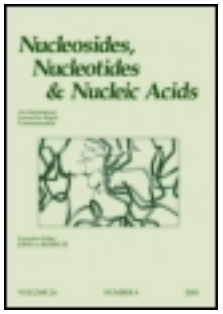

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Novel 4′-Branched Nucleosides

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NOVEL 4'-BRANCHED NUCLEOSIDES

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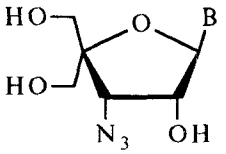
Total chemical synthesis of 4'-hydroxymethylnucleosides with an additional modification in a sugar residue was developed. The synthesis was made by condensation of corresponding protected sugars and nucleic bases with subsequent deprotection. In such a way 3'-azido- and 3'-amino-3'-deoxy-4'-hydroxymethylribonucleosides, 2',3'-anhydroribo- and 2',3'-anhydrolyxo-4'-hydroxymethylribonucleosides as well as 3'-deoxy-4'-hydroxymethylribonucleosides were prepared. At concentrations up to 100 μM none of them inhibited reproduction of human immunodeficiency virus type 1 in H9 and PBL cells as well as human herpes simplex virus type 2 and human cytomegalovirus in *vero* cells.

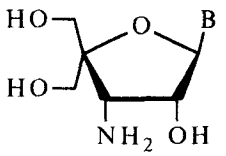
Recently, several highly active inhibitors of human immunodeficiency virus (HIV) reproduction in cell cultures have been found among 4'-substituted nucleosides [1-3], including 4'-azidothymidine, 4'-cyanothymidine, 4'-azido-2'-deoxycytidine. Intracellular triphosphorylation of 4'-azidothymidine followed by incorporation of the 5'-triphosphate into proviral DNA resulted in the total inhibition of proviral DNA biosynthesis catalyzed by HIV reverse transcriptase [4]. Thus it was demonstrated that modifications at 4'-position of nucleosides may be not crucial for the involvement of such nucleosides in intracellular anabolic processes.

Earlier several 4'-hydroxymethylnucleosides have been synthesized. Among them, 4'-hydroxymethylribonucleosides with adenine, cytosine, uracil [5,6], guanine [7] and modified nucleobases [8] should be mentioned. In these series, 4'-hydroxymethyl-2'-deoxyribonucleosides with thymine



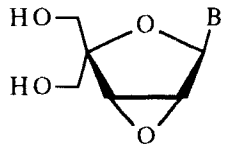
I

B=Ade, Cyt, Ura



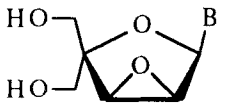
II

B=Ade, Cyt, Ura



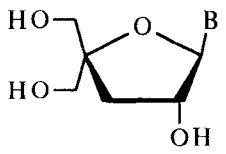
III

B=Ade, Gua



IV

B=Ade, Gua



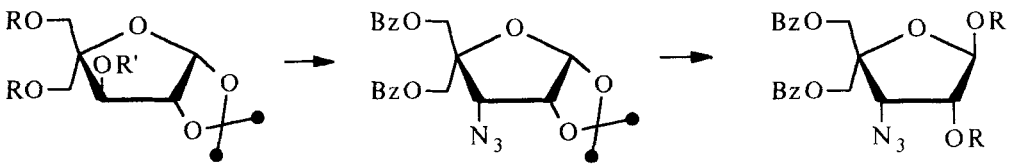
V

B=Ade, Cyt, Gua

FIGURE 1

[6,9] and adenine [10] bases, 4'-hydroxymethyl-3'-deoxyadenosine [10], 4'-hydroxymethylxylonucleosides with adenine and uracil bases [5,8,11], 4'-hydroxymethyl-2',3'-dideoxyribonucleosides with thymine, uracil [12,13], and adenine [10] bases, 4'-hydroxymethyl-2',3'-dideoxy-2',3'-didehydronucleosides with thymine [9] and adenine [10] bases were represented. 4'-Hydroxymethyl-3'-azido-3'-deoxythymidine [12], 4'-hydroxymethyl-2',3'-ribo- and 2',3'-lyxoanhydroadenosine [10], and 4'-hydroxymethyl-2'-deoxyxyloadenosine [10] have been synthesized. Recently a short communication dealt with the synthesis of 4'-hydroxymethyl-2',3'-ribo- and 2',3'-lyxoanhydroadenosine has been published [10]. Only 2'-deoxyderivatives have shown a marginal activity in HIV inhibition in cell cultures, the other compounds have not been active [9,10]. To obtain further information about the influence of 4'-hydroxymethyl group in nucleoside molecule on the inhibition of virus reproduction we have synthesized a number of 4'-hydroxymethylnucleosides.

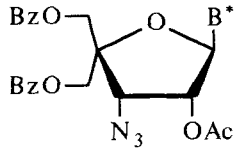
In this paper we describe the preparation of several groups of 4'-hydroxymethylnucleosides (**I-V**) (Figure 1) by the total chemical synthesis. 1,2-O-Isopropylidene-4-hydroxymethyl-α-D-xylofuranose (**VI**) was used as



VI R=R'=H
VII R=Bz, R'=H
VIII R=Bz, R'=Tfl

IX

X R=H
XI R=Ac



XII a, b, c

a. $B^*=N^6$-BzAde
b. $B^*=N^4$-AcCyt
c. B^*=Ura

Ia,b,c → IIa,b,c

Ia, IIa B=Ade
Ib, IIb B=Cyt
Ic, IIc B=Ura

Bz=COC_6H_5, Tfl=SO_2CF_3

SCHEME 1

starting material for the synthesis of compounds (**I-II**), (Scheme 1). Xylofuranose (**VI**) was obtained by periodate oxidation of 1,2-O-isopropylidene-α-D-glucopyranose with subsequent treatment by paraformaldehyde in alkaline solution according to [8,11]. The esterification of **VI** by benzoyl chloride at 0°C resulted in dibenzoyl derivative (**VII**). 3'-Hydroxy group in **VII** was reacted with trifluoromethanesulfonyl anhydride and the obtained **VIII** was treated with sodium azide according to [14]. The total yield of **IX** was 78% . Absorption at 2150 cm^{-1} in IR spectra of **IX** showed the presence of the N_3-residue. Transformation of xylosugar **VII** into ribosugar **IX** was detected by ^{1}H-NMR spectra, in which the signals of H-2 and H-3 protons shifted downfield to 0.19 and 0.18 ppm, respectively (Table 1). The coupling constant $J_{2,3}$ was increased to 4 Hz (Table 2). The removal of 1,2-O-isopropylidene group of **IX** by 75% HCOOH followed by acetylation of

TABLE 1. H^1-NMR data of the compounds shown in Scheme 1

Comp.	Chemical shifts, δ, ppm									Other protons
	H-1	H-2	H-3	H-5"a,5"b	H-5'a,5'b	H-5	H-6	H-2	H-8	
VI	5.86d	4.33dd	3.59d	3.50d	3.20d					1.10s,1.30s CH_3
VII	5.88d	4.61dd	4.32d	4.55d	4.35d					1.22s,1.50s CH_3
IX	5.78d	4.80dd	4.50d	4.65d	4.40d					1.22s,1.49s CH_3
XI	6.10s	5.32dd	4.45d	4.50s	4.48s					2.10s,1.83s OAc
XIIa	5.90d	5.64dd	5.39d	4.41s	4.65d			7.92s	8.24s	2.10s OAc
XIIb	5.65d	4.90 - 4.78 m		4.50d	4.62d	5.72d	7.55d			2.02s NHAc,
XIIc	5.92d	5.60dd	5.41d	4.34d	4.65d	5.20d	7.40d			1.98s OAc
Ia	5.76d	5.20dd	4.24d	3.60 - 3.02m				7.98s	8.19s	
Ib	5.78d	4.54dd	4.26d	3.64s		5.86d	7.56d			
Ic	5.82d	4.32dd	3.54d	3.80 - 3.60m		5.70d	7.72d			
IIa	5.90d	5.52dd	4.54d	3.49 - 3.09 m				7.90s	8.15s	
IIb	5.74d	4.62dd	4.14d	3.57d	3.50d	5.82d	7.66d			
IIc	5.80d	4.52dd	4.21d	3.54d	3.32d	5.24d	7.44d			

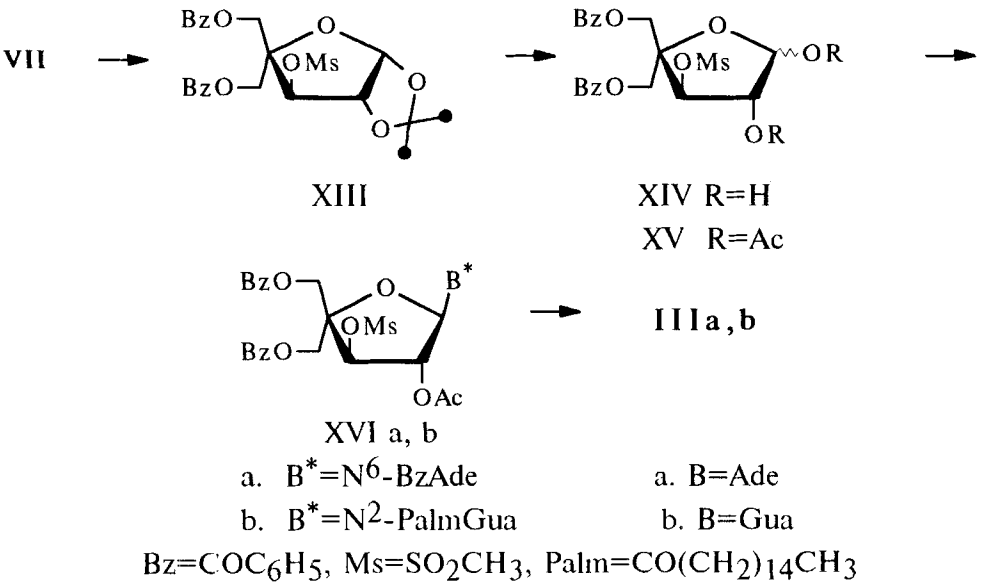
TABLE 2. Coupling constants of the compounds shown in Scheme 1

Comp.	Coupling constants, Hz				
	$J_{1,2}$	$J_{2,3}$	$J_{5'a,5'b}$	$J_{5''a,5''b}$	$J_{5,6}$
VI	4	2	11	12	
VII	4	1.5	10	9	
IX	3.8	4	10	12	
XI	0.5	6	-	12	
XIIa	7.5	6.5	11	-	
XIIb	4.8	5.8	12	-	8
XIIc	4	6	11	12	8
Ia	7	6.5	-	-	-
Ib	6	6	-	-	8
Ic	4	6	-	-	8
IIa	7	6	-	-	-
IIb	3	5.5	11	12	8
IIc	5	6	11	12	8

X with acetic anhydride in pyridine gave 1,2-di-O-acetyl-3-deoxy-3-azido-4-benzoyl-β-D-ribofuranose (**XI**) with the yield of 89%.

Nucleosides I were prepared by condensation of sugar **XI** with persilylated N^6-benzoyladenine, N^4-acetylcytosine, and uracil in the presence of $SnCl_4$, with subsequent deprotection of nucleosides **XII** by ammonia in methanol as in [15]. Reduction of **I** with triphenylphosphine in NH_4OH-pyridine gave aminonucleosides **II**, with the yields of 68-93%. The structure of **I** and **II** was confirmed by UV, IR, ^{1}H-NMR spectra data (Tables 1,2).

4'-Substituted anhydroribonucleosides **III** were prepared also from **VII** (Scheme 2). Activation of 3'-hydroxyl in **VII** by methanesulfonylation (**XIII**, yield 93%) followed by subsequent hydrolytic removal of isopropylidene group gave **XIV**. The latter was acetylated to give **XV** as a mixture of anomers, with the yield of 88% (from **XIII**).



SCHEME 2

Condensation of **XV** with persilylated N^6-benzoyladenine or N^2-palmitoylguanine in the presence of $SnCl_4$ or $F_3CSO_2SiMe_3$ as in [15] resulted in nucleosides **XVI** with the yields of 70 and 53%, respectively. They were deprotected subsequently with NH_3 in MeOH and then with NH_4OH in ethanol to afford **III**. Some physicochemical properties and ^{1}H-NMR data for the compounds in Scheme 2 are presented in Tables 3,4.

Anhydrolyxonucleosides with C4'-hydroxymethyl substituent (**IV**) were obtained according to Scheme 3. The key compound - 1,2-O-isopropylidene-4-hydroxymethyl-α-D-xylofuranose **VI** was benzoylated with 3 equivalents of BzCl and then **XVII** was converted to **XIX** as described above for **XI** with the yield of 84% and approximate α:β ratio 5:4.

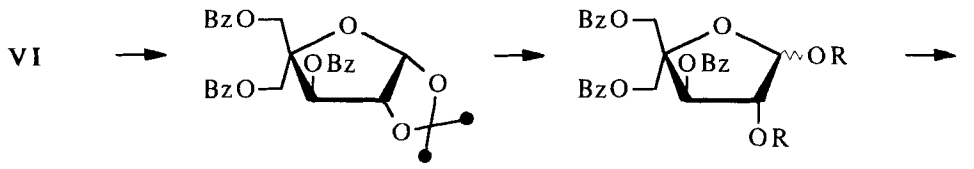
Condensation of **XIX** with persilylated N^4-benzoyladenine or N^2-palmitoylguanine gave **XXa** in the yield of 87%, **XXb** in the yield of 38%, N^7-isomer of **XXb** in the yield of 22%. Compounds **XX** were deacetylated by NH_3 - MeOH followed by mesylation to afford **XXII**. Anhydrolyxo ring formation was achieved as described above for **III**; **IVa** and **IVb** were isolated with 59 and 63% yields, respectively.

TABLE 3. H^1-NMR Data of the compounds shown in Schemes 2-3

Comp.	Chemical shifts, δ, ppm							Other protons
	H-1	H-2	H-3	H-5'a,5'b	H-5"a,5"b	H-2	H-8	
XIII	5.94d	4.80dd	5.20d	4.54d 4.77d	4.69s			2.92s OMs
α-XV	6.47d	5.75dd	5.55d	4.95 - 4.65m				3.20s OMs, 2.15s OAc
β-XV	6.30d	5.41d	5.34d	4.65 - 4.47m				3.10s OMs, 2.00s OAc
XVIa	6.15d	6.52t	5.59d	5.11d 4.97d	4.78s	8.26s	8.46s	3.10s OMs, 2.12s OAc
XVIb	5.97d	6.47t	5.57d	5.23d 4.91d	4.81s		8.35s	1.33s Plm
XVII	6.13d	4.85d	5.83d	4.57d 4.71ld	4.77s			1.41s,1.69s $C(CH_3)_2$
α-XIX	6.51d	5.78dd	6.05d	4.95 - 4.53m				2.15s OAc
β-XIX	6.31d	5.33dd	5.89d	4.88 - 4.46m				2.09s OAc
XXa	6.49d	6.55t	6.11d	5.25d 4.73d	4.85s	8.25s	8.69s	2.15s OAc
XXb	6.11d	6.50t	6.05d	5.61d 4.83d	4.89s		8.28s	2.11s OAc,1.34s Palm
XXIIa	6.43d	6.58t	6.13d	4.93d 4.77d	4.97d,4.73d	8.17s	8.58s	3.07s OMs
XXIIb	6.19d	6.39t	6.15d	5.59d 4.73d	4.89s		8.29s	3.01s OMs,1.34s Palm
IIIa	6.32s	4.60d	4.24d	3.89dd	3.60s	8.26s	8.46s	
IIIb	6.08s	4.50d	4.18d	3.67dd	3.72s		8.04s	
IVa	6.54s	4.42d	4.12d	3.86dd	3.42dd	8.26s	8.30s	
IVb	6.18s	4.25d	3.95d	3.79d 3.40d	3.52		7.74s	

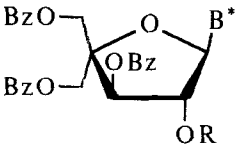
TABLE 4. Coupling constants for the compounds shown in Schemes 2-3

Comp.	Coupling constants, Hz			
	$J_{1,2}$	$J_{2,3}$	$J_{5'a,5'b}$	$J_{5''a,5''b}$
XIII	4	1	12	-
XV	α - 4.5, β - 1	α - 8, β - 1.5	-	-
XVIa	6	5	12	-
XVIb	6	5.5	12	-
XVII	4	4	12	-
XIX	α - 4.5, β - 1	α - 8, β - 2	-	-
XXa	5	4.5	12	-
XXb	7	6	12	-
XXIIa	5.5	5	11	12
XXIIb	6	5	12	-
IIIa	0	2	12	-
IIIb	0	2.5	12	-
VIa	0	3	11	12
VIb	0	3	11	12



XVII

XVIII R=H
XIX R=Ac

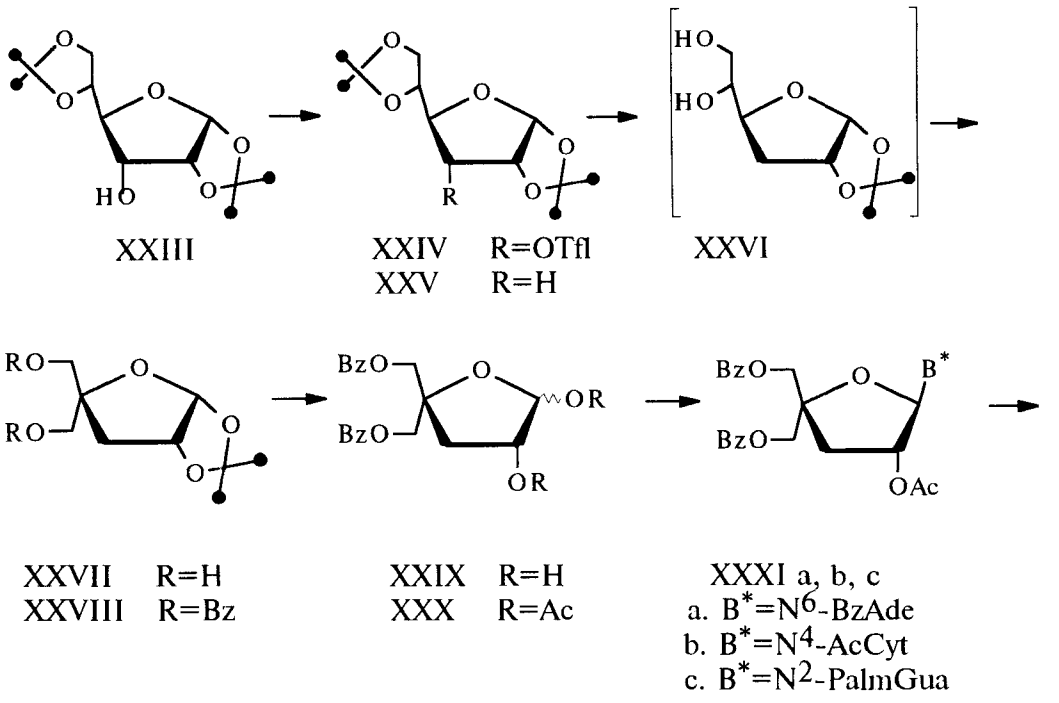


IVa,b

XX a, b R=Ac a. $B^*=N^6$-BzAde a. B=Ade
XXI a, b R=H b. $B^*=N^2$-PalmGua b. B=Gua
XXII a, b R=Ms

Bz=COC_6H_5, Ms=SO_2CH_3, Palm=$CO(CH_2)_{14}CH_3$

SCHEME 3



Va,b,c

a. B=Ade; b. B=Cyt; c. B=Gua

Bz=COC_6H_5, Tfl=SO_2CF_3, Palm=$CO(CH_2)_{14}CH_3$

SCHEME 4

The presence of anhydrorings in **III** and **IV** was confirmed by the appearance of singlets for 1'-H proton and characteristic doublets for 2'-H and 3'-H with $J_{2,3}$ = 1-1.5 Hz (Tables 3 and 4).

The compounds **V** were synthesized from 1,2;5,6-di-O-isopropylidene-α-D-allofuranose according to Scheme 4.

Triflation of 3'-hydroxyl group of 1,2;5,6-di-O-isopropylideneallose (**XXIII**) as in [16] with subsequent reduction by $NaBH_4$ as in [17] led to 1,2;5,6-di-O-isopropylidene-3-deoxy-D-*xylo*-hexofuranose (**XXV**). The removal of 5,6-isopropylidene group from **XXV** and the transformation of **XXVI** into 1,2-O-isopropylidene-3-deoxy-4-hydroxymethyl-α-D-*threo*-

TABLE 5. H^1-NMR Data of the compounds shown in Scheme 4

Comp.	Chemical shifts, δ, ppm					Other protons
	H-1	H-2	H-3a,b	H-5'a,5'b	H-5''a,5''b	
XXV	5.80d	4.60m	1.91ddd, 2.28ddd	4.25m	-	4.36m, H-4, 4.15m, H-6,6'
XXVII	5.90d	4.65dt	3.75 - 4.25m			1.55s, 1.40s 2x$\underline{CH_3}$
XXVIII	5.78d	4.64dt	2.01ddd, 2.21ddd	4.45s	4.25s	1.22s, 1.46s 2x$\underline{CH_3}$
α-XXX	6.15d	5.12m	2.55m	4.42s	4.34s	2.00s OAc
β-XXX	6.31d	5.25m	2.60m	4.40s	4.30s	2.15s OAc
XXXIa	6.08d	5.96m	3.12ddd, 2.25ddd	4.52dd	4.76dd	1.95s OAc
XXXIb	6.04d	5.34m	2.65ddd, 2.20ddd	4.48-4.60dd	4.30-4.70dd	1.90s OAc 2.10s NHAc
XXXIc	6.10d	5.60m	3.20ddd, 2.12ddd	4.36dd	4.72dd	2.11s OAc
Va	5.27d	4.60m	2.38ddd, 2.00ddd	3.42d	3.60d	8.46s H-8 8.26s H-2
Vb	5.70d	4.40m	2.20ddd, 1.80ddd	3.52s		5.82d H-6 7.60d H-5
Vc	5.74d	4.72m	2.54dd, 1.94dd	3.54s		8.04s H-8

TABLE 6. Coupling constants for the compounds shown in Scheme 4

Comp.	Coupling constants, Hz					
	$J_{1,2}$	$J_{2,3a}$	$J_{2,3b}$	$J_{3a,3b}$	$J_{5'a,5'b}$	$J_{5''a,5''b}$
XXV	4	4	7	14	-	-
XXVII	4	5	-	-	-	-
XXVIII	4	2	5	14	-	-
α-XXX	5	-	-	-	-	-
β-XXX	2	-	-	-	-	-
XXXIa	2	3	7	14	12	11
XXXIb	2	3	6	14	12	11
XXXIc	2	4	7	14	12	11
Va	5	7	7	14	11	10
Vb	5	6	7	14	-	-
Vc	5	7	7	14	-	-

pentofuranose **XXVII** as in [6] followed by benzoylation resulted in **XXVIII**. The key sugar **XXX** was synthesized from **XXVIII** by hydrolysis of the isopropylidene group and acetylation. Subsequent coupling with persilylated N^6-benzoyladenine, N^4-acetylcytosine, and N^2-palmitoylguanine to give nucleosides **XXXI** as in [15]. The latter compounds were deprotected to afford the target nucleosides **V**, as it was shown for **I**. All the compounds were characterized by ^{1}H-NMR spectra (Tables 5,6).

The signals of the protons in the ^{1}H-NMR spectra of the deoxynucleosides (**IIa-IIc, IIIa, IIIb, IVa, IVb, Va-Vc**) were in accordance with those of 3'-deoxyadenosine [18], 3'-amino-3'-deoxyadenosine [19], 2',3'-anhydroriboadenosine [20] and 2',3'-anhydrolyxoadenosine [21].

The presence of a 4'-hydroxymethyl group in nucleosides is confirmed by the appearance of two additional signals in ^{1}H-NMR spectra. The most difficult problem is to discriminate between the proton signals of 4'-hydroxymethyl group and those of C5' furanose residue.

None of the synthesized nucleosides inhibited HIV-1 reproduction in H9 and PBL cell cultures (Dr.B.W.Polsky, Memorial Sloan Kettering Cancer Center, New York, personal communication) as well as human herpes simplex virus type 2 and human cytomegalovirus in *Vero* cells (data of Dr.B.O'Hara, American Cyanamid Company, Pearl River, USA personal communication).

EXPERIMENTAL PART

Nucleic bases (Sigma), sodium azide, trifluoromethanesulfonyl anhydride and triphenylphosphine (Merck), other reagents and solvents (Russia) were used. UV spectra were registered in water on Beckman 25 spectrophotometer (USA), IR spectra - on Spectrometer 2000 (Hungary) in mineral oil. ^{1}H-NMR spectra of **I-V** were recorded on Varian XL-100-15 spectrometer (USA) in DMSO-d_6 - D_2O (2:1, v/v) with *tert.*-butanol as inner standard, those of all other compounds - in DMSO-d_6 or $CDCl_3$ with Me_4Si as internal standard, chemical shifts were given as δ values (ppm), coupling constants in Hz. The abbreviations used are as follows: s, singlet; d, doublet; t, triplet; dd, doublet of doublets; br s, broad singlet; m, multiplet. FAB-mass spectra were determined with a Kratos MS 50TC mass-spectrometer. Samples were mixed with glycerol in the probe tip. Xenon was used for the fast atom gun at 8 keV. TLC was performed on Silufol UV_{254} (Kavalier, Czechoslovakia) and silica gel 60 F_{254} (Merck) plates in systems (v/v): chloroform (A), chloroform - ethanol 20:1 (B), 9:1 (C), 4:1 (D) and 2-propanol - NH_4OH - water 7:1:2 (E). Column chromatography was performed on silica gel L40/100 (Chemapol, Czechoslovakia).

4-Hydroxymethyl-1,2-O-isopropylidene-α-D-xylofuranose (VI) was synthesized according to [8], ^{13}C-NMR (CD_3OD): 105.03 (C-1), 89.40 (C-2), 77.80 (C-3), 91.49 (C-4), 63.14 (C-5), 62.73 (C4'), 113.72 ($\underline{C}Me_3$), 26.62 and 27.24 (2 Me).

5-O-Benzoyl-4-benzoyloxymethyl-1,2-O-isopropylidene-α-D-xylofuranose (VII). Benzoyl chloride (6.38 g, 45.4 mmol) in CH_2Cl_2 (30 ml) was added during 1 h to the solution of **VI** (5 g, 22.7 mmol) at -4°C, the reaction mixture was stirred for 1.5 h at 0°C, poured into water with ice (500 ml), extracted with $CHCl_3$ (3 x 100 ml), the organic layer was

neutralized with saturated $NaHCO_3$ (3 x 50 ml), washed with water (3 x 50 ml), dried with Na_2SO_4, toluene (50 ml) was evaporated, then the residue and the product recrystallized from toluene. The yield was 7.18 g, 75%, m.p.148-150°C, Rf 0.2 (B), 0.57 (C), mass (m/z) 429 (M+H). UV (MeOH): λ_{max} 236 nm (ε 13 000). Anal. for $C_{35}H_{24}O_8$, %: C 64.46; H 5.65; found C 64.43, H 5.70.

3-Azido-4-benzoyloxymethyl-5-O-benzoyl-3-deoxy-1,2-O-isopropylidene-α-D-xylofuranose (IX). To a precooled to -20°C solution of **VII** (3 g, 7 mmol) in CH_2Cl_2 (20 ml) and pyridine (1.5 ml) trifluoromethanesulfonyl anhydride (2.56 g, 9.1 mmol) in CH_2Cl_2 (20 ml) was added for 30 min under intensive stirring. The reaction mixture was stirred with ethanol (1 ml) at room temperature for 10 min and poured into saturated $NaHCO_3$ in water (200 ml). The substances were extracted with $CHCl_3$, an organic solution was dried with Na_2SO_4, evaporated, the residue of **VIII** was dissolved in DMF (50 ml), sodium azide (1 g, 8.8 mmol) was added and the mixture was stirred for 2 h at 100°C. The reaction mixture was cooled, evaporated to dryness, diluted with $CHCl_3$ (200 ml) and water (100 ml), organic extract was washed with water (3 x 50 ml), dried with Na_2SO_4, concentrated and put on to silica gel column (9 x 4 cm). The title compound **IX** was eluted with $CHCl_3$ (1 l), fractions (TLC control) were evaporated. The yield was 2.49 g, 88%, Rf 0.34 (A), 0.71 (B). Mass (m/z) 453 (M+H). IR 2125 cm^{-1} (N_3). UV (MeOH): λ_{max} 239 nm (ε 13 500). Anal. for $C_{23}H_{23}N_3O_7$,%: C 60.91, H 5.21, N 9.27; found C 60.87, H 5.24, N 9.25.

1,2-Di-O-acetyl-3-azido-5-O-benzoyl-4-benzoyloxymethyl-3-deoxy-β-D-xylofuranose (XI). The solution of **IX** (2.37 g, 5.23 mmol) in 75% formic acid (38 ml) was heated for 2 hours at 50°C, then evaporated, the residue was subsequently reevaporated with 1-butanol (2 x 50 ml), toluene (2 x 50 ml) and pyridine (2 x 50 ml), the residue of **XI** was dissolved in acetic anhydride (2.76 ml, 20.92 mmol) in pyridine (20 ml) precooled to 0°C, and was stirred for 24 h at 20°C. The reaction mixture was poured into water with ice (300 g), extracted with $CHCl_3$ (3 x 50 ml), an organic layer was washed with saturated $NaHCO_3$ (3 x 50 ml), water (3 x 50 ml), dried with Na_2SO_4 and evaporated. The residue in $CHCl_3$ was chromatographed on a silica gel column (4 x 3 cm), the substance was

eluted with $CHCl_3$ and the eluate was evaporated. The yield was 2.33 g, 94%, Rf 0.5 (B), 0.9 (C). Mass (m/z) 498 (M+H). IR 2150 cm^{-1} (N_3). UV (MeOH): λ_{max} 237 nm (ε 13 700). Anal. for $C_{24}H_{23}N_3O_9$,%: C 57.93, H 4.66, N 8.45; found C 57.90, H 4.70, N 8.42.

9-(2-O-Acetyl-3-azido-5-O-benzoyl-4-benzoyloxymethyl-3-deoxy-β-D-ribofuranosyl)-N^6-benzoyladenine (XIIa). A solution of trimethylsilylated N^6-benzoyladenine (1.05 g, 2.75 mmol), prepared from N^6-benzoyladenine (0.65 g) in dichloroethane (20 ml), and a solution of $SnCl_4$ (1.78 g, 6.87 mmol) in dichloroethane (10 ml), were added to **XI** (1.14 g, 2.29 mmol) in dichloroethane (30 ml), the mixture was boiled for 2 hours, cooled, diluted with $CHCl_3$ (50 ml) and saturated $NaHCO_3$ (100 ml) and then filtered through Super Cell Hyflo (Gee Lawson Chemical, England). Organic extract was dried with Na_2SO_4, concentrated and purified on a silica gel column (9 x 4 cm) with $CHCl_3$ (1.5 l) elution. The yield was 1.4 g, 90%, Rf 0.32 (A), 0.59 (B). Mass (m/z) 678 (M+H). IR 2145 cm^{-1} (N_3). UV (MeOH): λ_{max} 280 nm (ε 19 940). Anal. for $C_{34}H_{28}N_8O_8$,%: C 60.34, H 4.17, N 16.57; found C 60.30, H 4.19, N 16.55.

1-(2-O-Acetyl-3-azido-5-O-benzoyl-4-benzoyloxymethyl-3-deoxy-β-D-ribofuranosyl)-N^4-acetylcytosine (XIIb). The solution of trimethylsilylated N^4-acetylcytosine (0.73 g, 3.25 mmol), prepared from N^4-acetylcytosine (0.5 g) in dichloroethane (20 ml) and $SnCl_4$ (2.11 g, 8.13 mmol) in dichloroethane (10 ml), was added to **XI** (1.35 g, 2.71 mmol) in dichloroethane (30 ml), the mixture was stirred for 2 hours at 20°C, diluted with $CHCl_3$ (50 ml) and then with saturated $NaHCO_3$ (100 ml) and filtered through Super Cell Hyflo. The organic extract was dried with Na_2SO_4, concentrated and purified on a silica gel column (9 x 1.5 cm) with $CHCl_3$ (0.5 l) elution. The yield was 1.3 g, 81%, Rf 0.25 (B), 0.63 (C). Mass (m/z) 591 (M+H). IR 2145 cm^{-1} (N_3). UV (MeOH): λ_{max} 236 nm (ε 24 200). Anal. for $C_{28}H_{26}N_6O_9$,%: C 56.94, H 4.44, N 14.23; found C 56.81, H 4.64, N 14.23.

1-(2-O-Acetyl-3-azido-5-O-benzoyl-4-benzoyloxymethyl-3-deoxy-β-D-ribofuranosyl)uracil (XIIc) was synthesized by the same procedure as **XIIa** from **XI** (1.16 g, 2.34 mmol), trimethylsilylated uracil (0.65 g, 2.57 mmol), in acetonitrile (70 ml) and $SnCl_4$ (0.86 g, 3.33 mmol). The yield was 0.95 g, 74%, Rf 0.34 (B), 0.66 (C). Mass (m/z) 550 (M+H). IR 2150

cm^{-1} (N_3). UV (MeOH): λ_{max} 257 nm (ε 9 440). Anal. for $C_{26}H_{23}N_5O_9$,%: C 56.82, H 4.22, N 12.75; found C 56.86, H 4.19, N 12.70.

3'-Azido-3'-deoxy-4'-hydroxymethylribonucleosides (Ia-Ic). Solutions of **XIIa-XIIc** in MeOH saturated with ammonia at 0°C were stirred at 20°C for 16 h, evaporated to dryness, solids were dissolved in minimum volumes of solvent system B and chromatographed on silica gel columns (8 x 1.5 cm). Nucleoside **Ia** was eluted with system A and nucleosides **Ib, Ic** - with B, the corresponding fractions were evaporated to dryness.

3'-Azido-3'-deoxy-4'-hydroxymethylriboadenosine (Ia) was crystallized from ethanol (10 ml), yield 0.5 g, 75%, m.p. 178°C Rf 0.15 (B), 0.87 (E). Mass (m/z) 323 (M+H). IR 2125 cm^{-1} (N_3). UV: pH 7 λ_{max} 259 nm (ε 15 600); pH 2 λ_{max} 257 nm (ε 14 800). Anal. for $C_{11}H_{14}N_8O_4$,%: C 40.98, H 4.38, N 34.78; found C 40.95, H 4.40, N 34.77.

3'-Azido-3'-deoxy-4'-hydroxymethylribocytidine (Ib), yield 0.52 g, 80%, Rf 0.07 (B), 0.50 (E). Mass (m/z) 300 (M+H). IR 2155 cm^{-1} (N_3). UV: pH 7 λ_{max} 272 nm (ε 9 200); pH 2 λ_{max} 281 nm (ε 14 000). Anal. for $C_{10}H_{14}N_6O_5$,%: C 40.28, H 4.70, N 28.18; found C 40.09, H 5.10, N 28.06.

3'-Azido-3'-deoxy-4'-hydroxymethylribouridine (Ic), yield 0.4 g, 78.4%, Rf 0.22 (D), 0.58 (E). Mass (m/z) 300 (M+H). IR 2150 cm^{-1} (N_3). UV: pH 7 λ_{max} 262 nm (ε 7 200); pH 2 λ_{max} 263 nm (ε 10 500). Anal. for $C_{10}H_{13}N_5O_6$,%: C 40.12, H 4.38, N 23.41; found C 40.08, H 4.35, N 23.44.

3'-Amino-3'-deoxy-4'-hydroxymethylribonucleosides (IIa-IIc). Triphenylphosphine (0.8 mmol) was added to **Ia-Ic** (0.4 mmol) in pyridine (5 ml) and solutions were stirred at 20°C for 2 h, then 25% NH_4OH in water (10 ml) was added and solutions were stirred for 8 hours at 20°C and the solvents were evaporated to dryness. The nucleosides **IIa** and **IIc** were purified by chromatography on silica gel columns (2 x 2 cm) with elution by system B. Fractions were evaporated to dryness. The nucleoside **IIb** was recrystallized from ethanol (5 ml).

3'-Amino-3'-deoxy-4'-hydroxymethylriboadenosine (IIa), yield 0.043 g, 62.4%, Rf 0.09 (D), 0.72 (E). Mass (m/z) 297 (M+H). UV: pH 7 λ_{max} 260 nm (ε 15 100). Anal. for $C_{11}H_{16}N_6O_4$,%: C 44.58, H 5.45, N 28.37; found C 44.55, H 5.49, N 28.40.

3'-Amino-3'-deoxy-4'-hydroxymethylribocytidine (IIb), yield 0.100 g, 93%, m.p. 148-150°C, Rf 0.28 (E). Mass (m/z) 274 (M+H). UV: pH 7 λ_{max} 272 nm (ε 8 900); pH 2 λ_{max} 281 nm (ε 14 000). Anal. for $C_{10}H_{16}N_4O_5$,%: C 44.11, H 5.92, N 20.58; found C 43.97, H 6.23, N 20.55.

3'-Amino-3'-deoxy-4'-hydroxymethylribouridine (IIc), yield 0.079 g, 73%, Rf 0.10 (D), 0.45 (E). Mass (m/z) 274 (M+H). UV: pH 7 λ_{max} 262 nm (ε 7 400). Anal. for $C_{10}H_{15}N_3O_6$,%: C 43.94, H 5.54, N 15.38; found C 43.98, H 5.57, N 15.35.

5-O-Benzoyl-4-benzoyloxymethyl-1,2-O-isopropylidene-3-O-methanesulfonyl-α-D-xylofuranose (XIII). Methanesulfonyl chloride (1.39 g, 12.14 mmol) in CH_2Cl_2 (20 ml) was added during 30 min to a precooled till -5°C solution of **VII** (4 g, 9.34 mmol) in pyridine (40 ml), the reaction mixture was stirred for 4 h at the same temperature, heated to 20°C, poured into water with ice (200 ml), extracted with $CHCl_3$ (3 x 100 ml), the organic layer was washed with saturated $NaHCO_3$ (3 x 100 ml), water (3 x 50 ml), it was dried with Na_2SO_4 and evaporated to dryness. The yield was 4.35 g, 92%, Rf 0.28 (A), 0.5 (B). Mass (m/z) 507 (M+H). UV (MeOH): λ_{max} 238 nm (ε 13 400). Anal. for $C_{24}H_{26}O_{10}S$, %: C 56.91; H 5.17; found C 56.87, H 5.20.

3,5-Di-O-benzoyl-4-benzoyloxymethyl-1,2-O-isopropylidene-α-D-xylofuranose (XVII) was synthesized from **VI** (5 g, 22.7 mmol) by the standard benzoylation procedure. The yield was 11.5 g, 95%, Rf 0.51 (A). Mass (m/z) 533 (M+H). UV (MeOH): λ_{max} 240 nm (ε 13 700). Anal. for $C_{30}H_{28}O_9$, %: C 67.66; H 5.37; found C 67.64, H 5.23.

1,2-Di-O-acetyl-5-O-benzoyl-4-benzoyloxymethyl-3-O-methanesulfonyl-D-xylofuranose (XV) was synthesized from **XIII** (4.10 g, 8.10 mmol) with subsequent acetylation of **XIV** by the same procedure as **XI**. The yield was 4.20 g, 89%, Rf 0.19 (A), 0.43 (B). Mass (m/z) 551 (M+H). UV (MeOH): λ_{max} 239 nm (ε 13 000). Anal. for $C_{25}H_{26}O_{12}S$, %: C 54.54, H 4.76, found C 54.57, H 4.73.

1,2-Di-O-acetyl-3,5-di-O-benzoyl-4-benzoyloxymethyl-D-xylofuranose (XIX) was obtained as **XI**, starting from **XVII** (11.18 g, 22.7 mmol) and subsequent acetylation of **XIV** with acetic anhydride (6.02 g, 59.02 mmol) in pyridine, 2 hours at 20°C. The yield was 12.78 g, 97.7%,

Rf 0.36 (A). Mass (m/z) 577 (M+H). UV (MeOH): λ_{max} 242 nm (ε 13 700). Anal. for $C_{31}H_{28}O_{11}$, %: C 64.74, H 4.73, found C 64.58, H 4.89.

9-(2-O-Acetyl-5-O-benzoyl-4-benzoyloxymethyl-3-O-methanesulfonyl-β-D-xylofuranosyl)-N^6-benzoyladenine (XVIa) was prepared from **XV** (2.27 g, 4.12 mmol) as described for **XIIa**. The yield was 2.11 g, 71%, foam, Rf 0.18 (A), 0.48 (C). Mass (m/z) 730 (M+H). UV (MeOH): λ_{max} 281 nm (ε 22 300), 235 nm (ε 10 000). Anal. for $C_{35}H_{31}N_5O_{11}S$, %: C 57.61, H 4.28, N 9.60; found C 57.57, H 4.23, N 9.63.

9-(2-O-Acetyl-3,5-di-O-benzoyl-4-benzoyloxymethyl-β-D-xylofuranosyl)-N^6-benzoyladenine (XXa) was prepared from sugar **XIX** (4 g, 6.94 mmol) by the same procedure as **XIIa**. The yield was 4.93 g, 86% m.p. 120°C (ethanol), Rf 0.13 (A), 0.5 (B). Mass (m/z) 757 (M+H). UV: (MeOH) λ_{max} 280 nm (ε 20 200), 235 nm (ε 10 100). Anal. for $C_{41}H_{33}N_5O_{10}$,%: C 65.16, H 4.40, N 9.27; found C 65.20, H 4.32, N 9.22.

9-(2-O-Acetyl-5-O-benzoyl-4-benzoyloxymethyl-3-O-methanesulfonyl-β-D-lyxofuranosyl)-N^2-palmitoylguanine (XVIb). The suspension of N^2-palmitoylguanine (4.49 g, 11.56 mmol) in hexamethyldi-silazane (80 ml) and trimethylchlorosilane (20 ml) was reflaxed till it became homogeneous, evaporated to dryness, the solid was dissolved in dichloroethane (40 ml), compound **XV** (5.3 g, 9.63 mmol) and trimethylsilyltrifluoromethane sulfonate (2.99 g, 13.49 mmol) in dichloroethane (40 ml) was added and the mixture was heated for 3 hours at 50°C. The reaction solution was poured into $CHCl_3$ (200 ml), washed with saturated $NaHCO_3$ (50 ml) and filtered through Super Cell Hyflo. The organic extract was dried with Na_2SO_4, evaporated to dryness, dissolved in $CHCl_3$ and chromatographed on a silica gel column (20 x 2.5 cm) with elution by $CHCl_3$-hexane (1:1 v/v) (0.5 l), $CHCl_3$ (1.5 l) and then by system B (0.3 l). Fractions with Rf 0.35 (C) were evaporated, yield 1.93 g, 22.7%, mass (m/z) 880 (M+H). Anal. for $C_{44}H_{57}N_5O_{12}S$,%: C 60.05, H 6.53, N 7.96; found C 60.09, H 6.58, N 8.02. Treatment of a sample with MeOH, saturated with ammonia at 0°C, (35 h, 20°C) resulted in N^7-isomer, λ_{max} 285 nm (ε 12 800).

Fractions with Rf 0.28 (C) were evaporated, **XVIb**, yield 4.91 g, 58%, mass (m/z) 880 (M+H). Anal. for $C_{44}H_{57}N_5O_{12}S$,%: C 60.05, H 6.53, N 7.96; found C 60.08, H 6.55, N 8.00. Treatment of an analytical

sample with ammonia saturated MeOH afforded N^9-isomer, λ_{max} 253 nm (ε 13 000), 274 nm (shoulder, ε 8 400).

9-(2-O-Acetyl-3,5-di-O-benzoyl-4-benzoyloxymethyl-β-D-xylo-furanosyl)-N^2-palmitoylguanine (XXb) was prepared as **XVIb** from sugar **XIX** (5g, 8.68 mmol), N^2-palmitoylguanine (3.71 g, 9.54 mmol) and trimethylsilyltrifluoromethane sulfonate (2.3 g, 10.4 mmol) in acetonitrile (120 ml). Purification was carried out by chromatography on a silica gel column (20 x 4 cm) and elution with $CHCl_3$ (2 l) and $CHCl_3$ - ethanol (50:1, 0.5 l). Fractions with Rf 0.53 (C) were evaporated, yield 1.71 g, 22%, mass (m/z) 907 (M+H). Anal. for $C_{50}H_{59}N_5O_{11}$,%: C 66.28, H 6.56, N 7.73; found C 66.18, H 6.62, N 7.81. Treatment of a sample with ammonia in MeOH (35 h, 20°C) afforded N^7-isomer, λ_{max} 285 nm (ε 12 900).

Fractions with Rf 0.42 (C) gave **XXb**, yield 3 g, 38%. Mass (m/z) 906 (M+H). Anal. for $C_{50}H_{59}N_5O_{11}$,%: C 66.28, H 6.56, N 7.73; found C 66.20, H 6.65, N 7.61. Treatment of a sample with MeOH, saturated with ammonia, afforded N^9-isomer, λ_{max} 253 nm (ε 13 500), 276 nm (shoulder, ε 8 800).

9-(3,5-Di-O-benzoyl-4-benzoyloxymethyl-2-O-methanesulfonyl-β-D-xylofuranosyl)-N^6-benzoyladenine (XXIIa) and N^2-palmitoylguanine (XXIIb). Methanol saturated at 0°C with ammonia (10 ml) was added at -10°C to nucleosides **XXa** and **XXb** (2.38 mmol) in tetrahydrofuran (50ml) and stirred for 24 h at -5°C. Then the solutions were evaporated to dryness, the solids **XXIIa** and **XXIIb** were reevaporated with pyridine (2 x 50 ml), dissolved in pyridine (50 ml), cooled to -5°C and methanesulfonyl chloride (0.37 ml, 4.76 mmol in both cases) were added. Reaction mixtures were stirred for 8 h at 0°C, water (1 ml) was added and the solutions were evaporated, solids were reevaporated with toluene (2 x 30 ml), dissolved in $CHCl_3$ (50 ml), washed with water (3 x 50 ml), dried with Na_2SO_4, evaporated and chromatographed on a silica gel column (20 x 2.5 cm) with elution by $CHCl_3$ (0.5 l).

Compound **XXIIa**, yield 1.65 g, 88%, Rf 0.16 (A), 0.44 (B). Mass (m/z) 792 (M+H). UV: λ_{max} 281 nm (ε 22 300). Anal. for $C_{40}H_{33}N_5O_{11}S$, %: C 60.68, H 4.20, N 8.84; found C 60.59, H 4.05, N 8.81.

Compound **XXIIb**, yield 1.69 g, 75%, Rf 0.21 (B). Mass (m/z) 943 (M+H). UV: λ_{max} 234 nm (ε 16 300), 254 nm (ε 8 900), 281 nm (ε 2 700).

Anal. for $C_{49}H_{59}N_5O_{12}S$, %: C 62.47, H 6.31, N 7.43; found C 62.32, H 6.45, N 7.51.

9-(2,3-Anhydro-4-hydroxymethyl-β-D-ribofuranosyl)adenine (IIIa) and 9-(4-hydroxymethyl-2,3-anhydro-β-D-ribofuranosyl)guanine (IIIb). Nucleosides **XVIa** and **XVIb** (1 mmol) were dissolved in methanol (30 ml), saturated at 0°C with ammonia, stirred for 36 h at 20°C, the solvents were evaporated, solids were dissolved in ethanol (20 ml) and 25% NH_4OH (40 ml), and the solutions were stirred for 24 h at 20°C. Solids after evaporation were recrystallized from ethanol (5 ml).

Compound **IIIa**, yield 0.22 g, 81.3%, m.p.210°C, Rf 0.5 (E). Mass (m/z) 280 (M+H). UV: pH 7 λ_{max} 261 nm (ε 14 600), pH 2 λ_{max} 256 nm (ε 14 700). Anal. for $C_{11}H_{13}N_5O_4$, %: C 47.69, H 4.69, N 25.08; found C 47.28, H 4.89, N 24.75.

Compound **IIIb**, yield 0.18 g, 62%, m.p.>300°C, Rf 0.40 (E). Mass (m/z) 296 (M+H). UV: pH 7 λ_{max} 252 nm (ε 12 900), 274 nm, shoulder (ε 8 300); pH 2 λ_{max} 256 nm (ε 10 700), 283 nm, shoulder (ε 7 500). Anal. for $C_{11}H_{13}N_5O_5$, %: C 44.73, H 4.44, N 23.73; found C 44.69, H 4.46, N 23.76.

9-(2,3-Anhydro-4-hydroxymethyl-β-D-lyxofuranosyl)adenine (IVa) and 9-(2,3-anhydro-4-hydroxymethyl-β-D-lyxofuranosyl)guanine (IVb) were synthesized from **XXIIa** and **XXIIb** (1.5 mmol) using the same procedure as for **III**.

Compound **IVa**, yield 0.22 g, 53%, m.p.279°C (ethanol), Rf 0.44 (E). Mass (m/z) 280 (M+H). UV: pH 7 λ_{max} 259 nm (ε 15 100), pH 2 λ_{max} 257 nm (ε 14 900). Anal. for $C_{11}H_{13}N_5O_4$, %: C 47.69, H 4.69, N 25.08; found C 46.98, H 4.41, N 24.86.

Compound **IVb**, yield 0.30 g, 69%, m.p.>300°C, Rf 0.38 (E). Mass (m/z) 296 (M+H). UV: pH 7 λ_{max} 253 nm (ε 14 900), 273 nm, shoulder (ε 8 300); pH 2 λ_{max} 256 nm (ε 10 700) 268 nm, shoulder (ε 7500). Anal. for $C_{11}H_{13}N_5O_5$, %: C 44.73, H 4.44, N 23.73; found C 44.52, H 4.26, N 24.03.

1,2:5,6-Di-O-isopropylidene-3-O-trifluoromethylsulfonyl-α-D-allofuranose (XXIV). Trifluoromethanesulfonyl anhydride (7.48 g, 26.53 mmol) in CH_2Cl_2 (20 ml) was added during 30 min to a solution of 1,2:5,6-di-O-isopropylidene-α-D-allofuranose **(XXIII)** (5.52 g, 21.53

mmol) and pyridine (4.19 g, 53.07 mmol) in CH_2Cl_2 (60 ml) precooled to -30°C. The mixture was stirred for 30 min at -20°C and methanol (5 ml) was added. The solution was washed with water (2 x 100 ml), organic phase was dried with Na_2SO_4, evaporated to dryness and the residue 8.3 g (91%) was used in subsequent step without any additional purification. An analytical sample of **XXIV** was purified on a silica gel column (3 x 1 cm), eluted with $CHCl_3$, Rf 0.5 (A), 0.81 (B). Mass (m/z) 393 (M+H). Anal. for $C_{13}H_{19}O_8F_3S$, %: C 39.79, H 4.88; found C 40.08, H 5.21.

3-Deoxy-1,2-O-isopropylidene-α-D-*xylo*-hexofuranose (XXV). Sodium borohydride (2.51 g, 67.8 mmol) was added to **XXIV** (8.3 g, 21.1 mmol) in acetonitrile (120 ml), the reaction mixture was stirred for 72 h at 20°C, diluted with acetone (10 ml) and the resulted homogeneous solution was evaporated to dryness. The residue was dissolved in $CHCl_3$ (100 ml), washed with water (3 x 100 ml), organic extract was dried with Na_2SO_4 and evaporated to dryness. The residue was dissolved in a mixture of methanol-AcOH-water (v/v) 1:1.23:1.4 (100 ml), the solution was heated for 12 h at 50°C, neutralized with $NaHCO_3$ and evaporated to dryness. The solid **XXV** was dissolved in water (100 ml), washed with $CHCl_3$ (2 x 50 ml), the aqueous solution was evaporated to dryness and used without additional purification.

3-Deoxy-4-hydroxymethyl-1,2-O-isopropylidene-α-D-*threo*-pentofuranose (XXVII) was synthesized from **XXV** with formation of intermediate **XXVI** according to [11]. ^{13}C-NMR (CD_3OD): 106.51 (C - 1), 88.46 (C - 2), 38.91 (C - 3), 91.50 (C - 4), 62.75 (C - 5), 62.10 (C - 4'), 113.52 (C ($CH_3)_2$), 25.94, 26.35 (2 x CH_3).

5-O-Benzoyl-4-benzoyloxymethyl-3-deoxy-1,2-O-isopropylidene-α-D-*threo*-pentofuranose (XXVIII) was obtained from **XXVII** (2.6 g, 12.7 mmol) by the standard benzoylation procedure. Yield 5.04 g, 96%, m.p.110°C, Rf 0.39 (A), 0.75 (B). Mass (m/z) 413 (M+H). UV (MeOH): λ_{max} 234 nm (ε 14 000). Anal. for $C_{23}H_{24}O_7$, %: C 66.97, H 5.87; found C 67.10, H 6.11.

5-O-Benzoyl-4-benzoyloxymethyl-3-deoxy-1,2-di-O-acetyl-D-*threo*-pentofuranose (XXX) was synthesized from **XXVIII** (5 g, 12.1 mmol) with subsequent acetylation of **XXIX** as for **XIX**; α/β ratio according to NMR-spectra is 5:1. Yield 6.32 g, 95%, Rf 0.25 (A), Rf 0.63 (B). Mass (m/z) 457

(M+H). UV (MeOH): λ_{max} 239 nm (ε 13 900). Anal. for $C_{24}H_{24}O_9$, %: C 63.14, H 5.30; found C 63.26, H 5.44.

9-(2-O-Acetyl-5-O-benzoyl-4-benzoyloxymethyl-3-deoxy-β-D-ribofuranosyl)-N^6-benzoyladenine (XXXIa) was synthesized from **XXX** by the procedure used for **XIIa**. Yield 1.12 g, 58%, Rf 0.10 (A), 0.32 (B). Mass (m/z) 636 (M+H). UV (MeOH): λ_{max} 281 nm (ε 19 100). Anal. for $C_{34}H_{29}N_5O_8$, %: C 64.23, H 4.60, N 11.02; found C 64.44, H 4.32, N 10.38.

1-(2-O-Acetyl-5-O-benzoyl-4-benzoyloxymethyl-3-deoxy-β-D-ribofuranosyl)-N^4-acetylcytosine (XXXIb) was synthesized from **XXX** (1.39 g, 3.46 mmol) and trimethylsilylated N^4-acetylcytosine [22], prepared from N^4-acetylcytosine (0.55 g), as it was done for **XIIa**. Yield 0.83 g, 51%, Rf 0.20 (A), 0.5 (B). Mass (m/z) 550 (M+H$^+$). UV (MeOH): λ_{max} 235 nm (ε 23 500). Anal. for $C_{28}H_{27}N_5O_9$, %: C 58.21, H 4.71, N 12.13; found C 58.03, H 4.92, N 12.24.

9-(2-O-Acetyl-5-O-benzoyl-4-benzoyloxymethyl-3-deoxy-β-D-ribofuranosyl)-N^2-palmitoylguanine (XXXIc) was synthesized from **XXX** (3.48 g, 7.63 mmol), N^2-palmitoylguanine (3.28 g, 8.45 mmol), and trimethylsililtrifluoromethane sulfonate (2.37 g, 10.68 mmol) in dichloroethane (100 ml) as it was done for **XXb**. The resulting substances were isolated on the silica gel column (20 x 4 cm), eluted with $CHCl_3$ (2 l). The fraction with Rf 0.33 (B) was evaporated to dryness, yield 2.01 g, 35%, mass (m/z) 786 (M+H). Anal. for $C_{43}H_{55}N_5O_9$, %: C 65.71, H 7.05, N 9.91; found C 65.56, H 7.20, N 8.74. Treatment of a sample with ammonia in MeOH (35 h, 20°C) gave the N^7-isomer, λ_{max} 284 nm (ε 12 100) in methanol.

Fraction with Rf 0.28 (B) was evaporated to dryness. **XXXIc**, yield 2.6 g, 45%, mass (m/z) 786 (M+H). UV (MeOH): λ_{max} 234 nm (ε 16 200), 253 nm (ε 8 700), 281 nm (ε 2 900). Anal. for $C_{43}H_{55}N_5O_9$, %: C 65.71, H 7.05, N 8.91; found C 65.93, H 6.90, N 8.85

3'-Deoxy-4'-hydroxymethylnucleosides (Va-Vc). Solutions of **XXXIa-XXXIc** (1.5 mmol) in methanol saturated with NH_3 (20 ml), were kept for 20 h at 20°C and evaporated to dryness. **Va** and **Vb** were dissolved in a minimum volume of chromatographic system B (200 ml) and poured on the columns (8 x 2 cm) with silica gel. The substances were eluted by system B (200 ml) and then by system C (300 ml), the corresponding

fractions were evaporated to dryness and solids were recrystallized from ethanol. The solution of **Vc** in water (20 ml) was washed with ethyl acetate (3 x 40 ml), evaporated, and the final residue was recrystallized from water (5 ml).

3'-Deoxy-4'-hydroxymethyladenosine (Va), yield 0.328 g, 78%, m.p.221°C, Rf 0.68 (E). Mass (m/z) 282 (M+H). UV (MeOH): pH 7 λ_{max} 259 nm (ε 15 500); pH 2 λ_{max} 257 nm (ε 14 500). Anal. for $C_{11}H_{15}N_5O_4$, %: C 46.97, H 5.38, N 24.90; found C 46.72, H 5.46, N 24.80.

3'-Deoxy-4'-hydroxymethylcytidine (Vb), yield 0.30 g, 79%, m.p.224°C (decomp.), Rf 0.52 (E). Mass (m/z) 257 (M+H). UV (MeOH): pH 7 λ_{max} 272 nm (ε 9 500), 281 nm (ε 9 500); pH 2 λ_{max} 281 nm (ε 13 500). Anal. for $C_{10}H_{15}N_3O_5$, %: C 46.69, H 5.88, N 16.38; found C 46.54, H 5.58, N 16.15.

3'-Deoxy-4'-hydroxymethylguanosine (Vc), yield 0.22 g, 50%, m.p.>300°C (decomp.), Rf 0.54 (E). Mass (m/z) 298 (M+H). UV (MeOH): pH 7, λ_{max} 252 nm (ε 12 800), 270 nm (shoulder) (ε 8 300); pH 2, λ_{max} 255 nm (ε 10 700), 271 nm (ε 7 500). Anal. for $C_{11}H_{15}N_5O_5$, %: C 44.44, H 5.09, N 23.56; found C 44.82, H 4.94, N 23.49.

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REFERENCES

1. Prisbe E.J., Maag H., Verheyden J.P.H., Rydzewsky R.M. in "Nucleosides and Nucleotides as Antitumor and Antiviral Agents" (Eds., Chu, C.K. and Baker D.C.), Plenum Press, New York, 1993, pp.101-113
2. Yang C.O., Wu H.Y., Praser-Smith E.B., Walker K.A.M. *Tetrahedron Lett.*, 1992, 33, 37-40.
3. Yang C.O., Kurz W., Eugui E.M., McRoberts M.J., Verheiden M.J., Kurz L.J., Walker K.A.M. *Tetrahedron Lett.*, 1992, 33, 41-44.

4. Chen M.S., Suttmann R.T., Wu V.C., Prisbe E.J. *J.Biol.Chem.*, 1992, **267**, 257-260.
5. Jones G.H., Taniguchi M., Tegg D., Moffatt J.G. *J.Org.Chem.*, 1979, **44**, 1309-1317.
6. Youssefych R., Togg D., Verheyden J.P.H., Jones G.H., Moffatt J.G. *Tetrahedron Lett.*, 1987, **18**, 435-438.
7. Martin J.C., Verheyden J.P.H. *Nucleosides & Nucleotides*, 1988, **7**, 365-374.
8. Youssefych R., Verheyden J.P.H., Moffatt J.G. *J.Org.Chem.*, 1979, **44**, 1301-1309.
9. O-Yang C., Kurz W., Eugui E.M., McRoberts M.J., Verheyden J.P.H., Kurz L.J., Walker K.A.M. *Tetrahedron Lett.*, 1992, **33**, 32-37.
10. Hrebabecky H., Dockal J., Holy A. *Coll.Czech.Chem. Commun., Symp.Issue,* 1993, **58**, 241-243.
11. Leland D.L., Kotick M.P. *Carbohydrate Res.*, 1974, **38**, C9-C11.
12. Ohryi H., Nishizaki T., Waga T., Meguro H. *Nucl.Acids Res. Symp.Ser.*, 1991, N25, 1-2.
13. O-Yang C., Wu H.Y., Eriser-Smith E.B., Walker K.A.M. *Tetrahedron Lett.*, 1992, **33**, 37-41.
14. Austin G.N., Baird P.D., Fleet G.W.J., Peach J.M. *Tetrahedron,* 1987, **43**, 3095-3108.
15. Niedballa U., Vorbruggen H. *J.Org.Chem.*, 1976, **41**, 2084-2092.
16. Hall Z.D., Miller D.C. *Carbohydrate Res.*, 1976, **47**, 299-305.
17. Paul E. *J.Org.Chem.*, 1984, **49**, 176-178.
18. Bazin H., Chattopadhyaya J. *Synthesis*, 1985, 1108-1110.
19. Lin T.-S., Chen M.S., McLaren C., Prusoff W.H. *J.Med.Chem.*, 1982, **30**, 440-444.
20. Martinez A.B., Calkins D.F., Reist J.J., Lee W.W., Goodman Z. *J.Heterocyclic Chem.*, 1970, **7**, 713-714.
21. Miyai K., Robins R.K., Tolman R.L. *J.Med.Chem.*, 1972, **15**, 1092-1098.
22. Okabe A.M., Sun R.-C., Zenchoff G.B. *J.Org.Chem.*. 1991, **56**, 4392-4397.

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