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Synthesis of 3′-deoxy-3′-*C*-methyl-β-D-ribonucleoside analogs

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Abstract—3′-Deoxy-3′-*C*-methyl-β-D-ribonucleoside analogs bearing the five canonical bases of nucleic acids have been synthesized. All these derivatives were prepared by glycosylation of the corresponding heterocyclic bases with a suitable peracylated 3-*C*-methyl sugar precursor. The synthesis of the 3-*C*-methyl sugar precursor is described following a new stereoselective synthetic pathway.

1. Introduction

Nucleoside analogs constitute an important class of therapeutic agents in the treatment of cancers and viral infections.[1] The mode of action of these derivatives is based upon their intracellular conversion to their phosphorylated forms (nucleotides), which can interact with different cellular or viral enzymatic systems involved in the nucleic acids biosynthesis. During the last decades, an intensive research was dedicated to the discovery of more effective, selective, and non-toxic new nucleoside derivatives.[2] These efforts have concerned the chemical modifications of the base and/or the sugar moiety of natural nucleosides. In the latter, the main modifications involved changes in the sugar moiety like, inversion of hydroxyl group configurations, their elimination leading to dideoxy-or dideoxy-didehydro-nucleosides, their substitution/functionalization by various synthetic groups, or cleavage of the sugar ring leading to acyclic nucleosides. Modifications of the sugar moiety of nucleosides may lead to significant changes in the spectrum of their biological activity and degree of selective toxicity, as well as in their physico-chemical properties. In the course of our ongoing research on the synthesis and biological evaluation of modified sugar nucleoside analogs, we became interested in a stereoselective strategy for the preparation of 3′-deoxy-3′-*C*-methyl-β-D-ribonucleoside analogs (Fig. 1). Surprisingly, although a tremendous work has been done in the synthesis of new series of nucleoside analogs, few work has been reported regarding the synthesis of 3′deoxy-3′-*C*-methyl nucleosides.[3] Except the adenine nucleoside derivative, which has been succinctly described,[4,5] all the target compounds are hitherto unknown. This fact prompted us to elaborate a synthetic route to reach such kind of compounds. Basically, nucleoside analogs can be obtained through the reaction of persylilated heterocyclic bases with a peracylated sugar precursor, in the presence of a Lewis acid as a catalyst, according to the Vorbrüggen's procedure. Under these conditions, the neighboring group participation of the 2-*C*-acyloxygroup controls the stereochemistry of the reaction leading exclusively to the formation of the β-nucleoside (*trans rule*).[6] Consequently, we embarked on the synthesis of an appropriate sugar precursor, namely, 1,2-di-*O*-acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-D-ribofuranose **1** (Fig. 1).

Herein, according to the literature data, we report on the different attempts for the preparation of this precursor and we describe here a new stereoselective synthetic pathway. Additionally, the synthesis of the corresponding 3′-deoxy-3′-*C*-methyl-β-D-ribonucleoside analogs bearing the five canonical bases of nucleic acids is also reported.

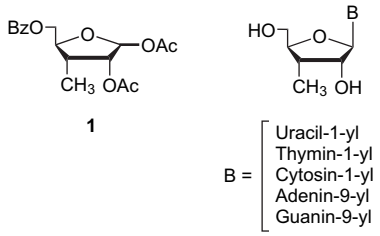

Figure 1. 3′-Deoxy-3′-*C*-methyl-β-D-ribonucleoside analogs.

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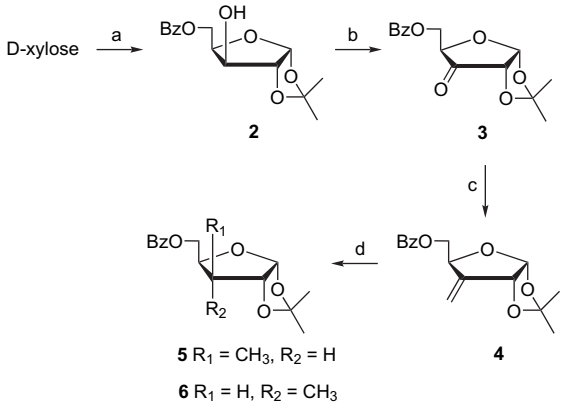
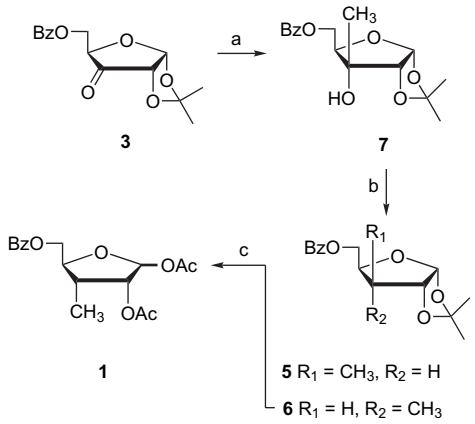
2. Results and discussion

Our first synthesis (Scheme 1) was centered on the catalytic hydrogenation of the olefin intermediate **4**. Such a reduction was described to be stereospecific leading only to the desired modified sugar with α-stereochemistry of the methyl group.[5,7] This result appeared to be consistent with previous observations of the approach of reducing agents to the β-face of furanosyl carbohydrates, with *erythro* or *ribo* configurations, bearing a 1,2-*O*-isopropylidene group in the α-stereochemistry.[8] The olefin should be readily available from the xylofuranoside **2** through an usual sequence involving the oxidation of unprotected secondary alcohol, followed by a Wittig reaction. Starting from D-xylose, precursor **2** was obtained in 70% overall yield according to a procedure involving the initial formation of the bis-isopropylidene derivative, selective deprotection of the six-membered isopropylidene ring, and selective benzoylation of the primary 5-hydroxyl group.[9] The preparation of the osidic precursor required introduction of a methyl group on position 3 of the sugar moiety. In our first synthetic pathway, this introduction involved reduction of an exocyclic methylene group previously obtained by a Wittig reaction on the keto sugar **3** (Scheme 1). Hydrogenation of the resulting exocyclic double bond in the presence of Pd/C 5% was not as stereoselective as previously reported and lead to the formation of two diastereoisomers **5** and **6** with a ratio 20:80 (as determined by ^{1}H NMR) in favor of the desired isomer **6**.



Scheme 1. Reagents and conditions: (a) Ref. 9; (b) Dess–Martin periodinane, CH_2Cl_2, 0 °C to rt, 95%; (c) Ph_3PCH_3Br, sodium *tert*-pentylate, THF, −78 °C then 5–6 °C, 87%; (d) H_2, Pd/C 5%, MeOH, rt, 98%, ratio **5/6**: 20:80.

The influence of pressure, temperature, nature of the solvent, and the catalyst on the stereoselectivity of the hydrogenation reaction has been investigated (data not shown). Whatever the conditions used, the two diastereoisomers have been obtained with a diastereoisomeric excess in favor of the desired compound **6** up to 60%. Furthermore, many attempts to separate the mixture of the two diastereoisomers have been performed including crystallization, chromatography on silica gel, and reverse phase, however, without any success. Therefore, at this stage of the synthesis, the compound **4** seemed not to be the ideal candidate for the preparation of an osidic precursor having a methyl group in position 3 with a *R* configuration. Thus, the synthesis of such a precursor was reconsidered from compound **3**. The modifications envisioned were the addition of an organomagnesium reagent, followed by a radical deoxygenation of the resulting tertiary alcohol. Thus, addition of methyl magnesium bromide in dry Et_2O at −20 °C to compound **3** (Scheme 2) gave stereoselectively[10] the 3-*C*-methyl sugar **7**. In contrast to the deoxygenation of alcohols using Barton–McCombie type methodology,[11] the use of methyl oxalyl esters provide good alternative for removal of hindered secondary or tertiary alcohols.[12] Thus, treatment of **7** with methyl oxalyl chloride in anhydrous dichloromethane gave the corresponding ester derivative, which was subsequently deoxygenated with tris(trimethylsilyl)silane hydride in the presence of AIBN to afford a mixture of compounds **5** and **6** with a ratio 2:98 (as determined by chiral HPLC, data not shown) in favor of **6**. From the diastereoisomeric mixture, we were able to separate by crystallization from petroleum ether pure compound **6**.

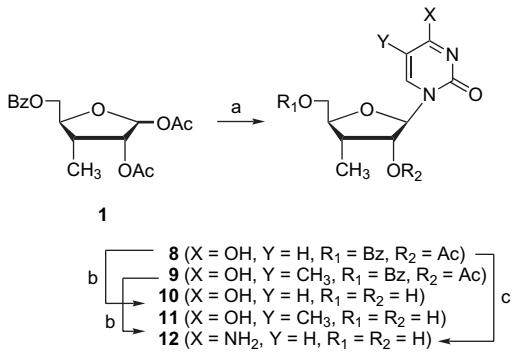


Scheme 2. Reagents and conditions: (a) CH_3MgBr, Et_2O, −20 °C, 80%; (b) (i) $MeCO_2COCl$, DMAP, CH_2Cl_2, 0 °C to rt, (ii) $(Me_3Si)_3SiH$, AIBN, toluene, reflux, 80% overall yield, ratio **5/6**: 2:98; (c) (i) TFA 80%, rt, (ii) Ac_2O, DMAP, pyridine, rt, 85% overall yield.

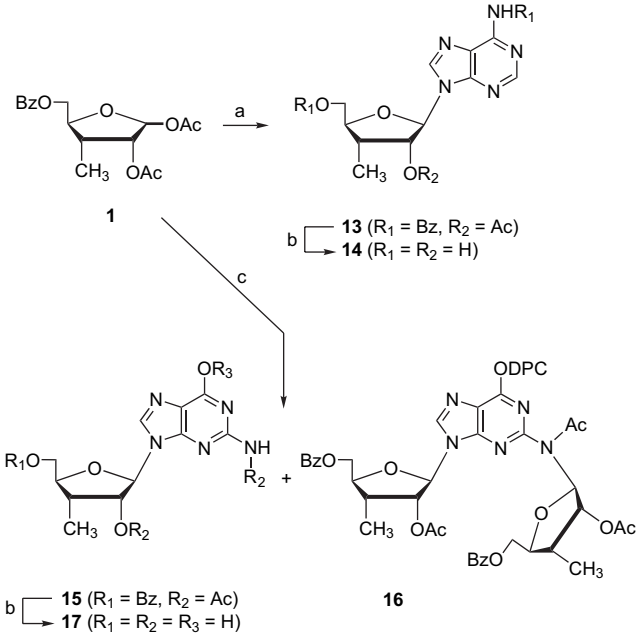
The stereoselectivity observed in this reaction, compared to the one obtained during the hydrogenation step can be justified on the basis of steric and stereoelectronic effects.[13] Indeed, after formation of the 3-*C*-methyl tertiary radical, the chirality of such a radical as well as its pyramidal shape[14] induce the preferential addition of the hydride on the less hindered sugar β-face.

Finally, compound **6** was converted in a two-step procedure into 1,2-di-*O*-acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-D-ribofuranose **1**, which was obtained in 85% after silica gel column chromatography.

The syntheses of the 3′-deoxy-3′-*C*-methyl-β-D-ribonucleoside pyrimidine and purine derivatives are depicted in Schemes 3 and 4. Glycosylation reactions with uracil, thymine, and sugar **1**, under Vorbrüggen conditions using (trimethylsilyl) trifluoromethane sulfonate (TMSOTf) as a catalyst in anhydrous acetonitrile, afforded compounds **8** and **9**. The target nucleosides **10** and **11** were obtained from **8** and **9** by following treatment with methanolic ammonia and purification on silica gel column chromatography. Subsequently, protected derivative **8** was converted into the corresponding cytosine derivative **12** via the formation of a thioamide intermediate followed by aminolysis.



Scheme 3. Reagents and conditions: (a) silylated uracil or thymine, TMSOTf, CH_3CN, 0 °C to rt, 82% for **8**, 64% for **9**; (b) $MeOH/NH_3$, rt, 92% for **10**, 83% for **11**; (c) (i) Lawesson's reagent, $(CH_2Cl)_2$, reflux, (ii) $MeOH/NH_3$, 100 °C, 92% overall yield.



Scheme 4. Reagents and conditions: (a) silylated N^6-benzoyl adenine, TMSOTf, CH_3CN, 0 °C to rt, 62%; (b) $MeOH/NH_3$, rt, 79% for **14**, 70% for **17**; (c) silylated N^2-acetyl-O^6-(DPC)guanine, TMSOTf, toluene, reflux, 55% for **15**, 14% for **16**.

A glycosylation reaction with N^6-benzoyl adenine and **1** provided compound **13**, which upon deprotection and purification gave the desired nucleoside **14**. In order to prepare the guanosine analog (**17**), a condensation reaction of N^2-acetyl-O^6-(diphenylcarbamoyl)guanine with **1** following Robins' procedure[15] was achieved to give the N^9-isomer **15** with 55% yield. No N^7-isomer was detected (^{1}H NMR) in the purified product as well as in the crude coupling mixture. However, compound **16**, a byproduct resulting from an attachment of a second sugar residue at N^2, was isolated with 14% yield. Such a kind of bis(sugar) byproduct has been previously reported.[15]

In summary, the syntheses of 3′-deoxy-3′-*C*-methyl-β-D-ribonucleoside analogs bearing the five naturally occurring nucleic acid bases were undertaken with the hope of discovering new nucleoside analogs endowed with potential biological properties. The target nucleosides were tested for their effects on the replication of HIV and several RNA viruses in cell culture experiments. However, none of these compounds did not show any significant antiviral activity nor cytoxicity at the highest concentration tested (usually 100 μM).

3. Experimental

3.1. General

Evaporation of solvents was carried out on a rotary evaporator under reduced pressure. Melting points were determined in open capillary tubes on a Büchi-545 and are uncorrected. UV spectra were recorded on an Uvikon 931 (Kontron). ^{1}H NMR and ^{13}C NMR spectra were recorded at ambient temperature on a Bruker 300 Avance and DRX 400. Chemical shifts (δ) are quoted in parts per million (ppm) referenced to the residual solvent peak ($CHCl_3$ fixed at 7.26 and 77 ppm, DMSO-d_5 fixed at 2.49 and 39.5 ppm) relative to tetramethylsilane (TMS). Deuterium exchange and COSY experiments were performed in order to confirm proton assignments. Coupling constants, *J*, are reported in hertz. 2D ^{1}H–^{13}C heteronuclear COSY were recorded for the attribution of ^{13}C signals. FAB mass spectra were recorded in the positive-ion or negative-ion mode on a JEOL JMS DX 300. The matrix was a mixture (50:50, v/v) of glycerol and thioglycerol (G/T). Specific rotations were measured on a Perkin–Elmer Model 341 spectropolarimeter (path length 1 cm), and are given in units of 10^{-1} cm^{-2} g^{-1}. Elemental analyses were carried out by the Service de Microanalyses du CNRS, Division de Vernaison (France). Thin layer chromatography was performed on precoated aluminum sheets of Silica 60 F_{254} (Merck, Art. 5554), visualization of products being accomplished by UV absorbency followed by charring with 5% ethanolic sulfuric acid and heating. All moisture-sensitive reactions were carried out under rigorous anhydrous conditions and under an argon atmosphere using over-dried glassware. Solvents were dried and distilled prior to use and solids were dried over P_2O_5 under reduced pressure.

3.1.1. 5-*O*-Benzoyl-1,2-*O*-isopropylidene-α-D-xylofuranose (2). Compound **2** was prepared from commercially available D-xylose following a protocol established in the literature.[9] ^{1}H NMR ($CDCl_3$) δ 1.25 (3H, s, C(CH_3)$_2$), 1.43 (3H, s, C(CH_3)$_2$), 3.15 (1H, sl, OH-3), 4.11 (1H, d, H-3, J_{3-4}=2.2), 4.32 (2H, m, H-4, H-5), 4.52 (1H, d, H-2, J_{2-1}=3.6), 4.73 (1H, m, H-5′), 5.89 (1H, d, H-1, J_{1-2}=3.6), 7.37–7.98 (5H, m, C_6H_5CO). Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.16. Found: C, 61.30, H 5.87.

3.1.2. 5-*O*-Benzoyl-3-deoxy-1,2-*O*-isopropylidene-α-D-*erythro*-3-pentulofuranose (3). Dess–Martin periodinane (60 g, 0.14 mol) was added to a solution of compound **2** (20.8 g, 0.07 mol) in anhydrous dichloromethane (400 mL) at 0 °C. The mixture was stirred for 4 h at room temperature, then concentrated, and diluted with diethyl ether (400 mL). The resulting precipitate was filtered. The clear filtrate was concentrated to dryness and coevaporated with anhydrous toluene to afford compound **3** as a white solid (19 g, 95%), which was crystallized from diethyl ether. Mp 93–95 °C (lit.[9] 97–98.5 °C); ^{1}H NMR ($CDCl_3$) δ 1.36 (3H, s,

$C(CH_3)_2$), 1.44 (3H, s, $C(CH_3)_2$), 4.39 (2H, m, H-2, H-5), 4.63 (2H, m, H-4, H-5′), 6.07 (1H, d, H-1, J_{1-2}=4.4), 7.37–7.88 (5H, m, C_6H_5CO). Anal. Calcd for $C_{15}H_{16}O_6 \cdot 1H_2O$: C, 58.06; H, 5.85. Found: C, 57.99; H, 5.89.

3.1.3. 5-*O*-Benzoyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methylidene-α-D-pentofuranose (4). To a suspension of methyl magnesium bromide (8.51 g, 23.8 mmol) in anhydrous THF (260 mL) was added sodium *tert*-pentylate (2.31 g, 21.0 mmol). The reaction mixture was stirred overnight at room temperature. The resulting orange solution was cooled down at −78 °C and a solution of compound **3** (3.46 g, 11.9 mmol) in anhydrous THF (52 mL) was added. The reaction mixture was stirred at 5–6 °C for 4 h, then diluted with ethyl acetate (200 mL), and successively washed with brine (100 mL), saturated $NaHCO_3$ solution (100 mL), and water (100 mL). The organic phase was dried over sodium sulfate and evaporated to dryness. Chromatography of the residue on a silica gel column using a stepwise gradient of ethyl acetate (0–20%) in cyclohexane afforded compound **4** (3 g, 87%), which was crystallized from petroleum ether. Mp 62–64 °C (lit.[16] 60–61.5 °C); ^{1}H NMR ($CDCl_3$) δ 1.32 (3H, s, $C(CH_3)_2$), 1.46 (3H, s, $C(CH_3)_2$), 4.33 (1H, dd, H-5, J_{5-2}=3.3, $J_{5-5'}$=11.8), 4.47 (1H, dd, H-5′, $J_{5'-2}$=5.5, $J_{5'-5}$=11.8), 4.88 (1H, m, H-2), 5.00 (1H, m, H-4), 5.23 (1H, m, =CH_2), 5.44 (1H, m, =CH_2), 5.85 (1H, d, H-1, J_{1-2}=4.0), 7.35–7.97 (5H, m, C_6H_5CO). Anal. Calcd for $C_{16}H_{18}O_5$: C, 66.20; H, 6.25. Found: C, 66.12; H, 6.24.

3.1.4. 5-*O*-Benzoyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-*threo*-pentofuranose (5) and 5-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-*erythro*-pentofuranose (6).

3.1.4.1. Hydrogenation. A solution of compound **4** (7.45 g, 25.7 mmol) in methanol (300 mL) was hydrogenated in the presence of Pd/C 5% (1 g) at room temperature and atmospheric pressure. After 15 h of stirring, the suspension was filtered through a sintered funnel covered with Celite and the filtrate was evaporated under reduced pressure to give an inseparable mixture of compounds **5** and **6** (7.35 g, 98%) in a ratio 20:80, as determined by ^{1}H NMR, respectively. ^{1}H NMR ($CDCl_3$) δ 0.97 (3H, d, CH_3-3 *threo*, J_{CH_3-3}=7.5), 1.18 (3H, d, CH_3-3 *erythro*, J_{CH_3-3}=6.9), 1.34 (3H, s, $C(CH_3)_2$ *threo*), 1.37 (3H, s, $C(CH_3)_2$ *erythro*), 1.56 (6H, s, $C(CH_3)_2$), 2.03 (1H, m, H-3 *erythro*), 2.45 (1H, m, H-3 *threo*), 4.11 (2H, m, H-4), 4.35–4.63 (6H, m, H-2, H-5, H-5′), 5.87 (1H, d, H-1 *erythro*, J_{1-2}=3.7), 5.91 (1H, d, H-1 *threo*, J_{1-2}=3.6), 7.40–8.05 (10H, m, C_6H_5CO).

3.1.4.2. Radical deoxygenation. To a solution of compound **7** (6 g, 19.5 mmol) and DMAP (7.2 g, 58.4 mmol) in anhydrous dichloromethane (64 mL) was added methyl oxalyl chloride (3.6 mL, 39 mmol) at 0 °C. The reaction mixture was stirred for 30 min at room temperature, and then washed with saturated $NaHCO_3$ solution (100 mL) and water (100 mL). The organic layer was dried over sodium sulfate, evaporated to dryness, and coevaporated with anhydrous toluene. The crude material was then dissolved in anhydrous toluene (175 mL), and AIBN (2.26 g, 13.6 mmol) and tris(trimethylsilyl)silane hydride (12 mL, 39 mmol) were added to it. The resulting solution was heated under reflux for 3 h. After cooling to room temperature, the solvent was removed under reduced pressure. Chromatography of the residue on a silica gel column using a stepwise gradient of ethyl acetate (0–8%) in petroleum ether afforded a mixture of compounds **5** and **6** (4.6 g, 80%) in 2:98 ratio. Crystallization from petroleum ether provided pure compound **6**. Mp 52–53 °C (lit.[17] 49 °C); *m/z* (FAB>0) 293 $(M+H)^+$; *m/z* (FAB<0) 291 $(M-H)^-$; ^{1}H NMR ($CDCl_3$) δ 1.08 (3H, d, CH_3-3, J_{CH_3-3}=6.9), 1.27 (3H, s, $C(CH_3)_2$), 1.47 (3H, s, $C(CH_3)_2$), 1.94 (1H, m, H-3), 4.02 (1H, m, H-4), 4.29 (1H, dd, H-5, J_{5-4}=5.3, $J_{5-5'}$=12.4), 4.50 (1H, dd, H-5′, $J_{5'-4}$=2.7, $J_{5'-5}$=12.4), 4.51 (1H, m, H-2), 5.78 (1H, d, H-1, J_{1-2}=3.7), 7.35–7.99 (5H, m, C_6H_5CO); ^{13}C NMR ($CDCl_3$) δ 9.7 (CH_3-3), 26.7 ($C(CH_3)_2$), 27.1 ($C(CH_3)_2$), 40.5 (C-3), 64.7 (C-5), 80.9 (C-4), 82.9 (C-2), 105.4 (C-1), 112.0 ($C(CH_3)_2$), 128.7–133.5 (C_{ar}), 166.8 (CO). Anal. Calcd for $C_{16}H_{20}O_5$: C, 65.74; H, 6.90. Found: C, 65.40; H, 7.16.

3.1.5. 5-*O*-Benzoyl-1,2-*O*-isopropylidene-3-*C*-methyl-α-D-ribofuranose (7). To a suspension of compound **3** (14.4 g, 49.4 mmol) in dry diethyl ether (250 mL) was added over 1 h a methyl magnesium bromide (3 M) solution in Et_2O (29.6 mL). The reaction mixture was stirred for 1 h at room temperature then 1 N NH_4Cl solution (50 mL) was added. The two layers were separated and the organic phase was washed with brine (100 mL) and water (100 mL), dried over sodium sulfate, and evaporated under reduced pressure. The residue was purified on silica gel column chromatography using a stepwise gradient of ethyl acetate (0–10%) in dichloromethane to afford compound **7** as a white solid (12.1 g, 80%), which was crystallized from diethyl ether/petroleum ether (1:1, v/v). Mp 110–111 °C; *m/z* (FAB>0) 309 $(M+H)^+$; ^{1}H NMR ($CDCl_3$) δ 1.19 (3H, s, CH_3-3), 1.30 (3H, s, $C(CH_3)_2$), 1.53 (3H, s, $C(CH_3)_2$), 2.67 (1H, s, OH), 4.04 (1H, dd, H-4, J_{4-5}=3.2, $J_{4-5'}$=8.0), 4.09 (1H, d, H-2, J_{2-1}=3.8), 4.31 (1H, dd, H-5′, $J_{5'-4}$=8.0, $J_{5'-5}$=11.9), 4.50 (1H, dd, H-5, J_{5-4}=3.2, $J_{5-5'}$=11.9), 5.76 (1H, d, H-1, J_{1-2}=3.8), 7.34–8.00 (5H, m, C_5H_6CO); ^{13}C NMR ($CDCl_3$) δ 18.3 (CH_3-3), 26.5 ($C(CH_3)_2$), 26.6 ($C(CH_3)_2$, 63.0 (C-5), 79.6 (C-4), 84.0 (C-2), 103.7 (C-1), 112.7 ($C(CH_3)_2$), 128.3–133.0 (C_{ar}), 166.4 (CO). Anal. Calcd for $C_{16}H_{20}O_6$: C, 62.33; H, 6.54. Found: C, 62.22; H, 6.52.

3.1.6. 1,2-Di-*O*-acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-α,β-D-ribofuranose (1). A solution of compound **6** (1 g, 3.42 mmol) in aqueous 80% trifluoroacetic acid (8.9 mL) was stirred at room temperature for 1 h and 30 min, and then trifluoroacetic acid was neutralized with addition of aqueous sodium hydrogen carbonate solution. After extractions with ethyl acetate, the organic phases were combined, dried over sodium sulfate, filtered, and evaporated under reduced pressure. The crude material was then dissolved in anhydrous pyridine (23.3 mL), and catalytic amount of DMAP and acetic anhydride (4.2 mL, 47.9 mmol) was added. The mixture was stirred for 30 min at room temperature, and then neutralized by aqueous sodium hydrogen carbonate solution. After extractions with diethyl ether, the organic phases were combined, dried over sodium sulfate, filtered, and evaporated to dryness. The residue was subjected to silica gel column chromatography, with a stepwise gradient of ethyl acetate (0–15%) in petroleum ether to afford compound **1** as a white solid (970 mg, 85%) and as

an anomeric α,β mixture (ratio α/β: 14:86, determined by ^{1}H NMR). An analytical sample of **1** was obtained after crystallization from petroleum ether providing the β anomer. Mp 89 °C; *m/z* (FAB>0) 337 $(M+H)^+$; ^{1}H NMR ($CDCl_3$) δ 1.04 (3H, d, C*H*$_3$-3, J_{CH_3-3}=6.9), 1.89 (3H, s, C*H*$_3$CO), 2.06 (3H, s, C*H*$_3$CO), 2.50 (1H, m, H-3), 4.14 (1H, m, H-4), 4.29 (1H, dd, H-5′, $J_{5'-4}$=4.8, $J_{5'-5}$=12.1), 4.52 (1H, dd, H-5, J_{5-4}=3.2, $J_{5-5'}$=12.1), 5.14 (1H, d, H-2, J_{2-3}=4.7), 6.05 (1H, s, H-1), 7.36–8.00 (5H, m, C$_6$*H*$_5$CO); ^{13}C NMR ($CDCl_3$) δ 10.0 (*C*H$_3$-3), 21.1 (*C*H$_3$CO), 21.4 (*C*H$_3$CO), 36.4 (C-3), 64.9 (C-5), 79.0 (C-2), 84.5 (C-4), 99.5 (C-1), 128.8–133.6 (C$_{ar}$), 166.7 (CO), 169.7 (CO), 170.4 (CO). Anal. Calcd for $C_{17}H_{20}O_7$: C, 60.71; H, 5.99. Found: C, 60.56; H, 6.21.

3.1.7. 1-(2-*O*-Acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-β-D-ribofuranosyl)uracil (8). A mixture of uracil (394 mg, 3.52 mmol), hexamethyldisilazane (35 mL), and a catalytic amount of ammonium sulfate was refluxed for 12 h. The resultant clear solution was concentrated to dryness under reduced pressure. TMSOTf (712 μL, 3.52 mmol) was added slowly at 0 °C to a solution of sugar **1** (592 mg, 1.76 mmol) and silylated base in dry acetonitrile (17 mL). The reaction mixture was stirred for 30 min at room temperature, poured into saturated sodium hydrogen carbonate solution, and extracted with dichloromethane. The organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. Chromatography of the residue on a silica gel column using as eluent a stepwise gradient of methanol (0–1%) in dichloromethane afforded compound **8** (557 mg, 82%) as a white foam. Mp 79 °C; $[\alpha]_D^{20}$ +15.0 (*c* 1.07, Me_2SO); UV λ_{max} (EtOH)/nm 259 (ε 10,700); *m/z* (FAB>0) 389 $(M+H)^+$, 277 $(S)^+$, 113 $(BH_2)^+$, 105 $(C_6H_5CO)^+$; *m/z* (FAB<0) 387 $(M-H)^-$, 121 $(C_6H_5CO_2)^-$, 111 $(B)^-$; ^{1}H NMR ($CDCl_3$) δ 1.04 (3H, d, C*H*$_3$-3′, $J_{CH_3-3'}$=6.8), 2.13 (3H, s, C*H*$_3$CO), 2.40 (1H, m, H-3′), 4.15 (1H, m, H-4′), 4.55 (1H, dd, H-5″, $J_{5''-4'}$=3.8, $J_{5''-5'}$=12.7), 4.67 (1H, dd, H-5′, $J_{5'-4'}$=2.4, $J_{5'-5''}$=12.7), 5.41 (1H, dd, H-2′, $J_{2'-1'}$=0.9, $J_{2'-3'}$=5.9), 5.47 (1H, dd, H-5, $J_{5\text{-NH}}$=2.0, J_{5-6}=8.2), 5.77 (1H, d, H-1′, $J_{1'-2'}$=0.9), 7.42–8.00 (6H, m, C$_6$*H*$_5$CO, H-6), 8.94 (1H, s, NH); ^{13}C NMR ($CDCl_3$) δ 8.2 (*C*H$_3$-3′), 19.6 (*C*H$_3$CO), 35.3 (C-3′), 61.7 (C-5′), 77.7 (C-2′), 82.8 (C-4′), 89.6 (C-1′), 101.2 (C-5), 127.6–132.6 (C$_{ar}$), 138.4 (C-6), 148.8 (C-2), 161.9 (C-4), 165.1 (CO), 168.5 (CO).

3.1.8. 1-(3-Deoxy-3-*C*-methyl-β-D-ribofuranosyl)-uracil (9). A solution of **8** (162 mg, 0.42 mmol) in methanolic ammonia (previously saturated at −10 °C and tightly stoppered) (15 mL) was stirred for 12 h at room temperature, and then evaporated to dryness. The residue was subjected to silica gel column chromatography, with a stepwise gradient of methanol (0–4%) in dichloromethane to afford compound **9** as a white solid (93 mg, 92%), which was crystallized from acetonitrile. Mp 208 °C; $[\alpha]_D^{20}$ +21.3 (*c* 1.08, Me_2SO); UV λ_{max} (EtOH)/nm 262 (ε 10,200); *m/z* (FAB>0) 243 $(M+H)^+$, 131 $(S)^+$, 113 $(BH_2)^+$; *m/z* (FAB<0) 241 $(M-H)^-$, 111 $(B)^-$; ^{1}H NMR (DMSO-d_6) δ 0.91 (3H, d, C*H*$_3$-3′, $J_{CH_3-3'}$=6.7), 2.07 (1H, m, H-3′), 3.54 (1H, m, H-5″), 3.78 (2H, m, H-4′, H-5′), 4.00 (1H, pt, H-2′), 5.14 (1H, pt, OH-5′), 5.54 (1H, d, H-5, J_{5-6}=8.1), 5.58 (1H, d, OH-2′, $J_{OH\text{-}2'}$=5.2), 5.60 (1H, s, H-1′), 8.13 (1H, d, H-6, J_{6-5}=8.1), 11.28 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ 10.0 (*C*H$_3$-3′), 35.7 (C-3′), 60.5 (C-5′), 77.9 (C-2′), 86.8 (C-4′), 91.9 (C-1′), 101.3 (C-5), 141.3 (C-6), 151.3 (C-2), 164.2 (C-4). Anal. Calcd for $C_{10}H_{14}N_2O_5$: C, 49.58; H, 5.83; N, 11.56. Found: C, 49.43; H, 5.67; N, 11.48.

3.1.9. 1-(2-*O*-Acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-β-D-ribofuranosyl)thymine (10). A mixture of thymine (712.5 mg, 5.66 mmol), hexamethyldisilazane (56.6 mL), and a catalytic amount of ammonium sulfate was refluxed for 12 h. The resultant clear solution was concentrated to dryness under reduced pressure. TMSOTf (1.14 mL, 5.66 mmol) was added slowly at 0 °C to a solution of sugar **1** (951 mg, 2.83 mmol) and silylated base in dry acetonitrile (26.5 mL). The reaction mixture was stirred for 30 min at room temperature, poured into saturated sodium hydrogen carbonate solution, and extracted with dichloromethane. The organic phase was dried over sodium sulfate, filtered, and evaporated to dryness. Chromatography of the residue on a silica gel column using as eluent a stepwise gradient of methanol (0–1%) in dichloromethane afforded compound **10** (726 mg, 64%) as a white foam. Mp 85 °C; $[\alpha]_D^{20}$ −7.1 (*c* 0.98, Me_2SO); UV λ_{max} (EtOH)/nm 265 (ε 10,000); *m/z* (FAB>0) 403 $(M+H)^+$, 277 $(S)^+$, 127 $(BH_2)^+$, 105 $(C_6H_5CO)^+$; *m/z* (FAB<0) 401 $(M-H)^-$, 125 $(B)^-$, 121 $(C_6H_5CO_2)^-$; ^{1}H NMR ($CDCl_3$) δ 1.02 (3H, d, C*H*$_3$-3′, $J_{CH_3-3'}$=6.9), 1.60 (3H, d, C*H*$_3$-5, J_{CH_3-6}=1.2), 2.09 (3H, s, C*H*$_3$CO), 2.47 (1H, m, H-3′), 4.09 (1H, m, H-4′), 4.45 (1H, dd, H-5″, $J_{5''-4'}$=4.2, $J_{5''-5'}$=12.6), 4.66 (1H, dd, H-5′, $J_{5'-4'}$=2.3, $J_{5'-5''}$=12.6), 5.37 (1H, dd, H-2′, $J_{2'-1'}$=1.8, $J_{2'-3'}$=6.4), 5.74 (1H, d, H-1′, $J_{1'-2'}$=1.8), 7.13 (1H, d, H-6, J_{6-CH_3}=1.2), 7.34–7.98 (5H, m, C$_6$*H*$_5$CO), 8.63 (1H, s, NH); ^{13}C NMR ($CDCl_3$) δ 9.6 (*C*H$_3$-3′), 12.3 (*C*H$_3$-5), 20.6 (*C*H$_3$CO), 36.6 (C-3′), 63.2 (C-5′), 78.5 (C-2′), 83.4 (C-4′), 90.4 (C-1′), 111.0 (C-5), 128.4–133.6 (C$_{ar}$), 135.3 (C-6), 149.9 (C-2), 163.4 (C-4), 166.2 (CO), 169.8 (CO).

3.1.10. 1-(3-Deoxy-3-*C*-methyl-β-D-ribofuranosyl)thymine (11). A solution of **10** (582 mg, 1.45 mmol) in methanolic ammonia (previously saturated at −10 °C and tightly stoppered) (50 mL) was stirred for 12 h at room temperature, and then evaporated to dryness. The residue was subjected to silica gel column chromatography with a stepwise gradient of methanol (0–5%) in dichloromethane to afford the compound **11** as a white solid (308 mg, 83%), which was lyophilized. Mp 202 °C; $[\alpha]_D^{20}$ +7.5 (*c* 1.06, Me_2SO); UV λ_{max} (EtOH)/nm 267 (ε 8400); *m/z* (FAB>0) 257 $(M+H)^+$, 131 $(S)^+$, 127 $(BH_2)^+$; *m/z* (FAB<0) 255 $(M-H)^-$, 125 $(B)^-$; ^{1}H NMR (DMSO-d_6) δ 0.92 (3H, d, C*H*$_3$-3′, $J_{CH_3-3'}$=6.8), 1.74 (3H, d, C*H*$_3$-5, J_{CH_3-6}=1.01), 2.12 (1H, m, H-3′), 3.55 (1H, m, H-5″), 3.77 (2H, m, H-4′, H-5′), 3.99 (1H, pt, H-2′), 5.16 (1H, pt, OH-5′), 5.53 (1H, d, OH-2′, $J_{OH\text{-}2'}$=5.0), 5.62 (1H, d, H-1′, $J_{1'-2'}$=0.8), 8.01 (1H, d, H-6, J_{6-CH_3}=1.0), 11.21 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ 9.2 (*C*H$_3$-3′), 12.2 (*C*H$_3$-5), 34.8 (C-3′), 59.7 (C-5′), 76.9 (C-2′), 85.8 (C-4′), 90.6 (C-1′), 108.0 (C-5), 136.3 (C-6), 150.3 (C-2), 163.9 (C-4).

3.1.11. 1-(3-Deoxy-3-*C*-methyl-β-D-ribofuranosyl)cytosine (12). Lawesson's reagent (75 mg, 0.19 mmol) was added to a solution of **8** (103 mg, 0.27 mmol) in anhydrous 1,2-dichloroethane (8.5 mL) and the reaction mixture was refluxed for 1 h. The solvent was then evaporated under reduced pressure and the residue was purified using silica

gel column chromatography with a stepwise gradient of methanol (0–1%) in dichloromethane to give the corresponding 4-thio intermediate as a yellow foam. A solution of the 4-thio intermediate in methanolic ammonia (3 mL) (saturated beforehand at −10 °C and stoppered tightly) was heated at 100 °C in a stainless-steel bomb for 12 h, and then cooled to room temperature. The solution was evaporated to dryness under reduced pressure and the residue was subjected to a silica gel column chromatography using a stepwise gradient of methanol (0–20%) in dichloromethane to afford the compound **12** as a white solid (59 mg, 92%), which was lyophilized. Mp 162 °C; $[\alpha]_D^{20}$ +38.8 (*c* 1.03, Me_2SO); UV λ_{max} (EtOH)/nm 272 (ε 8000); *m/z* (FAB>0) 242 $(M+H)^+$, 112 $(BH_2)^+$; *m/z* (FAB<0) 240 $(M-H)^-$; ^1H NMR (DMSO-d_6) δ 0.90 (3H, d, CH_3-3′, $J_{CH_3-3'}$=6.7), 1.99 (1H, m, H-3′), 3.55 (1H, m, H-5″), 3.77 (2H, m, H-4′, H-5′), 3.88 (1H, pt, H-2′), 5.09 (1H, pt, OH-5′), 5.51 (1H, d, OH-2′, $J_{OH-2'}$=4.9), 5.60 (1H, s, H-1′), 5.65 (1H, d, H-5, J_{5-6}=7.4), 7.10 (2H, 2×sl, NH_2), 8.09 (1H, d, H-6, J_{6-5}=7.4); ^{13}C NMR (DMSO-d_6) δ 8.6 (*C*H_3-3′), 34.1 (C-3′), 59.3 (C-5′), 77.0 (C-2′), 85.4 (C-4′), 91.2 (C-1′), 92.3 (C-5), 140.7 (C-6), 154.6 (C-2), 165.1 (C-4).

3.1.12. N^6-Benzoyl-9-(2-*O*-acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-β-D-ribofuranosyl)adenine (13). A mixture of N^6-benzoyl adenine (3.55 g, 14.9 mmol), *N*,*O*-bistrimethylsilylacetamide (7.3 mL, 29.8 mmol), and dry acetonitrile (104 mL) was refluxed under anhydrous conditions for 1 h. A solution of **1** (1 g, 2.97 mmol) in dry acetonitrile (27 mL) followed by TMSOTf (2.3 mL, 11.9 mmol) was added. The reaction mixture was refluxed for 6 h, and then partitioned between aqueous saturated sodium hydrogen carbonate solution and dichloromethane (100 mL). The organic layer was washed with water, dried over sodium sulfate, filtered, and concentrated in vacuo to give the crude product. Purification by silica gel column chromatography with a stepwise gradient of methanol (0–1.5%) in dichloromethane afforded the compound **13** (947 mg, 62%) as a white foam. Mp 93 °C; $[\alpha]_D^{20}$ −3.9 (*c* 1.03, Me_2SO); UV λ_{max} (EtOH)/nm 278 (ε 20,100); *m/z* (FAB>0) 516 $(M+H)^+$, 277 $(S)^+$, 240 $(BH_2)^+$, 105 $(C_6H_5CO)^+$; *m/z* (FAB<0) 514 $(M-H)^-$, 238 $(B)^-$, 121 $(C_6H_5CO_2)^-$; ^1H NMR (DMSO-d_6) δ 1.13 (3H, d, CH_3-3′, $J_{CH_3-3'}$=6.8), 2.18 (3H, s, CH_3CO), 3.21 (1H, m, H-3′), 4.23 (1H, m, H-4′), 4.51 (1H, dd, H-5″, $J_{5''-4'}$=4.8, $J_{5''-5'}$=12.8), 4.63 (1H, dd, H-5′, $J_{5'-4'}$=2.4, $J_{5'-5''}$=12.4), 5.84 (1H, dd, H-2′, $J_{2'-1'}$=0.8, $J_{2'-3'}$=6.0), 6.25 (1H, d, H-1′, $J_{1'-2'}$=1.2), 7.49–8.04 (10H, m, 2×C_6H_5CO), 8.62 (1H, s, H-2), 8.69 (1H, s, H-8), 11.2 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ 9.7 (*C*H_3-3′), 21.1 (*C*H_3CO), 36.8 (C-3′), 64.1 (C-5′), 78.8 (C-2′), 83.5 (C-4′), 88.9 (C-1′), 126.2 (C-5), 129.0–133.9 (C_{ar}), 143.9 (C-8), 151.0 (C-4), 152.0 (C-6), 152.3 (C-2), 166.0 (CO), 166.1 (CO), 170.5 (CO). Anal. Calcd for $C_{27}H_{25}N_5O_6$: C, 62.91; H, 4.89; N, 13.59; O, 18.62. Found: C, 62.47; H, 5.10; N, 13.18.

3.1.13. 9-(3-Deoxy-3-*C*-methyl-β-D-ribofuranosyl)-adenine (14). A solution of **13** (931 mg, 1.81 mmol) in methanolic ammonia (previously saturated at −10 °C and tightly stoppered) (36 mL) was stirred for 24 h at room temperature, and then evaporated to dryness. The residue was crystallized from methanol and water (8:2, v/v) to afford the compound **14** (377 mg, 79%). Mp 243 °C; $[\alpha]_D^{20}$ −41.6 (*c* 0.99, Me_2SO); UV λ_{max} (EtOH)/nm 260 (ε 14,500); *m/z* (FAB>0) 266 $(M+H)^+$, 136 $(BH_2)^+$; *m/z* (FAB<0) 264 $(M-H)^-$; ^1H NMR (DMSO-d_6) δ 0.99 (3H, d, CH_3-3′, $J_{CH_3-3'}$=6.8), 2.41 (1H, m, H-3′), 3.55 (1H, m, H-5″), 3.76 (1H, m, H-5′), 3.85 (1H, m, H-4′), 4.32 (1H, pt, H-2′, $J_{2'-OH}$=4.7, $J_{2'-3'}$=4.5), 5.14 (1H, t, OH-5′, $J_{OH-5'}$=$J_{OH-5''}$= 5.4), 5.70 (1H, d, OH-2′, $J_{OH-2'}$=4.9), 5.91 (1H, s, H-1′), 7.28 (2H, s, NH_2), 8.15 (1H, s, H-2), 8.42 (1H, s, H-8); ^{13}C NMR (DMSO-d_6) δ 9.7 (*C*H_3-3′), 35.6 (C-3′), 60.7 (C-5′), 76.8 (C-2′), 86.1 (C-4′), 90.2 (C-1′), 119.0 (C-5), 138.8 (C-8), 148.7 (C-4), 152.4 (C-2), 156.0 (C-6). Anal. Calcd for $C_{11}H_{15}N_5O_3$: C, 49.81; H, 5.70; N, 26.40; O, 18.09. Found: C, 49.82; H, 5.71; N, 26.26.

3.1.14. 2-*N*-Acetyl-9-(2-*O*-acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-β-D-ribofuranosyl)-6-*O*-diphenylcarbamoylguanine (15) and 2-*N*-acetyl-9-N_2-(2-*O*-acetyl-5-*O*-benzoyl-3-deoxy-3-*C*-methyl-β-D-ribofuranosyl)-6-*O*-diphenylcarbamoylguanine (16). BSA (1.7 mL, 7.12 mmol) was added to a suspension of 2-*N*-acetyl-6-*O*-diphenylcarbamoylguanine (1.38 g, 3.56 mmol) in anhydrous dichloroethane (25 mL), and stirring was continued at 80 °C for 1 h. The clear solution was evaporated and the residue was dissolved in toluene (25 mL). Then a solution of **1** (1 g, 2.97 mmol) in toluene (25 mL) was added followed by TMSOTf (918 μL, 4.75 mmol) at 0 °C. The solution was stirred at 80 °C for 1 h and 30 min, cooled down, and ethyl acetate was added. The organic phase was washed with saturated sodium hydrogen carbonate solution and water, dried over sodium sulfate, filtered, and evaporated. The residue was purified by silica gel column chromatography using a stepwise gradient of methanol (0–2%) in dichloromethane to give in order of elution compound **16** (396 mg, 14%) and compound **15** (1.08 g, 55%) as a white foam, which was recrystallized from acetonitrile. Compound **16**: mp 101 °C; $[\alpha]_D^{20}$ −17.3 (*c* 0.98, Me_2SO); UV λ_{max} (EtOH)/nm 270 (ε 25,400); *m/z* (FAB>0) 941 $(M+H)^+$, 389 $(BH_2)^+$, 277 $(S)^+$, 105 $(C_6H_5CO)^+$, 43 $(CH_3CO)^+$; *m/z* (FAB<0) 939 $(M-H)^-$, 387 $(B)^-$; ^1H NMR (DMSO-d_6) δ 0.90 (3H, d, CH_3-3′, $J_{CH_3-3'}$=6.8), 1.08 (3H, d, CH_3-3′, $J_{CH_3-3'}$=6.8), 1.99 (3H, s, CH_3CO), 2.09 (3H, s, CH_3CO), 2.14 (3H, s, CH_3CO), 2.33 (1H, m, H-3′), 2.94 (1H, m, H-3′), 3.89 (1H, m, H-4′), 3.99 (1H, m, H-5″), 4.22 (1H, m, H-4′), 4.31 (1H, m, H-5′), 4.47 (1H, m, H-5″), 4.56 (1H, m, H-5′), 5.76 (1H, dd, H-2′, $J_{2'-1'}$=1.6, $J_{2'-3'}$=6.4), 5.84 (1H, dd, H-2′, $J_{2'-1'}$=0.8, $J_{2'-3'}$=5.7), 6.04 (1H, d, H-1′, $J_{1'-2'}$=1.7), 6.18 (1H, d, H-1′, $J_{1'-2'}$=0.8), 7.31–7.76 (20H, m, 4×C_6H_5CO), 8.76 (1H, s, H-8); ^{13}C NMR (DMSO-d_6) δ 9.5 (*C*H_3-3′), 9.9 (*C*H_3-3′), 20.6 (*C*H_3CO), 20.8 (*C*H_3CO), 37.0 (C-3′), 37.4 (C-3′), 63.7 (C-5′), 65.1 (C-5′), 78.5 (C-2′), 79.0 (C-2′), 82.1 (C-4′), 84.1 (C-4′), 89.3 (C-1′), 92.7 (C-1′), 123.1 (C-5), 126.5–133.4 (C_{ar}), 143.5 (C-8), 150.1 (C-4), 153.8 (C-2), 156.0 (C-6), 166.3–171.4 (6×CO). Anal. Calcd for $C_{50}H_{48}N_6O_3$: C, 63.82; H, 5.14; N, 8.93; O, 22.10. Found: C, 63.73; H, 5.32; N, 8.56. Compound **15**: mp 211 °C; $[\alpha]_D^{20}$ +25.0 (*c* 1.01, Me_2SO); UV λ_{max} (EtOH)/nm 273 (ε 20,200); *m/z* (FAB>0) 665 $(M+H)^+$, 470 $(M-(C_6H_5)_2NCO+H)^+$, 389 $(BH_2)^+$, 277 $(S)^+$, 196 $((C_6H_5)_2NCO)^+$, 105 $(C_6H_5CO)^+$, 43 $(CH_3CO)^+$; *m/z* (FAB<0) 663 $(M-H)^-$, 468 $(M-(C_6H_5)_2NCO-H)^-$, 387 $(B)^-$; ^1H NMR (DMSO-d_6) δ 1.10 (3H, d, CH_3-3′, $J_{CH_3-3'}$=6.8), 2.13 (3H, s, CH_3CO), 2.14 (3H, s, CH_3CO), 3.66 (1H, m, H-3′), 4.18 (1H, m, H-4′), 4.48 (1H,

dd, H-5″, $J_{5''-4'}$=5.1, $J_{5''-5'}$=12.5), 4.58 (1H, dd, H-5′, $J_{5'-4'}$=2.6, $J_{5'-5''}$=12.5), 5.79 (1H, d, H-2′, $J_{2'-3'}$=6.2), 6.13 (1H, d, H-1′, $J_{1'-2'}$=0.8), 7.31–7.53 (15H, m, 3×C_6H_5CO), 8.52 (1H, s, H-8), 10.78 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ 9.7 (CH_3-3′), 21.0 (CH_3CO), 25.0 (CH_3CO), 36.4 (C-3′), 64.2 (C-5′), 79.1 (C-2′), 83.9 (C-4′), 89.7 (C-1′), 120.9 (C-5), 127.4–133.8 (C_{ar}), 142.0 (C-8), 150.5 (C-4), 154.1 (C-2), 155.7 (C-6), 165.9–170.5 (4×CO). Anal. Calcd for $C_{35}H_{32}N_6O_8$: C, 63.25; H, 4.85; N, 12.64; O, 19.26. Found: C, 63.13; H, 4.90; N, 12.59.

3.1.15. 9-(3-Deoxy-3-*C*-methyl-β-D-ribofuranosyl)guanine (17). A solution of **15** (450 mg, 0.68 mmol) in methanolic ammonia (30 mL, saturated at −10 °C) in a sealed flask was stirred at ambient temperature for 24 h. Volatiles were evaporated and the residue was crystallized from water to give compound **17** (133.4 mg, 70%). Mp 265 °C; $[\alpha]_D^{20}$ −15.2 (*c* 1.02, Me_2SO); UV λ_{max} (EtOH)/nm 255 (ε 11,700); *m/z* (FAB>0) 282 $(M+H)^+$, 152 $(BH_2)^+$; *m/z* (FAB<0) 280 $(M-H)^-$; ^{1}H NMR (DMSO-d_6) δ 0.97 (3H, d, CH_3-3′, $J_{CH_3-3'}$=6.7), 2.35 (1H, m, H-3′), 3.53 (1H, m, H-5″), 3.74 (2H, m, H-4′, H-5′), 4.19 (1H, t, H-2′, $J_{2'-3'}=J_{2'\text{-OH}}$=5.0), 5.01 (1H, t, OH-5′, $J_{\text{OH-5}'}=J_{\text{OH-5}''}$= 5.1), 5.56 (1H, d, OH-2′, $J_{\text{OH-2}'}$=5.1), 5.71 (1H, s, H-1′), 6.47 (2H, s, NH_2), 7.99 (1H, s, H-8), 10.62 (1H, s, NH); ^{13}C NMR (DMSO-d_6) δ 9.7 (CH_3-3′), 35.9 (C-3′), 60.8 (C-5′), 77.0 (C-2′), 85.8 (C-4′), 89.3 (C-1′), 116.6 (C-5), 135.1 (C-8), 150.5 (C-4), 153.5 (C-2), 156.7 (C-6). Anal. Calcd for $C_{11}H_{15}N_5O_4\cdot 0.5H_2O$: C, 45.51; H, 5.56; N, 24.13; O, 24.80. Found: C, 45.45; H, 5.74; N, 23.26.

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