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Synthesis of Glycosylated β-Amino Hydroxamates as New Class of Antimalarials☆

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Abstract—Glycosylated β-amino acids (**3–18, 38, 39**), obtained by hydrolysis of glycosylated β-amino esters on reaction with hydroxylamine hydrochloride in presence of DIC/DCC afforded glycosyl β-amino hydroxamates (**19–34, 40, 41**) in fair to good yields. Compounds (**19–34, 40, 41**) were screened against human malarial parasite *Plasmodium falciparum* in vitro for their schizontocidal activity. Compounds (**19**, **24, 26, 28, 40 and 41**) exhibited good activity at 2 μg/mL concentrations.

Introduction

Malaria, a parasitic disease caused mainly by Plasmodium, (*Plasmodium vivax, Plasmodium falciparum, Plasmodium ovale* and *Plasmodium malariae*) a protozoan is responsible globally for 500 million cases of clinical disease yearly.[1] Mortality from malaria exceeds 1 million per year, most of them being children under the age of 4 years and presents a public health problem for 2.4 billion people representing over 40% of world population in over 90 countries.[2] Out of different strains causing this disease *P. falciparum* is a deadly one and is very common in tropical Africa, South America and South East Asia including the Indian sub-continent and responsible for more than 95% of malaria related deaths.[3] Malaria control efforts include attempts to develop effective vaccine, eradicate mosquito vectors, and develop new drugs.[4]

Due to many reasons, availability of effective vaccine against malaria is not possible in the near future[5] and there are many hurdles in vector control too.[6] A number of drugs including mefloquine, halofantrin, doxycycline, azithromycin, artemisinin and its several analogues are known against this disease.[7] However, all of them are associated with one or more drawbacks.[8] The development of resistance against the currently used antimalarials[9] led to an additional urgency to explore and develop novel compounds by identification of novel chemotherapeutic targets[10] from the myriad of parasite's enzymes, receptors, metabolic pathways, and genomic data.

Iron (III) is important for intra-erythrocyte growth and development of the human malarial parasite to such an extent that its growth is arrested in the presence of iron chelators.[11–14] Certain hydroxamates (Fig. 1) are known to act as very good iron chelators and have shown antimalarial activity too.[15] The iron chelating property of hydroxamates is known to enhance the clearance of the parasites in mild malaria[16] and their combination with other antimalarials is known to hasten the recovery from deep coma in severe falciparum malaria.[17] Peptidyl deformylase, an enzyme present in malarial parasite (absent in mammals), is responsible for the co-translational removal of the *N*-formyl methionine in the protein biosynthesis during the chain elongation of peptides.[18] This enzyme has recently been identified as a target to develop new drugs. Further, hydroxamates are known to inhibit peptidyl deformylase where the hydroxamates group attached to the molecule can interact with the metal ion forming a transition state structure, which corresponds to formyl methionyl peptide bound to a ferrous ion at the site of the deformylase enzyme.[19]

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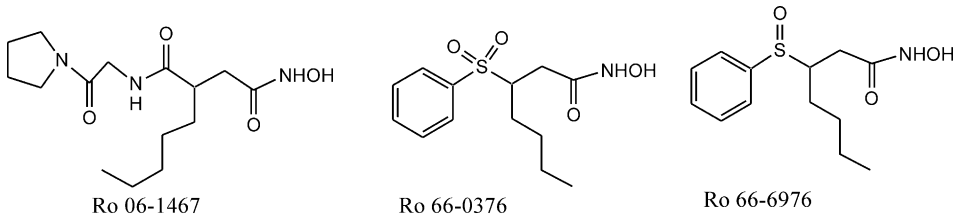


Figure 1.

In an our ongoing research programme towards the development of biologically active compounds from sugars, glycosylated amino acid derivatives have been shown to possess various biological activities including parasitic DNA topoisomerase-II, glutathione-*S*-transferase inhibitory, antitubercular and immunomodulatory activities.[20] Recognition of certain glycosylated amino acid derivatives by merozoits of the malarial parasite,[21] which divides in the red blood cells of the host has also been reported. Role of sugars in drug targeting and their good pharmacokinetic properties[22] as well as the chelating ability of hydroxamates[23] prompted us to synthesize certain glycosylated hydroxamic acids and evaluate them for antimalarial activities.

Materials and Methods

Chemicals and reagents

Chloroquine as free base was purchased from Sigma chemicals. *P. falciparum*-NF-54 (culture adapted strain) was used in the study. These parasites were maintained in continuous culture using 10% B +ve human serum, erythrocytes and RPMI-1640 medium supplemented with 2 g of glucose, 5.97 g of hepes 2.1 g of sodium bicarbonate/L. Parasites were synchronized repeatedly with 5% sorbitol to produce experimental cultures.

Determination of antimalarial activity in vitro. The antimalarial activity of the compounds and reference drug were assessed against NF-54 strain of *P. falciparum* by the Schizont maturation method.

Briefly a parasite suspension (180 μL/well) of infected erythrocytes in RPMI-1640 medium was added to each well containing 20 μL of drug concentrations prepared in culture medium. The final culture suspension had a hematocrit of 3–4% and a 1.0–2.0% infection of parasitized erythrocytes (>95% rings) in culture medium containing 10% human serum. Micro culture plates were incubated for 42 h at 37 °C in a candle jar having 5% O_2, 5% CO_2 and 90% N_2 to allow the development of malaria parasites. After incubation, culture plates were taken out and maximum supernatant medium was removed and thin blood smears of each well content were made and stained with 5% Giemsa stain. These smears were checked for the maturation of schizont relative to the controls. These tests, in vitro measure the drug sensitivity of *P. falciparum* following the WHO standard protocol with minor modifications for the assessment of the inhibition of schizont maturation.[28]

Table 1. Glycosyl amino acids and Hydroxamates synthesized

Entry	Glycosyl amino acid	Glycosyl hydroxamates	R	R_1
1	**3**	**19**	CH_3	Heptyl
2	**4**	**20**	CH_2Ph	Heptyl
3	**5**	**21**	CH_3	Dodecyl
4	**6**	**22**	CH_2Ph	Dodecyl
5	**7**	**23**	CH_3	Hexadecyl
6	**8**	**24**	CH_2Ph	Hexadecyl
7	**9**	**25**	CH_3	Benzyl
8	**0**	**26**	CH_2Ph	Benzyl
9	**11**	**27**	CH_3	Morpholyl
10	**12**	**28**	CH_2Ph	Morpholyl
11	**13**	**29**	CH_3	Veratryl
12	**14**	**30**	CH_2Ph	Veratryl
13	**15**	**31**	CH_3	Cyclopropyl
14	**16**	**32**	CH_2Ph	Cyclopropyl
15	**17**	**33**	CH_3	Furyl
16	**18**	**34**	CH_2Ph	Furyl
17	**38**	**40**	—	Heptyl
18	**39**	**41**	—	Hexadecyl

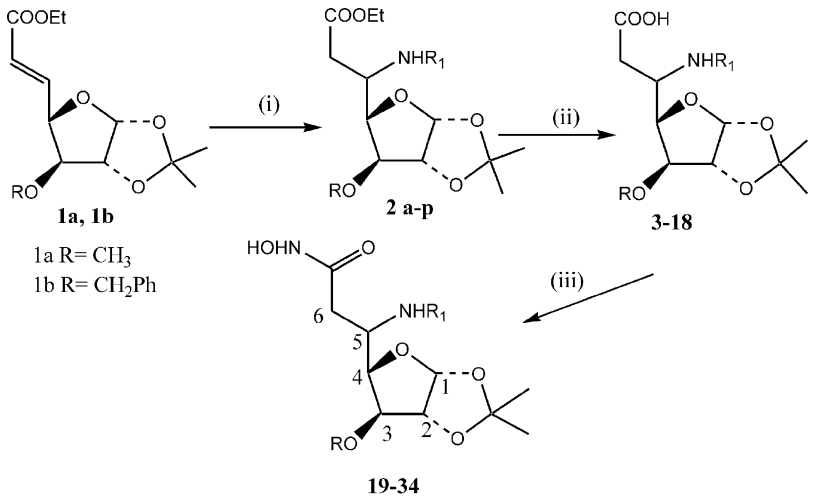
Conclusion

In conclusion we have synthesized glycosylated hydroxamates from glycosylated amino acids successfully and screened them for their in vitro antimalarial activity. One of the compounds screened (**24**) showing 100% inhibition at 2 μg/mL gave a lead for further exploration and development of new antimalarial agents.

Results and Discussion

Chemistry

The synthetic strategy begins with glycosylated β-amino acids (**3**–**18**, **38**, **39**) obtained from glycosylated amino esters (**2a**–**p**, and **36**, **37**), which were synthesized by our recently reported method.[24] Hydrolysis of these to their corresponding lithium salts of glycosylated β-amino acids (**3**–**18**, **38**, **39**) was carried out by lithium hydroxide in a mixture of THF and water. The free acids could never be isolated, even after acidification with dilute HCl. However, the free acids could be obtained in good yields by hydrolyzing the amino esters with a mixture of triethyl amine, ethanol and water (1:2:2), which required a very long reaction time. The



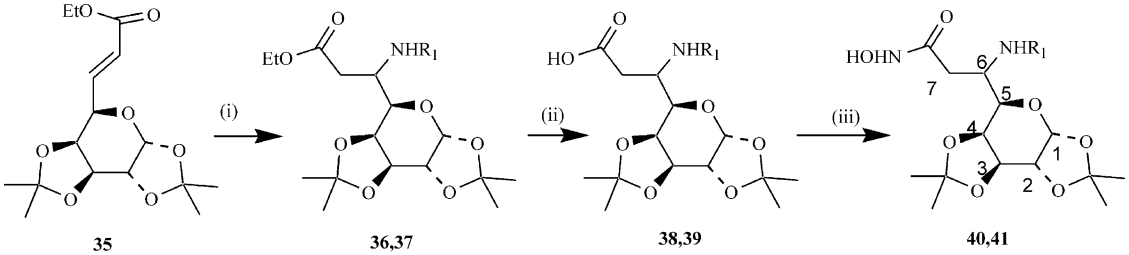
Scheme 1. Reagents and conditions: (i) R_1NH_2, Alcohol; (ii) Et_3N, EtOH and H_2O/LiOH.H_2O, THF; (iii) DCC, $NH_2OH.HCl$, Et_3N, CH_3CN.

lithium salts of the acids were converted to their respective hydroxamates (**19**–**34**, **40**, **41**) by reaction with hydroxylamine hydrochloride (Table 1). A number of reaction conditions employing a combination of different sets of reagents including (i) treatment of the acid with thionyl chloride followed by its reaction with hydroxylamine hydrochloride in acetonitrile; (ii) diisopropyl carbodiimide, hydroxylamine hydrochloride and triethyl amine in acetonitrile; and (iii) dicyclohexyl carbodiimide, hydroxylamine hydrochloride and triethyl amine in a mixture of acetonitrile and dichloromethane were optimized. The first set of reagent did not give the expected product, instead resulted in a black mass from which we could never isolate any product. The second set of reagents gave the expected product but in very poor yield along with undesired side products from which the diisopropyl ureas could only be isolated. However, the combination of third set of reagent gave expected glycosyl hydroxamates (**19**–**34**) in moderate to good yields with lesser side products. Since compound **24** has shown very good schizonticidal activity against *P. falciparum*, it prompted us to synthesize galactopyranosyl analogues (**40**, **41**) of the compound by reaction of galactopyranosyl amino acid (**38**, **39**) with hydroxylamine hydrochloride (Scheme 1).

The conversion of esters into corresponding acids was evidenced by their spectroscopic data. IR spectrum of these compounds exhibited absorption band around 1620 cm^{-1} corresponding to the salt of carboxylic acid. ^1H NMR spectra showed the disappearance of a quartet around δ 4.00 and a triplet around δ 1.00 for $OC\underline{H}_2CH_3$ and $OCH_2C\underline{H}_3$ respectively in all the compounds indicating the hydrolysis of ester into acid. Further in ^{13}C NMR spectrum down field shift of carbonyl signal from around δ 172 to around δ 173 in the compound confirms the presence of carboxyl group. Structure of the hydroxamates (**19**–**34**, **40**, **41**) obtained from acids were based on their IR, MS and NMR spectroscopic data. All the compounds showed $[M+H]^+$ 15 units higher than their corresponding acids indicating the conversion of COOH into CONHOH. This was further evidenced by IR spectrum of the hydroxamates where absorption band around 1660 cm^{-1} indicated the presence of CONHOH group. Further, in ^{13}C NMR spectrum the carbonyl signal shifted up field around δ 169 in comparison to acid where it appeared around δ 173 due to more shielding effect of nitrogen than oxygen, confirming the conversion of acids into hydroxamates (Scheme 2).

Biology

Glycosylated amino acids **3**–**18** and corresponding hydroxamates **19**–**34**, **40** and **41** were tested in vitro for their schizont maturation inhibitory activity. The compounds were dissolved initially in DMSO and concentrations of 50, 10, and 2 μg/mL were made in complete medium. Percentage of schizont inhibition at different concentrations has been depicted in Table 2. Among the glycosylated amino acids compounds **3**, **7**, **8**, **9**, **13**, **15**, and **17** although exhibited some activity at 50 μg/mL, but at lower concentration (2 μg/mL) only compound **15** showed schizont inhibition to the extent of 66% only. Among the hydroxamates although many com-



Scheme 2. Reagents and conditions. (i) R_1NH_2, EtOH; (ii) Et_3N, EtOH and H_2O or LiOH·H_2O, THF/H_2O; (iii) DCC, NH_2OHHCl, Et_3N, CH_3CN.

Table 2. Antimalarial activity of Glycosyl amino acids and hydroxamates

S. no.	Compd no.	% Inhibition of Schizont maturation		
		50 μg/mL	10 μg/mL	2 μg/mL
1	**3**	88.8	88.8	44.4
2	**4**		nd	
3	**5**		nd	
4	**6**		nd	
5	**7**	88.8	44.4	44.4
6	**8**	66.6	66.6	33.3
7	**9**	77.7	66.6	55.5
8	**10**	33.3	33.3	11.1
9	**11**		nd	
10	**12**		nd	
11	**13**	88.8	55.5	44.4
12	**14**	55.5	44.4	44.4
13	**15**	88.8	77.7	66.6
14	**16**		nd	
15	**17**	100.0	44.4	44.4
16	**18**	44.4	33.3	33.3
17	**19**	100	65.7	65.7
18	**20**	100	42.86	48.5
19	**21**	57.14	57.14	42.86
20	**22**	57.14	42.86	42.86
21	**23**	100	91.42	42.86
22	**24**	100	100	100
23	**25**	42.86	42.86	14.29
24	**26**	100	65.7	65.7
25	**27**	81.25	78.7	56.3
26	**28**	81.25	75.0	75.0
27	**29**	44.4	44.4	33.3
28	**30**	100.0	44.4	44.4
29	**31**	75.0	62.5	56.3
30	**32**	62.5	50.0	53.7
31	**33**	75.0	50.0	50.0
32	**34**	77.7	33.3	11.1
33	**38**		nd	
34	**39**		nd	
35	**40**	88.8	77.7	66.6
36	**41**	100	100	88.8
37	Chloroquine[a]	100	0.0	0.0

[a]The concentrations used are 100, 50 and 10 ng/mL.

pounds showed activity at 50 μg/mL concentration but at lower concentration (2 μg/mL) only compounds **19**, **24**, **26**, **28**, **40** and **41** have shown growth inhibition. While compounds **19**, **26**, **28** and **40** showed more than 65% inhibition of schizont formation at 50 μg/mL concentration. Three compounds **19**, **24** and **41** showed very good inhibition even at 2 μg/mL concentration. Compound **24** exhibited 100% inhibition at the same concentration and proved to be most potent compound. The rest of the tested compounds also showed inhibition in the process of normal development of malarial parasite. In this system chloroquine (free base) as a reference drug showed 100% inhibition at 100 ng/mL concentrations (Table 2).

Out of four species (*P. falciparum, P. vivax, P. malariae,* and *P. ovalae*), of malarial parasite causing malaria disease in human, the *P. falciparum* is most difficult to cure because of its prevalence, virulence and drug resistance.[25] The treatment of falciparum malaria consists in mainly killing the asexual parasites in the circulation as the sexual forms are important for drug resistance and are non-pathogenic. However, use of a combination of agents killing asexual parasite and supportive therapy with gametocytocidal agents enhances the benefits to the host. A number of drugs available today for the treatment of malaria are associated with one or more drawbacks, the prominent one being the development of resistance against them.[8,9] A number of targets both specific and nonspecific to the parasite have been chosen for drug development against this disease.[26] The proposed compounds in the present study having structural features of substituted amino acids and sugars are expected to give a novel class of antimalarial, as such compounds are known to enhance the immune status of the host.[27] Further, these compounds with hydroxamate moiety are expected to inhibit crucial enzymes, which are essential for the survival and propagation of this parasite.

A careful structure–activity relationship indicates that out of all the compounds screened for antimalarial efficacy in vitro, hydroxamates (**19**–**34**, **40**, **41**), in general, are more active than the corresponding acids (**3**–**18**, **38**, **39**). Further, activity in this class of compounds is dependent on the nature of substituent present on nitrogen of amine part as well as 3-*O*-substituent in the sugar ring.

The compounds having long straight alkyl amines as C-5 substituent were found to be more active than the rigid or cyclic amines as substituent at the same position. Thus compounds with morpholine, furfuryl, cyclopropyl and aryl (veratryl) amines as substituents result in drastic loss of antimalarial activity. The better activity in compound **24** and **41** with long straight alkyl chain may be due to its hydrophobic character, which might be required during binding with enzyme. Out of the two compound **24** and **41,** the former with glucofuranosyl residue exhibited better activity than the latter with galactopyranosyl skeleton, indicating the role of sugar. Glucofuranose ring contributes better towards the activity than galactopyranose ring.

Experimental

Thin layer chromatography was performed using silica gel 60 F_{254} plates with detecting agents iodine vapors, spraying with 5% sulphuric acid in ethanol followed by heating at 100 °C. Merck Silica gel (60–120 mesh) was used for column chromatography. Infrared spectra were recorded on a Perkin-Elemer RX-1FT-IR spectrophotometer. Melting points were determined on a Buchi 535 digital melting point apparatus and were uncorrected. Elemental analysis was performed on a Perkin-Elmer 2400 C, H, N analyzer and values were within ±0.4% of the calculated values. The optical rotations were measured in a 1.0 dm tube with Jasco dip-140 polarimeter in chloroform. The organic extracts were dried over anhydrous Na_2SO_4 and evaporation of the solvent was carried out on a rotary evaporator under reduced pressure.

General procedure for the preparation of the compounds 3–18

5,6-Dideoxy-5-heptylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuranuronic acid (3). Method A. A mixture of ethyl [5,6-dideoxy-5-heptylamino-3-*O*-

methyl-1,2-*O*-isopropylidene-β-L-*ido*-heptofuran]-uronate (**2a,** 1.6 g, 4.13 mmol) in THF (4.0 mL) and $LiOH{\cdot}H_2O$ (0.35 g, 8.26 mmol) in water (4.0 mL) was stirred magnetically at 25 °C for 18 h. The reaction mixture was neutralized with 2 N HCl at 0 °C and solvent evaporated to get a crude mixture, which was dissolved in dichloromethane and filtered. The filtrates dried (Na_2SO_4) and evaporated under reduced pressure to give a crude mass, which was chromatographed over SiO_2 column using chloroform–methanol (3:97) as eluant to give compound **3** as Colourless solid. Yield 90%, mp 112 °C, R_f 0.40 (chloroform–methanol, 20:1) $[\alpha]_D^{20}$ −36.8 (*c* 0.125 $CHCl_3$); MS (FAB) = *m*/*z* 366 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3440, 2934, 1616. ^1H NMR (200 MHz, $CDCl_3$): δ 5.89 (d, *J* = 3.7 Hz, 1H, H-1); 4.59 (d, *J* = 3.7 Hz, 1H, H-2); 4.31 (dd, *J* = 9.4 and 3.0 Hz, 1H, H-4); 3.73 (d, *J* = 3.0 Hz, 1H, H-3); 3.39 (s, 3H CH_3); 3.35 (m, 1H, H-5); 2.94 (m, 2H, $NHC\underline{H}_2$); 2.54 (dd, *J* = 16.5 and 4.4 Hz, 1H, $H\text{-}6_A$); 2.23 (dd, *J* = 16.5 and 7.1 Hz, 1H, $H\text{-}6_B$), 1.65 (m, 2H, $NHCH_2C\underline{H}_2$); 1.50 and 1.31 [each s, 6H 2×C $(CH_3)_2$], 1.27 (m, 8H, CH_2s); 0.88 (t, *J* = 7.1 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173 (C=O); 112.6 [$\underline{C}(CH_3)_2$]; 105.3 (C-1); 84.2 (C-2); 83.3 (C-4); 82.5 (C-3); 57.4 ($-OCH_3$); 47.2 (C-5); 46.3 ($-NH\underline{C}H_2$), 30.1 (C-6), 29.2, 27.2, 26.0, 23.07(CH_2s), 27.0 and 26.7 [C $(\underline{C}H_3)_2$], 14.4 ($-CH_2\underline{C}H_3$). Anal. calcd C, 59.17; H, 8.83; N, 3.83. Found: C, 59.66; H, 8.7; N, 3.64.

Method B

To the magnetically stirred solution of the ethyl [5,6-dideoxy-5-heptylamino-3-*O*-methyl-1,2-*O*-isopropylidene-β-L-*ido*-heptofuran]uronate (**2a**, 2.1 g, 5.42 mmol) in aq EtOH (50%, 40 mL), Et_3N (10.0 mL) was added and the contents were stirred magnetically for 72 h. Solvent evaporated under reduced pressure with an azeotrop of EtOH and $C_6H_5CH_3$ to give a residual mass which was subjected to column chromatography over SiO_2 column using chloroform–methanol (3:97) as eluant to give compound **3** as Colourless solid (Yield 85%) The compound was found to be identical in all respects to that obtained in method A.

3-*O*-Benzyl-5, 6-dideoxy-5-heptylamino-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronic acid (4). It was obtained by reaction of ethyl [3-*O*-benzyl-5,6-dideoxy-5-heptylamino-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronate **2b** (1.3 g, 2.81 mmol) and lithium hydroxide (0.24 g, 5.62 mmol) as above. Colourless solid, mp 105 °C, Yield 92% R_f 0.40 (chloroform–methanol, 19:1), $[\alpha]_D^{20}$ −13.77 (*c* 0.225 $CHCl_3$); MS (FAB) = *m*/*z* 436 $(M+H)^+$;IR (KBr) ν_{max} cm^{-1}: 2930.3, 1591 (>C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 5H, ArH); 5.88 (d, *J* = 3.5 Hz, 1H, H-1); 4.66 and 4.54 (each d, *J* = 11.9 Hz, 2H, OCH_2); 4.62 (d, *J* = 3.5 Hz, 1H, H-2), 4.22 (dd, *J* = 8.9 and 3.2 Hz, 1H, H-4); 3.94 (d, *J* = 3.2 Hz, 1H, H-3); 3.52 (m, 1H, H-5); 2.90 (m, 2H, $NHC\underline{H}_2$); 2.60 (dd, *J* = 16 and 5.2 Hz, 1H, $H\text{-}6_A$); 2.26 (dd, *J* = 16.0 and 8.6 Hz, 1H, $H\text{-}6_B$); 1.63 (m, 2H, $NHCH_2C\underline{H}_2$); 1.54 (bs, 1H, NH); 1.48 and 1.32 [each s, 6H, C $(C\underline{H}_3)_2$]; 1.27 (m, 8H, CH_2s); 0.87 (t, *J* = 7.1 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173 (C=O); 136.4 (each Ar–C); 129.2, 129.1 128.5, 127.9 (ArCH); 112.3 [$\underline{C}(CH_3)_2$]; 105.2 (C-1); 82.6 (C-2); 82.0 (C-4); 81.3 (C-3); 72.2 ($-O\underline{C}H_2Ph$); 54.5 (C-5), 47.3 ($-NH\underline{C}H_2$); 31.1 (C-6), 29.0, 27.3, 27.0(CH_2s), 26.7 and 26.9 [C($\underline{C}H_3)_2$]; 14.3 ($-CH_2\underline{C}H_3$). Anal. calcd C, 65.29; H, 8.22; N, 3.17. Found: C, 64.98; H, 8.42; N, 3.02.

5,6-Dideoxy-5-dodecylamino-1,2-*O*-isopropylidene-3-*O*-methyl - β - L - *ido* - heptofuranuronic acid (5). It was obtained by reaction of ethyl [5,6-dideoxy-5-dodecylamino-3-*O*-methyl-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronate **2c** (1.4 g, 3.06 mmol) and lithium hydroxide (0.26 g, 6.12 mmol) as above. Colourless solid. Yield 94%; mp 98 °C; R_f 0.40 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −29.53 (*c* 0.163 $CHCl_3$); MS (FAB) = *m*/*z* 436 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3443, 2927, 2856, 1618 (>C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 5.89 (d, *J* = 3.6 Hz, 1H, H-1); 4.59 (d, *J* = 3.6 Hz, 1H, H-2); 4.29 (dd, *J* = 9.1 and 2.5 Hz, 1H, H-4); 3.73 (d, *J* = 2.5 Hz, 1H, H-3); 3.40 (s, 3H CH_3); 3.35 (m, 1H, H-5); 2.90 (m, 2H, $NHC\underline{H}_2$); 2.58 (dd, *J* = 17.1 and 4.4 Hz, 1H, $H\text{-}6_A$); 2.33 (d, *J* = 17.1 Hz, 1H, $H\text{-}6_B$), 1.62 (m, 2H, $NHCH_2C\underline{H}_2$); 1.50 and 1.32 [each s, 6H, $C(CH_3)_2$], 1.25 (m, 18H, CH_2s); 0.88 (t, *J* = 7.1 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.1 (C=O); 112.2 [$\underline{C}(CH_3)_2$]; 105.4 (C-1); 84.3 (C-2); 81.2 (C-4); 81.4 (C-3); 57.6 ($-OCH_3$); 53.2 (C-5); 46.3 ($-NH\underline{C}H_2$), 32.1 (C-6), 30.1, 29.7, 29.5, 29.3, 27.2 (CH_2s), 27.5 and 26.6 [$C(\underline{C}H_3)_2$], 14.4 ($-CH_2\underline{C}H_3$). Anal. calcd C, 63.43; H, 9.72; N, 3.22. Found: C, 63.62; H, 9.64; N, 3.13.

3-*O*-Benzyl-5,6-dideoxy-5-dodecylamino-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronic acid (6). It was obtained by reaction of ethyl [3-*O*-benzyl-5,6-dideoxy-5-dodecylamino-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]uronate **2d** (1.5 g, 2.81 mmol) and lithium hydroxide (0.24 g, 5.62 mmol). Colourless solid Yield 94%; mp 126 °C; R_f 0.5 (chloroform–methanol, 20:1) $[\alpha]_D^{20}$ 43.73 (*c* 0.1875 $CHCl_3$); MS (FAB) = *m*/*z* 506 $(M+H)^+$; IR (KBr) ν_{max} $cm^{-1:}$ 3449, 2928, 1618. ^1H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 5H, ArH); 5.91 (d, *J* = 3.7 Hz, 1H, H-1); 4.67 and 4.47 (each d, *J* = 11.4 Hz, 2H, OCH_2Ph); 4.64 (d, *J* = 3.7 Hz, 1H, H-2); 4.06 (dd, *J* = 9.6 and 3.1 Hz, 1H, H-4); 3.97 (d, *J* = 3.1 Hz, 1H, H-3); 3.37 (m, 1H, H-5); 2.80 (t, *J* = 7.2 Hz, 2H, $NHC\underline{H}_2$); 2.51 (dd, *J* = 17.3 and 5.0 Hz, 1H, $H\text{-}6_A$); 2.16 (dd, *J* = 17.3 and 5.1 Hz, 1H, $H\text{-}6_B$); 1.57 (m, 2H, $NHCH_2C\underline{H}_2$); 1.48 and 1.31 [each s, 6H, C $(C\underline{H}_3)_2$]; 1.25 (m, 18H, CH_2s); 0.88 (t, *J* = 7.14 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.2 (C=O); 136.7 (each Ar–C); 128.6, 128.4,127.9 (ArCH); 111.8 [$\underline{C}(CH_3)_2$]; 104.6 (C-1); 82.1 (C-2); 81.8 (C-4); 80.7 (C-3); 72.4 ($-O\underline{C}H_2Ph$); 53.2 (C-5); 46.3 ($-NH\underline{C}H_2$); 32.7 (C-6); 30.3, 29.6, 27.3, 26.1, 23.02 (CH_2s); 27.1 and 26.6 [$C(\underline{C}H_3)_2$], 14.49 ($-CH_2\underline{C}H_3$). Anal. calcd C, 68.08; H, 9.06; N, 2.74. Found: C, 68.39; H, 9.33; N, 2.64.

5,6-Dideoxy-5-hexadecylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuranuronic acid (7). It was obtained by reaction of ethyl [5,6-dideoxy-5-hexadecylamino-3-*O*-methyl-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronate **2e** (1.6 g, 3.12 mmol) and lithium hydroxide (0.26 g, 6.24) as above, Colourless solid.

Yield 90% mp 108 °C. R_f 0.5 (chloroform–methanol, 19:1) $[\alpha]_D^{20}$ −36.95 (*c* 0.2625 $CHCl_3$), MS (FAB) = *m*/*z* 492 $(M+Li)^+$, IR (KBr) ν_{max} cm^{-1}: 3458, 2927, 1629, ^1H NMR (200 MHz, $CDCl_3$): δ 5.89 (d, *J* = 3.7 Hz, 1H, H-1); 4.59 (d, *J* = 3.7 Hz, 1H, H-2); 4.31 (dd, *J* = 8.8 and 2.6 Hz, 1H, H-4); 3.74 (d, *J* = 2.6 Hz, 1H, H-3); 3.40 (s, 3H-OCH_3); 3.37 (m, 1H, H-5); 2.89 (m, 2H, $NHC\underline{H}_2$); 2.63 and 2.37 (each m, 2H, H-6); 1.61 (m, 2H, $NHCH_2C\underline{H}_2$); 1.49 and 1.31 [each s, 6H, $C(CH_3)_2$], 1.25 (m, 26H, CH_2s); 0.87 (t, *J* = 6.1 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.3 (C=O); 112.1 [$\underline{C}(CH_3)_2$]; 105.3 (C-1); 84.2 (C-2); 82.4 (C-4); 80.2 (C-3); 57.6 ($-OCH_3$); 47.6 (C-5); 46.6 ($-NH\underline{C}H_2$), 32.1 (C-6), 30.3, 29.4, 27.5 (CH_2s), 27.1 and 26.6 [$C(\underline{C}H_3)_2$], 14.5 ($-CH_2\underline{C}H_3$). Anal. calcd C, 65.96; H, 10.25; N, 2.85. Found: C, 65.72; H, 10.35; N, 2.98.

3-*O*-Benzyl-5,6-dideoxy-5-hexadecylamino-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronic acid (8). It was obtained by reaction of ethyl [3-*O*-benzyl-5,6-dideoxy-5-hexadecylamino-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronate **2f** (1.5 g, 2.54 mmol) and lithium hydroxide (0.21 g, 5.08 mmol) as above, Colourless solid. Yield 90% mp 103 °C. R_f 0.40 (chloroform–methanol, 19:1) $[\alpha]_D^{20}$ −64 (*c* 0.1 $CHCl_3$), MS (FAB) = *m*/*z* 568 $(M+Li)^+$, IR (KBr) ν_{max} cm^{-1}: 3440, 1616 (>C=O); ^1H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 5H, ArH); 5.88 (d, *J* = 3.7 Hz, 1H, H-1); 4.63 and 4.51 (each d, *J* = 11.7 Hz, 2H, OCH_2Ph); 4.60 (d, *J* = 3.7 Hz, 1H, H-2); 4.24 (dd, *J* = 9.9 and 3.0 Hz, 1H, H-4); 3.41 (d, *J* = 3.0 Hz, 1H, H-3); 3.37 (m, 1H, H-5); 2.86 (m, 2H, $NHC\underline{H}_2$); 2.45 (m, 2H, H-6); 1.63 (m, 2H, $NHCH_2C\underline{H}_2$); 1.48 and 1.31 [each s, 6H, C $(CH_3)_2$]; 1.25 (m, 26H, CH_2s); 0.85 (t, *J* = 6.1 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR ($CDCl_3$): δ 173.3 (C=O); 112.1 [$\underline{C}(CH_3)_2$]; 105.3 (C-1); 84.6 (C-2); 82.4 (C-4); 80.3 (C-3); 60.2 ($-OCH_2Ph$); 47.6 (C-5); 46.7 ($-NH\underline{C}H_2$), 32.8 (C-6), 30.2, 29.5, 27.4 (CH_2s), 27.1 and 26.6 [$C(\underline{C}H_3)_2$], 14.5 ($-CH_2\underline{C}H_3$). Anal. calcd C, 69.81; H, 9.59;N, 2.47. Found: C, 69.63; H, 9.68;N, 2.21.

5-Benzylamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuranuronic acid (9). It was obtained by reaction of ethyl [5-benzylamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-i*do*-heptofuran]-uronate **2g** (1.3 g, 3.43 mmol) and lithium hydroxide (0.29 g, 6.86 mmol) as above, Colourless solid. Yield 98% mp 154 °C R_f 0.40 (chloroform–methanol, 19:1) $[\alpha]_D^{20}$ −5.2 (*c* 0.25 $CHCl_3$), MS (FAB) = *m*/*z* 358 $(M+Li)^+$, IR (KBr) ν_{max} cm^{-1}: 3447, 2987, 2834, 1596; ^1H NMR (200 MHz, $CDCl_3$): δ 7.46 (m, 5H, ArH); 5.97 (d, *J* = 3.6 Hz, 1H, H-1); 4.92 and 4.24 (each d, *J* = 12.9 Hz, 2H, $NHC\underline{H}_2Ar$); 4.75 (each d, *J* = 3.6 Hz, 1H, H-2); 4.37 (dd, *J* = 9.8 and 3.2 Hz, 1H, H-4); 3.83 (d, *J* = 3.2 Hz, 1H, H-3); 3.61 (m, 1H, H-5); 3.43 (s, 3H, $-OCH_3$); 2.47 (m, 2H, H-6); 1.48 and 1.33 [each s, 6H, $C(CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.1 (C=O); 139.4 (Ar–C); 129.3, 128.5, 127.2 (Ar–CH); 112.6 [$\underline{C}(CH_3)_2$]; 105.3 (C-1); 84.3 (C-2); 83.1 (C-4); 80.7 (C-3); 58.6 ($-OCH_3$); 53.2 (C-5); 50.5 ($-NH\underline{C}H_2$), 33.6 (C-6), 27.1 and 26.6 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 60.50; H, 6.77; N, 3.92. Found: C, 60.45; H, 6.63; N, 3.81.

5-Benzylamino-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuranuronic acid (10). It was obtained by reaction of ethyl [5-benzylamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-benzyl-β-L-i*do*-heptofuran]-uronate **2h** (1.6 g, 3.51 mmol) and lithium hydroxide (0.30 g, 7.02) as above, Colourless solid. Yield 98%; mp 134 °C; $[\alpha]_D^{20}$ −27.71 (*c* 0.35 $CHCl_3$); MS (FAB) = *m*/*z* 434 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3456, 2933, 2936 1621. ^1H NMR (200 MHz, $CDCl_3$): δ 7.32 (m, 10H, ArH); 5.91 (d, *J* = 3.7 Hz, 1H, H-1); 4.69 and 4.48 (each d, *J* = 11.5 Hz, 2H, OCH_2Ph); 4.66 (d, *J* = 3.7 Hz, 1H, H-2); 4.18 (dd, *J* = 9.6 and 3.2 Hz, 1H, H-4); 3.98 and 3.80 (each d, *J* = 12.3 Hz, 2H, $-NHC\underline{H}_2Ph$); 3.97 (d, *J* = 3.2 Hz, 1H, H-3); 3.46 (m, 1H, H-5); 2.59 (dd, *J* = 17.2 and 5.0 Hz, 1H, $H\text{-}6_A$); 2.15 (dd, *J* = 17.2 and 4.1 Hz, 1H, $H\text{-}6_B$); 1.49 and 1.31 [each s, 6H, $C(C\underline{H}_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.6 (C=O); 137.4 and 137.2 (Ar–C); 129.1, 128.5, 128.9, 128.2, 128.8, 127.4 (Ar–CH); 112.5 [$\underline{C}(CH_3)_2$]; 105.3 (C-1); 82.7 (C-2); 81.3 (C-4); 81.4 (C-3); 72.8 ($-O\underline{C}H_2Ph$); 53.6 (C-5); 51.9 ($-NH\underline{C}H_2$); 33.4 (C-6); 27.1 and 26.6 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 66.51; H, 6.51; N, 3.23. Found: C, 66.47; H, 6.73; N, 3.08.

5,6-Dideoxy-1,2-*O*-isopropylidene-5-(morpholin-1-yl)- 3-*O*-methyl-β-L-*ido*-heptofuranuronic acid (11). It was obtained by reaction of ethyl [5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-(morpholin-1-yl)β-L-i*do*-heptofuran]-uronate **2i** (1.2 g, 3.34 mmol) and lithium hydroxide (0.28 g, 6.68 mmol) as above. Colourless solid, Yield 88%; mp 139 °C; R_f 0. 45 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −56.0 (*c* 0.0875 $CHCl_3$); MS (FAB) = *m*/*z* 338; $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3409, 2987, 2934, 1623; ^1H NMR (200 MHz, $CDCl_3$): δ 5.89 (d, *J* = 3.6 Hz, 1H, H-1); 4.59 (d, *J* = 3.6 Hz, 1H, H-2); 4.22 (dd, *J* = 9.8 and 3.2 Hz, 1H, H-4); 3.82 (m, 4H, morpholinyl H); 3.58 (d, *J* = 3.2 Hz, 1H, H-3); 3.40 (s, 3H, $-OCH_3$); 3.34 (m, 1H, H-5); 2.87 (m, 4H, morpholinyl H); 2.42 (m, 2H, H-6); 1.48 and 1.32 [each s, 6H, $C(CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.2 (C=O); 112.5 [$\underline{C}(CH_3)_2$];105.7 (C-1); 84.3 (C-2); 80.2 (C-4); 79.6 (C-3); 67.1 (morpholinyl CH_2); 59.5 (C-5); 58.6 ($-OCH_3$); 53.3 (morpholinyl CH_2); 31.2 (C-6), 27.2 and 26.5 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 53.41; H, 7.17; N, 4.15.Found: C, 53.86; H, 7.42; N, 4.03.

3-*O*-Benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-(morpholin-1-yl)-β-L-*ido*-heptofuranuronic acid (12). It was obtained by reaction of ethyl [3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-(morpholin-1-yl)β-L-i*do*-heptofuran]-uronate **2j** (1.6 g, 4.38 mmol) and lithium hydroxide (0.42 g) as above. Colourless solid, Yield 88% mp 142 °C; R_f 0.55 (chloroform–methanol, 20:1); $[\alpha]_D^{20}$ −56.0 (*c* 0.1125 $CHCl_3$); MS (FAB) = *m*/*z* 414 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3407, 3017, 1634. ^1H NMR (200 MHz, $CDCl_3$): δ 7.33 (m, 5H, ArH); 5.93 (d, *J* = 3.6 Hz, 1H, H-1); 4.65 and 4.45 (each d, *J* = 11.3 Hz, each 1H, OCH_2Ph); 4.60 (d, *J* = 3.6 Hz, 1H, H-2); 4.14 (dd, *J* = 9.8 and 2.8 Hz, 1H, H-4); 3.79 (d, *J* = 2.8 Hz, 1H, H-3); 3.78 (m, 4H, morpholyl H); 3.34 (m, 1H, H-5); 2.81 (m, 4H, morpholyl H); 2.16 (m, 2H, H-6); 1.48 and 1.32 [each s, 6H, $C(C\underline{H}_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.5 (C=O); 136.2 (Ar–C); 129.3,

128.2,128.5 (Ar–CH); 112.5 [$\underline{C}(CH_3)_2$]; 105.2 (C-1); 82.3 (C-2); 81.4 (C-4); 80.3 (C-3); 72.6 (–O$\underline{C}H_2$Ph); 68.7 (morpholinyl CH_2); 59.8 (C-5);49.7 (morpholinyl CH_2); 32.33 (C-6); 27.2 and 26.6 [C($\underline{C}H_3)_2$]. Anal. calcd C, 61.01; H, 6.83; N, 3.39. Found: C, 61.38; H, 7.02; N, 3.14.

5,6-Dideoxy-5-(3,4-dimethoxybenzyl)amino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuranuronic acid (13). It was obtained by reaction of ethyl [5,6-dideoxy-5-(3,4-dimethoxybenzyl)amino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-i*do*-heptofuran]-uronate **2k** (1.9 g, 4.32 mmol) and lithium hydroxide (0.36 g, 8.64 mmol) as above. Colourless solid, Yield 98%; mp 133 °C; R_f 0. 55 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −12.17 (*c* 0.2875 $CHCl_3$); MS (FAB) = *m*/*z* 418 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3427,3026, 2984, 1624. ^1H NMR (200 MHz, $CDCl_3$): δ 6.87 (m, 3H, Ar–H); 5.90 (d, *J* = 3.4 Hz, 1H, H-1); 4.59 (d, *J* = 3.4 Hz, 1H, H-2); 4.15 (dd, *J* = 9.1 and 2.5 Hz, 1H, H-4); 3.98 (s, 2H, NHC$\underline{H}_2$) 3.85 (s, 6H, 2×Ar–OCH_3); 3.73 (d, *J* = 2.5 Hz, 1H, H-3); 3.43 (m, 1H, H-5); 3.37 (s, 3H, –OCH_3); 2.55 (dd, *J* = 17.0 and 4.5 Hz, 1H, H-6_A); 2.33 (dd, *J* = 17.0 and 6.3 Hz, 1H, H-6_B); 1.49 and 1.31 [each s, 6H, C($CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.9 (C=O); 149.6, 149.4 and 127.9 (ArC); 121.7, 112.6, 111.7 (ArCH); 112.4 [$\underline{C}(CH_3)_2$]; 105.3 (C-1); 83.7 (C-2); 81.3 (C-4); 81.0 (C-3); 57.9 (-OCH_3); 56.3 (2×Ar-OCH_3); 53.6 (C-5); 50.1 (-NH$\underline{C}H_2$), 32.3 (C-6), 27.1 and 26.6 [C($\underline{C}H_3)_2$]. Anal. Calcd. C, 57.55; H, 6.76; N, 3.36. Found: C, 57.89; H, 6.94; N, 3.26.

3-*O*-Benzyl-5,6-dideoxy-5-(3,4-dimethoxybenzyl)amino-1,2-*O*-isopropylidene-β-L-i*do*-heptofuranuronic acid (14). It was obtained by reaction of ethyl [3-*O*-benzyl-5,6-dideoxy - 5 - (3,4 - dimethoxybenzyl)amino - 1,2 - *O* - *iso*-propylidene-β-L-i*do*-heptofuran]-uronate **2l** (1.8 g, 4.33 mmol) and lithium hydroxide (0.36 g, 8.66 mmol) as above. Colourless solid, Yield 98%; mp 147 °C; R_f 0.45 (chloroform–methanol, 20:1); $[\alpha]_D^{20}$ −41.33 (*c* 0.225 $CHCl_3$); MS (FAB) = *m*/*z* 494 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3424, 2938, 1606. ^1H NMR (200 MHz, $CDCl_3$): δ 7.18 (m, 5H, ArH); 6.84 (m, 3H, ArH); 5.91 (d, *J* = 3.4 Hz, 1H, H-1); 4.65 (m, 2H, OCH_APh and H-2); 4.48 (d, *J* = 11.6 Hz, 1H, –OCH_BPh); 4.34 (dd, *J* = 9.2 and 2.8 Hz, 1H, H-4); 3.98 (s, 2H, NHC$\underline{H}_2$Ph) 3.81 (s, 6H, 2×Ar–OCH_3) 3.71 (d, *J* = 2.8 Hz, 1H, H-3); 3.49 (m, 1H, H-5); 2.48 (dd, *J* = 17.1 and 3.9 Hz, 1H, H-6_A); 2.24 (dd, *J* = 17.1 and 6.2 Hz, 1H, H-6_B); 1.47 and 1.31 [each s, 6H, C($C\underline{H}_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.9 (C=O); 149.6 and 149.5, 137.0 (Ar–C); 129.1, 128.7,128.2, 127.7, 121.92, 112.5, 111.7 (Ar–CH); 112.7 [$\underline{C}(CH_3)_2$]; 105.4 (C-1); 81.9 (C-2); 81.8 (C-4); 80.9 (C-3); 72.4 (–O$\underline{C}H_2$Ph); 56.3 (2×Ar–OCH_3); 53.6 (C-5); 50.3 (–NH$\underline{C}H_2$); 32.3 (C-6); 27.1 and 26.6 [C($\underline{C}H_3)_2$]. Anal. calcd C, 63.28; H, 6.54; N, 2.84. Found: C, 63.49; H, 6.73; N, 2.64.

5-Cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuranuronic acid (15). It was obtained by reaction of ethyl [5-cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-i*do*-heptofuran]-uronate **2m** (1.2 g, 3.64 mmol) and lithium hydroxide (0.30 g, 7.28 mmol) as above. Colourless solid, Yield 95%; mp 122 °C; R_f 0. 35 (chloroform–methanol, 19:1) $[\alpha]_D^{20}$ −24 (*c* 0.3375 $CHCl_3$); MS (FAB) = *m*/*z* 308 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3457, 2988, 2836, 1617. ^1H NMR (200 MHz, $CDCl_3$): δ 5.90 (d, *J* = 3.7 Hz, 1H, H-1); 4.62 (d, *J* = 3.7 Hz, 1H, H-2); 4.14 (dd, *J* = 9.8 and 3.1 Hz, 1H, H-4); 3.71 (d, *J* = 3.1 Hz, 1H, H-3); 3.45(m, 1H, H-5); 3.41 (s, 3H, –OCH_3); 2.74 (dd, *J* = 16.9 and 4.6 Hz, 1H, H-6_A); 2.33 (m, 2H, H-6_B and NHC$\underline{H}$); 1.47 and 1.31 [each s, 6H, C($CH_3)_2$]; 0.61 (m, 4H, cyclopropyl H). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 174.1 (C=O); 112.4 [$\underline{C}(CH_3)_2$]; 105.5 (C-1); 83.3 (C-2); 81.4 (C-4); 80.6 (C-3); 57.3 (–OCH_3); 54.8 (C-5); 31.2 (C-6); 28.3 (NHCH); 27.3 and 26.6 [C($\underline{C}H_3)_2$]; 6.9 and 5.7 (cyclopropyl 2×CH_2). Anal. calcd C, 54.72; H, 7.22; N, 4.56. Found: C, 54.91; H, 7.54; N, 4.48.

3-*O*-Benzyl-5-cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-i*do*-heptofuranuronic acid (16). It was obtained by reaction of ethyl [3-*O*-benzyl-5-cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronate **2n** (1.6 g, 3.95 mmol) and lithium hydroxide (0.33 g, 7.90 mmol) as above. Colourless solid, Yield 95%; mp 113 °C; R_f 0. 45 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −39.57 (*c* 0.2375 $CHCl_3$); MS (FAB) = *m*/*z* 384 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1} 3435, 2986, 1616. ^1H NMR (200 MHz, $CDCl_3$): δ 7.33 (m, 5H, ArH); 5.92 (d, *J* = 3.7 Hz, 1H, H-1); 4.66 (d, *J* = 3.7 Hz, 1H, H-2); 4.68 and 4.47 (each d, *J* = 11.5 Hz, 2H, –OCH_2Ph); 4.13 (dd, *J* = 9.8 and 3.1 Hz, 1H, H-4); 3. 95 (d, *J* = 3.1 Hz, 1H, H-3); 3.47 (m, 1H, H-5); 2.67 (dd, *J* = 16.9 and 5.9 Hz, 1H, H-6_A); 2.28 (m, 1H, NHC$\underline{H}$); 2.18 (dd, *J* = 16.9 and 5.1 Hz, 1H, H-6_B); 1.47 and 1.31 [each s, 6H, C($CH_3)_2$]; 0.57 (m, 4H, cyclopropyl H). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.4 (C=O); 137.1 (Ar–C); 129.1, 128.3,128.3 (Ar–CH); 112.6 [$\underline{C}(CH_3)_2$]; 105.4 (C-1); 82.3 (C-2); 81.6 (C-4); 80.5 (C-3); 72.2 (–O$\underline{C}H_2$Ph); 54.8 (C-5); 33.7 (C-6); 28.4 (–NH$\underline{C}$H); 27.2 and 26.6 [C($\underline{C}H_3)_2$]; 6.7 and 5.4 (cyclopropyl 2×CH_2). Anal. calcd C, 62.66; H, 6.84; N, 3.65. Found: C, 62.94; H, 7.05; N, 3.32.

5,6-Dideoxy-5-furylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuranuronic acid (17). It was obtained by reaction of ethyl [5,6-dideoxy-5-furylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β- L-i*do*-heptofuran]-uronate **2o** (1.3 g, 3.52 mmol) and lithium hydroxide (0.30 g, 7.04 mmol) as above. Colourless solid, Yield 92%; mp 163 °C; R_f 0.40 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −38.72 (*c* 0.3125 $CHCl_3$); MS (FAB) = *m*/*z* 342 $(M+H)^+$; IR (KBr) ν_{max} cm^{-1}: 3474, 2987, 2845, 1618. ^1H NMR (200 MHz, $CDCl_3$): δ 7.39 (s, 1H, furyl H); 6.31 (m, 2H, Furyl H); 5.88 (d, *J* = 3.7 Hz, 1H, H-1); 4.61 (d, *J* = 3.7 Hz, 1H, H-2); 4.13 (dd, *J* = 9.6 and 3.2 Hz, 1H, H-4); 3.94 (s, 2H, NHC$\underline{H}_2$); 3.71 (d, *J* = 3.2 Hz, 1H, H-3); 3.39 (s, 3H, –OCH_3); 3.35 (m, 1H, H-5); 2.59 (dd, *J* = 17.0 and 4.9 Hz, 1H, H-6_A); 2.24 (dd, *J* = 17.0 and 4.5 Hz, 1H, H-6_B); 1.47 and 1.31 [each s, 6H, C($CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 173.8 (C=O); 152.7 (Furyl C); 143.2 (Furyl CH); 112.6 [$\underline{C}(CH_3)_2$]; 110.9 and 107.5 (Furyl CH); 105.2 (C-1); 83.7 (C-2); 81.0 (C-4); 81.7 (C-3); 58.0 (–OCH_3); 53.7

(C-5); 44.9 (–NH$\underline{C}H_2$), 33.8 (C-6), 27.1 and 26.6 [C($\underline{C}H_3$)$_2$]. Anal. calcd C, 55.33; H, 6.39; N, 4.03. Found: C, 55.59; H, 6.72; N, 3.95.

3-*O*-Benzyl-5,6-dideoxy-5-furylamino-1,2-*O*-isopropylidene - β - L - i*do* - heptofuranuronic acid (18). It was obtained by reaction of ethyl [3-*O*-benzyl-5-furylamino-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronate **2p** (1.4 g, 3.14 mmol) and lithium hydroxide (0.26 g, 6.28 mmol) as above. Colourless solid, yield 92%; mp 124 °C; R_f 0.45 (chloroform–methanol, 25: 2); $[\alpha]_D^{20}$ −38.18 (*c* 0.275 $CHCl_3$); MS (FAB) = *m*/*z* 424 $(M+Li)^+$; IR (KBr) ν_{max} cm^{-1}: 3427, 2964, 1616. ^1H NMR (200 MHz, $CDCl_3$): δ 7.37 (m, 5H, ArH); 7.28 (m, 1H, Furyl H); 6.29 (m, 2H, Furyl H); 5.91 (d, *J* = 3.7 Hz, 1H, H-1); 4.65 and 4.46 (each d, *J* = 11.5 Hz, 2H, OCH_2Ph); 4.64 (d, *J* = 3.7 Hz, 1H, H-2); 4.13 (dd, *J* = 9.6 and 3.1 Hz, 1H, H-4); 3.95 (d, *J* = 3.1 Hz, 1H, H-3); 3.90 (s, 2H, NHC$\underline{H}_2$); 3.40 (m, 1H, H-5); 2.50 (dd, *J* = 17.1 and 4.8 Hz, 1H, H-6_A); 2.12 (dd, *J* = 17.1 and 4.6 Hz, 1H, H-6_B); 1.46 and 1.30 [each s, 6H, C($C\underline{H}_3$)$_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 172.9 (C=O); 150.4 143.2 and 137.06 (Ar–C); 129.1, 128.7,128.2, (Ar–CH); 110.8, 109.2 (Furyl CH); 112.6 [$\underline{C}(CH_3)_2$]; 105.3 (C-1); 82.2 (C-2); 81.7 (C-4); 81.1 (C-3); 72.4 (–O$\underline{C}H_2$Ph); 53.2 (C-5); 42.9 (–NH$\underline{C}H_2$); 32.3 (C-6); 27.1 and 26.6 [C($\underline{C}H_3$)$_2$]. Anal. calcd C, 62.41; H, 6.19; N, 3.31. Found: C, 62.69; H, 6.33; N, 3.12.

General procedure for the preparation of the compounds 19–34

N-Hydroxy-[-5,6-dideoxy-5-heptylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuran]-uronamide (19). 5,6-dideoxy-5-heptylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-i*do*-heptofuranuronic acid **3** (1.1 g, 3.06 mmol) in a mixture of anhydrous acetonitrile and dichloromethane (5.0 mL each) was magnetically stirred at 30 °C. To the stirring reaction mixture DCC (0.64 g, 3.1 mmol) was added followed by addition of followed by the addition of hydroxylamine hydrochloride (0.45 g, 6.42 mmol). The reaction mixture was stirred magnetically at 30 °C for 15 min and then transferred to 0 °C. Triethyl amine (0.88 mL, 6.42 mmol) was added and the reaction mixture is stirred at 0–4 °C for 10 h. The reaction mixture was filtered, filtrate was concentrated to get crude residue, which was dissolved in ethyl acetate (25 mL) washed with sodium bicarbonate soln. (2×15 mL) and water (2×15 mL). The organic layer dried over Na_2SO_4 and concentrated at reduced pressure to get crude product. The latter on column chromatography over SiO_2, using chloroform–methanol (97:3) as eluant gave the title compound. Colourless oil; Yield 48%; R_f 0.45 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −28.44 (*c* 0.1125 $CHCl_3$); MS (FAB) = *m*/*z* 375 $(M+H)^+$; IR (KBr) ν_{max} cm^{-1}: 3238, 2930, 1658. ^1H NMR (200 MHz, $CDCl_3$): δ 5.88 (d, *J* = 3.7 Hz, 1H, H-1); 4.60 (d, *J* = 3.8 Hz, 1H, H-2); 4.08 (dd, *J* = 9.3 and 2.9 Hz, 1H, H-4); 3.69 (d, *J* = 2.9 Hz, 1H, H-3); 3.44 (m, 1H, NHC$\underline{H}_A$); 3.40 (s, 3H CH_3); 3.20 (m, 1H, H-5); 2.70 (m, 1H, NHC$\underline{H}_B$); 2.59 (dd, *J* = 16.5 and 5.0 Hz, 1H, H-6_A); 2.26 (dd, *J* = 16.5 and 4.8 Hz, 1H, H-6_B), 1.43 and 1.28 [each s, 6H, 2×C (CH_3)$_2$], 1.31 (m, 10H, CH_2s) 0.88 (t, *J* = 7.1 Hz, 3H, –$CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169 (C=O); 112.8 [$\underline{C}(CH_3)_2$]; 105.4 (C-1); 84.0 (C-2); 83.8 (C-4); 82.9 (C-3); 57.9 (–OCH_3); 47.9 (C-5); 46.41 (–NH$\underline{C}H_2$), 30.1 (C-6), 29.2, 27.2, 26.0, 23.07 (CH_2s), 27.0 and 26.7 [C($\underline{C}H_3$)$_2$], 14.4 (–$CH_2\underline{C}H_3$). Anal. calcd C, 57.73; H, 9.15; N, 7.48. Found: C, 58.02; H, 9.34; N, 7.35.

***N*-Hydroxy-[3-*O*-benzyl-5,6-dideoxy-5-heptylamino-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronamide (20).** It was obtained by the reaction of compound **4** (1.0 g, 2.30 mmol) with hydroxylamine hydrochloride (0.34 g, 4.83 mmol) in presence of dicyclohexyl carbodiimide (0.49 g, 2.30 mmol) and triethyl amine (0.38 mL, 2.75 mmol) as above. Yellow oil; Yield 40%; R_f 0.55 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −40.0 (*c* 0.0875 $CHCl_3$), MS (FAB) = *m*/*z* 451 $(M+H)^+$; IR (KBr) ν_{max} $cm^{-1:}$ 3238, 2930, 2859, 1648. ^1H NMR (200 MHz, $CDCl_3$): δ 7.34 (m, 5H, ArH); 5.92 (d, *J* = 3.5 Hz, 1H, H-1); 4.69 and 4.57 (each d, *J* = 11.9 Hz, each 1H, OCH_APh and –OCH_BPh); 4.62 (d, *J* = 3.5 Hz, 1H, H-2), 4.20 (dd, *J* = 8.9 and 3.2 Hz, 1H, H-4); 3.99 (d, *J* = 3.2 Hz, 1H, H-3); 3.50 (m, 1H, H-5); 2.90 (m, 2H, NHC$\underline{H}_2$); 2.60 (dd, *J* = 16 and 5 Hz, 1H, H-6_A); 2.26 (dd, *J* = 16.0 and 8.0 Hz, 1H, H-6_B); 1.584 (bs, 1H, NH); 1.48 and 1.32 [each s, 6H, C ($C\underline{H}_3$)$_2$]; 1.25 (m, 10H, CH_2s); 0.86 (t, *J* = 7.14 Hz, 3H, –$CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 168 (C=O); 136.9 (each Ar–C); 129.0, 129. 128.8,127.92 (ArCH); 112.6 [$\underline{C}(CH_3)_2$]; 105.4(C-1); 82.2 (C-2); 82.1 (C-4); 81.7 (C-3); 72.5 (–O$\underline{C}H_2$Ph); 54.9 (C-5), 47.5 (–NH$\underline{C}H_2$); 31.9 (C-6), 29.1, 27.7, 27.1(CH_2s), 26.7 and 26.9 [C ($\underline{C}H_3$)$_2$]; 14.4 (–$CH_2\underline{C}H_3$). Anal. calcd C, 63.98; H, 8.50; N, 6.22. Found: C, 64.27; H, 8.73; N, 6.09.

***N*-Hydroxy-[5,6-dideoxy-5-dodecylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuran]-uronamide (21).** It was obtained by the reaction of compound **5** (1.0 g, 2.33 mmol) with hydroxylamine hydrochloride (0.34 g, 4.90 mmol) in presence of dicyclohexyl carbodiimide (0.48 g, 2.34 mmol) and triethyl amine (0.67 mL, 2.33 mmol) as above. Yellow oil; Yield 42%; R_f 0. 5 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −36.36 (*c* 0.1375 $CHCl_3$); MS (FAB) = *m*/*z* 444 $(M+H)^+$; IR (KBr) ν_{max} $cm^{-1:}$ 3019, 2933, 2861, 1658. ^1H NMR (200 MHz, $CDCl_3$): δ 5.88 (d, *J* = 3.4 Hz, 1H, H-1); 4.60 (d, *J* = 3.4 Hz, 1H, H-2); 4.16 (dd, *J* = 9.8 and 2.9 Hz, 1H, H-4); 3.73 (d, *J* = 2.9 Hz, 1H, H-3); 3.40 (s, 3H CH_3); 3.27 (m, 1H, H-5); 2.67 (m, 2H, NHC$\underline{H}_2$); 2.30 (dd, *J* = 16.0 and 8.0 Hz, 1H, H-6_A); 1.96 (d, *J* = 16 Hz, 1H, H-6_B), 1.48 and 1.31 [each s, 6H, C(CH_3)$_2$]; 1.25 (m, 18H, CH_2s); 0.88 (t, *J* = 7.1 Hz, 3H,–$CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 158.2 (C=O); 112.4 [$\underline{C}$ (CH_3)$_2$]; 105.2 (C-1); 84.0 (C-2); 81.6 (C-4); 81.1 (C-3); 57.9 (–OCH_3); 53.8 (C-5); 46.6 (–NH$\underline{C}H_2$), 32.3 (C-6), 30.3, 29.9, 29.8, 29.7, 27.5 (CH_2s), 27.5 and 26.6 [C ($\underline{C}H_3$) $_2$], 14.7 (–$CH_2\underline{C}H_3$). Anal. calcd C, 62.13; H, 9.97; N, 6.30. Found: C, 62.40; H, 10.08; N, 6.17.

***N*-Hydroxy-[3-*O*-benzyl-5,6-dideoxy-5-dodecylamino-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronamide (22).** It was obtained by the reaction of compound **6** (1.2 g, 2.37 mmol) with hydroxylamine hydrochloride (0.35 g,

4.98 mmol) in presence of dicyclohexyl carbodiimide (0.49 g, 2.37 mmol) and triethyl amine (0.68 mL, 4.98 mmol) as above. Yellow solid. Yield 40%; mp 113 °C; R_f 0.5 (chloroform–methanol, 20:1); $[\alpha]_D^{20}$ −45.09 (*c* 0.1375 $CHCl_3$); MS (FAB) = *m*/*z* 521 $(M+H)^+$; IR (KBr) ν_{max} cm^{-1}: 3403, 2926, 2855, 1654. ^1H NMR (200 MHz, $CDCl_3$): δ 7.32 (m, 5H, ArH); 5.90 (d, *J* = 3.7 Hz, 1H, H-1); 4.67 and 4.49 (each d, *J* = 11.9 Hz, 2H, OCH_2Ph); 4.64 (d, *J* = 3.7 Hz, 1H, H-2); 4.06 (dd, *J* = 7.2 and 3.0 Hz, 1H, H-4); 3.94 (d, *J* = 3.0 Hz, 1H, H-3); 3.48 (m, 1H, H-5); 3.2 (m, 2H, $NHC\underline{H}_2$); 2.55 (m, 1H, $H\text{-}6_A$); 2.20 (dd, *J* = 16.5 and 2.4 Hz, 1H, $H\text{-}6_B$); 1.84 (bs, 1H, NH); 1.48 and 1.31 [each s, 6H, $C(C\underline{H}_3)_2$]; 1.25 (m, 18H, CH_2s); 0.88 (t, *J* = 7.14 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 168.4 (C=O); 136.91 (each Ar–C); 128.65, 128.24,127.92 (ArCH); 111.98 [$\underline{C}(CH_3)_2$]; 104.76 (C-1); 82.01 (C-2); 81.58 (C-4); 80.37 (C-3); 72.04 ($-O\underline{C}H_2Ph$); 53.42 (C-5); 46.03 ($-NH\underline{C}H_2$); 32.47 (C-6); 30.0, 29.7, 27.6,26.0, 23.07(CH_2s); 27.14 and 26.60 [$C(\underline{C}H_3)_2$], 14.49 ($-CH_2\underline{C}H_3$). Anal. calcd C, 66.89; H, 9.29; N, 5.38. Found: C, 67.11; H, 9.43; N, 5.17.

***N*-Hydroxy-[5,6-dideoxy-5-hexadecylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuran]-uronamide (23).** It was obtained by the reaction of compound **7** (1.2 g, 2.47 mmol) with hydroxylamine hydrochloride (0.36 g, 5.2 mmol) in presence of dicyclohexyl carbodiimide (0.51 g, 2.47 mmol) and triethyl amine (0.71 mL, 5.2 mmol) as above. Yellow oil; yield 44%; R_f 0.5 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −39.4 (*c* 0.1875 $CHCl_3$); MS (FAB) = *m*/*z* 501 $(M+H)^+$; IR (KBr) ν_{max} cm^{-1}: 3403, 2912, 2845, 1657. ^1H NMR (200 MHz, $CDCl_3$): δ 5.88 (d, *J* = 3.7 Hz, 1H, H-1); 5.42 (bs, 1H, NHOH); 4.59 (d, *J* = 3.7 Hz, 1H, H-2); 4.20 (dd, *J* = 9.9 and 3.0 Hz, 1H, H-4); 3.41 (d, *J* = 3.0 Hz, 1H, H-3); 3.41 (s, 3H-OCH_3); 3.37 (m, 1H, H-5); 2.86 (m, 2H, $NHC\underline{H}_2$); 2.45 (m, 2H, H-6); 1.48 and 1.31 [each s, 6H, $C(CH_3)_2$]; 1.25 (m, 26H, CH_2s); 0.85 (t, *J* = 6.1 Hz, 3H, $-CH_2C\underline{H}_3$). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 168.9 (C=O); 112.2 [$\underline{C}(CH_3)_2$]; 105.1 (C-1); 84.4 (C-2); 82.5 (C-4); 80.7 (C-3); 57.5 ($-OCH_3$); 47.63 (C-5); 46.3 ($-NH\underline{C}H_2$), 32.3 (C-6), 30.1, 29.7, 27.7 (CH_2s), 27.1 and 26.6 [$C(\underline{C}H_3)_2$], 14.5 ($-CH_2\underline{C}H_3$). Anal. calcd C, 64.77; H, 10.47; N, 5.59. Found: C, 64.93; H, 10.70; N, 5.38.

***N*-Hydroxy-[3-*O*-benzyl-5,6-dideoxy-5-hexadecylamino-1,2-*O*-isopropylidene-β-L-*ido*-heptofuran]-uronamide (24).** It was obtained by the reaction of compound **8** (1.1 g, 2.85 mmol) with hydroxylamine hydrochloride (0.29 g, 4.12 mmol) in presence of dicyclohexyl carbodiimide (0.40 g, 2.85 mmol) and triethyl amine (0.57 mL, 4.12 mmol) as above. Yellow foam. Yield 45%; R_f 0.5 (chloroform–methanol, 20:1); $[\alpha]_D^{20}$ −36.0 (*c* 0.15 $CHCl_3$); MS (FAB) = *m*/*z* 577 $(M+H)^+$; IR (KBr) ν_{max} cm^{-1}: 2924, 2362, 1956, 1638, 1458, 1378; ^1H NMR (200 MHz, $CDCl_3$): δ 7.31 (m, 5H, ArH); 5.94 (d, *J* = 3.7 Hz, 1H, H-1); 4.66 and 4.46 (each d, *J* = 11.7 Hz, 2H, OCH_2Ph); 4.57 (d, *J* = 3.7 Hz, 1H, H-2); 4.11 (dd, *J* = 9.0 and 3.0 Hz, 1H, H-4); 3.78 (d, *J* = 3.0 Hz, 1H, H-3); 3.60 (m, 1H, H-5); 2.62 (m, 2H, $NHC\underline{H}_2$); 2.45 (m, 2H, H-6); 1.56 (bs, 1H, NH); 1.47 and 1.31 [each s, 6H, $C(C\underline{H}_3)_2$]; 1.25 (m, 26H, CH_2s); 0.87 (t, *J* = 7.14 Hz, 3H, $-CH_2C\underline{H}_3$); ^{13}C NMR (proton decoupled, $CDCl_3$): δ 162.7 (C=O); 137.2 (Ar–C); 129.1, 128.6,128.1 (Ar CH); 112.0 [$\underline{C}(CH_3)_2$]; 105.4 (C-1); 82.4 (C-2); 82.0 (C-4); 81.62 (C-3); 72.2 ($-O\underline{C}H_2Ph$); 49.8 (C-5); 47.4 ($-NH\underline{C}H_2$); 32.3 (C-6); 30.1, 29.8, 27.6, 23.1 (CH_2s); 27.2 and 26.7 [$C(\underline{C}H_3)_2$], 14.5 ($-CH_2\underline{C}H_3$). Anal. calcd C, 68.71; H, 9.79; N, 4.86. Found: C, 68.92; H, 9.95; N, 4.71.

***N*-Hydroxy-[5-benzylamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuran]-uronamide (25).** It was obtained by the reaction of compound **9** (1.0 g, 2.85 mmol) with hydroxylamine hydrochloride (0.41 g, 5.98 mmol) in presence of dicyclohexyl carbodiimide (0.59 g, 2.85 mmol) and triethyl amine (0.82 mL, 5.98 mmol) as above. White solid. Yield 70%; Mp 148 °C; R_f 0.5 (chloroform–methanol, 19:1) $[\alpha]_D^{20}$ −51.42 (*c* 0.2625 $CHCl_3$); MS (FAB) = *m*/*z* 367 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3206, 3015, 2936, 1658, 1458, 1379; ^1H NMR (200 MHz, $CDCl_3$): δ 7.36 (m, 5H, ArH); 5.88 (d, *J* = 3.6 Hz, 1H, H-1); 4.59 and 4.57 (each d, *J* = 3.6 Hz, 1H, H-2); 4.15 (dd, *J* = 9.8 and 3.2 Hz, 1H, H-4); 3.84 (s, 2H, $NHCH_2Ar$); 3.70 (d, *J* = 3.2 Hz, 1H, H-3); 3.38 (s, 3H, $-OCH_3$); 3.37 (m, 1H, H-5); 2.59 (dd, *J* = 16.5 and 4.0 Hz, 1H, $H\text{-}6_A$); 2.29 (dd, *J* = 16.5 and 5.2 Hz, 1H, $H\text{-}6_B$); 1.47 and 1.31 [each s, 6H, $C(CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169 (C=O); 139.0 (Ar C); 129.0, 128.8, 127.9 (Ar CH); 112.2 [$\underline{C}(CH_3)_2$];105.1 (C-1); 84.2 (C-2); 83.91 (C-4); 80.9 (C-3); 57.9 ($-OCH_3$); 53.6 (C-5); 50.1 ($-NH\underline{C}H_2$), 32.9 (C-6), 27.1 and 26.6 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 59.00; H, 7.15; N, 7.65. Found: C, 59.13; H, 7.24; N, 7.49.

***N*-Hydroxy-[5-benzylamino-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuran]-uronamide (26).** It was obtained by the reaction of compound **10** (1.0 g, 2.34 mmol) with hydroxylamine hydrochloride (0.34 g, 4.91 mmol) in presence of dicyclohexyl carbodiimide (0.48 g, 2.34 mmol) and triethyl amine (0.68 mL, 4.91 mmol) as above. Yellow solid. Yield 48%, mp 134 °C, R_f 0.5 (chloroform–methanol, 20:1), $[\alpha]_D^{20}$ −52.4 (*c* 0.1125 $CHCl_3$), MS (FAB) = *m*/*z* 443 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3217, 2987, 2932, 2361, 1957, 1660, 1556, 1495. ^1H NMR (200 MHz, $CDCl_3$): δ 7.30 (m, 5H, ArH); 5.91 (d, *J* = 3.6 Hz, 1H, H-1); 4.68 and 4.49 (each d, *J* = 11.2 Hz, each 1H, OCH_APh and $-OCH_BPh$); 4.60 (d, *J* = 3.6 Hz, 1H, H-2); 4.11 (m, 1H, H-4); 3.94 (d, *J* = 2.9 Hz, 1H, H-3); 3.88 and 3.70 (each d, *J* = 15.0 Hz, 1H, $NHCH_A$ and $NHCH_B$); 3.45 (m, 1H, H-5); 2.60 (m, 2H, H-6); 1.47 and 1.31 [each s, 6H, $C(C\underline{H}_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 168.9 (C=O); 137.0 and 137.2 (Ar–C); 129.0, 128.9,128.7, 128.5, 128.0, 127.6 (Ar–CH); 112.0 [$\underline{C}(CH_3)_2$]; 105.1 (C-1); 82.6 (C-2); 81.9 (C-4); 81.14 (C-3); 72.4 ($-O\underline{C}H_2Ph$); 53.64 (C-5); 51.6 ($-NH\underline{C}H_2$); 33.9 (C-6); 27.1 and 26.6 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 65.14; H, 6.83; N, 6.33. Found: C, 65.38; H, 6.98; N, 6.24.

***N*-Hydroxy-[5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-(morpholin-1-yl)-β-L-*ido*-heptofuran]-uronamide (27).** It was obtained by the reaction of compound **11** (0.9 g, 2.72 mmol) with hydroxylamine hydrochloride

(0.40 g, 5.77 mmol) in presence of dicyclohexyl carbodiimide (0.56 g, 2.72 mmol) and triethyl amine (0.82 mL, 5.77 mmol) as above. Colourless solid, yield 45%, mp 124 °C R_f 0.5 (chloroform–methanol, 19:1), $[\alpha]_D^{20}$ −58.46 (*c* 0.1625 $CHCl_3$), MS (FAB) = *m*/*z* 347 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3337, 2939, 1658, 1550, 1456; ^1H NMR (200 MHz, $CDCl_3$): δ 5.91 (d, *J* = 3.4 Hz, 1H, H-1); 4.57(d, *J* = 3.6 Hz, 1H, H-2); 4.13 (dd, *J* = 9.8 and 3.2 Hz, 1H, H-4); 3.75 (m, 4H, morpholinyl H); 3.58 (d, *J* = 3.2 Hz, 1H, H-3); 3.40 (s, 3H, –OCH_3); 3.26 (m, 1H, H-5); 2.82 (m, 4H, morpholinyl H); 2.33 (m, 2H, H-6); 1.48 and 1.32 [each s, 6H, $C(CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169.2 (C=O); 112.0 [$\underline{C}(CH_3)_2$];105.3 (C-1); 84.9 (C-2); 80.5 (C-4); 79.8 (C-3); 67.3 (morpholinyl CH_2); 59.3 (C-5); 57.8 (–OCH_3); 53.8 (morpholinyl CH_2); 30.9 (C-6), 27.2 and 26.5 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 52.01; H, 7.57; N, 8.09. Found: C, 52.32; H, 7.69; N, 7.92.

***N*-Hydroxy-[3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-(morpholin-1-yl)-β-L-*ido*-heptofuran]-uronamide (28).** It was obtained by the reaction of compound **12** (1.0 g, 2.46 mmol) with hydroxylamine hydrochloride (0.36 g, 5.17 mmol) in presence of dicyclohexyl carbodiimide (0.50 g, 2.46 mmol) and triethyl amine (0.72 mL, 5.17 mmol) as above. Yellow solid. Yield 52% mp 84 °C, R_f 0.5 (chloroform–methanol, 20:1) $[\alpha]_D^{20}$ −49.14 (*c* 0.175 $CHCl_3$), MS (FAB) = *m*/*z* 423 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3295, 2954, 2858, 1665, 1493, 1456; ^1H NMR (200 MHz, $CDCl_3$): δ 7.33 (m, 5H, ArH); 5.91 (d, *J* = 3.8 Hz, 1H, H-1); 4.64 and 4.46 (each d, *J* = 11.5 Hz, each 1H, OCH_APh and –OCH_BPh); 4.60 (d, *J* = 3.6 Hz, 1H, H-2); 4.16 (dd, *J* = 9.4 and 2.4 Hz, 1H, H-4); 3.78 (d, *J* = 2.4 Hz, 1H, H-3); 3.69 (m, 4H, morpholyl H); 3.27 (m, 1H, H-5); 2.99 (m, 4H, morpholyl H); 2.31 (dd, *J* = 15.7 and 11.6 Hz, 1H, H-6_A); 2.06 (m, 1H, H-6_B); 1.47 and 1.31 [each s, 6H, $C(C\underline{H}_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169.4 (C=O); 136.9 (Ar–C); 129.0, 128.7,128.6 (Ar–CH); 112.1 [$\underline{C}(CH_3)_2$]; 105.4 (C-1); 82.6 (C-2); 81.1 (C-4); 80.0 (C-3); 72.3 (–O$\underline{C}H_2$Ph); 68.0 (morpholinyl CH_2); 59.32 (C-5);49.5 (morpholinyl CH_2); 32.33 (C-6); 27.2 and 26.6 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 59.70; H, 7.16; N, 6.63. Found: C, 59.86; H, 7.32; N, 6.57.

***N*-Hydroxy-[5,6-dideoxy-5-(3,4-dimethoxybenzyl)amino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuran]-uronamide (29).** It was obtained by the reaction of compound **13** (1.3 g, 3.16 mmol) with hydroxylamine hydrochloride (0.46 g, 6.64 mmol) in presence of dicyclohexyl carbodiimide (0.65 g, 3.16 mmol) and triethyl amine (0.92 mL, 6.64 mmol) as above. Colourless foam. Yield 58%; R_f 0.35 (chloroform–methanol, 19:1); $[\alpha]_D^{20}$ −5.76 (*c* 0.3125 $CHCl_3$), MS (FAB) = *m*/*z* 427 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3436, 1638. ^1H NMR (200 MHz, $CDCl_3$): δ 6.83 (s, 3H, Ar–H); 5.88 (d, *J* = 3.3 Hz, 1H, H-1); 4.60 (d, *J* = 3.3 Hz, 1H, H-2); 4.15 (dd, *J* = 9.0 and 3.2 Hz, 1H, H-4); 3.89 and 3.87 (each s, 6H, 2×Ar–OCH_3); 3.73 (d, *J* = 3.2 Hz, 1H, H-3); 3.44 (m, 1H, H-5); 3.39 (s, 3H, –OCH_3); 2.63 (dd, *J* = 16.8 and 4.3 Hz, 1H, H-6_A); 2.33 (dd, *J* = 16.5 and 5.2 Hz, 1H, H-6_B); 1.48 and 1.32 [each s, 6H, $C(CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 164.2 (C=O); 149.65, 148.9 and 130.4 (Ar–C); 121.6, 112.7, 111.3 (ArCH); 112.1 [$\underline{C}(CH_3)_2$];105.5 (C-1); 84.3 (C-2); 81.2 (C-4); 78.7 (C-3); 57.9 (–OCH_3); 56.3 (2×Ar–OCH_3); 55.3(C-5); 52.9 (–NH$\underline{C}H_2$), 30.6 (C-6), 27.3 and 26.6 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 56.33; H, 7.09; N, 6.57. Found: C, 56.47; H, 7.22; N, 6.51.

***N*-Hydroxy-[3-*O*-benzyl-5,6-dideoxy-5-(3,4-dimethoxybenzyl)amino-1,2-*O*-isopropylidene-β-L-*ido*-heptofuran]-uronamide (30).** It was obtained by the reaction of compound **14** (1.2 g, 2.46 mmol) with hydroxylamine hydrochloride (0.36 g, 5.17 mmol) in presence of dicyclohexyl carbodiimide (0.51 g, 2.46 mmol) and triethyl amine (0.72 mL, 5.17 mmol) as above. Colourless foam. Yield 68%, R_f 0.5 (chloroform–methanol, 20:1) $[\alpha]_D^{20}$ −20.5 (*c* 0.4 $CHCl_3$), MS (FAB) = *m*/*z* 503 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3685, 3020, 1658. ^1H NMR (200 MHz, $CDCl_3$): δ 7.29 (m, 5H, ArH); 6.80 (m, 3H, ArH); 5.90 (d, *J* = 3.6 Hz, 1H, H-1); 4.65 (m, 2H, OCH_APh and H-2); 4.47 (d, *J* = 11.6 Hz, 1H, –OCH_BPh); 4.15 (dd, *J* = 9.5 and 2.9 Hz, 1H, H-4); 3.94 (d, *J* = 2.9 Hz, 1H, H-3); 3.86 and 3.85 (m, 7H, 2×Ar–OCH_3 and NHC$\underline{H}_A$); 3.70 (d, *J* = 16.2 Hz, 1H, NHC$\underline{H}_B$); 3.38 (m, 1H, H-5); 2.50 (dd, *J* = 16.4 and 3.9 Hz, 1H, H-6_A); 2.21 (dd, *J* = 16.4 and 5.4 Hz, 1H, H-6_B); 1.47 and 1.31 [each s, 6H, $C(C\underline{H}_3)_2$]; ^{13}C NMR (proton decoupled, $CDCl_3$): δ 168.9 (C=O); 137.0 and 137.2 (Ar–C); 129.0, 128.9, 128.7, 128.5, 128.0, 127.6 (Ar–CH); 112.0 [$\underline{C}(CH_3)_2$]; 105.1 (C-1); 82.6 (C-2); 81.9 (C-4); 81.14 (C-3); 72.4 (–O$\underline{C}H_2$Ph); 53.64 (C-5); 51.6 (–NH$\underline{C}H_2$); 33.9 (C-6); 27.1 and 26.6 [$C(\underline{C}H_3)_2$]. Anal. calcd C, 62.14; H, 6.82; N, 5.57. Found: C, 62.35; H, 6.91; N, 5.49.

***N*-Hydroxy-[5-cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuran]-uronamide (31).** It was obtained by the reaction of compound **15** (0.9 g, 3.0 mmol) with hydroxylamine hydrochloride (0.44 g, 6.3 mmol) in presence of dicyclohexyl carbodiimide (0.62 g, 3.0 mmol) and triethyl amine (0.87 mL, 6.3 mmol) as above. Colourless foam. Yield 48%, R_f 0.5 (chloroform–methanol, 19:1) $[\alpha]_D^{20}$ −24.85 (*c* 0.35 $CHCl_3$), MS (FAB) = *m*/*z* 317 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3427, 2992, 1654. ^1H NMR (200 MHz, $CDCl_3$): δ 5.88 (d, *J* = 3.7 Hz, 1H, H-1); 4.60 (d, *J* = 3.7 Hz, 1H, H-2); 4.11 (dd, *J* = 9.5 and 2.9 Hz, 1H, H-4); 3.69 (d, *J* = 2.9 Hz, 1H, H-3); 3.41 (s, 3H, –OCH_3); 3.32 (m, 1H, H-5); 2.69 (dd, *J* = 16.5 and 3.8 Hz, 1H, H-6_A); 2.37 (dd, *J* = 16.5 and 5.9 Hz, 1H, H-6_B); 2.16 (m, 1H, NHC$\underline{H}$); 1.47 and 1.31 [each s, 6H, $C(CH_3)_2$]; 0.45 (m, 4H, cyclopropyl H). ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169.5 (C=O); 112.2 [$\underline{C}(CH_3)_2$]; 105.1 (C-1); 83.9 (C-2); 81.8 (C-4); 80.8 (C-3); 57.9 (–OCH_3); 54.4 (C-5); 30.6 (C-6); 28.23 (NHCH); 27.3 and 26.6 [$C(\underline{C}H_3)_2$]; 6.7 and 5.4 (cyclopropyl 2×CH_2). Anal. calcd C, 53.15; H, 7.65; N, 8.86. Found: C, 53.42; H, 7.77; N, 8.79.

***N*-Hydroxy-[3-*O*-benzyl-5-cyclopropylamino-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-*ido*-heptofuran]-uronamide (32).** It was obtained by the reaction of compound **16** (1.1 g, 2.91 mmol) with hydroxylamine hydrochloride (0.42 g, 6.1 mmol) in presence of dicyclohexyl carbodiimide (0.60 g, 2.91 mmol) and triethyl amine (0.84

mL, 6.1 mmol) as above. Colourless foam. Yield 50%, R_f 0.45 (chloroform–methanol, 25:2) $[\alpha]_D^{20}$ −8.44 (*c* 0.0225 $CHCl_3$), MS (FAB) = *m*/*z* 393 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3430, 2986, 1656. ^1H NMR (200 MHz, $CDCl_3$): δ 7.34 (m, 5H, ArH); 5.91 (d, *J* = 3.5 Hz, 1H, H-1); 4.64 (m, 2H, OCH_APh and H-2); 4.49 (d, *J* = 11.5 Hz, 1H, $-OCH_BPh$); 4.12 (dd, *J* = 9.4 and 3.0 Hz, 1H, H-4); 3. 94 (d, *J* = 3.0 Hz, 1H, H-3); 3.38 (m, 1H, H-5); 2.59 (dd, *J* = 16.5 and 3.8 Hz, 1H, $H\text{-}6_A$); 2.28 (dd, *J* = 16.5 and 5.9 Hz, 1H, $H\text{-}6_B$); 2.13 (m, 1H, NHC<u>H</u>); 1.46 and 1.30 [each s, 6H, $C(CH_3)_2$]; 0.45 (m, 4H, cyclopropyl H); ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169.5 (C=O); 137.3 (ArC); 129.0, 128.6, 128.4 (Ar–CH); 112.3 [<u>C</u>$(CH_3)_2$]; 105.1 (C-1); 82.4 (C-2); 81.9 (C-4); 80.8 (C-3); 72.4 (–O<u>C</u>H_2Ph); 54.38 (C-5); 33.3 (C-6); 28.3 (–NH<u>C</u>H); 27.2 and 26.6 [C(<u>C</u>$H_3)_2$]; 6.7 and 5.4 (cyclopropyl 2×CH_2). Anal. calcd C, 61.21; H, 7.19; N, 7.14. Found: C, 61.43; H, 7.32; N, 7.08.

***N*-Hydroxy-[5,6-dideoxy-5-furylamino-1,2-*O*-isopropylidene-3-*O*-methyl-β-L-*ido*-heptofuran]-uronamide (33).** It was obtained by the reaction of compound **17** (1.0 g, 2.93 mmol) with hydroxylamine hydrochloride (0.43 g, 6.15 mmol) in presence of dicyclohexyl carbodiimide (0.61 g, 2.93 mmol) and triethyl amine (0.85 mL, 6.15 mmol) as above. Colourless foam. Yield 60%, R_f 0.5 (chloroform–methanol, 19:1) $[\alpha]_D^{20}$ −11.09 (*c* 0.3875 $CHCl_3$), MS (FAB) = *m*/*z* 357 $(M+H)^+$, IR (KBr) ν_{max} cm^{-1}: 3021, 1659. ^1H NMR (200 MHz, $CDCl_3$): δ 7.38 (d, *J* = 1 Hz, 1H, Furyl H); 6.30 (m, 1H, Furyl H); 6.21 (m, 1H, Furyl H); 5.88 (d, *J* = 3.8 Hz, 1H, H-1); 4.60 (d, *J* = 3.8 Hz, 1H, H-2); 4.08 (dd, *J* = 9.3 and 3.0 Hz, 1H, H-4); 3.83 (s, 2H, NHC<u>H</u>$_2$); 3.70 (d, *J* = 3.0 Hz, 1H, H-3); 3.39 (s, 3H, $-OCH_3$); 3.34 (m, 1H, H-5); 2.58 (dd, *J* = 16.5 and 4.3 Hz, 1H, $H\text{-}6_A$); 2.25 (dd, *J* = 16.5 and 5.4 Hz, 1H, $H\text{-}6_B$); 1.47 and 1.31 [each s, 6H, $C(CH_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169.1 (C=O); 152.9 (Furyl C); 142.6 (Furyl CH); 112.2 [<u>C</u>$(CH_3)_2$]; 110.7 and 107.9 (Furyl CH); 105.1 (C-1); 84.0 (C-2); 81.7 (C-4); 81.5 (C-3); 57.9 ($-OCH_3$); 53.3 (C-5); 43.4 (–NH<u>C</u>H_2), 33.6 (C-6), 27.1 and 26.6 [C(<u>C</u>$H_3)_2$]. Anal. calcd C, 53.92; H, 6.79; N, 7.86. Found: C, 54.03; H, 6.89; N, 7.82.

***N*-Hydroxy-[3-*O*-benzyl-5,6-dideoxy-5-furylamino-1,2-*O*-isopropylidene-β-L-i*do*-heptofuran]-uronamide (34).** It was obtained by the reaction of compound **18** (1.1 g, 2.63 mmol) with hydroxylamine hydrochloride (0.38 g, 5.52 mmol) in presence of dicyclohexyl carbodiimide (0.59 g, 2.63 mmol) and triethyl amine (0.76 mL, 5.52 mmol) as above. Colourless foam. Yield 45%, R_f 0.45 (chloroform–methanol, 20:1); $[\alpha]_D^{20}$ −19.85 (*c* 0.375 $CHCl_3$); MS (FAB) = *m*/*z* 433 $(M+H)^+$; IR (KBr) ν_{max} cm^{-1}: 3398, 2926, 1657. ^1H NMR (200 MHz, $CDCl_3$): δ 7.33 (m, 1H, furyl H); 7.30 (m, 5H, ArH); 6.29 (m, 1H, furyl H); 6.19 (s, 1H, furyl H); 5.90 (d, *J* = 3.7 Hz, 1H, H-1); 4.68 (m, 2H, $-OCH_APh$ and H-2); 4.48 (d, *J* = 11.5 Hz, 1H, OCH_BPh); 4.11 (dd, *J* = 9.3 and 2.9 Hz, 1H, H-4); 3.94 (d, *J* = 2.9 Hz, 1H, H-3); 3.81 (s, 2H, NHC<u>H</u>$_2$); 3.35 (m, 1H, H-5); 2.40 (m, 2H, H-6); 1.47 and 1.31 [each s, 6H, C(C<u>H</u>$_3)_2$]. ^{13}C NMR (proton decoupled, $CDCl_3$): δ 169.0 (C=O); 152.9 (furyl C), 142.6 furyl CH); 137.3 (Ar–C); 129.0, 128.5 and 128.3 (Ar–CH); 112.3 [<u>C</u>$(CH_3)_2$]; 110.6 and 107.8 (furyl CH); 105.2 (C-1); 82.3 (C-2); 81.9 (C-4); 81.4 (C-3); 72.4 (–O<u>C</u>H_2Ph); 53.2 (C-5); 43.5 (–NH<u>C</u>H_2); 33.5 (C-6); 27.1 and 26.6 [C(<u>C</u>$H_3)_2$]. Anal. calcd C, 61.10; H, 6.53; N, 6.48. Found: C, 61.19; H, 6.64; N, 6.42.

6,7-dideoxy-6-heptylamino-L-*threo*-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-octapyranuronic acid (38). It was obtained by reaction of **36** (1.1 g, 2.48 mmol) and lithium hydroxide (0.21 g, 4.96 mmol) as above. Colourless solid, Yield 92% mp 113 °C; R_f 0.47 (chloroform/methanol, 20:1); $[\alpha]_D^{20}$ −36.23 (*c* 0.2125, $CHCl_3$), MS (FAB) = *m*/*z* 422 $(M+Li)^+$; IR (Neat) ν_{max} cm^{-1} 2933, 1610, 1584; ^1H NMR (200 MHz, $CDCl_3$): δ 5.52 (d, *J* = 5.0 Hz, 1H, H-1), 4.61 (dd, *J* = 7.9 and 2.4 Hz, 1H, H-3), 4.33 (dd, *J* = 5.0 and 2.4 Hz, 1H, H-2), 4.28 (dd, *J* = 7.9 and 1.6 Hz, 1H, H-4), 3.83 (d, *J* = 9.4 Hz, 1H, H-5), 3.27 (m, 1H, H-6), 2.84 (m, 3H, NHC<u>H</u>$_2$ and $H\text{-}7_A$), 2.48 (dd, *J* = 17.2 and 4.9 Hz, 1H, $H\text{-}7_B$), 1.62 (m, 2H, $NHCH_2C\underline{H}_2$), 1.52 and 1.42 [each s, 6H, C(C<u>H</u>$_3)_2$], 1.31 [m, 14H, C(C<u>H</u>$_3)_2$ and 4×CH_2], 0.86 (t, *J* = 6.6 Hz, 3H, $-CH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$): δ 173.2, (C=O); 109.6 and 108.9 [<u>C</u>$(CH_3)_2$]; 97.0 (C-1); 72.0 (C-2); 71.5 (C-3); 71.0 (C-4); 68.7(C-5); 56.0 (C-6); 47.5 (–NH<u>C</u>H_2); 36.0 (C-7); 29.8 29.6, 25.3, 24.7, and 23.0 (CH_2s); 27.7, 26.8 and 26.3 [<u>C</u>$(CH_3)_2$]; 14.5 (CH_3). Anal. calcd C, 59.85; H, 8.61; N, 3.32. Found: C, 60.11; H, 8.69; N, 3.27.

6,7-dideoxy-6-hexadecylamino-L-*threo*-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-octapyranuronic acid (39). It was obtained by reaction of **37** (1.2 g, 2.10 mmol) and lithium hydroxide (0.18 g, 4.20 mmol) as above. Colourless solid, Yield 88%; mp 83 °C; R_f 0.55 (chloform/methanol, 20:1); $[\alpha]_D^{20}$ −42.22 (*c* 0.225, chloroform); MS (FAB) = *m*/*z* 549 $(M+Li)^+$; IR (Neat) ν_{max} cm^{-1}: 3413, 2924, 1608, 1594. ^1H NMR (200 MHz, $CDCl_3$): δ 5.52 (d, *J* = 4.9 Hz, 1H, H-1), 4.62 (dd, *J* = 7.8 and 2.3 Hz, 1H, H-3), 4.32 (m, 2H, H-2 and H-4), 3.99 (d, *J* = 8.8 Hz, 1H, H-5), 3.41 (m, 1H, H-6), 2.93 (m, 3H, NHC<u>H</u>$_2$ and $H\text{-}7_A$), 2.74 (dd, *J* = 9.6 and 4.8 Hz, 1H, $H\text{-}7_B$), 1.67 (m, 2H, $NHCH_2C\underline{H}_2$), 1.54, 1.43, 1.35 and 1.42 [each s, 12H, 2×C(C<u>H</u>$_3)_2$], 1.25 (m, 26H, CH_2s), 0.88 (t, *J* = 6.6 Hz, 3H,-$CH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$): δ 173.2, (C=O); 110.1 and 109.8 [<u>C</u>$(CH_3)_2$]; 96.7 (C-1); 71.0 (C-2); 70.9 (C-3); 70.6 (C-4); 67.8 (C-5); 55.9 (C-6); 46.6 (–NH<u>C</u>H_2); 32.3 (C-7); 30.5, 29.8 29.6, 25.3, 24.7, and 23.0 (CH_2s); 26.2, 25.2 and 24.5 [<u>C</u>$(CH_3)_2$]; 14.5 (CH_3). Anal. calcd C, 65.79; H, 9.94; N, 2.56. Found: C, 65.92; H, 10.14; N, 2.49.

***N*-Hydroxy-[6,7-dideoxy-6-heptylamino-L-*threo*-1,2:3,4-di-*O*-isopropylidene-α-D-galacto-octapyran]-uronamide (40).** It was obtained by the reaction of compound **38** (0.9 g, 2.13 mmol) with hydroxylamine hydrochloride (0.32 g, 4.48 mmol) in presence of dicyclohexyl carbodiimide (0.45 g, 2.15 mmol) and triethyl amine (0.6 mL, 4.30 mmol) as above. Colourless oil, Yield 45%; R_f 0.42 (chloform/methanol, 20:1); $[\alpha]_D^{20}$ −48 (*c* 0.125, chloroform); MS (FAB) = *m*/*z* 431 $(M+H)^+$; IR (Neat) ν_{max} cm^{-1} 2931, 1660. ^1H NMR (200 MHz, $CDCl_3$): δ 5.52 (d, *J* = 5.2 Hz, 1H, H-1), 4.60 (dd, *J* = 5.4 and 2.4 Hz, 1H, H-3), 4.31 (m, 2H, H-2 and H-4), 3.75 (d, *J* = 7.6

Hz, 1H, H-5), 3.50 (m, 1H, H-6), 2.74 (m, 2H, NHC$\underline{H}_2$), 2.48 (m, 2H, H-7), 1.60 (m, 2H, $NHCH_2C\underline{H}_2$), 1.50 and 1.43 [$C(C\underline{H}_3)_2$], 1.32 [m, 14H, $C(C\underline{H}_3)_2$ and $4\times CH_2$], 0.86 (t, $J=6.6$ Hz, 3H, $-CH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$): δ 168.9, (C=O); 109.4 and 108.2 [$\underline{C}(CH_3)_2$]; 96.5 (C-1); 72.3 (C-2); 71.4 (C-3); 71.2 (C-4); 68.2(C-5); 56.6 (C-6); 47.2 ($-NH\underline{C}H_2$); 36.4 (C-7); 29.5 29.3, 25.3, 24.7, and 23.3 (CH_2s); 27.3, 26.3 and 26.2 [$\underline{C}(CH_3)_2$]; 14.4 (CH_3). Anal. calcd C, 58.58; H, 8.90; N, 6.51. Found: C, 58.69; H, 9.11; N, 6.47.

_N_-Hydroxy-[6,7-dideoxy-6-hexadecylamino-L-_threo_-1,2:3,4-di-_O_-isopropylidene-α-D-galacto-octapyran]uronamide (41). It was obtained by the reaction of compound **39** (1.0 g, 1.82 mmol) with hydroxylamine hydrochloride (0.27 g, 3.82 mmol) in presence of dicyclohexyl carbodiimide (0.38 g, 1.85 mmol) and triethyl amine (0.52 mL, 3.7 mmol) as above. Colourless oil, Yield 42%; R_f 0.60 (chloform/methanol, 20:1); $[\alpha]_D^{20}$ −40.0 (*c* 0.0875, chloroform); MS (FAB) = *m*/*z* 557 $(M+H)^+$; IR (Neat) ν_{max} cm^{-1}: 3425, 2928, 1656. ^1H NMR (200 MHz, $CDCl_3$): δ 5.52 (d, $J=4.9$ Hz, 1H, H-1), 4.60 (dd, $J=7.7$ and 2.6 Hz, 1H, H-3), 4.33 (m, 2H, H-2 and H-4), 3.89 (d, $J=8.3$ Hz, 1H, H-5), 3.31 (m, 1H, H-6), 2.65 (m, 4H, NHC$\underline{H}_2$ and H-7), 1.64 (m, 2H, $NHCH_2C\underline{H}_2$), 1.51, 1.42 and 1.32 [each s, 12H, $2\times C(C\underline{H}_3)_2$], 1.25 [m, 26H, $13\times CH_2$], 0.87 (t, $J=6.6$ Hz, 3H, $-CH_2C\underline{H}_3$); ^{13}C NMR ($CDCl_3$): δ 169.3, (C=O); 109.2 and 108.6 [$\underline{C}(CH_3)_2$]; 97.2 (C-1); 72.4 (C-2); 71.3(C-3); 71.2 (C-4); 68.4 (C-5); 56.3 (C-6); 47.2 ($-NH\underline{C}H_2$); 36.2 (C-7); 29.8 29.6, 25.3, 24.7, 23.8, 23.6, 23.5 and 23.0 (CH_2s); 27.4, 26.6 and 26.2 [$\underline{C}(CH_3)_2$]; 14.5 (CH_3). Anal. calcd C, 64.72; H, 10.14; N, 5.03. Found: C, 64.88; H, 10.23; N, 4.98.

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References and Notes

1. Weiss, U. *Nature* **2002**, *415*, 669.
2. (a) *World Health Report*; World Health Organization: Geneva, 2000. (b) Greenwood, B.; Mutabingwa, T. *Nature* **2002**, *415*, 760.
3. (a) Westling, J.; Yowell, C. A.; Majer, P.; Erickson, J. W.; Dame, J. B.; Dunn, B. M. *Exp. Parasitol.* **1999**, *87*, 185. (b) Haque, T. S.; Skillman, A. G.; Lee, C. E.; Habashita, H.; Gluzman, I. Y.; Ewing, J. T. A.; Goldberg, D. E.; Kuntz, I. D.; Ellman, J. A. *J. Med. Chem.* **1999**, *42*, 1428.
4. Olliaro, P.; Cattani, J.; Wirth, D. *JAMA* **1996**, *275*, 230.
5. Hoffman S.L.; Miller, L.H. ASM: Washington, 1996; p 1–13.
6. (a) Alonso, P. L.; Lindsay, S. W.; Armstrong, J. R. M.; Conteh, M.; Hill, A. G.; David, P. H. *Lancet* **1991**, *337*, 1499. (b) Collins, F. H.; Bensansky, N. J. *Science* **1994**, *264*, 1874.
7. Panisko, D. M.; Keystone, J. S. *Drugs* **1990**, *39*, 160.
8. (a) White, J. J. *N. Engl J Med.* **1996**, *335*, 800. (b) Luzzi, G. A.; Peto, T. E. A. *Drug Safety* **1993**, *8*, 295. (c) Keystone, J. S. *Drugs* **1990**, *39*, 337.
9. Meinnel, T. *Parasitol. Today* **2000**, *16*, 165.
10. Olliaro, P.; Worth, D. *J. Pharm. Pharmacol.* **1997**, *49*, 29.
11. Raventos-Suarez, C.; Pollack, S.; Nagel, R. L. *Am. J. Trop. Med. Hyg.* **1982**, *31*, 919.
12. Whitehead, S.; Peto, T. E. A. *Blood* **1978**, *76*, 1250.
13. Hershko, C.; Peto, T. E. A. *J. Exp. Med.* **1988**, *168*, 375.
14. Fritsch, G.; Treumer, J.; Sipra, D. T.; Jung, A. *Exp. Parasitol.* **1985**, *60*, 171.
15. (a) Lytton, S. D.; Mester B, DayanI.; Glickstein, H.; Libman, J.; Shanzer, A.; Cabantchik, Z. I. *Blood* **1993**, *81*, 214 and references cited therein. (b) Hamadi, A.; Ramindrsoa, F.; Sinou, V.; Chritopher, R.; Fusai, T.; Bras, J.; Le Parzy, D.; Kunesch, G.; Pradines, B. *Biochem. Pharmacol.* **2003**, *65*, 1351.
16. Gourdeuk, V. R.; Thuma, P. E.; Brittenham, G. M.; Blemba, G.; Zulu, S.; Simwanza, G.; Simwanza, G.; Kallnee, P.; M'Hango, A.; Parry, D.; Poltera, A. A.; Aikawa, M. *Am. J. Trop. Med. Hyg.* **1993**, *48*, 193.
17. Gourdeuk, V. R.; Thuma, P. E.; Brittenham, G. M.; McLaren, C.; Parry, D.; Backenstose, A. et al. *N. Engl. J. Med.* **1992**, *327*, 1473.
18. Apfel, C. M.; Locher, H.; Evers, S.; Takacs, B.; Hubschwerlen, C.; Pirson, W.; Page, M. G. P.; Keck, W. *Antimicrob. Agents Chemother.* **2001**, *45*, 1058.
19. Apfel, C. M.; Banner, D. W.; Bur, D.; Dietza, M.; Hirata, T.; Hubschwerlen, C.; Locher, H.; Page, M. G. P.; Pirson, W.; Rosse, G.; Specklin, J. L. *J. Med. Chem.* **2000**, *43*, 2324.
20. (a) Srivastava, A. K.; Tripathi, R. P.; Khan, A. R.; Bhaduri, A. P. *Helminthologia* **1995**, *32*, 25. (b) Tripathi, R. P.; Rastogi, S. K.; Kundu, B.; Saxena, J. K.; Reddy, V. J. M.; Srivastava, S.; Chandra, S.; Bhaduri, A. P. *Combin. Chem. Highthroughput Screen.* **2001**, *4*, 237. (c) Khan, A. R.; Tripathi, R. P.; Tiwari, V. K.; Mishra, R. C.; Reddy, V. J. M.; Saxena, J. K. *J. Carbohydrate Chem.* **2002**, *21*, 591. (d) Greenwich Pharma Syntex. *Drugs Future* **1989**, *14*, 369.
21. Perkins, M. E.; Rocco, L. J. *J. Immunol.* **1988**, *141*, 3190.
22. Khan, A. R.; Tripathi, R. P.; Bhaduri, A. P.; Sahai, R.; Puri, A.; Tripathi, L. M.; Srivastava, V. M. L. *Eur. J. Med. Chem.* **2001**, *36*, 435.
23. Gourdeuk, V. R.; Thuma, P. E.; Brittenham, G. M.; McLaren, C.; Parry, D.; Backenstose, A. *N. Engl. J. Med.* **1992**, *327*, 1473.
24. Tripathi, R. P.; Tripathi, R.; Tiwari, V. K.; Bala, L.; Sinha, S.; Srivastava, A. K.; Srivastava, R.; Srivastava, B. S. *Eur. J. Med. Chem.* **2002**, *37*, 773.
25. Yuan, Z.; Trias, J.; White, R. J. *Drug Discov. Today* **2001**, *6*, 954.
26. Olliaro, P.; Yuthavong, Y. *Pharmacol. Ther.* **1999**, *93*, 306.
27. (a) Gordon, P. Strategic Med. Res. Corp. US 3939 145, DE 240965. (b) Hiromoni, K.; Yamaguschi, T. Onto Tokio Eur. Pat. Appl. E. P. 650974, C. A. *123*, 31439f, 1995. (c) Hopkins, S. J. *Drugs Future* **1985**, *10*, 301, and references cited therein.
28. Rieckmann, K. H.; Campbell, G. H.; Saf, L. J.; Mrema, J. E. *Lancet* **1978**, 22.