2′,3′-DIDEOXY- AND 3′-AZIDO-2′,3′-DIDEOXYNUCLEOSIDES OF 5-PHENYL-2(1*H*)-PYRIMIDINONE. PREPARATION OF 2′,3′-DIDEOXYPENTOFURANOSES

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The synthesis of methyl 3-azido-5-benzoyl-2,3-dideoxy-β-D-ribofuranoside (**10**) from methyl 2-deoxy-D-ribofuranoside (**1**) and its use for the preparation of 3′-azido-2′,3′-dideoxy-β-D-ribofuranosides is described. Reaction of methylglucoside **1** with benzoyl chloride in pyridine afforded 5-*O*-benzoyl derivative **2**, which on oxidation with complex of chromium trioxide, pyridine and acetic anhydride afforded 3-keto derivative **3**. This was reduced with sodium borohydride in ethanol to give a mixture of methyl 2-deoxyglycosides of α-D-*ribo*- (**4**) and β-D-*xylo*- (**5**) configuration. Their mesyl derivatives **6** and **7** were chromatographically separated. Compound **7** reacted with sodium azide in hot dimethylformamide to afford methyl 3-azido-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (**10**). 5-Phenyl-2(1*H*)-pyrimidinone was converted into silyl derivative **11** by treatment with hexamethyldisilazane. Reaction of compound **11** with the azido sugar **10**, catalyzed by trimethylsilyl trifluoromethanesulfonate, and subsequent methanolysis, furnished a mixture of anomeric 3′-azido-2′,3′-dideoxynucleosides **14** and **15**. Methyl 5-*O*-benzoyl-2,3-dideoxy-α-D-ribofuranoside (**17**) was prepared from methyl-α-glycoside **4** by reaction with thionyl chloride and subsequent reduction of the obtained 3-chloro derivative **16** with tributylstannane. Silyl derivative **11** reacted with 2,3-dideoxy sugar **17** under catalysis with trimethylsilyl triflate to give mainly 1-(5-*O*-benzoyl-2,3-dideoxy-α-D-*glycero*-pentofuranosyl)-5-phenyl-2(1*H*)-pyrimidinone (**19**) and minor amount of the β-anomer **18**. Their methanolysis afforded dideoxynucleosides **20** and **21**.

Key words: Nucleosides; Pyrimidine; Sugar-modified; AZT analogs; Dideoxynucleosides; 5-Phenyl-2(1*H*)-pyrimidinone.

This work represents a continuation of our preceding paper[1] concerning the preparation of nucleoside analogs derived from 5-phenyl-2(1*H*)-pyrimidinone. The reason for the study of this system is its relation with the uracil and cytosine systems in which substitution with an aromatic group often leads to marked biological effects, especially inhibition of uridine phosphorylase and thymidine phosphorylase.

In connection with the quest for compounds active against retroviruses, several 5-substituted pyrimidinone nucleosides containing 3′-azido-2′,3′-dideoxyribofuranose sugar component have been described: derivatives with a halogen atom (bromine or iodine) in position 5 (ref.[2]) and also the 5-methyl-2(1*H*)-pyrimidinone analog of AZT.

The latter exhibited a very strong anti-HIV activity[3], similar to that of the parent AZT. The analog was synthesized from protected AZT by deoxygenation in position 4 via the 4-triazolyl and the 4-hydrazino derivative, which was then converted into the pyrimidinone analog by heating with silver oxide[3,4].

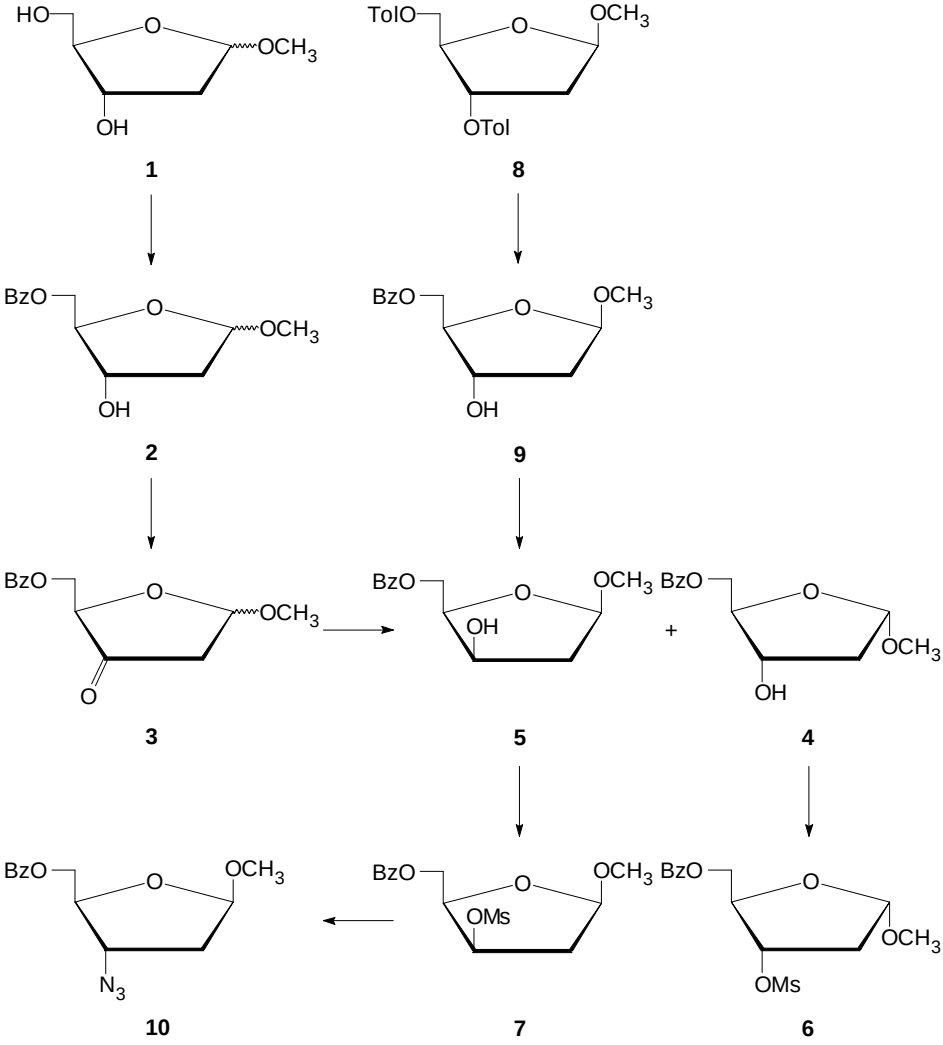
The paper on 5-halogeno substituted nucleosides with 3′-azido group[2] describes their synthesis by the nucleosidation reaction of the corresponding base with methyl 5-*O*-acetyl-3-azido-2,3-dideoxy-D-ribofuranoside. This azido sugar was prepared in seven steps from D-xylose according to the described procedures[5–7]. Apart from the low total yield (8%), this synthesis has a drawback in that the sugar is obtained as a mixture of anomers of the pyranose and furanose forms that are difficult to separate[2].

In order to avoid such complications, we first worked out a relatively simple preparation of protected methyl 3-azido-2,3-dideoxy-β-D-ribofuranoside from methyl 2-deoxy-D-ribofuranoside[8] (**1**) (Scheme 1).

The starting methyl glycoside **1** was first quantitatively and selectively benzoylated in position 5 with benzoyl chloride in pyridine. The obtained 5-*O*-benzoyl derivative **2** was oxidized with the chromium trioxide–pyridine–acetic anhydride complex to give 3-keto derivative **3** which was reduced with sodium borohydride in ethanol to a mixture of methyl glycosides **4** a **5**, the β-anomer **5** having the 2-*deoxyxylo*- and the α-anomer **4** the 2-*deoxyribo*-configuration. Although compounds **4** and **5** could not be separated by chromatography, their respective mesyl derivatives **6** and **7** were separable. The individual steps of the pathway **1–7** give high yields and, on a larger scale, the intermediates can be used without purification, the only one chromatography involved in the preparation being used in the separation of compounds **6** and **7**.

When performing this reaction sequence, we have repeatedly observed that the ratio of the obtained 3-*O*-mesyl-2-deoxyribo to the 3-*O*-mesyl-2-deoxyxylo derivative (**6** : **7**), as well as the ratio of the 2-deoxyribo to the 2-deoxyxylo derivative (**4** : **5**), determined by NMR spectroscopy, corresponded to the α : β anomer ratio in the starting methyl 2-deoxyriboside **1**. It follows that in the described oxidation–reduction reaction of the anomeric benzoyl derivative **2** the configuration in position 3 is changed only in the β-anomer, analogously to the same oxidation–reduction reaction of β-2′-deoxynucleosides[9], whereas the α-anomer of originally 2-*deoxyribo*-configuration gave again the α-2-deoxyriboside. We have confirmed this assumption by carrying out the whole reaction sequence starting from the anomerically pure methyl 5-*O*-benzoyl-2-deoxy-β-D-ribofuranoside (**9**) (Scheme 1). Since it was difficult to separate anomers of the starting methylglycoside **1**, we used its 3,5-bis(*O*-*p*-toluoyl) derivative **8** (ref.[8]), an easily accessible starting sugar for the synthesis of 2′-deoxynucleosides whose both anomers can be well separated by chromatography. The protecting groups were removed by methanolysis and the obtained methyl 2-deoxy-β-D-ribofuranoside was benzoylated under the same conditions as the anomer mixture **1**. Oxidation with chromium trioxide–pyridine–acetic anhydride complex and subsequent reduction with sodium borohydride

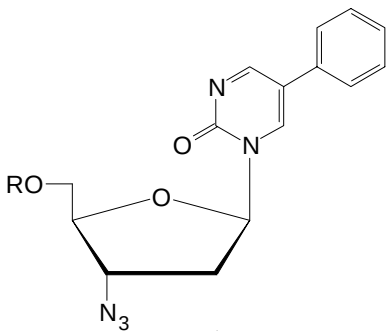
actually afforded methyl 5-*O*-benzoyl-2-deoxy-β-D-xylofuranoside (**5**) in high yield (85%). Compound **5** was further mesylated to afford the above-mentioned 2-deoxy-3-*O*-mesyl-β-D-xylo derivative **7**. This on heating with sodium azide furnished the desired methyl 3-azido-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (**10**) as the starting sugar for the preparation of 3′-azido-3′-deoxynucleosides.



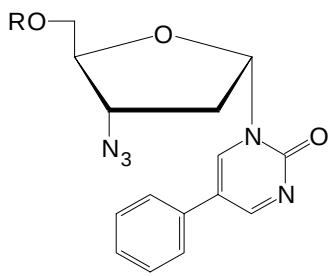
Bz, benzoyl
Ms, methanesulfonyl

SCHEME 1

For nucleosidation reactions with this synthon we have used 5-phenyl-2(1*H*)-pyrimidinone which was silylated with hexamethyldisilazane in the presence of ammonium sulfate. Reaction of the silylated base **11** with the azido sugar **10**, catalyzed with trimethylsilyl trifluoromethanesulfonate in acetonitrile, gave in high yield a mixture of anomeric 3′-azidonucleosides **12** and **13**. Finally, removal of the benzoyl protecting groups by treatment with methanolic ammonia gave free 3′-azido-2′,3′-dideoxy nucleosides **14** and **15**. It was advantageous to separate the anomers at the stage of free nucleosides. Whereas the protected derivatives **12** and **13** were chromatographically almost unseparable, the difference in chromatographic mobilities of the free β- and α-anomers **14** and **15** was sufficient for the separation.



	R
12	Bz
14	H



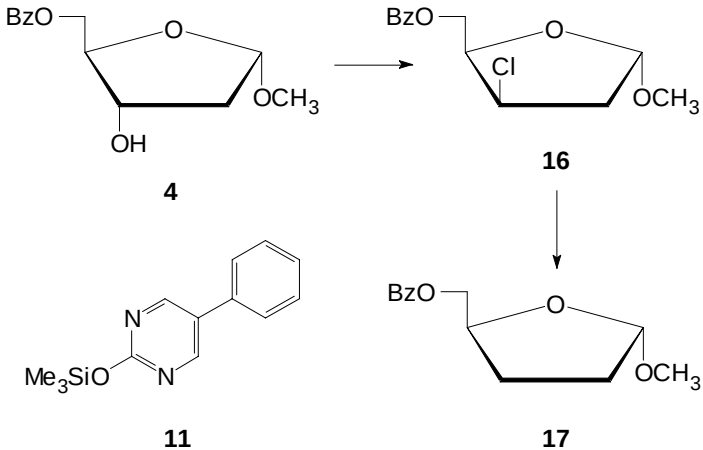
	R
13	Bz
15	H

The deblocking of compounds **12** and **13** with methanolic ammonia was not accompanied with intramolecular cyclization to O^2,5′-cyclo derivatives described for the pyrimidone nucleosides, e.g. for the synthesis of 3′-azidonucleosides of 5-halogeno-2-pyrimidones[2] which were obtained not in the individual form but only as equilibrium mixtures of the free nucleoside and its cyclic form.

As for 2′,3′-dideoxynucleosides, sugar synthons for the preparation of 2,3-dideoxy sugars have been recently synthesized from L-glutamic acid[10–13]. In the present communication we describe new synthesis of the starting sugar synthon from methyl 5-*O*-benzoyl-2,3-dideoxy-D-ribofuranoside (**17**) that makes use of the above-described 5′-benzoylated methyl glycoside **4**. This derivative was subjected to reaction with thionyl chloride and the obtained 3-chloro derivative **16** was reduced with tributylstannane to give dideoxy derivative **17** (Scheme 2). The compound **17** was pure α-anomer, however, for the described reaction sequence, as well as for the subsequent nucleosidation, the configuration at the anomeric center was not substantial.

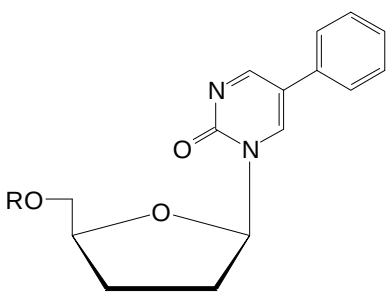
The nucleosidation reaction of silyl derivative **11** with the 2,3-dideoxy sugar **17** was performed at 0 °C in acetonitrile under catalysis with trimethylsilyl triflate. In our case,

the β-anomer **18** was obtained only in a low yield, the α-anomer **19** being the major product. The anomers were separated on silica gel and deblocked with methanolic ammonia to give dideoxynucleosides **21** and **20**.

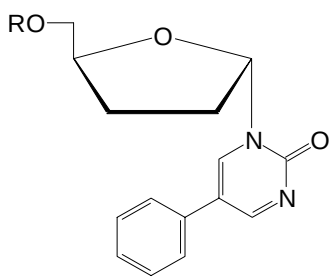


SCHEME 2

The configuration and anomeric purity of the compounds was verified by ^{1}H NMR (decoupled) and ^{13}C NMR spectra. The individual carbon atoms were assigned on the basis of J-modulated spectra (APT), which permit discrimination of C, CH, CH_2 and CH_3 carbon atoms. The observed chemical shifts and coupling constants are given in the Experimental and agree (allowing for the substitution effects) with the data published[14,15] for the anomeric pairs of 2-deoxyfuranosyl and 2,3-dideoxyfuranosyl derivatives.



	R
18	Bz
20	H



	R
19	Bz
21	H

None of the free 2′,3′-dideoxy and 3′-azido-2′,3′-dideoxynucleosides exhibited any cytostatic effects[16] on cell cultures L1210, HeLa and L929.

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–ethyl acetate 10 : 1; S2, toluene–ethyl acetate 8 : 1; S3, toluene–ethyl acetate 3 : 2; S4, toluene–ethyl acetate 1 : 1; S5, ethyl acetate; S6, ethyl acetate–acetone–ethanol–water 36 : 6 : 1 : 1. 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). NMR spectra (δ, ppm; *J*, Hz) were measured on Varian UNITY 200 (^{1}H at 200 MHz and ^{13}C at 50.3 MHz) or Varian UNITY 500 (^{1}H at 500 MHz and ^{13}C at 125.7 MHz) spectrometers in hexadeuteriodimethyl sulfoxide. The chemical shifts of protons were referenced to tetramethylsilane as internal standard whereas those of the carbon atoms to the solvent signal ($\delta(CD_3SOCD_3)$ = 39.7 ppm). 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).

Methyl 5-*O*-Benzoyl-2-deoxy-D-ribofuranoside (**2**)

Prior to the reaction, methyl 2-deoxy-D-ribofuranoside (**1**; 9.6 g, 65 mmol) was codistilled with pyridine (150 ml) and the residue was dissolved in dry pyridine (390 ml). A solution of benzoyl chloride (8.3 ml, 71 mmol) in pyridine (390 ml) was added dropwise during 8 h with stirring and cooling with ice. After addition of all the benzoyl chloride, the reaction mixture was stirred for another 30 min at 0 °C, quenched with methanol (30 ml) and the solution was set aside at room temperature overnight. The solvent was evaporated, the residue was codistilled with toluene and partitioned between water and ethyl acetate (500 ml each). The organic phase was washed successively with 1% hydrochloric acid to slightly acid reaction, water and saturated sodium hydrogen carbonate, dried over magnesium sulfate, and the solvent was evaporated. Yield 15.1 g (92%) of yellowish sirup. The obtained chromatographically homogeneous benzoyl derivative **2** (R_F 0.38, S4) was used without purification in the next step.

Methyl 5-*O*-Benzoyl-2-deoxy-3-*O*-methanesulfonyl-α-D-ribofuranoside (**6**) and Methyl 5-*O*-Benzoyl-2-deoxy-3-*O*- methanesulfonyl-β-D-xylofuranoside (**7**)

Chromium trioxide (14 g, 140 mmol) was added in portions to dry pyridine (110 ml) so as to keep the reaction mixture only slightly warm. A solution of compound **2** (7.6 g, 30.1 mmol) in pyridine (20 ml) was added to the resulting yellow-brown solution, the mixture was cooled with ice and acetic anhydride (10.5 ml) was added dropwise. The reaction mixture was stirred at 0 °C for 10 min and at room temperature for 10 min, diluted with ethyl acetate (1 l) and filtered through a layer (1 cm) of silica gel. The filtrate was taken down, the residue codistilled with toluene and then with absolute ethanol. The obtained crude 3-keto derivative **3** was dissolved in absolute ethanol (300 ml) cooled with ice and sodium borohydride (3.70 g, 98 mmol) was added. After stirring for 20 min at 0 °C, the reaction was quenched with saturated ammonium chloride (600 ml) and several drops of dilute (1 : 1) hydrochloric acid. The solution was concentrated to one half, the aqueous phase was extracted with ethyl acetate (2 × 500 ml), the combined extracts were dried over magnesium sulfate and the solvent was evaporated. Yield 5 g (66%) of a sirupy mixture of 2-deoxyribofuranosyl (**4**) and 2-deoxyxylofuranosyl (**5**) derivative.

The mixture was codistilled with pyridine (40 ml), the residue was dissolved in pyridine (60 ml) and methanesulfonyl chloride (7.8 ml, 100 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 15 min and at room temperature for 5 h. After cooling to 0 °C, methanol (25 ml) was added and the solvent was evaporated. The residue was mixed with ethyl acetate (300 ml) and washed with 1% hydrochloric acid to slightly acid reaction. The organic layer was further washed with water and saturated solution of sodium hydrogen carbonate, dried over magnesium sulfate and the solvent was evaporated. The residue was chromatographed on silica gel in system S3. First fractions afforded (R_F 0.38) the amorphous methyl 5-*O*-benzoyl-2-deoxy-3-*O*-methanesulfonyl-α-D-ribofuranoside (**6**): 2.6 g (40%). For $C_{14}H_{18}O_7S$ (330.4) calculated: 50.90% C, 5.49% H, 9.71% S; found: 50.77% C, 5.46% H, 9.89% S. ^{1}H NMR spectrum: 2.12 br, dt, 1 H, *J*(2a,1) = *J*(2a,3) = 1.0, *J*(gem) = 14.8 (H-2a); 2.49 ddd, 1 H, *J*(2b,3) = 7.8, *J*(2b,1) = 5.3 (H-2b); 3.26 s, 3 H (CH_3, mesyl); 3.29 s, 3 H (OCH_3); 4.37 dd, 1 H, *J*(5a,4) = 5.7, *J*(gem) = 12.8 (H-5a); 4.45 dd, 1 H, *J*(5b,4) = 4.0 (H-5b); 4.45 m, 1 H (H-4); 5.15 br d, 1 H (H-1); 5.24 ddd, 1 H, *J*(3,2b) = 7.8, *J*(3,2a) = 1.5, *J*(3,4) = 2.7 (H-3); 7.54 t, 2 H, 7.68 t, 1 H and 7.99 d, 2 H (H arom.). ^{13}C NMR spectrum: 37.65 (CH_3); 39.06 (C-2); 54.71 (OCH_3); 63.91 (C-5); 80.38 (C-3); 81.01 (C-4); 104.73 (C-1); 128.98, 2 C and 129.48 2 C and 129.52 and 133.69 (C arom.); 165.67 (C=O).

Further elution afforded amorphous methyl 5-*O*-benzoyl-2-deoxy-3-*O*-methanesulfonyl-β-D-xylofuranoside (**7**) (R_F 0.28, S3): 0.70 g (11%). For $C_{14}H_{18}O_7S$ (330.4) calculated: 50.90% C, 5.49% H, 9.71% S; found: 51.00% C, 5.48% H, 9.58% S. ^{1}H NMR spectrum: 2.21 dt, 1 H, *J*(2a,1) = *J*(2a,3) = 1.3, *J*(gem) = 14.8 (H-2a); 2.48 ddd, 1 H, *J*(2b,1) = 5.7, *J*(2b,3) = 6.2 (H-2b); 3.22 s, 3 H (OCH_3); 3.26 s, 3 H (CH_3, mesyl); 4.43 dd, 1 H, *J*(5a,4) = 7.1, *J*(gem) = 11.4 (H-5a); 4.45 dd, 1 H, *J*(5b,4) = 4.9 (H-5b); 4.52 dt, 1 H (H-4); 5.08 dd, 1 H (H-1); 5.38 ddd, 1 H, *J*(3,2b) = 6.6, *J*(3,2a) = 1.5, *J*(3,4) = 5.1 (H-3); 7.53 t, 2 H, 7.67 t, 1 H and 8.00 d, 2 H (H arom.). ^{13}C NMR spectrum: 37.77 (CH_3); 39.43 (C-2); 54.81 (OCH_3); 63.79 (C-5); 78.32 (C-3); 79.47 (C-4); 104.37 (C-1); 128.92, 2 C and 129.48 2 C and 129.66 and 133.63 (C arom.); 165.68 (C=O).

Methyl 5-*O*-Benzoyl-2-deoxy-β-D-xylofuranoside (**5**)

The β-anomer **9** (195 mg, 0.765 mmol) was oxidized with a mixture of chromium trioxide (360 mg, 3.6 mmol), pyridine (2 ml), and acetic anhydride (0.27 ml) as described for the anomeric mixture **2**. The obtained 3-keto derivative was reduced with sodium borohydride (100 mg, 2.64 mmol) in absolute ethanol (10 ml), reaction time 20 min. The reaction mixture was worked up as described for compound **2**. The crude product was chromatographically homogeneous and was purified on a column of silica gel (25 ml), elution with system S4 (R_F 0.39). Yield 116 mg (59%) of a sirupy residue, containing at least 85% of pure β-anomer of *xylo*-configuration **5**. ^{1}H NMR spectrum: 1.83 ddd, 1 H, *J*(2a,1) = 2.0, *J*(2a,3) = 3.3, *J*(gem) = 13.7 (H-2a); 2.28 ddd, 1 H, *J*(2b,1) = 5.9, *J*(2b,3) = 7.1 (H-2b); 3.24 s, 3 H (OCH_3); 4.22 ddd, 1 H, *J*(4,3) = 5.5, *J*(4,5a) = 8.1, *J*(4,5b) = 4.0 (H-4); 4.36 dd, 1 H, *J*(gem) = 11.5 (H-5a); 4.37 m, 1 H (H-3); 4.49 dd, 1 H (H-5b); 4.92 d, 1 H, *J*(OH,3) = 5.1 (3-OH); 4.96 dd, 1 H (H-1); 7.53 t, 2 H, 7.66 t, 1 H and 8.00 d, 2 H (H arom.). ^{13}C NMR spectrum: 41.17 (C-2); 54.66 (OCH_3); 65.53 (C-5); 69.65 (C-3); 79.75 (C-4); 104.70 (C-1); 129.00, 2 C and 129.44, 2 C and 130.08 and 133.57 (C arom.); 166.07 (C=O).

Methyl 3-Azido-5-*O*-benzoyl-2,3-dideoxy-β-D-ribofuranoside (**10**)

Finely ground sodium azide (1.29 g, 19.84 mmol) was added to a solution of mesyl derivative **7** (1.33 g, 4.03 mmol) in dimethylformamide (15 ml) and the mixture was stirred at 100 °C for 5 h under argon. The solid was filtered off, washed with a mixture of ethyl acetate and toluene, and the combined filtrates were concentrated. The residue was codistilled with toluene and partitioned between water and ethyl acetate. The organic layer was dried over magnesium sulfate, the solvent was

evaporated and the residue was chromatographed on silica gel (180 ml) in system S1 (R_F 0.34) to give 1.04 g (93%) of compound **10** as colorless oil. For $C_{13}H_{15}N_3O_4$ (277.3) calculated: 56.31% C, 5.45% H, 15.15% N; found: 56.49% C, 5.43% H, 14.95% N. IR spectrum (CCl_4): 2 103 cm^{-1} (N_3). ^{1}H NMR spectrum: 2.10 ddd, 1 H, *J*(2a,1) = 5.3, *J*(2a,3) = 7.1 *J*(gem) = 13.4 (H-2a); 2.32 ddd, 1 H, *J*(2b,1) = 1.8, *J*(2b,3) = 7.3 (H-2b); 3.20 s, 3 H (OCH_3); 4.19 q, 1 H (H-4); 4.31 dd, 1 H, *J*(5a,4) = 5.6, *J*(gem) = 11.5 (H-5a); 4.40 dd, 1 H, *J*(5b,4) = 5.1 (H-5b); 4.40 td, 1 H, *J*(3,4) = 5.3 (H-3); 5.08 dd, 1 H (H-1); 7.53 t, 2 H, 7.65 t, 1 H and 8.05 d, 2 H (H arom.). ^{13}C NMR spectrum: 38.39 (C-2); 54.56 (OCH_3); 61.11 (C-3); 65.06 (C-5); 81.10 (C-4); 104.67 (C-1); 128.89, 2 C and 129.44 2 C and 129.65 and 133.62 (C arom.); 165.66 (C=O).

Methyl 5-*O*-Benzoyl-3-chloro-2,3-dideoxy-α-D-xylofuranoside (**16**)

Thionyl chloride (0.7 ml, 9.6 mmol) was added at 0 °C to a solution of methyl 5-*O*-benzoyl-2-deoxy-α-D-ribofuranoside (**4**; 1.602 g, 6.35 mmol) in hexamethylphosphoric triamide (12 ml). After stirring at 0 °C for 10 min and then at room temperature for 6 h, the mixture was poured into saturated sodium hydrogen carbonate solution, the organic layer was dried over magnesium sulfate and the solvent was evaporated. Chromatography of the residue on silica gel in system S2 (R_F 0.53) afforded 1.31 g (76%) of compound **16** as colorless sirup. ^{1}H NMR spectrum: 2.40 ddd, 1 H, *J*(2a,1) = 3.9, *J*(2a,3) = 6.1, *J*(gem) = 14.9 (H-2a); 2.51 ddd, 1 H, *J*(2b,1) = 5.6, *J*(2b,3) = 2.0 (H-2b); 3.20 s, 3 H (OCH_3); 4.45 m, 3 H (H-4 and H-5); 4.89 ddd, 1 H, *J*(3,2a) = 6.1, *J*(3,2b) = 2.0, *J*(3,4) = 3.2 (H-3); 5.27 dd, 1 H (H-1); 7.55 t, 2 H, 7.68 t, 1 H and 7.99 d, 2 H (H arom.). ^{13}C NMR spectrum: 43.63 (C-2); 55.28 (OCH_3); 60.42 (C-3); 64.19 (C-5); 77.20 (C-4); 104.12 (C-1); 129.00, 2 C and 129.39, 2 C and 129.50 and 133.70 (C arom.); 165.58 (C=O).

Methyl 5-*O*-Benzoyl-2,3-dideoxy-α-D-ribofuranoside (**17**)

Tributylstannane in toluene (1 M, 5.3 ml) and azo-bis(isobutyronitrile) (175 mg) were added to a solution of 3-chloro derivative **16** (1.11 g, 4.10 mmol) in toluene (8 ml) at 120 °C. The reaction mixture was stirred at 120 °C for 1 h, cooled and the solvent was evaporated. Chromatography on silica gel (200 ml) in system S1 (R_F 0.30) gave 919 mg (95%) of dideoxy sugar **17** as colorless liquid. Mass spectrum (FAB; G + $CHCl_3$): 235.2 (M + H). ^{1}H NMR spectrum: 1.71 m, 1 H (H-3a); 1.77 m, 1 H (H-2a); 2.00 m, 1 H, *J*(2b,1) = 5.0, *J*(2b,3a) = *J*(2b,3b) = 9.0, *J*(gem) = 12.7 (H-2b); 2.05 m, 1 H (H-3b); 3.22 s, 3 H (OCH_3); 4.24 dd, 1 H, *J*(5a,4) = 6.8, *J*(gem) = 12.5 (H-5a); 4.31–4.35 m, 2 H (H-4 and H-5b); 5.03 dd, 1 H, *J* = 1.0 and 5.0 (H-1); 7.54 t, 2 H, 7.65 t, 1 H and 7.97 d, 2 H (H arom.). ^{13}C NMR spectrum: 25.52 (C-3); 31.63 (C-2); 54.21 (OCH_3); 66.52 (C-5); 75.40 (C-4); 105.04 (C-1); 128.99, 2 C and 129.36 2 C and 129.77 and 133.58 (C arom.); 165.81 (C=O).

1-(3-Azido-2,3-dideoxy-β-D-ribofuranosyl)-5-phenyl-2(1*H*)-pyrimidinone (**14**) and
1-(3-Azido-2,3-dideoxy-α-D-ribofuranosyl)-5-phenyl-2(1*H*)-pyrimidinone (**15**)

A suspension of 5-phenyl-2(1*H*)-pyrimidinone (800 mg, 4.65 mmol) and a catalytic amount of ammonium sulfate in hexamethyldisilazane (20 ml) was heated at 150 °C until it dissolved, and then for additional 2 h. The solvent was evaporated and the residue was codistilled with xylene (30 ml), leaving the silyl derivative **11**. A solution of the azido sugar **9** (970 mg, 3.50 mmol) in acetonitrile (25 ml) was added, the reaction mixture was cooled to 0 °C and trimethylsilyl trifluoromethanesulfonate (1.16 ml, 6.4 mmol) was added. The mixture was stirred at 0 °C for 40 min and the reaction was quenched with saturated solution of sodium hydrogen carbonate (100 ml). After stirring at room temperature for 15 min, the product was taken up in ethyl acetate (150 ml). The organic layer was dried over magnesium sulfate, the solvent was evaporated and the residue was chromatographed on silica

gel (250 ml) in ethyl acetate to give 1.2 g (82%) of chromatographically homogeneous mixture of anomers **12** and **13** as a white foam, R_F 0.50 (S5). Mass spectrum (FAB; G + dimethylformamide): 418.4 (M + H).

The obtained mixture of anomers in methanolic ammonia (about 100 ml) was allowed to stand in a refrigerator at 4 °C for 20 h. The solution was concentrated and the residue was chromatographed on silica gel (250 ml) in ethyl acetate. The β-anomer **14** (R_F 0.31, S5) was eluted first, yield 389 mg (47%) of white foam, collected after standing overnight with ethyl acetate–ether in a refrigerator. For $C_{15}H_{15}N_5O_3$ (313.3) calculated: 57.50% C, 4.83% H, 22.35% N; found: 57.38% C, 4.83% H, 22.32% N. IR spectrum ($CHCl_3$): 2 107 cm^{-1} (N_3). ^1H NMR spectrum: 2.55 m, 2 H (H-2′); 3.67 ddd, 1 H, J(5′a,4′) = 2.6, J(5′a,OH) = 4.7, J(gem) = 12.4 (H-5′a); 3.84 ddd, 1 H, J(5′b,4′) = 2.9, J(5′b,OH) = 4.7 (H-5′b); 3.98 m, 1 H (H-4′); 4.44 br q, 1 H, J(3′,4′) = 6.6 (H-3′); 5.58 t, 1 H (5′-OH); 6.09 br t, 1 H, J = 5.2 and 5.7 (H-1′); 7.30–7.55 m, 3 H and 7.65 m, 2 H (H arom.); 8.98 s, 1 H and 9.00 s, 1 H (H-4 and H-6). ^{13}C NMR spectrum: 38.11 (C-2′); 57.92 (C-3′); 59.62 (C-5′); 85.33 (C-1′); 86.72 (C-4′); 116.63 (C-5); 125.52, 2 C and 127.56 and 129.26, 2 C and 133.67 (C arom.); 141.30 (C-6); 154.24 (C-2); 164.63 (C-4).

Further elution with system S6 afforded the α-anomer **15** (R_F 0.26). Yield 420 mg (51%) of colorless amorphous compound. For $C_{15}H_{15}N_5O_3$ (313.3) calculated: 57.50% C, 4.83% H, 22.35% N; found: 57.78% C, 4.86% H, 22.11% N. IR spectrum ($CHCl_3$): 2 107 cm^{-1} (N_3). ^1H NMR spectrum: 2.27 dt, 1 H, J(2′a,1′) = J(2′a,3′) = 2.6, J(gem) = 14.5 (H-2′a); 2.87 dt, 1 H, J(2′b,1′) = J(2′b,3′) = 6.7 (H-2′b); 3.55 t, 2 H (H-5′); 4.43 dt, 1 H (H-3′); 4.59 td, 1 H, J(4′,3′) = 2.6, J(4′,5′) = 4.5 (H-4′); 5.11 t, 1 H, J(OH,5′) = 5.7 (5′-OH); 6.07 dd, 1 H (H-1′); 7.37 t, 1 H, 7.47 t, 2 H and 7.63 d, 2 H (H arom.); 8.36 d, 1 H (H-6); 8.99 d, 1 H, J(4,6) = 3.4 (H-4). ^{13}C NMR spectrum: 37.58 (C-2′); 61.13 (C-3′); 61.68 (C-5′); 87.33 (C-1′); 88.81 (C-4′); 116.74 (C-5); 125.83, 2 C and 127.70 and 129.30, 2 C and 133.61 (C arom.); 140.68 (C-6); 154.36 (C-2); 164.95 (C-4).

1-(5-*O*-Benzoyl-2,3-dideoxy-β-D-*glycero*-pentofuranosyl)-5-phenyl-2(1*H*)-pyrimidinone (**18**) and
1-(5-*O*-Benzoyl-2,3-dideoxy-α-D-*glycero*-pentofuranosyl)-5-phenyl-2(1*H*)-pyrimidinone (**19**)

5-Phenyl-2(1*H*)-pyrimidinone (800 mg, 4.65 mmol) was converted into the silyl derivative **11** as described for compounds **14** and **15**. The residue was mixed with a solution of the deoxy sugar **17** (850 mg, 3.6 mmol) in acetonitrile (30 ml), the solution was cooled to 0 °C and trimethylsilyl trifluoromethanesulfonate (1.16 ml, 6.4 mmol) was added. After stirring at 0 °C for 75 min, saturated solution of sodium hydrogen carbonate was added and the product was extracted with ethyl acetate. The organic phase was dried over magnesium sulfate, the solvent was evaporated and the residue was chromatographed on silica gel (400 ml) in ethyl acetate. The α-anomer **19** (R_F 0.21, S5), was eluted first, yield 515 mg (38%) of amorphous compound. For $C_{22}H_{20}N_2O_4$ (376.4) calculated: 70.20% C, 5.36% H, 7.44% N; found: 69.12% C, 5.50% H, 7.00% N. ^1H NMR spectrum: 1.95 m, 1 H (H-3′a); 2.15 m, 1 H (H-3′b); 2.20 m, 1 H, J(2′a,1′) = 3.3 (H-2′a); 2.60 m, 1 H, J(2′b,1′) = 6.4 (H-2′b); 4.36 dd, 1 H, J(5′a,4′) = 5.8, J(gem) = 11.7 (H-5′a); 4.44 dd, 1 H, J(5′b,4′) = 3.7 (H-5′b); 5.00 m, 1 H (H-4′); 6.10 dd, 1 H (H-1′); 7.36 t, 1 H, 7.45 t, 2 H, 7.55 t, 2 H, 7.64 d, 2 H, 7.68 t, 1 H and 8.00 d, 2 H (H arom.); 8.29 d, 1 H (H-6); 9.00 d, 1 H, J(4,6) = 3.3 (H-4). ^{13}C NMR spectrum: 25.67 (C-3′); 32.15 (C-2′); 66.37 (C-5′); 79.26 (C-4′); 89.63 (C-1′); 116.90 (C-5); 125.96, 127.62, 129.02, 129.06, 129.12, 129.16, 129.39, 2 C, 129.66, 133.62 and 133.68 (C arom.); 140.77 (C-6); 154.33 (C-2); 164.88 (C-4); 165.79 (C=O).

Further elution furnished the β-anomer **18**, yield 131 mg (10%) upon crystallization from ethyl acetate, m.p. 151.5–154.5 °C, R_F 0.14 (S5). For $C_{22}H_{20}N_2O_4$ (376.4) calculated: 70.20% C, 5.36% H, 7.44% N; found: 70.14% C, 5.40% H, 7.30% N. ^1H NMR spectrum: 1.94 dq, 1 H, J(3′a,2′a) = 8.2, J(3′a,2′b) = J(3′a,4′) = 8.6 (H-3′a); 2.11 ddd, 1 H, J(3′b,2′b) = 7.9, J(3′b,2′a) = 4.4, J(3′b,4′) = 6.2, J(gem) = 12.7 (H-3′b); 2.18 d pent, 1 H, J(2′a,1′) = 4.0, J(gem) = 13.7 (H-2′a); 2.58 ddd, 1 H, J(2′b,1′)

= 6.8 (H-2′b); 4.55 dtd, 1 H, *J*(4′,5′a) = 2.9, *J*(4′,5′b) = 6.0 (H-4′); 4.59 dd, 1 H, *J*(gem) = 12.2 (H-5′a); 4.63 dd, 1 H (H-5′b); 6.00 dd, 1 H (H-1′); 7.29 m, 3 H, 7.37 t, 2 H, 7.50 d, 2 H, 7.58 t, 1 H and 7.87 d, 2 H (H arom.); 8.36 d, 1 H (H-6); 8.95 d, 1 H, *J*(4,6) = 3.3 (H-4). ^{13}C NMR spectrum: 25.21 (C-3′); 32.34 (C-2′); 65.75 (C-5′); 79.68 (C-4′); 88.67 (C-1′); 116.79 (C-5); 125.63, 2 C and 127.53, and 128.85, 2 C and 129.11, 2 C and 129.27, 2 C and 129.34, 133.51, 133.62 (C arom.); 140.23 (C-6); 154.32 (C-2); 164.83 (C-4); 165.86 (C=O).

1-(2,3-Dideoxy-β-D-*glycero*-pentofuranosyl)-5-phenyl-2(1*H*)-pyrimidinone (**20**)

A mixture of 5′-*O*-benzoyl derivative **18** (100 mg, 0.266 mmol) and methanolic ammonia (10 ml) was stirred at room temperature for 48 h. After evaporation of the solvent, the residue was crystallized from ethyl acetate and ethanol, collected and washed with ethyl acetate and ether. Yield 60 mg (83%) of compound **20**, m.p. 174–177 °C, R_F 0.22 (S6). Mass spectrum (FAB; G + dimethyl sulfoxide): 273.3 (M + H). ^{1}H NMR spectrum: 1.82 dddd, 1 H, *J*(3′a,2′a) = 2.0, *J*(3′a,4′) = 5.5, *J*(3′a,2′b) = 7.9 (H-3′a); 1.91 dddd, 1 H, *J*(3′b,2′a) = 7.3, *J*(3′b,4′) = 10.2, *J*(3′b,2′b) = 11.9, *J*(gem) = 12.6 (H-3′b); 2.10 ddt, 1 H, *J*(2′a,1′) = 1.7, *J*(gem) = 13.6 (H-2′a); 2.47 ddt, 1 H (H-2′b); 3.63 ddd, 1 H, *J*(5′a,4′) = 2.5, *J*(5′a,OH) = 4.4, *J*(gem) = 12.3 (H-5′a); 3.91 ddd, 1 H, *J*(5′b,4′) = 2.5, *J*(5′b,OH) = 5.3 (H-5′b); 4.20 ddt, 1 H (H-4′); 5.45 br t, 1 H (5′-OH); 5.98 dd, 1 H, *J*(1′,2′a) = 1.7, *J*(1′,2′b) = 6.8 (H-1′); 7.34 t, 1 H, 7.43 t, 2 H and 7.63 d, 2 H (H arom.); 8.98 d, 1 H (H-6); 9.20 d, 1 H, *J*(4,6) = 3.5 (H-4). ^{13}C NMR spectrum: 23.01 (C-3′); 33.42 (C-2′); 60.78 (C-5′); 83.57 (C-4′); 87.81 (C-1′); 125.41, 2 C and 127.42 and 129.26, 2 C and 133.81 (C arom.); 141.62 (C-6); 154.38 (C-2); 164.14 (C-4).

1-(2,3-Dideoxy-α-D-*glycero*-pentofuranosyl)-5-phenyl-2(1*H*)-pyrimidinone (**21**)

A solution of compound **19** (485 mg, 1.29 mmol) in methanolic ammonia (40 ml) was allowed to stand at room temperature for 48 h. After evaporation of the solvent, the residue was chromatographed on silica gel (200 ml) in system S6 (R_F 0.16) to give 220 mg (63%) of amorphous compound **19**. According to NMR spectrum, the product contained small amount of the β-anomer, which had been formed in the debenzoylation. Mass spectrum (FAB; G + dimethyl sulfoxide): 273.1 (M + H). ^{1}H NMR spectrum: 1.80–2.50 m, 4 H, overlapped with signals of [D_6]-DMSO and the β-anomer (H-2′ and H-3′); 3.44 dd, 1 H, *J*(5′a,4′) = 4.8, *J*(gem) = 11.7 (H-5′a); 3.50 dd, 1 H, *J*(5′b,4′) = 4.4 (H-5′b); 4.62 m, 1 H, *J*(4′,3′) = 7.0 (H-4′); 6.02 dd, 1 H, *J*(1′,2′a) = 6.4, *J*(1′,2′b) = 3.5 (H-1′); 7.34–7.63 m, 5 H (H arom.); 8.23 d, 1 H (H-6); 8.96 d, 1 H, *J*(4,6) = 3.3 (H-4). ^{13}C NMR spectrum: 25.25 (C-3′); 32.32 (C-2′); 63.50 (C-5′); 82.70 (C-4′); 89.43 (C-1′); 116.86 (C-5); 140.49 (C-6); 156.32 (C-2); 164.72 (C-4). The aromatic carbon atom signals overlapped with those of the β-anomer.

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