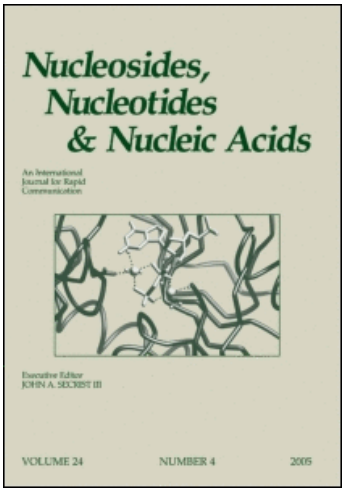

Nucleosides, Nucleotides and Nucleic Acids

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SYNTHESIS AND DNA TOPOISOMERASE-II INHIBITORY ACTIVITY OF UNNATURAL NUCLEOSIDES

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▫ *The synthesis and biological activities of a number of unnatural nucleosides (**23–43**) is described. Nucleosides have been synthesized by $SnCl_4$-catalyzed condensation of amino sugar acetates and silylated modified pyrimidines. Few of the 2′-O-acetyl derivatives of the nucleosides were hydrolyzed to the respective hydroxy derivatives by treatment with methanol saturated with ammonia. The compounds were screened against Filarial DNA-topoisomerase-II but only one of the compounds (**29**) inhibited this enzyme at 40 μg / mL of reaction mixture.*

Keywords Nucleosides, DNA topoisomerase-II, Brugia malayi, Aza pyrimidines, Glycosylated amino ester

INTRODUCTION

Unnatural nucleosides, until recently, have dominated as antiviral, antitumor, and anticancer agents because of their involvement with one or more aspects of nucleic acid biosynthesis.[1–7] They have been obtained by condensation of unnatural sugars or natural sugar glycosyl donors and natural or unnatural purine or pyrimidine bases.[8] Azanucleosides (e.g., 6-aza Cyd) are structural analogues of natural nucleosides showing anticancer, antimycoplasmal, and antiviral effects.[9] Very recently, 6-azauridine has been reported to be incorporated into the genome of HDV ribozyme active sites.[10] Modified nucleosides have also been reported to occur in various types of RNA and many of them have been used as tools for the study of nucleic acid metabolism.[11] Nucleosides with modifications both in sugars and bases have been isolated from RNAs.[12,13] Many antibiotics are composed of nucleosides with modified amino sugars and are inhibitors of DNA-dependent RNA

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TABLE 1 Glycosyl β-Amino/Amido Esters and Diacetates

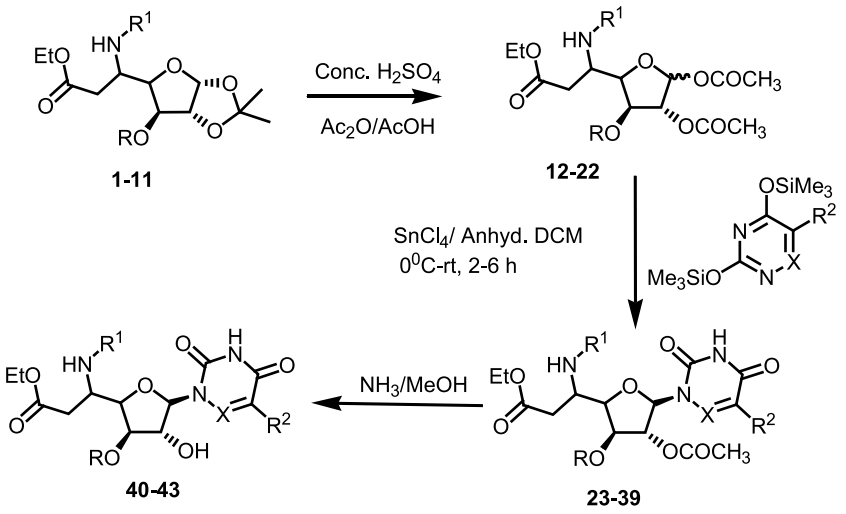
Sugar	Sugar acetate	R	R^1
1	**12**	CH_3	$H/COCH_3$
2	**13**	CH_2Ph	$H/COCH_3$
3	**14**	CH_3	Hexadecyl
4	**15**	CH_3	Cyclopropyl
5	**16**	CH_3	Furyl
6	**17**	CH_3	Benzyl
7	**18**	CH_3	$4\text{-}NO_2\text{-}COPh$
8	**19**	CH_2Ph	$4\text{-}NO_2\text{-}COPh$
9	**20**	CH_3	3-Cl-COPh
10	**21**	CH_2Ph	3-Cl-COPh
11	**22**	CH_2Ph	$CO(CH_2)_{12}CH_3$

polymerase of both prokaryotes and eukaryotes,[14–17] clearly pointing out their involvement in many reactions pertaining to the nucleic acid metabolism. Although β-nucleosides have extensively been studied for different biological activities,[18–31] α-nucleosides have received little attention in relation to biological activities. However, several such nucleosides are known to exhibit significant antimetabolic properties.[32] In an our ongoing program, we have recently shown that glycosyl amino esters and many other glycoconjugates developed by conventional and combinatorial approaches have proven to be very good DNA-topoisomerase-II inhibitor of filarial parasite.[33–35] Encouraged by this, we were interested to synthesize a few nucleosides from the amino sugars responsible for DNA-topoisomerase-II inhibitory activity. In the present study we describe the effect of unnatural nucleosides, obtained by condensation of glycosyl amino esters and modified pyrimidine bases onto the Filarial DNA-topoisomerase-II. Thus, in the present communication synthesis and DNA-topo-II inhibitory activity of such nucleosides is reported.

RESULTS AND DISCUSSION

The synthetic strategy begins with the glycosylated β-amino esters **1**, **2**, and **3–6** obtained by conjugate addition of ammonia and different primary amines as reported by us earlier.[33–35] However, the glycosyl amido esters **7–11** were obtained by the reaction of **1** or **2** with substituted carboxylic acids using DCC coupling procedure or with acid chloride in the presence of triethylamine, in very good yields.

The glycosyl donors, **14–22**, were prepared by the hydrolysis of 1,2-*O*-isopropylidene followed by acetylation of the resulting hemiacetal in one pot from **3–11** by concentrated H_2SO_4 in the presence of $Ac_2O/AcOH$ in good yields (Table 1) (Scheme 1). During the above reaction, acetylation of the amino group occurred in case of glycosyl amino esters **1** and **2** to give compounds **12** and **13**, respectively. The structures of all the products were determined on the basis of



SCHEME 1 Synthesis of unnatural nucleosides.

spectroscopic data; these were found to be mixtures of α- and β-anomers and were used as such without further purification. The glycosyl 1,2-di-*O*-acetates were obtained as epimeric mixtures of α- and β-anomers in a ratio of approximately 1:3 in all the cases reported. The α- and β-anomeric configuration was ascertained on the basis of coupling constant between H-1 (anomeric) and H-2. In glycosyl donors,

TABLE 2 Unnatural Nucleosides (**23–43**) Synthesized

Compound No.	R	R^1	X	R^2
23	CH_3	$COCH_3$	*N*	H
24	CH_3	$COCH_3$	*N*	CH_3
25	CH_3	$COCH_3$	*CH*	Br
26	CH_2Ph	$COCH_3$	*N*	H
27	CH_2Ph	$COCH_3$	*N*	CH_3
28	CH_3	Hexadecyl	*N*	CH_3
29	CH_3	Cyclopropyl	*N*	H
30	CH_3	Furyl	*N*	CH_3
31	CH_3	Benzyl	*N*	CH_3
32	CH_3	4-NO_2-COPh	*N*	H
33	CH_3	4-NO_2-COPh	*N*	CH_3
34	CH_3	4-NO_2-COPh	*CH*	Br
35	CH_2Ph	4-NO_2-COPh	*N*	CH_3
36	CH_2Ph	4-NO_2-COPh	*CH*	Br
37	CH_3	3-Cl-COPh	*N*	CH_3
38	CH_2Ph	3-Cl-COPh	*N*	H
39	CH_2Ph	$CO(CH_2)_{12}CH_3$	*N*	CH_3
40	CH_3	$COCH_3$	*N*	CH_3
41	CH_2Ph	$COCH_3$	*N*	H
42	CH_3	Cyclopropyl	*N*	H
43	CH_2Ph	4-NO_2-COPh	*N*	CH_3

signals for anomeric proton with J values 4.5 Hz and 0–1 Hz were assigned to α- and β-anomers respectively. Similarly, H-2 was a singlet in β-anomer, whereas it appeared as merged/overlapped *dd* in α-anomers, and is hence reported as *m*. Condensation of glycosyl donors with silyl derivatives of the pyrimidine bases was carried out using $SnCl_4$ as catalyst (Table 2).

6-Aza uracil, 5-bromo uracil, and 6-aza thymine bases were silylated to their corresponding *O*-silyl derivatives by reaction with HMDS in refluxing toluene in the presence of ammonium sulphate. Thus, glycosyl acetates (**12–22**), on condensation with silylated bases, afforded 2′-*O*-acetyl nucleosides (**23–39**) in good yields. The nucleosides were obtained as diastereoisomeric mixtures as the starting glycosyl acetates were diastereoisomeric mixtures. The structures of these nucleosides were established on the basis of spectroscopic data and analysis. The anomeric configuration was ascertained on the basis of proton magnetic resonance (^{1}H NMR) spectral data. As expected in the case of unsubstituted amino sugar, the anchimeric assistance due to 2′-acetyl group led to the formation of β-nucleosides stereoselectively. But, in the case of glycosyl donor having 5′-*N*-benzoyl substituents led to the formation of nucleosides with an α-configuration. The combined effect of 3′-*O*-substitution and the substituent at amine part has a greater effect on stereoselection, leading to formation of only the α-nucleosides in some of the cases (**27**, **35**, **39**). Nucleosides (**23–43**) in their MS (FAB) have characterstic $[M + H]^+$ signals corresponding to their molecular formulae. In IR spectrum of all the nucleosides, absorption bands at around 1680 cm^{-1} for the carbonyl group in the pyrimidine ring were present. The configuration anomeric center was determined on the basis of coupling constant of the anomeric proton (H-1′). In β-nucleosides $J_{1',2'}$ was found to be 0–2 Hz, while in α-nucleosides it was around 5.0 Hz; and the H-2′ appeared as overlapped/merged *dd* leading to an *m*-like signal. In ^{13}C NMR spectra of the above nucleosides, the anomeric C-1′ appeared at around δ 89–90. The C-2 and C-4 of the pyrimidine ring appeared at around δ 148.0 and 156.0, respectively, besides other usual signals. Analytical data were in accordance with the established structures.

Four of the above nucleosides (**24**, **26**, **29**, and **35**) were deacetylated by treatment with ammonia in methanol at ambient temperature to get 2′-hydroxy nucleosides (**40–43**) in quantitative yields. In deacetylated nucleosides the anomeric proton shifted to upfield in comparison to the acetylated ones. The structures of all these nucleosides were also established on the basis of spectroscopic data and analysis.

DNA Topoisomerase-II Inhibitory Activity

As shown in Figure 1, only one of the compounds synthesised (**29**) exhibited topoisomerase–II inhibitory activity up to only 40%, while the other compounds have no inhibition against this enzyme. However, compound **39** formed complex with DNA, and compounds **23**, **24**, **27**, **30**, and **31** caused degradation/cleavage of DNA. Topo inhibitors like TAS-103, a novel antineoplastic agent, also

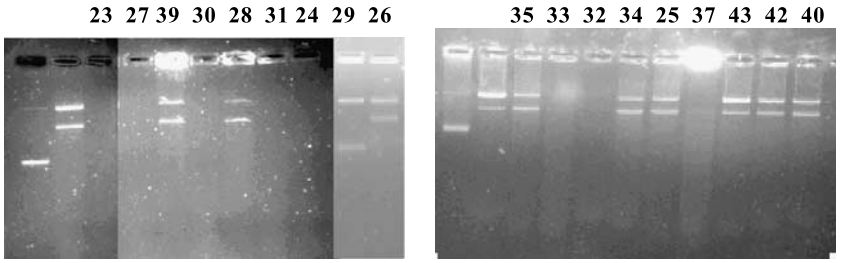


FIGURE 1 Inhibition of *Setaria cervi* topoisomerase-II by unnatural nucleosides. The enzyme activity was monitored as described in the text. In both figures, Lane 1, pBR322 DNA alone; Lane 2, DNA + *S. cervi* topoisomerase II.

caused topoisomerase-II–mediated DNA cleavage in treated cells, indicating that these, too, act as a novel antineoplastic agent.[36] Compounds 26 and 27 were tested against HEV (herpes encephalytis virus) and many of them were screened for their in vitro antimycobacterial activity, but none of them showed any significant activity.

DNA Topoisomerase II Estimation

Adult parasites of *Setaria cervi* were obtained from local abattoir and brought to the laboratory in 0.85% NaCl. Adult *Brugia malayi* were recovered from the peritoneal cavity of gerbil infected 90–180 days intraperitoneally. Worms were thoroughly washed in saline and homogenized in homogenizing medium (10% homogenate). Protein content was measured by the method of Lowry et al.[37] The reaction catalyzed by DNA topo-II was estimated as reported earlier.[38] The reaction mixture in a final volume of 20 µl contained 50 mM Tris-HCl, pH 7.5; 50 mM KCl; 10 mM $MgCl_2$; 1 mM ATP; 0.1 mM EDTA; 0.5 mM DTT; 30 µg/ml BSA; 0.25 µg pBR322 DNA; and enzyme protein. The reaction was carried out at 37°C for 30 min. and stopped by adding 5 µl of stop buffer. The samples were electrophoresed on 1% agarose gel in Tris-acetate buffer for 18 h at 20 V. Gels were stained with ethidium bromide (0.5 µg/mL) and visualized and photographed on a GDS 7500 UVP Trans-Illuminator (Ultraviolet Products, U.K.). Incubating enzyme protein with the inhibitor for 10 min. at 37°C and starting the reaction by addition of pBR322 measured the effect of inhibitors on the enzyme activity. The percent inhibition was measured by micro densitometry of the gel with a gel base/gel blot Progel analysis software programme.

EXPERIMENTAL

General Methods

Thin-layer chromatographies were carried out on silica gel (Kiesel 60-F254, Merck), spots were developed in iodine vapors and by spraying with 5% sulfuric

acid in alcohol followed by heating at 100°C. Column chromatographies were carried out on silica gel (120–230 mesh, Merck) using the indicated eluent. IR spectra of liquids were recorded as thin films on KBr plates with a Perkin Elmer 881 spectrophotometer. NMR spectra were recorded on Bruker spectrometers 200 MHz or 300 MHz and the reference used was $CDCl_3$. Chemical shifts were given as δ ppm values and *J* values were given in Hertz (Hz). Elemental analyses were performed on a Perkin-Elmer 2400 II elemental analyzer. The optical rotations were measured in a 1.0 dm tube with Jasco dip-140 polarimeter in chloroform, methanol, or ethyl acetate. The excess of the reagents or solvents were evaporated under reduced pressure at a bath temperature between 45 and 55°C.

General Procedure for the Synthesis of Compounds 7–10

Ethyl[5,6-dideoxy-1,2-di-O-isopropylidene-3-*O*-methyl-5-*N*-(4-nitrobenzoyl)amino]-α-D-*gluco* and-β-L-*ido*-hepto-1,4-furanuronate (7). A mixture of 4-nitrobenzoic acid (2.60 g, 7.58 mmol), dicyclohexyl carbodimide (2.10 g, 7.8 mmol), and dimethylamino pyridine (1.54 g, 3.8 mmol) in anhydrous dichloromethane (50.0 mL) was stirred magnetically at 0°C for five min. A solution of ethyl-5-amino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*gluco* and β-L-*ido*-1,4-heptofuranuronate (**1a**, 2.0 g, 4.10 mmol) in anhydrous dichloromethane (10.0 mL) was added drop-wise over a period of 30 min. to the stirring reaction mixture and stirring continued at ambient temperature for 6 h. After disappearance of starting material (tlc), the reaction mixture was filtered and the filtrate concentrated under reduced pressure. The residue thus obtained was dissolved in ethyl acetate, washed with aqueous NH_4Cl (2 × 25 mL) and water (2 × 20 mL). The organic layer was dried (Na_2SO_4) and concentrated under reduced pressure to give a crude mass, which was chromatographed over SiO_2 column using hexane:ethyl acetate (4:1) as eluent to give compound **7** as colorless foam 2.16 g (92%), Rf 0.50 (7:3 hexane/ethyl acetate); $[\alpha]_D^{25}$ − 32.33 (*c* 0.3, CH_3OH). MS (FAB): *m/z* 439 $(M + H)^+$; IR (Neat), ν_{max}: 3292, 2932, 1727, 1658, 1629, 1600, and 1527 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.28 and 7.92 (d, *J* = 8.8 Hz, 2H, ArH), 7.58, 7.04 (d, *J* = 8.1 Hz, 1H, diastereomeric NHCO); 5.94, 5.90 (d, *J* = 3.8 Hz, 1H, diastereomeric H-1); 4.94–4.72 (two m, 1H, diastereomeric H-5), 4.63–4.60 (m, 1H, diastereomeric H-2); 4.45–4.30 (m, 1H, diastereomeric H-4); 4.14 (q, *J* = 7.1 Hz, 2H, —O*C*H_2CH_3); 3.90, 3.75 (d, *J* = 3.2 Hz, 1H, diastereomeric H-3); 3.45, 3.39 (s, 3H, diastereomeric —OCH_3); 2.94–2.68 (m, 2H, H-6); 1.49, and 1.32 [s, 6H, $(CH_3)_2C$]; 1.25 (t, *J* = 7.1 Hz, 3H, —OCH_2C*H*$_3$). Anal. Calcd for $C_{20}H_{26}N_2O_9$: C, 54.79; H, 5.98; N, 6.39. Found: C, 54.92; H, 6.23; N, 6.11.

Ethyl[3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-*N*-(4-nitrobenzoyl)amino]-β-L-*ido*-hepto-1,4-furanuronate (8). Colorless solid, mp 181°C; yield 1.90 g (95%), Rf 0.55 (7:3 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 8.00 (*c* 0.275, CH_3OH). MS (FAB): *m/z* 514 $(M + H)^+$, IR(KBr) ν_{max}: 3336, 2985, 2929, 1738, 1656, 1600, 1547, 1519, 1460, and 1377 cm^{-1}. ^1H NMR

(200 MHz, $CDCl_3$): δ 8.15 and 7.74 (d, J = 8.4 Hz, 2H, ArH); 7.25 (m, 5H, ArH); 6.95 (d, J = 7.8 Hz, 1H, NHCO); 5.99 (d, J = 3.8 Hz, 1H, H-1); 4.88–4.84 (m, 1H, H-5); 4.69–4.64 (m, 2H, —OCH_APh and H-2); 4.48–4.41 (m, 2H, —OCH_BPh and H-4); 4.13 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.99 (d, J = 3.2 Hz, 1H, H-3); 2.72–2.66 (m, 2H, H-6); 1.49, 1.33 [s, 6 H, $(CH_3)_2C$]; 1.25 (t, J = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{26}H_{30}N_2O_9$: C, 60.69; H, 5.88; N, 5.44. Found: C, 61.01; H, 6.04; N, 5.23.

Ethyl[5-*N*-(3-chlorobenzoyl)amino-5,6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl]-α-D-*gluco* and-β-L-*ido*-hepto-1,4-furanuronate (9). Colorless foam; yield 2.32 g (89%), Rf 0.45 (7:3 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 2.28 (*c* 0.525, CH_3OH). MS (FAB): *m/z* 429 $(M + H)^+$, IR(KBr), ν_{max}: 3360, 2988, 2936, 1729, 1652, 1536, 1469, and 1377 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.75 (s, 1H, ArH); 7.63 (d, J = 7.5 Hz, 1H, ArH); 7.43–7.34 (m, 2H, ArH); 6.94 (d, J = 8.2 Hz, 1H, NHCO); 5.94 (d, J = 3.9 Hz, 1H, H-1); 4.95–4.78 (m, 1H, H-5); 4.60 (d, J = 3.9 Hz, 1H, H-2); 4.51–4.46 (m, 1H, H-4); 4.16 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.74 (d, J = 3.2 Hz, 1H, H-3); 3.38 (s, 3H, —OCH_3); 2.81–2.70 (m, 2H, H-6); 1.49, 1.32 [s, 3H, $(CH_3)_2C$]; 1.25 (t, J = 7.1 Hz, 6H, —OCH_2CH_3). Anal. Calcd for $C_{20}H_{26}ClNO_7$: C, 56.14; H, 6.12; N, 3.27. Found: C, 56.44; H, 6.41; N, 3.08.

Ethyl[3-*O*-benzyl-5-*N*-(3-chlorobenzoyl)amino-5,6-dideoxy-1,2-*O*-isopropylidene]-α-D-*gluco* and-β-L-*ido*-hepto-1,4-furanuronate (10). Colourless foam; yield 1.85 g (93%), Rf 0.50 (7:3 hexane/ethyl acetate), $[\alpha]_D^{25}$ −6.40 (*c* 0.250, CH_3OH). MS (FAB): *m/z* 504 $(M + H)^+$, IR(KBr), ν_{max}: 3368, 2983, 2928, 1730, 1658, 1570, 1536, and 1465, 1377 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.64 (s, 1H, ArH); 7.51–7.22 (m, 8H, ArH); 6.79 (d, J = 8.1 Hz, 1H, NHCO); 5.98 (d, J = 3.8 Hz, 1H, H-1); 4.87–4.74 (m, 1H, H-5); 4.68–4.63 (m, 2H, —OCH_APh and H-2); 4.47–4.42 (m, 2H, —OCH_BPh and H-4); 4.12 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.97 (d, J = 3.2 Hz, 1H, H-3); 2.84–2.57 (m, 2H, H-6); 1.59, 1.49 [s, 6H, $(CH_3)_2C$]; 1.23 (t, J = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{26}H_{30}NO_7Cl$: C, 61.96; H, 6.00; N, 2.78. Found: C, 62.23; H, 6.32; N, 2.57.

Ethyl[3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-5-*N*-(tetradecanoyl)amino]-β-L-*ido*-hepto-1,4-furanuronate (11). Ethyl[5-amino-3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene]-β-L-*ido*-1,4-heptofuranuronate (**1a**, 1.5 g, 4.10 mmol) was dissolved in anhydrous dichloromethane and stirred magnetically at 0°C for 10 min. followed by the addition of triethyl amine (1.0 mL, 9.0 mmol). Myristoyl chloride (2.6 mL, 4.20 mmol) was taken in anhydrous dichloromethane and added drop-wise over a period of 30 min. to the stirring reaction mixture and stirring continued at 30°C for 3 h. After disappearance of starting material (tlc), the reaction mixture was filtered, concentrated under reduced pressure, residue dissolved in ethyl acetate and washed with aqueous NH_4Cl (2 × 25 mL) and water (2 × 20 mL). The organic layer was dried (Na_2SO_4) and

concentrated under reduced pressure to give a crude mass, which was chromatographed over SiO_2 column using hexane:ethyl acetate (5:1) as eluent to give compound **11**. Colorless solid, mp 121–123°C, yield 2.24 g (95%), Rf 0.65 (7:3 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 12.57 (*c* 0.175, CH_3OH). MS (FAB): *m/z* 575 $(M + H)^+$, IR(KBr), ν_{max}: 2925, 2856, 1733, 1656, 1541, and 1459 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.35–7.32 (m, 5H, ArH); 5.99 (d, *J* = 8.0 Hz, 1H, NHCO); 5.94 (d, *J* = 3.8 Hz, 1H, H-1); 4.69–4.54 (m, 3H, —OCH_APh, H-2 and H-5); 4.40–4.35 (m, 2H, —OCH_BPh and H-4); 4.09 (q, *J* = 7.1 Hz, 2H, —OCH_2CH_3); 3.90 (d, *J* = 3.2 Hz, 1H, H-3); 2.64 (dd, *J* = 16.1 and 6.0 Hz, 1H, H-6_A); 2.49 (dd, *J* = 16.1 and 5.3 Hz, 1H , H-6_B); 2.06–1.98 (m, 2H, $COCH_2$); 1.48, 1.32 [s, 6H, $(CH_3)_2C$], 1.23 (m, 25H, 11 × CH_2 and OCH_2CH_3). Anal. Calcd for $C_{33}H_{53}NO_7$: C, 68.84; H, 9.28; N, 2.43. Found: C, 69.13; H, 9.54; N, 2.19.

General Procedure for the Synthesis of Compounds 12—22

Ethyl[5-*N*-(acetyl)amino-1,2-di-*O*-acetyl-5,6-dideoxy-3-*O*-methyl)]-α-D-*gluco* and β-L-*ido*-hepto-1,4-furanuronate (12). To a stirring solution of ethyl-5-amino-5, 6-dideoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*gluco* and β-L-*ido*-1,4-heptofuranuronate (**1a**, 3.0 g, 10.38 mmol) in glacial acetic acid (15.0 mL) at 0°C, acetic anhydride (1.5 mL) was added and stirring continued at the same temperature. After 10 min., concentrated sulfuric acid (0.2 mL) was added and the stirring further continued for 12 h. The reaction mixture was poured on crushed ice containing sodium bicarbonate and it was extracted repeatedly with chloroform. The organic layer dried (Na_2SO_4) and concentrated under reduced pressure to get a crude product, which on column chromatography (SiO_2) using chloroform/methanol (99:1) as eluent afforded compound **12** as yellowish foam; yield 3.68 g (89%), Rf 0.35 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 15.69 (*c* 0.325, CH_3OH). MS (FAB): *m/z* 376 $(M + H)^+$, IR(Neat) ν_{max}: 3377, 2987, 1741, 1662, 1543, 1440, and 1373 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 6.40 (d, *J* = 4.5 Hz, 1H, H-1, α-anomer); 6.09 (s, 1H, H-1, β-anomer); 5.21 (s, 1H, H-2, β-anomer); 5.17–5.12 (m, 1H, H-2, α-anomer); 4.68–4.51 (m, 2H, H-4 and H-5); 4.11 (q, *J* = 7.1 Hz, 2H, —OCH_2CH_3); 3.78 (d, *J* = 2.1 Hz, 1H, H-3); 3.47, 3.46, 3.45, and 3.42 (s, 3H, —OCH_3 of diastereomeric anomers); 2.68–2.64 (m, 2H, H-6); 2.11, 2.10, and 1.95 [s, 9H, 2 × $OCOCH_3$ and $NHCOCH_3$]; 1.25 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{16}H_{25}NO_9$: C, 51.20; H, 6.71; N, 3.73. Found: C, 51.43; H, 6.92; N, 3.60.

Ethyl[1,2-di-*O*-acetyl-3-*O*-benzyl-5-*N*-acetyl-5,6-dideoxy)]-β-L-*ido*-hepto-1,4-furanuronate (13). Yellow oil; yield 2.68 g (92 %), Rf 0.40 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ −7.66 (*c* 0.30, CH_3OH). MS (FAB): *m/z* 451 $(M + H)^+$, IR(Neat), ν_{max}: 3373, 2371, 1739, 1661, 1545, 1437, and 1373 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.35 (m, 5H, ArH); 6.41 (d, *J* = 4.5 Hz, 1H, H-1, α-anomer); 6.04 (d, *J* = 7.8 Hz, 1H, NHCO); 5.27 (s, 1H, H-1, β-anomer); 5.27–5.23 (m, 1H, H-2, α-anomer); 4.77(d, *J* = 11.8 Hz, 1H, OCH_APh); 4.64–4.51 (m, 3H,

OCH_APh, H-5 and H-4); 4.11 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.98 (d, J = 4.6 Hz, 1H, H-3); 2.62 (d, J = 5.4 Hz, 2H, H-6); 2.11, 2.0, and 1.81 [s, 9H, 2 × $OCOCH_3$ and $NHCOCH_3$]; 1.25 (t, J = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{22}H_{29}NO_9$: C, 58.53; H, 6.47; N, 3.10. Found: C, 58.82; H, 6.73; N, 3.01.

Ethyl[1,2-di-*O*-acetyl-5,6-dideoxy-5-hexadecylamino-3-*O*-methyl)]-β-L-*ido*-hepto-1,4-furanuronate (14). Yellow oil; yield 1.22 g (90%), Rf 0.60 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 23.41 (*c* 0.1375, CH_3OH). MS (FAB): *m/z* 558 $(M + H)^+$, IR(KBr), ν_{max}: 3341, 2983, 1730, 1247, 1177, 1028, and 757 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 6.42 (d, J = 4.6 Hz, 1H, H-1, α-anomer); 6.11 (s, 1H, H-1, β-anomer); 5.19 (s, 1H, H-2, β-anomer); 5.18–5.11 (m, 1H, H-2, α-anomer); 4.66–4.49 (m, 2H, H-4 and H-5); 4.03 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.68 (d, J = 2.1 Hz, 1H, H-3); 3.45, 3.41 (s, 3H, —OCH_3), 2.68–2.64 (m, 2H, H-6); 2.06, 2.04 (s, 6H, 2 × $OCOCH_3$); 1.55 (m, 2H, $NHCH_2CH_2$); 1.25 (m, 33H, − 15 × CH_2's and OCH_2CH_3). 0.87 (t, J = 6.9 Hz, 3H, —CH_2CH_3). Anal. Calcd for $C_{30}H_{55}NO_8$: C, 64.60; H, 9.94; N, 2.51. Found: C, 64.71; H, 10.23; N, 2.38.

Ethyl[1,2-di-*O*-acetyl-5-cyclopropylamino-5,6-dideoxy-3-*O*-methyl)]-β-L-*ido*-hepto-1,4-furanuronate (15). Colorless oil; yield 1.13 g (88%), Rf 0.50 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 12.72 (*c* 0.2625, CH_3OH). MS (FAB): *m/z* 374 $(M + H)^+$, IR(KBr), ν_{max}: 3355, 3048, 2978, 2923, 2845, and 1721 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 6.38 (d, J = 4.5 Hz, 1H, H-1, α-anomer); 6.12 (s, 1H, H-1, β-anomer); 5.24 (s, 1H, H-2, β-anomer); 5.21–5.18 (m, 1H, H-2, α-anomer); 4.68–4.51 (m, 2H, H-4 and H-5); 4.08 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.59 (d, J = 2.1 Hz, 1H, H-3); 3.47 and 3.45 (s, 3H, —OCH_3); 2.72–2.66 (m, 2H, H-6); 2.08, and 2.05 (s, 6H, 2 × $OCOCH_3$); 1.88 (m, 1H, NHCH); 1.26 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); 0.55–0.48 (m, 4H, cyclopropyl CH_2). Anal. Calcd for $C_{17}H_{27}NO_8$: C, 54.68; H, 7.29; N, 3.75. Found: C, 54.82; H, 7.53; N, 3.55.

Ethyl[1,2-di-*O*-acetyl-5,6-dideoxy-5-furylamino-3-*O*-methyl)]-β-L-*ido*-hepto-1,4-furanuronate (16). Colorless foam; yield 1.32 g (85%), Rf 0.45 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 11.32 (*c* 0.1750, CH_3OH). MS (FAB): *m/z* 415 $(M + H)^+$, IR(KBr), ν_{max}: 3341, 2983, 1730, 1247, 1177, 1028, and 757 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.42 (s, 1H, furyl H); 6.88–6.82 (m, 2H, furyl H); 6.40 (d, J = 4.5 Hz, 1H, H-1, α-anomer); 6.09 (s, 1H, H-1, β-anomer); 5.21 (s, 1H, H-2, β-anomer); 5.17–5.12 (m, 1H, H-2, α-anomer); 4.68–4.51 (m, 2H, H-4 and H-5); 4.11 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.78 (d, J = 2.1 Hz, 1H, H-3); 3.62 (s, 2H, NCH_2); 3.51, 3.49 (s, 3H, —OCH_3); 2.72–2.65 (m, 2H, H-6); 2.11, 2.10 [s, 6H, 2 × $OCOCH_3$]; 1.25 (t, J = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{19}H_{27}NO_9$: C, 55.20; H, 6.58; N, 3.39. Found: C, 54.92; H, 6.83; N, 3.15.

Ethyl[1,2-di-*O*-acetyl-5-benzylamino-5,6-dideoxy-3-*O*-methyl)]-α-D-*gluco* and β-L-*ido*-hepto-1,4-furanuronate (17). Colorless

foam; yield 1.20 g (90%), Rf 0.50 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 24.31 (*c* 0.1875, CH_3OH). MS (FAB): *m/z* 424 $(M + H)^+$, IR (Neat) ν_{max}: 3378, 2364, 1730, 1527, 1555, 1381, 1216, 1077, 759, and 670 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.27–7.24 (m, 5H, ArH); 6.38 (d, *J* = 4.5 Hz, 1H, H-1, α-anomer); 6.05 (s, 1H, H-1, β-anomer); 5.18 (s, 1H, H-2, β-anomer); 5.13–5.07 (m, 1H, H-2, α-anomer); 4.68–4.51 (m, 3H, H-4, H-5 and NCH_A); 4.38 (d, *J* = 15.6 Hz, 1H, and NCH_B); 4.02 (q, *J* = 7.1 Hz, 2H, —OCH_2CH_3); 3.82 (d, *J* = 2.1 Hz, 1H, H-3); 3.46, 3.44 (s, 3H, —OCH_3); 2.71–2.65 (m, 2H, H-6); 2.11, 2.10 [s, 6H, 2 × $OCOCH_3$]; 1.25 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{21}H_{29}NO_8$: C, 59.56; H, 6.90; N, 3.31; Found: C, 59.84; H, 7.22; N, 3.03.

Ethyl[1,2-di-*O*-acetyl-5,6-dideoxy-3-*O*-methyl-5-*N*-(4-nitrobenzoyl)amino]-α-D-*gluco* and-β-L-*ido*-hepto-1,4-furanuronate (18). Colorless oil; yield 1.8 g (96%), Rf 0.62 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ −12.16 (*c* 0.3125, CH_3OH). MS (FAB): *m/z* 483 $(M + H)^+$, IR(KBr) ν_{max}: 3344, 2935, 1741, 1660, 1601, 1529, 1348, and 1223 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.27 and 7.91 (d, *J* = 8.6 Hz, 2H, ArH); 6.86, 6.82 (d, *J* = 0.8 Hz, NHCO of anomers); 6.44 (d, *J* = 4.5 Hz, 1H, H-1, α-anomer); 6.13 (s, 1H, H-1, β-anomer); 5.26 (s, 1H, H-2, β-anomer); 5.20–5.15 (m, 1H, H-2, α-anomer); 4.90–4.71 (m, 1H, H-5); 4.68–4.50 (m, 1H, H-4); 4.11 (q, *J* = 7.1 Hz, 2H, —OCH_2CH_3); 3.87 (d, *J* = 2.1 Hz, 1H, H-3); 3.46, 3.43 (s, 6H, —OCH_3 of two anomers); 2.81–2.75 (m, 2H, H-6); 2.11, 2.09 (s, 3H, 2 × $OCOCH_3$); 1.26 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{21}H_{26}N_2O_{11}$: C, 52.28; H, 5.43; N, 5.81; Found: C, 52.54; H, 5.62; N, 5.70.

Ethyl[3-*O*-benzyl-1,2-di-*O*-acetyl-5,6-dideoxy-5-*N*-(4-nitrobenzoyl)]-β-L-*ido*-hepto-1,4-furanuronate (19). Colorless solid, mp 144°C; yield 1.6 g (98%), Rf 0.68 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 24.6 (*c* 0.17, CH_3OH). MS (FAB): *m/z* 559 $(M + H)^+$, IR(KBr) ν_{max}: 3421, 3022, 2931, 2859, 1740, 1663, 1602, 1528, 1488, and 1347 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.14 and 7.72 (d, *J* = 8.7 Hz, 2H, ArH); 7.29–7.21 (m, 5H, ArH); 6.88, 6.84 (d, *J* = 7.8 Hz, 1H, NHCO of anomers); 6.41 (d, *J* = 4.5 Hz, 1H, H-1, α-anomer); 6.18 (s, 1H, H-1, β-anomer); 5.32 (m, 1H, H-2, β-anomer); 5.28–5.26 (m, 1H, H-2, α-anomer); 4.86–4.78 (m, 1H, H-5); 4.74 (d, *J* = 11.4 Hz, 1H, OCH_APh); 4.66–4.51 (m, 2H, OCH_BPh and H-4); 4.13 (m, 3H, —OCH_2CH_3 and H-3); 2.78–2.74 (m, 2H, H-6); 2.13, 2.04, 2.10, and 2.09 (s, 6H, 2 × $OCOCH_3$ of anomers); 1.25 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{27}H_{30}N_2O_{11}$: C, 58.06; H, 5.41; N, 5.02; Found: C, 58.34; H, 5.73; N, 4.92.

Ethyl[1,2-di-*O*-acetyl-5-*N*-(3-chlorobenzoyl)-5,6-dideoxy-3-*O*-methyl]-α-D-*gluco* and-β-L-*ido*-hepto-1,4-furanuronate (20). Colorless oil; yield 1.75 g (94%), Rf 0.56 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ −27.29 (*c* 0.2125, CH_3OH). MS (FAB): *m/z* 473 $(M + H)^+$, IR (Neat) ν_{max}: 3328.9, 2988, 2935, 2855, 1743, 1655, 1538, 1471, 1426, and 1372 cm^{-1}; ^1H NMR (200MHz,

$CDCl_3$): δ 7.75 (s, 1H, ArH); 7.74–7.28 (m, 4H, ArH); 6.84, 6.81 (d, J = 7.8 Hz, 1H, –NHCO of anomers); 6.41, 6.36 (d, J = 4.5 Hz, 1H, H-1 diastereomeric α-anomers); 6.15, 6.12 (s, 1H, H-1 of β-anomers); 5.24, 5.21(s, 1H, H-2 of β-anomers); 4.95–4.55 (m, 2H, H-5 and H-4 of diastereomers); 4.14 (q, J = 7.1 Hz, 2H, —OCH_2CH$_3$); 3.92–3.86 (m, 1H, H-3 of diastereomers); 3.53 and 3.44 (s, 6H, —OCH_3 of two anomers); 2.84–2.72 (m, 2H, H-6); 2.11, 2.09 (s, 6H, 2 × $OCOCH_3$); 1.26 (t, J = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{21}H_{26}NO_9Cl$: C, 53.45; H, 5.55; N, 2.97. Found: C, 53.71; H, 5.82; N, 2.73.

Ethyl[1,2-di-*O*-acetyl-3-*O*-benzyl-5-*N*-(3-chlorobenzoyl)-5,6-dideoxy]-α-D-*gluco* and-β-L-*ido*-hepto-1,4-furanuronate (21). Colorless foam; yield 1.42 g (95%), Rf 0.00 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 9.84 (*c* 0.4875, CH_3OH). MS (FAB): *m/z* 549 $(M + H)^+$, IR(KBr) ν_{max}: 3431, 3019, 2930, 2858, 1741, 1661, 1568, 1523, 1469, and 1373 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.59 and 7.53 (s, 1H, ArH of anomers); 7.49–7.30 (m, 4H, ArH); 7.29–7.24 (m, 5H, ArH); 6.86, 6.82 (d, J = 8.1 Hz, 1H, NHCO of anomers); 6.43 (d, J = 4.5 Hz, 1H, H-1, α-anomer); 6.18 (s, 1H, H-1, β-anomer); 5.28 (m, 1H, H-2, β-anomer); 5.27–5.23 (m, 1H, H-2, α-anomer); 4.76–4.51 (m, 4H, —OCH_2Ph, H-4 and H-5); 4.17–4.06 (m, 3H, —OCH_2CH_3 and H-3); 2.78–2.71 (m, 2H, H-6); 2.11, 2.03, 2.07 and 2.06 (s, 6H, 2 × $OCOCH_3$ of anomers), 1.25 (t, J = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd for $C_{27}H_{30}NO_9Cl$: C, 59.18; H, 5.52; N, 2.56; Found: C, 59.42; H, 5.81; N, 2.32.

Ethyl[1,2-di-*O*-acetyl-3-*O*-benzyl-5-*N*-tetradecanoyl-5,6-dideoxy]-α-D-*gluco* and-β-L-*ido*-hepto-1,4-furanuronate (22). Colorless oil; yield 2.8 g (96%), Rf 0.70 (3:2 hexane/ethyl acetate), $[\alpha]_D^{25}$ − 12.57 (*c* 0.45, CH_3OH). MS (FAB): *m/z* 620 $(M + H)^+$, IR(KBr), ν_{max}: 3444, 2926, 2855, 2363, 1743, 1653, 1552, 1460, and 1379 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.36–7.34 (m, 5H, ArH); 6.41 (d, J = 4.5 Hz, 1H, H-1, α-anomer); 6.14 (s, 1H, H-1, β-anomer); 5.98 and 5.90 (d, J = 7.53 Hz, 1H, NHCO of anomers); 5.26 (m, 1H, H-2, β-anomer); 5.20–5.18 (m, 1H, H-2, α-anomer); 4.77 (d, J = 11.8 Hz, 1H, —OCH_BPh); 4.70–4.51 (m, 3H, —OCH_BPh, H-4 and H-5); 4.22–4.03 (m, 2H, —OCH_2CH_3); 3.97 (d, J = 4.77 Hz, 1H, H-3); 2.64 (d, J = 5.4 Hz, 2H, H-6); 2.11, 2.00 (s, 6H, 2 × $OCOCH_3$ of anomers); 1.50 (m, 2H, $COCH_2$); 1.25–1.19 (m, 25H, 11 × CH_2 and OCH_2CH_3); (t, J = 6.9 Hz, 3H, CH_2CH_3). Anal. Calcd for $C_{34}H_{53}NO_9$: C, 65.89; H, 8.62; N, 2.26; Found: C, 66.18; H, 8.96; N, 2.02.

General Procedure for the Synthesis of Compounds 23—39

6-Aza-1-[ethyl-(5′-*N*-acetylamino-2′-*O*-acetyl-5′,6′-dideoxy-3′-*O*-methyl-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil. (23). A mixture of ethyl[5-*N*-(acetyl)amino-1,2-di-*O*-acetyl-5,6-dideoxy-3-*O*-methyl)]-α-D-*gluco* and β-L-*ido*-hepto-1,4-furanuronate, **12** (1.20 g, 4.29 mmol) and the silylated 6-aza uracil (0.6 g, 5.0 mmol) were stirred at 0°C for 10 min. followed by the addition of $SnCl_4$ (1.0 mL, 5.0 mmol). The stirring was continued from 0°C

to rt for 4 h. After disappearance of the starting material (tlc) the reaction mixture was poured on crushed ice over sodium bicarbonate, extracted in chloroform (2 × 25 mL), dried (Na_2SO_4), and concentrated at reduced pressure to get crude residue, which on column chlromatography using chloroform:methanol (49:1) as eluent afforded **23** as colorless solid, mp 181°C; yield 0.55 g (61%), Rf 0.40 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 94.28 (*c* 0.175, CH_3OH). MS (FAB): *m/z* 429 $(M + H)^+$; IR (KBr) ν_{max}: 3426, 3020, 1702, 1654, 1522, and 1372 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.50 and 7.48 (s, 1H, H-5 of α and β anomers); 6.82 and 6.56 (d, *J* = 9.0 Hz, 1H, NHCO); 6.05 (d, *J* = 3.3 Hz, 1H, H-1′, β anomer); 6.02 (d, *J* = 5.0 Hz, 1H, H-1′, α anomer); 5.48 (m, 1H, H-2′); 4.73 (m, 1H, H-5′, β anomer); 4.53–4.51 (m, 2H, H-4′and H-5′ of α anomer); 4.34 (dd, J = 5.4 and 3.0 Hz, H-4′, β anomer); 4.12 (q, *J* = 7.1 Hz, 2H, —OCH_2); 4.03 (dd, *J* = 6.0 and 4.2 Hz , 1H, H-3′, α anomer); 3.89 (d, *J* = 4.5 Hz , 1H, H-3′, β anomer); 3.46, 3.44 (s, 3H, —OCH_3); 2.66–2.58 (m, 2H, H-6′); 2.11, 2.10, 1.98, 1.96 (s, 6H, $OCOCH_3$ and $NHCOCH_3$); 1.25, 1.24 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 172.3, 171.82, 170.67, 170.3, and 170.1 (*C*OOEt and O*C*OCH_3 NH*C*OCH_3 of anomers); 156.1 (C-4); 148.2 (C-2); 136.7, 136.6 (C-5); 89.6, 88.9 (C-1′); 84.5, 83.07 (C-2′); 81.1, 80.03 (C-4′); 77.9, 77.4 (C-3′); 61.2 (—OCH_2); 58.7, 58.0 (OCH_3); 46.1, 45.8 (C-5′); 36.6 (C-6′); 23.8, 23.7, 21.1, 21.0, and 14.50 (OCO*C*H_3, $NHCOCH_3$, and OCH_2CH_3). Anal. Calcd. for $C_{17}H_{24}N_4O_9$: C, 47.66; H, 5.65; N, 13.08; Found: C, 47.92; H, 5.84; N, 12.89.

6-Aza-1-[ethyl-(5′-N-acetylamino-2′-*O*-acetyl-5′,6′-dideoxy-3′-*O*-methyl-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] thymine (24): Yellow foam; yield 0.34 g (59%), Rf 0.45 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 60.30 (*c* 0.325, CH_3OH). MS (FAB): *m/z* 443 $(M + H)^+$, IR(KBr) ν_{max}: 3425, 2987, 2363, 1725, 1656, 1551, and 1442 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 9.70 and 9.28 (bs, 1H, NH); 6.01 (d, *J* = 2.5 Hz 1H, H-1′); 5.99 (d, *J* = 4.9 Hz 1H, H-1′ α anomer); 5.63–5.58 (m, 1H, H-2′); 4.56–4.48 (m, 1H, H-4′); 4.11 (q, *J* = 7.1 Hz, 2H, —O*C*H_2CH_3); 3.82 (m, 1H, H-5′); 3.48 (d, *J* = 5.4 Hz, 1H, H-3′); 3.44 (s, 3H, OCH_3); 2.66 (d, *J* = 5.8 Hz, each 2H, H-6); 2.30, 2.11, and 1.99 (s, 9H, $OCOCH_3$, $NHCOCH_3$ and = CCH_3); 1.27 (t, *J* = 7.1 Hz, 3H, —OCH_2C*H*$_3$). ^{13}C NMR ($CDCl_3$): δ 172.3, 171.8, 170.6, 170.2, and 170.1 (*C*OOEt, O*C*OCH_3 and NH*C*OCH_3 of anomers); 156.5 (C-4); 149.2 (C-2); 145.4, 145.0 (C-5); 89.5, 88.7 (C-1′); 84.4, 83.1 (C-2′); 81.1, 79.8 (C-4′); 77.5, 76.9 (C-3′); 61.1 (—OCH_2); 58.4, 57.8 (OCH_3); 46.3, 45.9 (C-5′); 36.5 (C-6′); 21.1, 16.8, and 14.50 (OCO*C*H_3, $NHCOCH_3$, and OCH_2CH_3). Anal Calcd. for $C_{18}H_{26}N_4O_9$: C, 48.87; H, 5.92; N, 12.66; Found: C, 49.17; H, 6.14; N, 12.52.

5-Bromo-1-[ethyl-(5′-*N*-acetylamino-2′-*O*-acetyl-5′,6′-dideoxy-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (25). Yellow solid, 163°C; yield 0.25 g (54%), Rf 0.55 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ + 13.33 (*c* 0.075, CH_3OH). MS (FAB): *m/z* 506 $(M + H)^+$, IR(KBr), ν_{max}: 3341, 2936, 1725, 1680, 1660, 1444, 1374, 1231, and 1059 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 9.15 (bs, 1H, NH); 8.18, 7.72 (s, 1H, H-6

of diastereomers); 6.49, 6.43 (d, J = 9.0 Hz, 1H, NHCO); 5.92 (s, 1H, H-1′); 5.25 (s, 1H, H-2′); 4.85–4.70 (m, 1H, H-5′); 4.50–4.32 (m, 1H, H-4′ of diastereomers); 4.13 (q, J = 7.1 Hz, 2H, —OCH_2); 3.68 (d, J = 2.8 Hz , 1H, H-3′); 3.49, 3.45 (s, 3H, —OCH_3); 2.72–2.58 (m, 2H, H-6′); 2.14, 2.08, 2.01, and 1.99 (s, 6H, $OCOCH_3$ and $NHCOCH_3$ of diastereomers); 1.26 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.1, 172.0, and 169.9 (*C*OOEt, O*C*OCH_3 and NH*C*OCH_3); 158.0 (C-4); 148.2 (C-2); 140.3 (C-6); 110.0 (C-5); 89.0 (C-1′); 82.4 (C-2′); 79.6 (C-4′); 72.2 (C-3′); 61.3 (—OCH_2); 58.3 (OCH_3); 44.4 (C-5′); 35.6 (C-6′); 23.8, 21.1, and 14.5 (OCO*C*H_3, NHCO*C*H_3, and OCH_2CH_3). Anal Calcd.for $C_{18}H_{24}BrN_3O_9$: C, 42.70; H, 4.78; N, 8.30; Found: C, 42.94; H, 4.91; N, 8.11.

6-Aza-1-[ethyl-(5′-*N*-acetylamino-2′-*O*-acetyl-3′-*O*-benzyl-5′,6′-dideoxy)-β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (26). Colorless solid, mp 148°C; yield 0.15 g (62%), Rf 0.45 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 9.6 (*c* 0.3125, CH_3OH). MS (FAB): *m/z* 505 $(M + H)^+$; IR (KBr) ν_{max}: 3275, 2927, 1739, 1657, 1562, and 1379 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.38–7.32 (m, 6H, ArH and H-5); 6.38 (d, J = 8.2 Hz, 1H, NHCO); 5.27 (s, 1H, H-1′); 5.18 (s, 1H, H-2′); 4.81, 4.57 (d, J = 11.6 Hz, 1H, OCH_APh and OCH_BPh); 4.64 (m, 1H, H-5′); 4.30 (m, 1H, H-4′); 4.12 (q, J = 7.1 Hz, 2H, —OCH_2); 3.99 (d, J = 5.3 Hz, 1H, H-3′); 2.58 (d, J = 5.73 Hz, 2H, H-6′); 2.09, 1.89 (s, 6H, OCO*C*H_3 and NHCO*C*H_3); 1.25 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 170.7, and 170.3 (*C*OOEt, and O*C*OCH_3 NH*C*OCH_3); 148.6, 145.0 (C-4 and C-2); 140.0 (C-5); 136.9 (ArC); 129.0, 128.8, and 128.6 (Ar-CH); 100.9 (C-5); 95.4 (C-1′); 81.6 (C-2′); 80.8 (C-4′); 80.1 (C-3′); 72.8 (—O*C*H_2Ph); 61.1 (—OCH_2), 46.7 (C-5′); 36.6 (C-6′); 23.7, 21.2, and 14.2 (OCO*C*H_3, NHCO*C*H_3, and OCH_2CH_3). Anal. Calcd. for $C_{23}H_{28}N_4O_9$: C, 54.76; H, 5.59; N, 11.11; O, 28.54; Found: C, 55.64; H, 5.98; N, 10.43.

6-Aza-1-[ethyl-(5′-*N*-acetylamino-2′-*O*-acetyl-3′-*O*-benzyl-5′,6′-dideoxy)-β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)]thymine (27). Colorless oil; yield 0.14 g (60%), Rf 0.50 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 64.00 (*c* 0.075, CH_3OH). MS (FAB): *m/z* 519 $(M + H)^+$; IR (KBr) ν_{max}: 3073, 2361, 1721, 1680, and 1543 cm^{-1}. ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.8 (bs, 1H, exchanges with D_2O, NH); 7.34 (m, 5H, ArH); 6.48 (d, J = 8.1 Hz, 1H, NHCO); 6.02 (d, J = 4.5 Hz, 1H, H-1′); 5.62 (m, 1H, H-2′); 4.71, 4.60 (d, J = 12.0 Hz, 1H, OCH_APh and OCH_BPh); 4.63 (m, 1H, H-5′); 4.46 (m, 1H, H-4′); 4.15 (m, 3H, —OCH_2 and H-3′); 2.64 (d, J = 6.3 Hz, 2H, H-6′); 2.23, 2.07, and 1.89 (s, 9H, OCO*C*H_3 NHCO*C*H_3 and = C*C*H_3); 1.24 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.4, 170.2, and 169.7 (*C*OOEt, and O*C*OCH_3 NH*C*OCH_3), 156.8, 148.6 (C-2 and C-4); 145.0 (C-5); 137.0 (ArC); 129.1, 128.4, and 128.0 (Ar-CH); 88.5 (C-1′); 80.6 (C-2′); 79.6 (C-4′); 77.3 (C-3′); 72.0 (—O*C*H_2Ph); 60.8 (—OCH_2); 46.1 (C-5′); 36.2 (C-6′); 23.4, 20.8, 16.5, and 14.2 (OCO*C*H_3, NHCO*C*H_3, = C*C*H_3 and OCH_2CH_3). Anal. Calcd. for $C_{24}H_{30}N_4O_9$: C, 55.59; H, 5.83; N, 10.81; Found: C, 55.64; H, 5.98; N, 10.43.

6-Aza-1-[ethyl-(2′-*O*-acetyl-5′,6′-dideoxy-5′-*N*-hexadecylamino-3′-*O*-methyl)-β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] thymine (28). Yellow oil; Yield 0.26 g (55%), Rf 0.65 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 9.90 (*c* 0.7875, CH_3OH). MS (FAB): *m/z* 625 $(M + H)^+$, IR(Neat) ν_{max}: 3414, 3021, 1703, 1636, 1542, 1423 cm^{-1} . ^1H NMR (200 MHz, $CDCl_3$): δ 6.02 (d, *J* = 3.2 Hz 1H, H-1′); 5.68 (d, *J* = 3.2 Hz, 1H, H-2′); 4.84 (dd, *J* = 7.9 and 3.0 Hz, 1H, H-4′); 4.12 (q, *J* = 7.1 Hz, 2H, —OCH_2); 3.88 (d, *J* = 3.0 Hz, 1H, H-3′); 3.41 (s, 3H, OCH_3); 3.28 (m, 1H, H-5′); 2.61 (m, 2H, H-6′); 2.20, 2.07 (s, 6H, $OCOCH_3$ and = CCH_3); 1.88–1.84 (m, 2H, $NHCH_2$); 1.28–1.23 (m, 31H, 14 × CH_2′s and —OCH_2CH_3), 0.88 (t, *J* = 6.9 Hz, 3H, –CH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.0, 170.5, (*C*OOEt, and O*C*OCH_3); 156.8 (C-4); 148.5 (C-2); 139.0 (C-5); 89.8 (C-1′); 83.5 (C-2′); 79.8 (C-4′); 74.8 (C-3′); 60.9 (—OCH_2); 57.3 (OCH_3); 35.6 (C-5′); 32.2 (C-6′); 30.1, 29.7, 27.2, and 25.9 (CH_2s); 21.2, 17.0, and 14.50 ($OCOCH_3$, OCH_2CH_3). Anal. Calcd. for $C_{32}H_{56}N_4O_8$: C, 61.51; H, 9.03; N, 8.97; Found: C, 61.73; H, 9.24; N, 8.69.

6-Aza-1-[ethyl-(2′-*O*-acetyl-5′-*N*-cyclopropylamino-5′,6′-dideoxy-3′-*O*-methyl)-β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (29). Yellow foam; yield 0.31 g (51%), Rf 0.40 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 18.08 (*c* 0.2875, CH_3OH). MS (FAB): *m/z* 427 $(M + H)^+$; IR (Neat) ν_{max}: 3296, 2931, 1735, 1684, and 1373 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.31 (s, 1H, H-5); 5.94–5.92 (m, 2H, H-1′ and H-2′); 4.14 (m, 3H, OCH_2 and H-4′); 3.93 (d, *J* = 4.7 Hz, 1H, H-3′); 3.63 (m, 1H, H-5′); 3.45 (s, 3H, OCH_3); 2.75–2.72 (m, 2H, H-6′); 2.08 (s, 3H, $OCOCH_3$); 2.11 (m, 1H, cyclopropyl CH), 1.27 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3), 0.45–0.36 (m, 4H, cyclopropyl 2 × CH_2); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.5, 170.6, (*C*OOEt, and O*C*OCH_3); 156.2 (C-4); 148.6 (C-2); 135.6 (C-5); 85.7 (C-1′); 81.1 (C-2′); 71.8 (C-4′); 71.4 (C-3′); 60.8 (—OCH_2); 57.4 (OCH_3); 54.7 (C-5′); 36.2 (C-6′); 28.67 (NHCH); 21.2, 14.50 ($OCOCH_3$ and OCH_2CH_3); 7.5, 5.5 (cyclopropyl CH_2). Anal. Calcd. for $C_{18}H_{26}N_4O_8$: C, 50.70; H, 6.15; N, 13.14; Found: C, 51.06; H, 6.51; N, 13.01.

6-Aza-1-[ethyl-(2′-*O*-acetyl-5′,6′-dideoxy-5′-*N*-furylamino-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] thymine (30). Yellow solid, mp 135°C; yield 0.250 g (45%), Rf 0.55 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 45.33 (*c* 0.075, CH_3OH). MS (FAB): *m/z* 481 $(M + H)^+$, IR (KBr) ν_{max}: 2990, 2826, 1727, 1680, 1641, 1450, and 1376 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 9.2 (bs, 1H, NH); 7.26 (s, 1H, furyl H); 6.29–6.26 (m, 1H, furyl H); 6.18, 6.13 (d, *J* = 3.2 and 2.6 Hz, 1 H, furyl H); 5.97, 5.93 (d, *J* = 3.2 and 2.6 Hz, H-1′ of diastereomers); 5.55, 5.53 (d, *J* = 3.2 and 2.6 Hz, 1H, H-2′); 4.85–4.81 (m, 1H, H-5′); 4.72, 4.24 (d, *J* = 15.0 Hz, 1H $NHCH_A$ and $NHCH_B$); 4.13–4.05 (m, 3H, OCH_2 and H-4′); 3.67 (d, *J* = 4.7 Hz, 1H, H-3′); 3.46, 3.39 (s, 3H, OCH_3 of diastereomers); 2.32–2.21 (m, 2H, H-6′); 2.16, 2.09 (s, 6H, $OCOCH_3$, = CCH_3); 1.71 (bs, 1H, NH); 1.25, 1.23 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR

(50 MHz, $CDCl_3$): δ 172.5, 171.8, and 170.2 (*C*OOEt, and O*C*OCH_3); 156.4 (C-4); 151.9 (Furyl C); 148.7 (C-2); 145.1 (C-5); 142.5, 141.4 (Furyl C); 111.1, 110.1, 108.8, and 108.3 (Furyl CH, diastereomeric); 89.2 (C-1′); 83.5 (C-2′); 78.2 (C-4′); 77.3 (C-3′); 61.3, 60.9 (—OCH_2); 57.2, 56.8 (OCH_3); 35.1, 34.6 (C-6′); 22.5, 21.1, 16.8, and 14.5 (OCO*C*H_3, C = CCH_3 and OCH_2*C*H_3). Anal. Calcd. for $C_{21}H_{28}N_4O_9$: C, 52.50; H, 5.87; N, 11.66; Found: C, 52.82; H, 6.14; N, 11.42.

6-Aza-1-[ethyl-(2′-*O*-acetyl-5′-*N*-benzylamino-5′,6′-dideoxy-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] thymine (31). Yellow solid, mp 163°C; yield 0.22 g (55%), Rf 0.45 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 46.00 (*c* 0.1, CH_3OH). MS (FAB): *m/z* 533 $(M + H)^+$, IR(KBr) ν_{max}: 3447, 2832, 2366, 1706, 1636, 1449, 1375, and 1307 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 7.30–7.32 (m, 5H, ArH); 5.98, 5.92 (d, *J* = 2.55 and 3.18 Hz, 1H, H-1′ of diastereomers); 5.53 (m, 1H, H-2′); 4.90 (m, 1H, H-5′); 3.98 (m, 5H, $NHCH_2$, —OCH_2 and H-4′); 3.69, 3.63 (d, *J* = 3.9 and 4.0 Hz, 1H, H-3′); 3.42, 3.36 (s, 6H, OCH_3 of two diastereomers); 2.90 (dd, *J* = 16.8 and 10.5 Hz, 1H, H-6_A′); 2.40 (m, 1H, H-6_B′); 2.20, 2.07 (s, 6H, OCO*C*H_3 and = CCH_3); 1.71 (bs, 1H, NH); 1.20, 1.12 (t, *J* = 7.1 Hz, 3H, —OCH_2C*H*$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.6, 172.9, 171.9, and 170.2 (*C*OOEt, and O*C*OCH_3); 158.0 (C-4); 148.7 (C-2); 145.1 (C-5); 139.0 (ArC); 128.6, 127.4, and 127.2 (ArCH); 89.6, 89.1 (C-1′); 83.7 (C-2′); 80.0 (C-4′); 76.2 (C-3′); 61.3, 60.9 (—OCH_2); 57.3, 56.8 (OCH_3); 46.2 ($NHCH_2$); 34.6 (C-6′); 23.7, 21.1, 14.5 (OCO*C*H_3, C = CCH_3 and OCH_2*C*H_3). Anal. Calcd. for $C_{23}H_{30}N_4O_8$: C, 56.32; H, 6.16; N, 11.42; Found: C, 56.64; H, 6.42; N, 11.19.

6-Aza-1-[ethyl-(2′-*O*-acetyl-5′-*N*-4-nitrobenzoylamino-5′,6′-dideoxy-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (32). Colorless solid, mp 148°C; yield 0.43 g (56%), Rf 0.38 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 48.66 (*c* 0.15, CH_3OH). MS (FAB): *m/z* 536 $(M + H)^+$; IR (KBr) ν_{max}: 3416, 3022, 1729, 1703, 1662, 1603, 1528, 1486, 1346, and 1222 cm^{-1}; ^1H NMR ($CDCl_3$): δ 9.06 (bs, 1H, NH); 8.28, 7.94 (d, *J* = 8.6 Hz, 2H, ArH); 7.58 (d, *J* = 8.2 Hz, 1H, NHCO); 7.41, 7.38 (s, 1H, H-5 of anomers); 6.08 (d, *J* = 3.2 Hz, 1H, H-1′, β anomer); 6.02 (d, *J* = 5.0 Hz, 1H, H-1′, α anomer); 5.58–5.55 (m, 1H, H-2′, α anomer); 5.53 (d, *J* = 3.2 Hz, 1H, H-1′, β anomer); 5.10–5.00 (m, 1H, H-5′, β anomer); 4.95–4.85 (m, 1H, H-5′, α anomer); 4.70–4.60 (m, 1H, H-4′, α anomer); 4.46–4.41 (m, 1H, H-4′, β anomer); 4.15 (q, *J* = 7.1 Hz, 2H, —OCH_2); 3.99 (d, *J* = 4.7 Hz, 1H, H-3′); 3.51, 3.44 (s, 3H, —OCH_3); 2.92–2.66 (m, 2H, H-6′); 2.12, 2.11 (s, 3H, OCO*C*H_3); 1.25, 1.26 (t, *J* = 7.1 Hz, 3H,—OCH_2C*H*$_3$); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.6, 170.7, and 165.6 (*C*OOEt, O*C*OCH_3 and NH*C*O); 155.9, 149.9 (C-4 and C-2); 148.1, 140.8 (ArC); 136.8 (C-5); 128.7, 124.1 (Ar-CH); 89.3 (C-1′); 83.4 (C-2′); 80.0 (C-4′); 77.6 (C-3′); 61.3 (—OCH_2); 58.7 (—OCH_3); 47.0 (C-5′); 36.6 (C-6′); 21.0, 14.5 (OCO*C*H_3 and OCH_2*C*H_3). Anal. Calcd. for $C_{22}H_{25}N_5O_{11}$: C, 49.35; H, 4.71; N, 13.08; Found: C, 49.74; H, 4.92; N, 12.89.

6-Aza-1-[ethyl-(2′-*O*-acetyl-5′-*N*-4-nitrobenzoylamino-5′,6′-dideoxy-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl] thymine (33). Colorless solid, mp 178°C; yield 0.47 g (60%), Rf 0.46 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 52.26 (*c* 0.1875, CH_3OH). MS (FAB): *m/z* 550 $(M + H)^+$, IR(KBr), ν_{max}: 3407, 2935, 2372, 1722, 1659, 1602, and 1527 cm^{-1}. ^1H NMR (200 MHz, $CDCl_3$): δ 8.72 (bs, 1H, NH); 8.27, 7.59 (d, *J* = 8.7 Hz, 2H, ArH); 7.59 (d, *J* = 8.2 Hz, 1H, NHCO); 6.08 (d, *J* = 3.1 Hz, 1H, H-1′); 5.61 (d, *J* = 3.1 Hz, 1H, H-2′); 5.00–4.96 (m, 1H, H-5′); 4.42–4.38 (m, 1H, H-4′); 4.17 (q, *J* = 7.1 Hz, 2H, —OCH_2); 3.98 (d, *J* = 4.4 Hz, 1H, H-3′); 3.53 (s, 3H, —OCH_3); 2.76 (dd, *J* = 16.8 and 5.8 Hz, 1H, H-6_A′); 2.65 (dd, *J* = 16.8 and 6.2 Hz, 1H, H-6_B′); 2.21, 2.12 (s, 3H, $OCOCH_3$ and = CCH_3); 1.24 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.9, 170.4, and 165.2 (*C*OOEt, O*C*OCH_3 and NH*C*O); 156.3, 150.0 (C-4 and C-2); 148.8 (C-5); 145.0, 140.0 (ArC); 128.5 and 124.1 (Ar-CH); 89.9 (C-1′); 84.9 (C-2′); 80.7 (C-4′); 77.3 (C-3′); 61.4 (—OCH_2); 57.8 (—OCH_3); 46.9 (C-5′); 35.9 (C-6′); 21.1, 16.8, and 14.5 ($OCOCH_3$, = CCH_3 and OCH_2CH_3). Anal. Calcd. for $C_{23}H_{27}N_5O_{11}$: C, 50.27; H, 4.95; N, 12.75; Found: C, 50.54; H, 5.16; N, 12.44.

5-Bromo-1-[ethyl-(2′-*O*-acetyl-5′,6′-dideoxy-3′-*O*-methyl-5′-*N*-4-nitrobenzoylamino)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (34). Yellow solid, mp 123°C; yield 0.23 g (48%), Rf 0.52 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ + 13.71 (*c* 0.0875, CH_3OH). MS (FAB): *m/z* 601 $(M + H)^+$; IR (KBr) ν_{max}: 3419, 3072, 2990, 1706, 1602, 1680, 1527, 1441, and 1346 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.73 (bs, 1H, NH); 8.29, 7.7 (d, *J* = 8.7 Hz, 2H, ArH); 8.20 (s, 1H, H-6); 7.42 (d, *J* = 8.2 Hz, 1H, NHCO); 5.93 (s, 1H, H-1′); 5.23 (s, 1H, H-2′); 5.06–4.97 (m, 1H, H-5′); 4.51 (dd, *J* = 8.9 and 3.3 Hz, 1H, H-4′); 4.22 (q, *J* = 7.2 Hz, 2H, —OCH_2); 3.74 (d, *J* = 4.4 Hz, 1H, H-3′); 3.49 (s, 3H, —OCH_3); 2.84 (dd, *J* = 16.8 and 5.0 Hz, 1H, H-6_A′); 2.68 (dd, *J* = 16.8 and 4.4 Hz, 1H, H-6_B′); 2.15 (s, 3H, $OCOCH_3$); 1.29 (t, *J* = 7.2 Hz, 3H, —OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.0, 169.9, and 165.6 (*C*OOEt, O*C*OCH_3 and NH*C*O); 159.4, 150.1 (C-4 and C-2); 140.6 (C-6); 149.8, 140.6 (ArC); 128.7, 124.2 (Ar-CH); 97.5 (C-5); 89.7 (C-1′); 83.2 (C-2′); 82.2 (C-4′); 79.0 (C-3′); 61.8 (—OCH_2); 58.4 (—OCH_3); 46.4 (C-5′); 35.5 (C-6′); 21.1, 14.5 ($OCOCH_3$ and OCH_2CH_3). Anal. Calcd. for $C_{23}H_{25}BrN_4O_{11}$: C, 45.04; H, 4.11; N, 9.13; Found: C, 45.35; H, 4.39; N, 9.02.

6-Aza-1-[ethyl-(2′-*O*-acetyl-3′-*O*-benzyl-5′,6′-dideoxy-5′-*N*-4-nitrobenzoylamino)-β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] thymine (35). Colourless solid, mp 184°C; yield 0.53 g (62%), Rf 0.55 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 16.69 (*c* 0.2875, CH_3OH). *m/z* 625 $(M + H)^+$, IR(KBr), ν_{max}: 3408, 3022, 1733, 1636, 1527, 1478, and 1340 cm^{-1} . ^1H NMR (200 MHz, $CDCl_3$): δ 8.2 (bs, 1H, NH); 8.09, 7.82 (d, *J* = 8.6 Hz, 2H, ArH); 7.52 (d, *J* = 8.2 Hz, 1H, NHCO); 7.27–7.22 (m, 5H, ArH); 6.08 (d, *J* = 4.32 Hz, 1H, H-1′);

5.89–5.86 (m, 1H, H-2′); 4.89–4.86 (m, 1H, H-5′); 4.74, 4.58 (d, J = 11.7 Hz, 1H, OCH_A and OCH_B); 4.56–4.52 (m, 1H, H-4′); 4.11 (q, J = 7.1 Hz, 2H, —OCH_2); 4.22–4.19 (m, 1H, H-3′); 2.72 (d, J = 6.5 Hz, 2H, H-6); 2.08, 2.07 (s, 6H, $OCOCH_3$ and = CCH_3); 1.24 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.8, 170.3, and 165.8 (*C*OOEt, O*C*OCH_3 and NH*C*O); 159.3, 154.8 (C-4 and C-2); 149.6 (C-5); 140.9, 137.6, and 135.6 (ArC); 128.9, 128.7, 128.3, and 123.7 (Ar-CH); 91.1 (C-1′); 81.6 (C-2′); 80.3 (C-4′); 77.5 (C-3′); 72.7 (—OCH_2Ph); 61.3 (—OCH_2); 47.5 (C-5′); 36.9 (C-6′); 21.2, 17.2, and 14.5 ($OCOCH_3$, = CCH_3 and OCH_2CH_3). Anal. Calcd. for $C_{29}H_{31}N_5O_{11}$: C, 55.68; H, 4.99; N, 11.19; Found: C, 55.94; H, 5.27; N, 10.94.

5-Bromo-1-[ethyl-(2′-*O*-acetyl-3′-*O*-benzyl-5′,6′-dideoxy-5′-*N*-4-nitrobenzoylamino)-β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (36). Colorless solid, mp 167°C; yield 0.21 g (48%), Rf 0.58 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 2.15 (*c* 0.025, CH_3OH). MS (FAB): *m/z* 690 $(M + H)^+$, IR(KBr), v_{max}: 3330, 2931, 1734, 1653, 1600, 1528, 1490, 1451, and 1345 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.19 and 7.84 (d, J = 8.8 Hz, 2H, ArH); 7.64 (d, J = 8.2 Hz, 1H, NHCO); 7.37–7.27 (m, 6H, ArH and H-6); 5.32 (s, 1H, H-1′); 5.20 (s, 1H, H-2′); 4.95–4.84 (m, 1H, H-5′); 4.77 (d, J = 11.7 Hz, 1H, OCH_A); 4.60–4.47 (m, 2H, H-4′and OCH_B); 4.12 (m, 3H, —OCH_2 and H-3′); 2.74–2.70 (m, 2H, H-6); 2.10 (s, 3H, $OCOCH_3$); 1.24 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.9, 170.0, and 165.6 (*C*OOEt, O*C*OCH_3 and NH*C*O); 159.4, 150.5 (C-4 and C-2); 149.8, 140.56, and 136.0 (ArC); 140.5 (C-6); 129.2, 128.9, 128.7, and 124.1 (Ar-CH); 97.5 (C-5); 89.8 (C-1′); 83.4 (C-2′); 79.7 (C-4′); 79.6 (C-3′); 72.2 (—OCH_2Ph); 61.7 (—OCH_2); 46.2 (C-5′); 35.4 (C-6′); 21.1, 14.5 ($OCOCH_3$ and OCH_2CH_3). Anal. Calcd. for $C_{29}H_{29}BrN_4O_{11}$: C, 50.52; H, 4.24; N, 8.13; Found: C, 50.82; H, 4.41; N, 8.04.

6-Aza-1-[ethyl-(2′-*O*-acetyl-5′-*N*-3-chlorobenzoylamino-5′,6′-dideoxy-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] thymine (37). Colorless oil; yield 0.21 g (52%), Rf 0.44 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 34.90 (*c* 0.1375, CH_3OH). MS (FAB): *m/z* 539 $(M + H)^+$; IR (KBr): 3413, 2931, 1725, 1680, 1660, 1569, 1530, 1455, 1375, 1303, and 1231 $v_{max}cm^{-1}$; ^{1}H NMR (200 MHz, $CDCl_3$): δ 9.1 (bs, 1H, NH); 7.70 (s, 1H, ArH); 7.48–7.34 (m, 3H, ArH); 6.09 (d, J = 2.9 Hz, 1H, H-1′); 5.60 (d, J = 2.9 Hz, 1H, H-2′); 5.06–4.82 (m, 1H, H-5′); 4.48–4.41 (m, 1H, H-4′); 4.14 (q, J = 7.1 Hz, 2H, —OCH_2); 3.96 (d, J = 4.5 Hz, 1H, H-3′); 3.52 (s, 3H, —OCH_3); 2.82–2.64 (m, 2H, H-6′); 2.18, 2.11 (s, 6H, $OCOCH_3$ and = CCH_3); 1.24 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR ($CDCl_3$): δ 171.9, 170.3, and 165.8 (*C*OOEt, O*C*OCH_3 and NH*C*O); 156.4, 148.8 (C-2 and C-4); 145.1 (C-5); 136.7, 135.0 (ArC); 131.9, 130.2, 127.6, and 125.4 (Ar-CH); 89.6 (C-1′); 84.8 (C-2′); 80.8 (C-4′); 78.2 (C-3′); 61.3 (—OCH_2); 57.7 (—OCH_3); 45.6 (C-5′); 36.1 (C-6′); 21.1, 16.8, and 14.5 ($OCOCH_3$, = CCH_3 and OCH_2CH_3). Anal. Calcd. for $C_{23}H_{27}ClN_4O_9$: C, 51.26; H, 5.05; N, 10.40; Found: C, 51.43; H, 5.24; N, 10.32.

6-Aza-1-[ethyl-(2′-*O*-acetyl-3′-*O*-benzyl-5′-*N*-3-chlorobenzoylamino-5′,6′-dideoxy)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (38). Yellow solid, mp 142°C; yield 0.19 g (49%), Rf 0.56 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 10.66 (*c* 0.1125, CH_3OH). MS (FAB): *m/z* 601 $(M + H)^+$, IR (KBr): 3355, 3048, 2978, 2923, 2845, and 1721 ν_{max} cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 8.21 (m, 2H, ArH and H-5); 7.64 (d, *J* = 8.2 Hz, 1H, NHCO); 7.46–7.20 (m, 8H, ArH); 6.12 (d, *J* = 3.0 Hz, 1H, H-1′); 5.62 (d, *J* = 3.0 Hz, 1H, H-2′); 4.99–4.88 (m, 1H, H-5′); 4.75–4.51 (m, 3H, OCH_2Ph and H-4′); 4.21–4.06 (m, 3H, —OCH_2 and H-3′); 2.73–2.70 (m, 2H, H-6); 2.04 (s, 3H, $OCOCH_3$); 1.21 (t, *J* = 7.1 Hz, 3H, —OCH_2CH_3). Anal. Calcd. for $C_{28}H_{29}ClN_4O_9$: C, 55.96; H, 4.86; N, 9.32; Found: C, 56.14; H, 4.97; N, 9.23.

6-Aza-1-[ethyl-(2′-*O*-acetyl-3′-*O*-benzyl-5′,6′-dideoxy-5′-*N*-tetradecanoylamino)-β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] thymine (39). Colourless solid, mp 124°C; yield 0.37 g (54%), Rf 0.65 (19:1 chloroform/methanol), $[\alpha]_D^{25}$ − 40.00 (*c* 0.150, CH_3OH). MS (FAB): *m/z* 687 $(M + H)^+$; IR(KBr) ν_{max}: 3019, 2928, 2402, 1733, 1634, and 1529 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$): δ 7.34–7.29 (m, 5H, ArH); 6.78 (d, *J* = 7.8 Hz, 1H, NHCO); 6.12 (d, *J* = 4.6 Hz, 1H, H-1′); 5.72 (m, 1H, H-2′); 4.72, 4.58 (d, *J* = 11.8 Hz, 1H, OCH_APh and OCH_BPh); 4.61 (m, 1H, H-5′); 4.42 (m, 1H, H-4′); 4.11 (m, 3H, —OCH_2CH_3 and H-3); 2.61 (d, *J* = 6.5 Hz, 2H, H-6′); 2.20 (s, 3H, $OCOCH_3$); 2.11 (t, *J* = 6.5 Hz, 2H, —$COCH_2$); 2.05 (s, 3 H, = CCH_3); 1.54 (m, 2H, $COCH_2CH_2$); 1.23 (m, 23H, 10 × CH_2s and OCH_2CH_3); 0.87 (t, *J* = 6.9 Hz, 3H, CH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 173.1, 171.8, and 170.4 (*C*OOEt, O*C*OCH_3 and NH*C*O); 159.1, 154.8 (C-4 and C-2); 137.6 (ArC); 135.2 (C-5); 128.8, 128.3, and 128.2 (Ar-CH); 89.8 (C-1′); 81.1 (C-2′); 79.9 (C-4′); 77.4 (C-3′); 72.1 (—OCH_2Ph); 61.0 (—OCH_2); 46.3 (C-5′); 37.1 (C-6′); 36.7 ($COCH_2$); 32.2, 30.1, 29.9, 29.8, 29.7, 29.6, 25.9, and 23.0 (CH_2s); 21.2, 17.3, and 14.5 ($OCOCH_3$, = CCH_3 and OCH_2CH_3). Anal. Calcd. for $C_{36}H_{54}N_4O_9$: C, 62.95; H, 7.92; N, 8.16; Found: C, 63.13; H, 8.09; N, 8.02.

General Procedure for the Synthesis of Compounds 40—43

6-Aza-1-[ethyl-(5′-*N*-acetylamino-5′,6′-dideoxy-2′-hydroxy-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronate-1′-yl)] thymine (40). 6-aza-1-ethyl[5′-*N*-acetyl-2′-*O*-acetyl-5′,6′-dideoxy-3′-*O*-methyl]-α-D-*gluco* and β-L-*ido*-hepto-1,4-furanuronat-1′yl) thymine, **24** (0.1 g, 0.23 mmol) was taken in dry methanolic ammonia solution (3.0 mL) in a sealed rb flask and stirred at rt for 1.5 h, solvents evaporated and the residue was chromatographed over an SiO_2 column using chloroform/methanol 9:1 as eluent to give **40** as Colourless solid, mp 168°C; yield 0.08 g (90%), Rf 0.50 (9:1 chloroform/methanol), $[\alpha]_D^{25}$ − 96.94 (*c* 0.2125, CH_3OH). MS (FAB): *m/z* 401 $(M + H)^+$; IR (KBr) ν_{max}: 3422, 2369, 1705, 1655, 1545, 1463, and 1378 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.88 (d, *J* = 8.7 Hz, 1H, NHCO); 5.88 (d, *J* = 6.7 Hz, 1H, H-1′); 4.72–4.67 (m, 1H, H-2′); 4.52–4.46

(m, 2H, H-5′ and H-4′); 4.04 (m, 3H, —OCH_2 and H-3′); 3.48 (s, 3H, OCH_3); 2.62–2.58 (m, 2H, H-6′); 2.28, 2.02 (s, 3H, $NHCOCH_3$ and = CCH_3); 1.25 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 171.8, 169.0 (*C*OOEt and $NHCOCH_3$); 157.3, 150.2, and 145.0 (C-4, C-2, and C-5); 90.0 (C-1′); 84.7 (C-2′); 78.8 (C-4′); 76.1 (C-3′); 61.1 (—OCH_2); 58.8 (—OCH_3); 51.1 (C-5′); 36.6 (C-6′); 23.7, 16.7 ($NHCOCH_3$ and OCH_2CH_3). Anal. Calcd. for $C_{16}H_{24}N_4O_8$: C, 48.00; H, 6.04; N, 13.99; Found: C, 48.24; H, 6.36; N, 13.81.

6-Aza-1-[ethyl-(5′-*N*-acetylamino-3′-*O*-benzyl-5′,6′-dideoxy-2′-hydroxy)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (41). Yellow solid, mp 162°C; yield 0.18 g (95%), Rf 0.55 (9:1 chloroform/methanol), $[\alpha]_D^{25}$ − 75.33 (*c* 0.3, CH_3OH). MS (FAB): *m/z* 463 $(M + H)^+$, IR(KBr) ν_{max}: 3346, 2986, 1703, 1657, 1544, and 1402 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.45 (s, 1H, H-5); 7.37–7.31 (m, 5H, ArH); 6.93, 6.68 (d, J = 8.2 Hz, 1H, NHCO of diastereomers); 5.96–5.91 (m, 1H, H-1′ of diastereomers); 5.82 (bs 1H, OH); 4.71–4.57 (m, 3H, —OCH_2Ph and H-2′); 4.43–4.39 (m, 1H, H-5′); 4.20–4.16 (m, 1H, H-4′); 4.06 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.61 (d, J = 1.1 Hz, H-3′); 2.64, 2.55 (m, 2H, H-6′); 1.87, 1.79 (s, 3H, $NHCOCH_3$ of diastereomers); 1.29, 1.18 (t, J = 7.1 Hz, 3H,—OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 174.3, 172.0, 171.1, and 170.4 (*C*OOEt and NH*C*O of diastereomers); 156.7, 156.5, 149.0, and 148.8 (C-4 and C-2); 137.8 (ArC); 136.8 (C-5); 128.9, 128.2, and 128.1 (Ar-CH); 90.5, 90.0 (C-1′); 84.2 (C-2′); 82.6 (C-4′); 80.2, 79.5 (C-3′); 72.7, 72.0 (—OCH_2Ph); 61.2 (—OCH_2); 47.0, 46.5 (C-5′); 37.1, 36.2 (C-6′); 23.5, 22.8, and 14.5 ($NHCOCH_3$ and OCH_2CH_3 of diastereomers). Anal. Calcd. for $C_{21}H_{26}N_4O_8$: C, 54.54; H, 5.67; N, 12.12; Found: C, 54.65; H, 5.81; N, 12.01.

6-Aza-1-[ethyl-(5′-*N*-cyclopropylamino-5′,6′-dideoxy-2′-hydroxy-3′-*O*-methyl)-α-D-*gluco* and β-L-*ido*-hepto-1′,4′-furanuronat-1′-yl)] uracil (42). Yellow foam; yield 0.11 g (93%), Rf 0.42 (9:1 chloroform/methanol), $[\alpha]_D^{25}$ − 10.90 (*c* 0.4125, CH_3OH). MS (FAB): *m/z* 385 $(M + H)^+$, IR(KBr), ν_{max}: 3421, 3022, 2931, 2859, 1740, 1663, 1602, 1528, 1488, and 1347 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 7.48 (s, 1H, H-5); 5.96 (d, J = 5.4 Hz, 1H, H-1′); 4.84–4.81 (m, 1H, H-2′); 4.30–4.27 (m, 1H, H-4′); 4.16 (q, J = 7.1 Hz, 2H, —OCH_2CH_3); 3.91–3.85 (m, 1H, H-5′); 3.61 (m, 1H, H-3′); 3.49 (s, 3H, —OCH_3); 2.69–2.63 (m, 2H, H-6′); 2.33–2.27 (m, 1H, NHC*H*); 1.25 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); 0.87, 0.39 (m, 2H, cyclopropyl H). Anal. Calcd. for $C_{16}H_{24}N_4O_7$: C, 49.99; H, 6.29; N, 14.58; Found: C, 50.24; H, 6.44; N, 14.49.

6-Aza-1-[ethyl-(3′-*O*-benzyl-5′,6′-dideoxy-5′-*N*-4-nitro-benzoyl)-β-L-*ido*-hepto-1′,4′-furanuronate-1′-yl)] thymine (43). Colorless solid, mp 181°C; yield 0.21 g (95%), Rf 0.58 (9:1 chloroform/methanol), $[\alpha]_D^{25}$ − 38.85 (*c* 0.0875, CH_3OH). MS (FAB): *m/z* 583 $(M + H)^+$; IR (KBr) ν_{max}: 3413, 1726, 1600, 1528, and 1347 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.09, 7.80 (d, J = 8.5

Hz, 2H, ArH); 7.71 (d, J = 5.8 Hz, 1H, NHCO); 7.25 (m, 5H, ArH); 6.40 (bs, 1H, NH, exchanges with D_2O); 6.00 (d, J = 4.7 Hz, 1H, H-1′); 4.88-4.83 (m, 1H, H-2′); 4.71 (d, J = 11.5 Hz, 1H, OCH_APh); 4.59–4.49 (m, 2H, H-5′ and OCH_BPh); 4.27–4.24 (m, 1H, H-4′); 4.07 (q, J = 7.1 Hz, 2H, —OCH_2); 3.61 (s, 1H, H-3′); 2.71 (s, 2H, H-6′); 1.92 (s, 3H, = CCH_3); 1.18 (t, J = 7.1 Hz, 3H, —OCH_2CH_3); ^{13}C NMR (50 MHz, $CDCl_3$): δ 172.2, 165.6 (*C*OOEt and NH*C*O); 158.8, 149.6, and 145.0 (C-4, C-2 and C-5), 155.5, 137.7 and 137.0 (ArC), 140.6 (C-5), 128.8, 128.3, and 123.9 (Ar-CH); 91.2 (C-1′); 83.4 (C-2′); 79.2 (C-4′); 72.0 (C-3′); 71.8 (—OCH_2Ph); 61.3 (—OCH_2); 52.3 (C-5′); 36.8 (C-6′); 17.1, 14.5 (= CCH_3, and OCH_2CH_3). Anal. Calcd. for $C_{27}H_{29}N_5O_{10}$: C, 55.57; H, 5.01; N, 12.00. Found: C, 55.74; H, 5.23; N, 11.87.

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