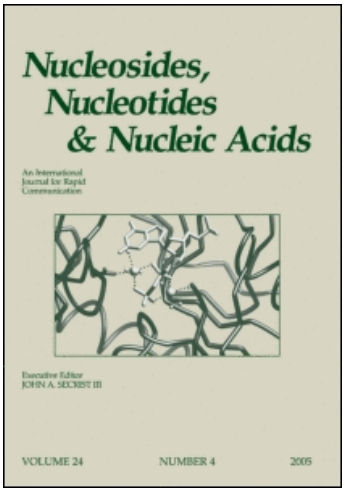

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New Non-Aromatic Triazinic Nucleosides: Synthesis and Antiretroviral Evaluation of β-Ribosylamine Nucleoside Analogs

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NEW NON-AROMATIC TRIAZINIC NUCLEOSIDES : SYNTHESIS AND ANTIRETROVIRAL EVALUATION OF β-RIBOSYLAMINE NUCLEOSIDE ANALOGS

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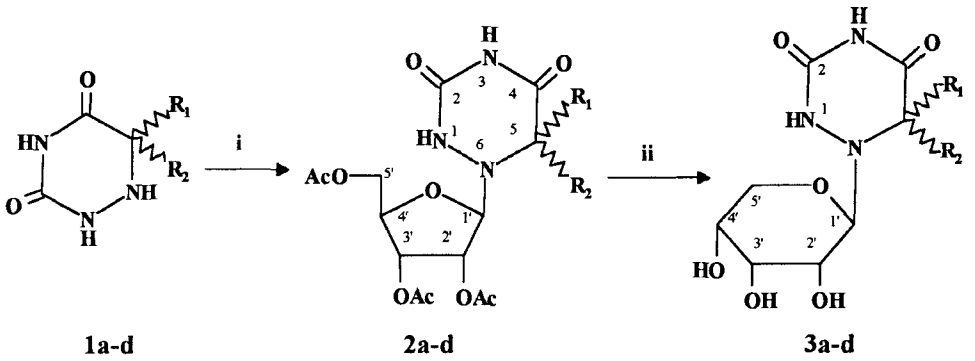
Abstract

Various 5-alkyl-6-aza-5,6-dihydrouridines and 6-(β-D-ribopyranosyl)-5-alkyl-6-aza-5,6-dihydrouracils have been synthesized. A new regioselective method is described for coupling triazinic bases to the sugar unit. Different epimers were isolated. Antiretroviral activity against Visna virus was evaluated.

A great variety of nucleoside analogs, among other compounds, have been used as broad antiviral and antibacterial as well as antitumor agents[1]. The study of non-aromatic triazinic nucleosides remains relatively unexplored in spite of potential activity as antiviral drugs[2,3]. In earlier work[4,5], we obtained a mixture of 1-(2',3',5'-tri-*O*-acetyl-β-D-ribofuranosyl)-5-alkyl-6-aza-5,6-dihydrouracils and of the corresponding N-6 nucleosides [6-(2',3',5'-tri-*O*-acetyl-β-D-ribofuranosyl)-5-alkyl-6-aza-5,6-dihydrouracils] by using the classic Vorbrüggen coupling method (HMDS, TMSCl, TMSTf)[6,7,8]. Some of the deprotected 5-alkyl-6-aza-5,6-dihydrouridine compounds, when tested against the Visna-Maedi retrovirus, proved to be promising despite their moderate activity. In this paper we report full details of our work including other triazinic bases and improved methods of regioselective synthesis for both N-1 and N-6 nucleoside analogs. We also discuss their sugar moiety conformation using NMR analysis.



1a-d **2a-d** **3a-d**

a : $R_1 = CH_3$, $R_2 = H$; **b** : $R_1 = (CH_2)_2CH_3$, $R_2 = H$; **c** : $R_1 = R_2 = CH_3$, **d** : $R_1 = R_2 = H$.
i : 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose (1 eq), TMSTf (1 eq).
ii : NH_3/MeOH.

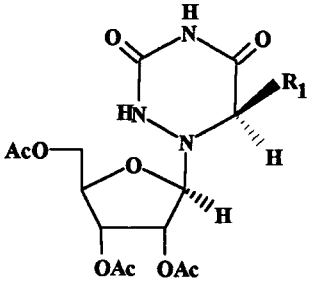
SCHEME 1

Results and Discussion

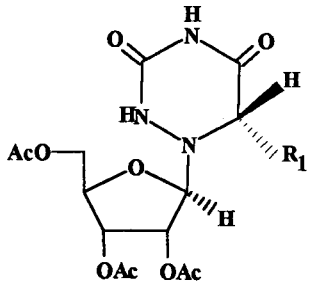
5-Alkyl and 5,5-dialkyl-6-aza-5,6-dihydrouracils (**1a-c**) have been prepared according to the method developed in our laboratory[9]. These heterocycles were synthesized by the reaction of semicarbazide with the appropriate α-bromo methyl alkanoate followed by cyclisation. Compound **1d** was obtained according to Gut *et al.*[10] by the reduction with Adams catalyst of the commercially available 6-azauracil. In order to regiospecifically link the 1,2,3,5-tetra-*O*-acetyl-β-D-ribofuranose and the triazinic bases (**1a-d**) at the N-6 position (Scheme 1), the sugar moiety was first treated with 1 eq of TMSTf at 50°C in dry acetonitrile before addition of the base.

By this route, TMSTf converted the *per*acetylated sugar into a reactive enoxonium species which exclusively reacts with the N-6 nitrogen, the most basic endocyclic nitrogen. Moreover, as a result of the participation of the neighbouring 2'-acetyl group[11], the N-6 nucleosides **2a-d**, with β-configuration, could be obtained in 49 %, 35%, 54% and 13% yields respectively. Their structures were determined using mass, ^1H and ^{13}C NMR spectroscopy. The C-5 epimers of **2a** (5*R* and 5*S*) and **2b** (5*R* and 5*S*) (Scheme 2) were separated with SiO_2 preparative chromatography (see Experimental) then identified by NOE experiment with H-1' proton saturation.

The relative 5*R* configuration for **2'a** is supported by the observation of a NOE at H-5 (δ 3.60 ppm) after saturation of the doublet at δ 4.67 ppm (H-1'). This result is in agreement



2'a,b (5*R*)

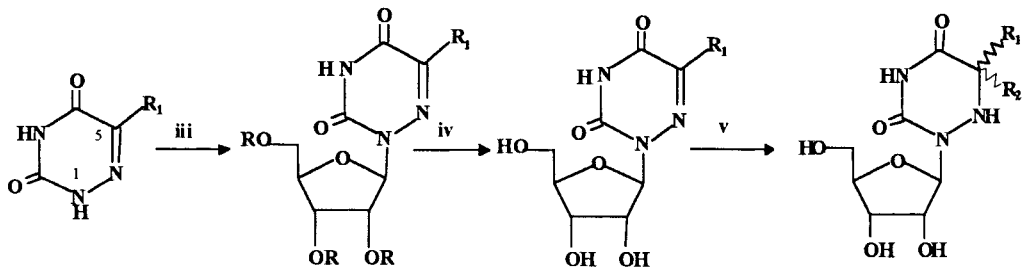


2"a,b (5*S*)

a : $R_1 = CH_3$; **b** : $R_1 = (CH_2)_2CH_3$.

SCHEME 2

with the assignement of the relative 5*S* configuration for **2"a** in which H-1' (δ 4.83 ppm) exhibits a NOE with the 5-methyl group (δ 1.44 ppm). This analysis is corroborated in the ^{13}C NMR of both compounds showing the upfield shift for C-1' (Δδ -3.2 ppm) and the 5-methyl group (Δδ -3.1 ppm) for **2"a** (5*S*) consequently to steric hindrance between the two carbon atoms. The products with higher R_f values using $CHCl_3$-EtOH (95:5) on silica gel have been assigned to the 5*R*-diastereoisomers. Nucleosides **2a-d** were deacetylated using methanolic ammonia (Scheme 1). Compounds **3a-d** were identified using ^1H and ^{13}C NMR to be β-ribopyranosyl-nucleosides[12-15]. In the ^1H NMR, the signals for the anomeric protons of **3a-d** are doublets (δ 4.17 - 4.47 ppm) with $J_{1',2'} = 9$ Hz which is consistent with a pyranose $^4C_1$ conformation for the sugar moiety of β-isomers[12-14]. The pyranose anomeric proton is known to exhibit an upfield shift of 0.3 - 0.4 ppm and an increase in its $J_{1',2'}$ coupling constant by approximately 3 Hz relative to that of the furanose[14]. Moreover, the experimental values of $J_{2',3'}$ and $J_{3',4'}$ (2.0 - 2.9 Hz) are in agreement with the calculated values ($J_{2',3'} = J_{3',4'} = 2.0$ Hz) for a $^4C_1$ ribopyranose conformation according Karplus[15]. In the ^{13}C NMR analysis, the upfield shift (7 ppm) of the C-4' resonance in ribopyranosyl-nucleosides **3a-d** as compared to that of **2a-d** is a consequence of the sugar ring expansion which moves the cyclic ether away from this carbon atom[14]. No furanose ring compounds were obtained after deacetylation of **2a-d**. Compounds **3a-d** proved stable when dissolved in D_2O (^1H NMR spectra identical after 17 hours). Thus it can be assumed that



4a : $R_1 = CH_3$ **5a** : $R_1 = CH_3$, R = Bz **6a** : $R_1 = CH_3$ **7a** : $R_1 = CH_3$, R_2 = H
4b : $R_1 = (CH_2)_2CH_3$ **5b** : $R_1 = (CH_2)_2CH_3$, R = Bz **6b** : $R_1 = (CH_2)_2CH_3$ **7c** : $R_1 = R_2$ = H
4c : R_1 = H **5c*** : R_1 = H, R = Ac **6c** : R_1 = H

iii : 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (1 eq), HMDS (2.65 eq), TMSCl (0.08 eq), $SnCl_4$ (0.7 eq).
iv : MeONa in MeOH.
v : H_2, PtO_2, AcOH / H_2O.
* : **5c** is commercially available.

SCHEME 3

deprotection of **2a-d** results in a rearrangement from furanose to pyranose for the ribose moiety which undoubtedly proceeds via the open-chain Schiff base[14]. This rearrangement was previously observed with the deacetylation in the same conditions of a N-(2',3',5'-tri-*O*-acetyl-ribofuranosyl)-anthranilonitrile which resulted in the formation of the more thermodynamically favoured β-pyranoside isomer[12].

To specifically obtain N-1 nucleosides (Scheme 3), we applied the method of Vorbrüggen[16] for glycosidation of the 6-aza-5-methyl (or *n*-propyl)-uracils **4a,b**[17]. The use of TMSTf led to a mixture of several compounds. Thus, **5a** and **5b** were obtained in 65% and 63% yields, respectively. These compounds along with the commercially available 1-(2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl)-6-azauracil **5c** were deprotected with 1M MeONa in methanol (Scheme 3, iv) to give **6a-c** in near quantitative yields. In our attempts to obtain the corresponding 5,6-dihydro-nucleosides, several hydrogenation and reduction pathways[14,18-22] were used and have proven unsuccessful. The catalytic hydrogenation, according to Gut *et al*[10] (*vide supra*) of the 5,6-double bond of a triazine ring could be applied successfully to the 6-aza-uracils **4a,c** but fails with nucleosides **6a-c**. In the same way, Gut *et al*[10] did not succeed in reducing the 1-methyl-6-azathymine, or the 1,3-

TABLE 1

Compounds	EC 50 (μM)[a]	CC 50 (μM)[b]
6a	650	>1500
6b	-	>1500
7c	-	>420
3'a (5*R*)	-	>650
3"a (5*S*)	-	>330
3'b (5*R*)	300	>330
3"b (5*S*)	-	60
3c	-	>800
3d	-	50
AZT	5	>500

[a] EC 50 is the concentration that protected 50% of infected cells.
[b] CC 50 is defined as the concentration required to reduce the viability of non infected cells by 50%.

dimethyl-6-azathymine, as a result of steric hindrance. However, an increase in the hydrogen pressure (4 bars) and a longer time (20 days) appeared to be effective, but only for **6a** and **6c**[*]. The 6-aza-5,6-dihydro-5-methyluridine **7a** and 6-aza-5,6-dihydrouridine **7c** were obtained after separation with 70% and 85% yields respectively, with **7a** as a mixture of C-5 epimers (**7a** 5*R* and 5*S*). As there was no modification in the UV spectra after 30 days, the hydrogenation of **6b** or **4b** was unsuccessful; this may be the result of steric hindrance caused by the bulky 5-propyl group. We were unable to separate the two epimers 5*R* and 5*S* of **7a**, nevertheless, their ratio could be estimated as 3 / 7 by using the heights of the two ^{13}C NMR signals for C-5. The analogy of the ^{1}H and ^{13}C NMR spectra of N-1 nucleosides **7a** and **7c** with those of **6a,c** indicates a furanosyl sugar ring. Furanose-pyranose isomerization was not observed for **7a** and **7c** due to the sufficient conjugative interaction between the electron-withdrawing carbonyl C-4, N-1 and the partial double bond character between C-2 and N-3 similar to that of dihydrouridine[14].

Biological tests

Compounds **6a**, **6b**, **7c**, **3'a** (5*R*), **3"a** (5*S*), **3'b** (5*R*), **3"b** (5*S*), **3c** and **3d** were evaluated for their antiviral activities *in vitro* against the Visna strain K 796 retrovirus in sheep choroid plexus cells (SCP cells). Antiviral activities and cytotoxicity were measured

by the MTT method[24] applied to adherent cells. Briefly, SCP cells were incubated in the presence of the tested compounds alone or with Visna virus at a multiplicity of infection 0.5. After 5 days of incubation, MTT was added and the formation of formazan was spectrophotometrically measured[25]. Results are shown in Table 1.

Compared to AZT, none of the tested compounds showed any significant antiviral activities *in vitro* in this cell culture system. Compounds **3"b** (5*S*) and **3d** were cytotoxic. The other compounds were not cytotoxic even at high concentrations.

EXPERIMENTAL SECTION

General methods

IR spectra were measured in cm^{-1} on solid samples in KBr with a Perkin Elmer 1310. UV-visible spectra were recorded on a Hewlett Packard 8452A spectrophotometer using 1 cm quartz cells in the indicated solvent, wavelengths were measured in nm and extinction coefficient in $cm^{-1}.mol^{-1}.l$. Rotatory dispersion were measured at 22°C in the indicated solvent with a JASCO (DIP-370) polarimeter. Proton and Carbon NMR spectra were recorded on a Bruker AC 200 with tetramethylsilane as internal standard at 200 MHz for ^1H and 50 MHz for ^{13}C. Chemical shifts are given in ppm and coupling constants in Hz in the indicated solvent. Electronic impact mass spectra (EI) were recorded on a SHIMADZU QP appartus by the "Laboratoire Départemental d'Analyse", Limoges. Chemical Ionization mass spectra (CI) were recorded on a R3010 Nermag. FAB^- mass spectra were performed on a ZAB 2-SEQ using triglycerol as matrix at the "Service Central d'Analyse", CNRS Solaize. Microanalyses were carried out by the "Service Régional de Microanalyse", Université Pierre et Marie Curie, Paris.

Chemicals

All solvents and reagents were purchased from Aldrich, Prolabo or Janssen. Acetonitrile and dichloroethane were distilled on CaH_2 and P_2O_5 before their use.

Chromatography

Analytical thin-layer chromatography (TLC) was performed on silica gel (Merck, $60F_{254}$). PLC was performed on coated silica gel plates ($60F_{254}$). Column chromatography was carried out on silica gel 60 ACC (15-40μm. Merck). The following solvent systems were used as eluents : A = $CHCl_3$-EtOH (95:5) ; B = $CHCl_3$-EtOH (9:1) ; C = AcOEt-pet. ether (4:1) ; D = $CHCl_3$-EtOH (7:3) ; E = $CHCl_3$-EtOH (1:1).

General method for the preparation of 6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-5-alkyl-6-aza-5,6-dihydrouracil (2a-d)

Trimethylsilyltrifluoromethane sulfonate, TMSTf, (0.185 ml, 1 mmol) was added to a solution of 1,2,3,5-tetra-*O*-acetyl-ß-D-ribofuranose (318 mg, 1 mmol) in dry acetonitrile (5 ml) at 50°C and the

mixture was stirred for 15 mn. A solution of 5-alkyl-6-aza-5,6-dihydrouracil **1a,b,c,d** (1 mmol) in dry acetonitrile (10ml) was then added. The reaction mixture was stirred for 5 hours at room temperature and neutralized at 0°C with a saturated aqueous solution of $NaHCO_3$. After separation of the organic layer, the solvent was then evaporated under reduced pressure and the residue was applied on silica gel PLC and eluted with system A (**a**), B (**b,d**) or C (**c**) to give the title compounds **2a-d**.

6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydro-5-methyluracil. (**2a**)

The reaction with 6-aza-5,6-dihydro-5-methyluracil (129 mg) gave two C-5 epimers **2'a** (5*R*) and **2"a** (5*S*) which were separated by silica gel PLC.

2'a (5*R*) (140 mg, 36%). White foam. R_f (system A) : 0.32. MS (EI) *m/z* : 387 $M^{+\cdot}$, 313 (M - $CH_3COOCH_2)^+$, 259, 129. IR : 3300, 3260 (NH amide), 2910 (CH_3), 1750 (CO acetate), 1720, 1690 (CO triazine). $[\alpha]_D$: -91.5° (c 0.2, $CHCl_3$). ^1H NMR($CDCl_3$) δ 1.43 (3H, d, *J*= 7.1 Hz, Me-5), 2.09, 2.10 and 2.13 (3H each, s, OAc), 3.60 (1H, q, *J* = 7.1 Hz, H-5), 4.05-4.30 (3H, m, H-4', H-5'a and H-5'b), 4.67 (1H, d, *J* = 7.3 Hz, H-1'), 5.24 (1H, dd, *J* = 5.6 and 2.0 Hz, H-3'), 5.42 (1H, dd, *J* = 5.7 and 7.3 Hz, H-2'), 7.21 (1H, br s, H-1), 7.94 (1H, br s, H-3). ^{13}C NMR($CDCl_3$) δ 16.4 (Me-5), 20.6 (Me, 3OAc), 58.5 (C-5), 63.2 (C-5'), 69.3 (C-3'), 71.2 (C-2'), 79.5 (C-4'), 96.4 (C-1'), 152.6 (C-2), 169.9, 170.1 and 170.5 (CO, OAc), 170.8 (C-4). Anal. Calcd for $C_{15}H_{21}N_3O_9$: C, 46.51; H, 5.46; N, 10.84. Found : C, 46.23; H, 5.67; N, 10.79.

2"a (5*S*) (50 mg, 13%). White foam. R_f (system A) : 0.26. MS (EI) *m/z* : 387 $M^{+\cdot}$, 313 (M - $CH_3COOCH_2)^+$, 259, 129. IR : 3300, 3260 (NH amide), 2950, 2910 (CH_3), 1750 (CO acetate), 1720, 1690 (CO triazine). $[\alpha]_D$: -77.8° (c 0.2, $CHCl_3$). ^1H NMR($CDCl_3$) δ 1.44 (3H, d, *J*= 7.2 Hz, Me-5), 2.09, 2.10 and 2.13 (3H each, s, OAc), 3.89 (1H, q, *J* = 7.1 Hz, H-5), 4.05-4.25 (3H, m, H-4', H-5'a and H-5'b), 4.83 (1H, d, *J* = 6.5 Hz, H-1'), 5.23 (1H, dd, *J* = 5.5 and 2.4 Hz, H-3'), 5.38 (1H, dd, *J* = 5.8 and 6.5 Hz, H-2'), 7.62 (1H, br s, H-1), 8.23 (1H, br s, H-3). ^{13}C NMR($CDCl_3$) δ 13.3 (Me-5), 20.5, 20.6 and 20.7 (Me, OAc), 54.8 (C-5), 63.4 (C-5'), 69.8 (C-3'), 71.1 (C-2'), 79.4 (C-4'), 93.2 (C-1'), 153.2 (C-2), 169.7, 169.9 and 170.8 (CO, OAc), 171.1 (C-4). Anal. Calcd for $C_{15}H_{21}N_3O_9$: C, 46.51; H, 5.46; N, 10.84. Found : C, 46.30; H, 5.62; N, 10.60.

6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydro-5-propyluracil. (**2b**)

The reaction with 6-aza-5,6-dihydro-5-propyluracil (157 mg) gave two C-5 epimers **2'b** (5*R*) and **2"b** (5*S*) which were separated by silica gel PLC.

2'b (5*R*) (50 mg, 17%). White foam. R_f (system A) : 0.35. MS (EI) *m/z* : 415 $M^{+\cdot}$, 341 (M - $CH_3COOCH_2)^+$, 259, 157. IR : 3300, 3260 (NH amide), 2950, 2910, 2840 (CH), 1750 (CO acetate), 1730, 1690 (CO triazine). $[\alpha]_D$: -58° (c 0.26, $CHCl_3$). ^1H NMR($CDCl_3$) δ 0.93 (3H, t, *J* = 7.2 Hz, Pr-5 γ-CH_3), 1.45 (2H, m, Pr-5 β-CH_2), 1.70 (2H, m, Pr-5 α-CH_2), 2.09, 2.11 and 2.12 (3H each, s, OAc), 3.43 (1H, dd, *J* = 5.5 and 9.0 Hz, H-5), 4.05-4.30 (3H, m, H-4', H-5'a and H-5'b), 4.61 (1H, d, *J* = 7.4 Hz, H-1'), 5.23 (1H, dd, *J* = 5.6 and 2.0 Hz, H-3'), 5.41 (1H, dd, *J* = 5.6 and 7.4 Hz, H-2'), 7.14 (1H, br s, H-1), 7.94 (1H,

br s, H-3). ^{13}C NMR($CDCl_3$) δ 13.3 (Pr-5γ), 18.9 (Pr-5β), 31.6 (Pr-5α), 20.5, 20.6 and 20.7 (Me, OAc), 62.6 (C-5), 63.2 (C-5'), 69.3 (C-3'), 71.1 (C-2'), 79.5 (C-4'), 96.8 (C-1'), 152.8 (C-2), 169.7, 170.2 and 170.8 (CO, OAc), 171.3 (C-4). Anal. Calcd for $C_{17}H_{25}N_3O_9$: C, 49.15; H, 6.06; N, 10.11. Found : C, 48.90; H, 6.31; N, 9.86.

2"b (5*S*) (60 mg, 17.5%). White foam. R_f (system A) : 0.28. MS (EI) *m/z* : 415 $M^{+\cdot}$, 341 $(M - CH_3COOCH_2)^+$, 259, 157. IR : 3300, 3260 (NH amide), 2950, 2910, 2840 (CH), 1740 (CO acetate), 1720, 1685 (CO triazine) $[\alpha]_D$: -7.5° (c 0.39, $CHCl_3$). ^1H NMR($CDCl_3$) δ 0.97 (3H, t, *J* = 7.2 Hz, Pr-5 γ-CH_3), 1.47 (2H, m, Pr-5 β-CH_2), 1.75 (2H, m, Pr-5 α-CH_2), 2.09, 2.11 and 2.12 (3H each, s, OAc), 3.68 (1H, dd, *J* = 6.3 and 8.7 Hz, H-5), 4.05-4.30 (3H, m, H-4', H-5'a and H-5'b), 4.87 (1H, d, *J* = 6.7 Hz, H-1'), 5.21 (1H, dd, *J* = 5.5 and 2.3 Hz, H-3'), 5.30 (1H, dd, *J* = 5.6 and 6.7 Hz, H-2'), 7.25 (1H, br s, H-1), 7.78 (1H, br s, H-3). ^{13}C NMR($CDCl_3$) δ 13.5 (Pr-5γ), 19.1 (Pr-5β), 30.1 (Pr-5α), 20.5 (Me, 3OAc), 57.8 (C-5), 63.5 (C-5'), 69.6 (C-3'), 71.1 (C-2'), 79.6 (C-4'), 95.3 (C-1'), 152.5 (C-2), 169.7, 169.9 and 170.5 (CO, OAc), 170.7 (C-4). Anal. Calcd for $C_{17}H_{25}N_3O_9$: C, 49.15; H, 6.06; N, 10.11. Found : C, 48.84; H, 6.16; N, 9.75.

6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydro-5,5-dimethyluracil. (**2c**)

The reaction with 6-aza-5,6-dihydro-5,5-dimethyluracil (148 mg) gave **2c** (217 mg, 54%) as a white foam. R_f (system C) : 0.4. MS (EI) *m/z* : 403 $(M+2H)^+$, 327 $(M - CH_3COOCH_2)^+$, 259. IR : 3300, 3260 (NH amide), 2975, 2880 (CH_3), 1750 (CO acetate), 1720, 1695 (CO triazine). $[\alpha]_D$: -86° (c 0.1, $CHCl_3$). ^1H NMR($CDCl_3$) δ 1.43 and 1.50 (3H, s, diMe-5), 2.11, 2.12 and 2.14 (3H each, s, OAc), 4.05-4.15 (2H, m, H-4' and H-5'b), 4.21 (1H, dd, *J* = 12.7 and 4.0 Hz, H-5'a), 4.89 (1H, d, *J* = 7.3 Hz, H-1'), 5.25 (1H, dd, *J* = 5.7 and 2.2 Hz, H-3'), 5.46 (1H, dd, *J* = 5.7 and 7.3 Hz, H-2'), 7.32 (1H, br s, H-1), 7.69 (1H, br s, H-3). ^{13}C NMR($CDCl_3$) δ 20.3 and 24.9 (diMe-5), 20.7 (Me, 3OAc), 59.4 (C-5), 63.3 (C-5'), 69.5 (C-3'), 71.3 (C-2'), 79.2 (C-4'), 91.0 (C-1'), 152.8 (C-2), 169.7, 170.2 and 170.9 (CO, OAc), 173.4 (C-4). Anal. Calcd for $C_{16}H_{23}N_3O_9$: C, 47.87; H, 5.77; N, 10.46. Found : C, 48.21; H, 5.82; N, 10.05.

6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydrouracil. (**2d**)

The reaction with 6-aza-5,6-dihydrouracil (115 mg) gave **2d** (50 mg, 13%) as a white foam. R_f (system A) : 0.45. MS (EI) *m/z* : 374 $(M+H)^+$, 373 $M^{+\cdot}$, 300 $(M - CH_3COOCH_2)^+$, 259. IR : 3300, 3260 (NH amide), 2920, 2850 (CH_2), 1740 (CO acetate), 1720, 1695 (CO triazine). $[\alpha]_D$: -89.1° (c 0.37, $CHCl_3$). ^1H NMR($CDCl_3$) δ 2.10[x2] and 2.13 (3H each, s, OAc), 3.61 and 3.95 (1H, d, *J* = 16.9 Hz, H-5a,b), 4.08-4.20 (3H, m, H-4', H-5'a and H-5'b), 4.70 (1H, d, *J* = 7.0 Hz, H-1'), 5.24 (1H, dd, *J* = 5.5 and 2.1 Hz, H-3'), 5.36 (1H, dd, *J* = 5.6 and 7.0 Hz, H-2'), 7.53 (1H, br s, H-1). ^{13}C NMR($CDCl_3$) δ 20.5[x2], 20.6 (Me, OAc), 52.9 (C-5), 63.2 (C-5'), 69.6 (C-3'), 71.1 (C-2'), 79.6 (C-4'), 96.6 (C-1'), 153.1 (C-2), 168.3, 169.7 and 170.1 (CO, OAc), 170.8 (C-4). Anal. Calcd for $C_{14}H_{19}N_3O_9$: C, 45.04; H, 5.13; N, 11.25. Found : C, 44.85; H, 5.21; N, 11.12.

General method for the preparation of 6-(ß-D-ribopyranosyl)-5-alkyl-6-aza-5,6-dihydrouracil (3a-d)

To 6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-5-alkyl-6-aza-5,6-dihydrouracil **2a-d** (0.1 mmol) in MeOH (2ml) was added NH_3/MeOH 2M (0.5 ml, 1 mmol). The reaction mixture was stirred at room temperature for 2 days and evaporated to dryness. The residue was applied on silica gel PLC and eluted with system D (**a,b,d**), or E (**c**) to give the title compounds **3a-d.**

6-(ß-D-ribopyranosyl)-6-aza-5,6-dihydro-5-methyluracil (**3a**)

Deacetylation of 6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydro-5-methyluracil **2'a** (5*R*) (38.7 mg) and **2"a** (5*S*) (38.7 mg) yielded **3'a** (5*R*) and **3"a** (5*S*) respectively.

3'a (5*R*) (20 mg, 77%). R_f (system D) : 0.33. MS (FAB⁻TG) *m/z* : 260 $(M - H)^-$. $[\alpha]_D$: -90° (c 0.07, H_2O). ^1H NMR(CD_3OD) δ 1.37 (3H, d, *J*= 7.2 Hz, Me-5), 3.52-3.65 (4H, m, H-2', H-4', H-5'a and H-5'b), 3.60 (1H, q, *J* = 7.0 Hz, H-5), 4.10 (1H, t, *J* = 2.0 Hz, H-3'), 4.20 (1H, d, *J* = 9.0 Hz, H-1'). ^{13}C NMR(CD_3OD) δ 16.7 (Me-5), 59.3 (C-5), 65.7 (C-5'), 68.1, 68.3 (C-3', C-2'), 72.5 (C-4'), 93.6 (C-1'), 155.8 (C-2), 175.3 (C-4). Anal. Calcd for $C_9H_{15}N_3O_6$: C, 41.38; H, 5.78; N, 16.08. Found : C, 41.22; H, 5.80; N, 15.82.

3"a (5*S*) (17 mg, 66%). R_f (system D) : 0.33. MS (FAB⁻TG) *m/z* : 260 $(M - H)^-$. $[\alpha]_D$: +17° (c 0.1, EtOH). ^1H NMR(CD_3OD) δ 1.36 (3H, d, *J*= 7.1 Hz, Me-5), 3.50-3.66 (4H, m, H-2', H-4', H-5'a and H-5'b), 3.78 (1H, q, *J* = 7.1 Hz, H-5), 4.08 (1H, t, *J* = 2.5 Hz, H-3'), 4.40 (1H, d, *J* = 9.1 Hz, H-1'). ^{13}C NMR(CD_3OD) δ 14.6 (Me-5), 54.1 (C-5), 65.8 (C-5'), 68.1, 68.3 (C-3', C-2'), 72.4 (C-4'), 91.5 (C-1'), 174.8 (C-4). Anal. Calcd for $C_9H_{15}N_3O_6$: C, 41.38; H, 5.78; N, 16.08. Found : C, 41.15; H, 5.95; N, 15.91.

6-(ß-D-ribopyranosyl)-6-aza-5,6-dihydro-5-propyluracil (**3b**)

Deacetylation of 6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydro-5-propyluracil **2'b** (5*R*) (41 mg) and **2"b** (5*S*) (41 mg) yielded **3'b** (5*R*) and **3"b** (5*S*) respectively.

3'b (5*R*) (6 mg, 21%). R_f (system D) : 0.5. MS (FAB⁻TG) *m/z* : 288 $(M - H)^-$. $[\alpha]_D$: -15° (c 0.06, EtOH). ^1H NMR(CD_3OD) δ 0.96 (3H, t, *J* = 7.0 Hz, Pr-5 γ-CH_3), 1.52 (4H, m, Pr-5 β and α-CH_2), 3.38 (1H, dd, *J* = 4.6 and 9.3 Hz, H-5), 3.52-3.65 (3H, m, H-4', H-5'a and H-5'b), 3.61 (1H, dd, *J* = 2.9 and 9.0 Hz, H-2'), 4.10 (1H, t, *J* = 2.9 Hz, H-3'), 4.17 (1H, d, *J* = 9.0 Hz, H-1'). ^{13}C NMR(CD_3OD) δ 13.9 (Pr-5γ), 20.0 (Pr-5β), 33.3 (Pr-5α), 63.4 (C-5), 65.7 (C-5'), 68.2, 68.3 (C-3', C-2'), 72.6 (C-4'), 93.9 (C-1'), 155.9 (C-2), 174.9 (C-4). Anal. Calcd for $C_{11}H_{19}N_3O_6$: C, 45.67; H, 6.62; N, 14.52. Found : C, 45.50; H, 6.89; N, 14.36.

3"b (5*S*) (11 mg, 40%). R_f (system D) : 0.5. MS (FAB⁻TG) *m/z* : 288 $(M - H)^-$. $[\alpha]_D$: +17° (c 0.1, EtOH). ^1H NMR(CD_3OD) δ 0.96 (3H, t, *J* = 7.1 Hz, Pr-5 γ-CH_3), 1.63 (4H, m, Pr-5 β and α-CH_2), 3.50-3.67 (4H, m, H-5, H-4', H-5'a and H-5'b), 3.51 (1H, dd, *J* = 2.9 and 9.0 Hz, H-2'), 4.05 (1H, t, *J* = 2.9 Hz, H-3'), 4.41 (1H, d, *J* = 9.0 Hz, H-1'). ^{13}C NMR(CD_3OD) δ 14.0 (Pr-5γ), 20.1 (Pr-5β), 32.3 (Pr-5α), 57.5

(C-5), 65.9 (C-5'), 68.2, 68.2 (C-3', C-2'), 72.1 (C-4'), 93.0 (C-1'), 155.8 (C-2), 174.5 (C-4). Anal. Calcd for $C_{11}H_{19}N_3O_6$: C, 45.67; H, 6.62; N, 14.52. Found : C, 45.48; H, 6.70; N, 14.25.

6-(ß-D-ribopyranosyl)-6-aza-5,6-dihydro-5,5-dimethyluracil (**3c**)

Deacetylation of 6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydro-5,5-dimethyluracil **2c** (40.1 mg) yielded **3c**. (16 mg, 58%). R_f (system D) : 0.4. MS (FAB⁻TG) *m/z* : 274 $(M - H)^-$. $[\alpha]_D$: -62.5° (c 0.16, H_2O). ^1H NMR(CD_3OD) δ 1.37 and 1.39 (3H, s, diMe-5), 3.43-3.60 (3H, m, H-4', H-5'a and H-5'b), 3.64 (1H, dd, *J* = 2.7 and 9.0 Hz, H-2'), 4.11 (1H, t, *J* = 2.7 Hz, H-3'), 4.47 (1H, d, *J* = 8.9 Hz, H-1'). ^{13}C NMR(CD_3OD) δ 20.4 and 25.3 (diMe-5), 59.3 (C-5), 65.3 (C-5'), 68.1, 68.3 (C-3', C-2'), 72.7 (C-4'), 87.5 (C-1'), 156.3 (C-2), 176.9 (C-4). Anal. Calcd for $C_{10}H_{17}N_3O_6$: C, 43.63; H, 6.22; N, 15.26. Found : C, 43.40; H, 6.31; N, 15.03.

6-(ß-D-ribopyranosyl)-6-aza-5,6-dihydrouracil (**3d**)

Deacetylation of 6-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-aza-5,6-dihydrouracil **2d** (37 mg) yielded **3d**. (13 mg, 53%). R_f (system D) : 0.43. MS (FAB⁻TG) *m/z* : 246 $(M - H)^-$. $[\alpha]_D$: +37.5° (c 0.05, EtOH). ^1H NMR(CD_3OD) δ 3.48-3.65 (4H, m, H-2', H-4', H-5'a and H-5'b), 3.59 and 3.76 (1H, d, *J* = 16.8 Hz, H-5a,b), 4.07 (1H, t, *J* = 2.5 Hz, H-3'), 4.36 (1H, d, *J* = 8.3 Hz, H-1'). Anal. Calcd for $C_8H_{13}N_3O_6$: C, 38.86; H, 5.30; N, 16.99. Found : C, 38.59; H, 5.42; N, 16.68.

General method for the preparation of 1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-5-alkyl-6-azauracil (**5a,b**)

To 5-alkyl-6-azauracil **4a,b** (5 mmol) was added hexamethyldisilazane HMDS (2.8 ml, 13.3 mmol) and trimethylsilyl chloride TMSCl (0.05 ml, 0.4 mmol). The mixture was refluxed for 2 hours. The excess of HMDS/TMSCl was removed by evaporation under reduced pressure. The resulting 2,4-bis(trimethylsilyloxy)-5-alkyl-6-azauracil was used immediately. To a solution of this protected uracil (5 mmol) in dry 1,2-dichloroethane (4 ml) was added a solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (2.522 g, 5 mmol) in the same solvent (30 ml). The reaction mixture was cooled to 0°C and anhydrous stannic chloride was added (0.65 ml, 3,5 mmol). This reaction mixture was stirred for 3 hours (**a**) and 8 hours (**b**) respectively at 25°C. A saturated aqueous solution of sodium hydrogen carbonate was then added to neutralize the mixture. After separation, the organic layer was evaporated under reduced pressure to give a foamy residue. This residue was applied on silica gel PLC and eluted with system A (**a** and **b**) to give the title compounds **5a,b**.

1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6-aza-5-methyluracil (**5a**)

The reaction with 6-aza-5-methyluracil (0.636 g) gave **5a** (1.846 g, 65%) as a white foam. R_f (system A) : 0.39. MS (CI) *m/z* : 589 MNH_4^+, 572 MH^+. UV λ(EtOH) 266 nm (ε 6742). IR : 3200, 3040(NH), 2950, 2800(CH), 1715-1670(CO), 1600(CN). $[\alpha]_D$: -78.5° (c 0.5, $CHCl_3$). ^1H NMR($CDCl_3$) δ 2.13 (3H, s, Me-5), 4.57 (1H, dd, *J* = 4.0 and 11.5 Hz, H-5'a), 4.73 (1H, m, H-4'), 4.78(1H, dd, *J* = 3.5

and 11.5 Hz, H-5'b), 5.95 (1H, t, J = 5.6 Hz, H-3'), 6.11 (1H, dd, J = 3.6 and 5.6 Hz, H-2'), 6.56 (1H, d, J = 3.6 Hz, H-1'), 7.37 (6H, m, H-3" and H-5" Bz), 7.55 (3H, m, H-4" Bz), 7.95, 7.96 and 8.08 (2H each, dd, J = 1.5 and 7.1 Hz, H-2" and H-6" Bz), 9.46 (1H, br s, NH). ^{13}C NMR($CDCl_3$) δ 16.2 (Me-5), 63.6 (C-5'), 71.5 (C-3'), 73.3 (C-2'), 79.8 (C-4'), 88.2 (C-1'), 128.4 (C-3" and C-5" Bz), 128.7, 128.8 and 129.6 (C-1" Bz), 129.7[x2], 129.8 (C-2" and C-6" Bz), 133.2, 133.5 and 133.6 (C-4" Bz), 145.4 (C-5), 148.3 (C-4), 155.9 (C-2), 165.2, 165.3 and 166.1 (C-7" Bz). Anal. Calcd for $C_{30}H_{25}N_3O_9$: C, 63.04; H, 4.40; N, 7.35. Found : C, 63.39; H, 4.47; N, 6.92.

1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6-aza-5-propyluracil (**5b**)

The reaction with 6-aza-5-propyluracil (0.775 g) gave **5b** (1.875 g, 62.5%) as a white foam. R_f (system A) : 0.37. MS (CI) *m/z* : 617 MNH_4^+, 600 MH^+. UV λ(EtOH) 266 nm (ε 8474). IR : 3200, 3050(NH), 2950, 2920(CH), 1712-1680(CO), 1600(CN). $[\alpha]_D$: -77.5° (c 0.1, $CHCl_3$). ^{1}H NMR($CDCl_3$) δ 0.95 (3H, t, J = 7.3 Hz, Pr-5 γ-CH_3), 1.67 (2H, sext., J = 7.3 Hz, Pr-5 β-CH_2), 2.40 (2H, 2t, J = 7.3 Hz, Pr-5 α-CH_2), 4.57 (1H, dd, J = 6.3 and 12.8 Hz, H-5'a), 4.71-4.79 (2H, m, H-4' and H-5'b), 5.95 (1H, t, J = 5.7 Hz, H-3'), 6.10 (1H, dd, J = 3.4 and 5.7 Hz, H-2'), 6.57 (1H, d, J = 3.4 Hz, H-1'), 7.39 (6H, m, H-3" and H-5" Bz), 7.55 (3H, m, H-4" Bz), 7.96[x2] and 8.08 (2H each, dd, J = 1.5 and 7.1 Hz, H-2" and H-6" Bz). ^{13}C NMR($CDCl_3$) δ 13.7 (Pr-5γ), 19.4 (Pr-5β), 31.7 (Pr-5α), 64.0 (C-5'), 71.7 (C-3'), 73.4 (C-2'), 79.7 (C-4'), 88.3 (C-1'), 128.4 (C-3" and C-5" Bz), 128.7, 128.8 and 129.5 (C-1" Bz), 129.8[x2], 129.9 (C-2" and C-6" Bz), 133.2, 133.5 and 133.7 (C-4" Bz), 148.1 (C-5), 148.2 (C-4), 155.5 (C-2), 165.2[x2] and 166.1 (C-7" Bz). Anal. Calcd for $C_{32}H_{29}N_3O_9$: C, 64.10; H, 4.87; N, 7.00. Found : C, 64.00; H, 5.04; N, 7.08.

General method for the preparation of 5-alkyl-6-azauridine (**6a,b,c**).

To 1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-5-alkyl-6-azauracil **5a,b** or 1-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-azauracil **5c** (0.25 mmol) in methanol (3.5 ml) was added a methanolic solution of MeONa 1M (0.5 ml, 0.5 mmol). The reaction mixture was stirred at 0°C and was neutralized with Amberlyst H^+ resin (0.5 g). The resin was filtered and the solvent was evaporated to dryness. Water (4 ml) was added to the residue and the precipitate of benzoic acid was separated on 0.22 μm filter (Millipore) for **5a,b**. The solvent was then evaporated under reduced pressure to give the title compounds **6a,b,c**.

6-aza-5-methyluridine (**6a**).

Debenzoylation of 1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6-aza-5-methyluracil **5a** (143 mg) was complete after 3 hours and yielded **6a** (60 mg, 93%). R_f (system B) : 0.54. MS (FAB⁻TG) *m/z* : 258 (M - H)⁻. UV λ(H_20) 260 nm (ε 7087). IR : 3600-3100(OH), 2940, 2800(CH), 1715-1680(CO), 1600(CN). $[\alpha]_D$: -75.8° (c 0.6, H_2O). ^{1}H NMR(CD_3OD) δ 2.17 (3H, s, Me-5), 3.60 (1H, dd, J = 5.5 and 11.9 Hz, H-5'a), 3.75 (1H, dd, J = 3.6 and 11.9 Hz, H-5'b), 3.96 (1H, dt, J = 3.7 and 5.6 Hz, H-4'), 4.27 (1H, t, J = 5.6 Hz, H-3'), 4.43 (1H, dd, J = 3.3 and 5.3 Hz, H-2'), 6.07 (1H, d, J = 3.5 Hz, H-1'). ^{13}C NMR(CD_3OD) δ

16.4 (Me-5), 63.6 (C-5'), 72.1 (C-3'), 74.5 (C-2'), 85.9 (C-4'), 91.6 (C-1'), 145.8 (C-5). Anal. Calcd for $C_9H_{13}N_3O_6$: C, 41.70; H, 5.05; N, 16.21. Found : C, 41.57; H, 5.40; N, 16.07.

6-aza-5-propyluridine (**6b**).

Debenzoylation of 1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6-aza-5-propyluracil **5b** (150 mg) was complete after 3 hours and yielded **6b** (68 mg, 95%). R_f (system B) : 0.66. MS (FAB⁻TG) *m/z* : 286 $(M - H)^-$. UV λ(H_2O) 260 nm (ε 4240). IR : 3600-3100(OH), 2950(CH), 1710-1680(CO), 1600(CN). $[\alpha]_D$:-65° (c 0.68, H_2O). ^1H NMR(CD_3OD) δ 0.98 (3H, t, *J* = 7.4 Hz, Pr-5 γ-CH_3), 1.68 (2H, sext., *J* = 7.4 Hz, Pr-5 β-CH_2), 2.55 (2H, t, *J* = 7.4 Hz, Pr-5 α-CH_2), 3.61 (1H, dd, *J* = 5.6 and 11.8 Hz, H-5'a), 3.75 (1H, dd, *J* = 3.6 and 11.9 Hz, H-5'b), 3.97 (1H, dt, *J* = 3.7 and 5.6 Hz, H-4'), 4.30 (1H, t, *J* = 5.4 Hz, H-3'), 4.41 (1H, dd, *J* = 2.4 and 5.3 Hz, H-2'), 6.13 (1H, d, *J* = 2.4 Hz, H-1'). ^{13}C NMR(CD_3OD) δ 14.1 (Pr-5γ), 20.4 (Pr-5β), 32.8 (Pr-5α), 63.7 (C-5'), 72.2 (C-3'), 74.8 (C-2'), 85.7 (C-4'), 91.8 (C-1'), 148.4 (C-5), 152.8 (C-4), 160.6 (C-2). Anal. Calcd for $C_{11}H_{17}N_3O_6$: C, 45.99; H, 5.96; N, 14.62. Found : C, 45.93; H, 6.24; N, 14.96.

6-azauridine (**6c**).

Deacetylation of 1-(2,3,5-tri-*O*-acetyl-ß-D-ribofuranosyl)-6-azauracil **5c** (93 mg) was complete after 15 minutes and yielded **6c** (57 mg, 95%). R_f (system B) : 0.50. MS (FAB⁻TG) *m/z* : 244 $(M - H)^-$. UV λ(H_2O) 264 nm (ε 5011). ^1H NMR(CD_3OD) δ 3.59 (1H, dd, *J* = 5.5 and 12.0 Hz, H-5'a), 3.73 (1H, dd, *J* = 3.7 and 12.1 Hz, H-5'b), 3.96 (1H, dt, *J* = 3.7 and 5.0 Hz, H-4'), 4.23 (1H, t, *J* = 5.2 Hz, H-3'), 4.42 (1H, dd, *J* = 2.9 and 5.2 Hz, H-2'), 6.08 (1H, d, *J* = 2.9 Hz, H-1'), 7.40 (1H, s, H-5).

General method for the preparation of 5-alkyl-6-aza-5,6-dihydrouridine (7a,c).

5-alkyl-6-azauridine **6a,c** (0.1 mmol) in water/acetic acid (7/1 v/v, 8 ml) was stirred with Adams catalyst PtO_2 (200 mg) under a H_2 pressure (4 bars). The reaction was followed with UV measurements by the disappearance of the 260 nm band. After 3 weeks, the solvent was evaporated under reduced pressure and the residue was applied on silica gel PLC and eluted with system D to give the title compounds **7a,c**.

6-aza-5,6-dihydro-5-methyluridine (**7a**).

The hydrogenation of 6-aza-5-methyluridine **6a** (21 mg) yielded **7a** as a mixture of C-5 epimers 5*R* and 5*S* (15 mg, 70%). R_f (system D) : 0.40. MS (EI) *m/z* : 261 M^+. UV λ(EtOH) 262 nm (ε 269). ^1H NMR(CD_3OD) δ 1.30 (3H, d, *J* = 7.0 Hz, Me-5), 3.60 (1H, dd, *J* = 5.2 and 12.0 Hz, H-5'a), 3.61 (1H, overlapped m, H-5), 3.72 (1H, dd, *J* = 3.8 and 12.0 Hz, H-5'b), 3.87 (1H, dt, *J* = 3.8 and 5.2 Hz, H-4'), 4.12 (1H, t, *J* = 5.2 Hz, H-3'), 4.30 (1H, dd, *J* = 4.2 and 5.3Hz, H-2'), 5.73 (1H, d, *J* = 4.2 Hz, H-1' 5-*S*), 5.76 (1H, d, *J* = 4.2 Hz, H-1' 5-*R*). ^{13}C NMR(CD_3OD) δ 13.2(C-7 5*S*), 55.4(C-5 5*S*), 58.3(C-5 5*R*), 63.6(C-5'), 72.0(C-3'), 73.5(C-2'), 84.9(C-4'), 90.4(C-1'). Anal. Calcd for $C_9H_{15}N_3O_6$: C, 41.38; H, 5.78; N, 16.08. Found : C, 41.15; H, 5.96; N, 15.92.

6-aza-5,6-dihydrouridine (**7c**).

The hydrogenation of 6-azauridine **6c** (24 mg) yielded **7c** (20 mg, 85%). R_f (system E) : 0.70. MS (EI) *m/z* : 247 $M^{+\cdot}$, 133, 115. UV λ(H_2O) 264 nm (ε 300). ^1H NMR(CD_3OD) δ 3.59 (1H, dd, *J* = 5.5 and 12.0 Hz, H-5'a), 3.60 (2H, s, H-5), 3.72 (1H, dd, *J* = 3.7 and 12.1 Hz, H-5'b), 3.85 (1H, dt, *J* = 3.7 and 5.3 Hz, H-4'), 4.13 (1H, t, *J* = 5.3 Hz, H-3'), 4.27 (1H, dd, *J* = 4.0 and 5.3 Hz, H-2'), 5.72 (1H, d, *J* = 4.0 Hz, H-1'). Anal. Calcd for $C_8H_{13}N_3O_6$: C, 38.86; H, 5.30; N, 16.99. Found : C, 38.60; H, 5.49; N, 16.72.

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REFERENCES

1. Robins, R.K. *Chem. Eng. News*, **1986**, *64*, 28.
2. Wierenga, W.; Woltersom, J.A. *J. Org. Chem.*, **1978**, *43*, 529.
3. Skulnick, H. *J. Org. Chem.*,**1978**, *43*, 3188.
4. Depelley, J.; Granet, R.; Krausz, P.; Piekarski, S.; Bosgiraud, C.; Beaussoleil, S. *Nucleosides & Nucleotides*, **1994**, *13*, 1007.
5. Beaussoleil, S.; Bosgiraud, C.; Depelley, J.; Granet, R.; Krausz, P.; Nicolas, J.A., Piekarski, S. French patent N° 9202401.
6. Vorbrüggen, H.; Höfle, G. *Chem. Ber.*, **1981**, *114*, 1256.
7. Vorbrüggen, H.; Bennua, B. *Chem. Ber.*, **1981**, *114*, 1279.
8. Vorbruggen, H.; Krolikiewicz, K.; Bennua, B. *Chem. Ber.*, **1981**, *114*, 1234.
9. Granet, R.; Piekarski, S. *C.R. Acad. Sci., Paris Série C*, **1975**, *280*, 585.
10. Gut, J.; Prystas, M.; Jonas, J.; Sorm, F. *Coll. Czech. Chem. Comm.*, **1961**, *26*, 974.
11. Fox, J.J.; Wempen, I. *Adv. Carbohydr. Chem.*,**1959**, *14*, 283.
12. Ferris, J.P.; Singh, S.; Newton, T.A. *J. Org. Chem.*, **1979**, *44*, 173.
13. Chavis, C.; De Gourcy, C.; Imbach, J.L. *Carbohydr. Res.*, **1984**, *135*,13.
14. Kelley, J.A.; Driscoll, J.S.; McCormack, J.J.; Roth, J.S.; Marquez, V.E. *J. Med. Chem.*, **1986**, *29*, 2351.
15. Karplus, M. *J. Am. Chem. Soc.*, **1963**, *85*, 2870.
16. Niedballa, U.; Vorbruggen, H. *J. Org. Chem.*, **1974**, *39*, 3654.
17. Maudet, D.; Granet, R.; Piekarski, S. *Bull. Soc. Chim.*, **1975**, *11-12*, 2696.
18. Freifelder, W.; Martin, W.B.; Stone, G.R.; Coffin, E.L. *J. Am. Chem. Soc.* ,**1961**, *26*, 383.
19. Skaric, V.; Gaspert, B.; Hohnjec, M. *J. Chem. Soc. (C)*, **1970**, 2444.
20. Skaric, V.; Gaspert, B.; Hohnjec, M. ; Lacan, G. *J. Chem. Soc. Perkin I*, **1974**, 267.
21. Borch, R.F.; Bernstein, M.D.; Dupont Durst, H. *J. Am. Chem. Soc.*, **1971**, *93*, 2897.

22. Ege, S.N.; Carter, M.L.C.; Ortwine, D.F.; Chou, S.S.P.; Richman, J.F. *J. Chem. Soc. Perkin I*, **1977**,1252.

23. Jonas, J.; Gut, J. *Coll. Czech. Chem. Comm.*, **1961**, *26*, 2155.

24. Pavwels, R.; Balzarini, J.; Baba, J.; Snoeck, M.; Schols, R.; Herdewyn, P.; Desmyster, J.; DeClercq, E. *J. Virological Methods*, **1988**, *20*, 309.

25. Delebassée, S.; Bosgiraud, C. To be published.

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