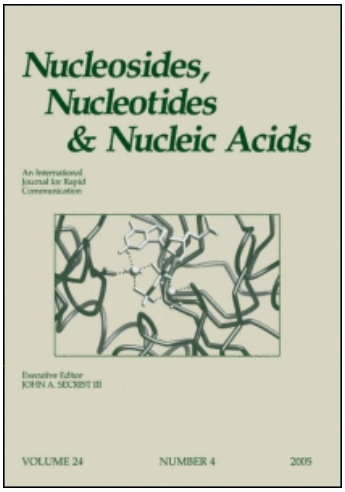

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Véronique Faivre-Buet[a]; Annie Grouiller[a]; Gérard Descotes[a]
[a] Laboratoire de Chimie Organique II Bât 308, Université Lyon I, Villeurbanne, (France)

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SYNTHESIS OF THYMINE NUCLEOSIDES DERIVED FROM 1-DEOXY-D-PSICOFURANOSE.

Véronique Faivre-Buet, Annie Grouiller * and Gérard Descotes
Université Lyon I, Laboratoire de Chimie Organique II Bât 308, URA CNRS 463
43, Boulevard du 11 Novembre 1918 - 69622 Villeurbanne (France)

Abstract. The use of D-(+)-ribonic γ-lactone **1a,b** as a chiral synthon leads to an efficient synthesis of the ketose 1-deoxy-D-psicofuranose **2a,b**. Condensation of the corresponding acetyl derivative **3a,b** with silylated thymine, followed by deprotection of **4a,b**, affords an anomeric mixture of ketosyl nucleoside **6** (predominately the β-anomer) in an improved overall yield of 49 %.

INTRODUCTION

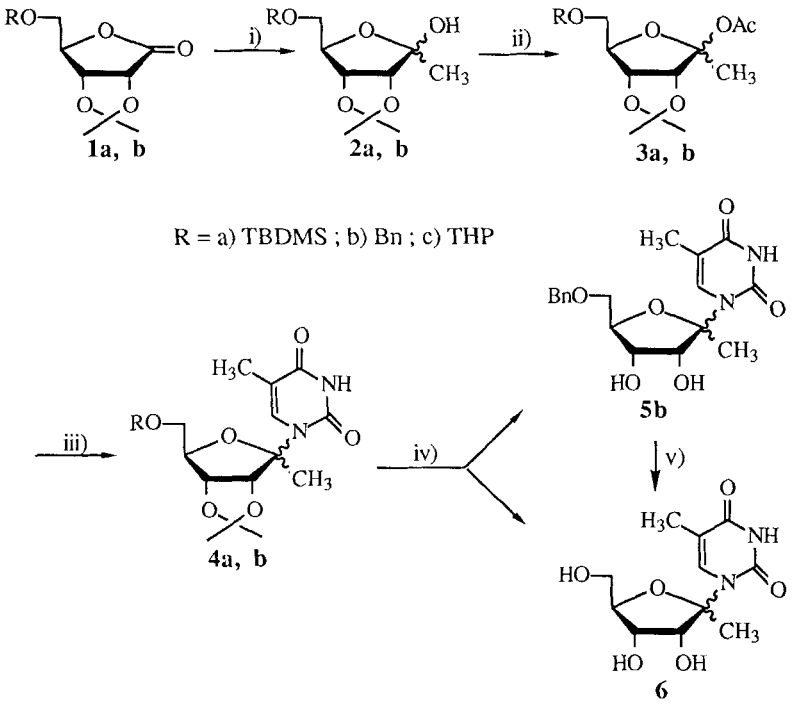
Concerning investigations on the potential anti-HIV activity of pyrimidine nucleosides derived from ketosugars, we have been interested in the preparation of 1(1-deoxy-β-D-psicofuranosyl)thymine **6** as the starting nucleoside for the synthesis of the corresponding analogues [1] of AZT and 2',3'-dideoxy-5-methyluridine.

Nucleoside **6** had been previously obtained by J. Farkàs et al [2] through the condensation of peracylated 1-bromo-1-deoxy-D-psicofuranosyl bromide with silylated thymine in the presence of mercuric acetate followed by reduction of the bromomethyl group and the hydroxyl deblocking, in an 11 % overall yield. In the present paper, we wish to report an improved synthesis of **6** from D-(+)-ribonic γ-lactone, a convenient chiral source for many biologically important molecules.

RESULTS AND DISCUSSION

The nucleophilic addition of equimolar methyllithium at -78°C to 2,3-*O*-isopropylidene-D-ribonolactone either silylated on the 5-hydroxyl group **1a** [3,4] or benzylated **1b** [5] affords the corresponding protected 1-deoxy-D-psicofuranoses **2a** and

2b which are inseparable from the starting lactone. Consequently they are directly converted into their acetyl derivatives **3a** and **3b**. The silylated lactone **1a** gives only one anomer, but the benzylated lactone **1b** gives both anomers in a 1 : 5 ratio as shown by the ^1H NMR spectrum. These spectra are the first for this class of derivatives to be reported fully assigned, even though such compounds were hitherto known : **3a** had been previously obtained by C.S. Wilcox et al [3] *via* the reaction of **1a** with a titanium carbene complex. These authors speculated that **3a** was produced solely as the β-isomer.



Key : i) MeLi / THF / -78°C; ii) Ac_2O/pyridine / DMAP; iii) $(Me_3Si)_2$ Thy / $EtAlCl_2$ / MeCN; iv) AG 50W-X4 resin / H_2O-MeOH 1: 2 / 50°C; v) $HCOONH_4$ /10% Pd-C / Me_2CO

The 5-tetrahydropyranyl derivative **2c** was also prepared as a α, β mixture through the nucleophilic addition of the carbanion generated from 2-lithio-1,3-dithiane to **1c**, followed by desulfurization with hydrogen-saturated Raney nickel [6]. Therefore, the stereochemistry of **2** seems to be dependent either on the strategy applied to **1** or on the steric bulk of R.

The nucleosides **4a** and **4b** are synthesized by treating the acetates **3a** and **3b** with 5-methyl-2,4-bis(trimethylsiloxy)pyrimidine in the presence of $EtAlCl_2$ as coupling reagent which may favor the β-anomeric stereoselectivity [7]. They are, respectively,

formed as inseparable 1: 3 and 1 : 9 mixtures of α and β anomers in 90 and 86 % yields. The hydroxyl groups in 3',4',6' positions of nucleoside **4a** and in 3',4' of nucleoside **4b** are deblocked by treatment with an H^+ resin, leading in 86 % and 80 % yields, respectively, to **6** and its 6'-benzylated analog **5b**. Only in the case of **5b** are the isomers separable, and deprotection of the hydroxymethyl group of the major isomer (*β*-anomer) by catalytic transfer hydrogenation, using 10% palladium on carbon with ammonium formate as the hydrogen donor [8], gives quantitatively and exclusively **6***β*. Other debenzylation methods (hydrogenolysis with palladium catalyst or reaction with BCl_3) were unsuccessful. It is noteworthy that the deblocking of **4b** into **5b** with H^+ resin gives the same ratio of anomers as in the starting nucleoside, but the deprotection of **4a** into **6** is accompanied with an enrichment in the *β* anomer from 1 : 3 to 1 : 6; in acidic medium at 50 °C, we have observed that,whereas the *β* anomer of **6** is stable, the *α* anomer is submitted to a certain decomposition.

The anomeric configurational assignments for the acetates **3a,b** and the nucleosides **4a,b**, **5b** and **6** were made on the basis of their ^1H and ^{13}C NMR spectra, with ^{13}C-^1H shift-correlated 2D, selective decoupling and NOE experiments.

The introduction of a methyl group at C-1' cuts down the number of vicinal proton-proton coupling constants from three (in ribofuranosyl derivatives) to two in these compounds; therefore the "trans" rule [9] which uses the value of $J_{1,2}$ for ascertaining *α*- and *β*-configurations cannot be applied in this case. In compensation, concerning the anomeric acetates **3b**, H-3 of the major isomer, at the opposite of H-5, is more deshielded than that of the minor isomer. This can be due to a deshielding effect of the neighboring acetoxy group and is in favour of a *β* major configuration, in line with that earlier reported for the addition of lithiopyridine to **1a** [10,11]. However, it was not possible to confirm this result by applying Imbach's rule [12], since the difference in chemical shifts of two methyl signals of the isopropylidene group (Δδ value) was not significant.

On the other hand, this rule was used for the configurational assignments of the nucleosides. Δδ values are 0.2 and 0.02 ppm for the isopropylidene group of the major and minor anomers of **4a,b** which thus are, respectively, the *β*- and *α*-isomers. The H-6 and 5-methyl resonances of the thymine moiety in the major isomers of **4a,b**, **5b** and **6** are also down- and upfield, respectively, in comparison with those of the minor isomer, which was previously reported for other *β*-D-anomers of thymine nucleosides [13]. The resonance of C-3' in the most *β*-isomers is also downfield of C-3'of the *α*-isomers, which has been observed before in normal nucleosides [14].The final corroboration arises from a NOE experiment performed on the separated isomers through saturation of H-1

methyl resonance of **4b** : a 1 % NOE effect was found for H-3' of the major isomer, whereas a 3 % effect was obtained for the minor isomer which is in favour of an NOE contact expected for an α configuration. Thus, the major anomer in the synthesis of 1(1-deoxy-D-psicofuranosyl)thymine is definitely β with a conformation previously determined as a preferential North-type puckered one [15].

In summary, a convenient synthesis of 1(1-deoxy-D-psicofuranosyl)thymine **6** was performed in an overall yield of 49 % starting from the easily available protected ribonolactones **1a,b**.

EXPERIMENTAL SECTION

^{1}H NMR spectra were recorded on a BRUKER AM 300 spectrometer in $CDCl_3$ unless otherwise specified. Chemical shifts were reported in parts per million (ppm) downfield from the internal standard tetramethylsilane. ^{13}C NMR spectra were recorded on a BRUKER AM 300 spectrometer, with chemical shifts reported in ppm and proton decoupling unless otherwise specified. Fast atom bombardment and high-resolution mass spectra (HRMS) were collected on a ZAB V.G mass spectra spectrometer.

Optical rotations were measured in 1-dm cells of 1-mL capacity with a Perkin-Elmer Model 241 polarimeter in chloroform. Concentration is reported in grams per deciliter. Solvents were dried by distillation from the appropriate drying agent. Triethylamine, pyridine, acetonitrile, were distilled from calcium hydride. Diethyl ether was distilled from lithium aluminium hydride.

All reactions were conducted under dry nitrogen atmosphere. Analytical thin-layer chromatography (TLC) was performed on Kieselgel 60F-254 plates (E. Merck).

Flash chromatography were conducted with Kieselgel 60 silica gel (250-400 mesh, E. Merck).

2-*O*-Acetyl-6-*O*-*tert*-butyldimethylsilyl-1-deoxy-3,4-*O*-isopropylidene-D-psicofuranose (3a) and 2-*O*-acetyl-6-*O*-benzyl-1-deoxy-3,4-*O*-isopropylidene-D-psicofuranose (3b). To a solution of methyllithium 1M in ether (10.5 mL) at -78 °C was added dropwise a solution of lactone **1a** (3.2 g, 10.5 mmol). The reaction mixture was stirred for 0.5 h., then allowed to warm to 0 °C and treated with 10 % aqueous ammonium chloride solution (100 mL). After extraction with ether (3 x 130 mL), the combined ether layers were washed with ice-cold water (2 x 75 mL) and dried over anhydrous magnesium sulfate. Filtration and concentration under reduced pressure yielded an oil which was applied to a silica gel column with ether-hexane 1 : 2

(v/v) as eluent. The obtained mixture contained both the inseparable lactone **1a** and expected compound **2a**. To a solution of the above mixture (3g dried by azeotropic removal of moisture with pyridine) in anhydrous pyridine (25 mL) was added acetic anhydride (9 mL, 9.7 mmol) and 4-dimethylaminopyridine (57 mg, 5 mole %). The reaction mixture was stirred at room temperature for 48 h. Ice-cold water (80 mL) was added and the aqueous phase was extracted with chloroform (3 x 60 mL). The combined organic phases were washed with a cold, saturated sodium hydrogen carbonate solution and with ice-cold water (3 x 50 mL), then dried over anhydrous magnesium sulfate. Evaporation to dryness under diminished pressure yielded an oil which was then chromatographed on a silica gel column (ethyl acetate/hexane, 1 :9, as eluent) to afford 1.7 g (62 % from **1a**) of compound **3a** :

Rf 0.60 (silica gel, EtOAc/hexane, 1 : 2); $[\alpha]^{23}_{D}$ - 26.3° (c 1.3, $CHCl_3$); IR (neat) 1740, 1375, 1370 cm^{-1}; ^1H NMR (DMSO-d_6) : δ 4.74 (d, 1H, $J_{3,4}$ = 6.0 Hz, H-3), 4.63 (dd, 1H, $J_{4,5}$ = 1.2 Hz, H-4), 3.98 (m, 1H, $J_{5,6b}$ = 9.7 Hz, $J_{5,6a}$ = 5.3 Hz, H-5), 3.55 (dd, 1H, J_{6gem} = 10 Hz, H-6a), 3.52 (t, 1H, H-6b), 1.88 (s, 3H, $OCOCH_3$), 1.34 (s, 3H, H-1), 1.34 and 1.21 (2s, 2x3H, CH_3 isoprop.), 0.81 [s, 9H, $(CH_3)_3$-C-Si], 0.06 [s, 6H, $(CH_3)_2Si$]; ^{13}C NMR (DMSO-d_6) : δ 169.0 (C = O), 113.8 (C-2), 111.9 (C quat. isoprop.), 87.0 (C-5), 84.1 (C-3), 81.6 (C-4), 63.5 (C-6), 26.2 and 24.7 (CH_3 isoprop.), 25.7 [($\underline{C}H_3$)$_3$-C-Si], 22.1 (C-1), 19.8 ($\underline{C}H_3$-C=O), 17.9 (C-Si), -5.3 and -5.5 [$(CH_3)_2Si$]; MS m/z: 301 (56, M^+ - OAc), 243 [9, M^+ -OAc-OC$(CH_3)_2$], 187 [5, M^+ -OAc-OC$(CH_3)_2$-tBu].

Anal. Calcd for $C_{17}H_{32}O_6Si$: C, 56.64; H, 8.94. Found : C, 56.40; H, 9.01.

The procedure described above for the preparation of **3a** was used for the conversion of the lactone **1b** into **3b**. After purification by column chromatography on silica gel with 1 : 4 (v/v) ethyl acetate/hexane as eluent, α and β anomers of **3b** were obtained separately in a 1 : 5 ratio (78 % overall yield).

β-Anomer : Rf 0.67 (silica gel, EtOAc/hexane, 1 : 1); ^1H NMR (DMSO-d_6) : δ 7.32 (s, 5H, H arom.), 4.77 (d, 1H, $J_{3,4}$ = 5.0 Hz, H-3), 4.74 (dd, 1H, $J_{4,5}$ = 0.9 Hz, H-4), 4.56 (s, 2H, CH_2Ph), 4.23 (t, 1H, H-5), 3.48 (m, 2H, J_{6gem} = 11.2 Hz, H-6), 1.89 (s, 3H, CH_3-C=O), 1.61 (s, 3H, H-1), 1.40 and 1.27 (2s, 2x3H, CH_3 isoprop.).

α-Anomer : Rf 0.66 (silica gel, EtOAc/hexane, 1 : 1); ^1H NMR (DMSO-d_6) : δ 7.31 (m, 5H, H arom.), 4.98 (td, 1H, $J_{5,6}$ = 3.7 Hz, $J_{5,4}$ = 7.7 Hz, H-5), 4.70 (t, 1H, $J_{4,3}$ = 7.1 Hz, H-4), 4.55 (d, 1H, H-3), 4.53 (s, 2H, CH_2Ph), 3.68 (d, 2H, H-6), 2.21 (s, 3H, CH_3-C=O), 2.02 (s, 3H, H-1), 1.55 and 1.38 (2s, 2x3H, CH_3 isoprop.).

Anal. Calcd for $C_{18}H_{24}O_6$: C, 64.27; H, 7.19. Found : C, 64.31; H, 7.10.

1(6-*O*-*tert*-butyldimethylsilyl-1-deoxy-3,4-*O*-isopropylidene-D-psicofuranosyl)-thymine (4a) and 1(6-*O*-benzyl-1-deoxy-3,4-*O*-isopropylidene-D-psicofuranosyl)-thymine (4b). A solution of compound **3a** (1g, 2.8 mmol) in acetonitrile (25 mL) was added to 5-methyl-2,4-bis(trimethylsiloxy)pyrimidine (1.5 g, 5.6 mmol). A 1.8 M solution of ethylaluminum dichloride in toluene (1.5 mL) was added dropwise and the reaction mixture was stirred at room temperature. The progress of the reaction was followed by TLC. After 30 min, TLC showed complete disappearance of the starting material. The reaction mixture was then poured into an ice-cold mixture of saturated sodium hydrogen carbonate solution (120 mL) and CH_2Cl_2 (200 mL) and stirred for 10 min.

The resulting solution was filtered through a pad of celite and the separated organic layer was washed with a saturated sodium hydrogen carbonate solution (100 mL), brine (2 x 100 mL) and finally dried over anhydrous magnesium sulfate. Filtration and removal of volatile compounds under reduced pressure afforded an oil (1.3 g). The oil was passed through a silica gel column (EtOAc/hexane, 2 : 1, eluent) to yield **4a** as a colorless foam (1.1 g, 2.6 mmol, 93 %) with an α :β ratio of 1:3.

Rf 0.50 (silica gel, EtOAc/hexane, 2 : 1); ^{1}H NMR ($CDCl_3$) : δ (**β-anomer**) : 9.46 (s, 1H, NH), 7.65 (s, 1H, H-6), 5.12 (d, 1H, $J_{3',4'}$ = 6.1 Hz, H-3'), 4.63 (dd, 1H, $J_{4',5'}$ = 2 Hz, H-4'), 4.44 (m, 1H, H-5'), 3.72 (dd, 1H, $J_{6'gem}$ = 11.5 Hz, $J_{6'a,5'}$ = 4.1 Hz, H-6'a), 3.62 (dd, 1H, $J_{6'b,5'}$ = 2.6 Hz, H-6'b), 1.88 (s, 3H, CH_3-5), 1.58 and 1.34 (2s, 2x3H, CH_3 isoprop), 1.56 (s, 3H, H-1'), 0.80 [s, 9H, $(CH_3)_3$-C-Si], 0.01 and 0.02 [2s, 2x3H, $(CH_3)_2$-Si]. (**α-anomer**) : 9.48 (s, 1H, NH), 7.58 (s, 1H, H-6), 4.88 (d, 1H, $J_{3',4'}$ = 5.7Hz, H-3'), 4.80 (dd, 1H, $J_{4',5'}$ = 3.5 Hz, H-4'), 4.21 (dd, 1H, $J_{5',6'}$ = 3Hz, H-5'), 3.83 (dd, 1H, $J_{6'gem}$ = 11.4 Hz, $J_{5',6'a}$ = 2.9 Hz, H-6'a), 3.72 (m, 1H, H-6'b), 1.91 (s, 3H, CH_3-5), 1.32 and 1.30 (2s, 2x3H, CH_3 isoprop), 1.80 (s, 3H, H-1'), 0.90 [s, 9H, $(CH_3)_3$-C-Si], 0.09 and 0.08 [2s, 2x3H,$(CH_3)_2$Si]. ^{13}C NMR ($CDCl_3$) : δ (**β-anomer**) : 164.7 (C-4), 150.2 (C-2), 136.5 (C-6), 112.9 (C quat. isoprop.), 108.9 (C-5), 101.5 (C-2'), 86.2 (C-3'), 85.6 (C-5'), 81.7 (C-4'), 63.7 (C-6'), 25.9 and 24.6 (CH_3 isoprop.), 25.7 [($\underline{C}H_3)_3$-C-Si], 23.6 (C-1'), 18.2 (C-Si), 12.8 (CH_3-5), -5.6 and -5.7 [$(CH_3)_2$-Si]. (**α-anomer**) : 164.8 (C-4), 150.1 (C-2), 135.9 (C-6), 113.4 (C quat. isoprop.), 108.5 (C-5), 98.1 (C-2'), 85.5 (C-3'), 85.4 (C-5'), 80.5 (C-4'), 63.3 (C-6'), 26.7 and 25.4 (CH_3 isoprop.), 25.7 [($\underline{C}H_3)_3$-C-Si], 25.3 (C-1'), 18.3 (C-Si), 12.6 (CH_3-5), -5.3 and -5.5 [$(CH_3)_2$-Si]; MS m/z : 427 (18, MH^+), 301 [100,$(M\text{-Base})^+$], 243 [8, M^+ - Base - $OC(CH_3)_2$], 187 [5, M^+ - Base - $O(CH_3)_2$ - tBu], 127 (12, Base + 2 H^+).

Anal. Calcd for $C_{20}H_{34}N_2O_6Si$: C, 56.31; H, 8.03. Found : C, 56.30; H, 8.10.

The procedure described above was applied to the compound **3b** (1g, 3.6 mmol) to yield **4b** (1.2 g, 86 %) with an $\alpha:\beta$ ratio of 1:9. In this case, the eluent used for flash chromatography was ethyl acetate.

Rf 0.59 (silica gel, $CHCl_3$/MeOH, 85 : 15); ^1H NMR ($CDCl_3$) : δ (**β-anomer**) : 8.98 (s, 1H, NH), 7.27 (m, 5H, H arom.), 7.65 (d, 1H, $J_{H6,CH3-5}$ = 1.1 Hz, H-6), 5.20 (d, 1H, $J_{3',4'}$ = 6.0 Hz, H-3'), 4.68 (dd, 1H, $J_{4',5'}$ = 1.1 Hz, H-4'), 4.55 (m, 1H, H-5'), 4.45 and 4.34 (d, 2 x 1H, $J_{CH2\ gem}$ = 11.7 Hz, CH_2Ph), 3.58 (dd, 1H, $J_{6'gem}$ = 10.5, $J_{6'a,5'}$ = 4.7 Hz, H-6'a), 3.48 (dd, 1H, $J_{6'b,5'}$ = 2.9 Hz, H-6'b), 1.85 (d, 3H, $J_{H6,CH3-5}$ = 1.1 Hz, CH_3-5), 1.62 (s, 3H, H-1'), 1.58 and 1.37 (2s, 2 x 3H, CH_3 isoprop.); (**α-anomer**) : 9.16 (s, 1H, NH), 7.63 (d, 1H, $J_{H6,CH3-5}$ = 1.1 Hz, H-6), 4.92 (d, 1H, $J_{3',4'}$ = 5.7 Hz, H-3'), 4.79 (dd, 1H, $J_{4',5'}$ = 3.8 Hz, H-4'), 460 (m, 1H, H-5'), 3.68 (dd, 1H, $J_{6'gem}$ = 10.5 Hz, $J_{6'a,5'}$ = 3.5 Hz, H-6'a), 3.60 (dd, 1H, $J_{6'b,5'}$ = 4.6 Hz, H-6'b), 1.94 (d, 3H, CH_3-5), 1.83 (s, 3H, H-1'), 1.33 and 1.31 (2s, 2x3H, CH_3 isoprop.); ^{13}C NMR ($CDCl_3$) : δ (**β-anomer**) : 164.4 (C-4), 150.1 (C-2), 136.9 (C quat. arom.), 136.3 (C-6), 128.5, 128.0, 127.1 (5C arom.), 112.9 (C quat. isoprop.), 108.7 (C-5), 101.6 (C-2'), 85.9 (C-3'), 84.0 (C-5'), 81.8 (C-4'),73.7 (CH_2Ph), 70.3 (C-6'), 26.2 and 24.7 (CH_3 isoprop.), 23.4 (C-1'), 12.6 (CH_3-5); MS m/z : 403 (6, MH^+), 277 [72,(M-Base)$^+$], 127 (10, Base + $2H^+$), 91 (100, CH_2Ph); accurate mass positive ion FAB MS m/z 403.1854 (MH^+, calcd 403.1869).

Anal. Calcd for $C_{21}H_{26}N_2O_6$: C, 62.69; H, 6.47; N, 6.96. Found : C, 62.50; H, 6.53; N, 7.06.

1(6-*O*-benzyl-1-deoxy-D-psicofuranosyl)thymine (5b). To a solution of nucleoside **4b** (1.2 g, 3 mmol) in water (56 mL) and MeOH (112 mL) was added 14 g of Bio-Rad H^+ resin. This mixture was stirred 6 h. at 50 °C. The resin was filtered off and the product lyophilised. The crude residue thus obtained (1.0 g) was applied to a column of silica gel ($CHCl_3$/MeOH, 10 : 1, eluent) to give 790 mg of β–anomer and 96 mg of α–anomer (80 % overall yield).

β-anomer : Rf 0.52 (silica gel, $CHCl_3$/MeOH, 90 : 10); $[\alpha]^{22}_D$ -47° (c 0.9, $CHCl_3$); ^1H NMR (DMSO-d_6) : δ 11.7 (s, 1H, NH), 7.80 (s, 1H, H-6), 7.31 (m, 5H, H arom.), 5.53 (d, 1H, $J_{3',OH}$ = 4.7 Hz, OH-3'), 5.01 (d, 1H, $J_{4',OH}$ = 6.6 Hz, OH-4'), 4.57 and 4.53 (2d, 2H, J_{gem} = 12.1 Hz, CH_2Ph), 4.49 (t, 1H, $J_{3',OH3'} = J_{3',4'}$ = 4.7 Hz, H-3'), 4.05 (m, 1H, H-5'), 3.95 (m, 1H, H-4'), 3.78 (dd, 1H, $J_{6'gem}$ = 11.3 Hz, $J_{6'a,5'}$ = 1.7 Hz, H-6'a), 3.53 (dd, 1H, $J_{6'b,5'}$ = 4.0 Hz, H-6'b), 1.55 and 1.48 (2s, 2 x 3H, CH_3-5 and H-1'); ^{13}C NMR (DMSO-d_6) : δ 168.3 (C-4), 154.4 (C-2), 142.2 (C quat. arom.), 140.4 (C-6), 132.4, 131.6, 131.0 (5C arom.), 111.6 and 102.8 (C-5 and C-2'), 85.5, 76.5, 73.2 (C-3', C-4', C-5'), 73.4, 77.6 (CH_2Ph and C-6'), 25.4 (C-1'), 16.2 (CH_3-

5).MS m/z : 363 (9, MH^+), 237 [72, $(M\text{-base})^+$], 219 (7, M^+-base-H_2O), 127 (21, base + $2H^+$), 91 (100, CH_2Ph^+); accurate mass positive ion FAB MS m/z 362.1462 (MH^+, Calcd 362.1477)

α-anomer : Rf 0.38 (silica gel, $CHCl_3$/MeOH, 90 : 10); $[\alpha]^{25}_D$ +2° (c 0.85, $CHCl_3$); ^1H NMR (DMSO-d_6) : δ 11.12 (s, 1H, NH), 7.58 (d, 1H, $J_{H6,CH3\text{-}5}$ = 0.9 Hz, H-6), 7.36 (m, 5H, H arom.), 5.33 (d, 1H, $J_{3',OH3'}$ = 4.0 Hz, OH-3'), 5.06 (s, 1H, OH-4'), 4.58 (s, 2H, CH_2Ph), 4.13 (m, 2H, H-3' and H-4'), 3.99 (m, 1H, H-5'), 3.76 (dd, 1H, $J_{6'gem}$ = 11.3 Hz, $J_{6'a,5'}$ = 1.0 Hz, H-6'a), 3.56 (dd, 1H, $J_{6'b,5'}$ = 5.1 Hz, H-6'b), 1.77 (d, 3H, CH_3-5), 1.60 (s, 3H, H-1'); ^{13}C NMR (DMSO-d_6) : δ 168.5 (C-4), 154.1 (C-2), 142.5 (C quat. arom.), 132.3, 131.4, 131.3 (5C arom.), 140.4 (C-6), 101.2 (C-2'), 76.4 (CH_2Ph), 73.5 (C-6'), 84.5, 78.3, 73.9 (C-3', C-4', C-5'), 29.3 (C-1'), 16.4 (CH_3-5).

Anal. Calcd for $C_{18}H_{22}N_2O_6$: C, 59.67; H, 6.08; N, 7.73. Found : C, 59.37; H, 6.33; N, 7.30.

1(1-Deoxy-D-psicofuranosyl)thymine (6).

Method A : The procedure described above for the preparation of **5b** was applied to 250 mg (0.58 mmol) of nucleoside **4a** to give 138 mg (86 %) of an anomeric mixture of **6** with an α :β ratio of 1:6.

Method B : To a solution of the pure β-anomer of **5b** (52 mg, 0.14 mmol) in acetone (4.3 mL) were added ammonium formate (86 mg) and 10 % palladium on carbon (140 mg). After 1h. refluxing, a second portion of palladium catalyst was added for completion of the reaction. The suspension was refluxed for another 1 h. Then the catalyst was filtered off and washed with the solvent. The filtrate was evaporated and the residue was purified by column chromatography on silica gel using CH_2Cl_2/MeOH, 10 : 1, as eluent to yield, quantitatively, 38 mg of the β-anomer of the titled compound. Rf 0.14 (silica gel, $CHCl_3$/MeOH 90 : 10).

β-anomer : ^1H NMR (DMSO-d_6) : δ 11.14 (s, 1H, NH), 8.03 (d, 1H, $J_{H6,CH3\text{-}5}$ = 0.9 Hz, H-6), 5.47 (d, 1H, $J_{3',OH}$ = 4.7 Hz, OH-3'), 5.01 (t, 1H, $J_{6',OH}$ = 5.1 Hz, OH-6'), 4.84 (d, 1H, $J_{4',OH}$ = 6.7 Hz, OH-4'), 4.44 (t, 1H, $J_{3',4'}$ = 4.4 Hz, H-3'), 3.89 (m, 1H, H-5'), 3.83 (m, 1H, $J_{4',5'}$ = 8.6 Hz, H-4'), 3.71 (ddd, 1H, $J_{6'gem}$ = 12.3 Hz, $J_{6'a,5'}$ = 2.7 Hz, H-6'a), 3.42 (dt, 1H, $J_{6'b,5'}$ = 4.5 Hz, H-6'b), 1.75 (d, 3H, CH_3-5), 1.55 (s, 3H, H-1'); ^{13}C NMR (DMSO-d_6): δ 164.1 (C-4), 150.2 (C-2), 136.5 (C-6), 107.2 (C-5), 98.4 (C-2'), 83.1 (C-5'), 74.1 (C-3'), 69.0 (C-4'), 59.6 (C-6'), 21.2 (C-1'), 12.1 (CH_3 5).

α-anomer : ^{1}H NMR (DMSO-d_6) : δ 11.05 (s, 1H, NH), 7.61 (s,1H, H-6), 5.21 (d, 1H, $J_{3',OH}$ = 4.5 Hz, OH-3'), 4.91 (d, 1H, $J_{4',OH}$ = 7.3 Hz, OH-4'), 4.79 (t, 1H, $J_{6',OH}$ = 5.8 Hz, OH-6'), 4.12 (m, 1H, H-3'), 1.77 (s, 3H, CH_3-5), 1.58 (s, 3H, H-1'); ^{13}C NMR (DMSO-d_6) : δ 164.4 (C-4), 150.0 (C-2), 136.3 (C-6), 106.1 (C-5), 96.7 (C-2'), 81.6 (C-5'), 77.4 (C-3'), 69.4 (C-4'), 60.8 (C-6'), 25.3 (C-1'), 12.2 (CH_3-5); MS m/z; 273 (11, MH^+), 147 (100, (M-base)$^+$), 127 (76, base + $2H^+$); accurate mass positive ion FAB MS m/z 273.1082 (MH^+, Calcd 273.1086).

Anal. Calcd. for $C_{11}H_{16}N_2O_6$, CH_3OH : C, 47.36; H, 6.58; N, 9.21. Found : C, 47.15; H, 6.59; N, 9.33.

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