Synthesis of 5-*N*-Glycosylaminopyrimidines. A New Class of Compounds with Potential Anti-aids Activity

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Received March 9, 2000

Reactions between 5,6-diaminopyrimidines **1a-c** and pentoses **2a-e** yield 5-*N*-glycosylaminopyrimidines or 7-polyhydroxyalkylpteridines, depending on the presence or absence of acetic acid. The "in vitro" anti-HIV activity of 6-amino-2-methoxy-3-methyl-5-*N*-D-ribosylaminopyrimidin-4(3*H*)-one **3e**, 6-amino-2-methoxy-3-methyl-5-*N*-β-D-xylopyranosylaminopyrimidin-4(3*H*)-one **3f**, and 6-amino-2-methylthio-5-*N*-β-L-xylopyranosylminopyrimidin-4(3*H*)-one **3k**, appears to be promising.

J. Heterocyclic Chem., **37**, 1511 (2000).

Introduction.

For many years there have been ongoing studies examining the relationship between the chemical and biological activity, and/or pharmacological applications, of various structures. Pyrimidine nucleoside analogues [1-8] and pteridines, particularly, are known to be amongst the most potent types of compounds because of their biological and pharmacological activities [9-16].

As part of our research dealing with the synthesis of potential biologically active agents, we became interested in the preparation of nucleosides derived from 5,6-diaminopyrimidines [17-20] as well as of 6- and 7-polyhydroxyalkylpteridines. The 5-*N*-glycosylaminopyrimidines are interesting and useful intermediates for the synthesis of other nucleoside analogues [21-23] and these types of compounds have not yet been intensively studied for their effects on the human immunodeficiency virus (HIV).

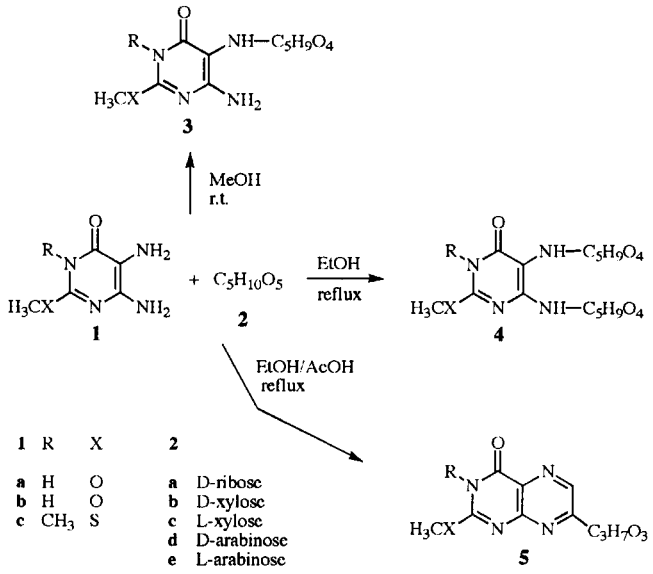
The compounds 6-amino-2-methoxy-3-methyl-5-*N*-D-ribosylaminopyrimidin-4(3*H*)-one **3e**, 6-amino-2-methoxy-3-methyl-5-*N*-β-D-xylopyranosylaminopyrimidin-4(3*H*)-one **3f,** and 6-amino-2-methylthio-5-*N*-β-L-xylopyranosylaminopyrimidin-4(3*H*)-one **3k,** have shown moderate activity [24] against HIV. Compared to other well established anti-HIV compounds, these products have relatively unusual structures. For this reason, studies of these compounds should constitute a new direction in the search for anti-viral agents.

In this paper, we describe the results of our studies involving the condensation of 5,6-diamino-2-methoxypyrimidin-4(3*H*)-one **1a**, 5,6-diamino-2-methoxy-3-methylpyrimidin-4(3*H*)-one **1b,** and 5,6-diamino-2-methylthiopyrimidin-4(3*H*)-one **1c**, with the pentoses D-ribose **2a**, D-xylose **2b**, L-xylose **2c**, D-arabinose **2d**, and L-arabinose **2e**. We also present the anti-HIV activity of the compounds generated.

Results and Discussion.

The reaction of 5,6-diaminopyrimidin-4(3*H*)-ones **1** with an equivalent amount of pentoses **2,** generated a range of products depending on the reaction conditions. If the reaction was carried out in absolute methanol at room temperature, 5-*N*-glycosylaminopyrimidine derivatives **3** were obtained. However, in refluxing ethanol, 5,6-diglycosylaminopyrimidines **4** were also formed in some cases. Finally, in the presence of acetic acid, the reaction generated 7-polyhydroxyalkylpteridines **5** (see Scheme 1, Table 1).

Scheme 1



The definitive 5-*N*-glycosidic structure of **3** was determined by comparing structural data with the corresponding C(6)-NH_2 glycosyl derivatives previously published by us [25]. Reacting **1a** and **1c** with D-ribose **2a**, gave a complex mixture of products unable to be resolved by usual chromatographic methods.

Study of the specific rotation values of the compounds **3** in water, demonstrated that these compounds exist in this medium as a mixture of α- and β-pyranosyl and furanosyl anomers, together with azomethine isomers that we have previously observed in other similar situations [17-20,26]. However, the ^{13}C-nmr spectra obtained in dimethyl-d_6 sulfoxide of compounds **3a-b**, **f-g**, **i-m**, show a signal in the 92.1-81.5 ppm range for C-1' and another in the 67.3-63.8 ppm range for C-5'. This indicates that a β-pyranosic

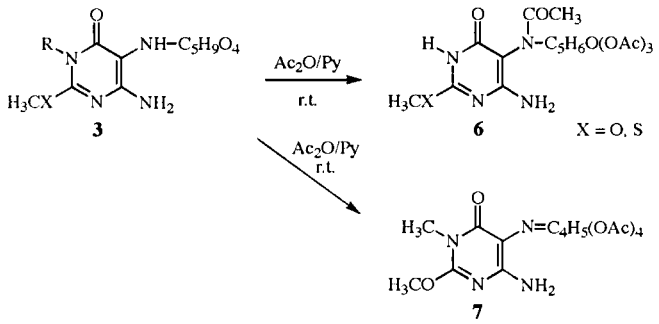
Table 1
Compounds Obtained in Condensation Reactions

Pyrimidine	Pentose	MeOH/r.t.	yield (%)	EtOH/AcOH/reflux	yield (%)
1a	**2a**	-	-	-	-
R= H, X= O	**2b**	**3a**	81	**3a**	69
	2c	**3b**	81	**3b**	15
	2d	**3c**	74	**3c**	10
	2e	**3d**	92	-	-
1b	**2a**	**3e**	77	**5a**	29
R= CH_3, X= O	**2b**	**3f**	45	**5b**	43
	2c	**3g**	78	**5c**	56
	2d	**3h**	84	**5a**	34
	2e	**3i**	77	**5d**	36
1c	**2a**	-	-	-	-
R= H, X= S	**2b**	**3j**	90	**3j**	60
	2c	**3k**	83	-	-
	2d	**3l**	81	-	-
	2e	**3m**	70	-	-

structure is present in this solvent. Four signals can be observed in the 66.7-61.0 ppm range for derivatives **3c-e** and **3h**, corresponding to the C-5' carbon atom of the above mentioned anomers.

Additional structural information about compound **3** has been obtained by acetylation in acetic anhydride and pyridine at room temperature. Depending on what is substituted at *N*-3, two types of acetyl derivatives have been obtained: glycopyranosides **6** for R = H and azomethinic compounds **7** for R = CH_3 (see Scheme 2, Table 2).

Scheme 2



3 **6** **7**

The 5-*N*-glycosylaminopyrimidine derivatives **3a-b, 3j-m,** acetylated as above, generate β-glycopyranosyl anomers **6a-b, 6e-h**. The ^{1}H-nmr spectra of these compounds indicate the β-pyranosyl configuration based on the chemical shifts values of H-1' (5.90-6.33 ppm) and the $J_{1',2'}$ coupling constants (9.5-9.9 Hz). In the ^{13}C-nmr spectra, the resonance of C-1' is in the 81.9-82.1 ppm range, which corresponds to the β-anomer [27]. The acetylation of **3c-d** generates **6c-d**, as a mixture of α- and β-glycopyranosyl anomers, unable to be separated, whose ^{1}H-nmr spectra shown a signal at 5.77 as a doublet for H-1' $J_{1',2'}$= 9.6 Hz for β-arabinopyranosil anomer and 6.38 as a doublet $J_{1',2'}$= 3.0 Hz for α-arabinopyranosil anomer. In the ^{13}C-nmr spectra

Table 2
Compounds Obtained in Acetylations Reactions for **3**

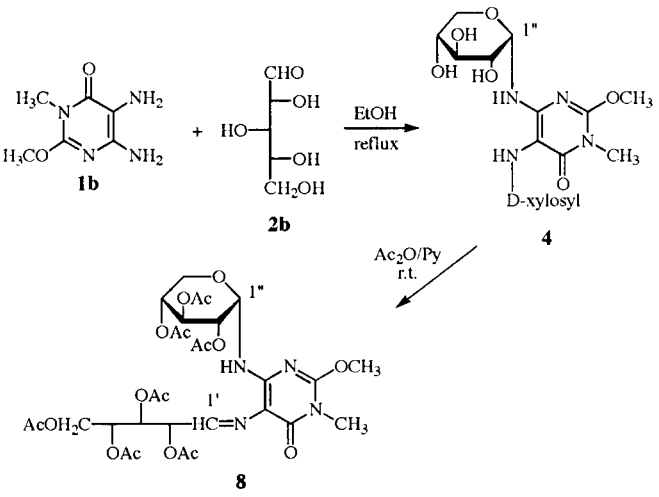
Starting material		Compound	Yield (%)
R= H	**3a**	**6a**	28
X= O	**3b**	**6b**	44
	3c	**6c** (α+β) anomers	24
	3d	**6d** (α+β) anomers	20
R= CH_3	**3e**	**7a**	12
X= O	**3f**	**7b**	34
	3g	**7c**	56
	3h	**7d**	50
	3i	**7e**	65
R= H	**3j**	**6e**	62
X= S	**3k**	**6f**	68
	3l	**6g**	24
	3m	**6h**	73

appear two signals at 64.9 and 63.3 ppm for **6c** and 65.4 and 64.0 ppm for **6d** assigned to C-5' of each anomer, respectively. The spectra of **7** indicate that these compounds possess an azomethinic structure [17-20, 26]. Thus, the N=CH proton appears as a doublet between 8.90-9.05 ppm with the coupling constant $J_{1',2'}$ = 2.7-3.1 Hz. In the ^{13}C-nmr spectra the resonance of C-1' appears at 151.1-151.8 ppm, corresponding to a tertiary carbon as seen in the DEPT experiment.

When condensations between **1** and **2** are undertaken in refluxing ethanol (see Scheme 1 and Scheme 3) only reaction between **1b** and **2b** generated a 10% yield of 5,6-diglycosylaminopyrimidine **4**. Compound **4** is probably formed by condensation of the C(6)-NH_2 group in **3f** with an additional molecule of D-xylose; similar products are obtained by reacting 6-aminopyrimidines with aldoses [25].

The study of the NMR spectra of **4** in dimethyl sulfoxide reveals, using the above considerations, that the glycosidic moiety at C-5 is pointing out as β-pyranose (C-1' 66.9 ppm), whereas, the anomeric centre at C-6 clearly possesses

Scheme 3



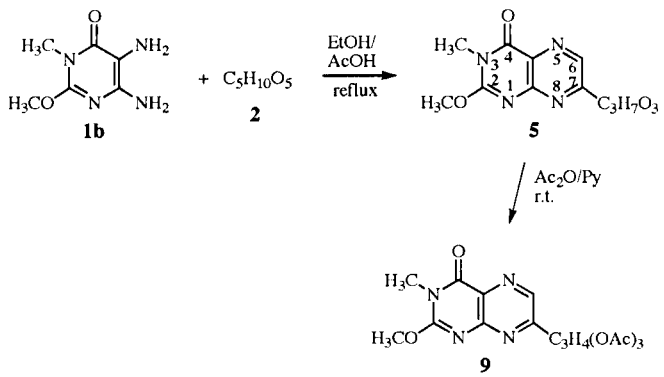
an α–pyranosic configuration (C-1" 59.6 ppm) confirmed in ^{1}H-nmr spectra on the basis of the $J_{1",2"}$ value (3.4 Hz). Acetylation of **4** generates **8**. In the ^{1}H-nmr spectrum of compound **8**, the N=CH and H-1" protons appear as doublets at 8.90 ppm ($J_{1',2'}$= 2.7 Hz) and 6.26 ppm ($J_{1",2"}$= 4.8 Hz), respectively.

Reacting **1b** with **2** in refluxing methanol or ethanol in the presence of an equivalent amount of acetic acid, generates 7-polyhydroxyalkylpteridines **5** (see Scheme 4, Table 1). The reaction of **1a** and **1c** leads basically to compounds **3**.

Starting from **3**, compounds **5** can be also obtained, then when we carried out the reaction of **3e** with double molar amount of acetic acid led to compound **5a** in 11 % yield which purity was comprobed by thin layer chromatography. We have concluded that substitution at C-7 occurs in the pteridine ring, based on our observations in other similar studies [17-20] and the ^{13}C- and ^{1}H-nmr chemical shifts in dimethyl-d_6 sulfoxide solution: C-6 at 144.0 ppm and H-6 at 8.80 ppm.

Compounds **5** are obtained from 5-*N*-glycosylaminopyrimidines **3** by an Amadori rearrangement [28,29] favored by the acidic medium. The structure of pteridines

Scheme 4



5 was confirmed after studying the corresponding acetyl derivatives **9** (see Scheme 4, Table 3).

Table 3

Compounds Obtained in Acetylations Reactions for **5**

Starting material	Compound	Yield (%)
5a	**9a**	22
5b	**9b**	22
5c	**9c**	42
5d	**9d**	52

Biological Results.

Biological tests were undertaken to establish the anti-HIV properties of glycosylaminopyrimidines and 7-polyhydroxyalkylpteridines. The "in vitro" anti-HIV activity of compounds **3**, **4**, **5** and **8** was determined by the National Cancer Institute (NCI) against T4 lymphocytes (CEM cell line) exposed to HIV at a virus-to-cell ratio of approximately 0.05, according to the general procedure described by this Institution [30]. Approximate values for 50% effective concentration (EC_{50}), 50% inhibitory concentration (IC_{50}) and therapeutic index (TI = IC_{50}/EC_{50}) were calculated for each test. The assays revealed moderate activity for 6-amino-2-methoxy-3-methyl-5-*N*-D-ribosylaminopyrimidin-4(3*H*)-one **3e**, 6-amino-2-methoxy-3-methyl-5-*N*-β-D-xylopyranosylaminopyrimidin-4(3*H*)-one **3f** and 6-amino-2-methylthio-5-*N*-β-L-xylopyranosylaminopyrimidin-4(3*H*)-one **3k** (see Table 4).

Table 4

Compound	IC_{50}(M)	EC_{50}(M)	TI_{50} (IC/EC)
3e	>8.3x10^{-4}	6.4x10^{-5}	>13.0
3f	>2.2x10^{-4}	1.4x10^{-4}	>1.6
3k	1.2x10^{-4}	1.1x10^{-5}	1.1x10^{+1}

EXPERIMENTAL

Melting points (mp) were determined in a Gallenkamp melting point apparatus and are uncorrected. ^{1}H-nmr spectra were recorded on a Hitachi Perkin Elmer R-600 spectrometer, Bruker AM-300 spectrometer and Bruker DPX-300 spectrometer using tetramethylsilane as internal standard. ^{13}C-nmr spectra were recorded on either a Bruker AM-300 spectrometer or a Bruker DPX-300 spectrometer. Optical rotation was measured in a Perkin Elmer 241 polarimeter. Ultraviolet (uv) spectra were recorded on Bausch-Lomb Spectronic 2000 and GBC UV/VIS 911 spectrophotometers. Elemental analyses (C, H and N) were performed on a Perkin Elmer 240 C analyzer. Mass spectra were recorded on a Hewlet Packard HP-5988-A spectrometer, using the direct injection and electron impact modes (70 eV). Flash column chromatography was performed on Merck Silica Gel 60 (0.040-0.030 mm). Reaction progress and products purity were monitored by thin layer chromatography (tlc) on Merck Silica Gel 60GF$_{254}$ (0.2 mm) aluminum pre-coated sheets with fluorescent indicators. The

spots were visualized by ultraviolet irradiation and by spraying the sheets with 4% sulfuric acid/methanol solution and subsequent heating.

Condensation Reactions.

Method A: Reactions in Methanol at Room Temperature.

Ten mmol 5,6-diaminopyrimidin-4(3*H*)-one **1**, was suspended in 70 ml absolute methanol (purged with argon at room temperature to ensure it was free from gases) and added to 10 mmol pentose **2**. The mixture was stirred at room temperature under a nitrogen atmosphere for 12 hours. The solid which appeared was collected by filtration and washed with ethanol and diethyl ether. Reaction products were purified by digestion in ethanol (**3a-e** and **3j-m**), or by recrystallization from methanol using activated charcoal (**3f-i**).

6-Amino-2-methoxy-5-*N*-β-D-xylopyranosylaminopyrimidin-4(3*H*)-one (**3a**).

Starting with 1.56 g of **1a** and 1.50 g of **2b**, 2.35 g (81%) of **3a** was obtained, mp 166-170 °C (d); Rf = 0.38 (tetrahydrofuran/acetone/water 5.7:3.6:0.7); $[\alpha]_D^{29°}$ = +2.0° to +7.0° after 33 minutes (c 1, water); ^{1}H-nmr (400 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.5 (bs, 1H, N_3-H deuterium oxide-exchangeable), 6.20 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.71 (bs, 1H, N_5-H), 4.86-4.00 (m, 3H, OH deuterium oxide-exchangeable), 3.22, 3.08, 2.92 (m, 4H, H-1', H-2', H-3', H-4'), 3.78 (m, 1H, H-5' overlapped with O-CH_3 signal), 3.61 (m, 1H, H-5'), 3.78 (s, 3H, O-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 162.8, 160.5, 154.5 (C-2, C-4, C-6), 99.0 (C-5), 92.0 (C-1'), 77.1, 72.6, 69.9 (C-2', C-3', C-4'), 67.3 (C-5'), 54.7 (O-CH_3); uv (water): λ max (nm) (ε) 205 (17300), 271 (10400).

Anal. Calcd. for $C_{10}H_{16}N_4O_6$: C, 41.67; H, 5.59; N, 19.44; Found: C, 41.73; H, 5.48; N, 19.16.

6-Amino-2-methoxy-5-*N*-β-L-xylopyranosylaminopyrimidin-4(3*H*)-one (**3b**).

Starting with 1.56 g of **1a** and 1.50 g of **2c**, 2.35 g (81%) of **3b** was obtained, mp 171-173 °C (d); $[\alpha]_D^{29°}$ = +0.4° to -5.5° after 40 minutes (c 1, water); Rf = 0.38 (tetrahydrofuran/acetone/water 5.7:3.6:0.7). ^{1}H-nmr (400 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.5 (bs, 1H, N_3-H deuterium oxide-exchangeable), 6.23 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.71 (bs, 1H, N_5-H), 4.86-3.98 (m, 3H, OH deuterium oxide-exchangeable), 3.20, 3.08, 2.93 (m, 4H, H-1',H-2', H-3', H-4'), 3.78 (m, 1H, H-5' overlapped with O-CH_3 signal), 3.63 (m, 1H, H-5'), 3.78 (s, 3H, O-CH_3). ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 162.7, 160.5, 154.5 (C-2, C-4, C-6), 99.0 (C-5), 92.0 (C-1'), 77.1, 72.6, 69.9, (C-2', C-3', C-4'), 67.3 (C-5'), 54.7 (O-CH_3). uv (water): λ max (nm) (ε) 205 (14730), 271 (8460).

Anal. Calcd. for $C_{10}H_{16}N_4O_6$: C, 41.67; H, 5.59; N, 19.44; Found: C, 41.73; H, 5.48; N, 19.16.

6-Amino-5-*N*-D-arabinosylamino-2-methoxypyrimidin-4(3*H*)-one (**3c**).

Starting with 1.56 g of **1a** and 1.50 g of **2d**, 2.14 g (74%) of **3c** was obtained, mp 156-158 °C (d); $[\alpha]_D^{29°}$ = -52.2° to +75.6° after 20 minutes (c 1, water); Rf = 0.59 (methylene chloride/ethanol 5:5); ^{1}H-nmr (very complex spectra) (300 MHz) selected data (dimethyl-d_6 sulfoxide) δ(ppm): 11.5 (bs, 1H, N_3-H), 6.30 (bs, 2H, NH_2), 3.95 (s, 3H, O-CH_3); ^{13}C-nmr selected data (dimethyl-d_6 sulfoxide) δ(ppm): 158.2, 153.9, 150.7 (C-2, C-4, C-6), 101.4 (C-5), 93.2 (C-1'), 75.9, 73.1, 70.4 (C-2', C-3', C-4'), 66.7, 63.5 61.7, 61.0, (C-5' for each anomer at the mixture), 54.7 (O-CH_3); uv (water): λ max (nm) (ε) 208 (20000), 272 (12670).

Anal. Calcd. for $C_{10}H_{16}N_4O_6$: C, 41.67; H, 5.59; N, 19.44; Found: C, 41.52; H, 5.54; N, 19.10.

6-Amino-5-*N*-L-arabinosylamino-2-methoxypyrimidin-4(3*H*)-one (**3d**).

Starting with 1.56 g of **1a** and 1.50 g of **2e**, 2.64 g (92%) of **3d** was obtained, mp 148-150 °C (d); $[\alpha]_D^{29°}$ = -30.2° to +47.5° after 40 minutes (c 1, water); Rf = 0.46 (methylene chloride/ethanol 5:5); ^{1}H-nmr (very complex spectra) selected data (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.5 (bs, 1H, N_3-H), 6.30 (bs, 2H, NH_2), 3.95 (s, 3H, O-CH_3); ^{13}C-nmr selected data (dimethyl-d_6 sulfoxide) δ(ppm): 162.2, 159.7, 154.0 (C-2, C-4, C-6), 99.2 (C-5), 91.4 (C-1'), 73.1, 69.9, 68.0 (C-2', C-3', C-4'), 68.7, 66.0, 63.0, 61.0 (C-5' for each anomer at the mixture), 54.2 (O-CH_3); uv (water): λ max (nm) (ε) 207 (9420), 273 (6220).

Anal. Calcd. for $C_{10}H_{16}N_4O_6$: C, 41.67; H, 5.59; N, 19.44; Found: C, 41.60; H, 5.62; N, 19.56.

6-Amino-2-methoxy-3-methyl-5-*N*-D-ribosylaminopyrimidin-4(3*H*)-one (**3e**).

Starting with 1.70 g of **1b** and 1.50 g of **2a**, 2.32 g (77%) of **3e** was obtained, mp 154-156 °C; $[\alpha]_D^{22°}$ = +4.8° to -0.6° after 21 hours (c 1, dimethyl sulfoxide); Rf = 0.62 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide): 6.15 (bs, 2H, NH_2), 4.85 (bs, 3H, OH deuterium oxide-exchangeable), 3.85 (s, 3H, O-CH_3), 3.15 (s, 3H, N-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.4, 157.7, 153.1 (C-2, C-4, C-6), 99.2 (C-5), 97.4 (C-1'), 74.7, 70.3, 70.0 (C-2', C-3', C-4'), 67.1, 64.3, 62.0, 61.0 (C-5' for each anomer at the mixture), 55.2 (O-CH_3), 27.5 (N-CH_3); ms: 302 ($M^{+\cdot}$, 2%); uv (water): λ max (nm) (ε) 207 (18140), 270 (9400).

Anal. Calcd. for $C_{11}H_{18}N_4O_6$: C, 43.70; H, 6.00; N, 18.54; Found: C, 43.29; H, 5.98; N, 19.01.

6-Amino-2-methoxy-3-methyl-5-*N*-β-D-xylopyranosylaminopyrimidin-4(3*H*)-one (**3f**).

Starting with 1.70 g of **1b** and 1.50 g of **2b**, 1.36 g (45%) of **3f** was obtained, mp 128-130 °C; $[\alpha]_D^{29°}$ = -11.8° to +3.6° after 78 hours (c 1, water); Rf = 0.43 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 6.20 (bs, 2H, NH_2), 5.55, 4.85 (s, 3H, OH deuterium oxide-exchangeable), 3.90 (s, 3H, O-CH_3), 3.20 (s, 3H, N-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.3, 157.8, 153.2 (C-2, C-4, C-6), 98.8 (C-5), 91.9 (C-1'), 77.0, 72.4, 69.6 (C-2', C-3', C-4'), 66.9 (C-5'), 55.2 (O-CH_3), 27.5 (N-CH_3); ms: 302 ($M^{+\cdot}$, 0.5%); uv (water): λ max (nm) (ε) 208 (18380), 272 (8930).

Anal. Calcd. for $C_{11}H_{18}N_4O_6$: C, 43.70; H, 6.00; N, 18.54; Found: C, 43.37; H, 5.97; N, 18.03.

6-Amino-2-methoxy-3-methyl-5-*N*-β-L-xylopyranosylaminopyrimidin-4(3*H*)-one, (**3g**).

Starting with 1.70 g of **1b** and 1.50 g of **2c**, 2.36 g (78%) of **3g** was obtained, mp 125-126°C; $[\alpha]_D^{29°}$ = +1.1° to -7.2° after 52 hours (c 1, water); Rf = 0.32 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 6.15 (bs, 2H, NH_2), 5.50, 4.88 (bs, 3H, OH deuterium oxide-exchangeable), 3.95 (s, 3H, O-CH_3), 3.20 (s, 3H, N-CH_3); ^{13}C-nmr (dimethyl-d_6

sulfoxide) δ(ppm): 161.1, 157.3, 153.0 (C-2, C-4, C-6), 99.3 (C-5), 91.2 (C-1'), 73.8, 70.4, 68.0 (C-2', C-3', C-4'), 66.5 (C-5'), 55.2 (O-CH_3), 27.5 (N-CH_3); ms: 302 ($M^{+\cdot}$, 14%); uv (water): λ max (nm) (ε) 209 (18830), 276 (9120).

Anal. Calcd. for $C_{11}H_{18}N_4O_6$: C, 43.70; H, 6.00; N, 18.54; Found: C, 43.27; H, 5.87; N, 18.07.

6-Amino-5-*N*-D-arabinosylamino-2-methoxy-3-methylpyrimidin-4(3*H*)-one (**3h**).

Starting with 1.70 g of **1b** and 1.50 g of **2d**, 2.54 g (84%) of **3h** was obtained, mp 155-156 °C; $[\alpha]_D^{29°}$ = +0.4° to -46.7° after 22 hours (c 1, water); Rf = 0.23 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 6.20 (bs, 2H, NH_2), 5.50, 4.70 (bs, 3H, OH deuterium oxide-exchangeable), 3.90 (s, 3H, O-CH_3), 3.20 (s, 3H, N-CH_3); ^{13}C-nmr selected data (dimethyl-d_6 sulfoxide) δ(ppm): 161.3, 157.5, 153.1 (C-2, C-4, C-6), 99.4 (C-5), 91.4 (C-1'), 76.3, 73.2, 70.2 (C-2', C-3', C-4'), 66.6 63.6, 61.8, 61.3 (C-5' for each anomer at the mixture), 55.1 (O-CH_3), 27.3 (N-CH_3); ms: 302 ($M^{+\cdot}$, 16%); uv (water): λ max (nm) (ε) 209 (17460), 274 (8700).

Anal. Calcd. for $C_{11}H_{18}N_4O_6$: C, 43.70; H, 6.00; N, 18.54; Found: C, 43.19; H, 6.00; N, 18.60.

6-Amino-5-*N*-β-L-arabinopyranosylamino-2-methoxy-3-methylpyrimidin-4(3*H*)-one (**3i**).

Starting with 1.70 g of **1b** and 1.50 g of **2e**, 2.33 g (77%) of **3i** was obtained, mp 134-136 °C; $[\alpha]_D^{29°}$ = +31.8° to +40.5° after 24 hours 50 minutes (c 1, water); Rf = 0.20 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 6.20 (bs, 2H, NH_2), 5.40, 4.40 (bs, 3H, OH deuterium oxide-exchangeable), 3.90 (s, 3H, O-CH_3), 3.20 (s, 3H, N-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.1, 157.3, 153.0 (C-2, C-4, C-6), 99.3 (C-5), 91.3 (C-1'), 73.1, 70.4, 69.6 (C-2', C-3', C-4'), 66.5 (C-5'), 55.2 (O-CH_3), 27.4 (N-CH_3); ms: 302 ($M^{+\cdot}$, 17%); uv (water): λ max (nm) (ε) 209 (18830), 282 (10400).

Anal. Calcd. for $C_{11}H_{18}N_4O_6$: C, 43.70; H, 6.00; N, 18.54; Found: C, 43.83; H, 6.05; N, 18.71.

6-Amino-2-methylthio-5-*N*-β-D-xylopyranosylaminopyrimidin-4(3*H*)-one (**3j**).

Starting with 1.72 g of **1c** and 1.50 g of **2b**, 2.74 g (90%) of **3j** was obtained, mp 172-173 °C (d); Rf = 0.62 (methylene chloride/ethanol 5:5); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.90 (bs, 1H, N_3-H deuterium oxide-exchangeable), 6.20 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.71 (bs, 1H, N_5-H), 4.88-3.80 (m, 3H, OH deuterium oxide-exchangeable), 3.22, 3.20, 3.08 (m, 4H, H-1', H-2', H-3', H-4'), 3.32 (m, 2H, H_2-5' overlapped with water signal), 2.42 (s, 3H, S-CH_3). ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.6, 158.5, 153.0 (C-2, C-4, C-6), 101.8 (C-5), 91.3 (C-1'), 77.1, 72.7, 69.4 (C-2', C-3', C-4'), 66.8 (C-5'), 12.5 (S-CH_3); uv (water): λ max (nm) (ε) 216 (sh), 224 (18860), 286 (9120).

Anal. Calcd. for $C_{10}H_{16}N_4O_5S$: C, 39.47; H, 5.30; N, 18.41; S, 10.54; Found: C, 39.34; H, 5.28; N, 18.40; S, 10.00.

6-Amino-2-methylthio-5-*N*-β-L-xylopyranosylaminopyrimidin-4(3*H*)-one (**3k**).

Starting with 1.72 g of **1c** and 1.50 g of **2c**, 2.52 g (83%) of **3k** was obtained, mp 170-172 °C (d); Rf = 0.60 (methylene chloride/ethanol 5:5); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.90 (bs, 1H, N_3-H deuterium oxide-exchangeable), 6.20 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.71 (bs, 1H, N_5-H), 4.87-3.82 (m, 3H, OH deuterium oxide-exchangeable), 3.23, 3.21, 3.09 (m, 4H, H-1', H-2', H-3', H-4'), 3.32 (m, 2H, H_2-5' overlapped with water signal), 2.40 (s, 3H, S-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.6, 158.5, 153.0 (C-2, C-4, C-6), 101.5 (C-5), 91.2 (C-1'), 77.0, 72.6, 69.5 (C-2', C-3', C-4'), 66.7 (C-5'), 12.5 (S-CH_3); uv (water): λ max (nm) (ε) 216 (sh), 224 (18530), 285 (8910).

Anal. Calcd. for $C_{10}H_{16}N_4O_5S$: C, 39.47; H, 5.30; N, 18.41; S, 10.54; Found: C, 39.27; H, 5.23; N, 18.02; S, 10.90.

6-Amino-5-*N*-β-D-arabinopyranosylamino-2-methylthiopyrimidin-4(3*H*)-one (**3l**).

Starting with 1.72 g of **1c** and 1.50 g of **2d**, 2.46 g (81%) of **3l** was obtained, mp 150-152 °C (d); Rf = 0.50 (methylene chloride/ethanol 5:5); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.90 (bs, 1H, N_3-H deuterium oxide-exchangeable), 6.20 (bs, 2H, NH_2 deuterium oxide-exchangeable), 4.89 (bs, 1H, N_5-H), 4.09, 3.81, 3.65 (m, 3H, OH deuterium oxide-exchangeable), 3.35, 3.22, 3.17 (m, 4H, H-1', H-2', H-3', H-4'), 3.32 (m, 2H, H_2-5' overlapped with water signal), 2.40 (s, 3H, S-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.6, 158.5, 156.1 (C-2, C-4, C-6), 101.8 (C-5), 91.3 (C-1'), 77.1, 72.7, 69.7 (C-2', C-3', C-4'), 67.0 (C-5'), 12.8 (S-CH_3); uv (water): λ max (nm) (ε) 216 (sh), 224 (19930), 285 (9910).

Anal. Calcd. for $C_{10}H_{16}N_4O_5S$: C, 39.47; H, 5.30; N, 18.41; S, 10.54; Found: C, 38.42; H, 5.04; N, 18.41; S, 10.50.

6-Amino-5-*N*-β-L-arabinopyranosylamino-2-methylthiopyrimidin-4(3*H*)-one (**3m**).

Starting with 1.72 g of **1c** and 1.50 g of **2e**, 2.13 g (70%) of **3m** was obtained, mp 148-149 °C (d); Rf = 0.55 (methylene chloride/ethanol 5:5); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.90 (bs, 1H, N_3-H deuterium oxide-exchangeable), 6.20 (bs, 2H, NH_2 deuterium oxide-exchangeable), 4.90 (bs, 1H, N_5-H), 4.11, 3.83, 3.62 (m, 3H, OH deuterium oxide-exchangeable), 3.37, 3.22, 3.15 (m, 4H, H-1', H-2', H-3', H-4'), 3.33 (m, 2H, H_2-5' overlapped with water signal), 2.40 (s, 3H, S-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.6, 158.5, 156.1 (C-2, C-4, C-6), 101.8 (C-5), 91.3 (C-1'), 77.3, 72.8, 69.5 (C-2', C-3', C-4'), 67.0 (C-5'), 12.8 (S-CH_3). λ max (nm) (ε) 216 (sh), 224 (17730), 285 (8910).

Anal. Calcd. for $C_{10}H_{16}N_4O_5S$: C, 39.47; H, 5.30; N, 18.41; S, 10.54; Found: C, 39.28; H, 5.29; N, 18.31; S, 10.15.

Method B: Reaction in Ethanol Under Reflux.

2-Methoxy-3-methyl-5-*N*-D-xylopyranosylamino-6-*N*-α-D-xylopyranosylaminopyrimidin-4(3*H*)-one (**4**).

Starting with 1.70 g (10 mmol) of 5,6-diamino-2-methoxy-3-methylpyrimidin-4(3*H*)-one, **1b**, and 1.50 g (10 mmol) of D-xylose, **2b**, in 100 ml absolute ethanol the mixture was stirred at room temperature for 12 hours. After this time, 25 ml of benzene were added and then the crude was concentrated to 50 ml at atmospheric pressure. Immediately following this, the mixture was stirred under reflux for 7 hours, generating 0.43 g (10%) of a solid identified as **4**, that was purified by digestion in ethanol, mp 184-186 °C (d); $[\alpha]_D^{19°}$ = -28.8° (c 1, dimethyl sulfoxide); Rf = 0 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 7.30 (d, 1H, N_6-H, $J_{NH,1'}$= 9.5 Hz deuterium oxide-exchangeable), 6.30 (m, 1H, H-1" + deuterium oxide→ d $J_{1",2"}$= 3.4 Hz), 5.50, 4.95, 4.45 (m, 6H deuterium oxide-exchangeable), 3.90

(s, 3H, O-CH_3), 3.20 (s, 3H, N-CH_3). ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 161.4, 155.3, 152.9 (C-2, C-4, C-6), 100.9 (C-5), 92.0 and 81.3 (C-1', C-1"), 78.9, 79.6, 76.9, 75.7, 72.4, 69.6 (C-2', C-3', C-4' and C-2", C-3", C-4"), 66.7 and 59.7 (C-5', C-5"), 55.2 (O-CH_3), 27.5 (N-CH_3); uv (water): λ max (nm) (ε) 209 (18830), 282 (9720).

Anal. Calcd. for $C_{16}H_{26}N_4O_{10}$: C, 44.23; H, 6.03; N, 12.90; Found: C, 44.23; H, 5.93; N, 13.38.

Method C: Reaction in Ethanol, Acetic Acid Under Reflux.

To 1.14 ml (20 mmol) of acetic acid was added 3.40 g (20 mmol) of 5,6-diamino-2-methoxy-3-methylpyrimidin-4(3*H*)-one **1b** and 3.00 g (22 mmol) of the pentoses **2a-e** in 100 ml of absolute ethanol. The mixture was refluxed for 1 hour, concentrated under vacuum to 50 ml and the residue kept at room temperature several days in an open flask. The brown solid that appeared was filtered off and washed with cold ethanol and diethyl ether. These compounds were purified by recrystallization from ethanol using activated charcoal.

2-Methoxy-3-methyl-7-[D-*erythro*]-α,β,γ-trihydroxypropyl-pteridin-4(3*H*)-one (**5a**).

Reaction between **1b** and **2a** generated 0.82 g (29%) of **5a**. From **1b** and **2d,** 0.48 g (34%) of **5a** was obtained, mp 170-172 °C. $[\alpha]_D^{20°}$ = +22.1° (c 1, water); Rf = 0.33 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.80 (s, 1H, H-6), 4.75 (m, 3H, OH-1', OH-2', H-1' + D_2O →d J = 5.5 Hz), 3.30 (s, 3H, N-CH_3), 4.05 (s, 3H, O-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 155.5 (C-7), 141.5 (C-6), 128.0 (C-4a), 160.5 (C-4), 152.0 (C-2), 163.3 (C-8a), 74.5, 73.3 (C-1', C-2'), 62.5 (C-3'), 56.1 (O-CH_3), 28.4 (N-CH_3); ms: 282 ($M^{+\cdot}$, 0.9%); uv (water): λ max (nm) (ε) 238 (16000), 262 (sh), 325 (7900).

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.85; Found: C, 46.72; H, 5.07; N, 19.44.

2-Methoxy-3-methyl-7-[D-*threo*]-α,β,γ-trihydroxypropyl-pteridin-4(3*H*)-one (**5b**).

Compounds **1b** and **2b** generated 1.20 g (43%) of **5b**, mp 172-176 °C. $[\alpha]_D^{20°}$ = -92.4° (c 1, water); Rf = 0.58 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.80 (s, 1H, H-6), 4.70 (m, 3H, OH-1', OH-2', H-1' + D_2O →d J = 2.0 Hz), 3.30 (s, 3H, N-CH_3), 4.05 (s, 3H, O-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 155.5 (C-7), 141.0 (C-6), 128.0 (C-4a), 160.5 (C-4), 152.0 (C-2), 164.3 (C-8a), 74.2, 74.4 (C-1', C-2'), 62.2 (C-3'), 56.1 (O-CH_3), 28.4 (N-CH_3); ms: 282 ($M^{+\cdot}$, 1%); uv (water): λ max (nm) (ε) 242 (24000), 263 (21200), 326 (8800).

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.85; Found: C, 46.80; H, 5.00; N, 20.18.

2-Methoxy-3-methyl-7-[L-*threo*]-α,β,γ-trihydroxypropyl-pteridin-4(3*H*)-one (**5c**).

Starting from **1b** and **2c** 3.16 g (56%) of **5c** was obtained, mp 172-176 °C. $[\alpha]_D^{20°}$ = +91.8° (c 1, water); Rf = 0.32 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.80 (s, 1H, H-6), 4.65 (m, 3H, OH-1', OH-2', H-1' + D_2O →d J = 2.0 Hz), 3.40 (s, 3H, N-CH_3), 4.10 (s, 3H, O-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 155.5 (C-7), 141.1 (C-6), 128.0 (C-4a), 160.5 (C-4), 152.0 (C-2), 164.4 (C-8a), 74.5, 73.2 (C-1', C-2'), 62.5 (C-3'), 56.1 (O-CH_3), 28.4 (N-CH_3); ms: 282 ($M^{+\cdot}$, 0.5%); uv (water): λ max (nm) (ε) 240 (20400), 258 (11900), 326 (9200).

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.85; Found: C, 46.89; H, 5.03; N, 19.86.

2-Methoxy-3-methyl-7-[L-*erythro*]-α,β,γ-trihydroxypropyl-pteridin-4(3*H*)-one (**5d**).

Reaction between **1b** and **2e** generated 2.03 g (36%) of **5d**, mp 170-172 °C. $[\alpha]_D^{20°}$ = -27.7° (c 1, water); Rf = 0.48 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.80 (s, 1H, H-6), 4.7 (m, 3H, OH-1', OH-2', H-1' + D_2O →d J = 5.5 Hz), 3.30 (s, 3H, N-CH_3), 4.05 (s, 3H, O-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 155.5 (C-7), 141.6 (C-6), 128.1 (C-4a), 160.5 (C-4), 152.0 (C-2), 163.3 (C-8a), 74.7, 73.6 (C-1', C-2'), 62.4 (C-3'), 56.1 (O-CH_3), 28.4 (N-CH_3); ms: 282 ($M^{+\cdot}$, 1%); uv (water): λ max (nm) (ε) 240 (16600), 258 (sh), 326 (7900).

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.00; N, 19.85; Found: C, 46.40; H, 5.05; N, 19.37.

Acetylation Reactions.

General Procedure for the Acetylation Reaction of 5-*N*-Glycosyl-aminopyrimidines.

Five mmol of the corresponding 5-*N*-glycosylaminopyrimidine **3** was added to a mixture of acetic anhydride and pyridine (50% v/v). The resulting solution was stirred at room temperature for 24 hours. The acetic anhydride and pyridine were then removed under vacuum and the residue was co-evaporated several times with methanol. Compounds **6** were crystallized from ethanol, whereas compounds **7** were crystallized from methanol.

5-Acetamido-6-amino-2-methoxy-5-*N*-β-D-(2,3,4-tri-*O*-acetyl)-xylopyranosylaminopyrimidin-4(3*H*)-one (**6a**).

Starting from 1.14 g of **3a**, 0.67 g (28%) of **6a** was obtained, mp 228-230 °C (d); $[\alpha]_D^{29°}$ = +49.9° (c 1, dimethyl sulfoxide); Rf = 0.52 (methylene chloride/ethanol 9:1); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.70 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.05 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.89 (d, 1H, H-1' J = 9.5 Hz), 5.26 (t, 1H, H-2' J = 9.5 Hz), 4.64 (t, 1H, H-3', J = 9.5 Hz), 4.73 (td,1H, H-4' J = 5.5 Hz J = 11.0 Hz, J = 11.0 Hz), 3.96 (dd, 1H, H-5'*cis* J = 11.0 Hz, J = 5.5 Hz), 3.56 (t, 1H, H-5'*trans* J = 11.0 Hz), 3.85 (s, 3H, O-CH_3), 1.99 (s, 3H, N_5-CO-CH_3), 1.88, 1.84, 1.81 (s, 9H, CO-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 172.8, 169.5, 169.4, 168.8 (CO-CH_3), 161.0, 160.4, 156.3 (C-2, C-4, C-6), 93.6 (C-5), 82.0 (C-1'), 73.5, 68.1, 67.8 (C-2', C-3', C-4'), 63.2 (C-5'), 54.5 (O-CH_3), 21.4, 20.6, 20.3, 20.2 (CO-CH_3); uv (methanol): λ max (nm) (ε) 209 (17110), 263 (8830).

Anal. Calcd. for $C_{18}H_{24}N_4O_{10}$•H_2O: C, 45.57; H, 5.52; N, 11.80; Found: C, 45.37; H, 5.30; N, 11.33.

5-Acetamido-6-amino-2-methoxy-5-*N*-β-L-(2,3,4-tri-*O*-acetyl)xylopyranosylaminopyrimidin-4(3*H*)-one (**6b**).

Starting from 1.14 g of **3b**, 1.05 g (44%) of **6b** was obtained, mp 224-226 °C (d); $[\alpha]_D^{29°}$ = -47.7° (c 1, dimethyl sulfoxide); Rf = 0.60 (methylene chloride/ethanol 9:1); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.70 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.05 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.90 (d, 1H, H-1' J = 9.5 Hz), 5.26 (t, 1H, H-2' J = 9.5 Hz), 4.68 (t, 1H, H-3' J = 9.5 Hz), 4.78 (td, 1H, H-4' J = 5.5 Hz, J = 11.0 Hz, J = 11.0 Hz), 3.97 (dd, 1H, H-5'*cis* J = 11.0 Hz,

J = 5.5 Hz), 3.59 (t, 1H, H-5'*trans* J = 11.00 Hz), 3.85 (s, 3H, O-CH_3), 1.96 (s, 3H, N_5-CO-CH_3), 1.86, 1.84, 1.81 (s, 9H, CO-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 172.9, 169.5, 169.4, 168.9 (CO-CH_3), 161.0, 160.4, 156.3 (C-2, C-4, C-6), 93.7 (C-5), 82.1 (C-1'), 73.6, 68.1, 67.8 (C-2', C-3', C-4'), 63.3 (C-5'), 54.5 (O-CH_3), 21.4, 20.7, 20.4, 20.2 (CO-CH_3); uv (methanol): λ max (nm) (ε) 209 (21840), 263 (11110).

Anal. Calcd. for $C_{18}H_{24}N_4O_{10}$•H_2O: C, 45.57; H, 5.52; N, 11.80; Found: C, 45.37; H, 5.33; N, 12.22.

5-Acetamido-6-amino-2-methoxy-5-*N*-D-(2,3,4-tri-*O*-acetyl)arabinopyranosylaminopyrimidin-4(3*H*)-one (**6c**).

Starting from 1.14 g of **3c**, 0.56 g (24%) of **6c** was obtained, as a solid foam. $[\alpha]_D^{28°}$ = -26.4° (c 1, dimethyl sulfoxide); Rf = 0.45 (methylene chloride/ethanol 9:1); ^{1}H-nmr selected data for α- and β-arabinopyranosil anomers (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.70 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.05 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.77 (d, 1H, H-1' J = 9.6 Hz for β-arabinopyranosil anomer), 6.38 (d, 1H, H-1' J = 3.0 Hz for α-arabinopyranosil anomer), 2.10, 1.98 (s, 6H, N_5-CO-CH_3), 2.10-1.81 (s, 24H, CO-CH_3 this appears in two symmetrical groups of signals); ^{13}C-nmr selected data (dimethyl-d_6 sulfoxide) δ(ppm): 172.9, 169.5, 169.4, 168.9 (CO-CH_3), 161.0, 160.4, 156.3 (C-2, C-4, C-6), 94.2, 94.0 (C-5 for each anomer), 88.3 (C-1' for each anomer) 81.9, 80.1, 77.8, 77.0, 71.9, 68.5 (C-2', C-3', C-4' for each anomer) 64.9, 63.3 (C-5' for each anomer), 54.6, 54.5 (O-CH_3 for each anomer), 21.5, 21.2, 20.8, 20.7, 20.6, 20.5, 20.3, 20.1 (CO-CH_3); uv (methanol): λ max (nm) (ε) 209 (29590), 263 (15130).

Anal. Calcd. for $C_{18}H_{24}N_4O_{10}$•1/2 H_2O: C, 46.45; H, 5.19; N, 12.03; Found: C, 46.95; H, 5.58; N, 11.96.

5-Acetamido-6-amino-2-methoxy-5-*N*-L-(2,3,4-tri-*O*-acetyl)arabipyranosylaminopyrimidin-4(3*H*)-one (**6d**).

Starting from 1.14 g of **3d**, 0.47 g (20%) of **6d** was obtained as a solid foam. $[\alpha]_D^{29°}$ = -47.7° (c 1, dimethyl sulfoxide); Rf = 0.46 (methylene chloride/ethanol 9:1); ^{1}H-nmr selected data for α- and β-arabinopyranosil anomers (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 11.70 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.05 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.77 (d, 1H, H-1' J = 9.5 Hz for β-arabinopyranosil anomer), 6.38 (d, 1H, H-1' J = 2.8 Hz for α-arabinopyranosil anomer), 3.85 (s, 6H, O-CH_3), 2.10, 1.98 (s, 6H, N_5-CO-CH_3), 2.10-1.81 (s, 24H, CO-CH_3 this appears in two simetrical groups of signals); ^{13}C-nmr selected data (dimethyl-d_6 sulfoxide) δ(ppm): 172.7, 169.9, 169.7, 168.3 (CO-CH_3), 160.9, 160.4, 156.2 (C-2, C-4, C-6), 94.2 (C-5 is the same for both anomers), 85.0 (C-1' are the same for both anomers), 81.9, 80.2, 77.8, 77.0, 71.9, 68.5 (C-2', C-3', C-4' for each anomer), 65.4, 64.0 (C-5' for each anomer), 54.6, 54.5 (O-CH_3 for each anomer), 21.5, 20.7, 20.7, 20.5 x 2, 20.3 x 2, 20.1 (CO-CH_3); uv (methanol): λ max (nm) (ε) 209 (17860), 263 (8740).

Anal. Calcd. for $C_{18}H_{24}N_4O_{10}$•1/2 H_2O: C, 46.45; H, 5.19; N, 12.03; Found: C, 46.51; H, 5.38; N, 12.03.

5-Acetamido-6-amino-2-methylthio-5-*N*-β-D-(2,3,4-tri-*O*-acetyl)-xylopyranosylaminopyrimidin-4(3*H*)-one (**6e**).

Starting from 1.52 g of **3j**, 1.47 g (62 %) of **6e** was obtained, mp 236-238 °C (d); $[\alpha]_D^{25°}$ = + 50.0° (c 1, dimethyl sulfoxide); Rf = 0.64 (methylene chloride/ethanol 9:1); ^{1}H-nmr (400 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 12. 10 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.00 (s, 2H, NH_2 deuterium oxide-exchangeable), 5.80 (d, 1H, H-1' J = 9.8 Hz), 5.15 (t, 1H, H-2' J = 9.8 Hz), 4.60 (t, 1H, H-3' J = 9.8 Hz), 4.73 (td, 1H, H-4' J = 5.5 Hz, J = 11.0 Hz, J = 11.0 Hz), 3.96 (dd, 1H, H-5'*cis* J = 11.0 Hz, J = 5.6 Hz,), 3.53 (t, 1H, H-5'*trans* J = 11.10 Hz), 2.46 (s, 3H, S-CH_3 overlapped with dimethyl-d_6 sulfoxide signal), 2.16 (s, 3H, N_5-CO-CH_3), 1.98, 1.83, 1.80 (s, 9H, CO-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 172.6, 169.5, 169.4, 168.8 (CO-CH_3), 160.1 x 3 (C-2, C-4, C-6), 95.3 (C-5), 82.0 (C-1'), 73.4, 68.0, 67.8 (C-2', C-3', C-4'), 63.2 (C-5'), 21.4, 20.6, 20.3, 20.2 (CO-CH_3), 12.6 (S-CH_3); uv (methanol): λ max (nm) (ε) 216 (10110), 231 (8090), 278 (4420).

Anal. Calcd. for $C_{18}H_{24}N_4O_9S$: C, 45.75; H, 5.12; N, 11.85; S, 6.78; Found: C, 45.79; H, 5.30; N, 11.75; S, 6.29.

5-Acetamido-6-amino-2-methylthio-5-*N*-β-L-(2,3,4-tri-*O*-acetyl)-xylopyranosylaminopyrimidin-4(3*H*)-one (**6f**).

Starting from 1.52 g of **3k**, 1.60 g (68 %) of **6f** was obtained, mp 242-243 °C (d); $[\alpha]_D^{25°}$ = -46.9° (c 1, dimethyl sulfoxide); Rf = 0.58 (methylene chloride/ethanol 9:1); ^{1}H-nmr (400 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 12.15 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.05 (s, 2H, NH_2 deuterium oxide-exchangeable), 5.85 (d, 1H, H-1' J = 9.8 Hz), 5.20 (t, 1H, H-2' J = 9.8 Hz), 4.65 (t, 1H, H-3' J = 9.8 Hz), 4.78 (td, 1H, H-4' J = 5.5 Hz, J = 11.0 Hz, J = 11.0 Hz), 4.0 (dd, 1H, H-5'*cis* J = 11.0 Hz, J = 5.6 Hz), 3.53 (t, 1H, H-5'*trans* J = 11.1 Hz), 2.50 (s, 3H, S-CH_3 overlapped with dimethyl-d_6 sulfoxide signal), 2.20 (s, 3H, N_5-CO-CH_3), 2.00, 1.95, 1.80 (s, 9H, CO-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 172.0, 169.1, 168.9, 168.5 (CO-CH_3), 160.1 x 3 (C-2, C-4, C-6), 95.0 (C-5), 82.0 (C-1'), 73.0, 68.5, 67.7 (C-2', C-3', C-4'), 63.2 (C-5'), 21.3, 20.5, 20.2, 20.0 (CO-CH_3), 12.6 (S-CH_3); uv (methanol): λ max (nm) (ε) 216 (10700), 231 (8070), 278 (4680).

Anal. Calcd. for $C_{18}H_{24}N_4O_9S$: C, 45.75; H, 5.12; N, 11.85; S, 6.78; Found: C, 45.80; H, 5.00; N, 11.90; S, 6.50.

5-Acetamido-6-amino-5-*N*-β-D-(2,3,4-tri-*O*-acetyl)arabinopyranosylamino-2-methylthiopyrimidin-4(3*H*)-one (**6g**).

Starting from 1.52 g of **3l** 0.58 g (24 %) of **6g** was obtained, mp 164-168 °C; $[\alpha]_D^{25°}$ = -110.0°(c 1, dimethyl sulfoxide); Rf = 0.64 (methylene chloride/ethanol 9:1); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 12.08 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.03 (s, 2H, NH_2 deuterium oxide-exchangeable), 6.40 (d, 1H, H-1' J = 9.9 Hz), 5.12 (dd, 1H, H-4' J = 3.4 Hz, J = 9.5 Hz, J = 9.5 Hz), 5.01 (bs, 1H, H-3'), 4.85 (t, 1H, H-2' J = 9.9 Hz), 3.88 (m, 2H, H_2-5'), 2.47 (s, 3H, S-CH_3 overlapped with dimethyl-d_6 sulfoxide signal), 2.16 (s, 3H, N_5-CO-CH_3), 1.99, 1.87, 1.86 (s, 9H, CO-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 172.0, 169.1, 168.2, 167.5 (CO-CH_3), 160.4 x 3 (C-2, C-4, C-6), 96.0 (C-5), 82.0 (C-1'), 72.0, 68.5, 65.6 (C-2', C-3', C-4'), 65.2 (C-5'), 21.4, 20.6, 20.8, 20.2 (CO-CH_3), 12.5 (S-CH_3); uv (methanol): λ max (nm) (ε) 216 (24500), 231 (20500), 278 (10700).

Anal. Calcd. for $C_{18}H_{24}N_4O_9S$•1/2 H_2O: C, 44.90; H, 5.23; N, 11.63; S, 6.66; Found: C, 44.50; H, 5.55; N, 11.50; S, 6.40.

5-Acetamido-6-amino-5-*N*-β-L-(2,3,4-tri-*O*-acetyl)arabinopyranosylamino-2-methylthiopyrimidin-4(3*H*)-one (**6h**).

Starting from 1.52 g of **3m**, 1.72 g (73 %) of **6h** was obtained, mp 167-169 °C; $[\alpha]_D^{25°}$ = +116.3° (c 1, dimethyl sulfoxide); Rf = 0.54 (methylene chloride/ethanol 9:1); ^{1}H-nmr (300 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 12.05 (bs, 1H, N_3-H deuterium oxide-exchangeable), 7.10 (s, 2H, NH_2 deuterium oxide-exchangeable), 6.33 (d, 1H, H-1' J = 9.9 Hz), 5.18 (dd, 1H, H-4' J = 3.5 Hz, J = 9.6 Hz, J =

9.6 Hz), 5.07 (bs, 1H, H-3'), 4.89 (t, 1H, H-2' J = 9.8 Hz), 3.94 (m, 2H, H_2-5'), 2.41 (s, 3H, S-CH_3 overlapped with dimethyl-d_6 sulfoxide signal), 2.10 (s, 3H, N_5-CO-CH_3), 1.94, 1.93, 1.92 (s, 9H, CO-CH_3); ^{13}C-nmr (dimethyl-d_6 sulfoxide) δ(ppm): 172.6, 169.9, 169.5, 168.9 (CO-CH_3), 160.0 x 3 (C-2, C-4, C-6), 95.7 (C-5), 81.9 (C-1'), 72.0, 68.5, 65.6 (C-2', C-3', C-4'), 65.1 (C-5'), 21.6, 21.0, 20.8, 20.4 (CO-CH_3), 12.7 (S-CH_3); uv (methanol): λ max (nm) (ε) 216 (22140), 231 (17730), 278 (9510).

Anal. Calcd. for $C_{18}H_{24}N_4O_9S$•1/2 H_2O: C, 44.90; H, 5.23; N, 11.63; S, 6.66; Found: C, 45.03; H, 4.93; N, 11.61; S, 6.33.

6-Amino-2-methoxy-3-methyl-5-*N*-D-(2,3,4,5-tetra-*O*-acetyl)-ribosylideniminopyrimidin-4(3*H*)-one (**7a**).

Starting from 1.52 g of **3e**, 0.28 g (12%) of **7a** was obtained, mp 140-142 °C; $[\alpha]_D^{29°}$ = +91° (c 1, chloroform); Rf = 0.64 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 9.05 (d, 1H, H-1' J = 3.1 Hz), 6.75 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.50 (m, 3H, H-2', H-3', H-4'), 4.25 (m, 2H, H_2-5'), 3.95 (s, 3H, O-CH_3), 3.20 (s, 3H, N-CH_3), 2.10, 2.05, 2.00, 1.95 (s, 12H, CO-CH_3); ^{13}C-nmr (deuteriochloroform) δ(ppm): 170.9, 170.3, 169.9 (CO-CH_3), 159.4, 157.8, 155.3 (C-2, C-4, C-6), 151.3 (C-1'), 103.2 (C-5), 74.1, 70.5, 69.3 (C-2', C-3', C-4'), 61.9 (C-5'), 55.7 (O-CH_3), 27.1 (N-CH_3), 21.0, 20.9, 20.7 x 2 (CO-CH_3); ms: 470 ($M^{+\cdot}$, 1%); uv (methanol): λ max (nm) (ε) 224 (15890), 279 (9060), 307 (10090).

Anal. Calcd. for $C_{19}H_{26}N_4O_{10}$: C, 48.51; H, 5.57; N, 11.92; Found: C, 48.22; H, 5.46; N, 11.98.

6-Amino-2-methoxy-3-methyl-5-*N*-D-(2,3,4,5-tetra-*O*-acetyl)-xylosylideniminopyrimidin-4(3*H*)-one (**7b**).

Starting from 1.51 g of **3f**, 0.80 g (34%) of **7b** was obtained, mp 143-145 °C; $[\alpha]_D^{20°}$ = +139.2° (c 1, chloroform); Rf = 0.78 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.90 (d, 1H, H-1' J = 2.7 Hz), 6.65 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.50 (m, 3H, H-2', H-3', H-4'), 4.15 (m, 2H, H_2-5'), 3.90 (s, 3H, O-CH_3), 3.10 (s, 3H, N-CH_3), 2.10, 2.05, 2.00, 1.95 (s, 12H, CO-CH_3); ^{13}C-nmr (deuteriochloroform) δ(ppm): 170.5, 170.3, 169.9 (CO-CH_3), 159.4, 157.8, 155.3 (C-2, C-4, C-6), 151.3 (C-1'), 103.1 (C-5), 73.4, 69.6, 69.3 (C-2', C-3', C-4'), 62.1 (C-5'), 55.7 (O-CH_3), 27.1 (N-CH_3), 20.9, 20.8, 20.7, 20.6 (CO-CH_3); ms: 470 ($M^{+\cdot}$, 1%); uv (methanol): λ max (nm) (ε) 224 (17930), 278 (10420), 307 (11740).

Anal. Calcd. for $C_{19}H_{26}N_4O_{10}$: C, 48.51; H, 5.57; N, 11.92; Found: C, 48.15; H, 5.51; N, 12.02.

6-Amino-2-methoxy-3-methyl-5-*N*-L-(2,3,4,5-tetra-*O*-acetyl)-xylosylideniminopyrimidin-4(3*H*)-one (**7c**).

Starting from 1.51 g of **3g** 1.32 g (56%) of **7c** was obtained, mp 146-148 °C; $[\alpha]_D^{20°}$ = -132.2° (c 1, chloroform); Rf = 0.81 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.95 (d, 1H, H-1' J = 2.7 Hz), 6.65 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.60 (m, 3H, H-2', H-3', H-4'), 4.25 (m, 2H, H_2-5'), 3.90 (s, 3H, O-CH_3), 3.15 (s, 3H, N-CH_3), 2.10, 2.00 (s, 12H, CO-CH_3); ^{13}C-nmr (deuteriochloroform) δ(ppm): 170.6, 170.2, 169.9 (CO-CH_3), 159.3, 157.8, 155.3 (C-2, C-4, C-6), 151.3 (C-1'), 103.0 (C-5), 72.6, 69.2, 68.6 (C-2', C-3', C-4'), 61.9 (C-5'), 55.7 (O-CH_3), 27.1 (N-CH_3), 20.9, 20.8, 20.7 (CO-CH_3); ms: 470 ($M^{+\cdot}$, 0.04%); uv (methanol): λ max (nm) (ε) 223 (17980), 278 (18780), 307 (11540).

Anal. Calcd. for $C_{19}H_{26}N_4O_{10}$: C, 48.51; H, 5.57; N, 11.92; Found: C, 48.15; H, 5.47; N, 12.23.

6-Amino-5-*N*-D-(2,3,4,5-tetra-*O*-acetyl)arabinosylidenimino-2-methoxy-3-methylpyrimidin-4(3*H*)-one (**7d**).

Starting from 1.51 g of **3h**, 1.18 g (50%) of **7d** was obtained, mp 155-156 °C; $[\alpha]_D^{20°}$ = -148.0° (c 1, chloroform); Rf = 0.70 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.90 (d, 1H, H-1' J = 2.7 Hz); 6.75 (bs, 2H, NH_2 deuterium oxide-exchangeable), 5.65 (m, 3H, H-1', H-2', H-3'), 4.25 (m, 2H, H_2-5'), 3.90 (s, 3H, O-CH_3), 3.15 (s, 3H, N-CH_3), 2.10, 2.00 (s, 12H, CO-CH_3); ^{13}C-nmr (deuteriochloroform) δ(ppm): 170.6, 170.5, 169.9 (CO-CH_3), 159.3, 157.7, 155.3 (C-2, C-4, C-6), 151.2 (C-1'), 102.9 (C-5), 72.6, 69.2, 68.6 (C-2', C-3', C-4'), 61.9 (C-5'), 55.6 (O-CH_3), 27.0 (N-CH_3), 20.9, 20.8, 20.7, 20.6 (CO-CH_3); ms: 470 ($M^{+\cdot}$, 1%); uv (methanol): λ max (nm) (ε) 224 (16200), 279 (9700), 308 (10800).

Anal. Calcd. for $C_{19}H_{26}N_4O_{10}$: C, 48.51; H, 5.57; N, 11.92; Found: C, 48.40; H, 5.60; N, 12.15.

6-Amino-5-*N*-L-(2,3,4,5-tetra-*O*-acetyl)arabinosylidenimino-2-methoxy-3-methylpyrimidin-4(3*H*)-one (**7e**).

Starting from 1.51 g of **3i**, 1.53 g (65%) of **7e** was obtained, mp 156-158 °C; $[\alpha]_D^{20°}$ = +143.3° (c 1, chloroform); Rf = 0.76 (methylene chloride/ethanol 8:2); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.90 (d, 1H, H-1' J = 2.9 Hz); 6.75 (bs, 2H, NH_2, deuterium oxide-exchangeable), 5.60 (m, 3H, H-2', H-3', H-4'), 4.25 (m, 2H, H_2-5'), 3.90 (s, 3H, O-CH_3), 3.15 (s, 3H, N-CH_3), 2.10, 2.00, (s, 12H, CO-CH_3); ^{13}C-nmr (deuteriochloroform) δ(ppm): 170.6, 170.2, 169.9 (CO-CH_3), 159.3, 157.8, 155.3 (C-2, C-4, C-6), 151.3 (C-1'), 102.9 (C-5), 72.6, 69.2, 68.6 (C-2', C-3', C-4'), 61.9 (C-5'), 55.7 (O-CH_3), 27.1 (N-CH_3), 20.9, 20.8, 20.7, 20.6 (CO-CH_3); ms: 470 ($M^{+\cdot}$, 2%); uv (methanol): λ max (nm) (ε) 224 (18140), 278 (18280), 305 (12020).

Anal. Calcd. for $C_{19}H_{26}N_4O_{10}$: C, 48.51; H, 5.57; N, 11.92; Found: C, 48.51; H, 5.44; N, 12.23.

Acetylation Reaction of **4**.

2-Methoxy-3-methyl-5-*N*-D-(2,3,4,5-tetra-*O*-acetyl)xylosylidenimino-6-*N*-α-D-(2,3,4,-tri-*O*-acetyl)xylopyranosylaminopyrimidin-4(3*H*)-one (**8**).

To 40 ml of a mixture of acetic anhydride and pyridine (50% v/v), 2.17 g (5 mmol) of **4** was added. The solution was stirred at room temperature for 24 hours. The acetic anhydride and pyridine were then removed under vacuum. The oily residue was purified by disolving in diethyl ether and hexane and was kept in the refrigerator overnight. The oily layer that appeared was filtered off and the mother liquors were evaporated under reduced pressure to dryness. The solid foam was identified as **8**, unable to be crystallized, 1.02 g (36%); Rf = 0.70 (methylene chloride/ethanol 9:1); ^{1}H-nmr (60 MHz) (dimethyl-d_6 sulfoxide) δ(ppm): 8.90 (d, 1H, H-1' J = 2.7 Hz), 7.05 (d, 1H, N_6-H J = 10.2 Hz deuterium oxide-exchangeable), 6.26 (dd, 1H, H-1" + deuterium oxide→ d J = 4.8 Hz), 5.50 (m, 5H, proton sugar signals), 4.40 (m, 5H, proton sugar signals), 4.05 (s, 3H, O-CH_3), 3.15 (s, 3H, N-CH_3), 2.00 (s, 21H, CO-CH_3).

General Procedure for the Acetylation Reaction of 7-Polyhydroxyalkylpteridines

The compound 7-polyhydroxyalkylpteridine **5** (0.42 g, 1.5 mmol) was stirred at room temperature for 24 hours in 20 ml of a mixture of acetic anhydride and pyridine (50%). The solvents were then removed under vacuum and the residue was co-evaporated

several times with methanol. The acetylated compounds were obtained as oily residues and were purified by preparative thin layer chromatography using methylene chloride/methanol 9.5:0.5 (double development) as eluent.

2-Methoxy-3-methyl-7-[D-*erythro*]-α,β,γ-tri-*O*-acetylpropyl-pteridin-4(3*H*)-one (**9a**).

Starting from **5a,** 0.18 g (22%) of **9a** was obtained; Rf = 0.76 (methylene chloride/ethanol 9:1); ^{1}H-nmr (60 MHz) (deuteriochloroform) δ(ppm): 8.75 (s, 1H, H-6), 6.15 (d, 1H, H-1' J = 6.2 Hz), 5.75 (m, 1H, H-2'), 4.40-4.65 (m, 3H, H-3' H_2-4'), 4.20 (s, 3H, O-CH_3), 3.60 (s, 3H, N-CH_3), 2.25, 2.05, 2.00 (s, 12H, CO-CH_3).

2-Methoxy-3-methyl-7-[D-*threo*]-α,β,γ-tri-*O*-acetylpropyl-pteridin-4(3*H*)-one (**9b**).

Starting from **5b**, 0.18 g (22%) of **9b** was obtained; Rf = 0.76 (methylene chloride/ethanol 9:1); ^{1}H-nmr (60 MHz) (deuteriochloroform) δ(ppm): 8.75 (s, 1H, H-6), 6.52 (d, 1H, H-1' J = 3.4 Hz), 5.70 (m, 1H, H-2'), 4.50-4.75 (m, 3H, H-3' H_2-4'), 3.80 (s, 3H, O-CH_3), 3.60 (s, 3H, N-CH_3), 2.20, 2.05, 2.00 (s, 12H, CO-CH_3).

2-Methoxy-3-methyl-7-[L-*threo*]-α,β,γ-tri-*O*-acetylpropyl-pteridin-4(3*H*)-one (**9c**).

Starting from **5c,** 0.26 g (42%) of **9c** was obtained; Rf = 0.76 (methylene chloride/ethanol 9:1); ^{1}H-nmr (60 MHz) (deuteriochloroform) δ(ppm): 8.75 (s, 1H, H-6), 6.20 (d, 1H, H-1' J = 4.8 Hz), 5.75 (m, 1H, H-2'), 4.40-4.55 (m, 3H, H-3' H_2-4'), 4.30 (s, 3H, O-CH_3), 3.60 (s, 3H, N-CH_3), 2.25, 2.05, 2.00 (s, 12H, CO-CH_3).

2-Methoxy-3-methyl-7-[L-*erythro*]-α,β,γ-tri-*O*-acetylpropyl-pteridin-4(3*H*)-one (**9d**).

Starting from **5d,** 0.32 g (52%) of **9d** was obtained; Rf = 0.78 (methylene chloride/ethanol 9:1); ^{1}H-nmr (60 MHz) (deuteriochloroform) δ(ppm): 8.75 (s, 1H, H-6), 6.20 (d, 1H, H-1' J = 6.2 Hz), 5.70 (m, 1H, H-2'), 4.20-4.65 (m, 3H, H-3', H_2-4'), 4.30 (s, 3H, O-CH_3), 3.60 (s, 3H, N-CH_3), 2.20, 2.05, 2.00 (s, 12H, CO-CH_3).

Acknowledgment.

Acknowlegment is made to the National Cancer Institute of Bethesda (Maryland, USA) where the biological assays of the compounds were undertaken.

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