofuran. The filtrate was evaporated under reduced pressure and the residue, thus obtained, was dissolved in ethyl acetate, washed with water, dried (anhyd. Na_2SO_4) and evaporated under reduced pressure to give a residual mass. The latter, on column chromatography over SiO_2 (60–120 mesh) using chloroform:methanol (97:3) as eluent gave compound **8**. Yield (0.91 g, 86%). Colourless oil $[\alpha]_D^{25} = -45.0^\circ$ (*c* 0.12, $CHCl_3$); MS FAB *m*/*z*: 687 $[M+H]^+$; IR (KBr, cm^{-1}) *v*: 3328 (NH), 2935 (CH_3 and CH_2 stretching); ^1H NMR (200 MHz, $CDCl_3$) δ: 7.31 (m, 5H, Ar–H), 5.92 (d, $J = 3.8$ Hz, 1H, H-1), 4.65 (m, 2H, H-2 and –OCH_APh), 4.39 (d, $J = 11.7$ Hz, 1H, –OCH_BPh), 4.17 (dd, $J = 3.0$ and 9.6 Hz, 1H, H-4), 3.81 (d, $J = 3.0$ Hz, 1H, H-3), 3.74 (m, 4H, –CH$_2$CH_2OH and NCH$_2$–), 3.17 (m, 1H, H-5), 2.74 (m, 2H, CH_2CH$_2$OH), 1.69 (m, 2H, NCH$_2$CH_2), 1.49 and 1.32 [each s, each 3H, 2× >C(CH_3)$_2$]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 137.3 (ArC), 128.9, 128.5, 128.4, 125.8 (ArCH), 112.0 [>*C*(CH$_3$)$_2$], 105.0 (C-1), 82.2 (C-2), 81.9 (C-4), 81.7 (C-3), 72.1 (O*C* H$_2$Ph), 62.3 (–*C* H$_2$OH), 57.1 (C-5), 44.5 (NCH$_2$), 31.3 (*C*H$_2$CH$_2$OH), 30.7, 29.7 (NCH$_2$*C* H$_2$), 27.1, 26.6 [>C(*C*H$_3$)$_2$]. Anal. Calcd for $C_{37}H_{54}N_2O_{10}$: C, 64.72; H, 7.87; N, 4.08. Found: C, 64.93; H, 8.12; N, 4.44%.

6.1.5. N^1,N^7-Bis-(3-*O*-benzyl-5(*S*)-hydroxyethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,7-diaminoheptane (9). Compound **9** was obtained by reduction of compound **3** (0.80 g, 0.96 mmol) with $LiAlH_4$ (0.36 g, 0.96 mmol) in anhydrous THF (15 mL) under nitrogen atmosphere as described above for compound **8** and isolated by column chromatography over SiO_2 (60–120 mesh) using chloroform:methanol (96:4) as eluent to give **9** as a colourless oil. Yield (0.68 g, 94%). $[\alpha]_D^{25} = -72.2^\circ$ (*c* 0.08, $CHCl_3$); MS FAB *m*/*z*: 743 $[M+H]^+$; IR (KBr, cm^{-1}) *v*: 3398 (NH), 2929, 2858 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz) δ: 7.33 (m, 5H, Ar–H), 5.93 (d, $J = 3.9$ Hz, 1H, H-1), 4.69 (d, $J = 11.7$ Hz, 1H, –OCH_APh), 4.65 (d, $J = 3.6$ Hz, 1H, H-2), 4.39 (d, $J = 11.7$ Hz, 1H, –OCH_BPh), 4.19 (dd, $J = 2.7$ and 9.6 Hz, 1H, H-4), 3.81 (d, $J = 3.0$ Hz, 1H, H-3), 3.71 (m, 2H, –CH_2OH), 3.23 (m, 1H, H-5), 3.25 (m, 2H, NCH_2), 2.46 (m, 2H CH_2CH$_2$OH), 1.59 and 1.38 [each s, each 3H, >C(CH_3)$_2$], 1.15 (m, 4H, CH_2s); ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 137.1 (ArC), 129.1, 129.0, 128.8, 128.6 (Ar–C), 112.3 [>*C*(CH$_3$)$_2$], 105.1 (C-1), 82.2 (C-2), 81.9 (C-4), 80.7 (C-3), 72.1 (–O*C*H$_2$Ph), 62.4 (–*C*H$_2$OH), 57.6 (C-5), 47.2 (NCH$_2$), 31.0 (–*C*H$_2$CH$_2$OH), 29.8, 29.6, 29.4, 29.2 (CH_2s), 27.1, 26.7 [>C(*C*H$_3$)$_2$]. Anal. Calcd for $C_{41}H_{62}N_2O_{10}$: C, 66.30; H, 8.35; N, 3.77. Found: C, 66.62; H, 8.02; N, 3.89%.

6.1.6. N^1,N^8-Bis-(3-*O*-benzyl-5(*S*)-hydroxymethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,8-diaminooctane (10). Reduction of above glycosyl amino ester **4** (0.50 g, 0.59 mmol) with $LiAl_4$ (0.02 g, 0.59 mmol) in anhydrous THF (5 mL) for 4 h as mentioned above followed by the work-up of the reaction mixture by column chromatography over SiO_2 (60–120 mesh) using chloroform:methanol (96:4) as eluent gave compound **10** as a colourless oil. Yield (0.36 g, 80%). $[\alpha]_D^{25} = -55.6^\circ$ (*c* 0.11, $CHCl_3$); MS FAB *m*/*z*: 757 $[M+H]^+$; IR (KBr, cm^{-1}) *v*: 3434 (–NH), 2931

(CH_3 and CH_2 stretching); ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.30 (m, 5H, Ar–H), 5.93 (d, J = 3.8 Hz, 1H, H-1), 4.65 (m, 2H, H-2 and OCH_APh), 4.39 (d, J = 11.7 Hz, 1H, –OCH_BPh), 4.20 (dd, J = 3.0 and 9.5 Hz, 1H, H-4), 3.82 (d, J = 3.0 Hz, 1H, H-3), 3.71 (m, 2H, CH_2OH), 3.23 (m, 1H, H-5), 2.67 (m, 4H, CH_2CH$_2$OH and NCH_2), 1.50 (m, 6H, CH_2s), 1.44 and 1.33 [each s, each 3H, >C(CH_3)$_2$]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 137.3 (ArC), 128.9, 128.5, 128.4 (Ar–CH), 112.0 [>C(CH$_3$)$_2$], 105.0 (C-1), 82.2 (C-2), 81.7 (C-4), 81.6 (C-3), 72.1 (OC H$_2$Ph), 62.6 (CH$_2$OH), 57.4 (C-5), 46.5 (NCH$_2$), 30.6 (C H$_2$CH$_2$OH), 29.7, 29.3, 27.4 (CH_2s), 27.1 and 26.6 [>C(CH$_3$)$_2$]. Anal. Calcd for $C_{42}H_{64}N_2O_{10}$:C, 66.66; H, 8.46; N, 3.70. Found: C, 67.01; H, 8.72; N, 3.49%.

6.1.7. N^1,N^9-Bis-(3-*O*-benzyl-5(*S*)-hydroxyethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,9-diaminononane (11). Compound **11** was obtained by the reduction of glycosyl amino ester **5** (1.0 g, 1.17 mmol) with $LiAlH_4$ (0.04 g, 1.17 mmol) in THF (25 mL) as usual and purification of the crude product over SiO_2 (60–120 mesh) column using chloroform:methanol (97:3) as eluent gave the desired compound **11** as a colourless oil. Yield (0.83 g, 92%). $[\alpha]_D^{25} = -72.8°$ (c 0.08, $CHCl_3$); MS FAB m/z: 771 [M+H]$^+$; IR (KBr, cm^{-1}) ν: 3339 (NH), 2933, 2857 (CH_3 and CH_2 stretching); ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.31 (m, 5H, Ar–H), 5.93 (d, J = 3.7 Hz, 1H, H-1), 4.67 (m, 2H, H-2 and OCH_APh), 4.39 (d, J = 11.7 Hz, 1H, –OCH_BPh), 4.20 (dd, J = 3.0 and 9.5 Hz, 1H, H-4), 3.82 (d, J = 3.0 Hz, 1H, H-3), 3.75 (m, 2H, CH_2OH), 3.25 (m, 1H, H-5), 2.68 (m, 2H, NCH$_2$), 2.36 (m, 2H, CH_2CH$_2$OH), 1.50 (m, 6H, CH_2s), 1.43 and 1.33 [each s, each 3H, >C(CH_3)$_2$]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 136.8 (ArC), 128.4, 128.1, 127.9 (Ar–CH), 111.5 [>C(CH$_3$)$_2$], 104.6 (C-1), 81.8 (C-2), 81.2 (C-4), 81.1 (C-3), 72.5 (OC H$_2$Ph), 62.2 (CH$_2$OH), 56.9 (C-5), 46.0 (NCH$_2$), 30.2 (CH$_2$CH$_2$OH), 29.3, 28.8, 27.1 (CH_2s), 26.6, 26.1 [>C(CH$_3$)$_2$]. Anal. Calcd for $C_{43}H_{66}N_2O_{10}$: C, 67.01; H, 8.57; N, 3.63. Found: C, 67.26; H, 8.96; N, 3.38%.

6.1.8. N^1,N^{10}-Bis-(3-*O*-benzyl-5(*S*)-hydroxyethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,10-diaminodecane (12). Reduction of the above glycosyl amino ester **6** (0.85 g, 0.97 mmol) with $LiAlH_4$ (0.03 g, 0.97 mmol) in anhydrous THF (15 mL) for 6 h as mentioned above and work-up of the reaction mixture resulted in a crude mass. The latter on purification over SiO_2 (60–120 mesh) column using chloroform:methanol (96:4) as eluent afforded compound **12** as a colourless oil. Yield (0.66 g, 87%); $[\alpha]_D^{25} = -65.6°$ (c 0.08, $CHCl_3$); MS FAB m/z: 785 [M+H]$^+$; IR (KBr,): cm^{-1} 3338 (–NH), 2987, 2923, 2853 (CH_3 and CH_2 stretching); ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 7.30 (m, 5H, Ar–H), 5.93 (d, J = 3.7 Hz, 1H, H-1), 4.65 (m, 2H, H-2 and OCH_APh), 4.39 (d, J = 11.7 Hz, 1H, –OCH_BPh), 4.22 (dd, J = 3.0 and 9.4 Hz, 1H, H-4), 3.83 (d, J = 3.0 Hz, 1H, H-3), 3.73 (m, 2H, CH_2OH), 3.25 (m, 1H, H-5), 2.67 (m, 2H, NCH$_2$), 1.50 (m, 8H, CH_2s), 1.46 and 1.33 [each s, each 3H, >C(CH_3)$_2$]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 137.2 (ArC), 128.9, 128.6, 128.4 (Ar–CH), 112.1 [>C(CH$_3$)$_2$], 105.0 (C-1), 82.1 (C-2), 81.7 (C-4), 81.4(C-3), 72.1 (OCH$_2$Ph), 62.4 (CH$_2$OH), 57.5 (C-5), 46.5 (NCH$_2$), 30.3 (CH$_2$CH$_2$OH), 29.7, 29.3, 27.4 (CH_2s), 27.1 and 26.6 [>C(CH$_3$)$_2$]. Anal. Calcd for $C_{44}H_{68}N_2O_{10}$: C, 67.34; H, 8.67; N, 3.57. Found: C, 67.70; H, 8.42; N, 3.40%.

6.1.9. N^1,N^{12}-Bis-(3-*O*-benzyl-5(*S*)-hydroxyethyl-5-deoxy-1,2-*O*-isopropylidene-α-D-xylofuranos-5-yl)-1,12-diaminododecane (13). Compound **13** was obtained by reduction of compound **7** (0.95 g, 1.06 mmol) with $LiAlH_4$ (0.04 g, 1.06 mmol) in anhydrous THF (15 mL) under nitrogen atmosphere as described above. Purification of the crude product over SiO_2 (60–120 mesh) column using chloroform: methanol (97:3) led to the isolation of compound **13** as a colourless oil. Yield (0.72 g, 84%), $[\alpha]_D^{25} = -70.5°$ (c 0.06, $CHCl_3$); MS FAB m/z: 813 [M+H]$^+$; IR (KBr, cm^{-1}) ν: 3398 (–NH), 2929, 2858 (CH_3 and CH_2 stretching); ^{1}H NMR ($CDCl_3$, 300 MHz) δ: 7.33 (m, 5H, Ar–H), 5.92 (d, J = 3.6 Hz, 1H, H-1), 4.69 (d, J = 12.0 Hz, 1H, –OCH_APh), 4.65 (d, J = 3.9 Hz, 1H, H-2), 4.39 (d, J = 11.7 Hz, 1H, –OCH_BPh), 4.18 (dd, J = 2.4 and 9.6 Hz, 1H, H-4), 3.82 (d, J = 2.4 Hz, 1H, H-3), 3.72 (m, 2H, –CH_2OH), 3.23 (m, 1H, CH_2CH$_2$OH), 2.68 (m, 2H NCH$_2$), 1.50 and 1.33 [each s, each 3H, >C(CH_3)$_2$], 1.22 (m, 10H, CH_2s); ^{13}C NMR ($CDCl_3$, 75 MHz) δ: 136.8 (ArC), 128.5, 128.2, 128.0 (Ar–C), 111.6 [>C(CH$_3$)$_2$], 104.6 (C-1), 81.8 (C-2, C-4), 81.1 (C-3), 71.6 (–OCH$_2$Ph), 62.4 (–CH$_2$OH), 57.1 (C-5), 46.1 (NCH$_2$), 30.4 (–CH$_2$CH$_2$OH), 29.5, 28.7, 27.2 (CH_2s), 26.7, 26.2 [>C(CH$_3$)$_2$]. Anal. Calcd for $C_{46}H_{72}N_2O_{10}$: C, 67.98; H, 8.86; N, 3.44. Found: C, 67.63; H, 8.60; N, 3.32%.

6.1.10. N^1,N^4-Bis-[(6*S*)-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,4-diaminobutane (14). A solution of (*E*)-ethyl 6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-6-eno-octopyranuronate **1b** (2.5 g, 7.62 mmol) and 1,4-diamino butane (0.38 g, 3.81 mmol) in ethanol (25 mL) was magnetically stirred at 30 °C for 16 h. The solvent was evaporated from the reaction mixture under reduced pressure. The crude product, thus obtained, was purified by column chromatography over SiO_2 using chloroform:methanol (98:2) as eluent to give title compound **14** as a colourless oil. Yield 2.46 g (87%); $[\alpha]_D^{20} = -40.0°$ (c 0.10, $CHCl_3$); MS (FAB) m/z: 745 (M+H)$^+$; IR (neat, cm^{-1}) ν_{max}: 3369 (–NH), 2985 and 2935 (CH_3 and CH_2 stretching) and 1734 (OC=O); ^{1}H NMR ($CDCl_3$, 200 MHz) δ: 5.54 (d, J = 5.1 Hz, 1H, H-1), 4.57 (dd, J = 7.9 and 2.0 Hz, 1H, H-3), 4.32 (m, 2H, H-2 and H-4), 4.12 (q, J = 7.1 Hz, 2H, –OCH$_2$), 3.86 (d, J = 7.2 Hz, 1H, H-5), 3.22 (m, 1H, H-6), 2.61 (m, 4H, CH$_2$CO and NHCH_2), 1.82 (bs, 1H, –NH), 1.51 and 1.44 [s, each 3H, C(CH$_3$)$_2$], 1.27 [m, 11H, C(CH$_3$)$_2$, NCH$_2$CH_2 and OCH$_2$CH_3]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.5 (OC=O), 109.6 and 108.9 [2× C(CH$_3$)$_2$], 96.9 (C-1), 71.8 (C-3), 71.4 and 70.9 (C-2 and C-4), 68.6 (C-5), 60.6 (–OCH$_2$), 55.8 (C-6), 47.3 (NCH$_2$), 35.7 (CH$_2$CO), 28.3 (NCH$_2$$CH_2$), 26.3, 25.3 and 24.7 [2× C(CH$_3$)$_2$], 14.5 (–OCH$_2$$CH_3$). Anal. Calcd for $C_{36}H_{60}N_2O_{14}$ (744): C, 58.06; H, 8.06; N, 3.76. Found: C, 58.20; H, 7.86; N, 3.89%.

6.1.11. N^1,N^7-Bis-[6-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,7-diaminoheptane (15) and (6*R*, 6*S*)N^1, N^7-Bis-[6-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,7-diaminoheptane (15a). Reaction of (*E*)-ethyl 6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-6-eno-octopyranuronate **1b** (3.0 g, 9.15 mmol) and 1,7-diamino heptane (0.59 g, 4.57 mmol) as described above and column chromatography of the crude product over SiO_2 using chloroform:methanol (97:3) as eluent gave the title compound **15** as diastereoisomeric mixture and **15a** as pure isomer. Yield (3.18 g, 89%); **15**, colourless oil; $[\alpha]_D^{20} = -57.5^\circ$ (*c* 0.20, $CHCl_3$); MS (FAB) *m/z*: 787 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3369 (–NH), 2983 and 2929 (CH_3 and CH_2 stretching) and 1729 (>C=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.54 (m, 1H, diastereomeric H-1), 4.31 (m, 3H, H-3, H-2 and H-4), 4.10 (q, $J = 7.1$ Hz, 2H, $-OCH_2$), 3.69 (m, 1H, diastereomeric H-5), 3.20 (m, 1H, H-6), 2.63 (m, 4H, CH_2CO and $NHCH_2$), 2.02 (bs, 1H, –NH), 1.51 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.24 [m, 15H, $C(CH_3)_2$, CH_2s and OCH_2CH_3]. Anal. Calcd for $C_{39}H_{66}N_2O_{14}$ (786): C, 59.54; H, 8.39; N, 3.56. Found: C, 59.28; H, 8.59; N, 3.36$[\alpha]_D^{20} = -36.0^\circ$ (*c*, 0.10, $CHCl_3$); MS (FAB) *m/z*: 787 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3402 (–NH), 2987 and 2932 (CH_3 and CH_2 stretching) and 1723 (OC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.54 (d, $J = 5.1$ Hz, 1H, H-1), 5.49 (d, $J = 5.0$ Hz, 1H, H-1′), 4.57 (m, 2H, H-3 and H-3′), 4.40 (m, 2H, H-4 and H-4′), 4.31 (dd, $J = 5.1$ and 2.3 Hz, 1H, H-2), 4.26 (dd, $J = 5.0$ and 2.2 Hz, 1H, H-2′), 4.12 (q, $J = 7.1$ Hz, 4H, $-OCH_2$ and $-OCH_2'$), 3.85 (d, 1H, $J = 7.5$ Hz, H-5), 3.67 (d, 1H, $J = 8.5$ Hz, H–5′), 3.22 (m, 2H, H-6 and H-6′), 2.57 (m, 8H, CH_2CO, CH_2CO', $NHCH_2$ and $NHCH_2'$), 1.65 (bs, 1H, –NH), 1.51 and 1.44 [s, each 6H, 2× $C(CH_3)_2$], 1.30 [m, 24H, 2× $C(CH_3)_2$, CH_2s and 2× $-OCH_2CH_3$]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 173.1 (OC=O), 172.7 (OC=O′), 109.6, and 109.3 [2× $C(CH_3)_2$], 108.9 and 108.7 [2× $C(CH_3)_2'$], 97.0 (C-1), 96.9 (C-1′), 71.9 (C-3), 71.5 (H-3′), 71.3 (C-4), 71.0 (C-2), 69.1 (C-5), 68.8 (C–5′), 60.6 (OCH_2), 60.5 (OCH_2'), 56.0 (C-6), 54.5 (C-6′), 47.5 (NCH_2), 47.3 (NCH_2'), 35.9 (CH_2CO), 35.5 (CH_2CO'), 30.8, 30.6, 29.8, 27.7 and 27.6 (CH_2s), 26.3, 25.3 and 24.7 [2× $C(CH_3)_2$], 14.5 ($-OCH_2CH_3$). Anal. Calcd for $C_{39}H_{66}N_2O_{14}$ (786): C, 59.54; H, 8.39; N, 3.56. Found: C, 59.38; H, 8.56; N, 3.36%.

6.1.12. N^1,N^8-Bis-[6-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,8-diaminooctane (16). Reaction of (*E*)-ethyl 6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-6-eno-octopyranuronate **1b** (3.0 g, 9.15 mmol) and 1,8-diamino octane (0.66 g, 4.57 mmol) as described above and column chromatography over SiO_2 using chloroform:methanol (97:3) as eluent gave the title compound **16** as a diastereoisomeric mixture. Yield (3.24 g, 89%); colourless oil; $[\alpha]_D^{20} = -68.0^\circ$ (*c* 0.10, $CHCl_3$); MS (FAB) *m/z*: 801 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3428 (–NH), 2986 and 2932 (CH_3 and CH_2 stretching) and 1724 (OC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.55 and 5.50 (each d, $J = 5.0$ Hz, each H, diastereomeric H-1), 4.57 (m, 1H, H-3), 4.37 (m, 2H, diastereomeric H-2 and H-4), 4.12 (q, $J = 7.1$ Hz, 2H, $-OCH_2$), 3.86 and 3.68 (each d, $J = 7.2$ and 8.5 Hz, 1H, diastereomeric H-5), 3.21 (m, 1H, H-6), 2.59 (m, 4H, CH_2CO and $NHCH_2$), 1.76 (bs, 1H, –NH), 1.51 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.29 [m, 15H, $C(CH_3)_2$,CH_2s and OCH_2CH_3]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 173.1 and 172.6 (diastereomeric OC=O), 109.6, 109.3, 108.9 and 108.7 [diastereomeric 2× $C(CH_3)_2$], 97.0 and 96.9 (C-1), 71.9 (C-3), 71.4 and 71.3 (diastereomeric C-4), 70.9 (C-2) 69.0 and 68.7 (diastereomeric C-5), 60.6 and 60.4 ($-OCH_2$), 56.0 and 54.4 (diastereomeric C-6), 47.4 and 47.2 (NCH_2), 35.8 and 35.5 (diastereomeric CH_2CO), 30.8, 30.5, 29.9 and 27.6 (CH_2s), 26.3, 25.3 and 24.7 [2× $C(CH_3)_2$], 14.5 ($-OCH_2CH_3$). Anal. Calcd for $C_{40}H_{68}N_2O_{14}$ (800): C, 60.0; H, 8.50; N, 3.50. Found: C, 59.71; H, 8.38; N, 3.21%.

6.1.13. N^1,N^9-Bis-[6-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,9-diaminononane (17) and (6*R*, 6*S*) N^1, N^9-bis-[6-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,9-diaminononane (17a). Reaction of (*E*)-ethyl 6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-6-eno-octopyranuronate **1b** (4.0 g, 12.2 mmol) and 1,9-diamino nonane (0.96 g, 6.1 mmol) as described above and column chromatography over SiO_2 using chloroform:methanol (97:3) as eluent gave the title compound **17** as a diastereoisomeric mixture and compound **17a** as a pure isomer. Yield (4.32 g 87%); **17**, colourless oil; $[\alpha]_D^{20} = -67.5^\circ$ (*c* 0.20, $CHCl_3$); MS (FAB) *m/z*: 815 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3363 (–NH), 2984 and 2929 (CH_3 and CH_2 stretching) and 1730 (OC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.54 (m, 1H, diastereomeric H-1), 4.56 (m, 1H, H-3), 4.31 (m, 2H, diastereomeric H-2 and H-4), 4.12 (q, $J = 7.2$ Hz, 2H, $-OCH_2$), 3.85 (d, $J = 7.2$ Hz, 1H, H-5), 3.0 (m, 1H, H-6), 2.47 (m, 5H, CH_2CO, $NHCH_2$ and NH), 1.51 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.27 [m, 17H, $C(CH_3)_2$, CH_2s and OCH_2CH_3]. Anal. Calcd for $C_{41}H_{70}N_2O_{14}$ (814): C, 60.44; H, 8.59; N, 3.43. Found: C, 59.98; H, 8.49; N, 3.16%. **17a,** colourless oil; $[\alpha]_D^{20} = -36.6^\circ$ (*c* 0.087, $CHCl_3$); MS (FAB) *m/z*: 815 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3415 (–NH), 2988 and 2930 (CH_3 and CH_2 stretching) and 1723 (>C=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.55 (d, $J = 5.1$ Hz, 1H, H-1), 5.49 (d, $J = 5.0$ Hz, 1H, H-1′), 4.57 (m, 2H, H-3 and H-3′), 4.45 (dd, $J = 8.0$ and 1.2 Hz, 1H, H-4), 4.29 (m, 3H, H-4′, H-2 and H-2′), 4.12 (q, $J = 7.1$ Hz, 4H, $-OCH_2$ and $-OCH_2'$), 3.85 (d, $J = 7.0$ Hz, 1H, H-5), 3.68 (d, $J = 8.4$ Hz, 1H, H-5′), 3.21 (m, 2H, H-6 and H-6′), 2.56 (m, 8H, CH_2CO, CH_2CO', $NHCH_2$ and $NHCH_2'$), 1.69 (bs, 1H, –NH), 1.50 and 1.44 [s, each 6H, 2× $C(CH_3)_2$], 1.29 [m, 26H, 2× $C(CH_3)_2$, CH_2s and 2× $-OCH_2CH_3$]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 173.1 (OC=O), 172.6 (OC=O′), 109.6, 109.2 [2× $C(CH_3)_2$], 108.9 and 108.7 [2× $C(CH_3)_2'$], 97.0 (C-1), 96.9 (C-1′), 72.0 (C-3), 71.5 (H-4), 71.3 (C-4′), 71.0 (C-2), 69.1 (C-5), 68.8 (C–5′), 60.6 (OCH_2), 60.4 (OCH_2'), 56.0 (C-6), 54.4 (C-6′), 47.5 (NCH_2), 47.3 (NCH_2'), 35.9 (CH_2CO), 35.6 (CH_2CO'), 30.9, 30.6, 29.9 and 27.7 (CH_2s), 26.3, 25.3 and 24.7 [2× $C(CH_3)_2$], 14.5 ($-OCH_2CH_3$). Anal. Calcd for $C_{41}H_{70}N_2O_{14}$ (814): C, 60.44; H, 8.59; N, 3.43. Found: C, 69.21; H, 8.46; N, 3.26%.

6.1.14. N^1,N^{10}-Bis-[6-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,10-diaminodecane (18). Reaction of (*E*)-ethyl 6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-6-eno-octopyranuronate **1b** (3.0 g, 9.15 mmol) and 1,10-diamino decane (0.80 g, 4.57 mmol) as described above and column chromatography over SiO_2 using chloroform:methanol (97:3) as eluent gave the title compound **18** as diastereoisomeric mixture. Yield (4.32 g, 87%); colourless oil; $[\alpha]_D^{20} = -50.0^\circ$ (*c* 0.10, $CHCl_3$); MS (FAB) *m/z*: 829 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3343 (–NH), 2985 and 2929 (CH_3 and CH_2 stretching) and 1730 (OC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.55 and 5.50 (each d, $J = 5.1$ and 4.9 Hz, each 1H, diastereomeric H-1), 4.59 (dd, $J = 7.9$ and 2.2 Hz, 1H, H-3), 4.36 (dd, $J = 7.9$ and 2.2 Hz, 1H, H-4), 4.30 (dd, $J = 5.1$ and 2.2 Hz, 1H, H-2), 4.12 (q, $J = 7.1$ Hz, 2H, $-OCH_2$), 3.85 (d, $J = 7.4$ Hz, 1H, H-5), 3.21 (m, 1H, H-6), 2.57 (m, 4H, CH_2CO and $NHCH_2$), 2.04 (bs, 1H, NH), 1.51 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.27 [m, 17H, $C(CH_3)_2$, CH_2s and OCH_2CH_3]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.6 (OC=O), 109.6, 109.3, 108.9 and 108.7 [diastereomeric 2× $C(CH_3)_2$], 97.0 (C-1), 71.9 (C-3), 71.5 (C-2), 71.0 (C-4), 69.0 and 68.8 (diastereomeric C-5), 60.6 ($-OCH_2$), 56.0 and 54.5 (diastereomeric C-6), 47.5 (NCH_2), 35.9 and 35.5 (diastereomeric CH_2CO), 31.2, 30.8, 30.5 and 27.7 (CH_2s), 26.3, 25.3 and 24.7 [2× $C(CH_3)_2$], 14.5 ($-OCH_2CH_3$). Anal. Calcd for $C_{42}H_{72}N_2O_{14}$ (828): C, 60.86; H, 8.69; N, 3.38. Found: C, 60.56; H, 8.43; N, 3.23%.

6.1.15. N^1,N^{12}-Bis-[6-carbethoxymethyl-6-deoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,12-diaminododecane (19). Reaction of (*E*)-ethyl 6,7-dideoxy-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-6-eno-octopyranuronate **1b** (2.5 g, 7.62 mmol) and 1,12-diamino dodecane (0.76 g, 3.81 mmol) as described above and column chromatography over SiO_2 using chloroform:methanol (97:3) as eluent gave the title compound **19** as diastereoisomeric mixture. Yield (2.85 g, 87%); colourless oil; $[\alpha]_D^{20} = -50.0^\circ$ (*c* 0.10, $CHCl_3$); MS (FAB) *m/z*: 858 $(M+2)^+$; IR (neat, cm^{-1}) ν_{max}: 3404 (–NH), 3020 and 2929 (CH_3 and CH_2 stretching) and 1722 (OC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.55 and 5.49 (each d, $J = 5.2$ and 5.0 Hz, each 1H, diastereomeric H-1), 4.60 (m, 1H, diastereomeric H-3), 4.31 (m, 2H, H-4 and H-2), 4.12 (q, $J = 7.1$ Hz, 2H, $-OCH_2$), 3.85 (d, $J = 7.0$ Hz, 1H, H-5), 3.21 (m, 1H, H-6), 2.58 (m, 4H, CH_2CO and $NHCH_2$), 1.51 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.27 [m, 19H, $C(CH_3)_2$, CH_2s and OCH_2CH_3];^{13}C NMR ($CDCl_3$, 50 MHz) δ: 172.8 and 172.3 (diastereomeric OC=O), 109.2, 108.9, 108.5 and 108.3 [diastereomeric 2× $C(CH_3)_2$], 96.6 and 96.5 (diastereomeric C-1), 71.6 (C-3), 71.1, 70.9, 70.6 and 70.4 (diastereomeric C-2 and C-4), 68.6 and 68.3 (diastereomeric C-5), 60.3 and 60.1 (diastereomeric $-OCH_2$), 55.6 and 54.0 (diastereomeric C-6), 47.1 and 46.9 (diastereomeric NCH_2), 35.4 and 35.1 (diastereomeric CH_2CO), 30.5, 30.2, 29.6 and 27.3 (CH_2s), 25.9, 24.9 and 24.3 [2× $C(CH_3)_2$], 14.2 ($-OCH_2CH_3$). Anal. Calcd for $C_{44}H_{76}N_2O_{14}$ (856): C, 61.68; H, 8.88; N, 3.27. Found: C, 61.48; H, 8.52; N, 3.13%.

6.1.16. N^1,N^4-Bis-[(6*S*)-deoxy-6-hydroxyethyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,4-diaminobutane (20). To a magnetically stirred slurry of $LiAlH_4$ (0.026 g, 0.67 mmol) in anhydrous THF (5.0 mL), a solution of galactopyranosyl amino ester **14** (0.5 g, 0.67 mmol) in anhydrous THF (5.0 mL) was added dropwise at 0 °C under N_2 atmosphere and stirred continuously for 30 min at 0 °C. The reaction mixture was further stirred magnetically for 2.5 h at ambient temperature. Excess of $LiAlH_4$ was quenched by saturated aqueous Na_2SO_4 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 (96:4) as eluent to give the galactopyranosyl amino alcohol **20** as a colourless oil. Yield (0.39 g, 90%); $[\alpha]_D^{20} = -27.4^\circ$ (*c*, 0.09, $CHCl_3$); MS (FAB) *m/z*: 661 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3399 (–NH), 2985 and 2935 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.52 (d, $J = 4.9$ Hz, 1H, H-1), 4.59 (d, $J = 7.8$ Hz, 1H, H-3), 4.30 (m, 2H, H-2 and H-4), 3.75 (m, 3H, OCH_2 and H-5), 3.08 (m, 1H, H-6), 2.75 (m, 2H, $NHCH_2$), 1.85 (m, 4H, CH_2CH_2OH and NH), 1.51, 1.44 and 1.32 [s, 3H, 3H and 6H, 2× $C(CH_3)_2$], 1.25 (m, 2H, NCH_2CH_2); ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 109.7 and 108.9 [2× $C(CH_3)_2$], 96.9 (C-1), 71.7 (C-3), 71.3 and 70.8 (C-2 and C-4), 68.0 (C-5), 62.4 (CH_2OH), 59.3 (C-6), 46.5 (NCH_2), 30.4 (CH_2CH_2OH), 27.5 (NCH_2CH_2), 26.3, 25.2 and 24.6 [2× $C(CH_3)_2$]. Anal. Calcd for $C_{32}H_{56}N_2O_{12}$ (660): C, 58.18; H, 8.48; N, 4.24. Found: C, 57.92; H, 8.16; N, 3.88%.

6.1.17. N^1,N^7-Bis-[6-deoxy-6-hydroxyethyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,7-diaminoheptane (21)]. Reduction of **15** (0.90 g, 1.14 mmol) with $LiAlH_4$ (0.044 g, 1.14 mmol) and work-up as described above followed by column chromatography over SiO_2 using chloroform:methanol (96:4) as eluent gave galactopyranosyl amino alcohol **21** as a colourless oil. Yield (0.75 g, 93%); $[\alpha]_D^{20} = -44.8^\circ$ (*c* 0.063, $CHCl_3$); MS (FAB) *m/z*: 704 $(M+2)^+$; IR (neat, cm^{-1}) ν_{max}: 3429 (–NH), 2929 and 2930 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.54 (m, 1H, diastereomeric H-1), 4.60 (dd, $J = 7.8$ and 2.1 Hz, 1H, H-3), 4.31 (m, 1H, diastereomeric H-2), 4.22 (dd, $J = 7.8$ and 1.5 Hz, 1H, H-4), 3.82 (m, 3H, $-OCH_2$ and H-5), 3.06 (m, 1H, H-6), 2.55 (m, 3H, NCH_2 and NH), 1.86 (m, 1H, CH_ACH_2OH), 1.64 (m, 1H, CH_BCH_2OH) 1.52 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.32 [m, 10H, $C(CH_3)_2$ and CH_2s]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 109.7. 109.6, 109.1 and 108.7 [diastereomeric 2× $C(CH_3)_2$], 96.9 (C-1), 71.7 (C-3), 71.4 (C-2), 70.9 (C-4), 68.3 (C-5), 63.1 and 62.4 (diastereomeric $-OCH_2$), 59.4 and 57.9 (diastereomeric C-6), 47.2 and 45.9 (diastereomeric NCH_2), 31.0, 30.7, 30.4, 29.7, 28.1 and 27.4 (diastereomeric CH_2s), 26.4, 26.3, 25.3, 25.2, 24.8 and 24.6 [diastereomeric 2× $C(CH_3)_2$]. Anal. Calcd for $C_{35}H_{62}N_2O_{12}$ (702): C, 59.83; H, 8.83; N, 3.99. Found: C, 59.62; H, 9.04; N, 3.77%.

6.1.18. N^1,N^8-Bis-[6-deoxy-6-hydroxyethyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,8-diaminooctane (22) and (6*S*, 6*S*) N^1,N^8-bis-[6-deoxy-6-hydroxyethyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,8-diaminooctane (22a). Reduction of **16** (1.2 g, 1.50 mmol) with $LiAlH_4$ (0.057 g, 1.50 mmol) and work-up as described above gave the crude product, which was purified by column chromatographed over SiO_2 using chloroform:methanol (97:3) as eluent to give galactopyranosyl amino alcohols **22** as a diastereoisomeric mixture and **22a** as the pure diastereoisomer. Yield (0.55 g, 55%); **22:** $[\alpha]_D^{20} = -32.0°$ (*c* 0.063, $CHCl_3$); MS (FAB) *m/z*: 717 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3405 (–NH), 2990 and 2932 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz): δ 5.54 (m, 1H, diastereomeric H-1), 4.59 (dd, *J* = 7.8 and 2.2 Hz, 1H, H-3), 4.32 (dd, *J* = 4.9 and 2.2 Hz, 1H, H-2), 4.27 (dd, *J* = 7.8 and 1.5 Hz, 1H, H-4), 3.82 (m, 3H, $-OCH_2$ and H-5), 3.1 (m, 1H, H-6), 2.60 (m, 2H, NCH_2), 1.69 (m, 2H, CH_2CH_2OH), 1.52 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.30 [m, 12H, $C(CH_3)_2$ and CH_2s]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 109.7. 109.1 and 108.8 [diastereomeric 2× $C(CH_3)_2$], 96.9 (C-1), 71.7 (C-3), 71.4 (C-2), 70.9 (C-4), 68.3 (C-5), 62.9 and 62.4 (diastereomeric $-OCH_2$), 59.5 and 57.8 (diastereomeric C-6), 47.2 and 45.9 (diastereomeric NCH_2), 30.8, 30.4, 30.3, 29.8, 28.0 and 27.5 (CH_2s), 26.3, 25.3, 25.2, 24.7 and 24.6 [diastereomeric 2× C($C H_3$)$_2$]. Anal. Calcd for $C_{36}H_{64}N_2O_{12}$ (716): C, 60.33; H, 8.94; N, 3.91. Found: C, 60.02; H, 8.62; N, 3.51%. **22a,** Yield (0.35 g, 35%); $[\alpha]_D^{20} = -64.0°$ (*c* 0.10, $CHCl_3$); MS (FAB) *m/z*: 717 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3410 (–NH), 2931 and 2857 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.55 (d, *J* = 5.0 Hz, 1H, H-1), 4.61 (dd, *J* = 7.9 and 2.1 Hz, 1H, H-3), 4.34 (dd, *J* = 5.0 and 2.1 Hz, 1H, H-2), 4.23 (d, *J* = 7.9 Hz, 1H, H-4), 3.84 (m, 3H, $-OCH_2$ and H-5), 3.10 (m, 1H, H-6), 2.55 (m, 3H, NCH_2 and NH), 1.65 (m, 2H, CH_2CH_2OH), 1.54 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.30 [m, 12H, $C(CH_3)_2$ and CH_2s]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 109.7 and 109.1 [2× $C(CH_3)_2$], 96.9 (C-1), 71.4 (C-3), 70.9 (C-2), 70.9 (C-4), 68.3 (C-5), 62.5 ($-OCH_2$), 57.8 (C-6), 45.9 (NCH_2), 30.7, 29.8, 27.9 and 27.5 (CH_2s), 26.3, 25.3 and 24.8 [2× C($C H_3$)$_2$]. Anal. Calcd for $C_{36}H_{64}N_2O_{12}$ (716): C, 60.33; H, 8.94; N, 3.91. Found: C, 60.22; H, 8.74; N, 3.65%.

6.1.19. N^1,N^9-Bis-[6-deoxy-6-hydroxyethyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,9-diaminononane (23). Reduction of **17** (0.40 g, 0.49 mmol) with $LiAlH_4$ (0.019 g, 0.49 mmol) and work-up as described above gave the crude product, which was purified by column chromatographed over SiO_2 column using chloroform:methanol (95:5) as eluent to get the galactopyranosyl amino alcohol **23** as a colourless oil. Yield (0.30 g, 86%); $[\alpha]_D^{20} = -43.0°$ (*c* 0.10, $CHCl_3$); MS (FAB) *m/z*: 731 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3425 (–NH), 2987 and 2929 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.54 (m, 1H, diastereomeric H-1), 4.60 (d, *J* = 7.8 Hz, 1H, H-3), 4.32 (m, 1H, diastereomeric H-2), 4.22 (d, *J* = 7.8 Hz, 1H, H-4), 3.79 (m, 3H, $-OCH_2$ and diastereomeric H-5), 3.08 (m, 2H, H-6 and NH), 2.79 and 2.59 (m, 2H, NCH_A and NCH_B), 1.87 and 1.60 (m, 2H, CH_ACH_2OH and CH_BCH_2OH), 1.52 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.32 [m, 14H, $C(CH_3)_2$ and CH_2s]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 109.7, 109.1 and 108.8 [diastereomeric 2× $C(CH_3)_2$], 96.9 (C-1), 71.7 (C-3), 71.4 (C-2), 70.9 (C-4), 68.3 (C-5), 63.1 and 62.3 (diastereomeric $-OCH_2$), 59.5 and 57.9 (diastereomeric C-6), 47.2 and 45.9 (diastereomeric NCH_2), 30.8, 30.4, 29.8, 28.0 and 27.5 (CH_2s), 26.3, 25.3, 25.2, 24.7 and 24.6 [diastereomeric 2× C($C H_3$)$_2$]. Anal. Calcd for $C_{37}H_{66}N_2O_{12}$ (730): C, 60.82; H, 9.41; N, 3.83. Found: C, 60.62; H, 9.23; N, 3.46%.

6.1.20. N^1,N^{10}-Bis-[6-deoxy-6-hydroxyethyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,10-diaminodecane (24). Reduction of **18** (0.60 g, 0.72 mmol) with $LiAlH_4$ (0.028 g, 0.72 mmol) and work-up as described above and column chromatography over SiO_2 column using chloroform : methanol (95:5) as eluent gave the galactopyranosyl amino alcohol **24** as a colourless oil. Yield (0.51 g, 95%); $[\alpha]_D^{20} = -88.0°$ (*c* 0.10, $CHCl_3$); MS (FAB) *m/z*: 745 $(M+H)^+$; IR (neat, cm^{-1}) ν_{max}: 3427 (–NH), 2928 and 2855 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.55 (m, 1H, diastereomeric H-1), 4.60 (d, *J* = 7.9 Hz, 1H, H-3), 4.33 (dd, *J* = 5.0 and 2.2 Hz, 1H, H-2), 4.22 (d, *J* = 7.9 Hz, 1H, H-4), 3.77 (m, 3H, $-OCH_2$ and H-5), 3.11 (m, 2H, H-6 and NH), 2.69 (m, 2H, NCH_2), 1.86 (m, 2H, CH_2CH_2OH), 1.52 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.29 [m, 14H, $C(CH_3)_2$ and CH_2s]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 109.7, 109.1 and 108.7 [diastereomeric 2× $C(CH_3)_2$], 96.9 (C-1), 71.7 (C-3), 71.4 (C-2), 70.9 (C-4), 68.3 (C-5), 63.2 and 62.5 (diastereomeric $-OCH_2$), 59.5 and 57.9 (diastereomeric C-6), 47.3 and 46.0 (diastereomeric NCH_2), 30.9, 30.7, 29.9, 28.0 and 27.6 (CH_2s), 26.3, 25.3 and 24.8 [2× C($C H_3$)$_2$]. Anal. Calcd for $C_{38}H_{68}N_2O_{12}$ (744): C, 61.29; H, 9.14; N, 3.76. Found: C, 60.92; H, 9.05; N, 3.59%.

6.1.21. N^1, N^{12}-Bis-[(6*S*)-deoxy-6-hydroxyethyl-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranos-6-yl]-1,12-diaminododecane (25). Reduction of **19** (0.50 g, 0.58 mmol) with $LiAlH_4$ (0.022 g, 0.58 mmol) and work-up as described above and column chromatography over SiO_2 column using chloroform:methanol (95:5) as eluent gave the galactopyranosyl amino alcohol **25** as a colourless oil. Yield (0.15 g, 33%); $[\alpha]_D^{20} = -66.4°$ (*c* 0.22, $CHCl_3$); MS (FAB) *m/z*: 774 $(M+2)^+$; IR (neat, cm^{-1}) ν_{max}: 3339 (–NH), 2986 and 2856 (CH_3 and CH_2 stretching); ^1H NMR ($CDCl_3$, 200 MHz) δ: 5.54 (d, *J* = 5.0 Hz, 1H, H-1), 4.60 (dd, *J* = 7.8 and 2.1Hz, 1H, H-3), 4.33 (dd, *J* = 5.0 and 2.1 Hz, 1H, H-2), 4.22 (d, *J* = 7.8 Hz, 1H, H-4), 3.86 (m, 3H, $-OCH_2$ and H-5), 3.12 (m, 2H, H-6 and NH), 2.70 (m, 2H, NCH_2), 1.86 (m, 2H, CH_2CH_2OH), 1.54 and 1.44 [s, each 3H, $C(CH_3)_2$], 1.29 [m, 16H, $C(CH_3)_2$ and CH_2s]; ^{13}C NMR ($CDCl_3$, 50 MHz) δ: 110.6 and 110.0 [2× $C(CH_3)_2$], 97.0 (C-1), 71.4 (C-3), 71.3 (C-2), 71.0 (C-4), 68.3 (C-5), 62.5 ($-OCH_2$), 57.9 (C-6), 46.0 (NCH_2), 31.0, 30.5, 29.9, 28.1 and 27.6 (CH_2s), 26.3, 25.3 and 24.8 [2× C($C H_3$)$_2$]. Anal. Calcd for $C_{40}H_{72}N_2O_{12}$ (772): C, 62.17; H, 9.32; N, 3.62. Found: C, 61.86; H, 9.12; N, 3.32%.

6.2. Biology

6.2.1. Activity against *M. tuberculosis* $H_{37}Ra$ strain. All the glycosyl amino alcohols synthesized were evaluated for their efficacy against *M. tuberculosis* $H_{37}Ra$ at concentration ranging from 50 to 1.56 μg/mL using twofold dilution in the initial screen. Log phase culture of *M. tuberculosis* $H_{37}Ra$ is diluted so as to give final $OD_{550\ nm}$ of 0.05 in Sauton's medium. In a 96-well white plate 190 μL of culture is dispensed in each well. A DMSO solution of test compounds is dispensed to 96-well plates so as to make final test concentration 25 μg/mL (5 μg test compound is dispensed in 10 μL of DMSO). Then the plate is incubated at 37 °C/5% CO_2 for 5 days. On the fifth day, 15 μL Alamar blue solution is added to the each well of the plate. The plate is again incubated overnight at 37 °C/5% CO_2 incubator. The fluorescence is read on BMG polar star with excitation frequency at 544 nm and emission frequency at 590 nm. The compounds, which were found active (>90% inhibition as compared with control) at this concentration, are then tested at six serial dilutions starting from 50 to 3.12 μg/mL.[19]

6.2.2. Activity against *M. tuberculosis* $H_{37}Rv$ strain. Drug susceptibility and determination of MIC of the test compounds/drugs against *M. tuberculosis* $H_{37}Rv$ was performed by agar microdilution method[20] where twofold dilutions of each test compound was added into 7H10 agar supplemented with OADC and organism. A culture of *M. tuberculosis* $H_{37}Rv$ growing on L-J medium was harvested in 0.85% saline with 0.05% Tween-80. A suspension of 1 μg/mL concentration of extracts/compounds was prepared in DMSO. This suspension was added to (in tubes) 7H10 middle brook's medium (containing 1.7 mL medium and 0.2 mL OADC supplement) at different concentration of compound keeping the volume constant, i.e., 0.1 mL. The medium was allowed to cool keeping the tubes in slanting position. These tubes were then incubated at 37 °C for 24 h followed by streaking of *M. tuberculosis* $H_{37}Rv$ (5×10^4 bacilli/tube). These tubes were then incubated at 37 °C. Growth of bacilli was seen after 30 days of incubation. Tubes having the compounds were compared with control tubes where the medium alone was incubated with $H_{37}Rv$. The concentration at which complete inhibition of colonies occurred was taken as active concentration of test compound.

6.2.3. In vivo screening. The activity of compound **13** was evaluated in vivo in experimental tuberculosis in mice as described previously.[21] Hence, the efficacy of the compound **13** against challenge of *M. tuberculosis* H37Rv was tested at 100 mg/kg. Mice were infected intravenously via lateral veins with 10^7 colony forming units, CFU. Mice were divided into two groups of 10 mice each after 2 days of infection. One was of compound **13** treated by intraperitoneal (i.p.) route, whereas the other group served as untreated control. At 25 mg /kg dose, the compound gives a marginal protection (Fig. 1). The compound seems to protect mice at nontoxic concentration against *M. tuberculosis* infection. However, at higher doses it causes toxicity in mice. It will be intresting to prepare analogues of compound **13** that will be nontoxic to eukaryotes but are strongly antitubercular.

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