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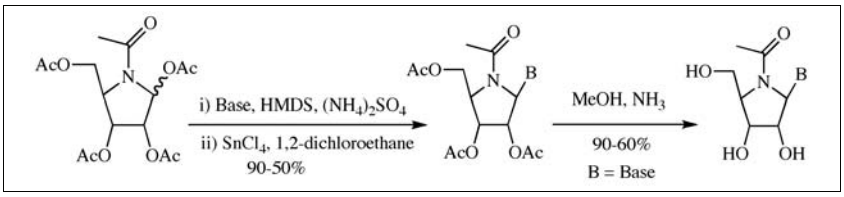
Received June 13, 2005



1,2,3,5-Tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-D-ribofuranose **5** was prepared from L-lyxose, which on condensation with silylated nucleoside bases gave the corresponding protected 4'-azanucleosides. The protecting groups were removed using methanolic ammonia to afford the *N*-acetyl-4'-azanucleosides, wherein the sugar ring oxygen is replaced with a substituted nitrogen atom, in good yields. Further, the 1-(4-deoxy-4-acetamido-β-D-ribofuranosyl)thymine **16** was transformed to the corresponding 2'-deoxy, 2',3'-dideoxy derivatives. The stereochemical assignments of the synthesized nucleosides were established based on NMR and X-ray studies.

J. Heterocyclic Chem., **43**, 325 (2006).

Introduction.

Modulation of the immune system offers an important paradigm in the control of diseases. Central to the balance between protection from disease versus mediating the pathophysiologic events of diseases [1] is the control of the levels of cytokines secreted by Th1/Th2 subsets of T helper (Th) cells [2]. Th-1 derived cytokines (IL-2, IFN-γ, TNF-α) are responsible primarily for cell-mediated immunity such as delayed hypersensitivity, whereas the Th-2 cytokines (IL-4, IL-5, IL-6, IL-9, IL-10, IL-13) are primarily involved in providing optimal help for humoral immune responses such as IgE and IgG4 antibody isotype switching [3]. Th1 and Th2 responses not only play different roles in protection but also promote different immunopathological reactions. Th1-type responses are involved in organ specific autoimmunity such as experimental autoimmune uveoretinitis [4] and experimental autoimmune encephalitis (EAE) [5], insulin dependent diabetes mellitus [6], in contact dermatitis [7] and in some chronic inflammatory disorders. In contrast, Th2-type responses are responsible for triggering allergic atopic disorders (against common environmental allergens) such as asthma [8]. They are thought to exacerbate infection with tissue-dwelling protozoa such as helminthes [9] and Leishmania major [10] and are preferentially induced in certain immunodeficiencies such as hpyer-IgE syndrome [11] and Omenn's syndrome [12] and are also associated with reduced ability to suppress HIV replication [13]. Thus, modulation of the cytokine profile of the aforementioned disease states would be of therapeutic benefit.

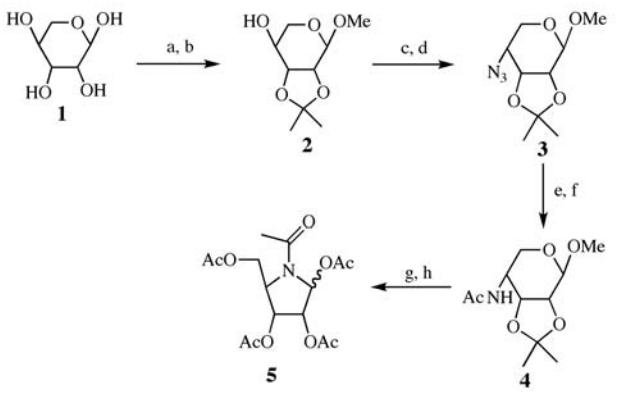
Ribavirin (1-β-D-ribofuranosyl-1,2,4-triazole-3-carboxamide) is a nucleoside analog that has demonstrated efficacy in treating viral disease as monotherapy (respiratory syncytial virus) [14] or in combination with interferon-alpha (hepatitis C) [15]. Recent collective studies have shown that the *in vivo* utility of ribavirin may be ascribed to more than the direct reduction in levels of circulating virus. The promotion of T-cell mediated immunity against viral infection has been shown to be a possible additional mechanism of antiviral activity by this nucleoside analog [16-18]. The central focus of this immunomodulatory effect of ribavirin is the augmentation of antiviral Type 1 cytokine expression (IL-2, IFN-γ, TNF-α) and concomitant suppression of Type 2 cytokine levels (IL-4, IL-5, IL-10) by activated T cells. The induction of a Type 1 cytokine bias by ribavirin, which was first demonstrated in humans *in vitro* [19], was shown to be functionally significant *in vivo* [20a] through the enhancement of a Type 1 cytokine-mediated contact hypersensitivity responses in BALB/c mice. Whereas L-ribavirin, wherein the ribose moiety was derived from unnatural sugar L-ribose, was shown [20b] to retain Type 1 cytokine enhancing activity similar to ribavirin. However these isomers differ markedly with respect to other biological properties [20c]. Thus the modification of ribose moiety selectively modulates ribavirin properties.

Our interest in 4'-azasugar nucleosides [21] coupled with the immunomodulatory properties of ribavirin prompted us to prepare ribavirin analogs and other monocyclic nucleosides containing azasugar **5**. Previously, a few groups have reported the synthesis of nucleosides having 4'-azasugar from different starting materials [22-26]. We now describe an improved method for the synthesis of 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-D-ribofuranose **5** from commercially available L-lyxose and certain monocyclic nucleosides derived from **5**.

Results and Discussion.

The desired protected aza-D-sugar **5** is synthesized as shown in Scheme 1 following the procedure developed earlier [21]. The key step involves the conversion of C_4 free hydroxyl group of **1** to a protected amino function with inversion of configuration to afford the desired D configuration. Then the pyranose derivative **4** was rearranged to the intermediate 4-aza-D-ribofuranose under aqueous acetic acid conditions with concomitant cleavage of acetonide. The azaribofuranose was then protected in presence of acetic acid, acetic anhydride and conc. H_2SO_4 to afford the target 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-D-ribofuranose **5**. The ^{1}H NMR spectrum of **5** showed the presence of α and β anomers in a ratio of 25:75 and correlated with 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-L-ribofuranose [21].

Scheme 1

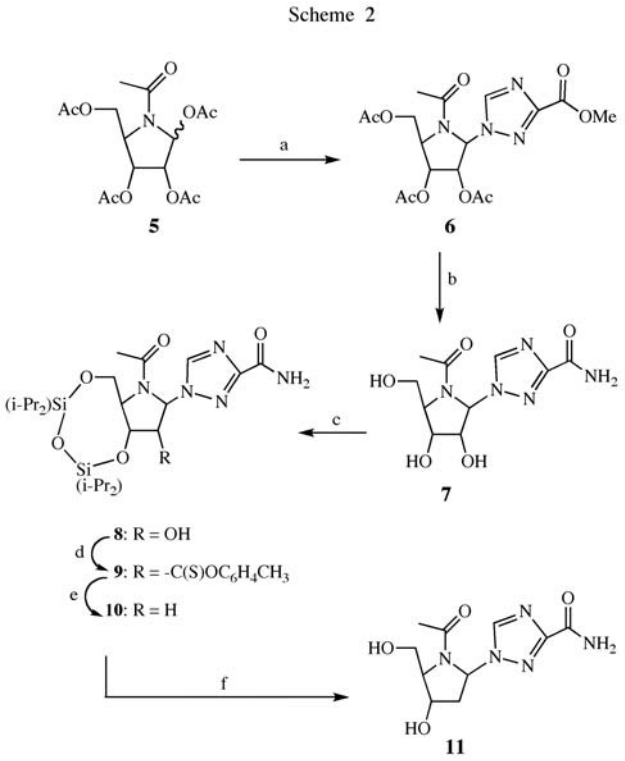


Reagents & Conditions: a) HCl/MeOH; b)HCl, acetone, 2,2-dimethoxypropane; c) $(CF_3SO_2)_2O$, DMAP, Py.; d) LiN_3, DMF; e) 5% Pd/C, MeOH; f) Ac_2O, DMAP, Py.; g) AcOH, H_2O; h) Ac_2O, AcOH, H_2SO_4

After accomplishing the synthesis of desired sugar **5**, it was then coupled to the triazole of ribavirin under Vorbrüggen conditions [27]. Accordingly the silylated methyl-1,2,4-triazole-3-carboxylate was reacted with **5** in presence of tin(IV) chloride to obtain the corresponding nucleoside **6** in moderate yield (51%). The ester **6** upon reaction with methanolic ammonia at room temperature for 16 h furnished the 4'-aza-D-ribavirin **7** in excellent yield.

The deoxy analog **11** of 4'-aza-ribavirin **7** was synthesized as follows. Thus reaction of 3' and 5' hydroxyl groups with Markiewicz reagent [28] readily gave the required cyclic silyl ether **8**. The corresponding 2' thiocarbonate **9**, obtained by reacting ether **8** with *p*-tolylthionochloroformate, upon exposure to tributyltin hydride [29] in presence of 2,2'-azobisisobutyronitrile (AIBN) in refluxing toluene afforded the protected deoxy-4'-aza-ribavirin **10**. The silyl groups of product **10** were removed with triethylamine trihydroflouride in dichloromethane to obtain the desired deoxy-4'-aza-ribavirin **11** in good yield.

Scheme 2



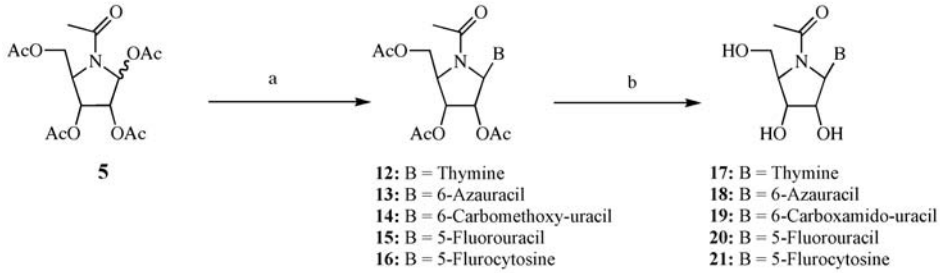
Reagents & conditions: a) i. Methyl-1,2,4-triazole-3-carboxylate, HMDS, $(NH_4)_2SO_4$; ii. $SnCl_4$, $ClCH_2CH_2Cl$; b) MeOH, NH_3; c) $TPDSiCl_2$, Py.; d) *p*-CH_3-$C_6H_4OC(S)Cl$, Py.; e) n-Bu_3SnH, AIBN, Toluene; f) 3HF.NEt_3, CH_2Cl_2

After successfully accomplishing the synthesis of **11**, we turned our attention to the coupling of **5** with thymine using Vorbrüggen glycosylation conditions. Accordingly, thymine was per-silylated with hexamethyldisilazane under reflux to give the corresponding silylated derivative which on treatment with **5** in the presence of $SnCl_4$ at –5 to 0 °C afforded 1-(2,3,5-tri-*O*-acetyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)thymine **12** in 87% yield. Exposure of **12** to methanolic ammonia at room temperature provided the target product *viz*., 1-(4-deoxy-4-acetamido-β-D-ribofuranosyl)thymine **17** in 79% yield.

Utilization of the similar coupling procedure for the preparation of a few other monocyclic 4'-aza-D-nucleosides (**13-16**) was found to be remarkably successful. In all these cases, β-isomers were obtained as the predominant products. These protected nucleosides upon deprotection afforded the corresponding deblocked nucleosides (**18**-**21**) in good yield. However, in general α isomers were also obtained as minor products during coupling but no further effort was made to deprotect them to obtain the corresponding α isomers of 4'-aza-ribonucleosides.

After accomplishing the synthesis of selected 4'-aza-D-ribonucleosides, we were interested in converting **17** to

Scheme 3



5

12: B = Thymine
13: B = 6-Azauracil
14: B = 6-Carbomethoxy-uracil
15: B = 5-Fluorouracil
16: B = 5-Flurocytosine

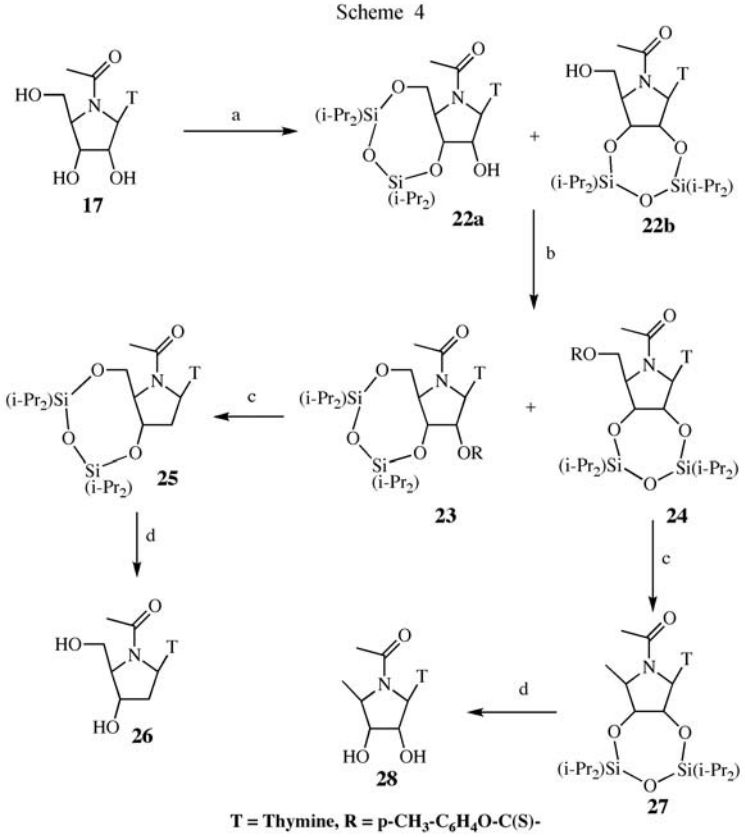
17: B = Thymine
18: B = 6-Azauracil
19: B = 6-Carboxamido-uracil
20: B = 5-Fluorouracil
21: B = 5-Flurocytosine

Reagents & Conditions: a) Base, HMDS, $(NH_4)_2SO_4$; ii) $SnCl_4$, 1,2-dichloroethane; b) MeOH, NH_3

the corresponding 2'-deoxy and 2',3'-dideoxy nucleosides. Thus, treatment of **17** with Markiewicz reagent ($TPDSiCl_2$) afforded an inseparable mixture of silyl ether derivatives **22a** and **22b**. The mixture on further reaction with *p*-tolyl chlorothionoformate and pyridine in CH_2Cl_2 afforded a readily separable mixture of thionoformate esters **23** and **24**. Radical mediated deoxygenation of **23** and **24** with tri-*n*-butyltin hydride in presence of AIBN in toluene under reflux furnished silyl-protected 4'-aza-D-thymidine **25** and 5'-deoxy-4'-aza-D-5-methyluracil **27** respectively. Removal of the silyl groups of **25** and **27** were accomplished with $Et_3N.3HF$ at room temperature to give 4'-deoxy-4'-(acetamido)-D-thymidine **26** and 4',5'-dideoxy-4'-(acetamido)-D-5-methyl-uracil **28** in high yields.

Finally, in view of the potent properties of 2',3'-dideoxy nucleosides, the synthesis of 1-(2,3,4-trideoxy-4-acetamido-*β*-D-ribofuranosyl)thymine **32** was pursued. Thus, selective protection of the 5'-hydroxyl group of **17** with TBDMSCl gave the corresponding silyl ether which upon treatment with methanesulfonyl chloride gave fully protected intermediate dimesylate **29**. The dimesylate upon

Scheme 4

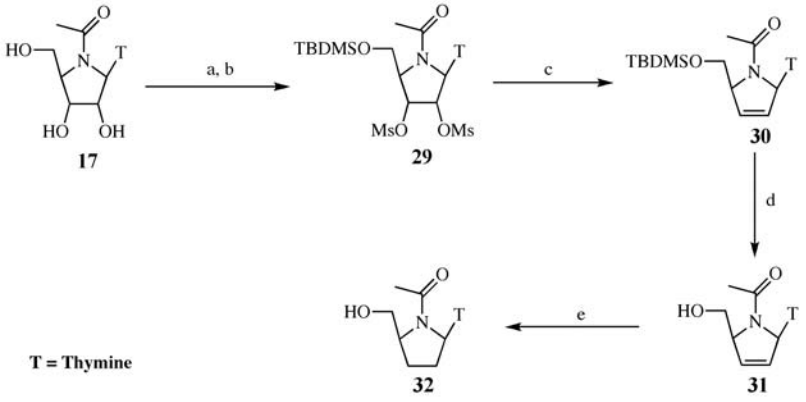


17 **22a** **22b** **25** **23** **24** **26** **28** **27**

T = Thymine, R = p-CH_3-C_6H_4O-C(S)-

Reagents & conditions: a) $TPDSiCl_2$, Py.;b) p-CH_3-$C_6H_4OC(S)Cl$, Py; c) n-Bu_3SnH, AIBN, Toluene; d) $3HF.NEt_3$, CH_2Cl_2

Scheme 5



Reagents & conditions: a) TBDMSCl, Py.;b) MsCl, NEt_3, CH_2Cl_2; c) Li_2Te, THF; d) 3HF.NEt_3, CH_2Cl_2; e) 10% Pd/C, MeOH

reaction with freshly prepared telluride dianion [30] in tetrahydrofuran at room temperature for 16 h afforded the silyl-protected 2',3'-didehydro-3'-deoxy-4'-aza-thymidine **30**. The silyl group in **30** was then removed using $Et_3N.3HF$ to afford 2',3'-didehydro-3',4'-dideoxy-4'-(acetamido)-D-thymidine **31** in 65% yield. Hydrogenation of **31** using Pd/C in methanol furnished the final target compound 3',4'-dideoxy-4'-aza-D-thymidine **32** in high yield.

The anomeric configurations of the monocyclic 4'-aza-D-nucleosides were assigned on the basis of ^{1}H NMR. For example the ^{1}H NMR spectrum of **6** indicated a doublet at δ 6.28 with a *J* value of 6.04 Hz supporting the assignment of β configuration [25] for $H_{1'}$. Further the *J* values for $H_{1'}$ of **12** were also in agreement with that of its L-isomer [21]. Additionally ^{1}H 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 ^{1}H NMR spectrum of **7** showed singlets at δ 8.69 (0.75H, major rotamer) and 8.95 (0.25H, minor rotamer) for H_5 and doublets at δ 6.03 (*J* = 6.04, 0.75H, major) and 6.81 (*J* = 4.13 Hz, 0.25H, minor) for $H_{1'}$ proton. On the other hand, $H_{2'}$, $H_{3'}$, $H_{4'}$ and $H_{5'}$ protons appeared as multiplets accounting for the rotamers. Also, the methyl protons of 4'-aminoacetyl appeared as singlets at δ 1.87 (0.75H, COCH_3, minor), 2.14 (2.25H, COCH_3, major). Interestingly, the silyl protected derivative of deoxy didehydro thymidine **30** showed very high ratio (99:1) of rotamers. The stereochemical assignments of the nucleosides were further confirmed by X-ray crystallographic studies of **6** (Figure 1). The N_2 atom of the base is located 1.3218 Å above the C_1-N_1-C_4 plane while C_9 atom lies 0.8627 Å above the defined plane. The $H_{1'}$ and $H_{4'}$ are below the plane as indicated by their negative values of bond lengths, -0.6615 and –0.8899 Å respectively. Further , as can be seen from the Figure 1, the azaribose ring adopts a typical $C_{3'}$ *endo* conformation. It's interesting to note the C=O group of N-acetyl is anchored away from the base thus minimizing the interactions between them. The N-acetyl group may also be responsible for the base to adopt an *exo* conformation. The above data clearly suggests that the triazole base of **6** has β orientation.

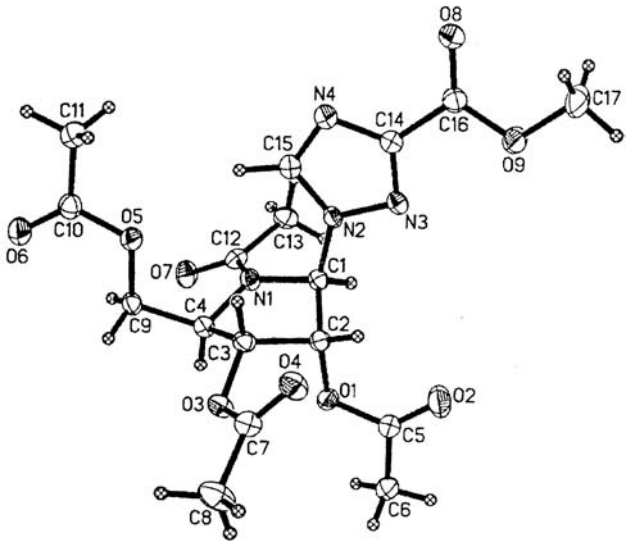


Figure 1. ORTEP diagram for **6**.

The compounds prepared in this report are yet to be evaluated for the Type 1 cytokine enhancing activity in activated human T cells in comparison to ribavirin, the positive control and the results will be reported elsewhere.

In summary, we have accomplished the synthesis of a fully protected 4-deoxy-4-(acetamido)-β-D-ribofuranose

as well as certain selected novel monocyclic D-nucleosides containing the 4-azasugar moiety.

EXPERIMENTAL

Melting points were measured on a Haake Büchler capillary melting point apparatus and are uncorrected. Nuclear magnetic resonance (^{1}H 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-L-lyxopyranoside (**2**).

To a methanolic HCl solution (0.5% w/v), prepared *in situ* by the reaction of 6 mL of acetyl chloride (84.44 mmol) with 600 mL MeOH (Fisher HPLC grade), was added 118 g (786.66 mmol) of L-lyxose (**1**) and the mixture was refluxed for 5 h under N_2 atmosphere. The reaction mixture was neutralized with 100 g amberlite basic resin IRA-410 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 which was recrystallized from 500 mL ethyl acetate to obtain white crystalline methyl glycoside 87 g (67% total from both 1st and 2nd crops).

Methyl β-L-lyxopyranoside (69 g, 420 mmol) suspended in 200 mL anhydrous acetone was treated with 200 mL 2,2-dimethoxy propane followed by the addition of 4 mL of 4 *M* solution of HCl in dioxane and the stirring was continued at 25 °C for 16 h. The reaction was quenched with 500 mg solid sodium bicarbonate and filtered. The filtrate was evaporated and the oily residue (pinkish) was purified by silica gel flash chromatography (CH_2Cl_2/ethyl acetate) to obtain 80 g (93.2%) product **2**.

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-D-riboparanoside (**3**).

Pyridine (3.2 mL, 39.85 mmol) and 50 mg (0.35 mmol) 4-(dimethylamino)pyridine in 300 mL anhydrous CH_2Cl_2 was treated slowly with 5.36 mL (32.5 mmol) trifluoromethanesulfonic anhydride at –20 °C under argon atmosphere. The reaction mixture was allowed to stir at –20 °C for 5 min. 5.1 g (25 mmol) of methyl 2,3-*O*-isopropylidene-α-L-lyxopyranoside in 100 mL CH_2Cl_2 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 250 mL mixture of ice-water 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 (2x150 mL) and brine (400 mL), dried (Na_2SO_4) and evaporated to give 8 g intermediate triflate product as pale yellow gummy solid.

The above crude intermediate methyl 4-*O*-trifluoromethanesulfonyl-2,3-*O*-isopropylidene-β-L-lyxopyranoside was dissolved in 150 mL DMF and then cooled (0 °C). 6.2 g (126.77 mmol) lithium azide was slowly added and stirred at room temperature for 3 h. The reaction mixture was diluted with 200 mL toluene and evaporated to dryness. The residue was dissolved in a mixture of 300 mL CH_2Cl_2 and 200 mL water. 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 silica gel flash chromatography (hexane/ethyl acetate) afforded 4.44 g, (78% overall yield for both the steps) pure azido product **3**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.35 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 3.42 (s, 3H, OCH_3), 3.6-3.8 (m, 3H), 4.01 (dd, 1H, *J* = 6.30 & 3.90 Hz), 4.45 – 4.52 (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-D-ribopyranoside (**4**).

To 6.5 g (28.38 mmol) of methyl 4-deoxy-4-azido-2,3-*O*-isopropylidene-β-D-ribopyranoside (**3**) in 40.0 mL MeOH was added 0.65 g Pd/C (5% w/w) and the reaction mixture was hydrogenated under H_2 atmosphere (50 psi) 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 150 mL CH_2Cl_2, 50 mg (0.36 mmol) DMAP and 13.70 mL (170.28 mmol) pyridine were added and cooled (0 °C). To the cold solution was added 13.4 mL (142.04 mmol) acetic anhydride at 0-5 °C and the reaction mixture was stirred for 16 h at room temperature. The reaction mixture quenched with the addition of 10 mL MeOH and the volatiles were evaporated. The residue was dissolved in 250 mL CH_2Cl_2 and washed with water (2x100 mL) and brine (200 mL), dried (Na_2SO_4) and evaporated. The residue was purified by flash silica gel chromatography (hexane/ethyl acetate) to obtain 6.2 g (89.39% overall yield for both the steps) product **4**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.31 (s, 3H, CH_3), 1.48 (s, 3H, CH_3), 1.97 (s, 3H, COCH_3), 3.35 (t, *J* = 10.65, 1H), 3.42 (s, 3H, OCH_3), 3.80 (dd, 1H, *J* = 10.44 & 5.77 Hz), 3.98 (dd, 1H, *J* = 6.04 & 4.67 Hz), 4.35 (dd, 1H, *J* = 6.04 & 4.12 Hz), 4.39 (d, 1H, *J* = 4.4 Hz), 4.49 (m, 1H), 5.79 (bd, 1H, *J* = 8.52 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)-β-D-ribofuranose (**5**).

Methyl 4-deoxy-4-acetamido-2,3-*O*-isopropylidene-β-D-ribopyranoside (**4**) (5.0 g, 20.40 mmol) was dissolved in 50 mL mixture (1:1) of distilled water and AcOH and 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 50 mL mixture (1:1) of glacial acetic acid and acetic anhydride and cooled (0 °C) and treated with 1 mL conc. H_2SO_4. The

reaction mixture was stirred at 0 °C for 30 min and then kept at 4 °C for 2 days. 10 g anhydrous NaOAc was added and stirred at room temperature for 30 min. The reaction mixture was then poured into 400 mL ice-water mixture and extracted with CH_2Cl_2 (2x150 mL). The combined organic layer was washed with water (2x200 mL) and brine (200 mL), dried (Na_2SO_4) and evaporated. The crude product was purified by flash silica gel chromatography (hexane/ethyl acetate) to obtain 3.71 g (50.82%) **5**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.0-2.16 (m, 15H, 5xCOCH_3), 4.18-4.51 (m, 3H), 5.33-5.36 (m, 1H), 5.45-5.55 (m, 1H), 6.36 (s, 0.75H, $H_{1'}$), 6.55 (d, 0.25H, J = 5.22 Hz, $H_{1'}$);

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.

Methyl-1-(2,3,5-triacetyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)-1,2,4-triazole-3-carboxylate (**6**).

Methyl-1, 2, 4-triazole-3-carboxylate (1.77 g, 13.97 mmol, 1.14 eq) and 177 mg ammonium sulphate were suspended in 40 mL hexamethyldisilazane and the mixture was refluxed for 2.5 h under N_2 atmosphere. The volatiles evaporated and the residue was resuspended in 50 mL 1,2-dichloroethane. It was then treated with 4.4 g (12.25 mmol) 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-D-ribofuranose (**5**) in 50 mL of 1,2-dichloroethane. The reaction mixture was then treated with 1.63 mL (13.97 mmol, 1.14 eq) fuming $SnCl_4$ at 0-5 °C. The reaction mixture was stirred at room temperature for 1 h. The reaction mixture was carefully quenched with aq. saturated solution of $NaHCO_3$ (50 mL) and then it was diluted with CH_2Cl_2 (200 mL). The mixture was filtered over 5 g celite bed. The organic layer of the filtrate was separated and the aqueous layer was extracted with CH_2Cl_2 (2x 100 mL). The combined organic layer was washed with water (2x300 mL) and brine (500 mL), dried (Na_2SO_4) and evaporated. The crude residue obtained so was recrystallized from 40 mL ethyl acetate to obtain 2.7 g, (51.71%) pure title product **6**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.03-2.16 (m, 12H, 4xCOCH_3), 3.95 (s, 3H, OCH_3), 4.21 (m, 1H, $H_{4'}$), 4.43 (m, 2H, $H_{5'}$), 5.65 (dd, J = 4.67 & 1.1 Hz, 1H, $H_{3'}$), 6.17 (t, 1H, J = 6.04 & 4.67 Hz, $H_{2'}$), 6.28 (d, 1H, J = 6.04 Hz, $H_{1'}$), 8.47 (s, 1H, H_5).

Anal. Calcd. for ($C_{17}H_{22}N_4O_9$): C, 47.89; H, 5.20; N, 13.14. Found: C, 47.81; H, 5.19; N, 13.10.

1-(4-Deoxy-4-acetamido-β-D-ribofuranosyl)-1,2,4-triazole-3-carboxamide (**7**).

Methyl-1-(2,3,5-triacetyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)-1,2,4-triazole-3-carboxylate (**6**) (2.7 g, 6.33 mmol) in 100 mL saturated methanolic ammonia was stirred at room temperature for 16 h. The volatiles were evaporated and the residue obtained was purified by flash alumina chromatography (eluant: decantant of the solvent mixture ethyl acetate/*n*-propyl alcohol/water: 64/4/32 to 57/14/29 %) to afford 1.7 g title product **7**. The product was wet with some (~5%) ethyl alcohol and also contaminated with acetamide. All our attempts to purify the product free of acetamide have summarily been failed. ^{1}H NMR (300 MHz, CD_3OD): δ 1.87 {s, 0.86, CH_3 (Ac), min.}, 2.14 {s, 2.14 H, CH_3 (Ac), maj.}, 3.87 (d, J = 6.59 Hz, 2H x $H_{5'}$), 4.01-4.10 (m, 1H, $H_{4'}$), 4.26 (d, J = 4.12 Hz, 0.75 H, $H_{3'}$, maj.), 4.31 (t, J = 3.8 Hz, 0.25 H, $H_{3'}$, min.), 4.54 (t, J = 4.1 Hz, 0.25 H, $H_{2'}$ min.), 4.85 (dd, J = 4.4 & 6.05 Hz, 0.75 H, $H_{2''}$, maj.), 6.03 (d, J = 6.04 Hz, 0.75 H, $H_{1'}$, maj.), 6.81 (d, J = 4.13 Hz, 0.25 H, $H_{1'}$ min.), 8.69 {s, 0.75 H, H_5, major rotamer (maj.)}, 8.95 {s, 0.25H, H_5, minor rotamer (min.)}. ES-MS: m/z 286 $(M+1)^+$.

1-{(3,5-*O*- (1,1,3,3-Tetraisopropyl-1,3-disiloxanediyl)-4-deoxy-4-acetamido-β-D-ribofuranosyl}-1,2,4-triazole-3-carboxamide (**8**).

1-(4-Deoxy-4-acetamido-β-D-ribofuranosyl)-1,2,4-triazole-3-carboxamide (**7**) (0.7 g, 2.45 mmol) was suspended in 15 mL pyridine and treated with 1.06 mL (3.31 mmol, 1.35 eq) 1,3-dichloro-1,1,3,3-tetraisopropyl-disiloxane and stirred at room temperature for 16 h. The reaction mixture was carefully quenched with 5 mL aq. saturated $NaHCO_3$ solution and then it was diluted with 100 mL CH_2Cl_2. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x25 mL). The combined organic layer was washed with water (2x100 mL) and brine (100 mL), dried (Na_2SO_4) and evaporated. The crude residue obtained so was purified by flash silica gel chromatography ($CHCl_3$/MeOH) to afford 0.7 g (54%) product **7**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94-1.18 (m, 24H, 4 x (CH_3)$_2$CHSi), 1.38 (m, 4H, 4 x (CH_3)$_2$C*H*Si), 2.02 {s, 0.9H, COCH_3, minor rotamer (min)}, 2.15 {s, 2.1H, COCH_3, major rotamer (maj)}, 3.33 (br s, 1H, O*H*, D_2O exchangeable), 3.82 {m, 0.7H, $H_{4'}$, (maj)}, 3.98-4.13 (m, 2.3 H, 2 x $H_{5'}$ & 0.3H, $H_{4'}$, min), 4.32 (d, J = 3.85 Hz, 0.3H, $H_{2'}$, min), 4.42 (d, J = 4.67 Hz, 0.7H, $H_{2'}$, maj), 4.52 (m), 4.65 (dd, J = 8.25 & 4.12 Hz, min), 5.29 (t, J = 4.95 Hz, 0.7H, $H_{3'}$, maj), 5.80 (br s, 0.7H, N*H*, maj., D_2O exchangeable), 5.94 (br s, 0.3 H, N*H*, min., D_2O exchangeable), 5.99 (s, 0.3H, $H_{1'}$, min), 6.40 (s, 0.7H, $H_{1'}$, maj), 6.91 (br s, 0.7H, N*H*, maj., D_2O exchangeable), 7.01 (br s, 0.3 H, N*H*, min., D_2O exchangeable), 8.38 (s, 0.7H, H_5, maj), 8.53 (s, 0.3H, H_5, min). ES-MS: m/z 528 $(M+1)^+$.

1-{2-*O*-(*p*-Tolylthionoformyl)-3,5-*O*-(1,1,3,3-tetraisopropyl-1,3-disiloxanediyl)-4-deoxy-4-acetamido-β-D-ribofuranosyl}-1,2,4-triazole-3-carboxamide (**9**).

1-{(3,5-*O*-(1,1,3,3-Tetraisopropyl-1,3-disiloxanediyl)-4-deoxy-4-acetamido-β-D-ribofuranosyl}-1,2,4-triazole-3-carboxamide (**8**) (0.6 g, 1.138 mmol) was dissolved in 10 mL mixture (9:1) of CH_2Cl_2 and pyridine. 0.219 mL (1.42 m mol, 1.25 eq) *O*-(*p*-tolyl)thionochloroformate was added and the reaction mixture was stirred at room temperature for 16 h. The reaction mixture was quenched with 5 mL aq. saturated $NaHCO_3$ solution and then it was diluted with 100 mL CH_2Cl_2. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2x25 mL). The combined organic layer was washed with water (2x100 mL) and brine (100 mL), dried (Na_2SO_4) and evaporated. The crude residue obtained so was purified over flash silica gel chromatography ($CHCl_3$/ethyl acetate) to afford 0.35 g (45%) product **9**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92-1.15 (m, 24H, 4 x (CH_3)$_2$CHSi), 1.30 (m, 4H, 4 x (CH_3)$_2$C*H*Si), 2.01 {s, 0.9H, COCH_3, minor rotamer (min)}, 2.19 {s, 2.1H, COCH_3, major rotamer (maj)}, 2.35 (s, 3H, ArCH_3), 3.92 {m, 0.7H, $H_{4'}$, (maj)}, 4.05 (m, 2 H, 1.7 x $H_{5'}$ & 0.3H, $H_{4'}$, min), 4.70 (m), 4.81 (m), 5.50 (t, J = 5.22 & 6.05 Hz, 1H, $H_{3'}$), 5.75 (br s, 0.7H, N*H*, maj., D_2O exchangeable), 5.89 (br s, 0.3 H, N*H*, min., D_2O exchangeable), 6.10 (d, J = 4.67 Hz, 1H, $H_{2'}$), 6.12 (s, 0.3H, $H_{1'}$, min), 6.54 (s, 0.7H, $H_{1'}$, maj), 6.87 (br s, 0.7H, N*H*, maj., D_2O exchangeable), 6.96 (br d, J = 8.24 Hz, 2.3H, 2H of aromatic ring & 0.3H N*H*, min., D_2O exchangeable), 7.21 (d, J = 8.24 Hz, 2H of aromatic ring), 8.41 (s, 0.7H, H_5, maj), 8.69 (s, 0.3H, H_5, min). ES-MS: m/z 678 $(M+1)^+$.

1-{(3,5-*O*-(1,1,3,3-Tetraisopropyl-1,3-disiloxanediyl)-2,4-dideoxy-4-acetamido-*β*-D-ribofuranosyl}-1,2,4-triazole-3-carboxamide (**10**).

1-{2-*O*-(*p*-Tolylthionoformyl)- 3,5-*O*- (1,1,3,3-tetraisopropyl-1,3-disiloxanediyl)-4-deoxy-4-acetamido-*β*-D-ribofuranosyl}-1,2,4-triazole-3-carboxamide (0.35 g, 0.516 mmol) (**9**) was dissolved in 20 mL toluene and was purged with argon for 20 min. and then treated with 0.084 g (0.516 mmol) 2,2'-azobisisobutyronitrile (AIBN) and 0.274 ml (1.03 mmol, 2 eq) tributyltin hydride. The reaction mixture was refluxed for 3 h under a stream of argon. The volatiles evaporated and the crude residue obtained so was purified by flash silica gel chromatography ($CHCl_3$/ethyl acetate) to afford 0.23 g (87 %) product **10**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.94-1.18 (m, 24H, 4 x $(CH_3)_2$-CHSi), 1.26 (m, 4H, 4 x $(CH_3)_2CH$Si), 2.00 {s, 0.75H, COCH_3, minor rotamer (min)}, 2.13 {s, 2.25H, COCH_3, major rotamer (maj)}, 2.42 (m, 1H, $H_{2'}$), 2.54 (m, 0.25H, $H_{2'}$, min.), 2.85 (dd, J = 13.5 & 7.5 Hz, 0.75H, $H_{2'}$, maj), 3.78 {m, 1H, $H_{4'}$), 3.88 (m, 2H, 2 x $H_{5'}$), 4.50 (m), 4.67 (m), 5.30 (m, 1H, $H_{3'}$), 5.88 (br s, 0.75H, NH, maj., D_2O exchangeable), 6.01 (br s, 0.25 H, NH, min., D_2O exchangeable), 6.14 (d, J = 6.0 Hz, 0.25H, $H_{1'}$, min), 6.40 (d, J = 7.8 Hz, 0.75H, $H_{1'}$, maj), 6.89 (br s, 0.75H, NH, maj., D_2O exchangeable), 7.03 (br s, 0.25 H, NH, min., D_2O exchangeable), 8.35 (s, 0.75H, H_5, maj), 8.55 (s, 0.25H, H_5, min). ES-MS: m/z 511 $(M+1)^+$.

1-(2,4-Dideoxy-4-acetamido-*β*-D-ribofuranosyl)-1,2,4-triazole-3-carboxamide (**11**).

1-{(3,5-*O*-(1,1,3,3-Tetraisopropyl-1,3-disiloxanediyl)-2, 4-dideoxy-4-acetamido-*β*-D-ribofuranosyl}-1,2,4-triazole-3-carboxamide (**10**) (0.23 g, 0.45 mmol) was dissolved in 5 mL CH_2Cl_2 and treated with 0.29 mL (1.79 mmol, 4 eq) triethylamine trishydrofluoride at room temperature. The reaction mixture was stirred for 48 h at room temperature. The volatiles were removed and the residue was purified by flash silica gel chromatography ($CHCl_3$/MeOH eluents) to afford 0.08 g (66%) product **11**. ^{1}H NMR (300 MHz, CD_3OD): δ 1.95 {s, 0.36, CH_3 (Ac), min.}, 2.16{s, 2.64 H, CH_3 (Ac), maj.}, 2.51(m, 1H, $H_{2'}$), 2.87 (m, 1H, $H_{2'}$), 3.82 (m, 2H, 1x $H_{5'}$ & H_4), 3.99 (t, J = 6.87 Hz, 1H, $H_{5'}$), 4.44 (d, J = 4.12 Hz, $H_{3'}$), 6.54 (t, J = 7.69 Hz, $H_{1'}$), 8.63 {s, 0.88H, H_5, major rotamer (maj.)}, 8.88 {s, 0.12H, H_5, minor rotamer (min.)}.

Anal. Calcd. for $C_{11}H_{16}N_4O_5$: C, 46.48; H, 5.67; N, 19.71. Found: C, 46.55; H, 5.72; N, 19.52.

1-(2, 3, 5-Tri-*O*-acetyl-4-deoxy-4-acetamido-*β*-D-ribofuranosyl)-thymine (**12a**) and 1-(2, 3, 5-Tri-*O*-acetyl-4-deoxy-4-acetamido-*α*-D-ribofuranosyl)thymine (**12b**).

Thymine (2.52 g, 20.0 mmol) and 250 mg ammonium sulphate were suspended in 50 mL hexamethyldisilazane and then heated at reflux for 3 h under N_2 atmosphere. The reaction mixture was evaporated to dryness and the residue was resuspended in 50 mL of 1,2-dichloroethane and cooled to 0 °C in an ice bath. 5.026 g (14.0 mmol) 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-*β*-D-ribofuranose (**5**) in 50 mL 1,2-dichloroethane was added followed by the addition of 2.34 mL (20.0 mmol) fuming $SnCl_4$ at 0°C. The reaction mixture was stirred at room temperature for 1 h. The reaction was carefully quenched with 50 mL aq. saturated $NaHCO_3$ solution and diluted with CH_2Cl_2 (200 mL). The mixture was filtered over 5 g celite bed 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 silica gel chromatography ($CHCl_3$/acetone) to give 5.35 g (90.0%) pure titled product *β*-isomer **12a** and 0.38 g (6.47%) *α*-isomer **12b**. ^{1}H NMR (300 MHz, $CDCl_3$) of *β*-isomer: *δ* 1.88-2.19 (m, 15H, 4xCOCH_3 & CH_3), 4.07 (m, 0.5H, $H_{4'}$), 4.36-4.55 (m, 2.5H, $H_{4'}$ & $H_{5'}$), 5.30 (m, 0.5H, $H_{3'}$), 5.47 (m, 1.5H, $H_{2'}$ & $H_{3'}$), 6.15 (br t, J = 6.05 & 5.77 Hz, 0.5H, $H_{1'}$), 6.37 (d, 0.5H, J = 6.59 Hz, $H_{1'}$), 7.16 (s, 0.5H, C_6H), 7.42 (s, 0.5H, C_6H), 9.13 (s, 0.5H, NH, D_2O exchangeable), 9.32 (s, 0.5H, NH, D_2O exchangeable). IR (KBr) ν_{max} 3350, 2970, 1700, 1412, 1236 cm^{-1}. ES-MS: m/z 426 $(M+1)^+$. ^{1}H NMR (300 MHz, $CDCl_3$) of *α*-isomer: *δ* 1.87-2.17 (m, 15H, 4xCOCH_3 & C_5CH_3), 4.25 (m, 1H, $H_{4'}$), 4.49-4.58 (m, 2H, $H_{5'}$), 5.15 (d, J = 9.9 Hz, 0.55H, $H_{3'}$), 5.17 (d, J = 10.5 Hz, 0.45H, $H_{3'}$), 5.40 (d, J = 5.1 Hz, 0.45H, $H_{2'}$), 5.79 (dd, J = 5.1 & 7.2 Hz, 0.55H, $H_{2'}$), 6.22 (s, 0.45H, $H_{1'}$), 6.47 (d, J = 7.2 Hz, 0.55H, $H_{1'}$) 7.07 (d, J = 1.2 Hz, 0.55H, C_6H), 7.15 (d, J = 1.2 Hz, 0.45H, C_6H), 9.04 (s, 0.55H, NH), 9.21 (s, 0.45H, NH). IR (KBr) ν_{max} 3354, 2968, 1702, 1410, 1240 cm^{-1}. ES-MS: m/z 426 $(M+1)^+$.

1-(2,3,5-Tri-*O*-acetyl-4-deoxy-4-acetamido-*β*-D-ribofuranosyl)-6-azauracil (**13**).

A suspension of 1.13 g (10.0 mmol) 6-azauracil and 113 mg ammonium sulphate in 25 mL hexamethyldisilazane was refluxed for 1 h under N_2 atmosphere. The reaction mixture was evaporated to dryness and the residue was resuspended in 25 mL 1,2-dichloroethane. To this stirred solution was added a solution of 2.51 g (7 mmol) 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-*β*-D-ribofuranose (**5**) in 25 mL 1,2-dichloroethane followed by the addition of 1.17 mL (10.0 mmol) fuming $SnCl_4$ at 0°C. After the addition of 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-*β*-D-ribofuranose (**5**) the reaction mixture was stirred at room temperature for 1 h. The reaction was carefully quenched with 50 mL aq. saturated $NaHCO_3$ solution and diluted with CH_2Cl_2 (200 mL). The mixture was filtered through 5 g celite 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 silica gel chromatography (hexane/ethyl acetate) to obtain 1.43 g (49.58%) title product **13** (*β*-isomer) and 0.8 g (27.74%) *α*-isomer. ^{1}H NMR (300 MHz, $CDCl_3$) of *β*-isomer: *δ* 2.01-2.14 (m, 15H), 4.11-4.48 (m, 3H, $H_{4'}$ & 2 x $H_{5'}$), 5.45 (d, J = 4.5 Hz, 0.55H, $H_{3'}$), 5.49 (d, J = 5.1 Hz, 0.45H, $H_{3'}$), 5.57 (t, J = 5.1 Hz, 0.35H, $H_{2'}$), 5.63 (dd, J = 6.9 & 4.5 Hz, 0.65H, $H_{2'}$), 6.41 (d, J = 4.8 Hz, 0.35H, $H_{1'}$), 6.52 (d, J = 7.2 Hz, 0.65H, $H_{1'}$), 7.23 (s, 0.35H, C_5H), 7.38 (s, 0.65H, C_5H), 9.59 (bs, 1H, NH, D_2O exchangeable). IR (KBr) ν_{max} 3210, 2983, 1678, 1336, 1017 cm^{-1}. ES-MS: m/z 413 $(M+1)^+$. ^{1}H NMR (300 MHz, $CDCl_3$) of *α*-isomer: *δ* 1.96-2.18 (m, 15H), 4.15 (m, 2H, 2 x $H_{5'}$), 4.49 (m, 0.5H, $H_{4'}$), 4.59 (dd, J = 3.6 & 3.0 Hz, 0.5H, $H_{4'}$), 5.25 (d, J = 5.7 Hz, 0.75H, $H_{3'}$), 5.32 (d, J = 5.4 Hz, 0.25H, $H_{3'}$), 5.65 (t, J = 6.9 & 5.7 Hz, 0.25H, $H_{2'}$), 5.72 (t, J = 6.3 & 6.0 Hz, 0.75H, $H_{2'}$), 6.49 (d, J = 6.3 Hz, 0.75H, $H_{1'}$), 6.60 (d, J = 6.9 Hz, 0.25H, $H_{1'}$), 7.24 (s, 0.65H, C_5H), 7.32 (s, 0.35H, C_5H), 9.85 (bs, 1H, NH, D_2O exchangeable). ES-MS: m/z 413 $(M+1)^+$.

Methyl 1-(2,3,5-Tri-*O*-acetyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)uracil-6-carboxylate (**14**).

6-Carbomethoxyuracil (1.7 g, 10.00 mmol) and 170 mg ammonium sulphate were suspended in 30 mL hexamethyldisilazane and was refluxed for 1 h under N_2 atmosphere. The volatiles were evaporated and the residue was resuspended in 1,2-dichloroethane (25 mL). To this was added 2.51 g (7.00 mmol) 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-D-ribofuranose (**5**) in 50 mL 1,2-dichloroethane and was followed by the addition of 1.17 mL, (10.00 mmol) fuming $SnCl_4$ at 0 °C. The reaction mixture was stirred at room temperature for 16 h, carefully quenched with 50 mL aq. saturated $NaHCO_3$ solution and diluted with CH_2Cl_2 (200 mL). The mixture was filtered over 5 g celite bed. 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 (hexane/ethyl acetate) to obtain 2.2 g (67%) pure titled product **14**; IR (KBr) ν_{max} 3204, 2983, 1764, 1372, 1217 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 1.99-2.13 (m, 12H), 3.90 (s, 0.75H, OC*H*$_3$), 3.92 (s, 2.25H, OC*H*$_3$), 3.96-4.06 (m, 1H, $H_{5'}$), 4.46-4.58 (m, 2H, $H_{4'}$ & $H_{5'}$), 5.43 (d, 0.2H, J = 5.7 Hz, $H_{3'}$), 5.48 (d, 0.8H, J = 4.50 Hz, $H_{3'}$), 6.13 (m, 0.2H, $H_{2'}$), 6.21 (dd, 0.8H, J = 5.10 & 8.40 Hz, $H_{2'}$), 6.31 (s, 0.8H, C_5H), 6.37 (s, 0.2H, C_5H), 6.57 (d, 0.2H, J = 6.30 Hz, $H_{1'}$, min), 6.67 (d, 0.8H, J = 8.40 Hz, $H_{1'}$, maj), 8.33 (bs, 0.80H, N*H*, maj), 8.50 (bs, 0.20H, N*H*, min). ES-MS: m/z 470 $(M+1)^+$.

1-(2,3,5-Tri-*O*-acetyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)-5-fluorouracil (**15**).

A suspension of 1.3 g (10 mmol) 5-fluorouracil and 130 mg ammonium sulphate in 25 mL hexamethyldisilazane was refluxed for 2 h under N_2 atmosphere. The reaction mixture was evaporated to dryness and the residue was resuspended in 50 mL 1,2-dichloroethane. The solution was then treated with a solution of 2.51 g (7 mmol) 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-D-ribofuranose (**5**) in 50 mL 1,2-dichloroethane followed by the addition of 1.17 mL (10 mmol) fuming $SnCl_4$ at 0 °C. The reaction mixture was stirred at room temperature for 3 h and carefully quenched with 50 mL aq. saturated $NaHCO_3$ solution and diluted with CH_2Cl_2 (200 mL). The mixture was filtered over 5 g celite bed 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 ($CHCl_3$/acetone: 80/20) to provide pure anomeric isomers of title product **15** (β-isomer, 2.35 g, 78.25%; α-isomer 0.4 g 13.32%). ^1H NMR (300 MHz, $CDCl_3$) of β-isomer: δ 2.03-2.22 (m, 12H), 4.10 (m, 0.45H, $H_{4'}$, min), 4.48 (m, 2.55H, $H_{4'}$ & $H_{5'}$), 5.31 (m, 0.45H, $H_{3'}$), 5.47-5.55 (m, 1.55H, $H_{2'}$ & $H_{3'}$), 6.10 (t, 0.45H, J = 5.4 & 5.7 Hz, $H_{1'}$), 6.29 (d, 0.55H, J = 6.0 Hz, $H_{1'}$), 7.49 (d, 0.45H, J = 6.05 Hz, C_6H), 7.95 (d, 0.55H, J = 5.77 Hz, C_6H), 9.37 (bs, 0.45H, N*H*), 9.54 (bs, 0.55H, N*H*). IR (KBr) ν_{max} 3400, 3063, 1708, 1394, 1245, 1085 cm^{-1}. ES-MS: m/z 430 $(M+1)^+$. ^1H NMR (300 MHz, $CDCl_3$) of α-isomer: δ 1.98-2.29 (m, 12H), 4.21-4.33 (m, 1.45H, $H_{4'}$ & $H_{5'}$), 4.50-4.62 (m, 1.55H, $H_{4'}$ & $H_{5'}$), 5.40 (d, 0.80H, J = 5.21 Hz, $H_{3'}$), 5.49 (d, 0.20H, J = 4.94 Hz, $H_{3'}$), 5.74 (dd, 0.20H, J = 7.69 & 5.22 Hz, $H_{2'}$), 5.82 (dd, 0.80H, J = 7.15 & 5.22 Hz, $H_{2'}$), 6.47 (dd, 0.80H, J = 7.15 & 1.38 Hz, $H_{1'}$), 6.52 (dd, 0.20H, J = 8.24 & 1.2 Hz, $H_{1'}$), 7.40 (dd, 0.20H, J = 9.62 & 6.32 Hz, C_6H), 7.51 (d, 0.80H, J = 6.33 Hz, C_6H), 9.28 (d, 0.80H, J = 4.8 Hz, N*H*), 9.34 (d, 0.20H, J = 4.8 Hz, N*H*). IR (KBr) ν_{max} 3408, 3060, 1710, 1394, 1240, 1082 cm^{-1}. ES-MS: m/z 430 $(M+1)^+$.

1-(2,3,5-Tri-*O*-acetyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)-5-fluorocytosine (**16**).

A suspension of 1.0 g (7.75 mmol) 5-fluorocytosine and 100 mg ammonium sulphate in 25 mL hexamethyldisilazane was refluxed for 2 h under N_2 atmosphere. The volatiles were evaporated and the residue was resuspended in 25 mL 1,2-dichloroethane. To this stirred solution was added a solution of 2.51 g (7 mmol) 1,2,3,5-tetra-*O*-acetyl-4-deoxy-4-(acetamido)-β-D-ribofuranose (**5**) in 1,2-dichloroethane (25 mL) followed by the addition of 1.17 mL (10 mmol) fuming $SnCl_4$ at 0 °C. The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was carefully quenched with aq. 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 ($CHCl_3$/acetone: 80/20) to obtain pure product isomers (β-isomer, 2.38 g, 79.44%; α-isomer 0.29 g 9.68%); β-isomer: ^1H NMR (300 MHz, $CDCl_3$) δ 1.97-2.18 (m, 12H), 4.05 (m, 0.25H, $H_{4'}$), 4.35-4.59 (m, 2.75H, $H_{4'}$ & $H_{5'}$), 5.28 (t, J = 4.4Hz, 0.75H, $H_{3'}$), 5.33 (d, J = 6.32 Hz, 0.25H, $H_{3'}$), 5.44 (t,, J = 4.67 Hz, 0.75H, $H_{2'}$), 5.54 (d, J = 3.85 Hz, 0.25H, $H_{2'}$), 5.72 (bs, 0.25H, NH_2), 5.95 (bs, 0.75H, NH_2), 6.25 (bt, 0.25H, $H_{1'}$), 6.34 (d, 0.75H, J = 3.57 Hz, $H_{1'}$), 7.47 (d, 0.25H, J = 5.49 Hz, C_6H), 7.93 (d, 0.75H, J = 6.05 Hz, C_6H), 8.36 (bs, 1H, NH_2): IR (KBr) ν_{max} 3346, 3098, 1766, 1511, 1209 cm^{-1}. ES-MS: m/z 429 $(M+1)^+$. ^1H NMR (300 MHz, $CDCl_3$) of α-isomer: δ 1.82-2.31 (m, 12H), 4.15 (m, 0.25H, $H_{4'}$), 4.38 (m, 2H, 2 x $H_{5'}$), 5.15 (d, J = 17.04 Hz, 0.75H, $H_{3'}$), 5.40 (d, J = 5.21 Hz, 0.25H, $H_{3'}$), 5.54 (d, J = 3.85 Hz, 0.25H, $H_{2'}$, min), 5.75 (bs, 0.75H, NH_2), 5.82 (dd, J = 7.42 & 5.49 Hz, 1H, $H_{2'}$), 6.18 (bs, 0.25H, NH_2), 6.26 (s, 0.45H, $H_{1'}$), 6.58 (dd, J = 7.41 & 1.92 Hz, 0.55H, $H_{1'}$), 7.30 (d, J = 6.32 Hz, 0.45H, C_6H), 7.46 (d, J = 6.59 Hz, 0.55H, C_6H), 8.04 (bs, 0.45H, NH_2, exchangeable), 8.35 (bs, 0.55H, NH_2, exchangeable); IR (KBr) ν_{max} 3346, 3098, 1766, 1511, 1209 cm^{-1}. ES-MS: m/z 429 $(M+1)^+$.

1-(4-Deoxy-4-acetamido-β-D-ribofuranosyl)thymine (**17**).

A solution of 3.7 g (8.7 mmol) 1-(2, 3, 5-tri-*O*-acetyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)thymine (**12a**) in 100 mL saturated methanolic ammonia 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 ($CHCl_3$/MeOH) to afford the titled product 2.28 g (87.78%) **17**; mp 201-203 °C (dec); IR (KBr) ν_{max} 3355, 2962, 2840, 1610, 1415, 1236 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): δ 1.84 (s, 1.35H, C_5CH_3), 1.85 (s, 1.65H, C_5CH_3), 1.94 (s, 1.65H, COC*H*$_3$), 2.13 (s, 1.35H, COC*H*$_3$), 3.75-4.18 (m, 4H, $H_{3'}$, $H_{4'}$ & 2 x $H_{5'}$), 4.36 (t, 0.55H, J = 4.8 Hz, $H_{2'}$, maj), 4.56 (dd, 0.45H, J = 4.2 & 6.6 Hz, $H_{2'}$, min), 5.87 (d, 0.45H, J = 6.9 Hz, $H_{1'}$, min), 6.11 (d,

0.55H, *J* = 5.1 Hz, $H_{1'}$, maj), 7.87 (s, 0.45H, C_6H, min), 8.24 (s, 0.55H, C_6H, maj).

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-(4-Deoxy-4-acetamido-*β*-D-ribofuranosyl)-6-azauracil (**18**).

A solution of 1.25 g (3.03 mmol) 1-(2,3,5-tri-*O*-acetyl-4-deoxy-4-acetamido-*β*-D-ribofuranosyl)-6-azauracil (**13**) in 30 mL saturated methanolic ammonia 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 ($CHCl_3$/MeOH) to afford 0.65 g (74.90%) titled product **18**; mp 225-228 °C (dec); IR (KBr) ν_{max} 3292, 2990, 1725, 1620, 1272 cm^{-1}; ^1H NMR (300 MHz, Me_2SO-d_6 + D_2O): *δ* 1.82 (s, 1.02H, $COCH_3$), 1.95 (s, 1.98H, $COCH_3$), 3.33-3.55 (m, 2H, $H_{4'}$ & $H_{5'}$), 3.72 (dd, *J* = 8.4 & 6.0 Hz, 0.6H, $H_{5'}$), 3.86 (dd, *J* = 8.1 & 5.1 Hz, 0.4H, $H_{5'}$), 4.01 (m, 1H, $H_{3'}$), 4.25 (m, 1H, $H_{2'}$), 5.97 (d, *J* = 7.20 Hz, 0.60H, $H_{1'}$), 6.04 (d, *J* = 6.0 Hz, 0.40H, $H_{1'}$), 7.43 (s, 0.60H, C_5H), 7.51 (s, 0.40H, C_5H).

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*-D-ribofuranosyl)uracil-6-carboxamide (**19**).

A solution of 1.6 g (3.41 mmol) methyl 1-(2,3,5-tri-*O*-acetyl-4-deoxy-4-acetamido-*β*-D-ribofuranosyl)uracil-6-carboxylate (**14**) in 25 mL saturated methanolic ammonia was stirred at room temperature in a steel bomb for 16 h. The steel bomb was cooled to 0 °C, opened and evaporated to dryness. The residue obtained was purified by flash chromatography over silica gel ($CHCl_3$/MeOH) to afford 0.7 g (62.55%) titled product **19**; mp 115-118 °C; IR (KBr) ν_{max} 3310, 2980, 1640, 1412, 1032 cm^{-1}; ^1H NMR (300 MHz, CD_3OD): *δ* 1.91 (s, 1.08H, $COCH_3$), 2.07 (s, 1.92H, $COCH_3$), 3.75-3.99 (m, 3H, $H_{4'}$ & 2 x $H_{5'}$), 4.16 (d, *J* = 4.5 Hz, 0.72H, $H_{3'}$), 4.21 (d, *J* = 4.5 Hz, 0.28H, $H_{3'}$), 4.96 (m, 1H, $H_{2'}$), 6.19 (s, 0.6H, $H_{1'}$), 6.26 (s, 0.4H, $H_{1'}$, min), 6.48 (d, *J* = 7.8 Hz, 0.60H, H_5), 6.53 (d, *J* = 6.9 Hz, 0.40H, H_5).

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*-D-ribofuranosyl)-5-fluorouracil (**20**).

A solution of 2.15 g (5.01 mmol) 1-(2,3,5-tri-*O*-acetyl-4-deoxy-4-acetamido-*β*-D-ribofuranosyl)-5-fluorouracil (**15**) in 60 mL saturated methanolic ammonia 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 ($CHCl_3$/MeOH) to afford 1.18 g (77.7%) titled product **20**; mp 125-127 °C (dec); IR (KBr) ν_{max} 3438, 3080, 2961, 1667, 1392, 1131 cm^{-1}; ^1H NMR (300 MHz, CD_2OD): *δ* 1.98 {s, 1.65H, $COCH_3$}, 2.14 {s, 1.65H, $COCH_3$}, 3.75-4.18 (m, 3H, $H_{3'}$, $H_{4'}$ & 2 x $H_{5'}$), 4.35 (t, *J* = 4.5 & 5.1 Hz, 0.55H, $H_{2'}$), 4.5 (dd, *J* = 4.2 & 6.3 Hz, 0.45H, $H_{2'}$), 5.94 (d, *J* = 6.6 Hz, 0.45H, $H_{1'}$), 6.11 (dd, *J* = 1.2 & 4.8 Hz, 0.55H, $H_{1'}$), 8.36 (d, *J* = 6.9 Hz, 0.45H, C_6H), 8.69 (d, *J* = 6.9 Hz, 0.55H, C_6H);

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*-D-ribofuranosyl)-5-fluorocytosine (**21**).

A solution of 2.25 g (5.25 mmol) 1-(2,3,5-tri-*O*-acetyl-4-deoxy-4-acetamido-*β*-D-ribofuranosyl)-5-fluorocytosine (**16**) in 35 mL saturated methanolic ammonia 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 ($CHCl_3$/MeOH) to afford 1.45 g (91.33%) titled product **21**; mp 106-108 °C (dec); IR (KBr) ν_{max} 3536, 2926, 1684, 1490, 1177 cm^{-1}; ^1H NMR (300 MHz, CD_3OD) *δ* 1.92 (s, 1.95H, $COCH_3$), 2.17(s, 1.05H, $COCH_3$), 3.75-3.93 (m, 2H, 2x$H_{5'}$), 4.02-4.07 (m, 0.35H, $H_{4'}$), 4.15-4.20 (m, 1.65H, $H_{4'}$ & $H_{3'}$), 4.26 (dd, *J* = 8.76 & 4.2 Hz, 0.8H, $H_{2'}$), 4.49 (t, *J* = 4.5 Hz, 0.2H, $H_{2'}$), 5.76 (d, *J* = 5.1 Hz, 0.34H, $H_{1'}$, min), 6.12 (dd, 0.66H, *J* = 1.2 & 3.9 Hz, $H_{1'}$, maj), 8.19 (d, 0.33H, *J* = 6.9 Hz, C_6H, min), 8.66 (d, *J* = 6.9 Hz, 0.66H, C_6H, maj).

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*-D-ribofuranosyl]thymine (**22a**) & 1-[2,3-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-*β*-D-ribofuranosyl]thymine (**22b**).

A suspension of 1.794 g (6.0 mmol) 1-(4-deoxy-4-acetamido-*β*-D-ribofuranosyl)thymine (**17**) in 60 mL pyridine was treated with 2.48 mL (7.5 mmol) 1,3-dichloro-1,1,3,3-tetraisopropyldisiloxane and stirred at room temperature for 16 h. The reaction mixture was carefully quenched with aq. 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) to afford a mixture of inseparable products **22a** & **22b** (2.17 g, 66.79%). The mixture was not characterized further and carried forward for the next reaction without purification.

1-[2-*O*-(*p*-Tolylthionoformyl)-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-*β*-D-ribofuranosyl]-thymine (**23**) & 1-[5-*O*-(*p*-Tolylthionoformyl)-2, 3-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-*β*-D-ribofuranosyl]thymine (**24**).

To 2.10 g (3.87 mmol) mixture of 1-[3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-*β*-D-ribofuranosyl]thymine (**22a**) & 1-[2,3-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-*β*-D-ribofuranosyl]thymine (**22b**) in 25 mL pyridine was added 0.83 mL (5.42 mmol) *p*-tolyl chlorothionoformate and the reaction mixture was stirred at room temperature for 16 h under argon atmosphere. The reaction mixture was quenched with aq. 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 (hexane/ethyl acetate) to afford 0.94 g faster moving product and 0.65 g slower moving product. The combined yield was 1.59 g (59.32%). The ^1H NMR analysis of the products indicated that the structure of slower product as **23** and the structure of the faster product as **24**. ^1H NMR (300 MHz, $CDCl_3$) of **23**: *δ* 0.98-1.06 (m, 24H), 1.92 (s, 3H, CH_3),

2.00 (s, 2H, COCH_3), 2.252 (s, 1H, COCH_3), 2.35 (s, 3H, CH_3), 3.89-4.38 (m, 3H, $H_{5'}$ & $H_{4'}$), 4.66-4.81 (m, 1.5H, $H_{2'}$ & $H_{3'}$), 5.3 & 5.67 (bs, 0.5H, $H_{2'}$ & $H_{3'}$), 6.01 (s, 1H, $H_{1'}$), 6.95 (d, J = 8.7 Hz, 2H, Ph-*H*), 7.19 (d, J = 8.4 Hz, 2H, Ph-*H*), 7.35 (s, 0.24H, C_6H), 7.57 (s, 0.76H, C_6H), 8.17 (bs, 0.24H, N*H*), 8.50 (s, 0.76H, N*H*). ES-MS: m/z 692 $(M+1)^+$. ^{1}H NMR (300 MHz, $CDCl_3$) of **24**: δ 1.00-1.07 (m, 24H), 1.88 (s, 3H, CH_3), 2.02 (s, 2.4H, COCH_3), 2.22 (s, 0.6H, COCH_3), 2.36 (s, 3H, CH_3), 4.17-4.55 (m, 2H, $H_{4'}$ & $H_{3'}$), 4.85-5.29 (m, 3H, $H_{2'}$ & 2 x $H_{5'}$), 6.01 (d, 1H, J = 3.00 Hz, $H_{1'}$), 6.94 (d, J = 8.4 Hz, 2H, Ph-*H*), 7.21 (d, 2H, J = 8.4 Hz, Ph-*H*), 7.78 (s, 1H, C_6H), 8.48 (bs, 0.16H, N*H*, min), 8.55 (s, 0.84H, N*H*, maj). ES-MS: m/z 692 $(M+1)^+$.

1-[3,5-*O*-(1,1,3,3-Tetraisopropyldisiloxane-1,3-diyl)-2,4-dideoxy-4-acetamido-β-D-ribofuranosyl]thymine (**25**).

A solution of 0.62 g (0.89 mmol) 1-[2-*O*-(*p*-tolylthionoformyl)-3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-β-D-ribofuranosyl]thymine (**23**) in dry toluene (20 mL) was purged with argon for 20 min. To this stirred solution was added 0.14 g (0.92 mmol) AIBN followed by the addition of 0.47 mL (1.78 mmol) tributyltin hydride. The reaction mixture was refluxed for 5 h under a stream of argon. The volatiles were evaporated and the crude residue was purified by flash chromatography over silica gel (hexane/ethyl acetate) to afford 0.35 g (74.3%) the desired product **25**. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98-1.08 (m, 24H), 1.92 (s, 3H, CH_3), 1.99 (s, 2.25H, COCH_3), 2.18 (s, 0.75H, COCH_3), 2.2-2.42 (m, 1.5H, $H_{2'}$), 2.68 (m, 0.5H, $H_{2'}$), 3.70 (m, 1H, $H_{5'}$), 4.04 (m, 0.75H, $H_{5'}$), 4.35 (m, 0.25H, $H_{5'}$), 4.64 (m, 1.55H, $H_{3'}$ & $H_{4'}$), 5.12 (m, 0.45H, $H_{3'}$), 5.73 (m, 0.15H, $H_{1'}$), 6.08 (m, 0.85H, J = 6.3 Hz, $H_{1'}$), 7.34 (s, 0.15H, C_6H), 7.55 (s, 0.85H, C_6H,), 8.45 (bs, 0.15H, N*H*,), 9.07 (s, 0.85H, N*H*). ES-MS: m/z 526 $(M+1)^+$.

1-(2, 4-Dideoxy-4-acetamido-β-D-ribofuranosyl)thymine (**26**).

A solution of 0.34 g (0.65 mmol) 1-[3,5-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-2,4-dideoxy-4-acetamido-β-D-ribofuranosyl]thymine (**25**) in 15 mL CH_2Cl_2 was treated with 0.53 mL (3.23 mmol) triethylamine trishydrofluoride 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 ($CHCl_3$/MeOH) to give the titled compound 0.16 g (87.29%) **26**; mp 119-121 °C; IR (KBr) ν_{max} 3420, 2828, 1632, 1418, 1127 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD): δ 1.83 (s, 1.71H, CH_3), 1.86 (d, J = 0.6 Hz, 1.29H, CH_3), 1.95 (s, 1.29H, COCH_3), 2.19 (s, 1.71H, COCH_3), 2.26-2.44 (m, 2H, 2 x $H_{2'}$), 3.74-4.06 (m, 3H, $H_{4'}$ & $H_{5'}$), 4.31 (d, J = 3.6 Hz, 0.57H, $H_{3'}$), 4.37 (bs, 0.43H, $H_{3'}$), 6.27 (t, J = 8.1 Hz, 0.57H, $H_{1'}$), 6.49 (t, J = 7.5 Hz, 0.43H, $H_{1'}$), 7.70 (d, J = 1.2 Hz, 0.57H, C_6H), 8.18 (d, J = 0.9 Hz, 0.43H, C_6H).

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-D-ribofuranosyl]thymine (**27**).

A solution of 0.91 g (1.32 mmol) 1-[5-*O*-(*p*-tolylthionoformyl)-2,3-O-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4-deoxy-4-acetamido-β-D-ribofuranosyl]thymine (**24**) in 25 mL dry toluene was purged with argon for 20 min. To this stirred solution was added 0.215 g (1.32 mmol) AIBN and 0.69 mL (2.63 mmol) tri-*n*-butyltin hydride. 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 (hexane/ethyl acetate) to give 0.69 g **27** in quantitative yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.98-1.04 (m, 24H), 1.06-1.16 (m, 2H), 1.22-1.36 (m, 2H). 1.45 (d, 0.99H, J = 6.9 Hz, $H_{5'}$), 1.51 (d, 2.01H, J = 7.2 Hz, $H_{5'}$), 1.89 (s, 1.98H, CH_3), 1.92 (s, 1.02H, CH_3), 1.93 (s, 1.98H, COCH_3), 2.09 (s, 1.02H, COCH_3), 3.86 (m, 0.6H, $H_{4'}$), 3.98 (m, 0.4H, $H_{4'}$), 4.09-4.19 (m, 1H, $H_{3'}$), 4.35 (m, 0.5H, $H_{2'}$), 5.18 (dd, J = 6.0 & 3.9 Hz, 0.5H, $H_{2'}$), 5.30 (d, J = 6.0 Hz, 0.6H, $H_{1'}$), 5.98 (t, 0.4H, J = 4.2 Hz, $H_{1'}$), 6.99 (s, 0.44H, C_6H), 7.09 (d, J = 0.6 Hz, 0.56H, C_6H), 8.56 (bs, 0.66H, N*H*), 8.69 (bs, 0.34H, N*H*). ES-MS: m/z 526 $(M+1)^+$.

1-(4,5-Dideoxy-4-acetamido-β-D-ribofuranosyl)thymine (**28**).

A solution of 1-[2,3-*O*-(1,1,3,3-tetraisopropyldisiloxane-1,3-diyl)-4,5-dideoxy-4-acetamido-β-D-ribofuranosyl]thymine (**27**) (0.75 g, 1.43 mmol) in 30 mL CH_2Cl_2 was treated with 0.7 mL (4.29 mmol) triethylamine trishydrofluoride 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 ($CHCl_3$/MeOH) to afford 0.385 g (95.23 %) **28**. 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, $H_{5'}$), 1.48 (d, 1.64H, J = 6.87 Hz, $H_{5'}$), 1.87 (s, 1.08H, CH_3), 1.91 (s, 1.92H, CH_3), 1.91 (s, 1.08H, COCH_3), 2.09 (s, 1.92H, COCH_3), 3.84-4.00 (m, 1H, $H_{4'}$), 4.06 (m, 0.60H, $H_{3'}$), 4.33 (m, 0.40H, $H_{3'}$), 4.66 (m, 1H, $H_{2'}$), 5.72 (d, J = 6.87 Hz, 0.64H, $H_{1'}$), 6.08 (d, J = 5.77 Hz, 0.36H, $H_{1'}$), 7.21 (s, 0.36H, C_6H), 7.27 (s, 0.64H, C_6H).

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*-*t*-Butyldimethylsilyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)-thymine (**29**).

A suspension of 2.3 g (1.92 mmol) 1-(4-deoxy-4-acetamido-β-D-ribofuranosyl)thymine (**17**) in 50 mL pyridine was treated with 1.45 g (9.61 mmol) *t*-butyldimethylsilyl chloride and stirred at room temperature for 16 h. The reaction mixture was carefully quenched with aq. 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 was purified by flash silica gel chromatography ($CHCl_3$/MeOH) to obtain 2.22 g (69.87%) title product **29**. ^{1}H NMR (300 MHz, CDO_3D): δ 0.15 (m, 6H, Si(CH_3)$_2$), 0.95 (m, 9H, SiC(CH_3)$_3$), 1.86 (s, 0.45H, CH_3), 1.90 (s, 0.55H, CH_3), 1.92 (s, 0.55H, COCH_3), 2.13 (s, 0.45H, COCH_3), 3.90-4.11 (m, 3H, $H_{4'}$ 2x $H_{5'}$), 4.38 (m, 0.5H, $H_{3'}$), 4.61 (m, 0.5H, $H_{3'}$), 5.81 (d, J = 7.2 Hz, 0.35H, $H_{1'}$), 6.15 (d, J = 6.60 Hz, 0.65H, $H_{1'}$), 7.48 (s, 0.35H, C_6H), 7.68 (s, 0.65H, C_6H). ES-MS: m/z 414 $(M+1)^+$.

1–(5-O-t-Butyldimethylsilyl-2,3,4-trideoxy-2,3-didehydro–4–acetamido-β-D–ribofuranosyl)-thymine (**30**).

A solution of 2.22 g (5.37 mmol) diol, 1-(5-*O*-*t*-butyldimethylsilyl-4-deoxy-4-acetamido-β-D-ribofuranosyl)-thymine (**29**), in 125 ml CH_2Cl_2 was treated with 0.93 mL (12.09 mmol) methanesulfonyl chloride in presence of 1.8 ml (13.44 mmol) triethylamine and stirred at room temperature for 4 h. The reaction mixture was quenched with aq. 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) to afford almost pure intermediate dimesylate product (2.82 g, 92.20%). The product was dried over P_2O_5 for 48 h at room temperature under vacuum before carrying forward to the next reaction.

Lithium triethylborohydride solution (13.0 mL, 13 mmol) in tetrahydrofuran (1 *M*) was added to 0.758 g (5.94 mmol) tellurium powder (200 mesh). The mixture was stirred at room temperature until a pinkish-milky white suspension was obtained. To this stirred mixture was added 6 mL solution of the above mesylate (1.4 g, 2.7 mmol) in anhydrous tetrahydrofuran. After the addition of mesylate, 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 ($CHCl_3$/ethyl acetate) to afford 0.61 g 960%) pure titled product **30**. Major rotamer: ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.10 (s, 3H, CH_3), 0.12 (s, 3H, CH_3), 0.92 (s, 9H, *tert*-butyl), 1.92 (d, 3H, *J*=1.2 Hz, C_5CH_3), 2.06 (s, 3H, COCH_3), 4.02-4.07 (dd, 1H, *J* = 11.10 & 3.15 Hz, $H_{5'}$), 4.14-4.19 (dd, 1H, *J* = 11.1 & 3.6 Hz, $H_{5'}$), 4.83 (bd, *J* = 1.8 Hz, 1H, $H_{4'}$), 5.75 (dt, *J* = 6.3 & 2.1 Hz, 1H, $H_{3'}$), 6.18 (dt, *J* = 6.3 & 1.8 Hz, 1H, $H_{2'}$), 7.03 (d, 1H, *J* = 1.5 Hz, $H_{1'}$), 7.62 (d, 1H, *J* = 1.2 Hz, C_6H), 8.94 (s, 1H, N*H*). Minor rotamer peaks were appeared in the ratio of 1-2% of major rotamer peaks and found difficult to designate. ES-MS: m/z 380 $(M+1)^+$.

1–(2,3,4-Trideoxy-2,3-didehydro–4–acetamido-β-D–ribofuranosyl)thymine (**31**).

A solution of 0.61 g (1.60 mmol) 1–(5-*O*-*t*-butyldimethylsilyl-2,3,4-trideoxy-2,3-didehydro–4–acetamido-β-D–ribofuranosyl)thymine (**30**) in 30 mL CH_2Cl_2 was treated with 1 mL (6.4 mmol) triethylamine trishydrofluoride 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 ($CHCl_3$/MeOH) to afford 0.425 g (99.64%) **31**. IR (KBr) ν_{max} 3349, 2835, 1710, 1402, 1125 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD) δ 1.79 (s, 0.9H, C_5CH_3), 1.82 (d, 2.1H, *J* = 1.2 Hz, C_5CH_3), 2.04 (s, 2.1H, COCH_3), 2.2 (s, 0.9H, COCH_3), 3.84 (dd, *J* = 12 & 2.1 Hz, 0.7H, $H_{5'}$), 3.93 (dd, *J* = 12.3 & 2.1 Hz, 0.3H, $H_{5'}$), 4.05 (dd, *J* = 12.6 & 3.15 Hz, 0.3H, $H_{5'}$), 4.20 (dd, *J* = 12.0 & 2.7 Hz, 0.7H, $H_{5'}$), 4.73 (bd, 1H, $H_{4'}$, min), 5.79 (dt, *J* = 6.3 & 1.8, 0.7H, $H_{3'}$), 5.85 (dt, *J* = 6.3 & 1.8, 0.3H, $H_{3'}$, min), 6.19 (dt, *J* = 6.3 & 1.3, 0.3H, $H_{2'}$), 6.24 (dt, *J* = 6.3 & 1.5, 0.7H, $H_{2'}$), 6.97 (bs, 0.3H, $H_{1'}$), 7.11 (d, 0.7H, *J* = 1.8 Hz, $H_{1'}$), 8.12 (s, 0.3H, C_6H), 8.33 (d, 0.7H, *J* = 1.8 Hz, C_6H,).

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-D-ribofuranosyl)thymine (**32**).

To 200 mg (0.75 mmol) of 1-(2,3,4-trideoxy-2,3-didehydro-4-acetamido-β-D-ribofuranosyl)thymine (**31**) in 20 mL methanol was added 20 mg Pd/C (10% w/w) under argon atmosphere. The reaction mixture was shaken well under H_2 atmosphere (40 psi) at room temperature for 2 h. The catalyst was filtered over celite bed and the filtrate was evaporated to afford 200 mg titled product **32** as colorless solid in quantitative yield. IR (KBr) ν_{max} 3345, 2840, 1718, 1408, 1125 cm^{-1}; ^{1}H 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), 2.34 (m, 0.55H, $H_{2'}$), 2.40 (m, 0.45H, $H_{2'}$), 3.68–3.74 (m, 1H, $H_{5'}$), 3.92 (dd, 0.45H, $H_{4'}$), 4.08-4.16 (m, 1H, $H_{5'}$), 4.28 (dd, 0.55H, $H_{4'}$), 6.11 (t, 0.45H, $H_{1'}$), 6.31 (m, 0.55H, $H_{1'}$), 7.74 (s, 0.45H, C_5H), 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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