PREPARATION OF 5-BENZYLURACIL AND 5-BENZYLCYTOSINE NUCLEOSIDES AS POTENTIAL INHIBITORS OF URIDINE PHOSPHORYLASE

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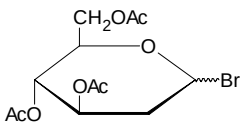
Reaction of 3,4,6-tri-*O*-acetyl-2-deoxyglucopyranosyl bromide (**1**) with silylated 5-benzyluracil and subsequent ammonolysis afforded α- and β-anomers of 5-benzyl-1-(2-deoxy-D-glucopyranosyl)uracil (**2** and **3**). Under catalysis with tin tetrachloride, silylated 5-benzyluracil reacted with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose to give 2′,3′,5′-tri-*O*-benzoyl-5-benzyluridine (**10**), which was converted into the 4-thio derivative **11** by reaction with Lawesson reagent. Debenzoylation of compound **11** afforded 5-benzyl-4-thiouridine (**12**), whereas its reaction with methyl iodide and deblocking gave 4-methylthiopyrimidine nucleoside **14**. Amonolysis of derivative **12** at elevated temperature afforded 5-benzylcytidine (**15**). This reacted with thionyl chloride at room temperature to give cyclic sulfite **16** which on heating at 100 °C in dimethylformamide was converted into 5-benzyl-2, 2′-cyclocytidine (**17**). Mild alkaline hydrolysis of compound **17** afforded 1-(β-D-arabinofuranosyl)-5-benzylcytosine (**18**). With boiling thionyl chloride, compound **15** formed 2′,3′-cyclic sulfite **19** which on alkaline hydrolysis gave 5-benzyl-5′-chloro-5′-deoxycytidine (**20**). Compound **20** was reduced with tributylstannane to 5-benzyl-5′-deoxycytidine (**21**). Reaction of silylated 5-benzyluracil with 2-deoxy-3,5-bis(*O*-*p*-toluoyl)-D-ribofuranosyl chloride, catalyzed with mercury(II) bromide, afforded 5-benzyl-2′-deoxy-3′,5′-bis(*O*-*p*-toluoyl)uridine (**22**) and its α-anomer **23**. With Lawesson reagent, compound **22** gave 5-benzyl-4-thiouracil derivative **24** which was ammonolyzed to give 5-benzyl-2′-deoxycytidine (**25**). Analogously, compound **23** was converted into 5-benzyl-2-deoxy-α-cytidine (**27**). 5′-*O*-Benzoyl-5-benzyluridine (**29**) was converted into the 2, 2′-anhydro derivative **30** which on reaction with hydrogen chloride afforded 3′-chloro-3′-deoxynucleoside **31**. This compound was reduced with tributylstannane and the obtained 2′-deoxynucleoside **32** on treatment with thionyl chloride gave a mixture of *erythro*- and *threo*-3′-chloro-2′,3′-dideoxynucleosides (**33** and **34**, respectively) which were reduced to 5′-*O*-benzoyl-5-benzyl-2′,3′-dideoxyuridine (**35**). Compound **35** reacted with Lawesson reagent under formation of 4-thiouracil derivative **36** and this was deblocked to 5-benzyl-4-thio-2′,3′-dideoxyuridine (**37**). On heating with ammonia, compound **37** was converted into 5-benzyl-2′,3′-dideoxycytidine (**38**). Reaction of 4-thiouracil derivative with methyl iodide and subsequent hydrazinolysis afforded 4-hydrazino derivative **40** which was heated with silver oxide in ethanol to give a mixture of anomeric 5-benzyl-1-(2,3-dideoxyribofuranosyl)-2(1*H*)-pyrimidinones (**42**).
Key words: 5-Benzyluracil; Pyrimidine; Nucleosides; Uridine phosphorylase.

In connection with our studies of uridine phosphorylase inhibitors we focused our attention on the preparation of some hitherto undescribed nucleosides derived from 5-benzyl-

uracil and 5-benzylcytosine. As shown by previous investigations in other laboratories, potent inhibitors have been found particularly among acyclic derivatives of 5-benzyluracil or 5-(3-benzyloxy)benzyluracil and also the 2,2′-anhydro derivatives of nucleoside analogs[1–5]. On the other hand, some 5-benzyluracil nucleosides (riboside, arabinoside, 2′-deoxyriboside amd 2′-bromo-2′-deoxyriboside) proved to be inactive[5]. Recently, a series of 5-benzyluracil nucleosides was prepared (e.g. 2′,3′-dideoxy-, 3′-azido-2′,3′-dideoxy- and 2′-deoxy-2′-fluoroarabinosyl derivatives[6,7]) which were studied as cytostatics or antivirals; however, their effect on uridine phosphorylase was not described. Save for several exceptions, no 5-benzylcytosine nucleosides have been prepared so far.

We considered it interesting to prepare particularly the 2′-deoxyglucopyranose derivative of 5-benzyluracil as a compound analogous to the so-called TdG, i.e. 1-(2-deoxy-β-D-glucopyranosyl)thymine[1,8] which represents one of the most effective



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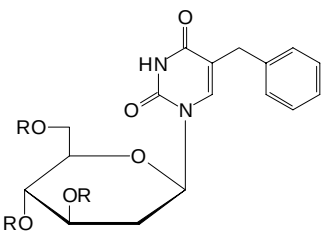
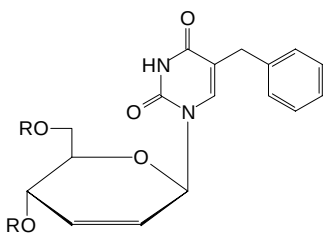
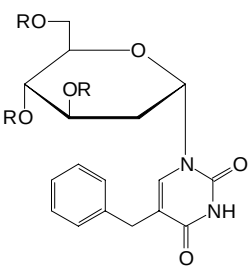


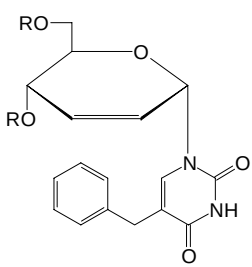
	R
2	Ac
6	H



	R
4	Ac
8	H



	R
3	Ac
7	H



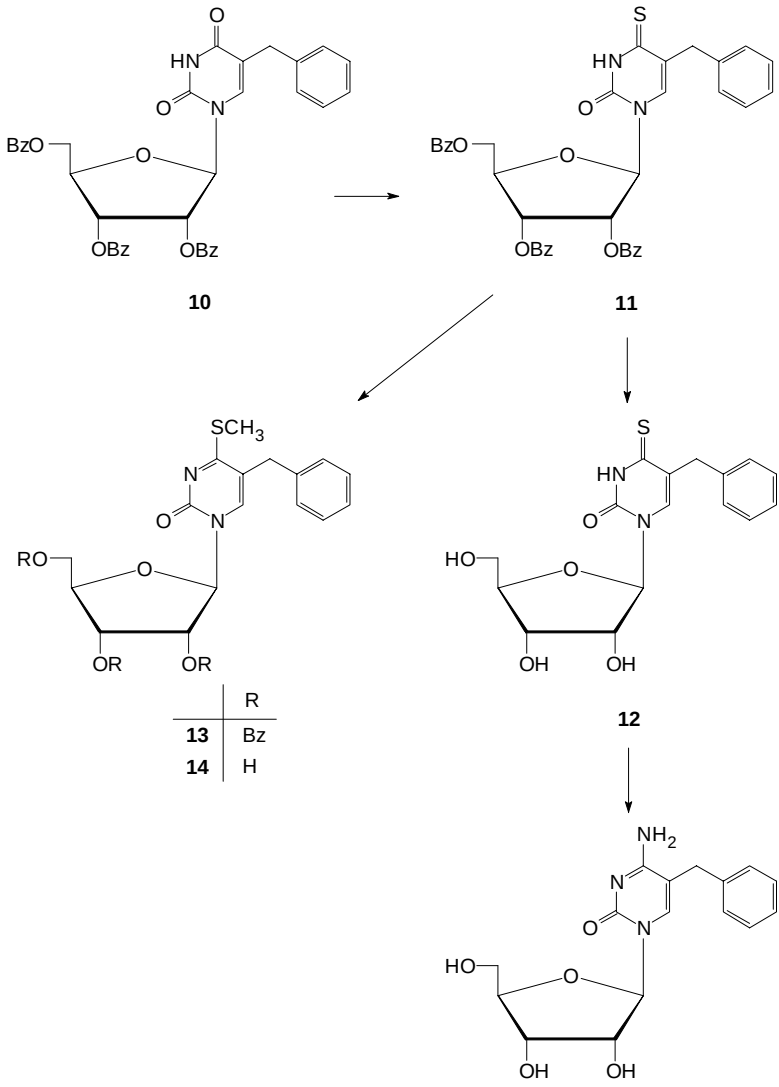
	R
5	Ac
9	H

uridine phosphorylase inhibitors. As the starting compound we have chosen 3,4,6-tri-*O*-acetyl-2-deoxyglucopyranosyl bromide (**1**), prepared by addition of hydrogen bromide to tri-*O*-acetyl-D-glucal[9]. The nucleosidation reaction of the 1-bromohexose **1** with silylated 5-benzyluracil was performed in acetonitrile under catalysis with trimethylsilyl triflate. As expected, the reaction gave both anomers of 5-benzyl-1-(2-deoxy-D-glucopyranosyl)uracil (**2** and **3**), the α-anomer predominating in the ratio of about 2 : 1, and didehydro derivatives **4** and **5**. Both anomers of the desired 2′-deoxynucleosides, as well as both the didehydro derivatives, differed only slightly in their chromatographic mobilities. In the case of acetylated nucleosides, the only pure product obtained was the α-anomer **3** which was deacetylated to give the free 2′-deoxyglucopyranosyl derivative **7**. To some extent, the nucleosidation was also accompanied by elimination leading to two 2′,3′-didehydro derivatives **4** and **5** which contaminated the acetylated β-anomer **2**. Only after deacetylation of this mixture of acetyl derivatives **2**, **4** and **5** with methanolic ammonia it was possible to separate chromatographically the individual products and to obtain 5-benzyl-1-(2-deoxy-β-D-glucopyranosyl)uracil (**6**) along with small amounts of the free didehydro derivatives **8** and **9**.

Nucleosidation reaction of silylated 5-benzyluracil with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose in 1, 2-dichloroethane, catalyzed with tin tetrachloride, afforded 2′,3′,5′-tri-*O*-benzoyl-5-benzyluridine (**10**) which was subsequently converted into 2′,3′,5′-tri-*O*-benzoyl-5-benzyl-4-thiouridine (**11**) by reaction with Lawesson reagent. The 4-thio derivative **11** was debenzoylated with methanolic ammonia to give free 5-benzyl-4-thiouridine (**12**). It was also converted into the protected 4-methylthio derivative **13** by reaction with methyl iodide in dimethylformamide. Compound **13** was methanolyzed to give free 1-(β-D-ribofuranosyl)-5-benzyl-4-methylthiopyrimidin-2-one (**14**). Reaction of the free 4-thiouridine derivative **12** with ammonia at elevated temperature in an autoclave gave 5-benzylcytidine (**15**) (Scheme 1).

5-Benzylcytidine was converted into other 5-benzylcytosine nucleosides as described below. Its reaction with thionyl chloride at ambient temperature gave cyclic sulfite **16** which on heating in dimethylformamide at 100 °C was quantitatively converted into 5-benzyl-2,2′-cyclocytidine (**17**). In an aqueous medium, treatment with an alkaline reagent such as potassium carbonate or Dowex 1 in the carbonate form resulted in fission of the anhydro bond in compound **17** under formation of 1-(β-D-arabinofuranosyl)-5-benzylcytosine (**18**), an analog of the known cytostatic araC. When the reaction of 5-benzylcytidine with thionyl chloride was performed at reflux, we isolated 2′,3′-cyclic sulfite **19** containing a chlorine atom in position 5′. This compound was hydrolyzed with a solution of potassium carbonate to give 5-benzyl-5′-chloro-5′-deoxycytidine (**20**) which was reduced with tributylstannane in a mixture of dimethyl sulfoxide and dioxane to 5-benzyl-5′-deoxycytidine (**21**). A similar sequence of reactions was used already earlier in the preparation of some analogs of unsubstituted cytosine nucleosides[10] (Scheme 2).

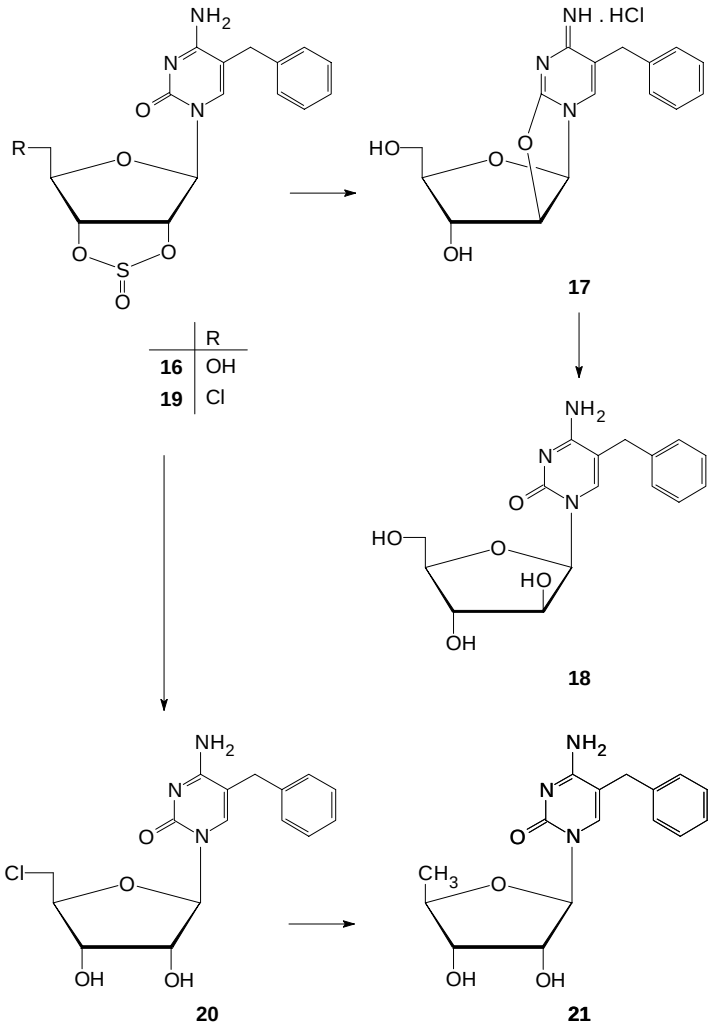
The preparation of 2′-deoxyribosides of 5-benzylcytosine consisted in the transformation of the corresponding uracil nucleosides via the 4-thiouracil derivatives. The nucleosidation reaction of silylated 5-benzyluracil with 2-deoxy-3,5-bis(*O*-*p*-toluoyl)-D-ribofuranosyl chloride was performed in acetonitrile in the presence of molecular sieves, with mercury(II) bromide as catalyst. This method is described[11] as very advantageous particularly for the preparation of 5-alkyl-2′-deoxyuridines because it gives



	R
13	Bz
14	H

SCHEME 1

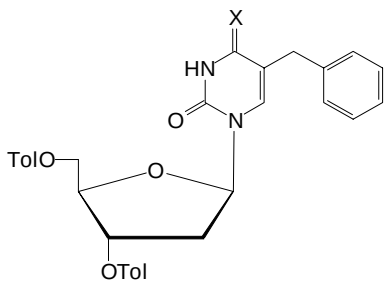
predominantly the β-anomers which, moreover, are easily isolable from the reaction mixture by crystallization. In our case, the β : α ratio (**22** : **23**) was 2 : 1, with high total yield of the nucleosidation reaction (88%). The obtained 5-benzyl-2′-deoxy-3′,5′-bis(*O*-*p*-toluoyl)uridine (**22**) was treated with Lawesson reagent in 1,2-dichloroethane to give 5-benzyl-4-thiouracil derivative **24** which, without purification, was deblocked with ammonia at room temperature and then further heated with ammonia in an autoclave under formation of 5-benzyl-2′-deoxycytidine (**25**). The same reaction course was used in the conversion of the protected α-anomer **23** into the 4-thio derivative **26** and then



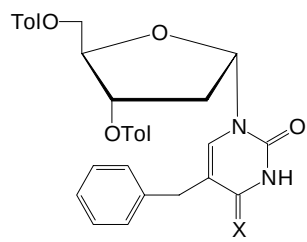
SCHEME 2

into 5-benzyl-1-(2-deoxy-α-D-ribofuranosyl)cytosine (5-benzyl-2-deoxy-α-cytidine) (**27**).

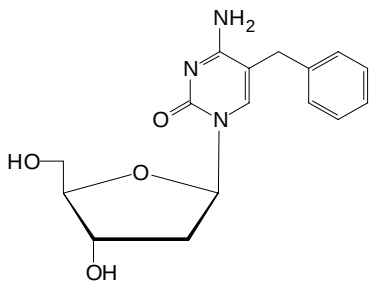
Another synthesized group of 5-benzylpyrimidine nucleoside derivatives prepared in this context were 2′,3′-dideoxynucleosides. So far, only one representative, 5-benzyl-2′,3′-dideoxyuridine, has been described[6]. Our synthesis started from 5′-*O*-benzoyl-5-benzyluridine (**29**) which was converted into 2′-chloro-2′-deoxynucleoside **31** via 2,2′-anhydronucleoside **30**. Compound **31** was reduced with tributylstannane and the obtained 2′-deoxyribonucleoside **32** was treated with thionyl chloride to give a mixture of *erythro*- and *threo*-3′-chloro-3′-deoxy derivatives **33** and **34**, respectively. Reductive dehalogenation with tributylstannane converted both the compounds **33** and **34** into 5′-*O*-benzoyl-5-benzyl-2′,3′-dideoxyuridine (**35**). This on reaction with Lawesson reagent afforded the 4-thiouracil derivative **36** which was deblocked to free 5-benzyl-4-thio-2′,3′-dideoxyuridine (**37**). Compound **37** on heating with ammonia gave 5-benzyl-2′,3′-dideoxycytidine (**38**). Using reactions generally used for transformation of uracil nucleosides into pyrimidinone derivatives[12], we converted the 4-thiouracil derivative **36** into 2′,3′-dideoxynucleosides derived from 5-benzyl-2-pyrimidinone: reaction with



	X
22	O
24	S



	X
23	O
26	S



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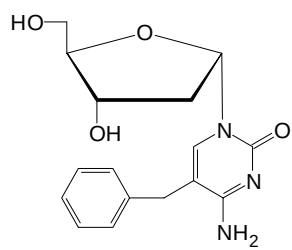

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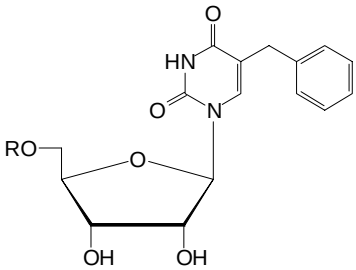
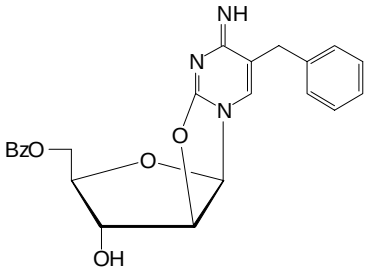


	R
28	H
29	Bz



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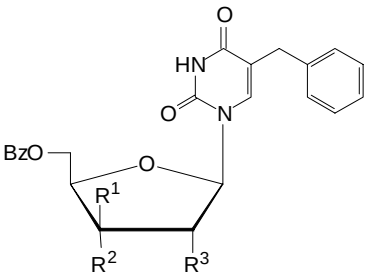
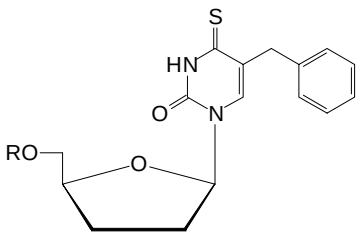
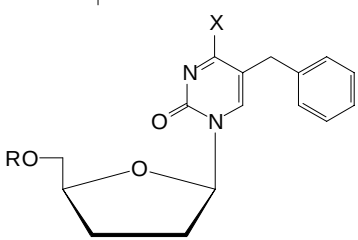


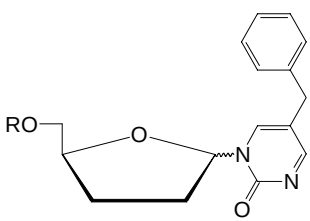
	R^1	R^2	R^3
31	H	OH	Cl
32	H	OH	H
33	H	Cl	H
34	Cl	H	H
35	H	H	H



	R
36	Bz
37	H



	X	R
38	NH_2	H
39	SCH_3	Bz
40	$NHNH_2$	Bz
43	$NHN{=}C(CH_3)_2$	Bz
44	$NHN{=}C(CH_3)_2$	H



	R
41	Bz
42	H

methyl iodide in dimethylformamide gave 4-methylthiopyrimidine **39** which on heating with hydrazine afforded 4-hydrazino derivative **40**. This was treated with silver oxide in ethanol[12] and the obtained intermediate **41** was deprotected to give 5-benzyl-1-(2,3-dideoxyribofuranosyl)-2(1*H*)-pyrimidinone (**42**).

The reaction with silver oxide was accompanied with anomerization of the nucleoside bond and both the compound **41** and the free pyrimidinone derivative **42** were obtained only as chromatographically inseparable mixture of anomers with the β : α anomer ratio of about 3 : 1. On the other hand, the dimethylhydrazone **43** (prepared by reaction of hydrazino derivative **40** with acetone) and the free nucleoside **44** (prepared from **43** by methanolysis) were pure β-anomers. Consequently, the mentioned anomerization took place only in the reaction with silver oxide and not already during the preparation of the hydrazino derivative **40**.

All the described free 5-benzyl derivatives were tested on cell cultures L1210, HeLa and L929 for cytostatic activity. Neither of them exhibited marked inhibitory effect on the cell growth. On the other hand, some of the compounds are effective inhibitors of uridine phosphorylase and their study will be described elsewhere[13].

EXPERIMENTAL

Unless stated otherwise, the solutions were evaporated at 40 °C/2 kPa and the compounds were dried over phosphorus pentoxide at 13 Pa. Thin-layer chromatography was performed on Silufol UV 254 foils (Kavalier, Czech Republic) in the systems S1, toluene–acetone 4 : 1; S2, toluene–acetone 3 : 1; S3, toluene–acetone 3 : 2; S4, toluene–ethyl acetate 6 : 1; S5, toluene–ethyl acetate 1 : 1; S6, ethyl acetate; S7, ethyl acetate–acetone–ethanol–water 18 : 3 : 1 : 1; S8, ethyl acetate–acetone–ethanol–water 18 : 3 : 2 : 2 . Spots were detected by UV light at 254 nm. Preparative column chromatography was carried out on silica gel (30–60 μm, Service Laboratory of the Institute) or Silpearl (Kavalier, Czech Republic). ^{1}H NMR spectra (δ, ppm; *J*, Hz) were measured on Varian UNITY 200 (200.01 MHz) or Varian UNITY 500 (499.8 MHz) spectrometers in hexadeuteriodimethyl sulfoxide with tetramethylsilane as internal standard. Mass spectra were obtained with a ZAB-EQ spectrometer (VG Analytical) using the FAB method (Xe, 8 kV, glycerol (G) or thioglycerol (TG) as matrices).

Reaction of 3,4,6-Tri-*O*-acetyl-2-deoxy-D-*arabino*-hexopyranosyl Bromide (**1**) with Silylated 5-Benzyluracil

Tri-*O*-acetyl-D-glucal (2.45 g, 9 mmol) was codistilled with toluene (2 × 20 ml) and then again dissolved in toluene (10 ml). The solution was saturated with gaseous hydrogen bromide at 0 °C for 45 min, the solvent was evaporated, the residue (compound **1**) was codistilled with toluene (3 × 20 ml) and dried in vacuo at room temperature for 1 h.

A mixture of 5-benzyluracil (2.02 g, 10 mmol), hexamethyldisilazane (30 ml) and a catalytic amount of ammonium sulfate was heated at 150 °C for 4 h (after 1 h the silylated base dissolved). After cooling, the solution was concentrated, the residue was codistilled with xylene (3 × 30 ml) and then dissolved in acetonitrile (20 ml). This solution was added to the 1-bromohexose **1** prepared above. The mixture was cooled to 0 °C, trimethylsilyl trifluoromethanesulfonate (2.2 ml, 12 mmol) was added and the solution was stirred at 0 °C for 30 min and at room temperature for 15 min. The mixture was poured into saturated solution of sodium hydrogen carbonate (250 ml) and the products

were extracted with ethyl acetate. The organic phase was dried over magnesium sulfate and the solvent evaporated. Chromatography of the residue on silica gel (500 ml) in system S2 afforded 1.4 g of a mixture containing compounds **2**, **4** and **5** (R_F 0.24). Further elution gave 1-(3,4,6-tri-*O*-acetyl-2-deoxy-α-D-*arabino*-hexopyranosyl)-5-benzyluracil (**3**), yield 1.60 g (38%), amorphous compound. For $C_{23}H_{26}N_2O_9$ (474.5) calculated: 58.22% C, 5.52% H, 5.90% N; found: 58.47% C, 5.51% H, 5.81% N. Mass spectrum (FAB; T + G, chloroform): 475.2 (M + H). ^{1}H NMR spectrum: 1.995 s, 3 H, 2.075 s, 3 H and 2.08 s, 3 H (3 × acetyl); 2.00 dt, 1 H, *J*(2′a,1′) ≈ *J*(2′a,3′) = 3.9, *J*(gem) = 14.2 (H-2′a); 2.48 ddd, 1 H, *J*(2′b,3′) = 3.9, *J*(2′b,1′) = 10.0 (H-2′b); 3.58 s, 2 H (CH_2); 4.20–4.26 m, 2 H (H-5′ and H-6′a); 4.36 dd, 1 H, *J*(6′b,5′) = 6.1, *J*(gem) = 11.5 (H-6′b); 4.76 t, 1 H, *J*(4′,3′) = 4.1, *J*(4′,5′) = 3.9 (H-4′); 5.16 br q, 1 H, (H-3′); 5.96 dd, 1 H, *J*(1′,2′a) = 3.7, *J*(1′,2′b) = 10.0 (H-1′); 7.10–7.30 m, 5 H (H arom); 7.61 s, 1 H (H-6); 11.44 s, 1 H (NH).

5-Benzyl-1-(2-deoxy-β-D-*arabino*-hexopyranosyl)uracil (**6**)

The mixture of acetates **2**, **4** and **5** (1.4 g), obtained in the above experiment, was stirred with methanolic ammonia at room temperature for 2 days. Evaporation of the solvent and chromatography of the residue on silica gel (200 ml) in system S7 gave as principal product 2′-deoxynucleoside **6** (R_F 0.30). The amorphous residue of the product **6** was dissolved in ethyl acetate–ether (1 : 1) and set aside in a refrigerator overnight. The deposited compound was collected and dried in vacuo, yield 650 mg (21% from compound **1**). Mass spectrum (FAB, G + dimethyl sulfoxide): 349.2 (M + H). ^{1}H NMR spectrum: 1.75 dt, 1 H, *J*(2′a,1′) ≈ *J*(2′a,3′) ≈ 11.4, *J*(gem) = 12.4 (H-2′a); 1.96 ddd, 1 H, *J*(2′b,1′) = 2.2, *J*(2′b,3′) = 4.9 (H-2′b); 3.08 td, 1 H, *J*(4′,3′) = 9.0, *J*(4′,OH) = 5.4, *J*(4′,5′) = 9.5 (H-4′); 3.25 ddd, 1 H, *J*(5′, 6′b) = 2.0, *J*(5′,6′a) = 5.9 (H-5′); 3.47 br pent, 1 H, *J*(6′a,OH) = 6.0, *J*(gem) = 12.0 (H-6′a); 3.56 br s, 2 H (CH_2); 3.52–3.60 m, 1 H (H-3′); 3.70 ddd, 1 H, *J*(6′b,OH) = 5.4 (H-6′b); 4.56 br t, 1 H (6′-OH); 5.05 d, 1 H (4′-OH); 5.13 d, 1 H, *J*(OH,3′) = 4.4 (3′-OH); 5.61 dd, 1 H, *J*(1′,2′a) = 11.2, *J*(1′,2′b) = 2.2 (H-1′); 7.15–7.30 m, 5 H (H arom.); 7.78 s, 1 H (H-6); 11.40 br, 1 H (NH).

Further chromatography afforded:

*5-Benzyl-1-(2,3-dideoxy-*β*-D-erythro-hex-2-enopyranosyl)uracil* (**8**); yield 120 mg (4% from compound **1**), amorphous compound, R_F 0.50 (S7). ^{1}H NMR spectrum: 3.45–3.50 m, 2 H and 3.65–3.69 m, 1 H (H-5′ and H-6′); 3.55 s, 2 H (CH_2); 3.96 m, 1 H, *J*(4′,5′) = 8.3 (H-4′); 4.77 t, 1 H, *J*(OH,6′) = 5.6 (6′-OH); 5.34 d, 1 H, *J*(OH,4′) = 6.8 (4′-OH); 5.66 dt, 1 H, *J* = 1.7, 2.0 and *J*(3′,2′) = 10.2 (H-3′); 6.08 dt, 1 H, *J* = 2.0, 2.0 and *J*(2′,3′) = 10.2 (H-2′); 6.26 br q, 1 H, *J* = 2.1 (H-1′); 7.15–7.30 m, 6 H (H arom. and H-6); 11.42 br s, 1 H (NH).

*5-Benzyl-1-(2,3-dideoxy-*α*-D-erythro-hex-2-enopyranosyl)uracil* (**9**); yield 130 mg (4.4% from compound **1**), amorphous compound, R_F 0.45 (S7). ^{1}H NMR spectrum: 3.34 ddd, 1 H, *J* = 2.2, 5.8 and 8.0 (H-5′); 3.47 pent, 1 H, *J* = 5.8, 5.8 and 12.0 (H-6′a); 3.52 s, 2 H (CH_2); 3.62 ddd, 1 H, *J* = 2.2, 5.4 and 12.0 (H-6′b); 3.90 q, 1 H (H-4′); 4.17 t, 1 H, *J*(OH,6′) = 5.8 (6′-OH); 5.20 d, 1 H, *J*(OH,4′) = 7.6 (4′-OH); 5.77 ddd, 1 H, *J*(3′,4′) = 2.0, *J*(3′,2′) = 10.2 (H-3′); 6.18 dt, 1 H, *J*(1′,2′) = *J*(1′,4′) = 2.2, *J*(1′,3′) = 3.0 (H-1′); 6.23 dt, 1 H, *J*(2′,4′) = 2.0 (H-2′); 7.17 t, 1 H, 7.21 d, 2 H and 7.26 t, 2 H (H arom.); 7.63 s, 1 H (H-6); 11.45 br s, 1 H (NH).

5-Benzyl-1-(2-deoxy-α-D-*arabino*-hexopyranosyl)uracil (**7**)

A solution of compound **3** (1.4 g, 2.95 mmol) in methanolic ammonia (100 ml) was stirred at room temperature for 2 days. Evaporation of the solvent, followed by chromatography on silica gel (100 ml) in system S7, afforded 700 mg (68%) of colorless amorphous compound **7** (R_F 0.30). Mass spectrum (FAB; T + G, methanol): 349.2 (M + H). ^{1}H NMR spectrum: 1.65 dt, 1 H, *J*(2′a,1′) = *J*(2′a,3′) = 3.6, *J*(gem) = 13.4 (H-2′a); 2.21 ddd, 1 H, *J*(2′b,3′) = 3.4, *J*(2′b,1′) = 10.0 (H-2′b); 3.38 m, 1 H (H-4′); 3.57 s, 2 H (CH_2); 3.54–3.60 m, 1 H (H-6′a); 3.74–3.79 m, 2 H (H-6′b and H-5′); 3.86 br pent, 1 H (H-3′); 4.61 t,

1 H, *J*(OH,6′) = 5.3 (6′-OH); 5.06 d, 1 H, *J*(OH,4′) = 5.4 (4′-OH); 5.22 d, 1 H, *J*(OH,3′) = 3.6 (3′-OH); 5.98 dd, 1 H (H-1′); 7.15–7.30 m, 5 H (H arom.); 7.70 s, 1 H (H-6); 11.25 br s, 1 H (NH).

2′,3′,5′-Tri-*O*-benzoyl-5-benzyluridine (**10**)

5-Benzyluracil (3.03 g, 15 mmol) was silylated as described for the preparation of compound **2**. A solution of 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribose (6.56 g, 13 mmol) in 1, 2-dichloroethane (50 ml) was added to the silylated base, followed by tin tetrachloride (3.5 ml, 30 mmol). After stirring for 2 h at room temperature, the reaction mixture was diluted with chloroform (1 000 ml) and poured into saturated solution of sodium hydrogen carbonate (500 ml). The mixture was shaken and filtered through Celite. The organic layer was separated, again washed with sodium hydrogen carbonate (3 × 250 ml) and dried over magnesium sulfate. Evaporation of the solvent afforded compound **10** (8.4 g, 100%) as white foam, chromatographically homogeneous (R_F 0.34, S1). To obtain an analytically pure sample, a part (200 mg) of the product was chromatographed on silica gel in system S1. For $C_{37}H_{30}N_20_9$ (646.7) calculated: 68.72% C, 4.68% H, 4.33% N; found: 68.51% C, 4.76% H, 4.37% N.

2′,3′,5′-Tri-*O*-benzoyl-5-benzyl-4-thiouridine (**11**)

Lawesson reagent (3.24 g, 8.0 mmol) was added to a solution of compound **10** (8.2 g, 12.7 mmol) in 1,2-dichloroethane (150 ml) and the mixture was refluxed under argon for 8 h. After cooling, the solution was chromatographed on a column of silica gel (750 ml) in system S4 (R_F: **11**, 0.42; **10**, 0.11). Yield 6.82 g (81%) of yellow foam. For $C_{37}H_{30}N_2O_8S$ (662.7) calculated: 67.06% C, 4.56% H, 4.23% N, 4.84% S; found: 66.78% C, 4.59% H, 3.81% N, 5.27% S. ^{1}H NMR spectrum: 3.71 d, 1 H and 3.82 d, 1 H, *J*(gem) = 14.9 (CH_2); 4.63 dd, 1 H, *J*(5′a,4′) = 5.6, *J*(gem) = 12.0 (H- 5′a); 4.68 dd, 1 H, *J*(5′b,4′) = 3.8 (H-5′b); 4.78 td, 1 H, *J*(4′,3′) = 5.6 (H-4′); 5.97 br t, 1 H (H-3′); 6.03 dd, 1 H, *J*(2′,1′) = 4.2, *J*(2′,3′) = 6.3 (H-2′); 6.20 d, 1 H (H-1′); 7.10–7.30 m, 5 H, 7.42–7.50 m, 6 H, 7.64 t, 3 H, 7.90 2 × d, 4 H and 8.03 d, 2 H (H arom.); 7.84 s, 1 H (H-6); 12.93 br s, 1 H (NH).

5-Benzyl-4-thiouridine (**12**)

Benzoyl derivative **11** (6.6 g, 9.96 mmol) in methanolic ammonia (100 ml) was stirred at room temperature for 72 h. Evaporation of the solvent and chromatography on silica gel in ethyl acetate afforded 2.99 g (86%) of yellow foam (R_F 0.33, S6). For $C_{16}H_{18}N_2O_5S$ (350.4) calculated: 54.85% C, 5.18% H, 7.99% N, 9.15% S; found: 54.58% C, 5.26% H, 7.88% N, 9.00% S. ^{1}H NMR spectrum: 3.51 br ddd, 1 H, *J* = 3.7, 3.9 and 12.2, decoupling OH: dd, *J*(5′a,4′) = 3.2 (H-5′a); 3.64 br ddd, 1 H, *J* = 3.6, 4.2 and 12.2, decoupling OH: dd, *J*(5′b,4′) = 3.2, *J*(gem) = 12.2 (H-5′b); 3.79 d, 1 H and 3.83 d, 1 H, *J*(gem) = 14.9 (CH_2); 3.87 dt, 1 H, *J*(4′,5′a) = *J*(4′,5′b) = 3.2, *J*(4′,3′) = 4.9 (H-4′); 3.96 br q, 1 H, decoupling OH: *J*(3′,4′) = 4.9 (H-3′); 4.04 br q, 1 H, decoupling OH: *J*(2′,3′) = 4.6 (H-2′); 5.10 d, 1 H, *J*(OH,3′) = 5.4 (3′-OH); 5.16 t, 1 H, *J*(OH,5′) = 5.0 (5′-OH); 5.48 d, 1 H, *J*(OH,2′) = 5.4 (2′-OH); 5.74 d, 1 H, *J*(1′,2′) = 4.4 (H-1′); 7.18 m, 1 H, 7.25 s, 2 H and 7.26 s, 2 H (H arom.); 8.03 s, 1 H (H-6); 12.30 br, 1 H (NH).

2′,3′,5′-Tri-*O*-benzoyl-5-benzyl-4-methylthiopyrimidine (**13**)

Finely ground potassium carbonate (100 mg) and methyl iodide (0.5 ml, 8 mmol) were added to a solution of the 4-thio derivative **11** (1.56 g, 2.35 mmol) in dimethylformamide (4 ml). The mixture was stirred at room temperature for 2 h, filtered and the filtrate was concentrated. The residue was partitioned between water and ethyl acetate (150 ml each), the organic layer was dried over magnesium sulfate and the solvent evaporated. The residue was chromatographed on silica gel (220 ml) in

system S1 (R_F: **13**, 0.15; **11**, 0.60) to give 1.0 g (63%) of white foam. For $C_{38}H_{32}N_2O_8S$ (676.8) calculated: 67.44% C, 4.77% H, 4.14% N, 4.74% S; found: 67.45% C, 4.69% H, 4.11% N, 4.68% S. ^{1}H NMR spectrum: 2.40 s, 3 H (CH_3); 3.65 and 3.69 2 × d, 2 H, *J*(gem) = 14.1 (CH_2); 4.65 dd, 1 H, *J*(5′a,4′) = 5.4, *J*(gem) = 12.2 (H-5′a); 4.72 dd, 1 H, *J*(5′b,4′) = 3.7 (H-5′b); 4.82 td, 1 H, *J*(4′,3′) = 6.1 (H-4′); 6.00 br t, 1 H, *J*(3′,2′) = 6.3 (H-3′); 6.03 dd, 1 H, *J*(2′,1′) = 3.8 (H-2′); 6.24 d, 1 H (H-1′); 7.16–7.28 m, 5 H, 7.42–7.48 m, 6 H, 7.60–7.67 m, 3 H, 7.88–7.92 m, 4 H and 7.99 m, 2 H (H arom.); 7.97 s, 1 H (H-6).

5-Benzyl-4-methylthiouridine (**14**)

A solution of benzoyl derivative **13** (760 mg, 1.12 mmol) in methanolic 0.1 M sodium methoxide (35 ml) was allowed to stand at room temperature for 4 h. The solution was neutralized with Dowex 50 (H^+ form), filtered and the filtrate was taken down. Crystallization of the residue from system S7 afforded compound **14** (100 mg), m.p. 155.5–157 °C. Another portion of the product was obtained by chromatography of the mother liquors on silica gel in system S7 (R_F 0.42); total yield 260 mg (64%). For $C_{17}H_{20}N_2O_5S$ (364.4) calculated: 56.03% C, 5.53% H, 7.69% N, 8.80% S; found: 56.23% C, 5.47% H, 7.71% N, 8.69% S. ^{1}H NMR spectrum: 2.36 s, 3 H (CH_3); 3.56 ddd, 1 H, *J*(5′a,4′) = 2.9, *J*(5′a,OH) = 4.9, *J*(gem) = 12.2 (H-5′a); 3.69 d, 1 H and 3.73 d, 1 H, *J*(gem) = 15.9 (CH_2); 3.75 ddd, 1 H, *J*(5′b,4′) = 2.9, *J*(5′b,OH) = 4.9 (H-5′b); 3.91 dt, 1 H, *J*(4′,3′) = 6.1 (H-4′); 3.97 br q, 1 H (H-3′); 3.995 m, 1 H (H-2′); 5.07 d, 1 H, *J*(OH,3′) = 5.9 (3′-OH); 5.22 t, 1 H, *J*(OH,5′) = 4.9 (5′-OH); 5.56 d, 1 H, *J*(OH, 2′) = 4.6 (2′-OH); 5.74 d, 1 H, *J*(1′,2′) = 2.7 (H-1′); 7.16–7.22 m, 3 H and 7.26–7.32 m, 2 H (H arom.); 8.29 s, 1 H (H-6).

5-Benzylcytidine (**15**)

5-Benzyl-4-thiouridine (**12**; 3.2 g, 9.1 mmol) was heated with methanolic ammonia (200 ml) at 120 °C for 1 h in an autoclave. After cooling, the solvent was evaporated, the residue was chromatographed on silica gel (500 ml) in system S8 (R_F 0.25) and the product was crystallized from the same solvent mixture. Yield 2.54 g (77%) of compound **15**, m.p. 211 °C. For $C_{16}H_{19}N_3O_5$ (333.3) calculated: 57.65% C, 5.74% H, 12.61% N; found: 57.58% C, 5.64% H, 12.66% N. ^{1}H NMR spectrum: 3.48 ddd, 1 H, *J* = 3.9, 5.1 and 12.0 (H-5′a); 3.63 ddd, 1 H, *J* = 3.2, 5.1 and 12.0 (H-5′b); 3.63 s, 2 H (CH_2); 3.83 dt, 1 H, *J* = 3.4, 3.4 and 5.1 (H-4′); 3.92 q, 1 H (H-3′); 3.96 q, 1 H (H-2′); 5.03 d, 1 H, *J*(OH,3′) = 5.6 (3′-OH); 5.07 t, 1 H, *J*(OH,5′) = 5.2 (5′-OH); 5.36 d, 1 H, *J*(OH,2′) = 5.4 (2′-OH); 5.77 d, 1 H, *J*(1′,2′) = 4.4 (H-1′); 7.20 t, 1 H, 7.24 d, 2 H and 7.29 t, 2 H (H arom.); 6.75 br s, 1 H and 7.43 br s, 1 H (NH_2); 7.60 s, 1 H (H-6).

2,2′-Anhydro-1-(β-D-arabinofuranosyl)-5-benzylcytosine Hydrochloride (**17**)

Thionyl chloride (0.15 ml, 2.06 mmol) was added to a suspension of 5-benzylcytidine (530 mg, 1.59 mmol) in acetonitrile (5 ml) and the mixture was stirred at room temperature for 1 h. After dilution with dry ether, the mixture was set aside in a refrigerator for 1 h, the crystalline material was collected on filter under exclusion of moisture, washed with ether and dried in vacuo. The obtained intermediate **16** (655 mg, 99%) was heated in dimethylformamide (15 ml) at 100 °C for 1 h. The solvent was evaporated and the residue codistilled with toluene (2 × 20 ml) and ethanol (20 ml). Precipitation with ether from methanolic solution afforded 537 mg (96%) of hygroscopic 2,2′-anhydro derivative **17**. ^{1}H NMR spectrum: 3.27 dd, 1 H, *J*(5′a,4′) = 3.7, *J*(gem) = 12.0 (H-5′a); 3.41 dd, 1 H, *J*(5′b,4′) = 3.2 (H-5′b); 3.85 d, 1 H and 3.89 d, 1 H, *J*(gem) = 16.1 (CH_2); 4.21 br td, 1 H, *J*(4′,3′) = 1.2, *J*(4′,5′) = 3.5 (H-4′); 4.48 br s, 1 H (H-3′); 5.06 br, 1 H (OH); 5.39 d, 1 H, *J*(2′,1′) = 5.9, *J*(2′, 3′) < 1 (H-2′); 6.18 br,

1 H (OH); 6.66 d, 1 H, *J*(1′,2′) = 5.9 (H-1′); 7.20–7.40 m, 5 H (H arom.); 8.14 s, 1 H (H-6); 8.86 s, 1 H, 9.01 br, 2 H and 9.44 s, 1 H (NH).

1-(β-D-Arabinofuranosyl)-5-benzylcytosine (**18**)

Dowex 1 (CO_3^{2-} form, 10 ml) was added to a solution of 2, 2′-anhydro derivative **17** (300 mg, 0.85 mmol) in water (10 ml) and the mixture was stirred at ambient temperature for 2 h. The ion exchanger was filtered off, the filtrate was taken down and the residue crystallized from methanol (with several drops of water) to give 216 mg (74%) of crystalline product, m.p. 215–217 °C. For $C_{16}H_{19}N_3O_5$. 0.5 H_2O (342.3) calculated: 56.13% C, 5.89% H, 12.27% N; found: 56.23% C, 5.89% H, 12.25% N. Mass spectrum (FAB; T + G, CH_3OH): 334.1 (M + H, $C_{16}H_{20}N_3O_5$). ^{1}H NMR spectrum: 3.42 dt, 1 H, *J* = 5.1, 5.1 and 11.5 (H-5′a); 3.50 dt, 1 H, *J* = 5.1, 5,1 and 11.5 (H-5′b); 3.61 s, 2 H (CH_2); 3.70 m, 1 H (H-4′); 3.86 m, 1 H (H-3′); 3.96 m, 1 H (H-2′); 4.97 t, 1 H, *J*(OH,5′) = 4.9 (5′-OH); 5.39 d, 2 H, *J* = 4.4 (2′-OH and 3′-OH); 6.04 d, 1 H, *J*(1′,2′) = 3.2 (H-1′); 6.64 br, 2 H (NH_2); 7.21 m, 3 H and 7.29 m, 2 H (H arom.); 7.37 s, 1 H (H-6).

5-Benzyl-5′-chloro-5′-deoxycytidine (**20**)

Thionyl chloride (0.55 ml, 7.5 mmol) was added to a suspension of 5-benzylcytidine (1.11 g, 3.33 mmol) in acetonitrile (25 ml) and the mixture was refluxed for 1.5 h. The solution of the formed sulfite **19** was cooled, concentrated to a half and added dropwise with stirring to ether (75 ml). The suspension formed was stirred for 15 min, filtered under exclusion of moisture and the product was washed with ether to neutral reaction. The thus-obtained intermediate **19** was dried in vacuo and dissolved in methanol (25 ml). A solution of potassium carbonate (10%, 20 ml) was added dropwise with stirring and the reaction mixture was stirred for 20 min. The deposited product was collected, washed with water to neutral reaction and then boiled with water. The suspension was allowed to stand overnight, filtered and the product was air-dried to give crystalline 5′-chloro derivative **20** (1.04 g, 89%), m.p. 223.5–226 °C. For $C_{16}H_{18}ClN_3O_4$ (351.8) calculated: 54.63% C, 5.16% H, 10.08% Cl, 11.94% N; found: 53.99% C, 5.11% H, 9.83% Cl, 12.22% N. ^{1}H NMR spectrum: 3.62 s, 2 H (CH_2); 3.63 dd, 1 H, *J*(5′a,4′) = 5.9, *J*(gem) = 12.2 (H-5′a); 3.81 dd, 1 H, *J*(5′b,4′) = 3.7 (H-5′b); 3.82 m, 1 H (H-3′); 3.93–3.99 m, 2 H (H-2′and H-4′); 5.26 d, 1 H, *J*(OH, 3′) = 4.2 (3′-OH); 5.44 d, 1 H, *J*(OH,2′) = 4.6 (2′-OH); 5.82 d, 1 H, *J*(1′,2′) = 4.4 (H-1′); 6.86 br, 1 H (NH); 7.19–7.33 m, 6 H (H arom. and H-6); 7.45 br, 1 H (NH).

5-Benzyl-5′-deoxycytidine (**21**)

A solution of tributylstannane in toluene (1 mol l^{-1}, 5 ml), followed by azobis(isobutyronitrile) (250 mg), was added at 130 °C to a solution of 5′-chloro derivative **20** (820 mg, 2.33 mmol) in dioxane–dimethyl sulfoxide (1 : 1, 10 ml). The reaction mixture was heated at 130 °C for 1 h, cooled and the solvent was evaporated. The residue was codistilled with xylene (4 × 20 ml) and chromatographed on silica gel (200 ml) in system S7 (R_F: **21**, 0.27; **20**, 0.34). Yield 400 mg (54%) of compound **21**, m.p. 224–226 °C (aqueous 2-propanol). For $C_{16}H_{19}N_3O_4$ (317.3) calculated: 60.56% C, 6.03% H, 13.24% N; found: 60.30% C, 5.98% H, 13.01% N. ^{1}H NMR spectrum: 1.01 d, 3 H, *J*(5′,4′) = 6.3 (H-5′); 3.41 td, 1 H, *J*(3′,2′) = 5.1, *J*(3′,4′) = *J*(3′,OH) = 6.3 (H-3′); 3.60 s, 2 H (CH_2); 3.78 pent, 1 H, *J* = 6.3 (H-4′); 3.83 td, 1 H, *J*(2′,1′) = 3.2, *J*(2′,3′) = *J*(2′,OH) = 5.0 (H-2′); 4.95 d, 1 H, *J*(OH,3′) = 6.1 (3′-OH); 5.30 d, 1 H, *J*(OH,2′) = 4.9 (2′-OH); 5.67 d, 1 H, *J*(1′,2′) = 3.2 (H-1′); 6.84 br, 1 H (NH); 7.01 s, 1 H (H-6); 7.24 m, 3 H and 7.33 m, 2 H (H arom.); 7.39 br, 1 H (NH).

5-Benzyl-2′-deoxy-3′,5′-bis(*O*-*p*-toluoyl)uridine (**22**) and 5-Benzyl-1-(2-deoxy-3,5-bis(*O*-*p*-toluoyl)-α-D-ribofuranosyl)uracil (**23**)

5-Benzyluracil (910 mg, 4.5 mmol) was silylated in the same manner as described for preparation of compound **2**. To the silylated base in acetonitrile (25 ml) was added 2-deoxy-3,5-bis(*O*-*p*-toluoyl)-D-ribofuranosyl chloride (1.36 g, 3.5 mmol) and molecular sieve 3Å (2 g), preheated at 200 °C in vacuo. Mercury(II) bromide (613 mg, 1.7 mmol) was added, the suspension was stirred at room temperature overnight, filtered, the solid was washed with a small amount of acetonitrile and then with chloroform. The chloroform filtrate was washed with 30% potassium iodide solution (3 × 75 ml) and water (100 ml) and dried over magnesium sulfate. Evaporation of the solvent and crystallization from ethanol afforded 715 mg (37%) of the product **22**.

The acetonitrile filtrate was taken down and the obtained mixture of anomers **22** and **23** was separated on silica gel in system S1. R_F: **22**, 0.34; **23**, 0.29. Total yield of the β-anomer **22** was 1.135 g (59%). Mass spectrum (FAB; G + DMSO): 555 (M + H). ^{1}H NMR spectrum and other physical constants were identical with those described in the literature[6]. The α-anomer **23** was obtained in the yield 600 mg (31%). Mass spectrum (FAB; G + DMSO): 555 (M + H). ^{1}H NMR spectrum and other physical constants were identical with those described in the literature[6].

5-Benzyl-2′-deoxycytidine (**25**)

Lawesson reagent (360 mg, 0.89 mmol) was added under argon to a solution of compound **22** (982 mg, 1.77 mmol) in 1,2-dichloroethane (20 ml) and the mixture was refluxed for 1 h. Another portion of the reagent (90 mg) was added and the refluxing continued for another 4 h. After cooling, the reaction mixture was applied onto a column of silica gel (300 ml) and chromatographed in toluene–acetone (8 : 1) to give 960 mg (95%) of derivative **24** (R_F 0.40, S1) as a yellow foam. The derivative **24** in methanolic ammonia was stirred at room temperature for 48 h. The solvent was evaporated, the residue was again dissolved in freshly made methanolic ammonia (70 ml) and heated at 120 °C for 1 h in an autoclave. After cooling, the solvent was evaporated and the residue chromatographed on silica gel (150 ml) in system S8 (R_F 0.29). Crystallization from 2-propanol–ethanol (1 : 1) afforded 364 mg (65%) of compound **25**, m.p. 192–194 °C. For $C_{16}H_{19}N_3O_4$ (317.3) calculated: 60.56% C, 6.03% H, 13.24% N; found: 60.30% C, 6.08% H, 13.40% N. ^{1}H NMR spectrum: 1.90 pent, 1 H, J(2′a,1′) = J(2′a,3′) = 6.1, J(gem) = 13.1 (H-2′a); 2.11 ddd, 1 H, J(2′b,1′) = 5.8, J(2′b,3′) = 3.4 (H-2′b); 3.44 m, 2 H (H-5′); 3.62 s, 2 H (CH_2); 3.74 br q, 1 H (H-4′); 4.16 m, 1 H (H-3′); 4.94 t, 1 H, J(OH,5′) = 5.2 (5′-OH); 5.19 d, 1 H, J(OH,3′) = 4.0 (3′-OH); 6.15 t, 1 H (H-1′); 6.73 br, 1 H (NH); 7.17–7.40 m, 6 H (H arom. and NH); 7.59 s, 1 H (H-6).

5-Benzyl-1-(2-deoxy-α-D-ribofuranosyl)cytosine (**27**)

The title compound was prepared from derivative **23** (428 mg, 0.77 mmol) in the same manner as described for the β-anomer **25**. Chromatography on silica gel in system S8 gave 181 mg (74%) of the α-anomer **27**, R_F 0.25. Mass spectrum (FAB; TG + G, methanol): 318 (M + H). ^{1}H NMR spectrum: 1.85 br dt, 1 H, J(gem) = 14.0 (H-2′a); 2.40–2.60 m, 1 H (H-2′b); 3.37 m, 2 H (H-5′); 3.63 s, 2 H (CH_2); 4.08 m, 1 H (H-4′); 4.18 m, 1 H (H-3′); 4.81 t, 1 H, J(OH,5′) = 4.6 (5′-OH); 5.15 d, 1 H, J(OH,3′) = 2.8 (3′-OH); 6.02 dd, 1 H, J(1′,2′a) = 2.4, J(1′,2′b) = 7.0 (H-1′); 6.60–6.90 br, 1 H (NH); 7.12–7.33 m, 6 H (H arom. and NH); 7.60 s, 1 H (H-6).

5-Benzyluridine (**28**)

A suspension of tribenzoyl derivative **10** (13 g, 20 mmol) in methanolic ammonia was stirred to homogeneity, the solution was set aside at room temperature for 3 days and the solvent was evaporated.

Crystallization from 2-propanol gave 4.2 g (63%) of 5-benzyluridine, m.p. 181–183 °C (reported[5] m.p. 182–183 °C). Chromatography of the mother liquors on a column of silica gel (150 g) in system S7 (R_F 0.51) and subsequent crystallization from 2-propanol gave additional 1.2 g (18%) of the same compound.

5′-*O*-Benzoyl-5-benzyluridine (**29**)

To a suspension of 5-benzyluridine **28** (5 g, 15 mmol) in acetone (75 ml) was added 2,2-dimethoxypropane (10 ml) and concentrated sulfuric acid (40 μl). The mixture was stirred at room temperature for 45 min and neutralized with finely ground sodium hydrogen carbonate. The insoluble portion was filtered off, washed with acetone, and the combined filtrates were taken down. The residue was dissolved in pyridine (80 ml), the solution was cooled in an ice bath, and benzoyl chloride (1.92 ml, 16.5 mmol) was added. The mixture was allowed to stand at 0 °C for 1 h and at room temperature for 4 h. Water (0.5 ml) was added and the mixture was taken down. The residue was partitioned between water (50 ml) and ethyl acetate (100 ml), the organic layer was washed successively with 2% hydrochloric acid to acid reaction of the aqueous phase, water (50 ml), and 5% sodium hydrogen carbonate solution, dried over magnesium sulfate and the solvent was evaporated. The residue was dissolved in 80% aqueous methanol (100 ml), Dowex 50 (H^+ form, 5 ml) was added and the mixture was refluxed for 7 h. Acetone (500 ml) was added and the mixture was again heated to the boil. The ion exchanger was filtered off, washed with acetone and the combined filtrates were concentrated to 25 ml. The product was collected and washed with methanol and ether. Yield 5.51 g (84%) of benzoyl derivative **29**, m.p. 206–208 °C. For $C_{23}H_{22}N_2O_7$ (438.4) calculated: 63.01% C, 5.06% H, 6.39% N; found: 62.73% C, 5.07% H, 6.41% N. ^{1}H NMR spectrum: 3.36 d, 1 H, J(gem) = 14.6 and 3.44 d, 1 H (CH_2); 4.07–4.23 m, 3 H (H-2′, H-3′, H-4′); 4.38 dd, 1 H, J(5a′,4′) = 5.2, J(5a′,5b′) = 11.9 (H-5a′); 4.55 dd, 1 H, J(5b′,4′) = 2.75 (H-5b′); 5.37 d, 1 H, J = 4.9 (OH); 5.53 d, 1 H, J = 5.2 (OH); 5.82 d, 1 H, J(1′,2′) = 5.2 (H-1′); 7.15 m, 5 H (H-benzyl); 7.48–8.00 m, 6 H (H-6, H-benzoyl); 11.41 s, 1 H (H-3).

2,2′-Anhydro-1-(5-*O*-benzoyl-β-D-arabinofuranosyl)-5-benzyluracil (**30**)

Thionyl chloride (1.7 ml, 23 mmol) was added to a suspension of benzoyl derivative **29** (5.26 g, 12 mmol) in acetonitrile (70 ml) and the mixture was stirred at room temperature for 24 h. After concentration to a half, the mixture was diluted with ethyl acetate (300 ml), washed with ice-cold 5% sodium hydrogen carbonate solution, dried over magnesium sulfate and the solvent was evaporated. The residue was dissolved in dimethylformamide (45 ml), imidazole (0.85 g, 12.5 mmol) was added and the solution was heated at 150 °C for 1 h. The solvent was evaporated and the residue was chromatographed on a column of silica gel (200 g) in ethyl acetate–ethanol (10 : 1), R_F 0.32. Crystallization from ethanol afforded 4.0 g (79%) of anhydronucleoside **30**, m.p. 179–182 °C. For $C_{23}H_{20}N_2O_6$ (420.4) calculated: 65.71% C, 4.79% H, 6.66% N; found: 65.67% C, 4.84% H, 6.64% N. ^{1}H NMR spectrum: 3.51 bs, 2 H (CH_2); 4.08 dd, 1 H, J(5a′,4′) = 8.1, J(5a′,5b′) = 12.1 (H-5a′); 4.27 dd, 1 H, J(5b′,4′) = 4.1 (H-5b′); 4.36–4.49 m, 2 H (H-3′, H-4′); 5.26 dd, 1 H, J(2′,1′) = 6.3, J(2′,3′) = 0.9 (H-2′); 6.10 d, 1 H, J(OH,3′) = 4.5 (3′-OH); 6.35 d, 1 H (H-1′); 7.15 s, 5 H (H-benzyl); 7.64 s, 1 H (H-6); 7.46–7.90 m, 5 H (H-benzoyl).

1-(5-*O*-benzoyl-2-deoxy-β-D-*erythro*-pentofuranosyl)-5-benzyluracil (**32**)

A solution of anhydro nucleoside **30** (3.57 g, 8.5 mmol) in 1 M hydrogen chloride in dimethylformamide was heated for 45 min at 100 °C. The solvent was evaporated, the residue was codistilled with xylene and then partitioned between ethyl acetate (200 ml) and 10% sodium hydrogen carbonate solution

(100 ml). The organic layer was separated, dried over magnesium sulfate and the solvent was evaporated. The thus-obtained chloro derivative **31** was dissolved in toluene (40 ml), the solution was heated at 100 °C and a solution of tributylstannane in toluene (1 mol l^{-1}, 17 ml), followed by azobis(isobutyronitrile) (170 mg), was added. After heating for 20 min, the reaction mixture was concentrated to a half and the deposited crystalline material was collected and washed with light petroleum. Crystallization from toluene–ethanol afforded 3.34 g (93%) of deoxy derivative **32**, m.p. 212–213 °C. For $C_{23}H_{22}N_2O_6$ (422.4) calculated: 65.40% C, 5.25% H, 6.63% N; found: 65.36% C, 5.26% H, 6.81% N. ^{1}H NMR spectrum: 2.09–2.14 m, 2 H (2 × H-2′); 3.36 d, 1 H, *J*(gem) = 14.7 and 3.44 d, 1 H (CH_2); 4.03–4.10 m, 1 H (H-4); 4.31–4.52 m, 3 H (H-3′, 2 × H-5′); 5.50 d, 1 H, *J*(OH,3′) = 3.7 (3′-OH); 6.22 t, 1 H, *J*(1′,2a′) = *J*(1′,2b′) = 6.7 (H-1′); 7.14 m, 5 H (H-benzyl); 7.46–7.98 m, 6 H (H-6, H-benzoyl); 11.36 s, 1 H (H-3).

1-(5-*O*-Benzoyl-2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-5-benzyluracil (**35**)

A solution of deoxy derivative **32** (3.3 g, 7.8 mmol) and thionyl chloride (0.88 ml, 12 mmol) in hexamethylphosphoric triamide (15 ml) was allowed to stand at room temperature overnight, then diluted with ethyl acetate (200 ml) and washed with 10% sodium hydrogen carbonate solution (3 × 100 ml). The organic layer was dried over magnesium sulfate and the solvent was evaporated. The obtained mixture of chloro derivatives **33** and **34** was dissolved in toluene (40 ml) and the solution was heated to the boil. A solution of tributylstannane in toluene (1 mol l^{-1}, 15 ml), followed by azobis(isobutyronitrile) (230 mg), was added and the mixture was refluxed for 1 h. Evaporation of the solvent and chromatography on a column of silica gel (300 g) in ethyl acetate–toluene (2 : 1) afforded 2.98 g (94%) of dideoxy derivative **35** as solid foam (R_F 0.40). For $C_{23}H_{22}N_2O_5$ (406.4) calculated: 67.97% C, 5.46% H, 6.89% N; found: 67.66% C, 5.29% H, 6.63% N. ^{1}H NMR spectrum: 1.82–2.43 m, 4 H (2 × H-2′, 2 × H-3′); 3.38 d, 1 H, *J*(gem) = 14.8 and 3.46 d, 1 H (CH_2); 4.26–4.52 m, 3 H (H-4′, 2 × H-5′); 6.03 dd, 1 H, *J*(1′,2a′) = 6.9, *J*(1′,2b′) = 4.3 (H-1′); 7.15 m, 5 H (H-benzyl); 7.43–8.00 m, 6 H (H-6, H-benzoyl); 11.35 s, 1 H (H-3).

1-(5-*O*-Benzoyl-2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-5-benzyl-4-thiouracil (**36**)

Lawesson reagent (850 mg, 2.1 mmol) was added to a solution of 5′-*O*-benzoyl-5-benzyl-2′,3′-dideoxyuridine (**35**; 1.38 g, 3.4 mmol) in 1,2-dichloroethane (30 ml) and the mixture was refluxed under argon for 3 h. After cooling, the solution was applied onto a column of silica gel (400 ml) and chromatographed in system S2 to give 1.11 g (77%) of compound **36** as yellow foam. R_F 0.28 (toluene–ethyl acetate 3 : 1). For $C_{23}H_{22}N_2O_4S$ (422.5) calculated: 65.38% C, 5.25% H, 6.63% N, 7.59% S; found: 64.95% C, 5.35% H, 6.35% N, 7.47% S. ^{1}H NMR spectrum: 1.78 m, 1 H (H-3′a); 2.09 m, 2 H (H-3′b and H-2′a); 2.38 m, 1 H (H-2′b); 3.63 d, 1 H and 3.79 d, 1 H, *J*(gem) = 15.1 (CH_2); 4.25 dd, 1 H, *J*(5′a, 4′) = 6.6, *J*(gem) = 11.7 (H-5′a); 4.35 ddd, 1 H, *J*(4′,5′a) = 6.6, *J*(4′,5′b) = 3.2, *J*(4′,3′) = 5.9 and 8.5 (H-4′); 4.40 dd, 1 H (H-5′b); 5.96 dd, 1 H, *J*(1′,2′) = 3.4 and 7.1 (H-1′); 7.10–7.20 m, 5 H (H arom.), 7.42 s, 1 H (H-6); 7.50 m, 2 H, 7.66 m, 1 H and 7.95 m, 2 H (H arom.); 12.76 s, 1 H (NH).

5-Benzyl-1-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-4-thiouracil (**37**)

A mixture of the protected 4-thio derivative **36** (1.11 g, 2.63 mmol) and methanolic ammonia (50 ml) was stirred for 3 days at room temperature. The solvent was evaporated and the residue was chromatographed on silica gel (240 ml) in system S3 (R_F 0.39) to give pure compound **37** (620 mg, 74%) as solid foam. For $C_{16}H_{18}N_2O_3S$ (318.4) calculated: 60.36% C, 5.70% H, 8.80% N, 10.07% S; found: 60.01% C, 5.70% H, 9.08% N, 9.82% S. ^{1}H NMR spectrum: 1.73 dddd, 1 H, *J*(3′a,2′a) = 7.6; *J*(3′a,4′) = 9.3, *J*(3′a,2′b) = 10.5, *J*(gem) = 12.5 (H-3′a); 1.86 dddd, 1 H, *J*(3′b,2′a) = 3.2, *J*(3′b,4′) = 5.9,

J(3′b,2′b) = 8.1 (H-3′b); 2.02 ddt, 1 H, *J*(2′a, 1′) = 2.7, *J*(gem) = 13.7 (H-2′a); 2.30 dddd, 1 H, *J*(2′b,1′) = 6.6 (H-2′b); 3.44 ddd, 1 H, *J*(5′a,4′) = 3.7, *J*(5′a,OH) = 5.0, *J*(gem) = 12.0 (H-5′b); 3.61 ddd, 1 H, *J*(5′b,4′) = 3.4, *J*(5′b,OH) = 5.1 (H-5′b); 3.80 s, 2 H (CH_2); 4.03 ddt, 1 H (H-4′); 5.10 t, 1 H (5′-OH); 5.90 dd, 1 H (H-1′); 7.18 m, 1 H and 7.26 m, 4 H (H arom.); 7.98 s, 1 H (H-6); 12.63 br, 1 H (NH).

5-Benzyl-1-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)cytosine (**38**)

A solution of 4-thio derivative **37** (450 mg, 1.41 mmol) in methanolic ammonia (50 ml) was heated at 120 °C for 1 h in an autoclave. After evaporation of the solvent, a mixture of ethyl acetate and acetone (5 : 1) was added, the mixture was briefly boiled and set aside at room temperature overnight. The crystalline product was collected, washed with acetone and ether and dried in vacuo; yield 255 mg (60%) of compound **38**. Further portion (65 mg, 15%) of the product was obtained from the mother liquors by chromatography on silica gel (50 ml) in system S8 (R_F 0.29) and subsequent crystallization from ethanol. M.p. 209–211 °C (ethanol–water). For $C_{16}H_{19}N_3O_3$. 0.25 H_2O (305.8) calculated: 62.83% C, 6.43% H, 13.74% N; found: 63.10% C, 6.44% H, 13.61% N. ^{1}H NMR spectrum: 1.65 ddt, 1 H, *J*(3′a,4′) = 8.5, *J*(3′a,2′) = 8.5 and 11.0, *J*(gem) = 12.5 (H-3′a); 1.78–1.87 m, 2 H (H-2′a and H-3′b); 2.24 dtd, 1 H, *J*(2′b,1′) = 6.6, *J*(2′b,3′b) = *J*(2′b, 3′a) = 9.O, *J*(gem) = 13.7 (H-2′b); 3.40 dt, 1 H, *J*(5′a,4′) = *J*(5′a,OH) = 4.5, *J*(gem) = 11.7 (H-5′a); 3.52 ddd, 1 H, *J*(5′b, 4′) = 4.1, *J*(5′b,OH) = 5.4 (H-5′b); 3.61 s, 2 H (CH_2); 3.97 ddt, 1 H, *J*(4′,3′) = 6.0 and 8.5 (H-4′); 4.97 t, 1 H (5′-OH); 5.92 dd, 1 H, *J*(1′,2′a) = 3.4, *J*(1′,2′b) = 6.6 (H-1′); 6.66 br, 1 H and 7.24 br, 1 H (NH_2); 7.18–7.27 m, 3 H and 7.30 m, 2 H (H arom.); 7.66 s, 1 H (H-6).

1-(5-*O*-Benzoyl-2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-5-benzyl-4-methylthiopyrimidine (**39**)

Finely ground potassium carbonate (200 mg) and methyl iodide (1 ml) were added to a solution of 4-thio derivative **36** (770 mg, 1.82 mmol) in dimethylformamide (5 ml). The mixture was stirred at room temperature for 30 min, the solid was filtered off and washed with ethyl acetate. The combined filtrates were taken down, the residue was codistilled with xylene (20 ml) and then partitioned between water (50 ml) and ethyl acetate (100 ml). The organic layer was dried over magnesium sulfate, the solvent evaporated and the residue chromatographed on silica gel (100 ml) in ethyl acetate (R_F in S6: **39**, 0.34; **36**, 0.82). Yield 702 mg (88%) of colorless foam, m.p. 122–124 °C (methanol). For $C_{24}H_{24}N_2O_4S$ (436.5) calculated: 66.04% C, 5.54% H, 6.42% N, 7.35% S; found: 65.79% C, 5.58% H, 6.42% N, 7.09% S. Mass spectrum (FAB; G + methanol): 437.1 (M + H). ^{1}H NMR spectrum: 1.75–1.83 m, 1 H, 2.03–2.12 m, 2 H and 2.37–2.50 m, 1 H (H-2′ and H-3′); 2.39 s, 3 H (SCH_3); 3.58 d, 1 H and 3.63 d, 1 H, *J* = 16.1 (CH_2); 4.36 dd, 1 H, *J*(5′a,4′) = 6.1, *J*(gem) = 11.7 (H-5′a); 4.42 dtd, 1 H, *J* = 2.7, 6.1, 6.1 and 8.7 (H-4′); 4.48 dd, 1 H, *J*(5′b,4′) = 2.9 (H-5′b); 5.96 dd, 1 H, *J*(1′,2′) = 3.4 and 6.8 (H-1′); 7.66 s, 1 H (H-6); 7.12 t, 2 H, 7.22 d, 2 H, 7.23 t, 1 H, 7.47 t, 2 H, 7.64 t, 1 H and 7.93 d, 2 H (H arom.).

1-(5-*O*-Benzoyl-2,3-dideoxy-D-*glycero*-pentofuranosyl)-5-benzyl-2(1*H*)-pyrimidinone (**41**)

Hydrazine hydrate (80%, 1 ml) was added to a solution of compound **39** (2.17 g, 4.97 mmol) in dioxane (30 ml) and the solution was refluxed for 2 h. After evaporation, the remaining hydrazino derivative **40** was codistilled with toluene (2 × 30 ml) and dissolved in ethanol (100 ml). Freshly prepared silver oxide (1.74 g, 7.5 mmol) was added and the stirred mixture was refluxed for 2.5 h. After standing overnight at room temperature, the suspension was filtered through Celite and the filtrate was taken down. The residue was dissolved in chloroform–methanol and the solution was mixed with silica gel (15 ml) and evaporated. This material was applied onto a column of silica gel (300 ml, ethyl acetate). The column was first washed with ethyl acetate and then the product **41** was eluted with system S6 (R_F 0.33, fluorescence in UV light). Yield 860 mg (43%) of amorphous material.

According to NMR, the compound was an inseparable mixture of anomers (β : α = 3 : 1). For $C_{23}H_{22}N_2O_4$ (390.4) calculated: 70.75% C, 5.68% H, 7.17% N; found: 69.53% C, 5.84% H, 7.11% N. Mass spectrum (FAB; bis(hydroxyethyl)disulfide + dimethyl sulfoxide): 391.1 (M + H). ^{1}H NMR spectrum (β-anomer): 1.79–1.87 m, 2.02–2.11 m and 2.50–2.56 m, 4 H (H-2′ and H- 3′); 3.57 d, 1 H and 3.65 d, 1 H, *J* = 15.2 (CH_2); 4.48 m, 1 H (H-4′); 4.49 dd, 1 H, *J*(5′a,4′) = 3.9, *J*(gem) = 13.9 (H-5′a); 4.57 dd, 1 H, *J*(5′b,4′) = 5.6 (H-5′b); 5.95 dd, 1 H, *J* = 3.4 and 6.6 (H-1′); 7.10–7.30 m, 5 H, 7.50–7.60 m, 2 H, 7.65 m, 1 H and 7.98 m, 2 H (H arom.); 7.99 d, 1 H and 8.47 d, 1 H, *J*(4,6) = 3.4 (H-4 and H-6). ^{1}H NMR spectrum (α-anomer): 1.91–1.98 m and 2.10–2.14 m, 4 H (H-2′and H-3′); 3.81 s, 2 H (CH_2); 4.35 dd, 1 H, *J*(5′a,4′) = 5.6, *J*(gem) = 11.7 (H-5′a); 4.41 dd, 1 H, *J*(5′b,4′) = 3.7 (H-5′b); 4.95 m, 1 H (H-4′); 6.04 dd, 1 H, *J* = 2.9 and 6.3 (H-1′); 7.10–7.30 m, 5 H, 7.50–7.60 m, 2 H, 7.65 m, 1 H and 7.98 m, 2 H (H arom.); 8.03 d, 1 H and 8.49 d, 1 H, *J*(4,6) = 3.4 (H-4 and H-6).

5-Benzyl-1-(2,3-dideoxy-D-*glycero*-pentofuranosyl)- 2(1*H*)-pyrimidinone (**42**)

A solution of benzoyl derivative **41** (850 mg, 2.18 mmol) in methanolic ammonia (20 ml) was allowed to stand at room temperature for 24 h. After evaporation, the residue was chromatographed on silica gel (200 ml) in system S7 (R_F 0.26) to give 500 mg (80%) of amorphous product, m.p. 168–174 °C (ethyl acetate–2-propanol). According to NMR, the product was a mixture of β and α anomers (about 5 : 2). ^{1}H NMR spectrum (signals common to both anomers): 1.70–2.10 m, 3 H and 2.35–2.45 m, 1 H (H-2′ and H-3′); 3.72 s, 2 H (CH_2); 5.23 t, 1 H, *J* = 4.9 (OH); 7.20–7.35 m, 5 H (H arom.). Exchange with CD_3COOD (β-anomer): 3.55 dd, 1 H, *J*(5′a,4′) = 3.2, *J*(gem) = 12.2 (H-5′a); 3.77 dd, 1 H, *J*(5′b,4′) = 2.9 (H-5′b); 4.12 m, 1 H (H-4′); 5.88 dd, 1 H, *J* = 2.9 and 6.6 (H-1′); 8.11 br s, 1 H and 8.44 br s, 1 H (H-4 and H-6). Exchange with CD_3COOD (α-anomer): 3.40 dd, 1 H, *J*(5′a,4′) = 4.9, *J*(gem) = 11.7 (H-5′a); 3.45 dd, 1 H, *J*(5′b,4′) = 4.6 (H-5′b); 4.48 m, 1 H (H-4′); 5.94 dd, 1 H, *J* = 2.9 and 6.3 (H-1′); 8.44 br s, 1 H and 8.58 br s, 1 H (H-4 and H-6).

1-(5-*O*-Benzoyl-2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-5-benzyl-4-(isopropylidenehydrazino)-2(1*H*)-pyrimidinone (**43**)

Hydrazine hydrate (80%, 0.1 ml) was added to a solution of compound **36** (643 mg, 1.47 mmol) in dioxane (20 ml) and the stirred mixture was refluxed for 1 h. The refluxing was continued for another 6 h during which further portions of hydrazine hydrate (total 0.6 ml) were added. After cooling to room temperature, acetone (1 ml) was added, the solution was stirred for 30 min and the solvent was evaporated. Chromatography on silica gel (250 ml) in system S5 (R_F: **43**, 0.33; **36**, 0.12) gave 494 mg (73%) of sirupy product. For $C_{26}H_{28}N_4O_4$ (460.5) calculated: 67.81% C, 6.13% H, 12.17% N; found: 67.77% C, 6.14% H, 11.82% N. Mass spectrum (EI): 460.2 (M^+), 256.1 (base + H). ^{1}H NMR spectrum: 1.87 s, 3 H and 1.95 s, 3 H (CH_3); 1.91 m, 1 H (H-3′a); 2.00 m, 1 H (H-2′a); 2.11 m, 1 H (H-3′b); 2.30 m, 1 H (H-2′b); 3.44 d, 1 H and 3.50 d, 1 H, *J*(gem) = 14.4 (CH_2); 4.29 m, 1 H (H-4′); 4.35 dd, 1 H, *J*(5′a,4′) = 6.3, *J*(gem) = 11.7 (H-5′a); 4.45 dd, 1 H, *J*(5′b,4′) = 2.9 (H-5′b); 6.06 dd, 1 H, *J* = 5.1 and 7.1 (H-1′); 7.04 s, 1 H (H-6); 7.12 m, 1 H, 7.19 m, 4 H, 7.51 t, 2 H, 7.65 t, 1 H and 7.99 d, 2 H (H arom.); 9.40 br s, 1 H (NH).

5-Benzyl-1-(2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-4-(isopropylidenehydrazino)-2(1*H*)-pyrimidinone (**44**)

A solution of benzoyl derivative **43** (450 mg, 0.98 mmol) in methanolic ammonia (15 ml) was set aside at room temperature for 24 h. After evaporation, the residue was chromatographed on silica gel (100 ml) in ethyl acetate (R_F 0.28). Yield 285 mg (82%) of yellow sirup. Mass spectrum (FAB; G + methanol): 357.3 (M + H). ^{1}H NMR spectrum: 1.75–1.84 m, 1 H, 1.87–1.94 m, 2 H and 2.18–2.26 m,

1 H (H-2′ and H-3′); 1.91 s, 3 H and 1.97 s, 3 H (CH_3); 3.46 dt, 1 H, *J*(5′a,4′) = *J*(5′a,OH) = 4.5, *J*(gem) = 11.7 (H-5′a); 3.58 dt, 1 H, *J*(5′b,4′) = *J*(5′b,OH) = 4.6 (H-5′b); 3.58 s, 2 H (CH_2); 3.97 m, 1 H (H-4′); 4.99 t, 1 H (5′-OH); 5.98 dd, 1 H, *J* = 3.9 and 7.3 (H-1′); 7.17 m, 1 H and 7.24–7.32 m, 4 H (H arom.); 7.35 s, 1 H (H-6); 9.38 br, 1 H (NH).

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