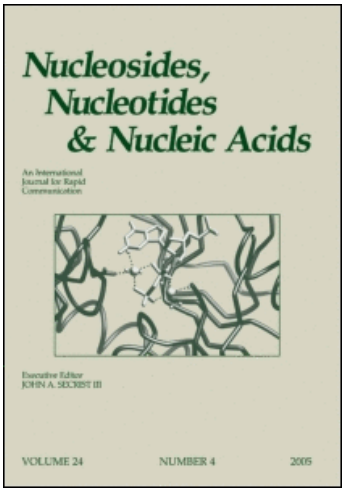

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Synthesis and Biological Evaluation of Some 5-Nitro- and 5-Amino Derivatives of 2'-Deoxycytidine, 2',3'-Dideoxyuridine, and 2',3'-Dideoxycytidine

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Synthesis and Biological Evaluation of Some 5-Nitro- and 5-Amino Derivatives of 2′-Deoxycytidine, 2′,3′-Dideoxyuridine, and 2′,3′-Dideoxycytidine

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ABSTRACT

In this article, we describe the synthesis of 5-nitro-1-(2-deoxy-α-D-*erythro*-pentofuranosyl)cytosine (**4α**), 5-nitro-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)cytosine (**4β**), 5-amino-1-(2-deoxy-α-D-*erythro*-pentofuranosyl)cytosine (**5α**), 5-nitro-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)cytosine (**5β**), 5-nitro-1-(2,3-dideoxy-β-D-ribofuranosyl)uracil (**6β**), 5-amino-1-(2,3-dideoxy-α,β-D-ribofuranosyl)uracil (**7**), 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl)cytosine (**8**) and 5-amino-1-(2,3-dideoxy-β-D-ribofuranosyl)cytosine (**9β**). The prepared compounds were tested for their activity against HIV and HBV viruses, but they did not show significant activity.

Key Words: 5-Substituted pyrimidine nucleoside analogues; HIV; HBV.

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INTRODUCTION

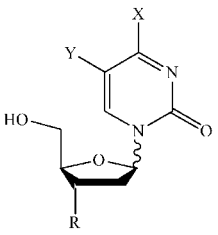
Nucleoside analogues represent one of the main classes of therapeutic agents in antiviral chemotherapy, and to date, near of twenty nucleoside analogues have been approved for the treatment of various viral diseases including Herpes viruses, Human Immunodeficiency Virus (HIV) and Hepatitis B virus (HBV) infections.[1] In order to discover new nucleoside derivatives endowed with potent antiviral activity, modifications of the base and/or the sugar moiety of natural nucleosides can be attempted. As a part of our ongoing research program on this topic we have synthesized pyrimidine nucleosides bearing a nitro or amino group at C-5.

Several pyrimidine nucleoside analogues, variously modified at C-5 of the base moiety, have been shown to present biological activity.[2] De Clercq et al. have reported the anti HSV-1 and HSV-2 activities of 5-nitro-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)cytosine (5-NO_2dC) (**4β**) (Fig. 1) as well as its inhibitory effect on mouse leukaemia L1210 cell growth.[3] Therefore we found it of interest to develop a new chemical synthesis for compound (**4β**) and its 5-amino counterpart (**5β**) (Fig. 1), all the more no biological data are available for the latter. Moreover, the synthesis of other hitherto unknown compounds such as 5-nitro and 5-amino-2′,3′-dideoxyuridine and cytidine derivatives (Fig. 1) as well as the biological evaluation concerning their potential antiviral activity against HIV and HBV are reported.

RESULTS AND DISCUSSION

The first synthesis of 5-NO_2dC (**4β**) was reported by Huang et al.[4] The nitro group on the pyrimidine ring of 2′-deoxycytidine was introduced by reaction of the corresponding 5′-monophosphate with NO_2BF_4/sulfolane. A dephosphorylation step to the free nucleoside (**4β**) was achieved by the action of alkaline phosphatase with a 1.5% overall yield.

In our first approach, we tried without any success to perform from a suitably protected 2′-deoxycytidine an Olah's nitration reaction,[5] already applied in the synthesis of 5-nitrouridine and 5-nitro-2′-deoxyuridine.[6] At this point a chemical conversion of the 5-nitrouracil moiety of the nucleoside to the corresponding nucleoside bearing 5-nitrocytosine seemed to be appropriate. Indeed, according to conventional routes, the C-4 position of the pyrimidine ring can be transformed in a two step reaction following three different methodologies. Thus, in a first step the C-4



	Compound	*X*	*Y*	*R*
(**4β**)	5-nitro-2'-deoxycytidine	NH_2	NO_2	OH
(**5β**)	5-amino-2'-deoxycytidine	NH_2	NH_2	OH
(**6β**)	5-nitro-2',3'-dideoxyuridine	OH	NO_2	H
(**7α/β**)	5-amino-2',3'-dideoxyuridine	OH	NH_2	H
(**8α/β**)	5-nitro-2',3'-dideoxycytidine	NH_2	NO_2	H
(**9β**)	5-amino-2',3'-dideoxycytidine	NH_2	NH_2	H

Figure 1.

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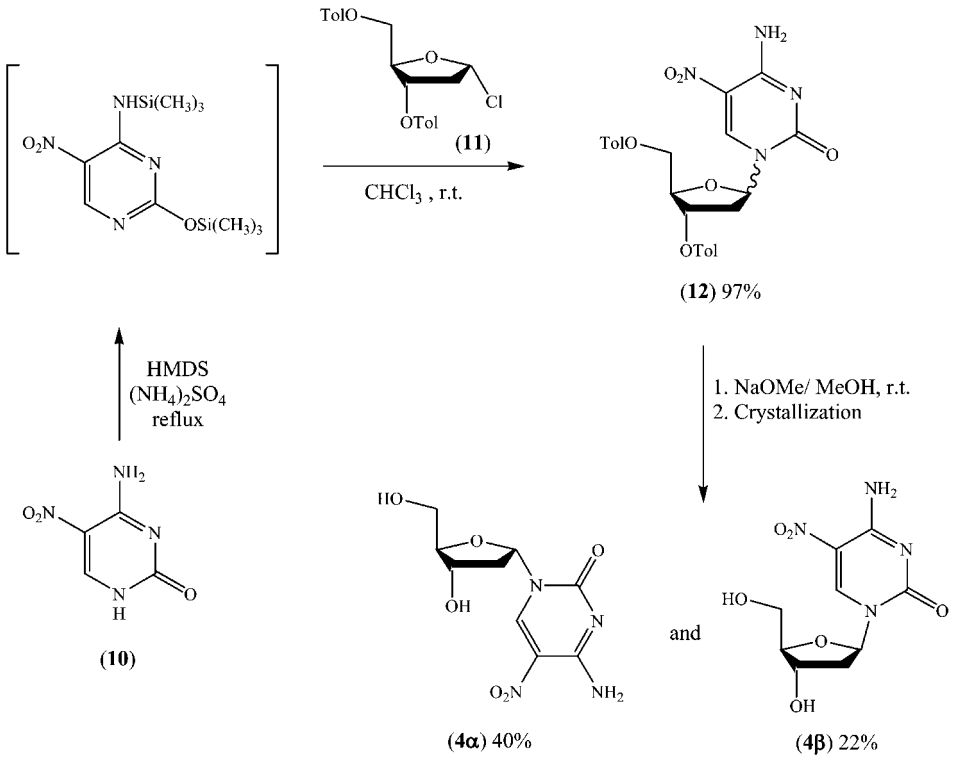
position of the uracil ring can be derivatized with a triazoyl-group,[7,8] an *O*-aryl group[9] or via a direct thionation reaction[10] to a C-4-thiocarbonyl. In a second step, ammonolysis should provided the cytosine nucleoside derivative. However, when these methodologies were applied to protected 5-nitro-2′-deoxyuridine, none of them provided the target 5-nitro-2′-deoxycytidine (**4β**). Thus, we chose another approach involving the coupling of a suitable protected carbohydrate moiety with 5-nitrocytosine[11] (**10**) through a glycosylation reaction.

Thus, glycosylation of silylated 5-nitrocytosine with 1-chloro-2-deoxy-3,5-di-*O*-(*p*-toluoyl)-α-D-*erythro*-pentofuranose[12] (**11**) in anhydrous $CHCl_3$, without any catalyst at room temperature, gave an anomeric mixture (α/β, ratio 1:1) of the protected nucleoside (**12**) which was isolated in a nearly quantitative yield (97%) (Sch. 1).

The anomeric ratio (α/β, ratio 1:1) of **12** was inferred from ^{1}H NMR spectroscopy studies using the chemical shift of H-6 protons of 5-nitrocytosine moiety because the H-1′ protons were overlapping. Our efforts to resolve the **12α** and **12β** anomers at their blocked stage were not successful. Thus, the protecting groups were removed by treatment with NaOMe/MeOH to give a mixture of anomers (**4α**/**4β**, ratio 1:1) in 72% yield. Fractional crystallization in MeOH at −18°C gave 5-nitro-1-(2-deoxy-α-D-ribofuranosyl)cytosine (**4α**) (40% yield) and 5-nitro-1-(2-deoxy-

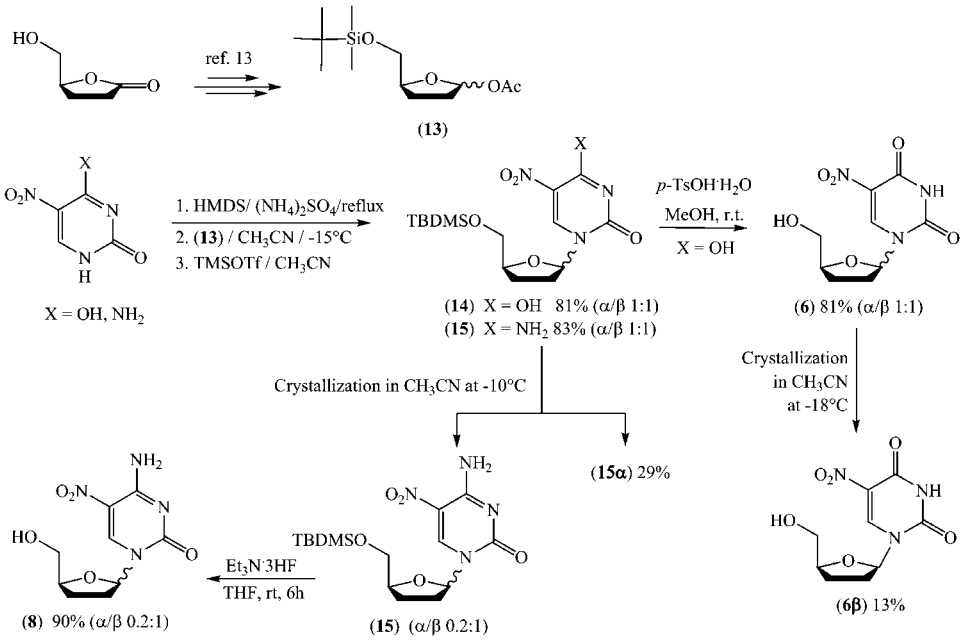


Scheme 1.

β-D-ribofuranosyl)cytosine (**4β**) (22% yield) separately (Sch. 1). The anomeric configuration of (**4α**) and (**4β**) was assigned through the comparison of their ^{1}H NMR spectra.[13] Indeed, protons that are *syn* to the nucleobase are more deshielded than those which are *anti*. Thus, the H-4′ proton of the α-anomer (4.38 ppm) appeared at a lower field than H-4′ proton of the β-anomer (3.90 ppm). Moreover, the H-5′ protons of the α-anomer (3.44 ppm) appeared at a higher field than those of the β-anomer (3.69 and 3.59 ppm). The structures of both compounds have been also verified by means of ^{1}H-NOE difference spectroscopy[14] since a NOE effect (12%) was observed between protons H-6 and H-4′ for the α-anomer (**4α**).

Then, we focused our attention on the synthesis of the hitherto unknown 5-nitro-1-(2,3-dideoxy-β-D-ribofuranosyl)uracil (**6β**) and 5-nitro-1-(2,3-dideoxy-α, β-D-ribofuranosyl)cytosine (**8**) (Sch. 2). For our purpose, we chose to synthesize a suitably protected 2,3-D-dideoxyribofuranose as key intermediate which can be further condensed with the appropriate heterocyclic moiety. 1-*O*-Acetyl-5-(*tert*-butyldimethylsilyl)-2,3-D-dideoxy-ribofuranose[13] (**13**) was obtained in three steps starting from commercially available (S)-γ-(hydroxymethyl)-γ-butyrolactone.

Sugar **13** was condensed with silylated 5-nitrouracil (Sch. 2) using TMSOTf as a catalyst in CH_3CN at −15°C to give 5-nitro-1-(5-*O*-*tert*-butyldimethylsilyl-2,3-dideoxy-D-ribofuranosyl)uracil (**14**) in 81% yield as a mixture of anomers (α/β, ratio 1:1). The reaction was instantaneous and prolonged reaction times provoked nucleoside decomposition. Treatment with *p*-toluenesulfonic acid monohydrate afforded an anomeric mixture of 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl) uracil (**6**) in 81% yield. The ratio of the two anomers (**6**) was determined by



Scheme 2.

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^{1}H-NMR by measuring the integral associated to the H-6 protons of both anomers. The β-anomer (**6β**) could be isolated with 13% yield after crystallization in acetonitrile at −18°C (Sch. 2). Correct assignment was made by comparing chemical shifts of H-6 proton in 5-nitro-2′,3′-dideoxyuridine (**6**) with those of 5-nitrouridine (9.74 ppm) and 5-nitro-2′-deoxyuridine (9.71 ppm) previously described.[6] The analysis of ^{1}H NMR spectrum of (**6**) displayed the presence of two singlets at 9.64 ppm and 8.81 ppm respectively. They were assigned to H-6 protons of the two anomers. Superposition of signals of H-1′ protons for both anomers prevented the exact attribution of stereochemistry.

Nevertheless, our attribution was confirmed by ^{1}H-NOE difference spectroscopy on the crystallized (**6β**) compound (Fig. 2), showing that H-1′ (5.85 ppm) proton is correlated to H-4′ proton (4.11 ppm) and that H-5″/H-5′ (3.78 ppm and 3.53 ppm) protons are correlated with H-6 proton (9.64 ppm).

On the other hand, 5-nitro-1-(5-[(*tert*-butyldimethylsilyl)-2,3-dideoxy-D-ribofuranosyl]cytosine (**15**) was obtained as a mixture of anomers (α/β, ratio 1:1) by condensing silylated 5-nitrocytosine with **13** in 83% yield (Sch. 2). Crystallization in acetonitrile at −10°C afforded pure α-anomer (**15α**) in 29% yield. The resulting filtrate provided an enriched β-anomeric mixture (α/β, ratio 0.2:1), which was directly deprotected by triethylamine tris(hydrogen fluoride) complex[15] (Et_3N, 3HF) at room temperature. An inseparable mixture of α- and β-anomer of 5-nitro-2′,3′-dideoxycytidine (**8**) was obtained in 90% yield (α/β, ratio 0.2:1) (Sch. 2).

Hydrogenation of 5-nitro-1-(2-deoxy-α-D-ribofuranosyl)cytosine (**4α**), 5-nitro-1-(2-deoxy-β-D-ribofuranosyl)cytosine (**4β**), 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl)uracil (**6**) and 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl)cytosine (**8**) afforded the corresponding 5-amino-1-(2-deoxy-α-D-ribofuranosyl)cytosine (**5α**), 5-amino-1-(2-deoxy-β-D-ribofuranosyl)cytosine (**5β**), 5-amino-1-(2,3-dideoxy-α,β-D-ribofuranosyl)uracil (**7**), 5-amino-1-(2,3-dideoxy-β-D-ribofuranosyl)cytosine (**9β**) (Sch. 3).

From the 5-amino nucleosides **5α**, **5β**, **7** and **9β**, only 5-amino-1-(2-deoxy-β-D-ribofuranosyl)cytosine[16,17] (**5β**) was previously reported, by treating 5-bromo-1-(2-deoxy-β-D-ribofuranosyl)cytosine with ammonia solution at 55°C for 4 days, giving (**5β**) with a low yield. In our approach, (**5β**) was obtained by simple reduction of (**4β**) with palladium on charcoal (5%) in methanolic acetic acid, at room temperature with a nearly quantitative yield (95%).

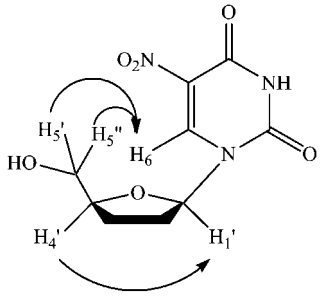

Figure 2.

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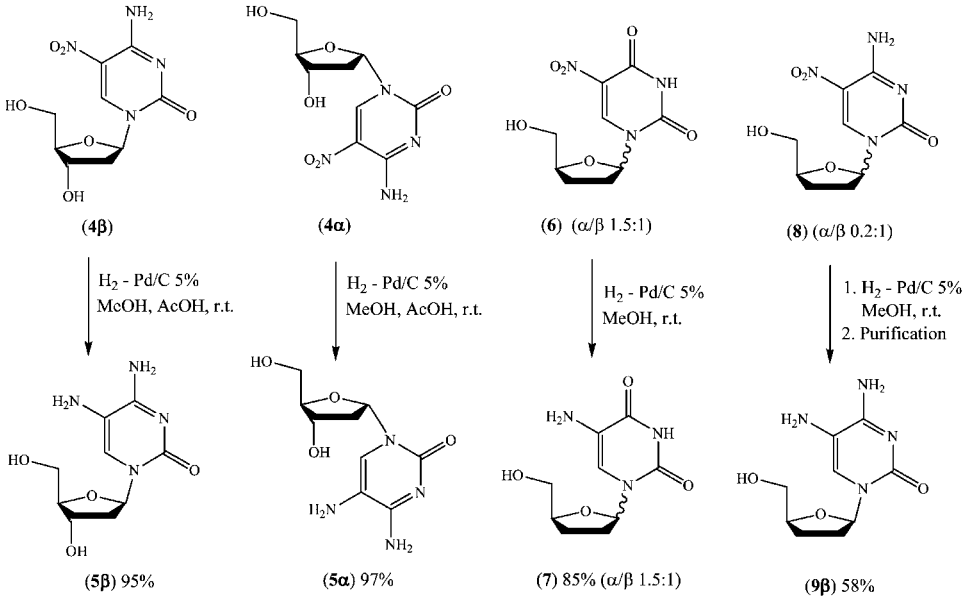

Scheme 3.

BIOLOGICAL EVALUATION

All the unprotected nucleosides (**4β**), (**4α**), (**5α**), (**5β**), (**6β**), (**7**), (**8**) and (**9β**) were tested for their in vitro inhibitory effects on the replication of HIV-1 in MT-4 cells. However, none of these compounds showed marked antiviral effects or detectable alteration of host-cell morphology at the highest concentration tested (generally 100 μM), with the exception of 5-nitro-1-(2-deoxy-β-D-ribofuranosyl)cytosine (**4β**) [MT-4 cells ($CC_{50} = 38\,\mu M$)] and 5-amino-1-(2,3-dideoxy-β-D-ribofuranosyl)cytosine (**9β**) [MT-4 cells ($CC_{50} = 13\,\mu M$)]. When evaluated in anti-HBV assays in HepG2 cells, none of the tested compounds showed antiviral effect (up to a concentration of 10 μM) nor cytotoxicity (up to the same concentration of 10 μM).

CONCLUSION

In this work, the syntheses of some nucleoside analogues bearing 5-nitro- or 5-amino-groups at C-5 position on uracil and cytosine were carried out. Glycosylation reactions of 5-nitro-uracil or –cytosine with a suitable 2-deoxy or 2,3-dideoxy sugar precursor followed by appropriate chemical modifications led to 5-nitro-1-(2-deoxy-α-D-*erythro*-pentofuranosyl)cytosine (**4α**), 5-nitro-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)cytosine (**4β**), 5-amino-1-(2-deoxy-α-D-*erythro*-pentofuranosyl)cytosine (**5α**), 5-nitro-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)cytosine (**5β**), 5-nitro-1-(2,3-dideoxy-β-D-ribofuranosyl)uracil (**6β**), 5-amino-1-(2,3-dideoxy-α,β-D-ribofuranosyl)uracil (**7**), 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl)cytosine (**8**)

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and 5-amino-1-(2,3-dideoxy-β-D-ribofuranosyl)cytosine (**9β**). All these compounds were tested against the replication of HIV and HBV but they did not show significant antiviral activities.

EXPERIMENTAL

^{1}H-NMR and ^{13}C-NMR spectra were recorded at room temperature with a Bruker DPX 200, AC 250 or DRX 400, in decoupled mode for ^{13}C-NMR. The chemical shifts for ^{1}H-NMR and ^{13}C-NMR are expressed in ppm with respect to the signal of residual DMSO-d_5 fixed at 2.49 ppm and 39.5 ppm. Deuterium exchange, COSY and DEPT experiments were performed in order to confirm proton assignments. Coupling constants *J* are expressed in Hertz (Hz). 2D ^{1}H-^{13}C heteronuclear COSY were recorded for the attribution of ^{13}C signals. Diastereoisomeric ratios (α and β) were determined by ^{1}H-NMR of anomeric mixture and the correct attribution of structures was made by NOE experiments. FAB mass spectra were recorded with JEOL JMS DX 300, by positive and negative FAB ionisation. The matrix was a mixture (50:50, v/v) of glycerol and thioglycerol (G-T) or 3-nitrobenzylic alcool (NBA). Specific rotations were measured on a Perkin-Elmer Model 241 spectropolarimeter (path length 1 cm), and are given in units of 10^{-1} deg cm^2 g^{-1}. Elemental analyses were carried out by the Service de Microanalyses du C.N.R.S. Division of Vernaison (France). Melting points are uncorrected and were measured by mean of a capillary with a Büchi melting point B-545. Ultra-Violet (U.V.) spectra were recorded with a spectrophotometre Uvikon-xs (BIO-TEK instruments). Thin layer chromatography (TLC) was performed on Silica Gel Merck 60 F_{254} (art. 5554), visualization of products being accomplished by UV absorbency followed by charring with 5% ethanolic sulfuric acid or by ninhydrine (200 mg) in abs. ethanol and heating. Column chromatography was carried out on Silica Gel 60 (Merck, art. 9385). After elution or extraction, compounds were filtered through Millex HV-4 (0.45 μm, Millipore) units. Reverse phase (C_{18}) purification was performed by Silica Merck LiChroprep RP-18 (25–40 μm). All moisture-sensitive reactions were carried out under rigorous anhydrous conditions under an argon atmosphere using oven-dried glassware. Solvents were dried and distilled prior to use and solids were dried over P_2O_5 under reduced pressure.

General Procedure for the Hydrogenation of Compounds 4β, 4α, 6, and 8. A solution of the nucleoside in MeOH (26 mL/mmol) and glacial acetic acid (44 μl/mmol, except for compound **6** and **8**) was hydrogenated in the presence of Pd/C 5% (100 mg/100 mg of nucleoside). After 20 min of stirring at room temperature, the suspension was filtered through a sintered funnel covered with Celite and the filtrate was evaporated to dryness and co-evaporated several times with toluene. The residue was subjected to a RP 18 column chromatography with water as eluent.

5-Nitro-1-(2-deoxy-3,5-di-*O*-*p*-toluoyl-α,β-D-*erythro*-pentofuranosyl)cytosine (12). A mixture of 5-nitrocytosine[11] (**10**) (3.5 g, 22.4 mmol), hexamethyldisilazane (160 mL) and a catalytic amount of ammonium sulfate was refluxed overnight. After distillation under vacuum, the crude was diluted with dry

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chloroform (40 mL) and a solution of 1-chloro-2-deoxy-3,5-di-*O*-*p*-toluoyl-α-D-*erythro*-pentofuranose[12] (6.09 g, 15.70 mmol) in dry chloroform (70 mL) was added. The mixture was stirred for 4h30 at room temperature, neutralised with a saturated solution of $NaHCO_3$ (100 mL), washed with water (2×100 mL), dried (sodium sulfate), and evaporated. Chromatography of the residue on a silica gel column using petroleum ether/ethyl acetate (75:25) as eluent gave a white foam which upon crystallization in MeOH at −18°C provided white crystals of **12** (7.74 g, 97% yield) as a mixture of anomers (α/β, ratio 1:1). R_f (system: $CHCl_3$/Methanol 98:2 v/v) 0.33 (α), 0.38 (β); δ_H[$(CD_3)_2SO$] 8.89 (s, 1H, 6-$H_{[\beta]}$), 8.85 (s, 1H, 6-$H_{[\alpha]}$), 8.43 (s, 1H, 4-$NH_{2[\alpha]}$ and 4-$NH_{2[\beta]}$), 7.94 (s, 1H, 4-$NH_{2[\beta]}$), 7.89 (s, 1H, 4-$NH_{2[\alpha]}$), 7.1–7.8 (m, 16H, $ArH_{[\alpha]}$ and $ArH_{[\beta]}$), 6.03 (m, 2H, 1′-$H_{[\alpha]}$ and 1′-$H_{[\beta]}$), 5.46 (m, 2H, 3′-$H_{[\alpha]}$ and 3′-$H_{[\beta]}$), 5.04 (m, 1H, 4′-$H_{[\alpha]}$), 4.59 (m, 1H, 4′-$H_{[\beta]}$), 5.53 (dd, 1H, $J_{5'\text{-}4'} = 3.6$, $J_{5'\text{-}5''} = 12.1$, 5′-$H_{[\beta]}$), 4.39 (m, 3H, 5″-$H_{[\beta]}$, 5′-$H_{[\alpha]}$ and 5″-$H_{[\alpha]}$), 2.86 (m, 1H, 2′-$H_{[\alpha]}$), 2.66 (m, 1H, 2′-$H_{[\beta]}$), 2.53 (m, 2H, 2″-$H_{[\alpha]}$ and 2′-$H_{[\beta]}$), 2.27 (s, 3H, $ArCH_3$), 2.24 (s, 6H, $ArCH_3$), 2.22 (s, 3H, $ArCH_3$); δ_C[$(CD_3)_2SO$] 166.34 (C = O), 166.29 (C = O), 166.1 (6-$C_{[\beta]}$), 165.5 (6-$C_{[\alpha]}$), 158.1 (4-$C_{[\alpha]}$ and 4-$C_{[\beta]}$), 147.2 (2-$C_{[\alpha]}$), 146.8 (2-$C_{[\beta]}$), 119.8 (5-$C_{[\alpha]}$), 119.7 (5-$C_{[\beta]}$), 89.8 (1′-$C_{[\alpha]}$), 89.4 (1′-$C_{[\beta]}$), 85.6 (4′-$C_{[\alpha]}$), 83.9 (4′-$C_{[\beta]}$), 75.8 (3′-$C_{[\beta]}$), 75.5 (3′-$C_{[\alpha]}$), 64.8 (5′-$C_{[\alpha]}$), 65.1 (5′-$C_{[\beta]}$), 39.1 (2′-$C_{[\alpha]}$), 38.8 (2′-$C_{[\beta]}$), 22.1 (CH_3); m/z (FAB > 0, G-T) 1017 $[2M + H]^+$, 509 $[M + H]^+$, 353 $[S]^+$, 157 $[BH_2]^+$, 119 $[CH_3PhCO]^+$; m/z (FAB < 0, G-T) 1015 [2M-H]$^-$, 507 [M-H]$^-$, 389 [M- CH_3PhCO]$^-$, 155 [B]$^-$. Anal. Calcd. for $C_{25}H_{24}N_4O_8 \cdot 0.3$ MeOH: C, 58.65; H, 4.90; N, 10.81. Found: C, 58.58; H, 4.84; N, 10.93.

5-Nitro-1-(2-deoxy-α-D-*erythro*-pentofuranosyl)cytosine (4α) and 5-Nitro-1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)cytosine (4β). 5-nitro-1-(2-Deoxy-3,5-di-*O*-*p*-toluoyl-α,β-D-*erythro*-pentofuranosyl)cytosine (**12**) (5.2 g, 10.2 mmol) in NaOMe/MeOH (102 mL, 0.2 N) was stirred at room temperature for 1h30 then MeOH (70 mL) was added. The resulting solution was neutralised with DOWEX (50×2, H^+-form), and the resin was filtered and washed several times with hot MeOH. The crude material was evaporated and the residue was diluted with water, washed with dichloromethane (3×100 mL) and evaporated to dryness. The residue was subjected to a RP 18 column chromatography and eluted with a stepwise gradient of acetonitrile (0-1%) in methanol to afford 1.99 g (72% yield) of 5-nitro-1-(2-deoxy-α,β-D-*erythro*-pentofuranosyl)cytosine as a mixture of its anomers (α/β, ratio 1:1). Crystallization with MeOH and a minimum amount of water at −10°C gave **4α** (1.1 g, 40% yield)) as white needles and **4β** (600 mg, 22% yield) as white flakes. R_f (system: Et_2O/MeOH 90:10 v/v) 0.13 (α), 0.18 (β); R_f (system: CH_3CN/MeOH 99:1 v/v) 0.16 (α), 0.24 (β).

(**4α**): m.p. 255°C (darkening); $[\alpha]_D^{20}$ +57.3 (*c* 1.1, Me_2SO); δ_H[$(CD_3)_2SO$] 9.11 (s, 1H, 6-H), 8.55 (s, 1H, 4-NH_2), 8.08 (s, 1H, 4-NH_2), 6.05 (dd, 1H, $J_{1'\text{-}2'} = 6.9$, 1′-H), 5.31 (d, 1H, $J_{3'\text{-}3'OH} = 2.5$, 3′-OH), 4.97 (t, 1H, $J_{5'\text{-}5'OH} = 5.7$, 5′-OH), 4.38 (dd, 1H, $J_{4'\text{-}5/5''} = 6.58$, $J_{4'\text{-}3'} = 11.5$, 4′-H), 4.26 (m, 1H, 3′-H), 3.44 (m, 2H, 5′-H et 5″-H), 2.59 (m, 1H, 2″-H), 2.54 (m, 1H, 2″-H); δ_C[$(CD_3)_2SO$] 158.7 (4-C), 152.7 (2-C), 147.9 (6-C), 119.3 (5-C), 91.9 (4′-C), 89.7 (1′-C), 73.1 (3′-C), 62.5 (5′-C), 41.1 (2′-C). Anal. Calcd. for $C_9H_{12}N_4O_6 \cdot CH_3OH$: C, 39.48; H, 5.30; N, 18.41: Found: C, 39.14; H, 5.07; N, 18.14.

(**4β**): m.p. 188°C (literature: 190°C);[4] $[\alpha]_D^{20}$ −60 (*c* 1.0, Me_2SO); $\lambda_{max}(H_2O)$/nm 322 (ε 9500); λ_{min} 278 (ε 3200); m/z (FAB > 0, G-T) 273 $[M+H]^+$, 157 $[BH_2]^+$, 117 $[S]^+$; m/z (FAB < 0, G-T) 271 $[M\text{-}H]^-$; $\delta_H[(CD_3)_2SO]$ 9.49 (s, 1H, 6-H), 8.49 (s, 1H, 4-NH_2), 8.03 (s, 1H, 4-NH_2), 6.01 (t, 1H, $J_{1'\text{-}2'/2'} = 5.8$, 1′-H), 5.31 (d, 1H, $J = 4.4$, 3′-OH), 5.22 (t, 1H, $J = 4.5$, 5′-OH), 4.23 (m, 1H, 3′-H), 3.90 (m, 1H, 4′-H), 3.69 (m, 1H, 5′-H), 3.59 (m, 1H, 5″-H), 2.34 (m, 1H, 2′-H); $\delta_C[(CD_3)_2SO]$ 58.2 (4-C), 152.6 (2-C), 147.8 (6-C), 119.9 (5-C), 88.9 (4′-C), 88.0 (1′-C), 70.1 (3′-C), 61.1 (5′-C), 42.1 (2′-C). Anal. Calcd. for $C_9H_{12}N_4O_6$: C, 39.71; H, 4.44; N, 20.58. Found: C, 39.45; H, 4.38; N, 20.45.

5-Nitro-1-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α,β-D-ribofuranosyl]uracil (14). A mixture of 5-nitrouracil (3.0 g, 19.1 mmol), hexamethyldisilazane (134 mL) and a catalytic amount of ammonium sulfate was refluxed under argon overnight. The solution was distilled under vacuum. The resultant oil was cooled at −15°C and a solution of **13**[13] (3.49 g, 12.7 mmol) in dry CH_3CN (130 mL) and trimethysilyltrifluromethane sulfonate (2.7 mL, 13.97 mmol) were added successively. The reaction mixture was immediately diluted with CH_2Cl_2 (130 mL) and neutralized with cooled 5% $NaHCO_3$. The organic layers were separated, washed with water (200 mL × 2), dried (Na_2SO_4) and evaporated in vacuo to dryness. The residue was purified on silica gel using a stepwise gradient of ethyl acetate (0-10%) in diethyl ether to afford a mixture of 5-nitro-1-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α,β-D-ribofuranosyl]uracil (**14**) (5.32 g; 81% yield). A crystallization in diethylether with a minimum amount of MeOH at −18°C afforded **14** (α/β, ratio 1:1) as white crystals: R_f (system: Et_2O/AcOEt 90:10 v/v) 0.65 (α); 0.52 (β); $\delta_H[(CD_3)_2SO]$ (α-anomer): 11.96 (s, 1H, 3-NH), 8.68 (s, 1H, 6-H), 5.84 (dd, 1H, $J_{1'\text{-}2'} = 6.3$, $J_{1'\text{-}2''} = 3.2$, 1′-H), 4.46 (m, 1H, 4′-H), 3.62 (dd, 1H, $J_{5'\text{-}4'} = 3.8$, $J_{5'\text{-}5''} = 11.1$, 5′-H), 3.54 (dd, 1H, $J_{5'\text{-}4'} = 4.6$, $J_{5'\text{-}5''} = 11.2$, 5″-H), 2.34 (m, 1H, 3′-H), 2.08 (m, 1H, 3″-H), 1.94 (m, 1H, 2′-H), 1.72 (m, 1H, 2″-H), 0.81 (s, 3H, $(CH_3)_3C$), 0.80 (s, 3H, $(CH_3)_3C$), 0.79 (s, 3H, $(CH_3)_3C$), 0.00 (s, 6H, $(CH_3)Si$); (β-anomer): 11.97 (s, 1H, 3-NH), 8.96 (s, 1H, 6-H), 5.85 (dd, 1H, $J_{1'\text{-}2'} = 2.8$, $J_{1'\text{-}2''} = 6.0$, 1′-H), 4.14 (m, 1H, 4′-H), 3.91 (dd, 1H, $J_{5'\text{-}4'} = 3.9$, $J_{5'\text{-}5''} = 11.2$, 5′-H), 3.69 (dd, 1H, $J_{5'\text{-}4'} = 3.8$, $J_{5'\text{-}5''} = 11.1$, 5″-H), 2.32 (m, 1H, 2′-H), 2.12 (m, 1H, 2″-H), 1.82 (m, 1H, 3′-H), 1.72 (m, 1H, 3″-H), 0.82 (s, 3H, $(CH_3)_3C$), 0.81 (s, 3H, $(CH_3)_3C$), 0.80 (s, 3H, $(CH_3)_3C$), −0.02 (s, 6H, (CH_3) Si); $\delta_C[(CD_3)_2SO]$ (α-anomer): 156.1 (4-C), 149.8 (2-C), 145.8 (6-C), 126.3 (5-C), 90.5 (1′-C), 83.4 (4′-C), 66.1 (5′-C), 33.1 (2′-C), 27.02 ($(\underline{C}H_3)_3C$), 26.0 (3′-C), 19.2 ($(CH_3)_3\underline{C}$), −4.14 (CH_3Si); (β-anomer): 155.7 (4-C), 149.5 (2-C), 145.5 (6-C), 125.7 (5-C), 88.9 (1′-C), 83.0 (4′-C), 64.7 (5′-C), 33.2 (2′-C), 26.68 ($(\underline{C}H_3)_3C$), 24.8 (3′-C), 19.1 ($(CH_3)_3\underline{C}$), −4.5 (CH_3Si), −4.64 (CH_3Si); m/z (FAB > 0, G-T) 743 $[2M+H]^+$; 372 $[M+H]^+$; 216 $[S]^+$; 158 $[BH_2]^+$; m/z (FAB < 0, G-T) 741 $[2M\text{-}H]^-$; 370 $[M\text{-}H]^-$; 156 $[B]^-$. Anal. Calcd. for $C_{15}H_{25}N_3O_6Si \cdot 1/2$ MeOH: C, 48.05; H, 7.02; N, 10.84. Found: C, 47.75 ; H, 6.77; N, 11.12.

5-Nitro-1-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α,β-D-ribofuranosyl]cytosine (15). A mixture of 5-nitrocytosine (**10**) (2.6 g, 16.4 mmol), hexamethyldisilazane (147 mL) and a catalytic amount of ammonium sulfate was refluxed overnight. After distillation under vacuum, the resultant oil was cooled at −15°C and a solution of **13**

(3.0 g, 10.9 mmol) in dry CH_3CN (110 mL) and trimethylsilyltrifluoromethane sulfonate (2.3 mL, 12.0 mmol) were successively added. The reaction mixture was immediately diluted with dichloromethane (100 mL) and neutralised with a cooled solution of 5% $NaHCO_3$. The organic layers were separated, washed with water (200 mL × 2), dried (Na_2SO_4) and evaporated under reduced pressure. The crude was purified on silica gel using a stepwise gradient of isopropanol (0-10%) in Et_2O to afford 5-nitro-1-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α,β-D-ribofuranosyl]-cytosine (**15**) (3.47 g, 86% yield) (α/β, ratio 1:1). R_f (system: Et_2O/isopropanol 90:10 v/v) 0.64 (α); 0.54 (β). Crystallization in CH_3CN at −10°C gave pure α-anomer (1.16 g, 29% yield). The resulting filtrate (2.2 g) provided a mixture enriched with β-anomer (α/β, ratio 0.2:1); λ_{max} (95% EtOH)/nm 319 (ε 8800), λ_{min} 277 (ε 1700); $\delta_H[(CD_3)_2SO]$ (α-anomer): 8.71 (s, 1H, 6-H), 8.42 (sl, 1H, 4-NH_2), 7.95 (sl, 1H, 4-NH_2), 5.81 (dd, 1H, $J_{1'-2'} = 2.66$, $J_{1'-2''} = 6.1$, 1′-H), 4.46 (m, 1H, 4′-H), 3.63 (dd, 1H, $J_{5'-4'} = 3.9$, $J_{5'-5''} = 11.1$, 5′-H), 3.55 (dd, 1H, $J_{5'-4'} = 4.6$, 5″-H), 2.36 (m, 1H, 3′-H), 1.98–1.88 (m, 2H, 2′-H and 3″-H), 1.71 (m, 1H, 2″-H), 0.82 (s, 9H, $(CH_3)_3C$), 0.00 (s, 6H, (CH_3) Si); (β-anomer): 8.96 (s, 1H, 6-H), 8.42 (sl, 1H, 4-NH_2), 7.95 (sl, 1H, 4-NH_2), 5.75 (t, 1H, $J_{1'-2'/2''} = 3.8$, 1′-H), 4.17 (m, 1H, 4′-H), 3.89 (dd, 1H, $J_{5'-4'} = 2.6$, $J_{5'-5''} = 11.7$, 5′-H), 3.68 (dd, 1H, 5″-H), 2.38 (m, 1H, 2′-H), 1.83 (m, 1H, 2″-H), 1.67 (m, 2H, 3′-H and 3″-H), 0.83 (s, 9H, $(CH_3)_3C$), 0.00 (s, 6H, (CH_3) Si); $\delta_C[(CD_3)_2SO]$ (α-anomer): 158.3 (4-C), 152.5 (2-C), 146.7 (6-C), 119.6 (5-C), 90.3 (1′-C), 82.9 (4′-C), 65.8 (5′-C), 33.1 (3′-C), 26.6 ($(\underline{C}H_3)_3C$), 25.6 (2′-C), 18.8 ($(CH_3)_3\underline{C}$), −4.5 (CH_3Si); (β-anomer): 158.2 (4-C), 152.6 (2-C), 146.9 (6-C), 119.4 (5-C), 89.3 (1′-C), 83.7 (4′-C), 64.9 (5′-C), 33.6 (3′-C), 26.7 ($(\underline{C}H_3)_3C$), 24.9 (2′-C), 19.0 ($(CH_3)_3\underline{C}$), −4.6 (CH_3Si), −4.7 (CH_3Si); m/z (FAB > 0, NBA) 371 $[M+H]^+$, 215 $[S]^+$, 157 $[BH_2]^+$; m/z (FAB < 0, G-T) 369 $[M\text{-}H]^-$, 155 $[B]^-$. Anal. Calcd. for $C_{15}H_{26}N_4O_5Si$: C, 48.63; H, 7.07; N, 15.12. Found: C, 48.50; H, 6.93; N, 14.74.

5-Nitro-1-(2,3-dideoxy-β-D-ribofuranosyl) Uracil (6β). To a solution of 5-nitro-1-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α,β-D-ribofuranosyl]uracil (**16**) (931 mg, 2.51 mmol) in MeOH (15 mL) and H_2O (2.3 mL) was added *p*-toluenesulfonic acid monohydrate (506 mg, 2.66 mmol). After stirring at room temperature for 20 min, MeOH (15 mL) was added and the solution was neutralised with DOWEX (1 × 2, OH^- form). The resin was filtered off and washed several times with hot methanol. The filtrate was concentrated and purified on a silica gel column using a stepwise gradient of MeOH (0–6%) in CH_2Cl_2 to afford of 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl) uracil (**6**) (522 mg, 81%) as a mixture of anomers (α/β, ratio 1:1). Crystallization in CH_3CN at −18°C afforded β-anomer (**6β**) (85 mg, 13.2% yield) as white needles. M.p. 230°C; R_f (system: Et_2O/AcOEt 90:10 v/v) 0.41 (α); 0.35 (β); $[\alpha]_D^{20}$ −71.3 (*c* 1.01 in Me_2SO); λ_{max} (95% EtOH)/nm λ_{max} 302 (ε 10900), λ_{min} 258 (ε 2500); $\delta_H[(CD_3)_2SO]$ 11.94 (s, 1H, 3-NH), 9.64 (s, 1H, 6-H), 5.85 (dd, 1H, $J_{1'-2'} = 1.2$, $J_{1'-2''} = 6.3$, 1′-H), 5.26 (t, 1H, $J = 4.6$, 5′-OH), 4.11 (m, 1H, 4′-H), 3.78 (m, 1H, 5′-H), 3.53 (m, 1H, 5″-H), 2.32 (m, 1H, 2′-H), 2.12 (m, 1H, 2″-H), 1.75–1.84 (m, 2H, 3′-H and 3″-H); $\delta_C[(CD_3)_2SO]$ 155.8 (4-C), 149.7 (2-C), 146.5 (6-C), 125.8 (5-C), 88.4 (1′-C), 84.3 (4′-C), 61.4 (5′-C), 33.7 (2′-C), 24.0 (3′-C); m/z (FAB > 0, G-T) 515 $[2M+H]^+$, 258 $[M+H]^+$, 158 $[BH_2]^+$, 101 $[S]^+$; m/z (FAB < 0, G-T)

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513 $[2M\text{-}H]^-$; 256 $[M\text{-}H]^-$; 156 $[B]^-$. Anal. Calcd. for $C_9H_{11}N_3O_6$: C, 42.03; H, 4.31; N, 16.34. Found: C, 42.07; H, 4.41; N, 16.22.

5-Nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl)cytosine (8). To a solution of 5-nitro-1-[5-*O*-(*tert*-butyldimethylsilyl)-2,3-dideoxy-α,β-D-ribofuranosyl] cytosine (**15**) (1.2 g, 3.24 mmol) (α/β 0.2:1) in dry THF (32 mL) was added triethylamine tris-(hydrogen fluoride) (3.2 mL, 19.44 mmol). The solution was stirred at room temperature for 6 h. Solvent was removed and the residue was purified on a silica gel column using a stepwise gradient of MeOH (0-8%) in CH_2Cl_2 to afford 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl)cytosine (**8**) (747 mg, 90% yield) as a mixture of anomers (α/β, ratio 0.2:1). R_f (system: Et_2O/Isopropanol 80:20 v/v) 0.21 (α); 0.33 (β); λ_{max} (95% EtOH)/nm 322 (ε 7400), λ_{min} 280 (ε 2100); $\delta_H[(CD_3)_2SO]$ (α-anomer): 8.81 (s, 1H, 6-H), 8.38 (sl, 1H, 4-NH_2), 7.94 (sl, 1H, 4-NH_2), 5.82 (m, 1H, 1′-H), 4.91 (t, 1H, $J = 5.8$, 5′-OH), 4.12 (m, 1H, 4′-H), 3.61 (m, 1H, 5′-H), 3.42 (m, 1H, 5″-H), 2.33 (m, 1H, 3′-H), 1.98–1.88 (m, 2H, 2′-H et 3″-H), 1.70 (m, 1H, 2″-H); (β-anomer): 9.63 (s, 1H, 6-H), 8.38 (sl, 1H, 4-NH_2), 7.94 (sl, 1H, 4-NH_2), 5.80 (m, 1H, 1′-H), 5.02 (t, 1H, $J = 4.5$, 5′-OH), 3.89 (m, 1H, 4′-H), 3.76 (m, 1H, 5′-H), 3.52 (m, 1H, 5″-H), 2.82 (m, 2H, 2′-H and 2″-H), 2.02 (m, 1H, 3′-H), 1.74 (m. 1H, 3″-H); $\delta_C[(CD_3)_2SO]$ (α-anomer): 158.3 (4-C), 152.7 (2-C), 147.9 (6-C), 119.6 (5-C), 88.2 (1′-C), 82.9 (4′-C), 61.6 (5′-C), 33.9 (3′-C), 24.4 (2′-C); (β-anomer): 158.3 (4-C), 152.7 (2-C), 146.9 (6-C), 119.6 (5-C), 88.7 (1′-C), 84.2 (4′-C), 61.6 (5′-C), 34.9 (3′-C), 23.9 (C-2′); m/z (FAB > 0, NBA) 513 $[2M + H]^+$, 257 $[M + H]^+$, 201 $[S]^+$, 157 $[BH_2]^+$; m/z (FAB < 0, G-T) 511 $[2M\text{-}H]^-$, 255 $[M\text{-}H]^-$, 155 $[B]^-$.

5-Amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)cytosine (5β). 5-nitro-1-(2-Deoxy-β-D-*erythro*-pentofuranosyl)cytosine (**4β**) (300 mg, 1.10 mmol) was hydrogenated following the general procedure to afford of 5-amino-1-(2-deoxy-β-D-*erythro*-pentofuranosyl)cytosine (**5β**) (247 mg, 95% yield) as a yellow powder. m.p. 165°C (darkening), 175°C (melting); $[\alpha]_D^{20}$ −21.9 (*c* 1.05, Me_2SO). R_f (system: CH_3CN/H_2O 90:10 v/v) 0.10; λ_{max} (95% EtOH)/nm λ_{max} 303 (ε 8400), λ_{min} 260 (ε 4100); $\delta_H[(CD_3)_2SO]$ 7.19 (sl, 1H, 4-NH_2), 7.13 (s, 1H, 6-H), 6.53 (sl, 1H, 4-NH_2), 6.10 (dd, 1H, $J_{1'\text{-}2'} = 6.0$, $J_{1'\text{-}2''} = 7.8$, 1′-H), 5.08 (d, 1H, $J = 4.1$, 3′-OH), 4.80 (t, 1H, $J = 5.3$, 5′-OH), 4.07 (m, 1H, 3′-H), 3.80 (sl, 2H, 5-NH_2), 3.62 (m, 1H, 4′-H), 3.42 (m, 2H, 5′-H and 5″-H), 1.92 (m, 1H, 2′-H), 1.78 (m, 1H, 2′-H); $\delta_C[(CD_3)_2SO]$ 61.6 (4-C), 154.7 (2-C), 122.7 (6-C), 116.9 (5-C), 87.7 (4′-C), 85.2 (1′-C), 71.6 (3′-C), 62.7 (5′-C), 40.5 (2′-C); m/z (FAB > 0, NBA) 485 $[2M + H]^+$, 243 $[M + H]^+$, 127 $[BH_2]^+$; m/z (FAB < 0, NBA) 241 $[M\text{-}H]^-$. Anal. Calcd. for $C_9H_{14}N_4O_4 \cdot 1/2$ H_2O: C, 43.03; H, 6.02; N, 22.30. Found: C, 43.37; H, 5.85; N, 21.95.

5-Amino-1-(2-deoxy-α-D-*erythro*-pentofuranosyl)cytosine (5α). 5-nitro-1-(2-Deoxy-*a*-D-*erythro*-pentofuranosyl)cytosine (**4α**) (500 mg, 1.84 mmol) was hydrogenated following the general procedure to afford 5-amino-1-(2-deoxy-*a*-D-*erythro*-pentofuranosyl)cytosine (**5α**) (434 mg, 97% yield) as a white powder. m.p. 132°C; $[\alpha]_D^{20} + 16.2$ (*c* 1.05, Me_2SO). R_f (system: CH_3CN/H_2O 90:10 v/v) 0.10; λ_{max} (95% EtOH)/nm 303 (ε 8400), λ_{min} 260 (ε 4100); $\delta_H[(CD_3)_2SO]$ 7.24 (s, 1H, 6-H), 7.09 (sl, 1H, 4-NH_2),6.03 (sl, 1H, 4-NH_2), 6.07 (dd, 1H, $J_{1'\text{-}2'} = 4.0$, $J_{1'\text{-}2''} = 7.3$, 1′-H),

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5.27 (sl, 1H, 3′-OH), 4.84 (sl, 1H, 5′-OH), 4.18 (m, 1H, 3′-H), 4.05 (m, 1H, 4′-H), 3.93 (sl, 2H, 5-NH_2), 3.43 (m, 2H, 5′-H et 5″-H), 2.50 (m, 1H, 2′-H), 1.76 (m, 1H, 2″-H); δ_C[$(CD_3)_2SO$] 161.6 (4-C), 154.7 (2-C), 123.8 (6-C), 116.4 (5-C), 89.0 (4′-C), 86.5 (1′-C), 71.3 (3′-C), 62.6 (5′-C), 41.4 (2′-C); m/z (FAB > 0, NBA) 485 $[2M+H]^+$, 243 $[M+H]^+$, 127 $[BH_2]^+$; m/z (FAB < 0, G-T) 483 [2M-H]$^-$, 241 [M-H]$^-$, 125 [B]$^-$. Anal. Calcd. for $C_9H_{14}N_4O_4$ 6.7 H_2O: C, 44.63; H, 5.83; N, 23.13. Found: C, 44.03; H, 5.88; N, 25.49.

5-Amino-1-(2,3-dideoxy-α,β-D-ribofuranosyl)uracil (7). 5-nitro-1-(2,3-dideoxy-α,β-D-ribofuranosyl)uracil (**6**) (α/β 1.5:1) (430 mg, 1.67 mmol) was hydrogenated following the general procedure. The residue was purified on a silica gel column using a stepwise gradient of MeOH (0-6%) in CH_2Cl_2 to afford of 5-amino-1-(2,3-dideoxy-α,β-D-ribofuranosyl) uridine (**7**) (322 mg, 85% yield) (α/β, ratio 1.5:1) as a yellow powder. R_f (system: CH_2Cl_2/MeOH 80:20 v/v) 0.49 (α); 0.34 (β); λ_{max} (H_2O)/nm 298 (ε 7300), λ_{min} 261 (ε 2500); δ_H[$(CD_3)_2SO$] 11.21 (sl, 2H, 3-$NH_{[\alpha]}$ and 3-$NH_{[\beta]}$), 6.96 (s, 1H, 6-$H_{[\beta]}$), 6.83 (s, 1H, 6-$H_{[\alpha]}$), 6.06 (dd, 1H, $J_{1'\text{-}2'}$ = 4.7, $J_{1'\text{-}2''}$ = 6.5, 1′-$H_{[\alpha]}$), 6.02 (dd, 1H, $J_{1'\text{-}2'}$ = 4.3, $J_{1'\text{-}2''}$ = 6.9, 1′-$H_{[\beta]}$), 4.82 (t, 1H, J = 5.6, 5′-$OH_{[\beta]}$), 4.74 (t, 1H, J = 5.6, 5′-$OH_{[\alpha]}$), 4.30 (m, 1H, 4′-$H_{[\alpha]}$), 4.08 (sl, 2H, 5-$NH_{2[\alpha]}$ and 5-$NH_{2[\beta]}$), 3.97 (m, 1H, 4′- $H_{[\beta]}$), 3.56 (m, 2H, 5′-$H_{[\beta]}$ and 5″-$H_{[\beta]}$), 3.40 (m, 2H, 5′-$H_{[\alpha]}$ and 5″-$H_{[\alpha]}$), 2.50 (m, 2H, 2′-$H_{[\alpha]}$ and 2″-$H_{[\alpha]}$), 2.23 (m, 2H, 2′-$H_{[\beta]}$ and 2″-$H_{[\beta]}$), 1.88 (m, 2H, 3′-$H_{[\alpha]}$ and 3″-$H_{[\alpha]}$), 1.80 (m, 2H, 3′-$H_{[\beta]}$ and 3″-$H_{[\beta]}$); δ_C[$(CD_3)_2SO$] 161.4 (4-$C_{[\alpha]}$ and 4-$C_{[\beta]}$), 149.6 (2-$C_{[\alpha]}$ and 2-$C_{[\beta]}$), 123.8 (6-$C_{[\alpha]}$ and 6-$C_{[\beta]}$), 115.7 (5-$C_{[\alpha]}$ and 5-$C_{[\beta]}$), 86.1 (1′-$C_{[\alpha]}$), 85.1 (1′-$C_{[\beta]}$), 82.1 (4′-$C_{[\alpha]}$), 81.5 (4′-$C_{[\beta]}$), 64.4 (5′-$C_{[\alpha]}$), 63.9 (5′-$C_{[\beta]}$), 31.8 (2′-$C_{[\alpha]}$), 31.5 (2′-$C_{[\beta]}$), 26.9 (3′-$C_{[\alpha]}$ and 3′-$C_{[\beta]}$); m/z (FAB > 0, G-T) 455 $[2M+H]^+$, 228 $[M+H]^+$, 128 $[BH_2]^+$, 101 $[S]^+$; m/z (FAB < 0, G-T) 453 [2M-H]$^-$, 226 [M-H]$^-$. HRMS calcd. for $C_9H_{13}N_3O_4$ 228.0984, found 228.1008.

5-Amino-1-(2,3-dideoxy-β-D-ribofuranosyl)cytosine (9β). 5-nitro-1-(2,3-Dideoxy-α,β-D-ribofuranosyl)cytosine (**8**) (α/β, ratio 0.2:1) (300 mg, 1.17 mmol) in MeOH (30 mL) was hydrogenated following the general procedure to afford 5-amino-1-(2,3-dideoxy-β-D-ribofuranosyl)cytosine (**9β**) (125 mg, 58% yield) as a yellow powder. R_f (system: CH_2Cl_2/MeOH 80:20 v/v) 0.12 (β). λ_{max} (95% EtOH)/nm 305 (ε 6500); λ_{min} 267 (ε 3400); δ_H[$(CD_3)_2SO$] 7.21 (s, 1H, 6-H), 6.02 (dd, 1H, $J_{1'\text{-}2'}$ = 3.8, $J_{1'\text{-}2''}$ = 6.9, 1′-H), 4.95 (t, 1H, J = 5.4, 5′-OH), 4.05–4.00 (m, 3H, 4′-H and 5-NH_2), 3.65 (m, 2H, 5′-H and 5″-H), 2.41-2.23 (m, 2H, 2′-H and 2″-H), 1.98 (m, 1H, 3′-H), 1.82 (m, 1H, 3″-H); δ_C[$(CD_3)_2SO$] 161.5 (4-C), 154.7 (2-C), 122.9 (6-C), 116.6 (5-C), 86.1 (1′-C), 81.6 (4′-C), 63.9 (5′-C), 32.4 (2′-C), 26.8 (3′-C); m/z (FAB > 0, G-T) 453 $[2M+H]^+$, 227 $[M+H]^+$, 127 $[BH_2]^+$, 101 $[S]^+$; m/z (FAB < 0, G-T) 225 [M-H]$^-$, 125 [B]$^-$. HRMS calcd. for $C_9H_{14}N_4O_3$ 226.2326, found 226.2330.

BIOLOGICAL METHODS

The anti-HIV and anti-HBV assays on cell culture were performed by following previously established procedures.[18]

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