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Synthesis and Bioevaluation of Glycosyl Ureas as α-Glucosidase Inhibitors and Their Effect on Mycobacterium†

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Abstract—Glycosyl amino esters (**2**–**13**) on reaction with different isocyanates resulted in quantitative conversion to glycosyl ureas (**14**–**32**). Few of the selected ureas (**15**–**20**, **22**–**28**, **30** and **32**) on cyclative amidation with DBU/TBAB/4 Å MS gave respective dihydropyrimidinones in fair to good yields (**33**–**47**). The compounds were screened for α-glucosidase inhibitory activity and two (**19** and **23**) of them showed strong inhibition against rat intestinal α-glucosidase. The compounds were also screened against *Mycobacterium aurum*, however, only one (**19**) of them exhibited marginal antitubercular activity. ©2000 Elsevier Science Ltd. All rights reserved.

Introduction

Type-2 noninsulin dependent diabetes mellitus (NIDDM),[1,2] a multifactorial disease accounts for 90–95% of all diabetes and affects about 150 million people globally. Among the non-infectious diseases (NID) it is a major killer disease and therefore been declared as priority disease by WHO. Although several drugs[3] for NIDDM with the known targets exist today, yet they are associated with many drawbacks such as liver toxicity,[4] adverse gastrointestinal symptoms[5] and raising the symptoms and risk factors of heart disease. Therapeutic approaches of herbal medicines also exist[6] but lack of well organized and rigorous clinical trial evidence to advocate their scientific merit warrants the introduction of new synthetic drugs against diabetes. In general, glycosidases are well known targets in the design and development of antidiabetic,[7,8] antiviral,[7,9] antibacterial[7,10] and anticancer[11] agents. In NIDDM, delaying glucose absorption after meals by inhibition of α-glucosidase is beneficial in therapy.[12,13] A pseudosachharide (acarbose) and an azasugar (miglitol) are being clinically used[14–16] for this purpose in the management of diabetes but these are associated with severe side effects including adverse gastrointestinal effects and abdominal discomfort. Spirosugars and glycosylamino acids both in acyclic and cyclic forms are known for their antidiabetic potential[17] affecting glycogen phosphorylase, a well known target in controlling the blood glucose level (Fig. 1).

Certain phenyl ureas exhibit antidiabetic[18] effect; however, they are associated with many drawbacks and it is envisaged that a hybrid of ureidyl pharmacophores and

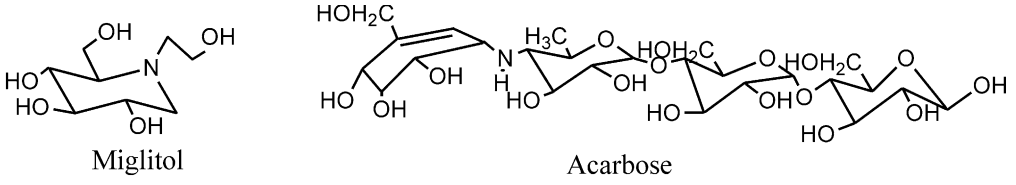

Figure. 1. α-Glucosidase inhibitors used as drugs.

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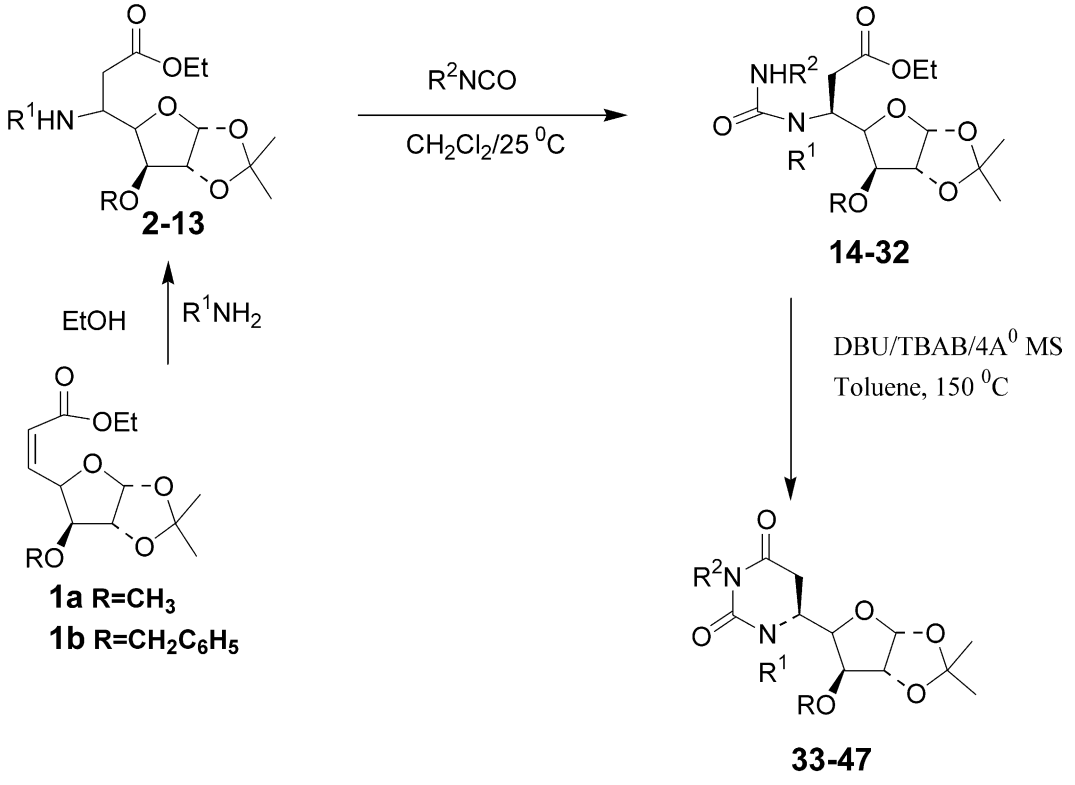
sugars, which are known for drug targeting[19] and better pharmacokinetics[20] may offer new leads against diabetes. Keeping in mind the above and in continuation of our work[21] on the development of chemotherapeutic agents from sugars, we have synthesized glycosyl ureas, both in flexible and rigid conformations, and evaluated for α-glucosidase inhibitory activity. Since we are also involved in a new drug development programme against tuberculosis, it was interesting for these compounds to be screened against *Mycobacterium aurum* because of the fact that glycosidase inhibitors are known for antitubercular activity.

Results and Discussion

Chemistry

The synthesis of compounds reported in the present study is given in Scheme 1. The starting glycosyl amino esters **2**–**13** are prepared by conjugate addition of different primary amines to the sugar derived olefinic esters **1a** and **1b**, by the method already reported by us.[21b–d] Compounds **2**–**13** on simple addition to different isocyanates including phenyl, benzyl, 3-acetyl phenyl, 4-fluorophenyl, 4-chlorophenyl isocyanates gave respective glycosyl ureides (**14**–**32**) in quantitative yields. Further compounds (**15**–**20**, **22**, **24**–**28**, **30** and **32**) on cyclative amidation with DBU/4 Å MS/Tetrabutyl ammonium bromide (TBAB) in refluxing toluene gave the corresponding glycosyl dihydropyrimidinones (**33**–**47**) in fair to good yields.

The structures of ureidyl derivatives are based on their spectroscopic data and analysis. Absorption around 1660 cm^{-1} in these compounds indicated the presence of CONH group. For SAR we were intended to synthesize the rigid analogues of those ureidyl derivatives, which have shown any inhibition against α-glucosidase. The structures of all the compounds are based on spectroscopic data and analysis. The stereochemistry at C-5 in ureidyl derivatives is always that of starting amino ester,[22] since the addition of isocyanates to the amines and the cyclative amidation does not involve C-5 chiral centre but the amino group attached to it, thus the configuration in the resulting compounds will not be changed at C-5 in glycosyl ureas and at C-6 in corresponding cyclic compounds. The configuration in glycosyl aminoesters have already established[21a–c,23] at C-5 as '*S*' and '*R*' in the major and minor isomers, respectively, and it was observed that in '*S*' isomer J_{4-5} (9.5 Hz) is always higher than J_{4-5} (7.2 Hz) of '*R*' isomer. Since amino esters (**3**, **5**–**8**, **10**–**13**) with '*S*' configuration have been used in isocyanates addition, hence, the configuration at C-5 in glycosyl ureas (**14**, **16**–**22**, **24**–**32**) and that of C-6 in corresponding cyclic analogues (**33**–**47**) would be '*S*' only. Further, trans relationship between H-4′ and H-6 protons in cyclic compounds was also evidenced by the ^{1}H NMR of the nucleosides (ca. compound **34**) the $J_{4',6}$ is 9.5 Hz in '*S*' isomer and 7.2 Hz in '*R*' isomer (not included in the Experimental). The amino esters (**3** and **9**) are a mixture of diastereoisomers and hence the resulting ureides (**15** and **23**) are a diastereoisomeric mixture. However, corresponding cyclised products (**33** and **40**) are isolated as pure isomers by column chromatography.



Scheme 1.

Biology

Out of several targets for NIDDM α-glucosidase inhibitors are gaining much importance as they are important both in breakdown of polysachharides into monosachharides and in the absorption of glucose in the enterocytes of the small intestine. Two of the well-known drugs acarbose and miglitol have undergone into extensive clinical trial. However, these and other known inhibitors of this enzyme have some demerits. Further furanose sugar derivatives are known to inhibit liver gluconeogenesis[24] and glycogenolysis and thereby show antidiabetic activity. Spirosugars having glycosyl amino acid and ureidyl components have shown inhibition of glycogen phosphorylase and many other glycosidases, it was contemplated that the designed compounds with ureidyl and amino acid components hybridized with sugars would offer a new class of antidiabetic agents. As evident from Table 1 compounds **16**, **17**, **19**, **23**, **24** and **30** show strong inhibition of α-glucosidase either at 250 or 100 μM concentrations. The standard drug acarbose inhibited this enzyme to the extent of 68% at 50 μM.

A close examination of structure activity relationship indicates that acyclic glycosyl ureas (**16**, **17**, **19**, **23**, **24** and **30**) with flexible conformation are stronger inhibitor of α-glucosidase than cyclic compounds (**34**, **35**, **37**, **40**, **41** and **46**) with rigid conformation. Three compounds **19**, **23** and **30** showed good enzyme inhibitory effect in dose dependent manner. IC_{50} values for compounds **23** and **30** were 140 and 40 μmol, respectively (Fig. 2).

N^1 unsubstituted compound **23** is equipotent to compounds with butyl or dodecyl substituents (**17** and **19**). However, N^3 phenyl with chloro or fluoro substituents results in better enzyme inhibition than unsubstituted or acetyl phenyls. N^1-cyclopropyl and N^1-*n*-butyl also showed inhibitory effect depending upon the substituents in the aromatic ring at N^3 and 3-*O*-substituent in sugar ring. Hence, no generalization can be made on the dependence of enzyme inhibitory activity at N^1,N^3 and 3-*O*-substituents of the sugar moiety and it is their combined effect, which results in good enzyme inhibition.

Out of curiosity that glycosidase inhibitors possess antibacterial activity, these compounds were screened against *M. arum*. However, only one (**19**) of them with dodecyl as N^1 and 4-chlorophenyl as N^3 substituent

Table 1. α-Glucosidase inhibitory activity of flexible and rigid analogues of Glycosyl Ureas

Compd	R	R_1	R_2	% Inhibition of α-glucosidase[a]
14	CH_3	H	4-Cl (phenyl)	47.0
15	CH_3	Cyclopropy	4-Cl (phenyl)	4.3
16	CH_3	Cyclopropyl	Benzyl	81.7
17	CH_3	*n*-Butyl	4-F(Phenyl)	85.6
18	CH_3	Heptyl	Benzyl	13.7
19	CH_3	Dodecyl	4-Cl (phenyl)	93.5
20	CH_3	Hexadecyl	Phenyl	34.8
21	CH_3	Hexadecyl	4-Cl (phenyl)	31.5
22	CH_3	Oleyl	Benzyl	16.4
23	CH_2Ph	H	4-Cl (phenyl)	97.2
24	CH_2Ph	Cyclopropyl	3-Acetyl(phenyl)	74.7
25	CH_2Ph	Cyclopropyl	4-Cl (phenyl)	15.3
26	CH_2Ph	Cyclopropyl	Benzyl	40.5
27	CH_2Ph	*n*-Butyl	4-F (phenyl)	49.3
28	CH_2Ph	Dodecyl	3-Acetyl(phenyl)	11.9
29	CH_2Ph	Dodecyl	4-F (phenyl	20.9
30	CH_2Ph	Dodecyl	4-Cl (phenyl	94.3
31	CH_2Ph	Dodecyl	Benzyl	10.8
32	CH_2Ph	Oleyl	Benzyl	12.3
33	CH_3	Cyclopropyl	4-Cl (phenyl)	11.7
34	CH_3	Cyclopropyl	Benzyl	35.2
35	CH_3	*n*-Butyl	4-F (phenyl)	13.5
36	CH_3	Heptyl	Benzyl	0.72
37	CH_3	Dodecyl	4-Cl (phenyl)	5.7
38	CH_3	Hexadecyl	Phenyl	5.0
39	CH_3	Oleyl	Benzyl	20.2
40	CH_2Ph	H	4-Cl(phenyl)	2.5
41	CH_2Ph	Cyclopropyl	3-Acetyl(phenyl)	47.0
42	CH_2Ph	Cyclopropyl	4-Cl(phenyl)	Nil
43	CH_2Ph	Cyclopropyl	Benzyl	61.8
44	CH_2Ph	*n*-Butyl	4-F (phenyl)	17.3
45	CH_2Ph	Dodecyl	3-Acetyl(phenyl)	28.5
46	CH_2Ph	Dodecyl	4-Cl(phenyl)	41.4
47	CH_2Ph	Oleyl	Benzyl	48.5
Acarbose				68[b]

[a]At 100 μM.
[b]At 50 μM.

exhibited mild antitubercular activity with MIC of 25 μg/mL only.

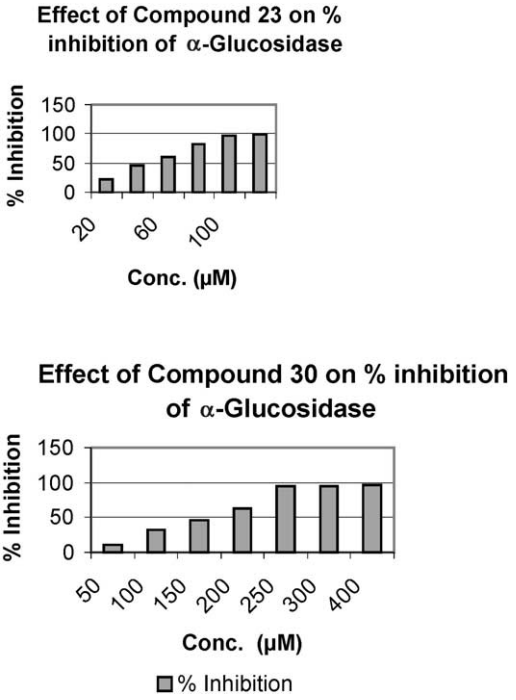


Figure 2.

In conclusion, we have synthesized glycosyl ureidyl uronates and C-nucleosides manner in an efficient manner. The compounds have been screened against rat intestinal α-glucosidase, showing good inhibition comparable to standard drug acarbose (Table 1).

Experimental

Chemistry

All glasswares were dried in an open flame before use in connection with an inert atmosphere. Solvents were evaporated under reduced pressure and evaporation was carried out at temperature $<50\,^{\circ}C$. Thin layer chromatography was performed using silica gel 60 F_{254} plates with detecting agents iodine vapours, spraying with 5% sulphuric acid in ethanol followed by heating at 100 °C, or by spraying with Dragendorf reagent. Silica gel (60–120 mesh) was used for column chromatography. Tetramethylsilane (0.0 ppm) was used as an internal standard in ^1H NMR and $CDCl_3$ (77.0 ppm) was used in ^{13}C NMR. The abbreviations used to indicate the peak multiplicity were; s, singlet; bs, broad singlet; d, doublet; dd, double doublet; t, triplet; q, quartet; m, multiplet; Hz, Hertz. FAB MS was recorded on Jeol (Japan)/SX-102. Infrared spectrum was taken with KBr on Perkin-Elmer RX-1. 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, methanol or ethyl acetate. Anhydrous sodium sulphate (Na_2SO_4) was used as drying agent for the organic phases containing the compounds. Unless otherwise stated, all materials were obtained from commercial suppliers Sigma Aldrich Company, Lancaster, SRL and Spectrochem Pvt. Ltd. and were used without further purification.

General procedure for the synthesis of compounds 14–46 and their physical data

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1, 2-*O*-isopropylidene-3-*O*-methyl-5-{N^3-(4-chlorophenyl)-1-ureidyl}-1,4-heptofuranos-5-yl]-uronoate (14). To a magnetically stirring solution of glycosyl amino ester **2** (1.0 g, 3.46 mmol) in anhydrous dichloromethane (10 mL), 4-chloro phenyl isocyanate (0.42 mL, 3.46 mmol) was added at 30 °C and stirring continued for 4 h. The solvent was evaporated under reduced pressure and the residue, thus obtained, was chromatographed over SiO_2 column using hexane/ethyl acetate (4:1) as eluent to give colourless foam. Yield 95%; $[\alpha]_D^{25}$ 26.66 (*c* 0.11, $CHCl_3$); MS FAB *m*/*z* = 443 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3359 (NH), 2937 (CH), 1726 (C=O), 1661 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.18 (m, 4H, Ar–H), 5.91 (d, *J* = 3.8 Hz, 1H, H-1), 5.60 (m, 1H, NH), 4.59 (d, *J* = 3.8 Hz, 1H, H-2), 4.40 (m, 2H, H-4 and H-5), 4.13 (q, 2H, OCH_2CH_3), 3.70 (d, *J* = 2.2 Hz, 1H, H-3), 3.38 (s, 3H, OCH_3), 2.69 (m, 2H, H-6), 1.78 (s, 1H, NH), 1.47 and 1.31 [each s, each 3H, $C(CH_3)_2$], 1.25 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 172.2 (OC=O); 155.7 (NC=O); 138.2 (Ar–C); 129.1, 127.12, 127.9, 121.3 (Ar–CH); 112.2 [$C(CH_3)_2$]; 105.1(C-1); 84.50 (C-2); 81.7 (C-4); 80.7 (C-3); 61.2 (OCH_2CH_3); 58.1(OCH_3), 47.3 (C-5); 37.3 (C-6); 27.1, 26.6, [$>C(CH_3)_2$]. Anal. calcd for $C_{20}H_{27}N_2O_7Cl$: C, 54.29; H, 6.11; N, 6.33; Found: C, 54.30; H, 5.88; N, 6.38.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*R*/*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-{N^1- cyclopropyl-N^3(4-chlorophenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (15). This was obtained by the reaction of compound **3** (1.50 g, 4.55 mmol) and 4-chlorophenyl isocyanate (0.55 mL, 4.55 mmol) as described above and isolated as colourless foam, Yield 92%. $[\alpha]_D^{25}$ −31.56 (*c* 0.47, $CHCl_3$); MS FAB *m*/*z* = 483 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3434 (NH), 2936 (CH), 1729 (C=O), 1673 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.37 (m, 4H, Ar–H); 5.88 (d, *J* = 3.78 Hz, 1H, H-1); 4.86 (dd, *J* = 9.1 Hz and 3.0 Hz, 1H, H-4), 4.59 (d, *J* = 3.8 Hz, 1H, H-2); 4.13 (m, 3H, H-5, OCH_2CH_3); 3.68 and 3.60 (each d, *J* = 3.0 Hz, each 1H, diastereomeric H-3); 3.38 and 3.34 (each s, 3H, diastereomeric OCH_3); 2.82 (m, 1H, diastereomeric H-6_A); 2.52 (m. 1H, cyclopropyl CH), 2.25 (dd, *J* = 15.6 Hz and 5.8 Hz, 1H, H-6_B), 1.50, 1.47 and 1.30 [each s, 3H, $C(CH_3)_2$], 1.22 (t, *J* = 7.2 Hz, 3H,OCH_2CH_3), 0.92 (m, 4H, cyclopropyl CH_2S).^{13}C NMR ($CDCl_3$): (some of the peaks were duplicated due to diastereomeric nature of the product) δ 173.1, 172.1 (OC=O); 156.9, 156.1 (NC=O); 138.1 (Ar–C); 129.1, 128.0, 127.9, 121.1 (Ar–CH); 112.2 [$>C(CH_3)_2$]; 105.1, 105.0 (C-1); 84.0, 83.9 (C-2); 81.7, 81.4 (C-4); 80.5, 79.5 (C-3); 61.0, 60.8 (OCH_2CH_3); 57.7, 57.4 (OCH_3); 36.2, 35.2 (C-6);

27.2,26.8 [$>C(CH_3)_2$]; 14.5 (OCH_2CH_3), 9.46, 9.13 (cyclopropyl CH_2). Anal. calcd for $C_{23}H_{31}N_2O_7Cl$: C, 57.26; H, 6.43; N, 5.81; Found: C, 57.27; H, 6.43; N, 5.13.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-(N^1-cyclopropyl-N^3-benzyl- 1-ureidyl)-1,4-heptofuranos-5-yl-]-uronoate (16). This was obtained by the reaction of compound **3** (1.0 g, 3.03 mmol) and benzyl isocyanate (0.37 mL, 3.03 mmol) as described above and isolated as colourless foam. Yield 96%; $[\alpha]_D^{25}$ −86.52 (*c* 0.39, $CHCl_3$); MS FAB *m*/*z* = 462 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3455 (NH), 2936 (CH), 1730 (C=O), 1653 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.37 (m, 4H, Ar–H); 5.88 (d, *J* = 3.78 Hz, 1H, H-1); 4.94 (m, 2H, H-4), 4.59 (d, *J* = 3.8 Hz, 1H, H-2); 4.42 (m, 2H, NCH_2Ph), 4.13 (m, 3H, H-5, OCH_2CH_3); 3.58 (d, *J* = 3.0 Hz, 1H, H-3); 3.38 (s, 3H, OCH_3); 2.72 (m. 2H, cyclopropyl CH and H-6_A), 2.38 (dd, *J* = 15.2 Hz and 4.2 Hz, 1H, H-6_B), 1.74 (bs, 1H, NH), 1.47 and 1.30 [each s, 3H, $C(CH_3)_2$], 1.22 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 0.92 (m, 4H, cyclopropyl CH_2s). ^{13}C NMR ($CDCl_3$): δ 172.3(OC=O); 159.1 (NC=O); 140.4 (Ar–C); 128.8, 127.6, 127.2 (Ar–CH); 112.1 [$>C(CH_3)_2$]; 105.0 (C-1); 84.1(C-2); 81.8 (C-4); 79.8 (C-3); 60.6 (OCH_2CH_3); 57.2 (OCH_3); 44.5 (NCH_2), 35.8 (C-6); 31.6 (cyclopropyl CH), 27.3, 26.9 [$>C(CH_3)_2$]; 14.5 (OCH_2CH_3), 10.1, 9.0 (cyclopropyl CH_2s).

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-{N^1- butyl-N^3-(4-fluorophenyl-1-ureidyl)-1,4-heptofuranos-5-yl-]-uronoate (17). This was obtained by the reaction of compound **4** (0 .96 g, 2.77 mmol) and 4-fluorophenyl isocyanate (0.03 mL, 2.77 mmol) as described above and isolated as colourless foam. Yield 92%; $[\alpha]_D^{25}$ −26.2 (*c* 0.08, CH_3OH); MS FAB *m*/*z* = 484 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3346 (NH), 2935 (CH), 1723 (C=O), 1661 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.28 and 6.98 (two d, *J* = 10.2 Hz and 8.7 Hz, 4H, Ar–H); 5.90 (d, *J* = 3.8 Hz, 1H, H-1); 4.62 (d, *J* = 3.8 Hz, 1H, H-2); 4.42 (m, 2H, NH and H-4); 4.17 (m, 3H, H-5, OCH_2CH_3); 3.61 (d, *J* = 3.0 Hz, 1H, H-3); 3.39 (s, 3H, OCH_3); 3.24 (dd, *J* = 6.6 Hz and 9.0 Hz, 1H, NCH_2); 2.8–1.5 (m, 4H, H-6 and NCH_2CH_2); 1.48 and 1.32 [each s, 3H, t, $C(CH_3)_2$], 1.26 (m, 4H, $NCH_2CH_2CH_2$, OCH_2CH_3), 0.92 [t, *J* = 6.5 Hz, 3H, $(CH_2)_3CH_3$].^{13}C NMR ($CDCl_3$): δ 172.1 (OC=O); 158.1 (NC=O); 138.1 (Ar–C); 129.2, 128.3, 128.9, 120.6 (Ar–CH); 112.1 [$>C(CH_3)_2$]; 105.2 (C-1); 82.5 (C-2); 82.0 (C-4); 81.9 (C-3); 61.1 (OCH_2CH_3); 58.0 (OCH_3), 38.8 (NCH_2); 32.4 (C-6); 27.2, 26.6 [$>C(CH_3)_2$]; 22.0 ($CH_2CH_2CH_3$); 14.5 (OCH_2CH_3, CH_2CH_3).

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-(N^1-heptyl-N^3-benzyl-1-ureidyl)-1,4-heptofuranos-5-yl]-uronoate (18). This was obtained by the reaction of compound 5 (0.77 g, 1.98 mmol) and benzyl isocyanate (0.24 mL, 1.98 mmol) as described above and isolated as colourless foam. Yield 91%. $[\alpha]_D^{25}$ −25 (*c* 0.15, CH_3OH); MS FAB *m*/*z* = 521 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3371 (NH), 2930 (CH), 1730 (C=O), 1639 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.29 (m, 5H, Ar–H), 5.85 (d, *J* = 3.8 Hz, 1H, H-1), 4.58 (d, *J* = 3.8 Hz, 1H, H-2), 4.38 (m, 4H, H-4, H-5 and NCH_2Ph), 4.10 (m, 2H, OCH_2CH_3), 3.59 (d, *J* = 3.0 Hz, 1H, H-3), 3.35 (s, 3H, OCH_3), 3.17 (m, 2H, NCH_2), 2.82 (m, 1H, H-6_A), 2.44 (dd, *J* = 4.0 Hz and 15.5 Hz, 1H, H-6_B), 1.61 (bs, 2H, NCH_2), 1.47 and 1.31 [each s, each 3H, $C(CH_3)_2$], 1.25–1.18 (m, 13H, OCH_2CH_3 and CH_2 s), 0.85 (t, *J* = 6.8 Hz, 3H, $CH_2CH_2CH_3$). ^{13}C NMR ($CDCl_3$): δ 171.7 (OC=O); 158.7 (NC=O); 140.3 (Ar–C); 128.8, 127.7, 127.2 (Ar–CH); 112.0 [$>C(CH_3)_2$]; 105.0 (C-1); 84.1(C-2); 81.5 (C-4); 79.8 (C-3); 72.1, 71.7 (NCH_2Ph), 61.1 (OCH_2CH_3); 57.6 (OCH_3), 44.9, 44.5 (NCH_2); 36.0 (C-6); 32.2 (CH_2S), 27.6, 26.7 [$C(CH_3)_2$]; 22.9 ($CH_2CH_2CH_3$); 14.5 (OCH_2 CH_3). Anal. calcd for $C_{28}H_{44}N_2O_7$: C, 64.6; H, 8.46; N, 5.38; Found: C, 64.64; H, 8.50; N, 5.42.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-{N^1-dodecyl-N^3-4-chlorophenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (19). This was obtained by the reaction of compound **6** (1.23 g, 0. 50 mmol) and 4-chloro phenyl isocyanate (0.06 mL, 0.50 mmol) as described above and isolated as colourless oil. Yield 90%. $[\alpha]_D^{25}$ −13 (*c* 0.10, CH_3OH); MS FAB *m*/*z* = 612 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3294 (NH), 2926 (CH), 1723 (C=O), 1632 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.28 and 7.19 (each d, *J* = 8.9 Hz and 9.0 Hz, 4H, Ar–H), 5.89 (d, *J* = 3.8 Hz, 1H, H-1), 4.61 (d, *J* = 3.8 Hz, 1H, H-2), 4.40 (m, 2H, H-4 and H-5), 4.18 (q, 2H, OCH_2CH_3), 3.60 (d, *J* = 3.0 Hz, 1H, H-3), 3.39 (s, 3H, OCH_3), 3.20 (m, 2H, NCH_2), 2.80 and 2.39 (each m, each 1H, H-6), 1.63 (m, 2H, NCH_2CH_2), 1.48 and 1.32 [each s, each 3H, $C(CH_3)_2$], 1.28 (m, 21 protons, OCH_2CH_3 and CH_2s), 0.87 (t, *J* = 6.6 Hz, 3H, $(CH_2)_{11}CH_3$). ^{13}C NMR ($CDCl_3$): δ 173.4 (OC=O); 156.6 (NC=O); 138.9 (Ar–C); 129.1, 127.2, 120.1 (Ar–CH); 112.1 [$>C(CH_3)_2$]; 105.2 (C-1); 84.1 (C-2); 81.6 (C-4); 79.5 (C-3), 61.5 (OCH_2CH_3),58.1 (OCH_3), 36.3 (C-6); 32.2, 30.1, 29.7, 27.8 (CH_2's), 27.1, 26.5 [$C(CH_3)_2$]; 22.9 ($CH_2CH_2CH_3$); 14.5 (OCH_2 CH_3 CH_2CH_3). Anal. calcd for $C_{32}H_{49}N_2O_7Cl$: C, 62.8; H, 7.36; N, 4.58; Found: C, 62.82; H, 7.39; N, 4.62.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-(N^1-hexadecyl-N^3-phenyl)-1-ureidyl)-1,4-heptofuranos-5-yl-]-uronoate (20). Obtained by the reaction of compound **7** (1.10 g, 2.14 mmol) and phenyl isocyanate (0.23 mL, 2.14 mmol) as described above and isolated as colourless oil. Yield 84%. $[\alpha]_D^{25}$ −26.4 (*c* 0.125, CH_3OH); MS FAB *m*/*z* = 633 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3352 (NH), 2926 (CH), 1724 (C=O), 1660 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.30 (m, 5H, Ar–H), 5.90 (d, *J* = 3.8 Hz, 1H, H-1), 4.62 (d, *J* = 3.8 Hz, 1H, H-2), 4.45 (m, 1H, H-4), 4.19 (q, 2H, OCH_2CH_3), 3.61 (d, *J* = 3.0 Hz, 1H, H-3), 3.39 (s, 3H, OCH_3), 3.23 (m, 2H, NCH_2), 2.81 (m, 1H, H-6_A), 2.44 (dd, *J* = 5.8 Hz and 17.4 Hz, 1H, H-6_B), 1.57 (m, 2H, NCH_2CH_2), 1.48 and 1.32 [each s, each 3H, $C(CH_3)_2$], 1.24 (m, 29H, CH_2's and OCH_2CH_3], 0.87 [t, *J* = 6.6 Hz, 3H, CH_3]. ^{13}C NMR ($CDCl_3$) δ 171.9 (OC=O); 158 (NC=O); 129.3, 129.0 122.7, 120.0, 119.6 (Ar–CH); 112.17 [$>C(CH_3)_2$]; 105.06 (C-1); 84.14 (C-2); 81.46

(C-4); 79.88 (C-3); 61.48 (NCH_2Ph and OCH_2CH_3); 57.72 (C-5); 35.71 (C-6), 32.31 (NCH_2CH_2), 30.08, 30.04, 29.85, 29.74, 29.58, 27.78 ($CH_{2'}s$); 27.22 and 26.68 [$>C(CH_3)_2$]; 23.0 (CH_2CH_3); 14.57 (OCH_2CH_3); 14.49 (CH_2CH_3).

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-{N^1-hexadecyl-N^3-(4-chlorophenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (21). This was obtained by the reaction of compound **7** (1.0 g, 1.94 mmol) and 4-chloro phenyl isocyanate (0.23 mL, 1.94 mmol) as described above and isolated as colourless foam. Yield 89%. $[\alpha]_D^{25}$ −26.4 (*c* 0.125, $CHCl_3$); MS FAB *m*/*z* = 667 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3339 (NH), 2927 (CH), 1718 (C=O), 1669 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 8.29 (s, 1H, NH), 7.36 and 7.26 (each d, *J* = 8.8 Hz, each 2H, Ar–H), 5.86 (d, *J* = 3.7 Hz, 1H, H-1), 4.55 (d, *J* = 3.7 Hz, 1H, H-2), 4.21 (m, 3H, H-4 and OCH_2CH_3), 3.67 (d, *J* = 3.0 Hz, 1H, H-3), 3.35 (m, 1H, H-5), 3.30 (s, 3H, OCH_3), 2.90–2.72 (m, 4H, H-6 and NCH_2), 1.59 (m, 1H, NH), 1.50 and 1.32 [each s, each 3H, $C(CH_3)_2$], 1.24 (m, 31H, CH_{2S} and OCH_2CH_3], 0.87 [t, *J* = 6.6 Hz, 3H, $(CH_2)_{14}CH_3$]. ^{13}C NMR ($CDCl_3$): δ 173.6 (OC=O); 156.7 (NC=O); 139.1 (Ar–C), 129.0, 127.0, 120.2 (Ar–CH); 112.2 [$>C(CH_3)_2$]; 105.3 (C-1); 84.0 (C-2); 81.5 (C-4); 79.9 (C-3); 61.6 (OCH_2CH_3), 58.0 (OCH_3); 53.4 (C-5), 36.2 (C-6), 32.3 (NCH_2), 30.0, 29.8, 29.7, 27.6 ($CH_{2'S}$), 27.1, 26.4 [$>C(CH_3)_2$]; 23.0 (CH_2CH_3), 14.5 (OCH_2CH_3). Anal. calcd for $C_{36}H_{59}N_2O_7Cl$: C, 64.86; H, 8.86; N, 4.20; Found: C, 64.25; H, 8.95; N, 4.88.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-(N^1-oleyl-N^3-benzyl)-1-ureidyl)-1,4-heptofuranos-5-yl-]-uronoate (22). This was obtained by the reaction of compound **8** (0.18 g, 0.33 mmol) and benzyl isocyanate (0.44 mL, 0.33 mmol) as described above and isolated as colourless oil. Yield 91%. $[\alpha]_D^{25}$ −25.6 (*c* 0.18, CH_3OH); MS FAB *m*/*z* = 674 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3404 (NH), 2930 (CH), 1723 (C=O), 1633 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.29 (m, 5H, Ar–H), 5.86 (d, *J* = 3.7 Hz, 1H, H-1), 5.35 (m, 2H, CH=CH), 4.59 (d, *J* = 3.8 Hz, 1H, H-2), 4.40 (m, 3H, H-4 and NCH_2Ph), 4.15 (m, 3H, H-5 and OCH_2CH_3), 3.59 (d, *J* = 2.7 Hz, 1H, H-3), 3.37 (s, 3H, OCH_3), 3.16 (m, 2H, NCH_2), 2.94 (m, 1H, H-6_A), 2.45 (dd, *J* = 4.03 Hz and 15.2HZ, 1H, H-6_B), 1.99 (m, 4H, $CH_2CH{=}CHCH_2$), 1.60 (bs, 2H, NCH_2CH_2), 1.47 and 1.31 [each s, each 3H, $C(CH_3)_2$], 1.22 (m, 25H, $CH_{2'}S$ and OCH_2CH_3), 0.87 (t, *J* = 6.48 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$) δ 170.4 (OC=O); 157.2 (NC=O); 139.0 (Ar–C), 130.3, 128.7, 127.7, 127.2 (Ar–C); 110.7 [$>C(CH_3)_2$]; 105.0 (C-1); 84.1 (C-2); 81.5 (C-4); 79.9 (C-3); 61.0 (NCH_2Ph), 57.6 (OCH_3); 44.9 (NCH_2), 36.0 (C-6), 32.9, 32.3, 30.1, 30.0, 29.9, 29.8, 29.7, 29.6, 27.6 ($CH_{2'}S$), 27.2, 26.7 [$>C(CH_3)_2$]; 23.0 (CH_2CH_3), 14.5, 14.4 (OCH_2CH_3, CH_2CH_3).

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*R*/*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N^3-(4-chloro phenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (23). This was obtained by the reaction of compound **9** (1.0 g, 2.73 mmol) and 4-chloro phenyl isocyanate (0.33 mL, 2.73 mmol) as described above and isolated as colourless foam. Yield 90%. $[\alpha]_D^{25}$ −25.45 (*c* 0.14, $CHCl_3$); MS FAB *m*/*z* = 519 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3361 (NH), 2935 (CH), 1725 (C=O), 1661 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.32–7.10 (m, 9H, Ar–H), 5.92 (d, *J* = 3.8 Hz, 1H, H-1), 5.55 (m, 1H, NH), 4.63 and 4.46 (each d, *J* = 12.0 Hz, each 1H, OCH_2Ph), 4.62 (d, *J* = 3.8 Hz, 1H, H-2), 4.30 (m, 1H, H-4), 4.12 (m, 3H, H-5 and OCH_2CH_3), 3.91 (d, *J* = 3.0 Hz, 1H, H-3), 2.72 (m, 1H, H-6_A), 2.56 (d, *J* = 5.48 Hz, 1H, H-6_B), 2.0 (s, 1H, NH), 1.46 and 1.30 [each s, each 3H, $C(CH_3)_2$], 1.25 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3). ^{13}C NMR ($CDCl_3$): (peaks were duplicated due to diastereoisomeric nature of product) δ 173.0, 172.1, 171.6 (OC=O); 155.5 (NC=O); 138.2, 138.1, 137.3, 137.1 (Ar–C); 129.2, 129.0, 128.9, 128.5, 128.4, 128.1, 127.8, 121.3, 121.2 (Ar–CH); 112.3, 112.2 [$C(CH_3)_2$]; 105.3, 105.1 (C-1); 82.4, 82.3 (C-2); 82.1, 819 (C-4); 80.8, 80.6 (C-3); 72.5, 72.2 (OCH_2Ph), 61.2, 61.1 (OCH_2CH_3); 47.2 (C-5); 37.3 (C-6); 27.1, 26.6, [$>C(CH_3)_2$], 14.5 (OCH_2CH_3). Anal. calcd for $C_{26}H_{31}N_2O_7Cl$: C, 60.23; H, 5.98; N, 5.40; Found: C, 58.89; H, 5.53; N, 5.40.

Ethyl-[(1*R*,2*R*,3*S*,4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N^1-cyclopropyl-N^3-(3-acetyl phenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (24). This was obtained by the reaction of compound 10 (0.50 g, 1.23 mmol) and 3-acetylphenyl isocyanate (0.16 mL, 1.23 mmol) as described above and isolated as colourless oil. Yield 90%; $[\alpha]_D^{25}$ −35.29 (*c* 0.1, $CHCl_3$); MS FAB *m*/*z* = 567 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3432 (NH), 1730 (C=O), 1676 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.86 (s, 1H, Ar–H), 7.77 and 7.58 (each d, *J* = 8.0 Hz, each 1H, Ar–H),7.56 (s, 1H, Ar–H), 7.34 (s, 5H, Ar–H); 5.91 (d, *J* = 3.7 Hz, 1H, H-1); 4.88 (m, 1H, H-4), 4.72 and 4.44 (each d, *J* = 11.8 Hz, each 1H, OCH_2Ph), 4.66 (d, *J* = 3.7 Hz, 1H, H-2); 4.20 (m, 1H, H-5), 4.06 (q, 2H, OCH_2CH_3); 3.81 (d, *J* = 3.0 Hz, 1H, H-3); 3.42 (m, 1H, cyclopropyl CH), 2.88 (m, 1H, H-6A), 2.58 (s,3H, $COCH_3$), 2.05 (dd, *J* = 2.8 Hz and 15.3 Hz,1H, H-6_B), 1.69 (s, 1H, NH), 1.48 and 1.31 [each s, 3H, $C(CH_3)_2$], 1.21 (t, *J* = 7.1 Hz, 3H, OCH_2CH_3), 1.11 (m, 4H, cyclopropyl CH_2s).^{13}C NMR ($CDCl_3$): δ 198.5 (CH_3C=O); 172.0 (OC=O), 156.3 (NC=O); 140.0, 138.0, 137.3 (Ar–C); 129.4, 128.9, 128.5, 128.4, 124.7, 123.0, 119.4 (Ar–CH); 112.2 [$>C(CH_3)_2$]; 105.1 (C-1); 82.4 (C-2); 81.3 (C-4); 79.4 (C-3); 71.9 (OCH_2Ph), 60.8 (OCH_2CH_3); 34.5 (C-6); 27.2, 26.8 [$>C(CH_3)_2$]; 14.5 (OCH_2CH_3), 9.96, 9.43 (cyclopropyl CH_2). Anal. calcd for $C_{31}H_{38}N_2O_8$: C, 65.72; H, 6.71; N, 4.95; Found: C, 64.62; H, 6.94; N, 5.74.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N^1-cyclopropyl-N^3-(4-chloro phenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (25). This was obtained by the reaction of compound **10** (0.80 g, 1.97 mmol) and 4-chloro phenyl isocyanate (0.24 mL, 1.97 mmol) as described above and isolated as colourless oil. Yield 85%; $[\alpha]_D^{25}$ −35.64 (*c* 0.41, $CHCl_3$); MS FAB *m*/*z* = 459 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3436 (NH), 2935 (CH), 1730 (C=O), 1672 (NC=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.42–7.19 (m, 9H, Ar–H); 5.90 (d, *J* = 3.78 Hz, 1H, H-1); 4.91 (m, 1H, H-4), 4.76

and 4.43 (each d, $J=11.8$ Hz, each 1H, OCH_2Ph), 4.65 (d, $J=3.8$ Hz, 1H, H-2); 4.20 (m, 1H, H-5), 4.08 (q, 2H, OCH_2CH$_3$); 3.80 (d, $J=3.0$ Hz,1H, H-3); 3.40 (m. 1H, H-6$_A$), 2.80 (m, 1H, cyclopropyl CH), 1.08 (dd, $J=3.2$ Hz and 15.6 Hz, 1H, H-6$_B$), 1.57 (each s, 1H, NH),1.46 and 1.30 [each s, 3H, C(CH_3)$_2$], 1.20 (t, $J=7.2$ Hz, 3H,OCH$_2$CH_3), 0.87 (m, 4H, cyclopropyl CH$_2$'s). ^{13}C NMR (CDCl$_3$): δ 172.0 (OC=O); 156.2 (NC=O); 138.1, 137.3 (Ar–C); 129.1, 128.9, 128.5, 128.4, 127.9, 121.2 (Ar–CH); 112.3, 109.9 [>C(CH$_3$)$_2$]; 105.1 (C-1); 82.4 (C-2); 81.4 (C-4); 79.4 (C-3); 71.9 (OCH$_2$Ph), 60.8 (OCH$_2$CH$_3$); 57.8 (C-5), 34.5 (C-6); 27.3, 26.9 [>C(CH$_3$)$_2$]; 14.5 (OCH$_2$CH$_3$), 9.96, 9.43 (cyclopropyl CH$_2$). Anal. calcd for $C_{31}H_{38}N_2O_8$: C, 62.36; H, 6.27; N, 5.02; Found: C, 62.95; H, 6.26; N, 4.98.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-(N^1-cyclopropyl-N^3-benzyl)-(1-ureidyl)-1,4-heptofuranos-5-yl-]-uronoate (26). This was obtained by the reaction of compound **10** (0.50 g, 1.23 mmol) and benzyl isocyanate (0.15 mL, 1.23 mmol) as described above and isolated as colourless oil. Yield 92%; $[\alpha]_D^{25}$ −42.86 (*c* 0.17, CHCl$_3$); MS FAB $m/z=539$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3459 (NH), 2935 (CH), 1729 (C=O), 1653 (*NC=O*); ^{1}H NMR (CDCl$_3$, 200 MHz) δ 7.34–7.21 (m, 10H, Ar–H); 5.91 (d, $J=3.7$ Hz, 1H, H-1); 4.93 (dd, $J=9.6$ Hz and 2.6 Hz, 1H, H-4), 4.68 and 4.47 (each d, $J=11.9$ Hz, each 1H, OCH_2Ph), 4.64 (d, $J=3.8$ Hz, 1H, H-2); 4 44 (m, 2H, NCH_2Ph), 4.13 (q, 2H, OCH_2CH$_3$); 4.04 (m, 1H, H-5), 3.79 (d, $J=3.0$ Hz, 1H, H-3); 3.34 (m, 1H, diastereomeric H-6$_A$), 2.68 (m. 1H, cyclopropyl CH), 2.08 (dd, $J=3.4$ Hz and 15.0 Hz, 1H, H-6$_B$), 1.60 (s, 1H, NH), 1.47 and 1.30 [each s, 3H, C(CH_3)$_2$], 1.25 (t, $J=7.2$ Hz, 3H,OCH$_2$CH_3), 0.88 (m, 4H, cyclopropyl CH$_2$s). ^{13}C NMR (CDCl$_3$): δ 173.0, 172.2 (OC=O); 159.3 (NC=O); 140.4 (Ar–C); 137.8, 137.5 (Ar–C), 128.9, 128.8, 128.7,128.4, 128.3, 127.7, 127.6, 127.2 (Ar–CH); 112.2 [>C(CH$_3$)$_2$]; 105.0 (C-1); 82.7 (C-2); 81.5 (C-4); 79.7 (C-3); 71.9 (OCH$_2$Ph), 57.8 (OCH$_2$CH$_3$); 44.8 (NCH$_2$Ph), 36.6, 35.1 (C-6); 27.3, 26.9 [>C(CH$_3$)$_2$]; 14.6 (OCH$_2$CH$_3$), 10.0, 9.3 (cyclopropyl CH$_2$). Anal. calcd for $C_{30}H_{38}N_2O_8$: C, 66.91; H, 7.06; N, 5.20; Found: C, 66.96; H, 6.98; N, 5.14.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N^1-butyl-N^3-(4-fluorophenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (27). This was obtained by the reaction of compound **11** (2.26 g, 5.36 mmol) and 4-fluoro phenyl isocyanate (1.61 mL, 5.36 mmol) as described above and isolated as colourless foam. Yield 85%; $[\alpha]_D^{25}$ −15.3 (*c* 0.13, CH$_3$OH); MS FAB $m/z=559$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3301 (NH), 2929 (CH), 1713 (C=O), 1668 (*NC=O*); ^{1}H NMR (CDCl$_3$, 200 MHz) δ 8.20 (s, 1H, NH), 7.19 (m, 7H, Ar–H); 6.85 (d, $J=8.7$ Hz, 2H, Ar–H), 5.90 (d, $J=3.5$ Hz, 1H, H-1); 4.56 (m, 4H, H-2, H-4, OCH$_2$Ph), 4.18 (m, 3H, H-5, OCH_2CH$_3$); 3.95 (d, $J=3.5$ Hz, 1H, H-3); 3.48 (m, 2H, NCH$_2$), 2.97 (m, 3H, NCH_2CH_2 and H-6$_A$); 2.73 (m, 1H, H-6$_B$), 1.62 (s, 1H, NH), 1.49 and 1.32 [each s, 3H, C(CH_3)$_2$], 1.22 (m, 5H, NCH$_2$CH$_2$CH_2, OCH$_2$CH_3), 0.89 [t, $J=7.1$ Hz, 3H, (CH$_2$)$_3$CH_3].^{13}C NMR (CDCl$_3$): δ 171.5 (OC=O); 160.8, 156.6, 156.0 (NC=O); 135.9 (Ar–C); 128.6, 128.3, 128.2, 121.3, 121. 115.3, 114.9 (Ar–CH); 111.8 [>C(CH$_3$)$_2$]; 105.1 (C-1); 81.7 (C-2); 80.7 (C-4); 79.2 (C-3); 71.4 (OCH$_2$Ph); 61.0 (OCH$_2$CH$_3$); 34.6 (NCH$_2$); 31.2 (C-6); 27.1, 26.6 [>C(CH$_3$)$_2$]; 20.5 (CH$_2$CH$_3$), 14.1,13.8 (OCH$_2$CH$_3$, CH$_2$CH$_3$). Anal. calcd for $C_{30}H_{39}N_2O_7F$: C, 64.5; H, 6.98; N, 5.0; Found: C, 64.48; H, 7.0; N, 4.96.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N^1-dodecyl-N^3-(3-acetylphenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (28). This was obtained by the reaction of compound **12** (1.0 g, 1.87 mmol) and 3-acetylphenyl isocyanate (0.25 mL, 1.87 mmol) as described above and isolated as colourless oil. Yield 90%; $[\alpha]_D^{25}$ −13 (*c* 0.12, CHCl$_3$); MS FAB $m/z=695$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3355 (NH), 2927 (CH), 1726 (C=O), 1671 (*NC=O*); ^{1}H NMR (CDCl$_3$, 200 MHz) δ 7.87 (s, 1H, Ar–H$_A$), 7.55 (m, 3H, Ar–H$_B$, –H$_C$ and –H$_D$),); 7.35 (m, 5H, Ar–H), 5. 94 (d, $J=3.6$ Hz, 1H, H-1); 4.74 and 4.41 (each d, $J=11.9$ Hz, each 1H, OCH$_2$Ph), 4.68 (d, $J=3.6$ Hz, 1H, H-2), 4.58 (m, 1H, H-4), 4.35 (m, 1H, H-5), 4.15 (q, 2H, OCH_2CH$_3$), 3.79 (d, $J=3.0$ Hz, 1H, H-3); 3.23 (m, 2H, NCH$_2$), 2.58 (s, 3H, COCH$_3$); 2.08–1.89 (m, 2H, H-6), 1.62 (m, 2H, NCH$_2$CH_2), 1.48 and 1.32 [each s, 3H, C(CH_3)$_2$], 1.24 (m, 21H, CH$_{2S}$ and OCH$_2$CH_3), 0.87 [t, $J=6.8$ Hz, 3H, CH$_2$CH_3]. ^{13}C NMR (CDCl$_3$): δ 198.7 (COCH$_3$), 171.8 (OC=O); 156.8, (NC=O); 140.8, 138.0, 136.9 Ar–C); 129.2, 129.0, 128.7 (Ar–CH); 112.2 [>C(CH$_3$)$_2$]; 105.1 (C-1); 82.1 (C-2); 80.9 (C-4); 79.5 (C-3); 71.8 (OCH$_2$Ph); 61.5 (OCH$_2$CH$_3$); 34.8 (C-6); 32.9 (NCH$_2$); 30.0, 29.8, 29.7, 29.4, 27.7 (CH$_2$s), 27.2 (COCH$_3$), 27.1, 26.6 [>C(CH$_3$)$_2$]; 23.0 (CH$_2$CH$_3$), 14.5, 14.4 (OCH$_2$CH$_3$, CH$_2$CH$_3$). Anal. calcd for $C_{40}H_{58}N_2O_8$: C, 69.16; H, 8.35; N, 4.03; Found: C, 69.19; H, 8.37; N, 4.07.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N^1-dodecyl-N^3-(4-fluorophenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (29). This was obtained by the reaction of compound **12** (0.60 g, 1.12 mmol) and 4-fluoro phenyl isocyanate (0.12 mL, 1.12 mmol) as described above and isolated as colourless foam. Yield 95%; $[\alpha]_D^{25}$ −20.9 (*c* 0.13, CH$_3$OH); MS FAB $m/z=671$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3387 (NH), 2925 (CH), 1732 (C=O), 1647 (*NC=O*); ^{1}H NMR (CDCl$_3$, 200 MHz) δ 7.28 (m, 5H, Ar–H); 6.94 (m, 4H, Ar–H), 5.93 (d, $J=3.5$ Hz, 1H, H-1); 4.73 and 4.40 (each d, $J=11.9$ Hz, each 1H, OCH$_2$Ph), 4.66 (d, $J=3.5$ Hz, 1H, H-2), 4.57 (m, 1H, H-4), 4.31 (m, 1H, H-5), 4.14 (q, 2H, OCH_2CH$_3$), 3.79 (d, $J=2.5$ Hz, 1H, H-3); 3.15 (m, 2H, NCH$_2$), 2.63 (m, 1H, H-6$_A$); 2.04 (dd, $J=2.1$ Hz, 16.4 Hz, 1H, H-6$_B$), 1.57 (m, 2H, NCH$_2$CH_2), 1.47 and 1.32 [each s, 3H, C(CH_3)$_2$], 1.25 (m, 21H, CH$_{2S}$ and OCH$_2$CH_3), 0.85 [t, $J=6.8$ Hz, 3H, CH$_2$CH_3]. ^{13}C NMR (CDCl$_3$): δ 171.9 (OC=O); 156.6, (NC=O); 139.0, 136.9 (Ar–C); 129.0, 128.9, 128.7, 128.6, 127.2, 121.0 (Ar–CH); 112.2 [>C(CH$_3$)$_2$]; 105.1 (C-1); 82.1 (C-2); 81.1(C-4); 79.5 (C-3); 71.8 (OCH$_2$Ph); 61.5 (OCH$_2$CH$_3$); 34.9 (NCH$_2$); 32.3 (C-6); 30.0, 29.8, 29.7, 29.5, 27.7 (CH$_2$s), 27.1, 26.6 [>C(CH$_3$)$_2$]; 23.0 (CH$_2$CH$_3$), 14.5, 14.4 (OCH$_2$CH$_3$, CH$_2$CH$_3$).

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N^1-dodecyl-N^3-(4-chlorophenyl)-1-ureidyl}-1,4-heptofuranos-5-yl-]-uronoate (30). This was obtained by the reaction of compound **12** (1.20 g, 2.25 mmol) and 4-chloro phenyl isocyanate (0.27 mL, 2.25 mmol) as described above and isolated as colourless oil. Yield 90%; $[\alpha]_D^{25}$ −44 (*c* 0.11, $CHCl_3$); MS FAB *m*/*z* = 688 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3378 (NH), 2929 (CH), 1718 (C=O), 1631 (*NC=O*); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.25 (m, 9H, Ar–H); 5.92 (d, *J* = 3.7 Hz, 1H, H-1); 4.73 and 4.41 (each d, *J* = 11.9 Hz, each 1H, OCH_2Ph), 4.66 (d, *J* = 3.7 Hz, 1H, H-2), 4,52 (m, 1H, H-4), 4.25 (m, 1H, H-5), 4.13(q, 2H, OCH_2CH_3), 3.79 (d, *J* = 2. 5 Hz, 1H, H-3); 3.17 (m, 2H, NCH_2), 2.64 (m, 1H, H-6$_A$); 2.05 (dd, *J* = 2.1 Hz, 16.0 Hz, 1H, H-6$_B$), 1.69 (m, 2H, NCH_2CH_2), 1.47 and 1.32 [each s, 3H, $C(CH_3)_2$], 1.23–1.16 (m, 21H, CH_{2S} and OCH_2CH_3), 0.87 [t, *J* = 6.0 Hz, 3H,CH_2CH_3]. ^{13}C NMR ($CDCl_3$): δ 171.9 (OC=O); 156.6, (NC=O); 139.0, 136.9 (Ar–C); 129.0, 128.9, 128.7, 128.6, 127.2, 121.0 (Ar–CH); 112.2 [$>C(CH_3)_2$]; 105.1 (C-1); 82.1 (C-2); 81.1 (C-4); 79.5 (C-3); 71.8 (OCH_2Ph); 61.5 (OCH_2CH_3); 34.9 (NCH_2); 32.3 (C-6); 30.0, 29.8, 29.7, 29.5, 27.7 (CH_{2S}), 27.1, 26.6 [$>C(CH_3)_2$]; 23.0 (CH_2CH_3), 14.5, 14.4 (OCH_2CH_3, CH_2CH_3). Anal. calcd for $C_{38}H_{55}N_2O_7Cl$: C, 66.47; H, 8.01; N, 4.08; Found: C, 66.5; H, 8.03; N, 4.10.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5, 6-dideoxy-1,2-*O*-isopropylidene-5-(N^1-dodecyl-N^3-benzyl-1-ureidyl)-1,4-heptofuranos-5-yl-]-uronoate (31). This was obtained by the reaction of compound **12** (0.80 g, 1.50 mmol) and benzyl isocyanate (0.18 mL, 1.50 mmol) as described above and isolated as colourless oil. Yield 88%; $[\alpha]_D^{25}$ −20.0 (*c* 0.5, CH_3OH); MS FAB *m*/*z* = 667 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3387(NH), 2925 (CH), 1732 (C=O), 1647 (*NC=O*); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.25 (m, 9H, Ar–H); 5.88 (d, *J* = 3.7 Hz, 1H, H-1); 5.03 (bs, 1H, NH), 4.69 and 4.42 (each d, *J* = 11.8 Hz, each 1H, OCH_2Ph), 4.63 (d, *J* = 3.7 Hz, 1H, H-2), 4.42 (m, 4H, H-4, H-5, NCH_2 Ph); 4.06 (q, 2H, OCH_2CH_3), 3.78 (d, *J* = 3.7 Hz, 1H, H-3); 3.14 (m, 2H, NCH_2), 2.80 (m, 1H, H-6$_A$); 2.07 (dd, *J* = 2.0 Hz and 17.4 Hz, 1H, H-6$_B$), 1.84 (m, 2H, NCH_2CH_2), 1.47 and 1.31 [each s, 3H, $C(CH_3)_2$], 1.25–1.16 (m, 21H,CH_{2S} and OCH_2CH_3), 0.87 [t, *J* = 6.0 Hz, 3H,CH_2CH_3].^{13}C NMR ($CDCl_3$): δ 171.6 (OC=O); 156.8, (NC=O); 140.5, 137.2 (Ar–C); 128.9, 1287, 128.5, 128.4, 127.6, 127.1 (Ar–CH); 112.0 [$>C(CH_3)_2$]; 105.0 (C-1); 82.2 (C-2); 81.4 (C-4); 79.7 (C-3); 71.8 (OCH_2Ph); 61.0 (OCH_2CH_3); 44.9 (NCH_2Ph), 35.3 (NCH_2); 32.3 (C-6); 30.0, 29.8, 29.7, 29.6, 27.7 (CH_{2S}), 27.2, 26.8 [$>C(CH_3)_2$]; 23.0 (CH_2CH_3), 14.55, 14.50 (OCH_2CH_3, CH_2CH_3). Anal. calcd for $C_{39}H_{58}N_2O_7$: C, 70.20; H, 8.70; N, 4.20; Found: C, 70.24; H, 8.73; N, 4.22.

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-(N^1-oleyl-N^3-benzyl-1-ureidyl)-1,4-heptofuranos-5-yl-]-uronoate (32). This was obtained by the reaction of **13** (0.42 g, 0.68 mmol) and benzyl isocyanate (0.08 mL, 0.68 mmol) as described above and isolated as colourless oil. Yield 91%; $[\alpha]_D^{25}$ −4.0 (*c* 0.15, CH_3OH); MS FAB *m*/*z* = 749 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3390 (NH), 2926 (CH), 1732 (C=O), 1647 (*NC=O*); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.3 (m, 10H, Ar–H$_A$), 5..88 (d, *J* = 3.8 Hz, 1H, H-1); 5.34 (m, 2H, CH=CH), 5.1 (bs, 1H, NH), 4.69 and 4.42 (each d, *J* = 11.8 Hz, each 1H, OCH_2Ph), 4.65 (d, *J* = 3.8 Hz, 1H, H-2), 4.38 (m, 4H, NCH_2Ph, H-4 and H-5), 4.04 (q, 2H, OCH_2CH_3), 3.78 (d, *J* = 2.0 Hz, 1H, H-3); 3.14 (m, 2H, NCH_2), 2.76 (m, 1H, H-6$_A$), 2.10 (m, 5H, H-6$_B$, and allylic CH_2); 1.60 (m, 2H, NCH_2CH_2), 1.47 and 1.31 [each s, 3H, $C(CH_3)_2$], 1.25 (m, 21H, CH_{2S} and OCH_2CH_3)), 0.87 [t, *J* = 5.9 Hz, 3H,CH_2CH_3].^{13}C NMR ($CDCl_3$): δ 171.6 (OC=O); 158.8 (NC=O); 140.5, 137.2 (Ar–C); 130.7, 130.3, 130.2, 128.9, 128.7, 128.5, 128.4, 127.6, 127.1 (Ar–CH); 112.1 [$>C(CH_3)_2$]; 105.0 (C-1); 82.2 (C-2); 81.4 (C-4); 79.7 (C-3); 71.8 (OCH_2Ph); 61.0 (OCH_2CH_3); 44.9 (NCH_2Ph), 35.3 (NCH_2), 30.1 (C-6); 30.0, 29.9, 29.8, 29.6, 27.7, 27.6 (CH_{2S}), 27.2, 26.8 [$>C(CH_3)_2$]; 23.0 (CH_2CH_3), 14.5, 14.4 (OCH_2CH_3, CH_2CH_3). Anal. calcd for $C_{35}H_{68}N_2O_7$: C, 72.10; H, 9.0; N, 3.7; Found: C, 72.13; H, 9.04; N, 3.74.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-cyclopropyl-N^3-(4-chlorophenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-methyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2, 4-dione (33). A solution of above compound **15** (1.0 g, 2.07 mmol), 4 Å MS (0.020 g), TBAB (0.010 g) and DBU (0.31 mL, 2.07 mmol) in anhydrous toluene (15 mL) was refluxed for 2.5 h. Solvent evaporated and the residue obtained was chromatographed over SiO_2 column using a gradient of hexane–ethylacetate (3:1), to give the compound as colourless oil. Yield 88%. $[\alpha]_D^{25}$ −86.6 (*c* 0.45, $CHCl_3$), MS FAB *m*/*z* = 437 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3380 (NH), 3010, 2935 (CH), 1670 (*NC=O*); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.40 and 7.05 (each d, each *J* = 8.8 Hz, each 2H, Ar–H), 5.94 (d, *J* = 3.8 Hz, 1H, H-1′), 4.62 (d, *J* = 3.8 Hz, 1H, H-2′), 4.40 (dd, *J* = 9.6 Hz and 3.0 Hz, 1H, H-4′), 3.96 (m, 1H, H-6), 3.72 (d, *J* = 3.0 Hz, 1H, H-3′), 3.42 (s, 3H, OCH_3), 3.01 (m, 1H, CH-cyclopropyl ring), 2.92 (d, *J* = 8.5 Hz, 1H, H-5$_A$), 2.63 (d, *J* = 17.8 Hz, 1H, H-5$_B$), 1.47 and 1.33 [each s, each 3H, $C(CH_3)_2$)]; 0.93–0.79 (m, 4H, CH_2- cyclopropyl ring). ^{13}C NMR ($CDCl_3$): δ 168.7 and 153.7 (C=O), 134.6, 134.2, 130.4 and 129.6 (Ar–C), 112.3 [*C* $(CH_3)_2$)], 105.6 (C-1′), 84.3 (C-2′), 81.0 (C-4′), 80.7 (C-3′), 57.8 (OCH_3), 53.2 (C-6), 35.4 (C-5), 32.1 (CH-cyclopropyl ring), 27.2 and 26.53 [$C(CH_3)_2$)], 10.1 and 7.0 (CH_2-cyclopropyl ring). Anal. calcd for $C_{23}H_{31}N_2O_7Cl$: C, 57.27; H, 6.43; N, 5.81; Found: C, 57.27; H, 6.63; N, 5.72.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-cyclopropyl-N^3-benzyl-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-methyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (34). This was obtained by refluxing a solution of **16** (1.2 g, 2.60 mmol), 4 Å MS (0.02 g), TBAB (0.012 g) and DBU (0.40 mL, 2.60 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield 75%. $[\alpha]_D^{25}$ −78.15 (*c* 0.39, $CHCl_3$), MS FAB *m*/*z* = 417$(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3375 (NH), 3019, 2935 (CH), 1671 (*NC=O*); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.40–7.25 (m, 5H, Ar–H), 5.87 (d, *J* = 3.8 Hz, 1H, H-1′), 4.53 (d, *J* = 3.8 Hz, 1H, H-2′), 4.09 (dd, *J* = 9.6 Hz and 3.0 Hz, 1H, H-4′), 3.82 (m, 1H, H-6), 3.62 (d,

$J = 3.0$ Hz, 1H, H-3′), 3.36 (s, 3H, OCH_3), 2.97 (m, 1H, CH-cyclopropyl ring), 2.74 (d, $J = 8.4$ Hz, 1H, H-5_A), 2.49 (d, $J = 17.8$ Hz, 1H, H-5_B), 1.25 and 1.21 [each s, each 3H, $C(CH_3)_2$)]; 0.93–0.50 (m, 4H, CH_2-cyclopropyl ring). ^{13}C NMR ($CDCl_3$): δ 168.6 and 154.0 (C=O), 138.2, 129.2, 128.8, 127.7 (Ar–C), 112.2 [$C(CH_3)_2$)], 105.5 (C-1′), 84.3 (C-2′), 81.0 (C-4′), 80.8 (C-3′), 57.7 (OCH_3), 53.1 (C-6), 43.9 (NCH_2), 34.8 (C-5), 31.9 (CH-cyclopropyl ring), 27.1 and 26.5 [$C(CH_3)_2$)], 10.3 and 6.9 (CH_2-cyclopropyl ring). Anal. calcd for $C_{21}H_{25}N_2O_6Cl$: C, 57.80; H, 5.73; N, 6.42; Found: C, 56.96; H, 5.68; N, 6.35.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-butyl-N^3-(4-fluorophenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-methyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (35). This was obtained by refluxing a solution of **17** (1.0 g, 2.07 mmol), 4 Å MS (0.020 g), TBAB (0.008 g) and DBU (0.32 mL, 2.07 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield 85%. $[\alpha]_D^{25}$ −13.0 (*c* 0.09, CH_3OH); MS FAB $m/z = 437$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3400 (NH), 2938 (CH), 1721 (C=O), 1677 (*NC=O*); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.10 (m, 4H, Ar–H); 5.93 (d, $J = 3.8$ Hz, 1H, H-1′); 4.61 (d, $J = 3.8$ Hz, 1H, H-2′), 4.36 (dd, $J = 3.1$ Hz and 9.4 Hz, 1H, H-4′), 3.97 (m, 1H, NCH_A), 3.85 (m, 1H, H-6), 3.71 (d, $J = 3.2$ Hz, 1H, H-3′), 3.42 (s, 3H, OCH_3), 3.22 (m, 1H, NCH_B), 2.8 (m, 1H, H-5_A), 2.68 (m, 1H, H-5_B), 1.64 (m, 4H, CH_2CH_2), 1.32 and 1.28 [each s, 3H, $C(CH_3)_2$], 0.93 (t, 3H, CH_2CH_3).^{13}C NMR ($CDCl_3$): δ 172.0 (CO), 166.1 (NC=O); 131.6, 130.8 (Ar–C); 116.5, 116.0, 115.5 (Ar–CH); 112.2, 111.8 [$>C(CH_3)_2$]; 105.4, 105.0 (C-1′); 84.0 (C-2′); 82.5 (C-4′); 81.5 (C-3′); 60.7, 59.3 (NCH_2), 54.8 (OCH_3),49.2, 49.1, 47.5,38.3, 37.6, 36.7, 35.1 (CH_2CH_2), 32.6, 30.5 (C-6); 29.3, 27.1 [$>C(CH_3)_2$]; 14.5, 14.2 (CH_2CH_3).

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-heptyl-N^3-benzyl-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-methyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (36). This was obtained by refluxing a solution of **18** (0.50 g, 0.96 mmol), 4 Å MS (0.020 g), TBAB (0.012 g) and DBU (0.14 mL, 0.96 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield 85%. $[\alpha]_D^{25}$ −27.6 (*c* 0.13,CH_3OH); MS FAB $m/z = 437$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3436 (NH), 2930 (CH), 1711 (C=O), 1667 (*NC=O*); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.28 (m, 5H, Ar–H); 5.84 (d, $J = 3.8$ Hz, 1H, H-1′); 4.97 (s, 2H, NCH_2Ph), 4.53 (d, $J = 3.8$ Hz, 1H, H-2′), 4.00 (dd, $J = 3.2$ Hz and 7.8 Hz, 1H, H-4′), 3.93 (m, 1H, NCH_A), 3.72 (m, 1H, H-6), 3.64 (d, $J = 3.2$ Hz, 1H, H-3′), 3.37 (s, 3H, OCH_3), 3.09 (m, 1H, NCH_B), 2.84 (dd, $J = 6.7$ Hz and 16.8 Hz,1H, H-5_A), 2.50 (d, $J = 16.8$ Hz, 1H, H-5_B), 1.55 (m, 4H, $NCH_2CH_2CH_2$), 1.25 [m, 12H, $C(CH_3)_2$ and CH_2′s], 0.87 (t, $J = 5.0$ Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.6 (C=O), 152.6 (NC=O); 138.2, 128.8, 127.6 (Ar–C); 112.3 [$>C(CH_3)_2$]; 105.4 (C-1′); 84.1 (C-2′); 81.1 (C-4′); 80.9 (C-3′); 57.8 (OCH_3), 51.1 (C-6), 49.4 (NCH_2Ph), 43.9 (NCH_2CH_2), 34.6 (C-5), 32.1, 29.4, 28.6, 27.2 (CH_2S), 27.0, 26.5 [$>C(CH_3)_2$], 22.9 (CH_2CH_3), 14.4(CH_2CH_3)].

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-dodecyl-N^3-(4-chlorophenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-methyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (37). This was obtained by refluxing a solution of **19** (0.40 g, 0.65 mmol), 4 Å MS (0.020 g), TBAB (0.009 g) and DBU (0.10 mL, 0.65 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield 80%. $[\alpha]_D^{25}$ −15 (*c* 0.08, CH_3OH), MS FAB $m/z = 565$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3389 (NH), 2927 (CH), 1722 (C=O);1682 (*NC=O*N). ^1H NMR ($CDCl_3$, 200 MHz) δ 7.36 (m, 5H, Ar–H), 5.92 (d, $J = 3.8$ Hz, 1H, H-1′), 4.62 (d, $J = 3.8$ Hz, 1H, H-2′); 4.40 (dd, $J = 9.5$ Hz and 3.2 Hz, 1H, H-4′); 3.9 (m, 2H, NCH_A, H-6), 3.72 (d, $J = 3.0$ Hz, H-3′); 3.42 (OCH_3), 3.20 (m, 1H, NCH_B), 3.13 (dd, $J = 16.6$ Hz and 6.6 Hz, 1H, H-5_A), 2.35 (d, $J = 16.6$ Hz, 1H, H-5_B), 1.63 (m, 4H, $NCH_2CH_2CH_2$), 1.47 and 1.32 [each s, each 3H, $C(CH_3)_2$)]; 1.25 (s, 16H, CH_2S),0.92 (t, $J = 6.4$ Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.6 (C=O), 152.1 (*NC=O*N), 134.3, 130.4, 129.6 (Ar–C), 112.3 [$C(CH_3)_2$)], 105.4 (C-1′), 84.1 (C-2′), 81.7 (C-4′), 80.9 (C-3′), 57.8 (OCH_3), 51.3 (C-6), 51.3 (C-6), 49.6 (NCH_2), 35.1 (C-5), 32.3, 30.0, 29.7, 28.5, (CH_2′S), 27.1, 26.5 [$C(CH_3)_2$], 23.0 (CH_2CH_3), 14.4 (CH_3). Anal. calcd for $C_{30}H_{45}N_2O_6Cl$: C, 67.3; H, 7.6; N, 4.3; Found: C, 67.74; H, 7.10; N, 4.36.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-hexadecyl-N^3-phenyl-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-methyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (38). This was obtained by refluxing a solution of **20** (0.85 g, 1.34 mmol), 4 Å MS (0.022 g), TBAB (0.008 g) and DBU (0.20 mL, 1.34 mmol) in dry toluene (15 mL) as described above and isolated as colourless oil. Yield 82%. $[\alpha]_D^{25}$ −29.7 (*c* 0.17, $CHCl_3$), MS FAB $m/z = 587$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3433 (NH), 2926, 2854 (CH), 1723, 1683 (C=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.39–7.15 (m, 5H, Ar–H), 5.92 (d, $J = 3.8$ Hz, 1H, H-1′), 4.60 (d, $J = 3.8$ Hz, 1H, H-2′); 4.41 (dd, $J = 9.4$ Hz and 3.0 Hz, 1H, H-4′); 3.97 (m, 1H, NCH_A), 3.85 (m, 1H, H-6), 3.7 (d, $J = 3.0$ Hz, 1H, H-3′); 3.42 (s, 3H, OCH_3), 3.18 (m, 1H, NCH_B); 3.06 (dd, $J = 16.7$ and 6.5 Hz, 1H, H-5_A), 2.64 (d, $J = 17.0$ Hz, 1H, H-5_B);1.60 (m, 2H, NCH_2CH_2), 1.48 and 1.32 [each s, each 3H, $C(CH_3)_2$)]; 1.25 (m, 26H, CH_2′S), 0.87 (t, $J = 6.7$ Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.7, 152.8 (C=O), 135.9, 129.5, 129.0, 128.6 (Ar–C), 112.3 [$C(CH_3)_2$)], 105.5 (C-1′), 84.2 (C-2′), 81.1 (C-4′), 80.9 (C-3′), 57.8 (OCH_3), 51.5 (C-6), 49.5 (NCH_2), 35.2 (C-5), 32.3, 30.1, 29.9, 29.7, 28.5, 27.9, 23.1 (CH_2′S), 27.2 and 26.3 [$C(CH_3)_2$)], 14.5 (CH_3). Anal. calcd for $C_{34}H_{54}N_2O_6$: C, 69.6; H, 9.2; N, 4.7; Found: C, 69.58; H, 9.24; N, 4.73.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-oleyl-N^3-benzyl-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-methyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (39). This was obtained by refluxing a solution of 22 (0.95 g, 1.41 mmol), 4 Å MS (0.020 g), TBAB (0.012 g) and DBU (0.21 mL, 1.41 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield 88%; $[\alpha]_D^{25}$ −28.8 (*c* 0.12, $CHCl_3$), MS FAB $m/z = 627$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3372 (NH), 2928 (CH), 1710 (C=O);1669 (*NC=O*N). ^1H NMR ($CDCl_3$, 200 MHz) δ 7.34 (m, 5H, Ar–H), 5.84 (d, $J = 3.7$ Hz, 1H,

H-1′), 5.36 (m, 2H, CH=CH), 4.97 (s, 2H, NCH_2Ph), 4.53 (d, $J=3.7$ Hz, 1H, H-2′), 4.03 (m, 2H, H-4′, NCH_A), 3.80 (m, 1H, H-6); 3.64 (d, $J=3.1$ Hz, H-3′); 3.37 (s, 3H, OCH_3), 3.1 (m, 1H, NCH_B), 2.90 (dd, $J=6.0$ Hz and 17.0 Hz, 1H, H-5_A), 2.55 (d, $J=17.0$ Hz, 1H, H-5_B), 2.02 (m, 4H, allylic CH_{2S}), 1.65 (m, 4H, CH_2′s), 1.41 [m, 26, $C(CH_3)_2$ and CH_{2S}], 0.88 (t, $J=7.0$ Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.6 (C=O), 152.6 (*NC*=*O*N), 138.2, 130.3, 128.9, 128.8, 127.6 (Ar–C), 112.3 [*C*$(CH_3)_2$)], 105.4 (C-1′), 84, 1 (C-2′), 81.1 (C-4′), 80.9 (C-3′), 71.9 (OCH_2Ph), 59.5 (NCH_2Ph), 57.7 (OCH_3), 51.9 (C-6), 49.4 (NCH_2), 34.6 (C-5), 32.9, 30.8, 30.0, 29.8, 29.7, 29.6, 28.6, 27.6, 27.2 (CH_2S), 27.1, 26.5 [C(*C*$H_3)_2$)], 23.0 (*C*H_2CH_3), 14.0 (CH_2*C*H_3). Anal. calcd for $C_{37}H_{58}N_2O_6$: C, 70.9; H, 9.2; N, 4.4; Found: C, 70.5; H, 9.23; N, 4.43.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^3-benzyl-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (40). This was obtained by refluxing a solution of **23** (0.80 g, 1.69 mmol), 4 Å MS (0.012 g), TBAB (0.008 g) and DBU (0.26 mL, 1.69 mmol) in anhydrous toluene (15 mL) as described above. On column chromatography of the reaction mixture only the main isomer could be isolated as white solid. Yield 80%. $[\alpha]_D^{25}$ −29.7 (*c* 0.08, $CHCl_3$); MS FAB $m/z=473$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3371 (NH), 2926 (CH), 1712 (C=O); 1660 (*NC*=*O*N); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.45–7.22 (m, 7H, Ar–H), 7.14 (d, $J=8.4$ Hz, 2H, Ar–H), 6.06 (bs, 1H, NH), 6.01 (d, $J=3.6$ Hz, 1H, H-1′), 4.79 and 4.50 (each d, $J=11.7$ Hz, each 1H, OCH_2Ph), 4.72 (d, $J=3.6$ Hz, 1H, H-2′), 4.15 (m, 1H, H-4′), 4.03 (d, $J=3.0$ Hz, 1H, H-3′), 3.98 (m, 1H, H-6), 2.73 (m, 2H, H-5), 1.53 and 1.38 [each s, each 3H, C(C*H*$_3)_2$], ^{13}C NMR ($CDCl_3$): δ 168.8 and 156.1 (C=O); 138.0, 137.5, 130.7, 129.7, 128.5, 121.1 (Ar–C), 111.6 [*C*$(CH_3)_2$]; 105.6 (C-1′); 82.4 (C-2′), 81.6 (C-4′), 80.6 (C-3′), 72.4 (OCH_2Ph), 46.7 (C-6); 34.6 (C-5); 27.2, 26.6, [>C(*C*$H_3)_2$].

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-cyclopropyl-N^3-(3′-acetylphenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin 2,4-dione (41). This was obtained by refluxing a solution of **24** (0.60 g, 1.06 mmol), 4 Å MS (0.022 g), TBAB (0.012 g) and DBU (0.16 mL, 1.06 mmol) in anhydrous toluene (10 mL) as described above and isolated as colourless oil. Yield 85%. $[\alpha]_D^{25}$ −16.0 (*c* 0.44, $CHCl_3$), MS FAB $m/z=521$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3370 (NH), 3012, 2928 (CH), 1710, 1668 (CO); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.95 (d, $J=7.8$ Hz, 1H, Ar–H), 7.67 (s, 1H, Ar–H), 7.52–7.29 (m, 7H, Ar–H), 5.98 (d, $J=3.8$ Hz, 1H, H-1′), 4.73 and 4.49 (each d, $J=11.6$ Hz, each 1H, OCH_2Ph), 4.67 (d, $J=3.8$ Hz, 1H, H-2′), 4.03 (dd, $J=9.6$ Hz and 3.1 Hz, 1H, H-4′), 4.03 (m, 1H, H-6), 3.95 (d, $J=3.1$ Hz, 1H, H-3′), 2.82 (m, 1H, CH-cyclopropyl ring), 2.76 (dd, $J=8.4$ Hz and 17.1 Hz, 1H, H-5_A), 2.55 (s, 3H, CH_3), 2.35 (d, $J=17.1$ Hz, 1H, H-5_B), 1.33 and 1.22 [each s, each 3H, $C(CH_3)_2$)]; 0.97–0.78 (m, 4H, CH_2-cyclopropyl ring). ^{13}C NMR ($CDCl_3$): δ 197.1, 168.6 and 153.8 (C=O), 138.5, 136.9, 136.2, 133.8, 129.7, 129.3, 128.9, 128.5 (Ar–C), 112.4 [*C*$(CH_3)_2$)], 105.6 (C-1′), 81.9 (C-2′), 81.8 (C-4′), 80.8 (C-3′), 72.3 (OCH_2Ph), 53.1 (C-6), 35.2 (C-5), 32.2 (CH-cyclopropyl ring), 27.2, 26.9 and 26.6 [OC*C*H_3 and C(*C*$H_3)_2$)], 10.0 and 7.1 (CH_2-cyclopropyl ring). Anal. calcd for $C_{29}H_{32}N_2O_7$: C, 68.55; H, 6.91; N, 4.26; Found: C, 67.95; H, 6.51; N, 4.10.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-cyclopropyl-N^3-(4-chlorophenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin- 2, 4-dione (42). This was obtained by refluxing a solution of **25** (0.75 g, 1.34 mmol), 4 Å MS (0.025 g), TBAB (0.006 g) and DBU (0.20 mL, 1.34 mmol) in anhydrous toluene (10 mL) as described above and isolated as colourless oil. Yield 82%. $[\alpha]_D^{25}$ −32.48 (*c* 0.42, $CHCl_3$), MS FAB $m/z=513$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3397 (NH), 3016, 2932 (CH), 1696 (C=O); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.39–7.29 (m, 7H, Ar–H), 7.03 (d, $J=8.5$ Hz, 2H, Ar–H), 5.97 (d, $J=3.8$ Hz, 1H, H-1′), 4.73 and 4.44 (each d, $J=11.7$ Hz, each 1H, OCH_2Ph), 4.67 (d, $J=3.8$ Hz, 1H, H-2′), 4.40 (dd, $J=9.6$ Hz and 3.1 Hz, 1H, H-4′), 4.0 (m, 1H, H-6), 3.92 (d, $J=3.1$ Hz, 1H, H-3′), 3.02 (m, 1H, CH-cyclopropyl ring), 2.80 (dd, $J=17.1$ Hz and 6.4 Hz, 1H, H-5_A), 2.34 (d, $J=17.1$ Hz, 1H, H-5_B), 1.46 and 1.32 [each s, each 3H, C(C*H*$_3)_2$)]; 0.94–0.77 (m, 4H, CH_2-cyclopropyl ring). ^{13}C NMR ($CDCl_3$): δ 168.5 and 153.7 (C=O), 136.9, 134.5, 130.4, 129.6, 129.2, 128.9, 128.5 (Ar–C), 112.3 [*C*$(CH_3)_2$)], 105.6 (C-1′), 81.9 (C-2′), 81.8 (C-4′), 80.8 (C-3′), 72.3 (OCH_2Ph), 53.0 (C-6), 35.2 (C-5), 32.2 (CH-cyclopropyl ring), 27.2 and 26.6 [C(*C*$H_3)_2$)], 10.3 and 7.0 (CH_2-cyclopropyl ring). Anal. calcd for $C_{27}H_{29}N_2O_6Cl$: C, 63.28; H, 5.66; N, 5.47; Found: C, 64.02; H, 5.69; N, 5.24.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-cyclopropyl-N^3-benzyl-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (43). This was obtained by refluxing a solution of **26** (0.85 g, 1.57 mmol), 4 Å MS (0.024 g), TBAB (0.012 g) and DBU (0.24 mL, 1.57 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield $[\alpha]_D^{25}$-36.50 (*c* 0.18, $CHCl_3$), MS FAB $m/z=493$ $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3375 (NH), 3015, 2932 (CH), 1668 (*NC*=*O*); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.38–7.18 (m, 10H, Ar–H), 5.88 (d, $J=3.8$ Hz, 1H, H-1′), 4.93 (s, 2H, NC*H*$_2$Ph), 4.68 and 4.41 (each d, $J=11.6$ Hz, each 1H, OC*H*$_2$Ph), 4.56 (d, $J=3.8$ Hz, 1H, H-2′), 4.03 (dd, $J=9.6$ Hz and 3.1 Hz, 1H, H-4′), 3.87 (m, 1H, H-6), 3.84 (d, $J=3.1$ Hz, 1H, H-3′), 2.98 (m, 1H, C*H*-cyclopropyl ring), 2.61 (d, $J=8.4$ Hz, 1H, H-5_A), 2.24 (d, $J=17.1$ Hz, 1H, H-5_B), 1.25 and 1.20 [each s, each 3H, C(C*H*$_3)_2$)]; 0.98–0.75 (m, 4H, C*H*$_2$-cyclopropyl ring). ^{13}C NMR ($CDCl_3$): δ 168.5 and 154.0 (C=O), 138.1, 137.0, 129.1, 128.8, 128.4, 127.6 (Ar–C), 112.3 [*C*$(CH_3)_2$], 105.5 (C-1′), 82.1 (C-2′), 81.8 (C-4′), 80.9 (C-3′), 72.3 (O*C*H_2Ph), 52.9 (C-6), 43.9 (N*C*H_2), 34.7 (C-5), 32.1 (*C*H-cyclopropyl ring), 27.1 and 26.6 [C(*C*$H_3)_2$)], 10.3 and 7.0 (CH_2-cyclopropyl ring). Anal. calcd for $C_{28}H_{32}N_2O_6$: C, 68.29; H, 6.50; N, 5.69; Found: C, 67.69; H, 6.39; N, 5.37.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-butyl-N^3-(4-fluorophenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2, 4-dione (44). This was obtained by refluxing a solution of **27** (1.0 g, 1.79

mmol), 4 Å MS (0.020 g), TBAB (0.014 g) and DBU (0.27 mL, 1.79 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield $[\alpha]_D^{25}$ −18 (*c* 0.12 $CHCl_3$), MS FAB *m*/*z* = 513 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3501 (NH), 2935 (CH), 1738 (C=O); ^1H NMR ($CDCl_3$, 200 MHz) δ 7.35 (m, 5H, Ar–H), 7.06 (m, 4H, Ar–H), 5.95 (d, *J* = 3.7 Hz, 1H, H-1′), 4.73 and 4.45 (each d, *J* = 11.6 Hz, each 1H, OCH_2Ph), 4.65 (d, *J* = 3.7 Hz, 1H, H-2′); 4.38 (dd, *J* = 9.7 Hz and 3.1 Hz, 1H, H-4′); 3.95 (d, *J* = 3.2 Hz, H-3′); 3.86 (m, 2H, NCH_2), 2.90 (dd, *J* = 16.8 Hz and 6.5 Hz, 1H, H-5_A), 2.38 (d, *J* = 16.8 Hz, 1H, H-5_B), 1.66 (m, 4H, $NCH_2CH_2CH_2$), 1.47 and 1.32 [each s, each 3H, $C(CH_3)_2$)]; 0.87 (t, *J* = 6.4 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.7 (C=O), 152 (N*C*=ON), 136.9, 131.6 (Ar=C), 130.8, 130.6, 129.2, 128.9, 128.5, 116.6, 116.1 (Ar–CH), 112.4 [$C(CH_3)_2$)], 105.5 (C-1′), 81.8 (C-2′), 81.7 (C-4′), 81.1 (C-3′), 72.3 (OCH_2Ph), 51.3 (C-6), 49.4 (NCH_2), 34.9 (C-5), 30.6 (NCH_2CH_2), 27.1, 26.5 [$C(CH_3)_2$)], 20.4 (CH_2CH_3),14.2 (CH_3).

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-dodecyl-N^3-(3-acetylphenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (45). This was obtained by refluxing a solution of **28** (0.80 g, 1.15 mmol), 4 Å MS (0.022 g), TBAB (0.014 g) and DBU (0.17 mL, 1.15 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield $[\alpha]_D^{25}$ −15 (*c* 0.08, CH_3OH), MS FAB *m*/*z* = 648 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3372 (NH), 1710 (C=O); 1669 (*NC*=*O*N). ^1H NMR ($CDCl_3$, 200 MHz) δ 7.68–7.26 (m, 5H, Ar–H), 5.96 (d, *J* = 3.7 Hz, 1H, H-1′), 4.74 and 4.45 (each d, *J* = 11.6 Hz, each 1H, OCH_2Ph); 4.66 (d, *J* = 3.7 Hz, 1H, H-2′), 4.40 (m, 1H, H-4′), 3.97 (d, *J* = 3.1 Hz, H-3′); 3.88 (m, 1H, H-6); 3.31–3.20 (m, 5H, $COCH_3$ and NCH_2), 2.88 (dd, *J* = 16.8 Hz and 3.2 Hz, 1H, H-5_A), 2.58 (m, 2H, NCH_2CH_2), 2.35(d, *J* = 16.6 Hz, 1H, H-5_B), 1.64 (m, 4H, CH_2S), 1.48 and 1.33 [each s, each 3H, $C(CH_3)_2$], 1.25 (s, 14H, $CH_{2'S}$), 0.87 (t, *J* = 7.0 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 199.2, 197.1 ($COCH_3$), 168.6 (C=O), 152.5 (*NC*=*O*N), 138.4, 136.8, 136.3, 133.8, 130.3, 129.6, 129.1, 128.9, 128.7, 127.5 (Ar–C), 112.4 [$C(CH_3)_2$)], 105.5 (C- 1′), 81.8 (C-2′), 81.7 (C-4′), 81.0 (C-3′), 72.3 (OCH_2Ph), 54.3 (OCH_3), 51.3 (C-6), 49.7 (NCH_2), 34.9 (C-5), 32.3, 30.0, 29.9, 29.7, 28.5 ($CH_{2'}S$), 27.2, 26.9, 26.5 [$COCH_3$ and $C(CH_3)_2$)], 23.0 (CH_2CH_3), 14.5 (CH_2CH_3). Anal. calcd for $C_{38}H_{52}N_2O_7$: C, 70.3; H, 8.02; N, 4.32; Found: C, 70.34; H, 8.05; N, 4.36.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-dodecyl-N^3-(4-chlorophenyl)-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (46). This was obtained by refluxing a solution of **30** (0.80 g, 1.16 mmol), 4 Å MS (0.020 g), TBAB (0.012 g) and DBU (0.18 mL, 1.16 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield 78%. $[\alpha]_D^{25}$ −35.80 (*c* 0.16, $CHCl_3$), MS FAB *m*/*z* = 641$(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3404 (NH), 2930 (CH), 1723 (C=O), 1681 (*NC*=*O*). ^1H NMR ($CDCl_3$, 200 MHz) δ 7.39–7.30 (m, 7H, Ar–H); 7.11 (d, *J* = 9 Hz, 2H, Ar–H); 5.93 (d, *J* = 3.9 Hz, 1H, H-1′); 4.76 and 4.44 (each d, *J* = 11.7 Hz, each 1H, OCH_2Ph); 4.66 (d, *J* = 3.9 Hz, 1H, H-2′); 4.32 (dd, *J* = 10.8 and 3.3 Hz, 1H, H-4′); 3.99 (d, *J* = 3.3 Hz, 1H, H-3′); 3.84 (m, 1H, NCH_A); 3.76 (dd, *J* = 10.8 and 5.4 Hz, 1H, H-6); 3.25 (d, *J* = 17.0 Hz, 1H, H-5_A); 2.89 (dd, *J* = 17.0 and 6.6 Hz, 1H, H-5_B); 2.78 (m, 1H, NCH_B); 1.47 and 1.33 [each s, each 3H, $C(CH_3)_2$)]; 1.25 (m, 10H, $CH_{2'}S$); 0.88 (t, *J* = 6.0 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.8, 152.8 (C=O), 136.7, 124.0, 130.2, 129.1, 128.7, 128.3, 127.7 (Ar–C), 112.0 [$C(CH_3)_2$)], 105.0 (C-1′), 82.4 (C-2′), 81.5 (C-4′), 79.8 (C-3′), 71.7 (OCH_2Ph), 50.4 (C-6), 47.3 (NCH_2), 34.2 (C-5), 31.9, 29.6, 29.5, 29.3, 28.11,25.4, 22.6 ($CH_{2'}S$), 27.7 and 26.2 [$C(CH_3)_2$)], 14.1(CH_3). Anal. calcd for $C_{36}H_{49}N_2O_6Cl$: C, 67.3; H, 7.64; N, 4.36; Found: C, 67.35; H, 7.62; N, 4.4.40.

(1′*R*,2′*R*,3′*S*,4′*R*,6*S*)-N^1-oleyl-N^3-benzyl-5,6-dihydro-(1′,2′-*O*-isopropyledene-3′-*O*-benzyl-1′,2′,3′,4′-tetrahydrofuranos-4′-yl)-pyrimidin-2,4-dione (47). This was obtained by refluxing a solution of **32** (0.50 g, 0.66 mmol), 4 Å MS (0.022 g), TBAB (0.010 g) and DBU (0.10 mL, 0.66 mmol) in anhydrous toluene (15 mL) as described above and isolated as colourless oil. Yield 70%. $[\alpha]_D^{25}$ −28 (*c* 0.15, CH_3OH), MS FAB *m*/*z* = 703 $(M+H)^+$; IR (neat): ν_{max} cm^{-1} 3371 (NH), 2926 (CH), 1711 (C=O);1669 (*NC*=*O*N). ^1H NMR ($CDCl_3$, 200 MHz) δ 7.31 (m, 10H, Ar–H), 5.87 (d, *J* = 3.7 Hz, 1H, H-1′), 5.34 (m, 2H, CH=CH), 4.95 (s, 2H, NCH_2Ph), 4.64 and 4.45 (each d, *J* = 11.6 Hz, each 1H, OCH_2Ph); 4.56 (d, *J* = 3.7 Hz, 1H, H-2′), 4.25 (dd, *J* = 9.2 Hz and 2.9 Hz, 1H, H-4′), 3.86 (d, *J* = 3.1 Hz, H-3′); 3.78 (m, 1H, H-6); 3.48 (m, 1H, NCH_A), 3.33 (m, 2H, H-5), 3.20 (m, 1H, NCH_B), 2.01 (m, 4H, allylic CH_{2S}), 1.66 (m, 4H, $CH_{2'S}$), 1.48 [m, 26, $C(CH_3)_2$ and CH_{2S}], 0.87 (t, *J* = 7.0 Hz, 3H, CH_2CH_3). ^{13}C NMR ($CDCl_3$): δ 168.5 (C=O), 152.6 (*NC*=*O*N), 138.2, 136.9, 130.3, 129.1, 128.8, 128.4, 127.5 (Ar–C), 112.3 [$C(CH_3)_2$)], 105.4 (C-1′), 81.8 (C-2′), 81.6 (C-4′), 81.1 (C-3′), 72.3 (OCH_2Ph), 59.5 (NCH_2Ph), 51.0 (C-6), 43.9 (C-5), 34.4, 30.0, 29.6, 28., 27.5, 27.2 (CH_{2S}), 27.0, 26.5 [$C(CH_3)_2$)], 23.0, 20.1(CH_2CH_3), 14.5 (CH_3).

Biology

Preparation of α-Glucosidase from rat intestinal mucosa. α-Glucosidase was prepared according to a slight modification of the procedure reported earlier.[25,26] Intestine of male albino rats (CF strain average body weight 200 ± 20 g) were excised, opened and the mucosa was collected and pooled. A 10% homogenate was prepared in 150 mM KCl using Potter Elvejhem glass homogeniser fitted with Teflon pestle. The homogenate was centrifuged at 1000*g* for 15 min and the supernatant was decanted and stored at 4 °C. The supernatant was dialyzed at 4 °C against 50 mM Tris–HCl buffer pH 7.0 with two to three changes of buffer. The dialyzed supernatant was saturated with ammonium sulphate to a final concentration of 30%. The sample was kept at 4 °C overnight and then centrifuged to collect the precipitate and the supernatant separately. The 30% ammonium sulphate saturated supernatant was further saturated to 60% with ammonium sulphate. Again the precipitate and supernatant were separated by centrifugation. Finally, the 60% ammonium sulphate

Table 2. α-Glucosidase activity

Source	Protein (mg/kg)	Specific activity	Fold purification
Crude extract	1.50±0.03	288.94±10.1	1.0
1000*g* supernatant	0.74±0.09	483.81±89.7	1.68
0–30% dialyzed precipitate	0.18±0.02	552.69±38.9	1.91
30–60% dialyzed precipitate	0.31±0.03	723.36±94.2	2.50
60–100% dialyzed precipitate	0.60±0.06	1370.91±53.8	4.74
100% saturated supernatant precipitate	0.12±0.02	Nil	

Maximum activity was observed in 60–100% saturated dialyzed precipitate.

saturated supernatant was further saturated to 100% with further addition of ammonium sulphate. The precipitate and supernatant was once again separated and all the samples were analysed for α-glucosidase activity using *p*-nitrophenyl-α-D-glucopyranoside as substrate. When it was observed that the enzyme activity is maximum in 60–100% ammonium sulphate precipitate (Table 2), it was stored at 4 °C and used as a source of enzyme for studying the effect of test compounds on α-glucosidase inhibition.

α-Glucosidase inhibitory activity determination. 50 μg of semi-purified α-glucosidase from rat intestinal mucosa and 100 μg of glutathione (1.0 mg/mL) was added to 0.67 mM phosphate buffer (pH 6.8). The reaction mixture was incubated at room temperature for 10 min before the addition of 0.1 mL *p*-nitrophenyl-α-D-glucopyranoside (PNPG) 0.01 M followed by change in optical density at 400 nm for a period of 20 min in the presence of 50 μg of desired test compound in the 1.0 mL assay system. Activity was expressed as nmol/min using molar extinction coefficient value as 9.6×10^3.

Antitubercular activity determination. The activity of compounds was tested against bioluminescent *M. aurum* expressing firefly luciferase.[27] The cells were grown to an optical density of 0.03 at 600 nm. Two-fold dilutions of compounds were prepared and added to 100 μL culture ($A_{600}=0.03$) in microtitre plate. The plate was incubated at 37 °C for 6 h and bioluminiscence was measured for each well. Two controls (with no drug) and two standard drugs (rifampicin and sparfloxacin) were also included. For measurement of bioluminescence, 100 μL of culture was mixed with 250 μL of sodium citrate buffer (0.1 M, pH 5.0) in the tube and was placed in the luminometer (Lumat LB 9507, EG & G Berthold) 100 μL of 1 mM luciferase substrate was infected and luminescence was measured as relative light units (RLU) for 10 s.

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