

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

Neetu Tewari,^a V. K. Tiwari,^a R. C. Mishra,^a R. P. Tripathi,^{a,*} A. K. Srivastava,^b
R. Ahmad,^b R. Srivastava^c and B. S. Srivastava^c

^aDivision of Medicinal Chemistry, Central Drug Research Institute, Lucknow-226001, India

^bDivision of Biochemistry, Central Drug Research Institute, Lucknow-226001, India

^cDivision of Microbiology, Central Drug Research Institute, Lucknow-226001, India

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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.

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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 drugs³ for NIDDM with the known targets exist today, yet they are associated with many drawbacks such as liver toxicity,⁴ adverse gastrointestinal symptoms⁵ and raising the symptoms and risk factors of heart disease. Therapeutic approaches of herbal medicines also exist⁶ 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 anticancer¹¹ agents. In NIDDM, delaying glucose absorption after meals by inhibition of α -glucosidase is beneficial in therapy.^{12,13} A pseudo-sachharide (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 potential¹⁷ affecting glycogen phosphorylase, a well known target in controlling the blood glucose level (Fig. 1).

Certain phenyl ureas exhibit antidiabetic¹⁸ effect; however, they are associated with many drawbacks and it is envisaged that a hybrid of ureidyl pharmacophores and

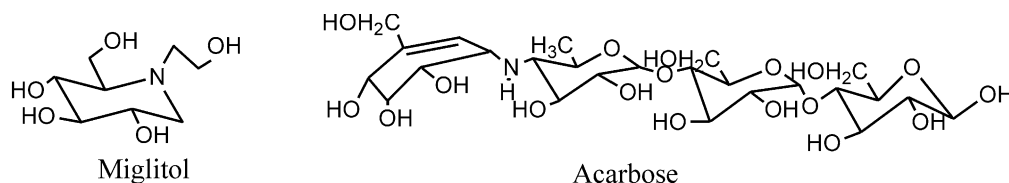


Figure 1. α -Glucosidase inhibitors used as drugs.

*Corresponding author. Tel.: +91-522-221-2412-418x4382; e-mail: rpt_56@yahoo.com

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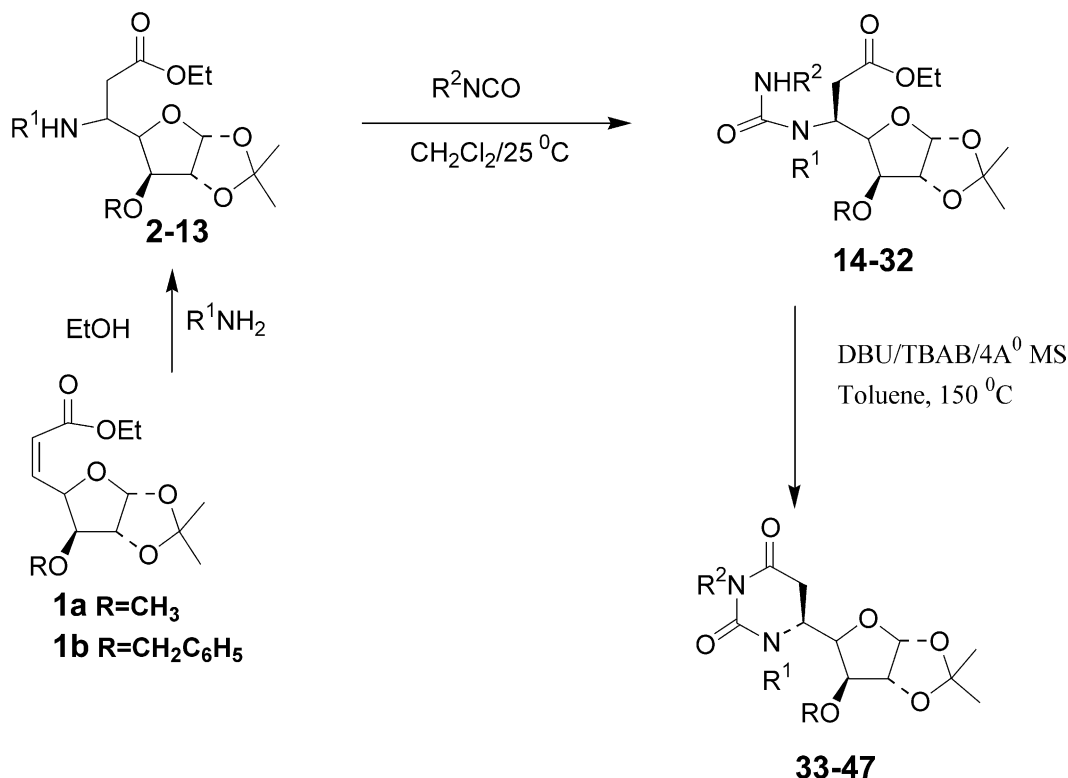
sugars, which are known for drug targeting¹⁹ and better pharmacokinetics²⁰ may offer new leads against diabetes. Keeping in mind the above and in continuation of our work²¹ on the development of chemotherapeutic agents from sugars, we have synthesized glycosyl ureas, both in flexible and rigid conformations, 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 anti-tubercular 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 ^1H 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 gluconeogenesis²⁴ 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 μ M concentrations. The standard drug acarbose inhibited this enzyme to the extent of 68% at 50 μ M.

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. IC₅₀ values for compounds **23** and **30** were 140 and 40 μ mol, respectively (Fig. 2).

N¹ unsubstituted compound **23** is equipotent to compounds with butyl or dodecyl substituents (**17** and **19**). However, N³ phenyl with chloro or fluoro substituents results in better enzyme inhibition than unsubstituted or acetyl phenyls. N¹-cyclopropyl and N¹-*n*-butyl also showed inhibitory effect depending upon the substituents in the aromatic ring at N³ and 3-*O*-substituent in sugar ring. Hence, no generalization can be made on the dependence of enzyme inhibitory activity at N¹, N³ 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 N¹ and 4-chlorophenyl as N³ 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	Cyclopropyl	4-Cl (phenyl)	4.3
16	CH ₃	Cyclopropyl	Benzyl	81.7
17	CH ₃	<i>n</i> -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 ₂ Ph	H	4-Cl (phenyl)	97.2
24	CH ₂ Ph	Cyclopropyl	3-Acetyl(phenyl)	74.7
25	CH ₂ Ph	Cyclopropyl	4-Cl (phenyl)	15.3
26	CH ₂ Ph	Cyclopropyl	Benzyl	40.5
27	CH ₂ Ph	<i>n</i> -Butyl	4-F (phenyl)	49.3
28	CH ₂ Ph	Dodecyl	3-Acetyl(phenyl)	11.9
29	CH ₂ Ph	Dodecyl	4-F (phenyl)	20.9
30	CH ₂ Ph	Dodecyl	4-Cl (phenyl)	94.3
31	CH ₂ Ph	Dodecyl	Benzyl	10.8
32	CH ₂ Ph	Oleyl	Benzyl	12.3
33	CH ₃	Cyclopropyl	4-Cl (phenyl)	11.7
34	CH ₃	Cyclopropyl	Benzyl	35.2
35	CH ₃	<i>n</i> -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 ₂ Ph	H	4-Cl(phenyl)	2.5
41	CH ₂ Ph	Cyclopropyl	3-Acetyl(phenyl)	47.0
42	CH ₂ Ph	Cyclopropyl	4-Cl(phenyl)	Nil
43	CH ₂ Ph	Cyclopropyl	Benzyl	61.8
44	CH ₂ Ph	<i>n</i> -Butyl	4-F (phenyl)	17.3
45	CH ₂ Ph	Dodecyl	3-Acetyl(phenyl)	28.5
46	CH ₂ Ph	Dodecyl	4-Cl(phenyl)	41.4
47	CH ₂ Ph	Oleyl	Benzyl	48.5
Acarbose				68 ^b

^aAt 100 μ M.

^bAt 50 μ M.

exhibited mild antitubercular activity with MIC of 25 $\mu\text{g/mL}$ only.

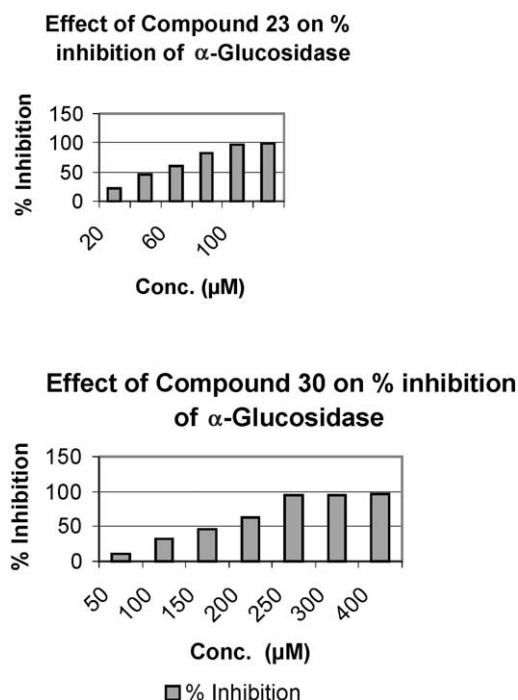


Figure 2.

In conclusion, we have synthesized glycosyl ureidyluronates 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 $< 50^\circ\text{C}$. Thin layer chromatography was performed using silica gel 60 F₂₅₄ plates with detecting agents iodine vapours, spraying with 5% sulphuric acid in ethanol followed by heating at 100°C , or by spraying with Dragendorff 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 $\pm 0.4\%$ 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-[(1R, 2R, 3S, 4R, 5S)-5,6-dideoxy-1, 2-O-isopropylidene-3-O-methyl-5-{N³-(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-chlorophenyl 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%; $[\alpha]_{\text{D}}^{25}$ 26.66 (c 0.11, CHCl_3); MS FAB $m/z = 443$ ($\text{M} + \text{H}$)⁺; 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, $\text{C}(\text{CH}_3)_2$], 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 [$\text{C}(\text{CH}_3)_2$]; 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, [$>\text{C}(\text{CH}_3)_2$]. Anal. calcd for $\text{C}_{20}\text{H}_{27}\text{N}_2\text{O}_7\text{Cl}$: C, 54.29; H, 6.11; N, 6.33; Found: C, 54.30; H, 5.88; N, 6.38.

Ethyl-[(1R, 2R, 3S, 4R, 5R/S)-5,6-dideoxy-1,2-O-isopropylidene-3-O-methyl-5-{N¹-cyclopropyl-N³-(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%. $[\alpha]_{\text{D}}^{25}$ -31.56 (c 0.47, CHCl_3); MS FAB $m/z = 483$ ($\text{M} + \text{H}$)⁺; 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, $\text{C}(\text{CH}_3)_2$], 1.22 (t, $J = 7.2$ Hz, 3H, OCH_2CH_3), 0.92 (m, 4H, cyclopropyl CH_2 S). ^{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 [$>\text{C}(\text{CH}_3)_2$]; 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_2 s). ¹³C 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_2 s).

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, $(CH_2)_3CH_3$]. ¹³C 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, $CH_2CH_2CH_3$). ¹³C 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_2CH_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_2 s), 0.87 (t, $J = 6.6$ Hz, 3H, $(CH_2)_{11}CH_3$). ¹³C 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_2CH_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]. ¹³C 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 (NCH₂Ph and OCH₂CH₃); 57.72 (C-5); 35.71 (C-6), 32.31 (NCH₂CH₃), 30.08, 30.04, 29.85, 29.74, 29.58, 27.78 (CH₂s); 27.22 and 26.68 [$>C(CH_3)_2$]; 23.0 (CH₂CH₃); 14.57 (OCH₂CH₃); 14.49 (CH₂CH₃).

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*S*)-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-5-{N¹-hexadecyl-N³-(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, CHCl₃); MS FAB $m/z = 667$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3339 (NH), 2927 (CH), 1718 (C=O), 1669 (NC=O); ¹H NMR (CDCl₃, 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 OCH₂CH₃), 3.67 (d, *J* = 3.0 Hz, 1H, H-3), 3.35 (m, 1H, H-5), 3.30 (s, 3H, OCH₃), 2.90–2.72 (m, 4H, H-6 and NCH₂), 1.59 (m, 1H, NH), 1.50 and 1.32 [each s, each 3H, C(CH₃)₂], 1.24 (m, 31H, CH₂s and OCH₂CH₃), 0.87 [t, *J* = 6.6 Hz, 3H, (CH₂)₁₄CH₃]. ¹³C NMR (CDCl₃): 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 (OCH₂CH₃), 58.0 (OCH₃); 53.4 (C-5), 36.2 (C-6), 32.3 (NCH₂), 30.0, 29.8, 29.7, 27.6 (CH₂s), 27.1, 26.4 [$>C(CH_3)_2$]; 23.0 (CH₂CH₃), 14.5 (OCH₂CH₃). Anal. calcd for C₃₆H₅₉N₂O₇Cl: 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-(N¹-oleyl-N³-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, CH₃OH); MS FAB $m/z = 674$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3404 (NH), 2930 (CH), 1723 (C=O), 1633 (NC=O); ¹H NMR (CDCl₃, 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 NCH₂Ph), 4.15 (m, 3H, H-5 and OCH₂CH₃), 3.59 (d, *J* = 2.7 Hz, 1H, H-3), 3.37 (s, 3H, OCH₃), 3.16 (m, 2H, NCH₂), 2.94 (m, 1H, H-6_A), 2.45 (dd, *J* = 4.03 Hz and 15.2 Hz, 1H, H-6_B), 1.99 (m, 4H, CH₂CH=CHCH₂), 1.60 (bs, 2H, NCH₂CH₂), 1.47 and 1.31 [each s, each 3H, C(CH₃)₂], 1.22 (m, 25H, CH₂s and OCH₂CH₃), 0.87 (t, *J* = 6.48 Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃) 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 (NCH₂Ph), 57.6 (OCH₃); 44.9 (NCH₂), 36.0 (C-6), 32.9, 32.3, 30.1, 30.0, 29.9, 29.8, 29.7, 29.6, 27.6 (CH₂s), 27.2, 26.7 ($>C(CH_3)_2$); 23.0 (CH₂CH₃), 14.5, 14.4 (OCH₂CH₃, CH₂CH₃).

Ethyl-[(1*R*, 2*R*, 3*S*, 4*R*, 5*R/S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N³-(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, CHCl₃); MS FAB $m/z = 519$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3361 (NH), 2935 (CH), 1725 (C=O), 1661 (NC=O); ¹H NMR (CDCl₃, 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, OCH₂Ph), 4.62 (d, *J* = 3.8 Hz, 1H, H-2), 4.30 (m, 1H, H-4), 4.12 (m, 3H, H-5 and OCH₂CH₃), 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(CH₃)₂], 1.25 (t, *J* = 7.2 Hz, 3H, OCH₂CH₃). ¹³C NMR (CDCl₃): (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(CH₃)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 (OCH₂Ph), 61.2, 61.1 (OCH₂CH₃); 47.2 (C-5); 37.3 (C-6); 27.1, 26.6, [$>C(CH_3)_2$], 14.5 (OCH₂CH₃). Anal. calcd for C₂₆H₃₁N₂O₇Cl: 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-{N¹-cyclopropyl-N³-(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, CHCl₃); MS FAB $m/z = 567$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3432 (NH), 1730 (C=O), 1676 (NC=O); ¹H NMR (CDCl₃, 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, OCH₂Ph), 4.66 (d, *J* = 3.7 Hz, 1H, H-2); 4.20 (m, 1H, H-5), 4.06 (q, 2H, OCH₂CH₃); 3.81 (d, *J* = 3.0 Hz, 1H, H-3); 3.42 (m, 1H, cyclopropyl CH), 2.88 (m, 1H, H-6_A), 2.58 (s, 3H, COCH₃), 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(CH₃)₂], 1.21 (t, *J* = 7.1 Hz, 3H, OCH₂CH₃), 1.11 (m, 4H, cyclopropyl CH₂s). ¹³C NMR (CDCl₃): δ 198.5 (CH₃C=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 (OCH₂Ph), 60.8 (OCH₂CH₃); 34.5 (C-6); 27.2, 26.8 [$>C(CH_3)_2$]; 14.5 (OCH₂CH₃), 9.96, 9.43 (cyclopropyl CH₂). Anal. calcd for C₃₁H₃₈N₂O₈: 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-{N¹-cyclopropyl-N³-(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, CHCl₃); MS FAB $m/z = 459$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3436 (NH), 2935 (CH), 1730 (C=O), 1672 (NC=O); ¹H NMR (CDCl₃, 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, $\text{C}(\text{CH}_3)_2$], 1.20 (t, $J=7.2$ Hz, 3H, OCH_2CH_3), 0.87 (m, 4H, cyclopropyl CH_2 s). ^{13}C NMR (CDCl_3): δ 172.0 ($\text{OC}=\text{O}$); 156.2 ($\text{NC}=\text{O}$); 138.1, 137.3 (Ar–C); 129.1, 128.9, 128.5, 128.4, 127.9, 121.2 (Ar–CH); 112.3, 109.9 [$>\text{C}(\text{CH}_3)_2$]; 105.1 (C-1); 82.4 (C-2); 81.4 (C-4); 79.4 (C-3); 71.9 (OCH_2Ph), 60.8 (OCH_2CH_3); 57.8 (C-5), 34.5 (C-6); 27.3, 26.9 [$>\text{C}(\text{CH}_3)_2$]; 14.5 (OCH_2CH_3), 9.96, 9.43 (cyclopropyl CH_2). Anal. calcd for $\text{C}_{31}\text{H}_{38}\text{N}_2\text{O}_8$: C, 62.36; H, 6.27; N, 5.02; Found: C, 62.95; H, 6.26; N, 4.98.

Ethyl-[(1R, 2R, 3S, 4R, 5S)-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene-5-(N¹-cyclopropyl-N³-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%; $[\alpha]_{\text{D}}^{25} -42.86$ (c 0.17, CHCl_3); MS FAB $m/z = 539$ ($\text{M} + \text{H}^+$); IR (neat): ν_{max} cm^{-1} 3459 (NH), 2935 (CH), 1729 ($\text{C}=\text{O}$), 1653 ($\text{NC}=\text{O}$); ^1H 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, $\text{C}(\text{CH}_3)_2$], 1.25 (t, $J=7.2$ Hz, 3H, OCH_2CH_3), 0.88 (m, 4H, cyclopropyl CH_2 s). ^{13}C NMR (CDCl_3): δ 173.0, 172.2 ($\text{OC}=\text{O}$); 159.3 ($\text{NC}=\text{O}$); 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 [$>\text{C}(\text{CH}_3)_2$]; 105.0 (C-1); 82.7 (C-2); 81.5 (C-4); 79.7 (C-3); 71.9 (OCH_2Ph), 57.8 (OCH_2CH_3); 44.8 (NCH_2Ph), 36.6, 35.1 (C-6); 27.3, 26.9 [$>\text{C}(\text{CH}_3)_2$]; 14.6 (OCH_2CH_3), 10.0, 9.3 (cyclopropyl CH_2). Anal. calcd for $\text{C}_{30}\text{H}_{38}\text{N}_2\text{O}_8$: C, 66.91; H, 7.06; N, 5.20; Found: C, 66.96; H, 6.98; N, 5.14.

Ethyl-[(1R, 2R, 3S, 4R, 5S)-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene-5-(N¹-butyl-N³-(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%; $[\alpha]_{\text{D}}^{25} -15.3$ (c 0.13, CH_3OH); MS FAB $m/z = 559$ ($\text{M} + \text{H}^+$); IR (neat): ν_{max} cm^{-1} 3301 (NH), 2929 (CH), 1713 ($\text{C}=\text{O}$), 1668 ($\text{NC}=\text{O}$); ^1H 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_2Ph), 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, $\text{C}(\text{CH}_3)_2$], 1.22 (m, 5H, $\text{NCH}_2\text{CH}_2\text{CH}_2$, OCH_2CH_3), 0.89 [t, $J=7.1$ Hz, 3H, $(\text{CH}_2)_3\text{CH}_3$]. ^{13}C NMR (CDCl_3): δ 171.5 ($\text{OC}=\text{O}$); 160.8, 156.6, 156.0 ($\text{NC}=\text{O}$); 135.9 (Ar–C); 128.6, 128.3,

128.2, 121.3, 121.1, 115.3, 114.9 (Ar–CH); 111.8 [$>\text{C}(\text{CH}_3)_2$]; 105.1 (C-1); 81.7 (C-2); 80.7 (C-4); 79.2 (C-3); 71.4 (OCH_2Ph); 61.0 (OCH_2CH_3); 34.6 (NCH_2); 31.2 (C-6); 27.1, 26.6 [$>\text{C}(\text{CH}_3)_2$]; 20.5 (CH_2CH_3), 14.1, 13.8 (OCH_2CH_3 , CH_2CH_3). Anal. calcd for $\text{C}_{30}\text{H}_{39}\text{N}_2\text{O}_7\text{F}$: C, 64.5; H, 6.98; N, 5.0; Found: C, 64.48; H, 7.0; N, 4.96.

Ethyl-[(1R, 2R, 3S, 4R, 5S)-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene-5-(N¹-dodecyl-N³-(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%; $[\alpha]_{\text{D}}^{25} -13$ (c 0.12, CHCl_3); MS FAB $m/z = 695$ ($\text{M} + \text{H}^+$); IR (neat): ν_{max} cm^{-1} 3355 (NH), 2927 (CH), 1726 ($\text{C}=\text{O}$), 1671 ($\text{NC}=\text{O}$); ^1H 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_2Ph), 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_2CH_2), 1.48 and 1.32 [each s, 3H, $\text{C}(\text{CH}_3)_2$], 1.24 (m, 21H, CH_2 s and OCH_2CH_3), 0.87 [t, $J=6.8$ Hz, 3H, CH_2CH_3]. ^{13}C NMR (CDCl_3): δ 198.7 (COCH_3), 171.8 ($\text{OC}=\text{O}$); 156.8, ($\text{NC}=\text{O}$); 140.8, 138.0, 136.9 (Ar–C); 129.2, 129.0, 128.7 (Ar–CH); 112.2 [$>\text{C}(\text{CH}_3)_2$]; 105.1 (C-1); 82.1 (C-2); 80.9 (C-4); 79.5 (C-3); 71.8 (OCH_2Ph); 61.5 (OCH_2CH_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 [$>\text{C}(\text{CH}_3)_2$]; 23.0 (CH_2CH_3), 14.5, 14.4 (OCH_2CH_3 , CH_2CH_3). Anal. calcd for $\text{C}_{40}\text{H}_{58}\text{N}_2\text{O}_8$: C, 69.16; H, 8.35; N, 4.03; Found: C, 69.19; H, 8.37; N, 4.07.

Ethyl-[(1R, 2R, 3S, 4R, 5S)-3-O-benzyl-5,6-dideoxy-1,2-O-isopropylidene-5-(N¹-dodecyl-N³-(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%; $[\alpha]_{\text{D}}^{25} -20.9$ (c 0.13, CH_3OH); MS FAB $m/z = 671$ ($\text{M} + \text{H}^+$); IR (neat): ν_{max} cm^{-1} 3387 (NH), 2925 (CH), 1732 ($\text{C}=\text{O}$), 1647 ($\text{NC}=\text{O}$); ^1H 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_2Ph), 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_2CH_2), 1.47 and 1.32 [each s, 3H, $\text{C}(\text{CH}_3)_2$], 1.25 (m, 21H, CH_2 s and OCH_2CH_3), 0.85 [t, $J=6.8$ Hz, 3H, CH_2CH_3]. ^{13}C NMR (CDCl_3): δ 171.9 ($\text{OC}=\text{O}$); 156.6, ($\text{NC}=\text{O}$); 139.0, 136.9 (Ar–C); 129.0, 128.7, 128.6, 127.2, 121.0 (Ar–CH); 112.2 [$>\text{C}(\text{CH}_3)_2$]; 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_2 s), 27.1, 26.6 [$>\text{C}(\text{CH}_3)_2$]; 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*S*)-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-{N¹-dodecyl-N³-(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, CHCl₃); MS FAB m/z = 688 ($M+H$)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3378 (NH), 2929 (CH), 1718 (C=O), 1631 (*NC=O*); ¹H NMR (CDCl₃, 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, OCH₂Ph), 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, OCH₂CH₃), 3.79 (d, *J*=2.5 Hz, 1H, H-3); 3.17 (m, 2H, NCH₂), 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, NCH₂CH₂), 1.47 and 1.32 [each s, 3H, C(CH₃)₂], 1.23–1.16 (m, 21H, CH₂S and OCH₂CH₃), 0.87 [t, *J*=6.0 Hz, 3H, CH₂CH₃]. ¹³C NMR (CDCl₃): 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 (OCH₂Ph); 61.5 (OCH₂CH₃); 34.9 (NCH₂); 32.3 (C-6); 30.0, 29.8, 29.7, 29.5, 27.7 (CH₂S), 27.1, 26.6 [$>C(CH_3)_2$]; 23.0 (CH₂CH₃), 14.5, 14.4 (OCH₂CH₃, CH₂CH₃). Anal. calcd for C₃₈H₅₅N₂O₇Cl: 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-(N¹-dodecyl-N³-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, CH₃OH); MS FAB m/z = 667 ($M+H$)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3387(NH), 2925 (CH), 1732 (C=O), 1647 (*NC=O*); ¹H NMR (CDCl₃, 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, OCH₂Ph), 4.63 (d, *J*=3.7 Hz, 1H, H-2), 4.42 (m, 4H, H-4, H-5, NCH₂ Ph); 4.06 (q, 2H, OCH₂CH₃), 3.78 (d, *J*=3.7 Hz, 1H, H-3); 3.14 (m, 2H, NCH₂), 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, NCH₂CH₂), 1.47 and 1.31 [each s, 3H, C(CH₃)₂], 1.25–1.16 (m, 21H, CH₂S and OCH₂CH₃), 0.87 [t, *J*=6.0 Hz, 3H, CH₂CH₃]. ¹³C NMR (CDCl₃): δ 171.6 (OC=O); 156.8, (NC=O); 140.5, 137.2 (Ar-C); 128.9, 128.7, 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 (OCH₂Ph); 61.0 (OCH₂CH₃); 44.9 (NCH₂Ph), 35.3 (NCH₂); 32.3 (C-6); 30.0, 29.8, 29.7, 29.6, 27.7 (CH₂S), 27.2, 26.8 [$>C(CH_3)_2$]; 23.0 (CH₂CH₃), 14.55, 14.50 (OCH₂CH₃, CH₂CH₃). Anal. calcd for C₃₉H₅₈N₂O₇: 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-(N¹-oleyl-N³-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, CH₃OH); MS FAB m/z = 749 ($M+H$)⁺; IR (neat): $\nu_{\max}$

cm⁻¹ 3390 (NH), 2926 (CH), 1732 (C=O), 1647 (*NC=O*); ¹H NMR (CDCl₃, 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, OCH₂Ph), 4.65 (d, *J*=3.8 Hz, 1H, H-2), 4.38 (m, 4H, NCH₂Ph, H-4 and H-5), 4.04 (q, 2H, OCH₂CH₃), 3.78 (d, *J*=2.0 Hz, 1H, H-3); 3.14 (m, 2H, NCH₂), 2.76 (m, 1H, H-6_A), 2.10 (m, 5H, H-6_B, and allylic CH₂); 1.60 (m, 2H, NCH₂CH₂), 1.47 and 1.31 [each s, 3H, C(CH₃)₂], 1.25 (m, 21H, CH₂S and OCH₂CH₃), 0.87 [t, *J*=5.9 Hz, 3H, CH₂CH₃]. ¹³C NMR (CDCl₃): 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 (OCH₂Ph); 61.0 (OCH₂CH₃); 44.9 (NCH₂Ph), 35.3 (NCH₂), 30.1 (C-6); 30.0, 29.9, 29.8, 29.6, 27.7, 27.6 (CH₂S), 27.2, 26.8 [$>C(CH_3)_2$]; 23.0 (CH₂CH₃), 14.5, 14.4 (OCH₂CH₃, CH₂CH₃). Anal. calcd for C₃₅H₆₈N₂O₇: 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*)-N¹-cyclopropyl-N³-(4-chlorophenyl)-5,6-dihydro-(1',2'-*O*-isopropylidene-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 SiO₂ 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, CHCl₃), MS FAB m/z = 437 ($M+H$)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3380 (NH), 3010, 2935 (CH), 1670 (*NC=O*); ¹H NMR (CDCl₃, 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, OCH₃), 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(CH₃)₂]; 0.93–0.79 (m, 4H, CH₂-cyclopropyl ring). ¹³C NMR (CDCl₃): δ 168.7 and 153.7 (C=O), 134.6, 134.2, 130.4 and 129.6 (Ar-C), 112.3 [C(CH₃)₂], 105.6 (C-1'), 84.3 (C-2'), 81.0 (C-4'), 80.7 (C-3'), 57.8 (OCH₃), 53.2 (C-6), 35.4 (C-5), 32.1 (CH-cyclopropyl ring), 27.2 and 26.53 [C(CH₃)₂], 10.1 and 7.0 (CH₂-cyclopropyl ring). Anal. calcd for C₂₃H₃₁N₂O₇Cl: 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*)-N¹-cyclopropyl-N³-benzyl-5,6-dihydro-(1',2'-*O*-isopropylidene-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, CHCl₃), MS FAB m/z = 417($M+H$)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3375 (NH), 3019, 2935 (CH), 1671 (*NC=O*); ¹H NMR (CDCl₃, 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, OCH₃), 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(CH₃)₂]; 0.93–0.50 (m, 4H, CH₂-cyclopropyl ring). ¹³C NMR (CDCl₃): δ 168.6 and 154.0 (C=O), 138.2, 129.2, 128.8, 127.7 (Ar-C), 112.2 [C(CH₃)₂], 105.5 (C-1'), 84.3 (C-2'), 81.0 (C-4'), 80.8 (C-3'), 57.7 (OCH₃), 53.1 (C-6), 43.9 (NCH₂), 34.8 (C-5), 31.9 (CH-cyclopropyl ring), 27.1 and 26.5 [C(CH₃)₂], 10.3 and 6.9 (CH₂-cyclopropyl ring). Anal. calcd for C₂₁H₂₅N₂O₆Cl: 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,6S)-N¹-butyl-N³-(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, CH₃OH); MS FAB $m/z = 437$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3400 (NH), 2938 (CH), 1721 (C=O), 1677 (NC=O); ¹H NMR (CDCl₃, 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, OCH₃), 3.22 (m, 1H, NCH_B), 2.8 (m, 1H, H-5_A), 2.68 (m, 1H, H-5_B), 1.64 (m, 4H, CH₂CH₂), 1.32 and 1.28 [each s, 3H, C(CH₃)₂], 0.93 (t, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): 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 (NCH₂), 54.8 (OCH₃), 49.2, 49.1, 47.5, 38.3, 37.6, 36.7, 35.1 (CH₂CH₂), 32.6, 30.5 (C-6); 29.3, 27.1 [$>C(CH_3)_2$]; 14.5, 14.2 (CH₂CH₃).

(1'R,2'R,3'S,4'R,6S)-N¹-heptyl-N³-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, CH₃OH); MS FAB $m/z = 437$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3436 (NH), 2930 (CH), 1711 (C=O), 1667 (NC=O); ¹H NMR (CDCl₃, 200 MHz) δ 7.28 (m, 5H, Ar-H); 5.84 (d, $J = 3.8$ Hz, 1H, H-1'); 4.97 (s, 2H, NCH₂Ph), 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, OCH₃), 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, NCH₂CH₂CH₂), 1.25 [m, 12H, C(CH₃)₂ and CH₂s], 0.87 (t, $J = 5.0$ Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): 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 (OCH₃), 51.1 (C-6), 49.4 (NCH₂Ph), 43.9 (NCH₂CH₂), 34.6 (C-5), 32.1, 29.4, 28.6, 27.2 (CH₂S), 27.0, 26.5 [$>C(CH_3)_2$], 22.9 (CH₂CH₃), 14.4 (CH₂CH₃).

(1'R,2'R,3'S,4'R,6S)-N¹-dodecyl-N³-(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, CH₃OH), MS FAB $m/z = 565$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3389 (NH), 2927 (CH), 1722 (C=O); 1682 (NC=ON). ¹H NMR (CDCl₃, 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 (OCH₃), 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, NCH₂CH₂CH₂), 1.47 and 1.32 [each s, each 3H, C(CH₃)₂]; 1.25 (s, 16H, CH₂S), 0.92 (t, $J = 6.4$ Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): δ 168.6 (C=O), 152.1 (NC=ON), 134.3, 130.4, 129.6 (Ar-C), 112.3 [C(CH₃)₂], 105.4 (C-1'), 84.1 (C-2'), 81.7 (C-4'), 80.9 (C-3'), 57.8 (OCH₃), 51.3 (C-6), 51.3 (C-6), 49.6 (NCH₂), 35.1 (C-5), 32.3, 30.0, 29.7, 28.5, (CH₂S), 27.1, 26.5 [C(CH₃)₂], 23.0 (CH₂CH₃), 14.4 (CH₃). Anal. calcd for C₃₀H₄₅N₂O₆Cl: 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,6S)-N¹-hexadecyl-N³-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, CHCl₃), MS FAB $m/z = 587$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3433 (NH), 2926, 2854 (CH), 1723, 1683 (C=O); ¹H NMR (CDCl₃, 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, OCH₃), 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, NCH₂CH₂), 1.48 and 1.32 [each s, each 3H, C(CH₃)₂]; 1.25 (m, 26H, CH₂S), 0.87 (t, $J = 6.7$ Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): δ 168.7, 152.8 (C=O), 135.9, 129.5, 129.0, 128.6 (Ar-C), 112.3 [C(CH₃)₂], 105.5 (C-1'), 84.2 (C-2'), 81.1 (C-4'), 80.9 (C-3'), 57.8 (OCH₃), 51.5 (C-6), 49.5 (NCH₂), 35.2 (C-5), 32.3, 30.1, 29.9, 29.7, 28.5, 27.9, 23.1 (CH₂S), 27.2 and 26.3 [C(CH₃)₂], 14.5 (CH₃). Anal. calcd for C₃₄H₅₄N₂O₆: 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,6S)-N¹-oleyl-N³-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, CHCl₃), MS FAB $m/z = 627$ (M + H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3372 (NH), 2928 (CH), 1710 (C=O); 1669 (NC=ON). ¹H NMR (CDCl₃, 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, NCH₂Ph), 4.53 (d, $J=3.7$ Hz, 1H, H-2'), 4.03 (m, 2H, H-4', NCH₂Ph), 3.80 (m, 1H, H-6); 3.64 (d, $J=3.1$ Hz, H-3'); 3.37 (s, 3H, OCH₃), 3.1 (m, 1H, NCH₂Ph), 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 CH₂S), 1.65 (m, 4H, CH₂S), 1.41 [m, 26, C(CH₃)₂ and CH₂S], 0.88 (t, $J=7.0$ Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): δ 168.6 (C=O), 152.6 (NC=ON), 138.2, 130.3, 128.9, 128.8, 127.6 (Ar-C), 112.3 [C(CH₃)₂], 105.4 (C-1'), 84.1 (C-2'), 81.1 (C-4'), 80.9 (C-3'), 71.9 (OCH₂Ph), 59.5 (NCH₂Ph), 57.7 (OCH₃), 51.9 (C-6), 49.4 (NCH₂), 34.6 (C-5), 32.9, 30.8, 30.0, 29.8, 29.7, 29.6, 28.6, 27.6, 27.2 (CH₂S), 27.1, 26.5 [C(CH₃)₂], 23.0 (CH₂CH₃), 14.0 (CH₂CH₃). Anal. calcd for C₃₇H₅₈N₂O₆: 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,6S)-N³-benzyl-5,6-dihydro-(1',2'-O-isopropylethene-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, CHCl₃); MS FAB m/z = 473 (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3371 (NH), 2926 (CH), 1712 (C=O); 1660 (NC=ON); ¹H NMR (CDCl₃, 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, OCH₂Ph), 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(CH₃)₂], ¹³C NMR (CDCl₃): 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(CH₃)₂]; 105.6 (C-1'); 82.4 (C-2'), 81.6 (C-4'), 80.6 (C-3'), 72.4 (OCH₂Ph), 46.7 (C-6); 34.6 (C-5); 27.2, 26.6, [$>C(CH_3)_2$].

(1'R,2'R,3'S,4'R,6S)-N¹-cyclopropyl-N³-(3'-acetylphenyl)-5,6-dihydro-(1',2'-O-isopropylethene-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, CHCl₃), MS FAB m/z = 521 (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3370 (NH), 3012, 2928 (CH), 1710, 1668 (CO); ¹H NMR (CDCl₃, 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, OCH₂Ph), 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, CH₃), 2.35 (d, $J=17.1$ Hz, 1H, H-5_B), 1.33 and 1.22 [each s, each 3H, C(CH₃)₂]; 0.97–0.78 (m, 4H, CH₂-cyclopropyl ring). ¹³C NMR (CDCl₃): 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(CH₃)₂], 105.6 (C-1'), 81.9 (C-2'), 81.8 (C-4'), 80.8 (C-3'), 72.3 (OCH₂Ph), 53.1 (C-6), 35.2

(C-5), 32.2 (CH-cyclopropyl ring), 27.2, 26.9 and 26.6 [OCH₂CH₃ and C(CH₃)₂], 10.0 and 7.1 (CH₂-cyclopropyl ring). Anal. calcd for C₂₉H₃₂N₂O₇: 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,6S)-N¹-cyclopropyl-N³-(4-chlorophenyl)-5,6-dihydro-(1',2'-O-isopropylethene-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, CHCl₃), MS FAB m/z = 513 (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3397 (NH), 3016, 2932 (CH), 1696 (C=O); ¹H NMR (CDCl₃, 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, OCH₂Ph), 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(CH₃)₂]; 0.94–0.77 (m, 4H, CH₂-cyclopropyl ring). ¹³C NMR (CDCl₃): 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(CH₃)₂], 105.6 (C-1'), 81.9 (C-2'), 81.8 (C-4'), 80.8 (C-3'), 72.3 (OCH₂Ph), 53.0 (C-6), 35.2 (C-5), 32.2 (CH-cyclopropyl ring), 27.2 and 26.6 [C(CH₃)₂], 10.3 and 7.0 (CH₂-cyclopropyl ring). Anal. calcd for C₂₇H₂₉N₂O₆Cl: 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,6S)-N¹-cyclopropyl-N³-benzyl-5,6-dihydro-(1',2'-O-isopropylethene-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, CHCl₃), MS FAB m/z = 493 (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3375 (NH), 3015, 2932 (CH), 1668 (NC=O); ¹H NMR (CDCl₃, 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, NCH₂Ph), 4.68 and 4.41 (each d, $J=11.6$ Hz, each 1H, OCH₂Ph), 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, CH-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(CH₃)₂]; 0.98–0.75 (m, 4H, CH₂-cyclopropyl ring). ¹³C NMR (CDCl₃): 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(CH₃)₂], 105.5 (C-1'), 82.1 (C-2'), 81.8 (C-4'), 80.9 (C-3'), 72.3 (OCH₂Ph), 52.9 (C-6), 43.9 (NCH₂), 34.7 (C-5), 32.1 (CH-cyclopropyl ring), 27.1 and 26.6 [C(CH₃)₂], 10.3 and 7.0 (CH₂-cyclopropyl ring). Anal. calcd for C₂₈H₃₂N₂O₆: 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,6S)-N¹-butyl-N³-(4-fluorophenyl)-5,6-dihydro-(1',2'-O-isopropylethene-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 CHCl₃), MS FAB $m/z = 513$ (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3501 (NH), 2935 (CH), 1738 (C=O); ¹H NMR (CDCl₃, 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, OCH₂Ph), 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, NCH₂), 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, NCH₂CH₂CH₂), 1.47 and 1.32 [each s, each 3H, C(CH₃)₂]; 0.87 (t, *J* = 6.4 Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): δ 168.7 (C=O), 152 (NC=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(CH₃)₂], 105.5 (C-1'), 81.8 (C-2'), 81.7 (C-4'), 81.1 (C-3'), 72.3 (OCH₂Ph), 51.3 (C-6), 49.4 (NCH₂), 34.9 (C-5), 30.6 (NCH₂CH₂), 27.1, 26.5 [C(CH₃)₂], 20.4 (CH₂CH₃), 14.2 (CH₃).

(1'R,2'R,3'S,4'R,6S)-N¹-dodecyl-N³-(3-acetylphenyl)-5,6-dihydro-(1',2'-O-isopropylethene-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, CH₃OH), MS FAB $m/z = 648$ (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3372 (NH), 1710 (C=O); 1669 (NC=ON). ¹H NMR (CDCl₃, 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, OCH₂Ph); 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, COCH₃ and NCH₂), 2.88 (dd, *J* = 16.8 Hz and 3.2 Hz, 1H, H-5_A), 2.58 (m, 2H, NCH₂CH₂), 2.35 (d, *J* = 16.6 Hz, 1H, H-5_B), 1.64 (m, 4H, CH₂S), 1.48 and 1.33 [each s, each 3H, C(CH₃)₂], 1.25 (s, 14H, CH₂S), 0.87 (t, *J* = 7.0 Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): δ 199.2, 197.1 (COCH₃), 168.6 (C=O), 152.5 (NC=ON), 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(CH₃)₂], 105.5 (C-1'), 81.8 (C-2'), 81.7 (C-4'), 81.0 (C-3'), 72.3 (OCH₂Ph), 54.3 (OCH₃), 51.3 (C-6), 49.7 (NCH₂), 34.9 (C-5), 32.3, 30.0, 29.9, 29.7, 28.5 (CH₂S), 27.2, 26.9, 26.5 [COCH₃ and C(CH₃)₂], 23.0 (CH₂CH₃), 14.5 (CH₂CH₃). Anal. calcd for C₃₈H₅₂N₂O₇: 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,6S)-N¹-dodecyl-N³-(4-chlorophenyl)-5,6-dihydro-(1',2'-O-isopropylethene-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, CHCl₃), MS FAB $m/z = 641$ (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3404 (NH), 2930 (CH), 1723 (C=O), 1681 (NC=O). ¹H NMR (CDCl₃, 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, OCH₂Ph); 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(CH₃)₂]; 1.25 (m, 10H, CH₂S); 0.88 (t, *J* = 6.0 Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): 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(CH₃)₂], 105.0 (C-1'), 82.4 (C-2'), 81.5 (C-4'), 79.8 (C-3'), 71.7 (OCH₂Ph), 50.4 (C-6), 47.3 (NCH₂), 34.2 (C-5), 31.9, 29.6, 29.5, 29.3, 28.11, 25.4, 22.6 (CH₂S), 27.7 and 26.2 [C(CH₃)₂], 14.1 (CH₃). Anal. calcd for C₃₆H₄₉N₂O₆Cl: C, 67.3; H, 7.64; N, 4.36; Found: C, 67.35; H, 7.62; N, 4.440.

(1'R,2'R,3'S,4'R,6S)-N¹-oleyl-N³-benzyl-5,6-dihydro-(1',2'-O-isopropylethene-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, CH₃OH), MS FAB $m/z = 703$ (M+H)⁺; IR (neat): $\nu_{\max}$ cm⁻¹ 3371 (NH), 2926 (CH), 1711 (C=O); 1669 (NC=ON). ¹H NMR (CDCl₃, 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, NCH₂Ph), 4.64 and 4.45 (each d, *J* = 11.6 Hz, each 1H, OCH₂Ph); 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 CH₂S), 1.66 (m, 4H, CH₂S), 1.48 [m, 26, C(CH₃)₂ and CH₂S], 0.87 (t, *J* = 7.0 Hz, 3H, CH₂CH₃). ¹³C NMR (CDCl₃): δ 168.5 (C=O), 152.6 (NC=ON), 138.2, 136.9, 130.3, 129.1, 128.8, 128.4, 127.5 (Ar-C), 112.3 [C(CH₃)₂], 105.4 (C-1'), 81.8 (C-2'), 81.6 (C-4'), 81.1 (C-3'), 72.3 (OCH₂Ph), 59.5 (NCH₂Ph), 51.0 (C-6), 43.9 (C-5), 34.4, 30.0, 29.6, 28., 27.5, 27.2 (CH₂S), 27.0, 26.5 [C(CH₃)₂], 23.0, 20.1 (CH₂CH₃), 14.5 (CH₃).

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 Elvehjem glass homogeniser fitted with Teflon pestle. The homogenate was centrifuged at 1000g 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 $\pm$ 0.03	288.94 $\pm$ 10.1	1.0
1000g supernatant	0.74 $\pm$ 0.09	483.81 $\pm$ 89.7	1.68
0–30% dialyzed precipitate	0.18 $\pm$ 0.02	552.69 $\pm$ 38.9	1.91
30–60% dialyzed precipitate	0.31 $\pm$ 0.03	723.36 $\pm$ 94.2	2.50
60–100% dialyzed precipitate	0.60 $\pm$ 0.06	1370.91 $\pm$ 53.8	4.74
100% saturated supernatant precipitate	0.12 $\pm$ 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 μ g of semi-purified α -glucosidase from rat intestinal mucosa and 100 μ g 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 μ g 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 μ L culture (A_{600} =0.03) in microtitre plate. The plate was incubated at 37°C for 6 h and bioluminescence 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 μ L of culture was mixed with 250 μ L 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 μ L of 1 mM luciferase substrate was infected and luminescence was measured as relative light units (RLU) for 10 s.

References and Notes

- (a) Kingh, H.; Aubert, R. E.; Herman, W. H. *Diabetes Care* **1998**, *21*, 1414. (b) Harris, M. I.; Flegal, K. M.; Cowie, C. C.; Eberhardt, M. S.; Goldstein, D. E.; Little, R. K.; Wiedmeyer, H. M.; Byrd-Holt, D. D. *Diabetes Care* **1998**, *21*, 518.
- (a) Pablos, M. A.; Ravigliione, M. C. L. *N. Engl. J. Med.* **1998**, *338*, 1641. (b) Zimmet, P. J. *Intern. Med.* **2000**, *247*, 301. (c) Zimmet, P. *Diabetologia* **1999**, *42*, 499. (d) Groop, L. J. *Intern. Med.* **1997**, *241*, 95. (e) Huebner, R. E.; Castro, K. G. *Ann. Rev. Med.* **1995**, *46*, 47.
- Lebovitz, H. E. *Drugs* **1992**, *44* (Suppl. 3), 21.
- Gale, E. A. M. *Lancet* **2001**, *357*, 1870.
- Moller, D. E. *Nature* **2001**, *414*, 821.
- Emst, E. *Br. J. Med.* **2000**, *321*, 395.
- (a) Paulsen, H.; Todt, K. *Adv. Carbohydr. Chem.* **1968**, *23*, 115. (b) Fellows, L. E. *Chem. Br.* **1987**, *23*, 842. (c) Truscheit, E.; Frommer, W.; Junge, B.; Muller, L.; Schmidt, D.; Winkler, W. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 744. (d) Inouge, S.; Tsuruoka, T.; Ito, A.; Niida, T. *Tetrahedron* **1968**, *24*, 2125. (e) Muller, L. In *Biotechnology*; Rehn, H. J., Reed, G., Eds., VCH: Weinheim, 1985; Vol. 4, Chapter 18.
- Bayer, A. G.; Kinast, G.; Schuller, M.; Schroder, T.; Ger Offen, D. R.; Anzeveno, P. B.; Creemer, L. J.; Daniel, J. K.; King, C. H. R.; Liu, P. S. *J. Org. Chem.* **1989**, *54*, 2539.
- Yoshikuni, Y.; Ezure, Y.; Aoyagi, Y.; Enomoto, H. *J. Pharmacobiol. Dyn.* **1988**, *111*, 356.
- (a) Karpus, A.; Fleet, G. W. J.; Dwek, R. A.; Petrusson, S.; Namgoong, S. K.; Ramsden, N. G.; Jacob, G. S.; Rademacher, T. W. *J. Proc. Natl. Acad. Sci. U.S.A.* **1988**, *85*, 9229. (b) Walker, B. D.; Kowalski, M.; Goh, W. C.; Kozarsky, K.; Krieger, M.; Rosen, C.; Rohrschneider, L.; Haseltine, W. A.; Sodroski, J. *J. Proc. Natl. Acad. Sci. U.S.A.* **1987**, *84*, 8120. (c) Winkler, D. A.; Holan, G. *J. Med. Chem.* **1989**, *32*, 2084.
- Evans, S. V.; Fellows, L. E.; Shing, K. T. M.; Flee, G. W. *Phytochemistry* **1985**, *24*, 1953.
- Humphries, M. J.; Matsumoto, K.; White, S. L.; Olden, K. *Cancer Res.* **1986**, *46*, 5215.
- Bischoff, H. *Eur. J. Clin. Invest.* **1994**, *24*, 3.
- Toeller, M. *Eur. J. Clin. Invest.* **1994**, *24*, 31.
- Porus, J. R. *Drugs Future* **1986**, *11*, 729.
- Bayer, A. G. *Drugs Future* **1986**, *11*, 1039.
- Kajimoto, T.; Liu, K. K. C.; Pederson, R. L.; Zhong, Z.; Ichikawa, Y.; John, A.; Porco, W.; Wong, C. H., Jr. *J. Am. Chem. Soc.* **1991**, *113*, 6187, and references cited therein.
- Frank, S. *Angew. Chem., Int. Ed.* **2002**, *41*, 230.
- Scozzafava, A.; Mastrolorenzo, A.; Suparan, C. T. *J. Enzyme Inhib.* **2001**, *16*, 425.
- Fischer, J. F.; Harrison, A. W.; Bundy, G. L.; Wilkinson, K. F.; Rush, B. D.; Ruwart, M. J. *J. Med. Chem.* **1991**, *34*, 3140.
- Negre, J.; Chance, M. L.; Hanboulia, S. Y.; Monsigny, M.; Roche, A. C.; Mayer, R. M.; Hommel, M. *Antimicrob. Agents Chemother.* **1992**, *36*, 2228.
- (a) Tiwari, V. K.; Tripathi, R. P. *Indian J. Chem.* **2002**, *41B*, 1681. (b) Tripathi, R. P.; Tripathi, R.; Tiwari, V. K.; Bala, L.; Sinha, S.; Srivastava, A.; Srivastava, R.; Srivastava, B. S. *Eu. J. Med. Chem.* **2002**, *37*, 773. (c) Khan, A. R.; Tripathi, R. P.; Tiwari, V. K.; Mishra, R. C.; Reddy, V. J. M. J. K. Saxena *J. Carbohydr. Chem.* **2002**, *21*, 587. (d) Mishra, R. C.; Tewari, N.; Arora, K.; Ahmad, R.; Tripathi, R. P.; Tiwari, V. K.; Walter, R. D.; Srivastava, A. K. *Comb. Chem. Highthroughput Screen.* **2003**, *6*, 37. (e) Tewari, N.; Mishra, R. C.; Tiwari, V. K.; Tripathi, R. P. *Synlett* **2002**, *11*, 1779.
- Patil, N. T.; Tilekar, J. N.; Dhavale, D. D. *J. Org. Chem.* **2001**, *66*, 1065.
- Hirama, M.; Shigemoto, T.; Yamazaki, Y.; Ito, S. *J. Am. Chem. Soc.* **1985**, *107*, 1797.
- Hanson, R. L.; Ho, R. S.; Wiseberg, J. J.; Simpson, R.; Younathan, E. S.; Blair, J. B. *J. Biol. Chem.* **1984**, *259*, 218.
- Cogoli, A.; Mosimann, H.; Vock, C.; Balthazar, A. K. V.; Semenza, G. *Eur. J. Biochem.* **1972**, *30*, 7.
- Matsui, T.; Yoshimoto, S.; Osajima, K.; Oki, T.; Osajima, Y. *Biosci. Biotech. Biochem.* **1996**, *60*, 2019.
- Deb, D. K.; Srivastava, K. K.; Srivastava, R.; Srivastava, B. S. *Biochem. Biophys. Res. Commun.* **2000**, *279*, 457.