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Synthesis and Structural Studies of Monocyclic 4'-Aza-L-Nucleosides

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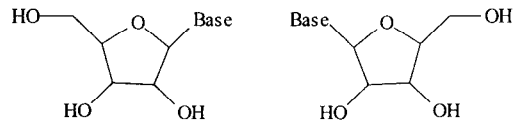
Abstract: Monocyclic 4'-Aza-L-Nucleosides in which the sugar ring oxygen is replaced with a nitrogen atom are synthesized from D-lyxose. The configurational assignments of the structures of newly derived compounds were established by 1D and 2D ^{1}H NMR experiments.

Keywords: Azasugars, L-nucleosides, 1D, 2D ^{1}H NMR studies

INTRODUCTION

Nucleosides derived from natural D-ribose play a vital role for the treatment of human viral diseases.[1] Among them, Ribavirin,[2] AZT,[3] ddI,[4] ddC[4] are the most prominent drugs that are in the market today. In addition, other types of nucleosides with D-configuration have been explored to treat different diseases.[5] Lately, reports of L-nucleosides, the mirror image of D-nucleosides, as antiviral agents have increased dramatically due to their potent biological activity and lower toxicity than their counterpart D-nucleosides.[6-11] The most active L-nucleosides include L-thymidine (L-T),[7] L-3'-thiacytidine (3TC),[8] L-5-fluoro-3'-thiacytidine (FTC),[8a,9] L-2',3'-dideoxycytidine (L-ddC),[10] L-5-fluoro-2',3'-dideoxycytidine (L-FddC),[10b,10c] and 2'-fluoro-5-methyl-β-L-arabinofuranosyluracil (L-FMAU).[11]



D-Nucleoside L-Nucleoside

Figure 1

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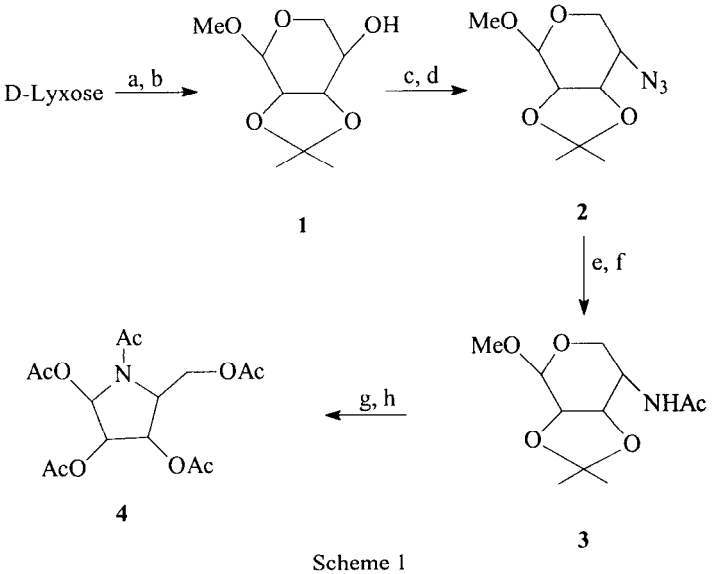
In recent years, the design of novel "ribose" rings by introducing different hetero atoms[12] has resulted in the discovery of effective antiviral and antitumor agents. For example, the replacement of the furanose ring with 1,3-dioxolane,[13] 1,3-oxathiolane,[14] 4'-thio[15] heterocylic moieties have produced potent antiviral compounds. Nucleosides containing tetrahydrothiophene,[16] isoxazole,[17] oxazolidine,[18] thiazolidine[19] and pyrrolidine[20] ring systems are also known. In addition, an L-nucleoside analogue 3TC which contains an 1,3-oxathiolane moiety, has been approved for the treatment of AIDS caused by human immunodeficiency virus (HIV) and hepatitis B (HBV). Our interest to synthesize novel L-nucleoside analogs coupled with the idea of replacing the furanose ring oxygen with nitrogen led us to examine L-nucleosides derived from azasugar (**4**).

Azasugars are structurally related to sugars in which the pentose ring oxygen is replaced by nitrogen. The azasugars by themselves have attracted considerable interest due to their ability to inhibit glycosidases.[21] Further, they have been introduced into nucleoside synthesis and used as effective molecular probes.[22] In addition, the antibiotic anisomycin[23] that has an azasugar was found active against protozoa and certain fungi. Furthermore, azasugars were found to have antidiabetic[24] and anticancer activity.[25] Nucleosides derived from pyrrolidine have also been incorporated into oligonucleotides and studied as antisense agents.[26]

Previously, a few groups have reported the synthesis of 4'-amino-sugar nucleosides from amino acids as the starting materials.[27,28] While Huang *et al* constructed 4'-acetamido-2'-deoxythymidine from 3,5-di-*O*-benzyl-2-deoxy-D-ribose dibenzyldithioacetal,[29] others prepared a 4'-acetamidoadenosine from L-Lyxose derivative.[30] Recently, C-nucleosides containing 4-



Scheme 1

Reagents and conditions: a) HCl/MeOH; b) HCl/Acetone/2,2-dimethoxy propane; c) DMAP/$(CF_3SO_2)_2O$/Py; d) LiN_3/DMF; e) 5%Pd/C/MeOH; f) DMAP/AC_2O/Py; g) AcOH/H_2O; h) H_2SO_4/Ac_2O/AcOH.

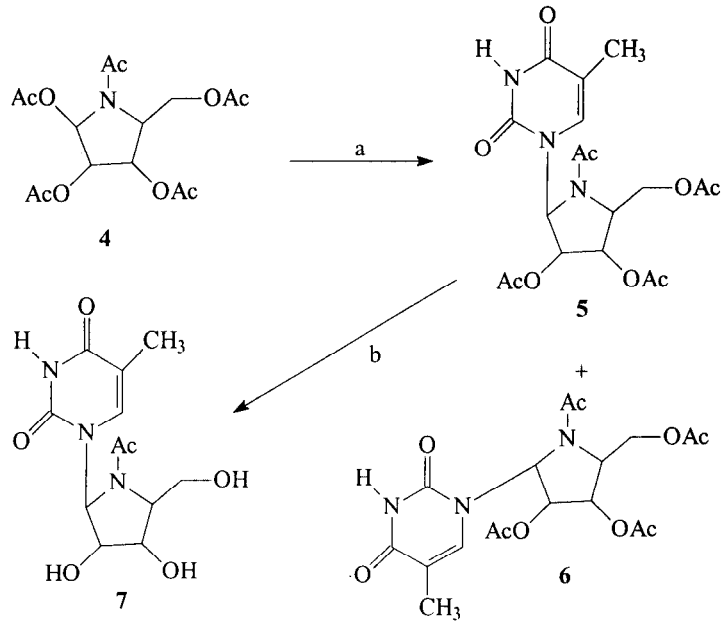
azasugar moiety have also been described.[31] Thus, there is a continuing interest in the synthesis of nucleosides containing azasugars. However, the preparation of 4'-aza-L-ribonucleosides has not been reported. We now describe a convenient methodology for the synthesis of 1, 2, 3, 5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-L-ribofuranose (**4**) from commercially available D-lyxose, coupling of **4** with different mono-heterocycles and their structural studies.

SYNTHESIS OF 4-AMINO-4-DEOXY-L-RIBOSE DERIVATIVE

The synthetic methodology employed for preparation of the protected aza-L-sugar **4** is shown in Scheme 1. Here, we elected to use D-lyxose as our starting material. Refluxing of D-lyxose in methanolic HCl (0.5%) for 5 h followed by treatment of the intermediate with 2,2-dimethoxypropane in acetone at room temperature for 16 h provided the corresponding methyl 2,3-isopropylidene-α-D-lyxopyranose (**1**) in 64% yield. Next, the key step is to convert the free hydroxyl group of **1** to an amino function with inversion of configuration to afford the desired L-configuration at C_4. This was accomplished by using the following sequence of steps. First, the secondary hydroxyl group of **1** was activated with trifluoromethanesulfonic anhydride in pyridine at –20 °C which on further reaction with lithium azide in dry DMF afforded the azido derivative (**2**) in good yield (78%). On the other hand, reaction of mesylate or tosylate derivatives of **1** with either sodium azide or lithium azide produced a mixture of products in low yields with recovered starting material. We believe that the triflate displacement reaction occurred smoothly with LiN_3 due to the increase in solubility of LiN_3 than NaN_3 in DMF by better solvation and activation of triflate group by Li-oxygen chelation. Reduction of the azide **2** with 5% Pd/C furnished methyl 4-amino-4-deoxy-2,3-isopropylidene-α-L-ribopyranoside which on acetylation with acetic anhydride gave the corresponding acetyl derivative (**3**). The pyranose derivative **3** was then transformed to the intermediate 4-aza-L-ribofuranose (**4**) in a two-step process: 1) Cleavage of the acetonide group with dilute acetic acid and concomitant ring opening and closure. 2) Acetylation with acetic acid and acetic anhydride in the presence of conc. H_2SO_4. The ^1H NMR spectrum of **4** showed the presence of α and β anomers in the ratio of 25:75 and correlated with 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(trifluoroacetamido)-D-ribofuranose.[31a]

RESULTS AND DISCUSSION

After successfully accomplishing the synthesis of **4**, we turned our attention to the coupling of **4** with thymine using Vorbrüggen glycosylation conditions.[32] Accordingly, thymine was per-silylated with hexamethyldisilazane under reflux to give the corresponding silylated derivative which on treatment with **4** in the presence of $SnCl_4$ at –5 to 0 °C afforded 1-(2,3,5-tri-*O*-acetyl-4-deoxy-4-acetamido-β-L-ribofuranosyl)thymine (**5**) in 87% yield and 5% α-isomer (**6**). Exposure of **5** to methanolic ammonia at room temperature provided one of the target product viz., 1-(4-deoxy-4-acetamido-β-L-ribofuranosyl)thymine (**7**) in 79% yield.

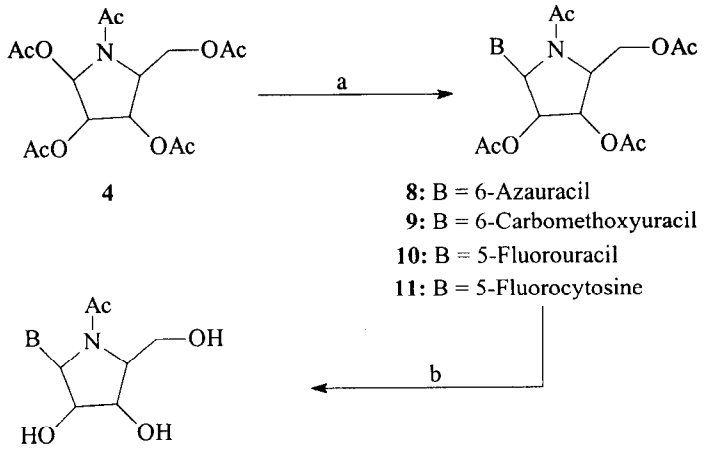


Scheme 2

Reagents and conditions: a) i. Thymine/HMDS/$(NH_4)_2SO_4$; ii. $SnCl_4$/ $ClCH_2CH_2Cl$; b) MeOH/NH_3.

Utilization of the similar coupling procedure for the preparation of a few other monocyclic 4'-aza-L-nucleosides (**8** – **11**) was found to be remarkably successful. These protected nucleosides upon deprotection afforded the corresponding deblocked nucleosides (**12** – **15**) in good yield. In all these cases, β-isomers were obtained as the predominant products. However, in a few cases minor products were detected on tlc but no further effort was made to separate and characterize the products.

After accomplishing the synthesis of selected 4'-aza-L-ribonucleosides, we were interested in converting **7** to the corresponding 2'-deoxy and 2',3'-dideoxy nucleosides. Thus, treatment of **7** with Markiewicz reagent ($TPDSiCl_2$)[33] afforded an inseparable mixture of silyl ether derivatives (**16**) and (**17**). The mixture on further reaction with *p*-tolyl chlorothionoformate and pyridine in CH_2Cl_2 afforded a readily separable mixture of thionoformate esters (**18**) and (**19**). Radical mediated deoxygenation[34] of **18** and **19** with tri-n-butyltin hydride in presence of AIBN in toluene under reflux furnished silyl-protected 4'-aza-L-thymidine (**20**) and 5'-deoxy-4'-aza-L-5-methyluracil (**22**) respectively. Removal of the silyl groups of **20** and **22** was accomplished with $Et_3N.3HF$ at room temperature to give 4'-deoxy- 4'-(acetamido)-L-thymidine (**21**) and 4',5'-dideoxy-4'-(acetamido)-L-5-methyluracil (**23**) in high yields.



4

8: B = 6-Azauracil
9: B = 6-Carbomethoxyuracil
10: B = 5-Fluorouracil
11: B = 5-Fluorocytosine

12: B = 6-Azauracil
13: B = Uracil-6-carboxamide
14: B = 5-Fluorouracil
15: B = 5-Fluorocytosine

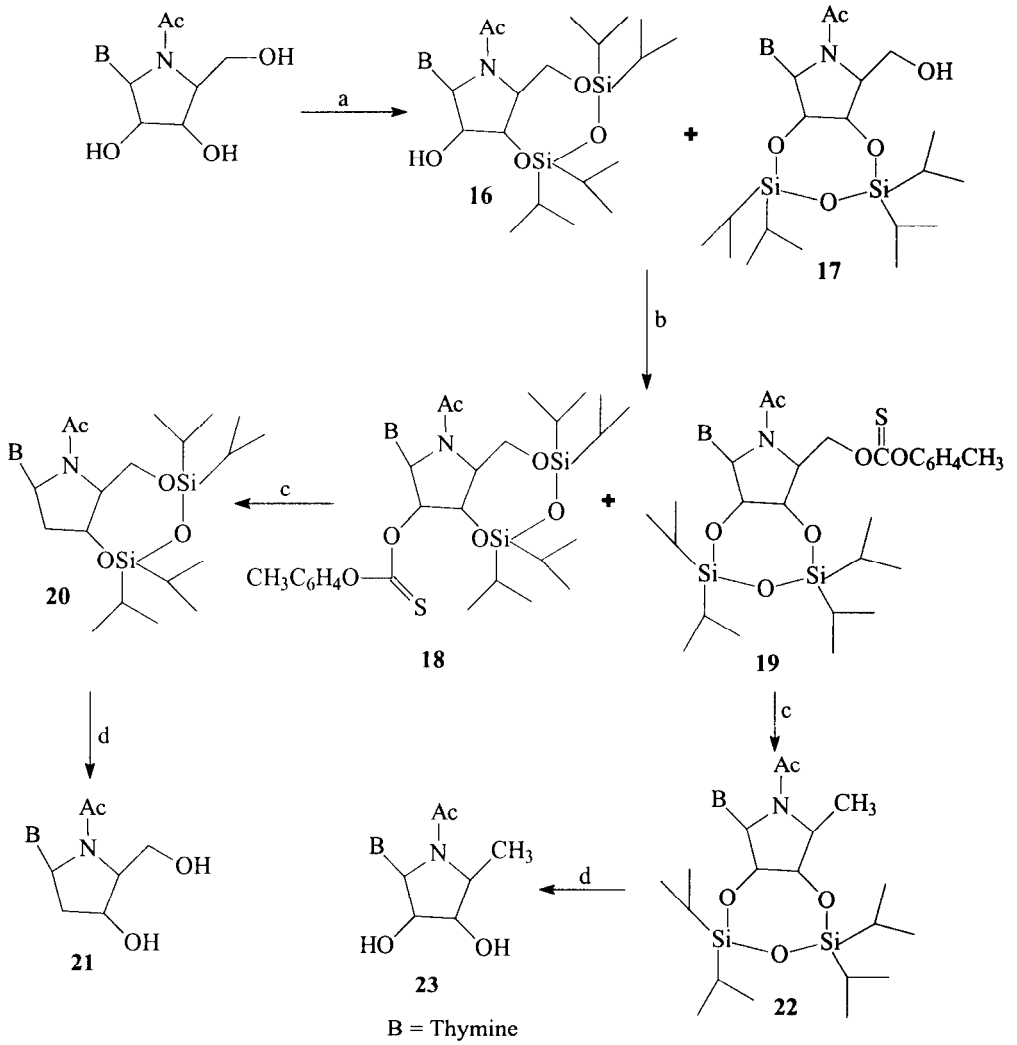
Scheme 3

Reagents and conditions: a) i. Base/HMDS/$(NH_4)_2SO_4$; ii. $SnCl_4$/ $ClCH_2CH_2Cl$; b) MeOH/NH_3.

Finally, in view of the potent properties of 2',3'-dideoxy nucleosides, the synthesis of 1-(2,3,4-trideoxy-4-acetamido-β-L-ribofuranosyl)thymine **27** was pursued. Thus, selective protection of the 5'-hydroxyl group of **7** with TBDMSCl followed by treatment with methanesulfonyl chloride gave fully protected derivative **24**. The dimesylate **24** upon reaction with freshly prepared Telluride dianion[35] in THF at room temperature for 16 h afforded the silyl-protected 2',3'- didehydro-3'-deoxythymidine intermediate (**25**). The silyl group in **25** was then removed using $Et_3N.3HF$ to afford 2',3'-didehydro-3',4'-dideoxy-4'-(acetamido)-L-thymidine (**26**) in 65% yield. Hydrogenation of **26** using Pd/C in methanol furnished the final target compound 3',4'-dideoxy-4'-aza-L-thymidine (**27**) in high yield.

STRUCTURAL STUDIES

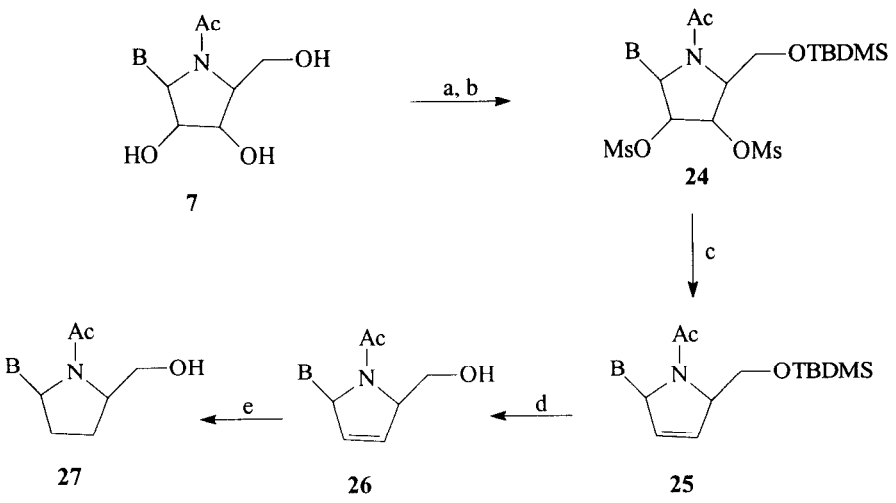
The anomeric configurations of the monocyclic 4'-aza-L-nucleosides were assigned on the basis of 1D and 2D ^1H NMR studies. Resonance assignments were made by a combination of standard 2D 1H-1H pulsed-field gradient COSY and phase-sensitive (TPPI) NOESY experiments. For NOESY experiments, mixing time was set to 0.4 second. The percentage of NOE's were calculated from DPFGSE one-dimensional NOE experiments.[36] For each of the compounds, two inter-convertible conformations exist, as indicated by the appearance of



Scheme 4

Reagents and conditions: a) TPDSiCl$_2$/Py; b) $CH_3C_6H_4OC(S)Cl$/Py; c) Bu_3SnH/AIBN/Toluene/reflux; d) $Et_3N.3HF/CH_2Cl_2$.

duplicate resonance lines for most protons and carbons. The exchange between the two conformations was evidenced by strong positive cross-peaks in NOESY spectra. Peaks were assigned to each conformation when possible according to COSY and NOESY connectivities. The α-isomer exhibited a NOE between signals of C_6H and $H_{4'}$ while no correlation between signals of C_6H and $H_{4'}$ of the β-isomer was observed. Additionally, we also observed a NOE between C_6H and $H_{2'}$ of the β-isomer while no such correlation exhibited in the α-isomer.



B = Thymine

Scheme 5

Reagents and conditions: a) i. TBDMSiCl/Py; b) CH_3SO_2Cl; c) Li_2Te/THF; d) $Et_3N.3HF/CH_2Cl_2$; e) 10% Pd/C/MeOH.

Furthermore, the $H_{1'}$ of β-isomer of **5** had an upfield chemical shift (6.15 & 6.37 ppm) compared to that of the α-isomer **6** (6.47ppm) which is deshielded by the heterocyclic ring. ^1H NMR spectra of **7, 12, 13, 14, 15, 21, 23** and **27** indicated the presence of a mixture of rotational isomers in varying ratios. However, the ratio of peaks for all the protons in a single compound was maintained constant. For example, the ^1H NMR spectrum of **7** showed singlets at δ 8.01 (0.55H, major rotamer) and 7.68 (0.45H, minor rotamer) for C_6H and doublets at δ 5.89 (J = 5.77, 0.55H, major) and 5.74 (J = 6.6 Hz, 0.45H, minor) for $H_{1'}$ proton. On the other hand, $H_{2'}$, $H_{3'}$, $H_{4'}$ and $H_{5'}$ protons appeared as multiplets and accounting for the rotamers. Also, the methyl protons of 4'-aminoacetyl and thymine methyl groups appeared as singlets at δ 1.99 (1.65H, Ac, major), 1.71 (1.35H, Ac, minor), 1.78 (1.65H, CH_3, thymine, major) and 1.74 (1.35H, CH_3, thymine, minor). In order to verify whether the compound **7** exists as rotational isomers, the ^1H NMR measurement of **7** was carried out at various temperatures. When the ^1H NMR was measured at 70 °C on the β-type isomer, the major and minor peaks that appeared at different chemical shifts coalesced into one single rotamer peak. The similar phenomenon has been reported for nucleosides containing azasugrs.[37]

A typical 500 MHz 1D ^1H NMR spectrum for α (Bottom) and β (Top) anomers of compound **14** is shown in Figure 2. In both cases, selective inversion was done on base C_6H (horizontal arrows). For **14α**, NOEs are observed from C_6H to $H_{4'}$ (0.43%) and from C_6H to 3'-OH and 2'-OH (0.98% total). In contrast, for **14β**, NOEs are observed from C_6H to $H_{2'}$ (1.9%) and to $H_{3'}$ (1.8%), but not to $H_{4'}$ at all. Thus, the NOE data indicates that **14α** isomer is in the alpha configuration whereas **14β** isomer is in the beta configuration, as the C_6H proton "sees"

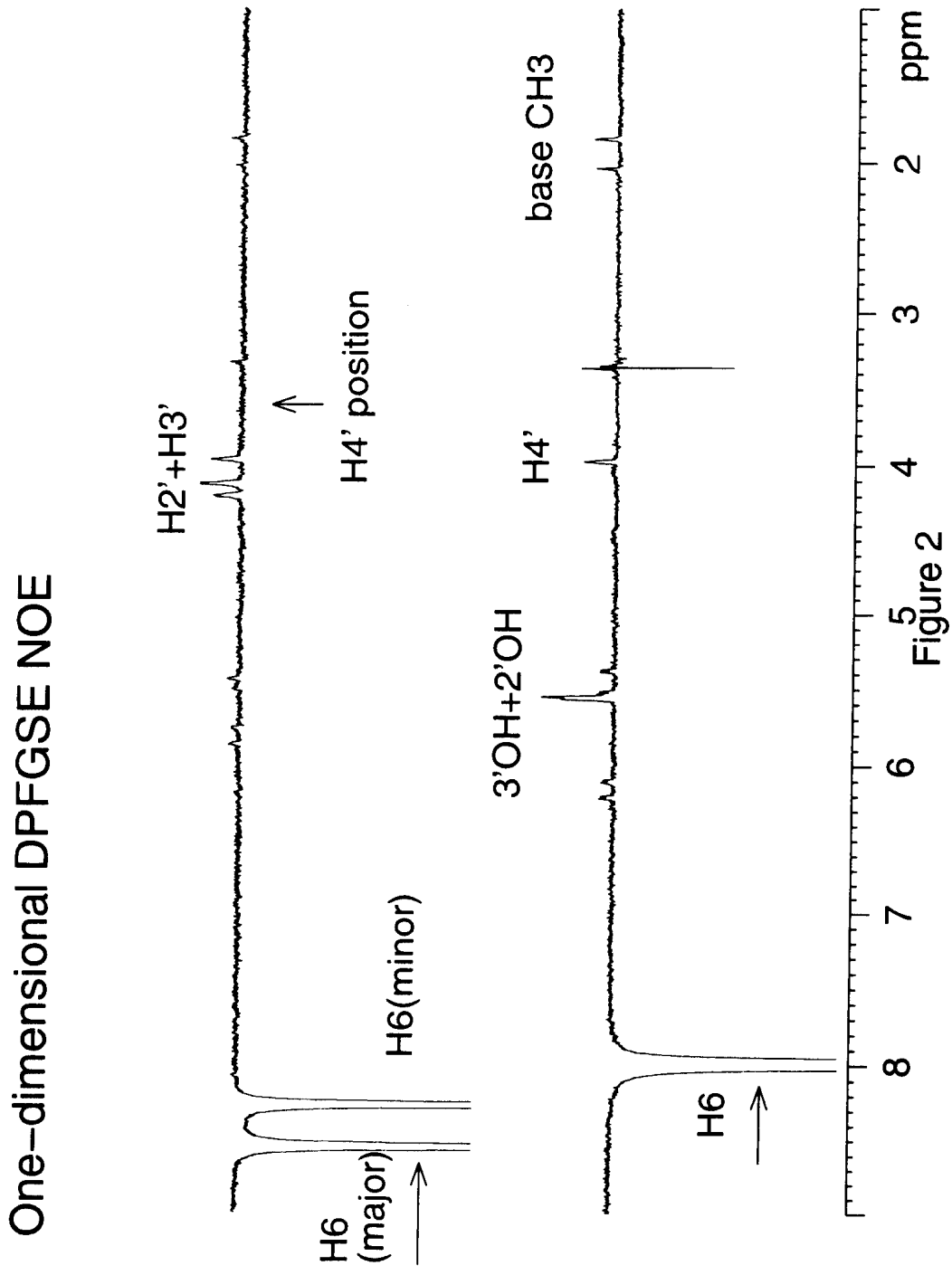

One–dimensional DPFGSE NOE
H2'+H3'
H4' position
H6(minor)
H6 (major)
3'OH+2'OH
H4'
base CH3
H6
8
7
6
5
4
3
2
ppm

Figure 2

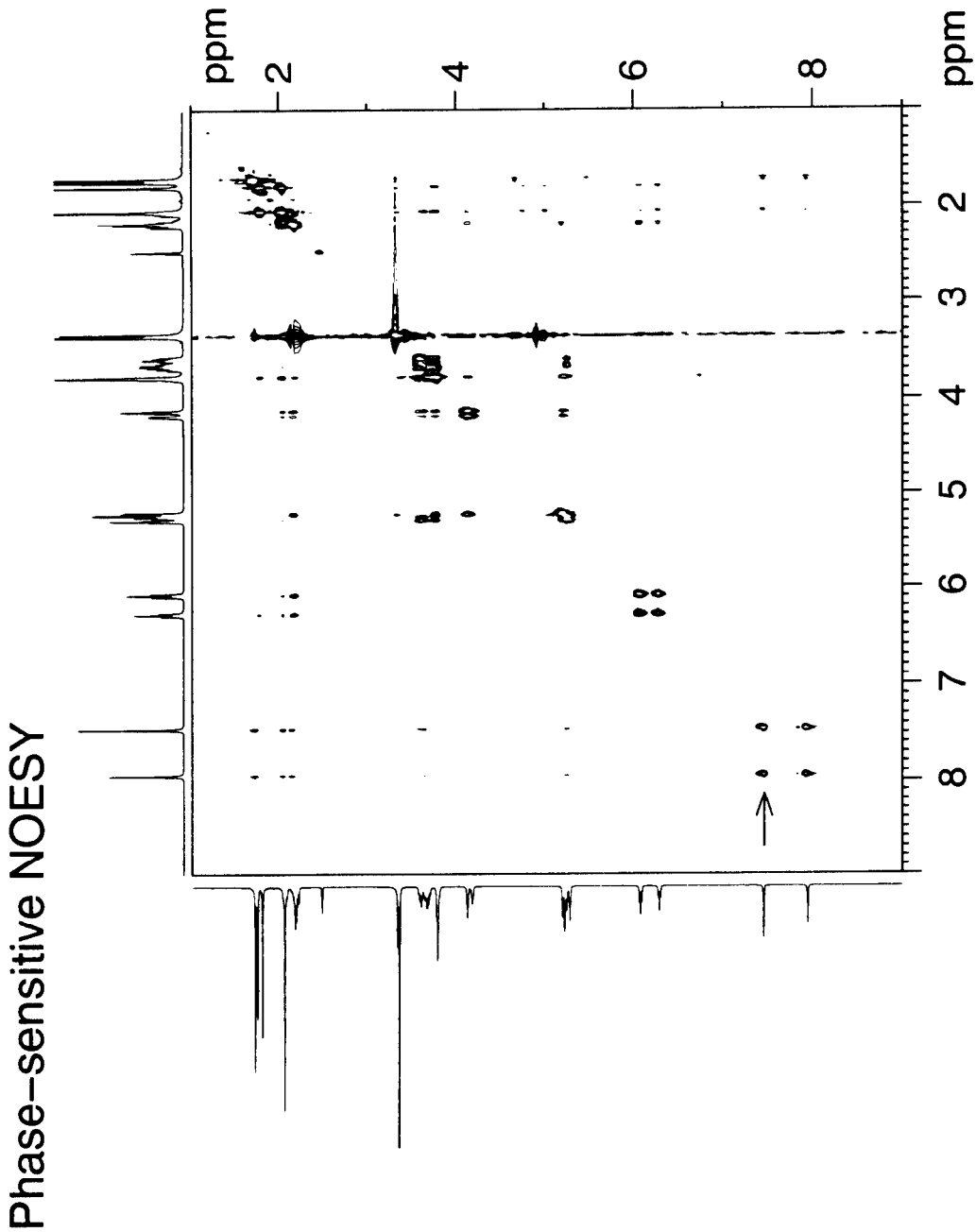


Figure 3

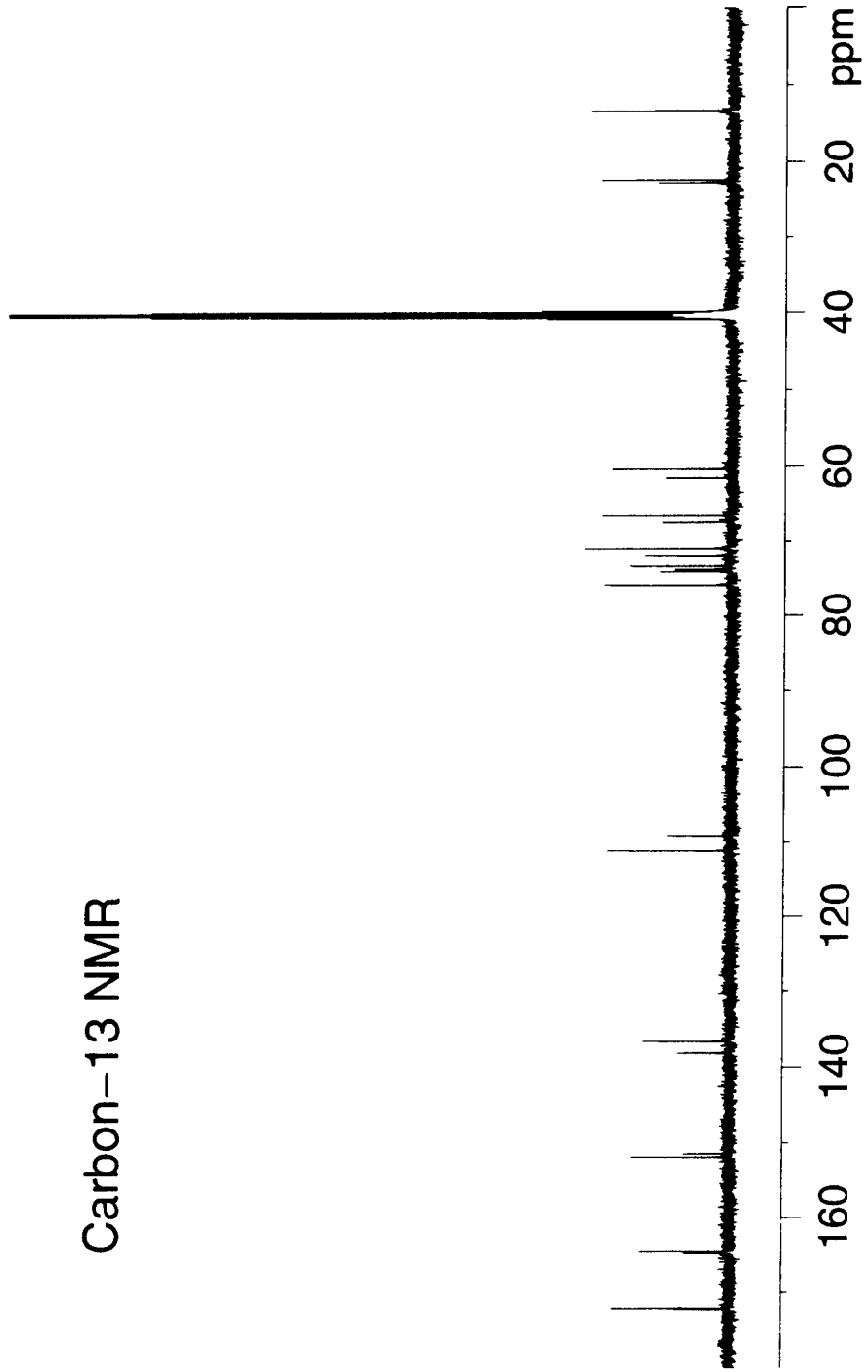


Figure 4

only the azasugar protons on the same side of the 5-member ring. Also, two exchangeable conformations of **14** are clear in the bottom spectrum (Figure 2). The exchange between C_6H in the two conformations is evidenced by a huge (~100%) negative peak at the C_6H of the minor conformer. Selected spectral parameters are: mixing time: 0.4 s; selective inversion pulse: 40 ms Gaussian shaped pulse; PFG pulses: 1 ms sine-bell shaped pulse followed by 200 us recovery delay.

Figure 3 shows the 500 MHz two-dimensional phase-sensitive (TPPI) NOESY spectrum for **21**. Both positive and negative contours are plotted. The exchange between the two (major and minor) conformers are observed as strong cross peaks that are in phase with the diagonal peaks. One such exchange peak [exchange between C_6H (major) and C_6H (minor)] is marked by an arrow. Some small NOE peaks are not visible at the contour level settings here. Selected spectral parameters are: mixing time: 0.4 s; time-domain data size: 2048X256; relaxation delay: 1 s; 8 scans per t1 increment; window functions: cosine squared in both dimensions. Figure 4 shows the ^{13}C NMR (125 MHz) spectrum for **7**. Most of the carbon resonances (see experimental) appear as doublets due to the presence of rotational isomers.

Preliminary studies of compounds **14**, **15** and **27** were found to be inactive when tested *in vitro* against human cytomegalovirus, herpes simplex virus type 1, influenza, respiratory syncytial virus, and parainfluenza type 3 virus.

In summary, we have accomplished the synthesis of a fully protected 4-deoxy-4-(acetamido)-L-ribofuranose as well as certain selected novel monocyclic L-nucleosides containing the 4-azasugar moiety. In addition, we have established the configurations of the aza-L-nucleosides using NOE and COSY experiments.

EXPERIMENTAL

Melting points were measured on a Haake Büchler capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance (^1H NMR & ^{13}C) spectra were recorded on Varian mercury 300 MHz and Bruker DRX 500 MHz spectrometer. The chemical shifts are expressed in δ values (ppm) relative to tetramethylsilane as internal standard. IR spectra were recorded using a MIDAC Grams/380 Prospect FT-IR spectrometer. Elemental analyses were performed by Quantitative technologies Inc., Whitehouse, NJ. Thin layer chromatography (TLC) was performed on plates of silica gel $60F_{254}$ coated on aluminum sheets (5x10 cm; EM Science) using different solvents prepared freshly. ICN silica gel 18-32 (60 Å) was used for flash column chromatography. All solvents used were reagent grade. Most of the dry solvents were purchased from Fluka and used as such without further purification. Most of the reactions were conducted under argon atmosphere. Evaporations were carried out under reduced pressure with the bath temperature below 35 °C.

Methyl 2, 3-*O*-isopropylidene-α-D-lyxopyranoside (1): To a methanolic HCl solution [500 mL, 0.5% w/v, prepared *in situ* by the reaction of acetyl chloride (5 mL, 70.37 mmol) with MeOH (Fisher HPLC grade)] was added D-lyxose (100 g, 666.66 mmol) and the mixture was refluxed for 5 h under N_2 atmosphere. The reaction mixture was neutralized with amberlite

basic resin IRA-410 (100.0 g) under stirring. The resin was filtered and washed with methanol (3x125 mL). The filtrate and the washings were combined and evaporated to give colorless syrup (110 g, quantitative yield) which was carried forward for the next reaction without further purification

To a stirred suspension of methyl β-D-lyxopyranoside (110 g, 666.66 mmol) in anhydrous acetone (400 mL) was added 2,2-dimethoxy propane (400 mL) followed by a solution of HCl in dioxane (4M, 8.0 mL) and the stirring was continued at 25 °C for 16 h. The reaction was quenched with solid sodium bicarbonate (500 mg) and filtered. The filtrate was evaporated and the oily residue (pinkish) was purified by silica gel flash chromatography using $CH_2Cl_2 \rightarrow$ ethyl acetate as the eluent to obtain **1** (87 g, 64%, overall yield for both steps). Anal. Calcd. for $C_9H_{16}O_5$: C, 52.93; H, 7.89. Found: C, 52.70; H, 7.82.

Methyl 4-deoxy-4-azido-2,3-*O*-isopropylidene-β-L-ribopyranoside (2): To a mixture of pyridine (6.4 mL, 79.9 mmol) and 4-(dimethylamino)pyridine (105 mg, 0.75 mmol) in anhydrous CH_2Cl_2 (600 mL) was added slowly trifluoromethanesulfonic anhydride (10.72 mL, 65 mmol) at –20 °C under argon atmosphere. The reaction mixture was allowed to stir at –20 °C for 5 min. A solution of **1** (10.2 g, 50 mmol) in CH_2Cl_2 (100.0 mL), was then added and the stirring was continued at –20 °C for additional 15 min. The TLC (15% ethyl acetate/hexane) indicated completion of the reaction. The reaction mixture was poured into a mixture of ice-water (500 mL) and the organic layer was separated. The aqueous phase was extracted with CH_2Cl_2 (2x100 mL). The combined organic layer was washed with water (2x250 mL) and brine (500 mL), dried ($NaSO_4$) and evaporated to give the intermediate triflate product as a pale yellow gummy solid (16 g).

A solution of the above methyl 4-*O*-trifluoromethanesulfonyl-2,3-*O*-isopropylidene-β-D-lyxopyranoside (16 g) in DMF (300 mL) was cooled to 0 °C. Lithium azide (12.5 g, 255.6 mmol) was slowly added and stirred at 23 °C for 3 h. The reaction mixture was diluted with toluene (200 mL) and evaporated to dryness. The residue was dissolved in a mixture of CH_2Cl_2 (500 mL) and water (200 mL). The organic layer was separated and washed with water (2x250 mL) and brine (300 mL), dried (Na_2SO_4) and evaporated to obtain an oily residue which on purification by flash chromatography using hexane → ethyl acetate as the eluent afforded pure azido product **2** (8.89 g, 78%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 3H, CH_3), 1.55 (s, 3H, CH_3), 3.44 (s, 3H, OCH_3), 3.7-3.9 (m, 3H), 4.03 (dd, 1H, J = 6.32 & 3.85 Hz), 4.49 – 4.58 (m, 2H). Anal. Calcd. for $C_9H_{15}N_3O_4$: C, 47.15; H, 6.59; N, 18.33. Found: C, 47.19; H, 6.50; N, 18.29.

Methyl 4-deoxy-4-acetamido-2,3-*O*-isopropylidene-β-L-ribopyranoside (3): To a solution of **2** (12.1 g, 52.83 mmol) in MeOH (40.0 mL) was added Pd/C (5% w/w, 1.2 g) and the reaction mixture was hydrogenated under H_2 (50 psi) atmosphere for 1 h. The reaction mixture was filtered over celite bed and evaporated to dryness. The residue was co-evaporated with toluene (2x50 mL) and followed by pyridine (2x25 mL). The residue was then carried forward to the next reaction without further purification.

To the above crude product in CH_2Cl_2 (250 mL) was added DMAP (0.7g, 5.0 mmol) and pyridine (25 mL, 310.55 mmol) and cooled to 0 °C. To the cold stirred solution was added acetic anhydride (25 mL, 265.0 mmol) at 0-5 °C (ice-acetone bath). After the addition of acetic anhydride, the ice bath was removed and the reaction mixture was stirred for 16 h. MeOH (10 mL) was added and the volatiles were evaporated. The residue was dissolved in CH_2Cl_2 (300 mL) and washed with water (2x200 mL) and brine (200 mL), dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography using hexane → ethyl acetate as the eluent to obtain **3** (11.49 g, 89%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34 (s, 3H, C*H*$_3$), 1.51 (s, 3H, C*H*$_3$), 1.99 (s, 3H, COC*H*$_3$), 3.37 (t, 1H), 3.44 (s, 3H, OC*H*$_3$), 3.83 (dd, 1H, *J* = 5.77 & 5.49 Hz), 4.01 (t, 1H, *J* = 5.77 & 4.67 Hz), 4.35 (t, 1H, *J* = 5.5 & 4.67 Hz), 4.40 (d, 1H, *J* = 4.4 Hz), 4.54 (m, 1H), 5.76 (bd, 1H, *J* = 7.97 Hz). Anal. Calcd. for $C_{11}H_{19}NO_5$: C, 53.86; H, 7.81; N, 5.71. Found: C, 53.78; H, 7.80; N, 5.67.

1,2,3,5-Tetra-*O*-acetyl-4-deoxy-4-(acetamido)-L-ribofuranose (4): A solution of **3** (8.9 g, 36.33 mmol) in a mixture of distilled water and AcOH (1:1, 100 mL) was heated at 70-75 °C for 1.5 h. Absolute EtOH (2x50 mL) was added and co-evaporated to give dry solid residue. The solid was treated with a mixture of glacial acetic acid and acetic anhydride (100 mL, 1:1), cooled to 0 °C (ice-water bath) and treated with conc. H_2SO_4 (1.0 mL). The reaction mixture was stirred at 0 °C for 30 min and then kept at 4 °C for 2 days. Anhydrous NaOAc (10.0 g) was added and stirred at room temperature for 30 min. The reaction mixture was then poured into ice-water mixture (400 mL) and extracted with CH_2Cl_2 (2x250 mL). The combined organic layer was washed with water (2x500 mL) and brine (400 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash chromatography using hexane → ethyl acetate as the eluent to obtain **4** (6.6 g, 51%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.0-2.16 (m, 15H, 5xCOC*H*$_3$), 4.18-4.51 (m, 3H), 5.33-5.36 (m, 1H), 5.45-5.55 (m, 1H), 6.36 (s, 0.75H), 6.55 (d, 0.25H, *J* = 5.22 Hz); ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.1, 20.4, 20.4, 20.7, 21.6, 59.1, 61.3, 61.6, 71.1, 71.9, 73.9, 80.0, 84.3, 168.9, 169.2, 169.6, 170.2, 170.3. Anal. Calcd. for $C_{15}H_{21}NO_9$: C, 50.13; H, 5.89; N, 3.89. Found: C, 50.06; H, 5.61; N, 3.67.

1-(2, 3, 5-Tri-*O*-acetyl-4-deoxy-4-acetamido-β-L-ribofuranosyl)thymine (5) and 1-(2, 3, 5-Tri-*O*-acetyl-4-deoxy-4-acetamido-α-L-ribofuranosyl)thymine (6): A suspension of thymine (1.26 g, 10.00 mmol) and ammonium sulphate (126 mg) in hexamethyldisilazane (25 mL) was heated at reflux for 5 h under N_2 atmosphere. The reaction mixture was evaporated to dryness and the residue suspended in 1,2-dichloroethane (50 mL) and cooled to 0 °C in an ice bath. A solution of **4** (2.51 g, 7.00 mmol) in 1, 2-dichloroethane (50 mL) was added followed by fuming $SnCl_4$ (1.17 mL, 10 mmol) at 0-5 °C. The reaction mixture was stirred at room temperature for 1 h. The reaction was carefully quenched with saturated $NaHCO_3$ solution (50 mL) and diluted with CH_2Cl_2 (200 mL). The mixture was filtered over a celite bed (5 g) and washed with CH_2Cl_2 (100 mL). The organic layer of the filtrate was separated and the aqueous layer was extracted with CH_2Cl_2 (2x100 mL). The combined organic extract was washed with water (2x300 mL) and brine (500 mL), dried (Na_2SO_4) and evaporated. The residue was purified by flash chromatography over silica gel using $CHCl_3$ → acetone as the eluent to give pure titled

products **5** & **6** (β-isomer **5**, 2.6 g, 87%; α-isomer **6**, 0.15 g, 5%). ^{1}H NMR (300 MHz, $CDCl_3$) of β-isomer: δ 1.80-2.2 (m, 15H, 4x$COCH_3$ & CH_3), 4.08 (m, 0.5H, $H_{5'}$), 4.37-4.56 (m, 2.5H, $H_{4'}$ & $H_{5'}$), 5.32 (m, 0.5H, $H_{3'}$), 5.47 (m, 1.5H, $H_{2'}$ & $H_{3'}$), 6.15 (m, 0.5H, $H_{1'}$), 6.37 (d, 0.5H, J = 6.6 Hz, $H_{1'}$), 7.16 (s, 0.5H, C_6H), 7.44 (s, 0.5H, C_6H), 9.02 (s, 0.5H, NH), 9.20 (s, 0.5H, NH). IR (KBr) ν_{max} 3350, 2970, 1700, 1412, 1236 cm^{-1}; Anal. Calcd. for $C_{18}H_{23}N_3O_9$: C, 50.82; H, 5.45; N, 9.88. Found: C, 50.89; H, 5.41; N, 9.77. ^{1}H NMR (300 MHz, $CDCl_3$) of α-isomer: δ 1.90-2.16 (m, 15H, 4x$COCH_3$ & C_5CH_3), 4.25 (m, 1H, $H_{4'}$), 4.36-4.56 (m, 2H, $H_{5'}$), 5.39 (d, 1H, J = 5.1 Hz, $H_{3'}$), 5.79 (dd, 1H, J = 5.1 & 7.2 Hz, $H_{2'}$), 6.47 (d, 1H, J = 7.2 Hz, $H_{1'}$), 7.15 (d, 1H, C_6H), 9.03 (s, 1H, NH). IR (KBr) ν_{max} 3354, 2968, 1702, 1410, 1240 cm^{-1}. Anal. Calcd. for $C_{18}H_{23}N_3O_9$: C, 50.82; H, 5.45; N, 9.88. Found: C, 50.76; H, 5.61; N, 9.67.

1-(4-Deoxy-4-acetamido-β-L-ribofuranosyl)thymine (7): A solution of **5** (3.1 g, 7.29 mmol) in saturated methanolic ammonia (100 mL) was stirred at room temperature in a steel bomb for 16 h. The steel bomb was cooled to 0 °C, opened and the contents were evaporated to dryness. The residue was purified by flash silica gel chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to afford the titled product **7** (1.72 g, 79%); mp 201-203 °C (dec); IR (KBr) ν_{max} 3349, 2961, 2835, 1613, 1412, 1236 cm^{-1}; ^{1}H NMR (300 MHz, Me_2SO-d_6 + D_2O) δ 1.70 (s, 1.35H, $COCH_3$, minor rotamer (min)), 1.73 (s, 1.35H, C_5CH_3, min), 1.77 (s, 1.65H, C_5CH_3, major rotamer (maj)), 1.98 (s, 1.65H, $COCH_3$, maj), 3.40-3.84 (m, 3H, $H_{4'}$ & $H_{5'}$), 3.94 (m, 1H, $H_{3'}$), 4.14 (t, 0.55H, J = 4.67 Hz, $H_{2'}$, maj), 4.20 (dd, 0.45H, J = 4.4 Hz, $H_{2'}$, min), 5.74 (d, 0.45H, J = 6.6 Hz, $H_{1'}$, min), 5.86 (d, 0.55H, J = 5.77 Hz, $H_{1'}$, maj), 7.68 (s, 0.45H, C_6H, min), 8.00 (s, 0.55H, C_6H, maj); ^{13}C NMR (500 MHz, Me_2SO-d_6): δ 13.2, 13.3, 22.4, 22.8, 60.3, 61.5, 66.6, 70.9, 72.1, 73.4, 74.1, 75.9, 109.2, 111.9, 136.6, 138.1, 151.4, 151.9, 164.6, 164.8, 172.1, 172.3. Anal. Calcd. for $C_{12}H_{17}N_3O_6$: C, 48.16; H, 5.73; N, 14.04. Found: C, 48.23; H, 5.81; N, 14.29.

1-(2,3,5-Tri-*O*-acetyl-4-deoxy-4-acetamido-β-L-ribofuranosyl)-6-azauracil (8): A suspension of 6-azauracil (0.91 g, 8.05 mmol) and ammonium sulphate (100 mg) in hexamethyldisilazane (20 mL) was refluxed for 2 h under N_2 atmosphere. The reaction mixture was evaporated to dryness and the residue was suspended in 1,2-dichloroethane (50 mL). To this stirred solution was added a solution of **4** (2.51 g, 7 mmol) in 1,2-dichloroethane (50 mL) followed by fuming $SnCl_4$ (0.94 mL, 8.05 mmol) at 0-5 °C (ice-water bath). After the addition of **4**, the reaction mixture was stirred at room temperature for 16 h. The reaction was carefully quenched with saturated $NaHCO_3$ solution (50 mL) and diluted with CH_2Cl_2 (200 mL). The mixture was filtered through celite (5 g) and washed with CH_2Cl_2 (100 mL). The organic layer of the filtrate was separated and the aqueous layer was extracted with CH_2Cl_2 (2x 100 mL). The combined organic extract was washed with water (2x300 mL) and brine (500 mL), dried (Na_2SO_4) and evaporated. The crude residue was purified by flash chromatography over silica gel using hexane → ethyl acetate as the eluent to obtain the titled product **8** (0.5 g, 17%). IR (KBr) ν_{max} 3210, 2983, 1678, 1336, 1017 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.01-2.15 (m, 12H), 4.12-4.48 (m, 3H, $H_{4'}$ & $H_{5'}$), 5.47 (m, 1H, $H_{3'}$), 5.57 (m, 0.2H, $H_{2'}$, minor rotamer (min)), 5.64 (m, 0.8H, $H_{2'}$, major rotamer (maj)), 6.41 (d, 0.2H, J = 5.4 Hz, $H_{1'}$, min), 6.52 (d, 0.8H, J =

7.2 Hz, $H_{1'}$, maj), 7.39 (s, 0.6H, C_5H, maj), 7.54 (s, 0.4H, C_5H, min), 9.80 (bs, 0.6H, N*H*, maj), 10.12 (bs, 0.4H, N*H*, min). Anal. Calcd. for $C_{16}H_{20}N_4O_9$: C, 46.60; H, 4.89; N, 13.58. Found: C, 46.76; H, 4.74; N, 13.54.

Methyl 1-(2,3,5-tri-*O*-acetyl-4-deoxy-4-acetamido-β-L-ribofuranosyl)uracil-6-carboxylate (9): A suspension of 6-carbomethoxyuracil (1.7 g, 10.00 mmol) and ammonium sulphate (170 mg) in hexamethyldisilazane (25 mL) was refluxed for 2 h under N_2 atmosphere. The volatiles were evaporated and the residue was suspended in 1,2-dichloroethane (50 mL). To this was added a solution of **4** (2.51 g, 7.00 mmol) in 1,2-dichloroethane (50 mL) followed by fuming $SnCl_4$ (1.17 mL, 10.00 mmol) at 0-5 °C (ice-water bath). The reaction mixture was stirred at room temperature for 16 h, carefully quenched with saturated $NaHCO_3$ solution (50 mL) and diluted with CH_2Cl_2 (200 mL). The mixture was filtered over a celite bed (5 g). The organic layer of the filtrate was separated and the aqueous layer was extracted with CH_2Cl_2 (2x100 mL). The combined organic extract was washed with water (2x300 mL) and brine (500 mL), dried (Na_2SO_4) and evaporated. The crude residue was purified by flash chromatography over silica gel using hexane → ethyl acetate as the eluent to obtain pure titled product **9** (2.2 g, 67%); mp 78-80 °C; IR (KBr) ν_{max} 3204, 2983, 1764, 1372, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.99-2.10 (m, 12H), 3.92 (s, 2.25H, OCH_3, major rotamer (maj)), 3.98 (s, 0.75H, OCH_3, minor rotamer (min)), 4.00-4.07 (m, 1H, $H_{5'}$), 4.54 (m, 2H, $H_{4'}$ & $H_{5'}$), 5.48 (d, 0.8H, J = 4.67 Hz, $H_{3'}$, maj), 5.54 (d, 0.2H, J = 4.94 Hz, $H_{3'}$, min), 6.13 (m, 0.2H, $H_{2'}$, min), 6.20 (dd, 0.8H, J = 4.67 & 7.96 Hz, $H_{2'}$, maj), 6.30 (s, 0.8H, C_5H, maj), 6.37 (s, 0.2H, C_5H, min), 6.58 (d, 0.2H, J = 6.87 Hz, $H_{1'}$, min), 6.68 (d, 0.8H, J = 7.99 Hz, $H_{1'}$, maj), 8.70 (bs, 0.80H, N*H*, maj), 8.89 (bs, 0.20H, N*H*, min); ^{13}C NMR (500 MHz, $CDCl_3$): δ 14.1, 20.4, 20.7, 20.7, 21.5, 21.7, 53.9, 54.2, 62.6, 62.7, 69.5, 71.4, 71.9, 104.2, 104.5, 138.0, 138.7, 149.4, 160.5, 162.5, 169.7, 170.2, 170.8, 171.2. Anal. Calcd. for $C_{19}H_{23}N_3O_{11}$: C, 48.61; H, 4.94; N, 8.95. Found: C, 48.60; H, 4.74; N, 8.90.

1-(2,3,5-Tri-*O*-acetyl-4-deoxy-4-acetamido-β-L-ribofuranosyl)-5-fluorouracil (10): A suspension of 5-fluorouracil (1.3 g, 10 mmol) and ammonium sulphate (130 mg) in hexamethyldisilazane (25 mL) was refluxed for 4 h under N_2 atmosphere. The reaction mixture was evaporated to dryness and the residue was suspended in 1,2-dichloroethane (50 mL). The solution was then treated with a solution of **4** (2.51 g, 7 mmol) in 1,2-dichloroethane (50 mL) followed by fuming $SnCl_4$ (1.17 mL, 10 mmol) at 0-5 °C (ice-water bath). The reaction mixture was stirred at room temperature for 16 h, carefully quenched with saturated $NaHCO_3$ solution (50 mL) and diluted with CH_2Cl_2 (200 mL). The mixture was filtered over a celite bed (5 g) and washed with CH_2Cl_2 (100 mL). The organic layer of the filtrate was separated and the aqueous layer was extracted with CH_2Cl_2 (2x100 mL). The combined organic extract was washed with water (2x300 mL) and brine (500 mL), dried (Na_2SO_4) and evaporated. The crude residue was purified by flash chromatography over silica gel using $CHCl_3$/acetone (80/20) as the eluent to provide pure **10** as a mixture of anomeric isomers (β-isomer, 1.00 g, 33%; α-isomer 0.4 g 13%). ^1H NMR (300 MHz, $CDCl_3$) of β-isomer: δ 2.02-2.21 (m, 12H), 4.10 (m, 0.45H, $H_{5'}$, min), 4.40-4.60 (m, 2.55H, $H_{4'}$ & $H_{5'}$), 5.30 (m, 0.45H, $H_{3'}$, min), 5.42-5.56 (m, 1.55H, $H_{2'}$ &

$H_{3'}$), 6.09 (t, 0.45H, J = 6.32 & 4.94 Hz, $H_{1'}$, min), 6.28 (d, 0.55H, J = 4.94 Hz, $H_{1'}$, maj), 7.48 (d, 0.45H, J = 5.77 Hz, C_6H, min), 7.95 (d, 0.55H, J = 5.77 Hz, C_6H, maj), 9.19 (bs, 0.45H, NH, min), 9.34 (bs, 0.55H, NH, maj). IR (KBr) ν_{max} 3400, 3063, 1708, 1394, 1245, 1085 cm^{-1}. Anal. Calcd. for $C_{17}H_{20}FN_3O_9$: C, 47.55; H, 4.69; N, 9.78. Found: C, 47.44; H, 4.74; N, 9.60. ^1H NMR (300 MHz, $CDCl_3$) of α-isomer: δ 1.99-2.25 (m, 12H), 4.20-4.38 (m, 1.45H, $H_{4'}$ & $H_{5'}$), 4.50-4.62 (m, 1.55H, $H_{4'}$ & $H_{5'}$), 5.42 (d, 0.80H, J = 5.40 Hz, $H_{3'}$, maj), 5.48 (d, 0.20H, J = 4.8 Hz, $H_{3'}$, min), 5.76 (dd, 0.20H, J = 7.5 & 4.8 Hz, $H_{2'}$, min), 5.82 (dd, 0.80H, J = 6.9 & 4.8 Hz, $H_{2'}$, maj), 6.48 (dd, 0.80H, J = 7.2 & 1.8 Hz, $H_{1'}$, maj), 6.54 (dd, 0.20H, J = 7.5 & 1.2 Hz, $H_{1'}$, min), 7.38 (d, 0.20H, J = 6.3 Hz, C_6H, min), 7.52 (d, 0.80H, J = 6.33 Hz, C_6H, maj), 9.28 (d, 0.80H, J = 4.8 Hz, NH, maj), 9.34 (d, 0.20H, J = 4.8 Hz, NH, min). IR (KBr) ν_{max} 3408, 3060, 1710, 1394, 1240, 1082 cm^{-1}. Anal. Calcd. for $C_{17}H_{20}FN_3O_9$: C, 47.55; H, 4.69; N, 9.78. Found: C, 47.60; H, 4.74; N, 9.79.

1-(2,3,5-Tri-*O*-acetyl-4-deoxy-4-acetamido-β-L-ribofuranosyl)-5-fluorocytosine (11): A suspension of 5-fluorocytosine (1.29 g, 10 mmol) and ammonium sulphate (322 mg) in hexamethyldisilazane (40 mL) was refluxed for 4 h under N_2 atmosphere. The volatiles were evaporated and the residue was suspended in 1,2-dichloroethane (50 mL). To this stirred solution was added a solution of **4** (2.51 g, 7 mmol) in 1,2-dichloroethane (50 mL) followed by fuming $SnCl_4$ (1.17 mL, 10 mmol) at 0-5 °C (ice-water bath). The reaction mixture was stirred at room temperature for 16 h. The reaction mixture was carefully quenched with saturated $NaHCO_3$ solution (50 mL) and diluted with CH_2Cl_2 (200 mL). The mixture was filtered over a celite bed (5 g). The organic layer of the filtrate was separated and the aqueous layer was extracted with CH_2Cl_2 (2x100 mL). The combined organic extract was washed with water (2x300 mL) and brine (500 mL), dried (Na_2SO_4) and evaporated. The crude residue was purified by flash chromatography over silica gel using $CHCl_3$/acetone (80/20) to obtain pure product **11** (1.00 g, 34%); mp 72-75 °C; IR (KBr) ν_{max} 3346, 3098, 1766, 1511, 1209 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.98-2.18 (m, 12H), 4.08 (m, 0.25H, $H_{4'}$, minor rotamer (min)), 4.36-4.62 (m, 2.75H, $H_{4'}$ & $H_{5'}$), 5.28 (m, 1H, $H_{3'}$), 5.44 (t, 0.8H, J = 4.67 Hz, $H_{2'}$, major rotamer (maj)), 5.55 (d, 0.2H, J = 4.39 Hz, $H_{2'}$, min), 5.76 (bs, 1H, NH_2), 6.27 (bt, 0.23H, $H_{1'}$, min), 6.37 (d, 0.77H, J = 3.57 Hz, $H_{1'}$, maj), 7.49 (d, 0.23H, J = 5.77 Hz, C_6H, min), 7.79 (bs, 1H, NH_2), 7.94 (d, 0.77H, J = 6.32 Hz, C_6H, maj); ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.4, 20.5, 20.7, 21.6, 21.9, 60.5, 62.4, 69.6, 72.1, 73.9, 79.0, 123.2, 123.4, 130.9, 131.2, 136.4, 138.4, 153.4, 153.9, 158.1, 158.2, 169.4, 169.6, 170.8, 172.3. Anal. Calcd. for $C_{17}H_{21}FN_4O_8$: C, 47.66; H, 4.94; N, 13.08. Found: C, 47.60; H, 5.11; N, 12.99.

1-(4-Deoxy-4-acetamido-β-L-ribofuranosyl)-6-azauracil (12): A solution of **8** (0.45 g, 1.09 mmol) in saturated methanolic ammonia (10 mL) was stirred in a steel bomb at room temperature for 16 h. The steel bomb was cooled, opened and evaporated to dryness. The residue was purified by flash chromatography over silica gel using $CHCl_3 \rightarrow$ MeOH as the eluent to afford the titled product **12** (0.18 g, 58%); mp 225-228 °C (dec); IR (KBr) ν_{max} 3292, 2990, 1725, 1620, 1272 cm^{-1}; ^1H NMR (300 MHz, Me_2SO-d_6) δ 1.84 (s, 1.35H, COCH_3, minor rotamer (min)), 1.95 (s, 1.65H, COCH_3, major rotamer (maj)), 3.46-3.85 (m, 3H, $H_{4'}$ & $H_{5'}$),

4.01 (m, 1H, $H_{3'}$), 4.22 (m, 1H, $H_{2'}$), 4.89 (m, 0.45H, O*H*, min), 5.01 (m, 0.55H, O*H*, maj),), 5.15 (m, 0.45H, O*H*, min), 5.28 (m, 0.55H, O*H*, maj), 5.39 (d, 0.45H, J = 6.86 Hz, O*H*, min), 5.50 (d, 0.55H, J = 5.7 Hz, O*H*, maj), 6.00 (d, 0.45H, J = 7.15 Hz, $H_{1'}$, min), 6.05 (d, 0.55H, J = 5.5 Hz, $H_{1'}$, maj), 7.50 (s, 0.45H, C_5H, min), 7.62 (s, 0.55H, C_5H, maj), 12.20 (bs, 1H, N*H*). ^{13}C NMR (500 MHz, Me_2SO-d_6): δ 21.4, 60.4, 61.4, 66.2, 69.7, 70.6, 73.1, 74.3, 74.4, 135.6, 137.5, 147.9, 148.6, 156.6, 170.2, 170.8. Anal. Calcd. for $C_{10}H_{14}N_4O_6$: C, 41.96; H, 4.93; N, 19.57. Found: C, 42.03; H, 5.11; N, 19.64.

1-(4-Deoxy-4-acetamido-β-L-ribofuranosyl)uracil-6-carboxamide (13): A solution of **9** (2.0 g, 4.26 mmol) in saturated methanolic ammonia (20 mL) was stirred at room temperature in a steel bomb for 16 h. The steel bomb was cooled, opened and evaporated to dryness. The residue that obtained was purified by flash chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to afford the titled product **13** (1.0 g, 72%); mp 115-118 °C; IR (KBr) ν_{max} 3310, 2980, 1640, 1412, 1032 cm^{-1}; ^{1}H NMR (300 MHz, Me_2SO-d_6 + D_2O) δ 1.70 (s, 1H, $COCH_3$, minor rotamer (min)), 1.89 (s, 2H, $COCH_3$, major rotamer (maj)), 3.44-3.97 (m, 4H, $H_{3'}$, $H_{4'}$ & $H_{5'}$), 4.73 (m, 1H, $H_{2'}$), 6.08-6.26 (m, 2H, C_5H & $H_{1'}$). ^{13}C NMR (500 MHz, Me_2SO-d_6): δ 14.1, 21.4, 21.5, 61.2, 61.5, 68.4, 69.5, 69.9, 70.5, 71.1, 99.6, 99.8, 143.1, 144.2, 161.4, 161.5, 163.0, 163.7, 169.6, 169.8. Anal. Calcd. for $C_{12}H_{16}N_4O_7$: C, 43.90; H, 4.91; N, 17.07. Found: C, 43.99; H, 5.06; N, 17.21.

1-(4-Deoxy-4-acetamido-β-L-ribofuranosyl)-5-fluorouracil (14): A solution of **10** (β-isomer, 1.0 g, 2.33 mmol) in saturated methanolic ammonia (20 mL) was stirred in a steel bomb at room temperature for 16 h. The steel bomb was cooled to 0 °C, opened and evaporated to dryness. The residue was purified by flash chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to afford the titled product **14** (0.6 g, 85%); mp 125-127 °C (dec); IR (KBr) ν_{max} 3438, 3080, 2961, 1667, 1392, 1131 cm^{-1}; ^{1}H NMR (500 MHz, Me_2SO-d_6) δ 1.85 (s, 1.35H, $COCH_3$, minor rotamer (min)), 2.02 (s, 1.65H, $COCH_3$, major rotamer (maj)), 3.15-3.96 (m, 5H, $H_{2'}$, $H_{3'}$, $H_{4'}$ & $H_{5'}$), 4.07 (dd, 0.55H, $C_{5'}OH$, maj), 4.33 (t, 0.45H, $C_{5'}OH$, min), 5.10 (d, 0.45H, $C_{3'}OH$, min), 5.20 (d, 0.55H, $C_{3'}OH$, maj), 5.40 (d, 0.45H, $C_{2'}OH$, min), 5.55 (d, 0.55H, $C_{2'}OH$, maj), 5.76 (t, 0.45H, J = 5.77 Hz, $H_{1'}$, min), 5.86 (d, 0.55H, J = 4.1 Hz, $H_{1'}$, maj), 8.27 (bd, 0.45H, C_6H, min), 8.55 (bd, 0.55H, C_6H, maj), 11.72 (bs, N*H*), 11.86 (bs, N*H*); ^{13}C NMR (500 MHz, Me_2SO-d_6): δ 21.7, 21.9, 48.6, 59.3, 60.5, 65.5, 67.0, 70.0, 71.4, 73.3, 73.5, 75.1, 124.2, 124.5, 125.8, 138.7, 139.7, 141.5, 149.3, 149.6, 156.9, 157.0, 157.2, 157.2, 171.6, 171.7. Anal. Calcd. for $C_{11}H_{14}FN_3O_6$: C, 43.57; H, 4.65; N, 13.86. Found: C, 43.40; H, 4.71; N, 13.80.

A solution of **10** (α-isomer, 0.4g, 0.93 mmol) in saturated methanolic ammonia (20 mL) was stirred in a steel bomb at room temperature for 16 h. The steel bomb was cooled to 0 °C, opened and evaporated to dryness. The residue was purified by flash chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to afford the α-isomer of **14** (0.6 g, 85%); mp 155-158 °C (dec); IR (KBr) ν_{max} 3436, 3088, 2691, 1672, 1392, 1131 cm^{-1}; ^{1}H NMR (500 MHz, Me_2SO-d_6) δ 1.85 (s, 1.35H, $COCH_3$, minor rotamer (min)), 2.04 (s, 1.65H, $COCH_3$, major rotamer (maj)), 3.42 (m, 1H, $H_{5'}$), 3.52 (m, 1H, $H_{4'}$), 3.98 (m, 1H, $H_{5'}$), 4.04 (m, 1H, $H_{3'}$), 4.44 (m, 1H, $H_{2'}$), 4.82 (t, 0.55H, $C_{5'}OH$, maj), 5.14 (t, 0.45H, $C_{5'}OH$, min), 5.40 (d, 0.45H, O*H*,

min), 5.54 (d, 0.55H, O*H*, maj), 5.58 (m, 1H, O*H*), 6.19 (d, 0.45H, J = 2.1 Hz, $H_{1'}$, min), 6.22 (d, 0.55H, J = 1.8 Hz, $H_{1'}$, maj), 7.99 (m, 1H, C_6H), 11.68 (bs, N*H*), 11.84 (bs, N*H*); ^{13}C NMR (500 MHz, Me_2SO-d_6): δ 22.1, 22.4, 58.5, 61.1, 66.4, 68.5, 69.3, 69.9, 71.6, 72.9, 126.5, 126.8, 127.1, 137.8, 138.4, 140.2, 149.7, 149.9, 157.1, 157.1, 157.3, 157.3, 170.2, 170.3. Anal. Calcd. for $C_{11}H_{14}FN_3O_6$: C, 43.57; H, 4.65; N, 13.86. Found: C, 43.40; H, 4.71; N, 13.80.

1-(4-Deoxy-4-acetamido-β-L-ribofuranosyl)-5-fluorocytosine (15): A solution of **11** (1.00 g, 2.33 mmol) in saturated methanolic ammonia (20 mL) was stirred in a steel bomb at room temperature for 16 h. The steel bomb was cooled, opened and evaporated to dryness. The residue was purified by flash chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to afford the titled product **15** (0.64 g, 91%); mp 106-108 °C (dec); IR (KBr) ν_{max} 3536, 2926, 1684, 1490, 1177 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 1.92 (s, 2H, $COCH_3$, major rotamer (maj)), 2.17(s, 1H, $COCH_3$, minor rotamer (min)), 3.75-3.93 (m, 2H, $H_{5'}$), 4.16-4.28 (m, 1.5H, $H_{3'}$ & $H_{4'}$), 4.49 (t, 0.5H, J = 4.4 & 4.94 Hz, $H_{3'}$), 4.65 (s, 1H, $H_{2'}$), 5.77 (d, 0.34H, J = 5.22 Hz, $H_{1'}$, min), 6.12 (dd, 0.66H, J = 1.92 & 4.12 Hz, $H_{1'}$, maj), 8.19 (d, 0.34H, J = 6.86 Hz, C_6H, min), 8.66 (d, 0.66H, J = 7.15 Hz, C_6H, maj); ^{13}C NMR (500 MHz, Me_2SO-d_6): δ 21.6, 22.2, 58.8, 59.7, 64.9, 69.7, 70.7, 73.3, 74.2, 75.3, 125.3, 125.6, 127.2, 134.8, 135.6, 136.8, 137.5, 153.7, 153.8, 157.2, 157.4, 171.5, 171.7. Anal. Calcd. for $C_{11}H_{15}FN_4O_5$: C, 43.71; H, 5.00; N, 18.54. Found: C, 43.77; H, 5.17; N, 18.79.

1-[3, 5-*O*-(1, 1, 3, 3-Tetraisopropyldisiloxane-1, 3-diyl)-4-deoxy-4-acetamido-β-L-ribofuranosyl]thymine (16) & 1-[2, 3-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-β-L-ribofuranosyl]thymine (17): A suspension of **7** (1.72 g, 5.75 mmol) in pyridine (25 mL) was treated with 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane (2.75 mL, 8.59 mmol) and stirred at room temperature for 16 h. The reaction mixture was carefully quenched with saturated $NaHCO_3$ solution (50 mL) and diluted with CH_2Cl_2 (100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x25 mL). The combined organic extract was washed with water (2x100 mL) and brine (100 mL), dried (Na_2SO_4) and evaporated. The crude residue was purified by flash chromatography over silica gel using hexane → ethyl acetate as the eluent to afford a mixture of inseparable products **16** & **17** (2.15 g, 69%).

1-[2-*O*-(*p*-Tolylthionoformyl)-3, 5-*O*-(1, 1, 3, 3-tetraisopropyldisiloxane-1, 3-diyl)-4-deoxy-4-acetamido-β-L-ribofuranosyl]thymine (18) & 1-[5-*O*-(*p*-Tolylthionoformyl)-2, 3-*O*-(1, 1, 3, 3-tetraisopropyldisiloxane-1, 3-diyl)-4-deoxy-4-acetamido-β-L-ribofuranosyl]thymine (19): To a mixture of **16** and **17** (2.00 g, 3.69 mmol) in pyridine (20 mL) was added *p*-tolyl chlorothionoformate (0.71 mL, 4.43 mmol) and the reaction mixture was stirred at room temperature for 16 h under argon atmosphere. The reaction mixture was quenched with saturated $NaHCO_3$ solution (50 mL) and diluted with CH_2Cl_2 (100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x25 mL). The combined organic extract was washed with water (2x100 mL) and brine (100 mL), dried (Na_2SO_4) and evaporated to dryness. The crude residue was purified by flash chromatography over silica gel using hexane → ethyl acetate as the eluent to afford a faster moving product (0.9 g) and a slower moving

product (0.8 g). The combined yield was 1.7 g (67%). The ^{1}H NMR analysis of the products indicated that the structure of slower product as **18** and the structure of the faster product as **19**. ^{1}H NMR (300 MHz, $CDCl_3$) of **18**: δ 0.96-1.18 (m, 24H), 1.92 (s, 3H, C*H*$_3$), 2.00 (s, 2H, COC*H*$_3$, major rotamer (maj)), 2.25 (s, 1H, COC*H*$_3$, minor rotamer (min)), 2.34 (s, 3H, C*H*$_3$), 3.85-4.40 (m, 3H, *H*$_{5'}$ & *H*$_{4'}$), 4.62-4.82 (m, 1.5H, *H*$_{2'}$ & *H*$_{3'}$, maj), 5.3 & 5.64 (bs, 0.5H, *H*$_{2'}$ & *H*$_{3'}$, min), 6.02 (s, 1H, *H*$_{1'}$), 6.95 (d, 2H, *J* = 8.52 Hz, Ph-*H*), 7.20 (d, 2H, *J* = 8.52 Hz, Ph-*H*), 7.35 (s, 0.24H, C$_6$*H*, min), 7.57 (s, 0.76H, C$_6$*H*, maj), 8.23 (bs, 0.24H, N*H*, min), 8.64 (s, 0.76H, N*H*, maj). Anal. Calcd. for $C_{32}H_{49}N_3O_8Si_2$: C, 55.54; H, 7.14; N, 6.07. Found: C, 55.50; H, 7.11; N, 6.23. ^{1}H NMR (300 MHz, $CDCl_3$) of **19**: δ 1.00-1.06 (m, 24H), 1.87 (s, 3H, C*H*$_3$), 2.02 (s, 2.4H, COC*H*$_3$, major rotamer (maj)), 2.22 (s, 0.6H, COC*H*$_3$, minor rotamer (min)), 2.34 (s, 3H, C*H*$_3$), 4.22-4.56 (m, 3H, *H*$_{4'}$ & *H*$_{5'}$), 4.84 (m, 1H, *H*$_{3'}$), 5.24 (m, 1H, *H*$_{2'}$), 6.02 (d, 1H, *J* = 3.02 Hz, *H*$_{1'}$), 6.96 (d, 2H, *J* = 8.24 Hz, Ph-*H*), 7.22 (d, 2H, *J* = 8.52 Hz, Ph-*H*), 7.78 (s, 1H, C$_6$*H*), 8.38 (bs, 0.16H, N*H*, min), 8.44 (s, 0.84H, N*H*, maj). Anal. Calcd. for $C_{32}H_{49}N_3O_8Si_2$: C, 55.54; H, 7.14; N, 6.07. Found: C, 55.52; H, 7.20; N, 6.17.

1-[3, 5-*O*-(1, 1, 3, 3-Tetraisopropyldisiloxane-1, 3-diyl)-2, 4-dideoxy-4-acetamido-β-L-ribofuranosyl]thymine (20): A solution of **18** (0.74 g, 1.07 mmol) in dry toluene (25 mL) was purged with argon for 20 min. To this stirred solution was added 2,2'-azobisisobutyronitrile (AIBN, 0.17 g, 1.07 mmol) followed by tri-n-butyltin hydride (0.56 mL, 2.11 mmol). The reaction mixture was refluxed for 6 h under a stream of argon. The volatiles were evaporated and the crude residue was purified by flash chromatography over silica gel using hexane → ethyl acetate as the eluent to afford **20** (0.45 g, 80%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90-1.08 (m, 24H), 1.60 (s, 2H), 1.90 (s, 3H, C*H*$_3$), 1.97 (s, 2.25H, COC*H*$_3$, major rotamer (maj)), 2.17 (s, 0.75H, COC*H*$_3$, minor rotamer (min)), 2.2-2.4 (m, 1.5H, *H*$_{2'}$, maj), 2.65 (m, 0.5H, *H*$_{2'}$, min), 3.68 (m, 1H, *H*$_{5'}$), 4.02 (m, 0.75H, *H*$_{5'}$), 4.32 (m, 0.25H, *H*$_{5'}$, min), 4.64 (m, 1.55H, *H*$_{3'}$ & *H*$_{4'}$), 5.12 (m, 0.45H, *H*$_{3'}$, min), 5.71 (m, 0.15H, *H*$_{1'}$, min), 6.05 (m, 0.85H, *J* = 6.05 Hz, *H*$_{1'}$, maj), 7.33 (s, 0.15H, C$_6$*H*, min), 7.53 (s, 0.85H, C$_6$*H*, maj), 8.23 (bs, 0.15H, N*H*, min), 8.76 (s, 0.85H, N*H*, maj). Anal. Calcd. for $C_{24}H_{43}N_3O_6Si_2$: C, 54.82; H, 8.24; N, 7.99. Found: C, 54.76; H, 8.29; N, 7.90.

1-(2, 4-Dideoxy-4-acetamido-β-L-ribofuranosyl)thymine (21): A solution of **20** (0.38 g, 0.72 mmol) in CH_2Cl_2 (10 mL) was treated with triethylamine trihydrofluoride (0.59 mL, 3.6 mmol) at room temperature. The reaction mixture was stirred for 48 h and evaporated to dryness. The residue was purified by flash chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to give the titled compound **21** (0.19 g, 93%); mp 119-121 °C; IR (KBr) ν_{max} 3420, 2828, 1632, 1418, 1127 cm^{-1}; ^{1}H NMR (500 MHz, Me_2SO-*d*$_6$) δ 1.72 (s, 1.65H, C*H*$_3$, major rotamer (maj)), 1.75 (s, 1.35H, C*H*$_3$, minor rotamer (min)), 1.80 (s, 1.35H, COC*H*$_3$, min), 2.06 (s, 1.65H, COC*H*$_3$, maj), 2.07 (m, 0.55H, *H*$_{2'}$-β, maj), 2.18 (m, 0.45H, *H*$_{2'}$-β, min), 2.19 (m, 1H, *H*$_{2'}$-α), 3.59-3.78 (m, 3H, *H*$_{4'}$ & *H* $_{5'}$), 4.13 (t, 0.55H, *H*$_{3'}$, maj), 4.18 (bs, 0.45H, *H*$_{3'}$, min), 5.19 (d, 0.45H, C$_{3'}$O*H*, min), 5.21 (d, 0.55H, C$_{3'}$O*H*, maj), 5.23 (t, 0.45H, C$_{5'}$O*H*, min), 5.29 (t, 0.55H, C$_{5'}$O*H*, maj), 6.08 (t, 0.45H, *H*$_{1'}$, maj), 6.29 (t, 0.45H, *H*$_{1'}$, min), 7.45 (s, 0.55H, C$_6$*H*, maj), 7.94 (s, 0.45H, C$_6$*H*, min), 11.18 (s, N*H*, maj), 11.38 (s, N*H*, min); ^{13}C NMR (500 MHz,

Me_2SO-d_6): δ 12.5, 12.6, 21.7, 22.7, 60.1, 61.4, 68.2, 68.8, 69.3, 69.4, 70.6, 108.5, 110.5, 135.5, 136.0, 150.4, 150.7, 163.7, 164.0, 171.2, 171.4. Anal. Calcd. for $C_{12}H_{17}N_3O_5.1/2H_2O$: C, 49.31; H, 6.21; N, 14.38. Found: C, 49.49; H, 6.43; N, 14.51.

1-[2, 3-*O*-(1, 1, 3, 3-Tetraisopropyldisiloxane-1, 3-diyl)-4, 5-dideoxy-4-acetamido-β-L-ribofuranosyl]thymine (22): A solution of 19 (1.35 g, 1.95 mmol) in dry toluene (40 mL) was purged with argon for 20 min. To this stirred solution was added 2,2'-azobisisobutyronitrile (AIBN, 0.32 g, 1.95 mmol) and tri-n-butyltin hydride (1.04 mL, 3.91 mmol). The reaction mixture was refluxed for 1.5 h under a stream of argon. The reaction mixture was evaporated to dryness. The crude residue was purified by flash chromatography over silica gel using hexane → ethyl acetate as the eluent to give 22 (0.7 g, 68 %). ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.98-1.05 (m, 24H), 1.46 (d, 1.2H, $H_{5'}$, minor rotamer (min)), 1.52 (d, 2.8H, J = 6.9 Hz, $H_{5'}$, major rotamer (maj)), 1.62 (bs, 1H), 1.89 (s, 1.2H, $COCH_3$, min), 1.93 (s, 3H, CH_3), 2.09 (s, 1.8H, $COCH_3$, maj), 3.86 (m, 0.6H, $H_{4'}$, maj), 3.98 (m, 0.4H, $H_{4'}$, min), 4.12-4.20 (m, 1H, $H_{3'}$), 4.36 (m, 0.5H, $H_{2'}$), 5.18 (m, 0.5H, $H_{2'}$), 5.30 (d, 0.6H, J = 6.05 Hz, $H_{1'}$, maj), 5.98 (d, 0.4H, J = 3.57 Hz, $H_{1'}$, min), 6.99 (s, 0.4H, C_6H, min), 7.08 (s, 0.6H, C_6H, maj), 8.53 (bs, 0.6H, NH, maj), 8.66 (bs, 0.4H, NH, min). Anal. Calcd. for $C_{24}H_{43}N_3O_6Si_2$: C, 54.82; H, 8.24; N, 7.99. Found: C, 54.89; H, 8.19; N, 7.79.

1-(4, 5-Dideoxy-4-acetamido-β-L-ribofuranosyl)thymine (23): A solution of **22** (0.6 g, 1.14 mmol) in CH_2Cl_2 (20 mL) was treated with triethylamine trihydrofluoride (0.56 mL, 3.42 mmol) at room temperature. The reaction mixture was stirred at room temperature for 20 h and the volatiles were evaporated to dryness. The residue was purified by flash chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to afford **23** (0.2 g, 62%). IR (KBr) ν_{max} 3484, 2978, 1728, 1478, 1252 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 1.40 (d, 1.36H, J = 6.87 Hz, $H_{5'}$, minor rotamer (min)), 1.48 (d, 1.64H, J = 6.87 Hz, $H_{5'}$, major rotamer (maj)), 1.87 (s, 1.08H, CH_3), 1.91 (s, 1.92H, CH_3), 1.91 (s, 1.08H, $COCH_3$, min), 2.09 (s, 1.92H, $COCH_3$, maj), 3.84-4.00 (m, 1H, $H_{4'}$), 4.06 (m, 0.60H, $H_{3'}$, maj), 4.33 (m, 0.40H, $H_{3'}$, min), 4.66 (m, 1H, $H_{2'}$), 5.72 (d, 0.64H, J = 6.87 Hz, $H_{1'}$, maj), 6.08 (d, 0.36H, J = 5.77 Hz, $H_{1'}$, min), 7.21 (s, 0.36H, C_6H, min), 7.27 (s, 0.64H, C_6H, maj); ^{13}C NMR (500 MHz, Me_2SO-d_6): δ 12.3, 12.4, 17.9, 18.7, 21.55, 21.7, 59.7, 60.9, 72.3, 73.5, 74.2, 74.3, 74.5, 108.7, 110.9, 135.2, 137.6, 150.5, 150.9, 163.7, 164.0, 170.7, 171.0. Anal. Calcd. for $C_{12}H_{17}N_3O_5$: C, 50.88; H, 6.05; N, 14.83. Found: C, 50.91; H, 6.23; N, 14.91.

1-(5-*O*-*Tert*-butyldimethylsilyl-2, 3-*O*-di-methanesulfonyl-4-deoxy-4-acetamido-β-L-ribofuranosyl)thymine (24): A suspension of 1-(4-deoxy-4-acetamido-β-L-ribofuranosyl)thymine 7 (0.58 g, 1.92 mmol) in pyridine (10 mL) was treated with *tert*-butyldimethylsilyl chloride (0.41 g, 2.68 mmol) and stirred at room temperature for 16 h. The reaction mixture was carefully quenched with saturated $NaHCO_3$ solution (5 mL) and diluted with CH_2Cl_2 (100 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x25 mL). The combined organic extract was washed with water (2x100 mL) and brine (100 mL), dried (Na_2SO_4) and evaporated. The crude residue that obtained was treated with methanesulfonyl chloride (0.37 mL, 4.8 mmol) and stirred at room temperature for 16 h. The reaction mixture

was quenched with saturated $NaHCO_3$ solution (5 mL) and the volatiles were evaporated to dryness. The residue that obtained was suspended in water (50 mL) and filtered. The solid was washed with water (200 mL) and then purified over flash silica gel chromatography using $CHCl_3$ → MeOH as the eluent to afford the pure titled product (0.5 g, 46%). The pure product was dried over P_2O_5 at 40 °C under vacuum before carrying forward to the next reaction. ^1H NMR (300 MHz, Me_2SO-d_6 + D_2O) δ 0.04 (bs, 6H, 2xCH_3), 0.82 (s, 9H, *tert*-butyl), 1.70 (s, 1.65H, C_5CH_3, major rotamer (maj)), 1.74 (s, 1.35H, C_5CH_3, minor rotamer (min)), 1.80 (s, 1.35H, $COCH_3$, min), 2.04 (s, 1.65H, $COCH_3$, maj), 3.12-24 (m, 6H, 2xSO_2CH_3), 3.90-4.06 (m, 2H, $H_{5'}$), 4.32 (m, 1H, $H_{4'}$), 5.10 (dd, 1H, J = 4.2 Hz, $H_{3'}$), 5.36-5.44 (dd, 1H, J = 7.5 & 4.5 Hz, $H_{2'}$), 6.03 (d, 0.55H, J = 7.8 Hz, $H_{1'}$, maj), 6.22 (d, 0.45H, J = 6.0 Hz, $H_{1'}$ min), 7.38 (s, 0.55H, C_6H, maj), 7.44 (s, 0.45 H, C_6H, min).

1–(5-*O*-*Tert*-butyldimethylsilyl-2,3,4-trideoxy-2,3-didehydro–4–acetamido-β-L–ribofuranosyl)thymine (25): A THF solution of lithium triethylborohydride (1M, 4.24 mL, 4.24 mmol) was added to Tellurium powder (200 mesh, 0.25 g, 1.93 mmol) and stirred at room temperature until a pinkish-milky white suspension was obtained. To this stirred mixture was added a solution of **24** (0.5 g, 0.88 mmol) in dry THF (6 mL). After the addition of **24**, the stirring was continued at room temperature for 48 h and filtered over a celite bed. The filtrate was evaporated and the residue was purified by flash chromatography over silica gel using $CHCl_3$ → ethyl acetate as the eluent to afford pure titled product **25** (0.2 g, 60%). Major rotamer: ^1H NMR (300 MHz, $CDCl_3$) δ 0.08 (s, 6H, 2xCH_3), 0.88 (s, 9H, *tert*-butyl), 1.89 (d, 3H, J=1.2 Hz, C_5CH_3), 2.02 (s, 3H, $COCH_3$), 3.98-4.08 (dd, 1H, J = 11.12 & 3.15 Hz, $H_{5'}$), 4.10-4.18 (dd, 1H, J = 10.85 & 3.71 Hz, $H_{5'}$), 4.79 (m, 1H, $H_{4'}$), 5.72 (m, 1H, $H_{3'}$), 6.14 (m, 1H, $H_{2'}$), 7.00 (d, 1H, J = 1.8 Hz, $H_{1'}$), 7.58 (d, 1H, J = 1.2 Hz, C_6H), 9.17 (s, 1H, NH). Minor rotamer peaks were appeared in the ratio of 1-2% of major rotamer peaks and found difficult to designate. Anal. Calcd. for $C_{18}H_{29}N_3O_4Si$: C, 56.96; H, 7.70; N, 11.07. Found: C, 56.79; H, 7.52; N, 11.15.

1–(2,3,4-Trideoxy-2,3-didehydro–4–acetamido-β-L–ribofuranosyl)thymine (26): A solution of **25** (0.27 g, 0.69 mmol) in CH_2Cl_2 (20 mL) was treated with triethylamine trihydrofluoride (0.32 mL, 1.38 mmol) at room temperature. The reaction mixture was stirred for 20 h and the volatiles were removed under reduced pressure. The residue was purified by flash chromatography over silica gel using $CHCl_3$ → MeOH as the eluent to afford **26** (0.16 g, 87%). IR (KBr) ν_{max} 3349, 2835, 1710, 1402, 1125 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) δ 1.79 (s, 0.6H, C_5CH_3, minor rotamer (min)), 1.82 (s, 2.4H, C_5CH_3, major rotamer (maj)), 2.04 (s, 2.4H, $COCH_3$, maj), 2.2 (s, 0.6H, $COCH_3$, min), 3.84 (dd, 1H, J = 12 & 2.85 Hz, $H_{5'}$), 4.0 (dd, 1H, J = 12 & 2.85 Hz, $H_{5'}$), 4.62 (m, 0.2H, $H_{4'}$, min), 4.73 (t, 0.8H, J = 2.1 Hz, $H_{4'}$, maj), 5.78 (d, 0.8H, J = 6.3 Hz, $H_{3'}$, maj), 5.85 (m, 0.2H, $H_{3'}$, min), 6.18 (m, 0.2H, $H_{2'}$, min), 6.23 (d, 0.8H, $H_{2'}$, J = 6.3 Hz, maj), 6.96 (m, 0.2H, $H_{1'}$, min), 7.11 (dd, 0.8H, J = 3.3 & 1.5 Hz, $H_{1'}$, maj), 8.12 (s, 0.2H, C_6H, min), 8.34 (s, 0.8H, C_6H, maj). Anal. Calcd. for $C_{12}H_{15}N_3O_4$: C, 54.33; H, 5.70; N, 15.84. Found: C, 54.11; H, 5.84; N, 15.68.

1-(2,3,4-Trideoxy–4–acetamido-β-L-ribofuranosyl)thymine (27): To a solution of **26** (90 mg, 0.34 mmol) in methanol (10 mL) was added Pd/C (10%, 10 mg) under argon atmosphere.

The reaction mixture was shaked under H_2 atomosphere (40 psi) at room temperature for 3 h. The catalyst was filtered and the filtrate was evaporated to afford the titled product as colorless solid (90 mg, quantitative). IR (KBr) ν_{max} 3345, 2840, 1718, 1408, 1125 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 1.84 (s, 1.65H, C_5CH_3, major rotamer (maj)), 1.86 (s, 1.35H, C_5CH_3, minor rotamer (min)), 1.97 (s, 1.65H, $COCH_3$, maj), 2.00-2.16 (m, 3H, $H_{2'}$ & $H_{3'}$), 2.19 (s, 1.35H, $COCH_3$, min), 2.34 (m, 0.55H, $C_{2'}$-β, maj), 2.40 (m, 0.45H, $C_{2'}$-β, min), 3.68–3.74 (m, 1H, $H_{5'}$), 3.92 (dd, 0.45H, $H_{4'}$, min), 4.08-4.16 (m, 1H, $H_{5'}$), 4.28 (dd, 0.55H, $H_{4'}$, maj), 6.11 (t, 0.45H, $H_{1'}$, min), 6.31 (dd, 0.55H, $H_{1'}$, maj), 7.74 (s, 0.45H, C_5H, min), 8.33 (s, 0.55H, C_5H, maj), 11.08 (bs, N*H*), 11.21 (bs, N*H*). Anal. Calcd. for $C_{12}H_{17}N_3O_4$: C, 53.92; H, 6.41; N, 15.72. Found: C, 53.99; H, 6.13; N, 15.49.

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