

Nucleosides. Part LXVI.¹ Syntheses and properties of pterin ribonucleosides

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Dedicated to Professor Harri Lönnerberg on the occasion of his 60th birthday

Abstract

Several pterin derivatives (**1-8**) have been ribosylated in form of their trimethylsilyl derivatives (**9**) with 1-bromo-(**10**) and 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-D-ribofuranose (**11**) under the catalysis of HgO/HgBr₂, BF₃-etherate and trimethylsilyl triflate, respectively. Mixtures of the N-1- (**19-25**) and N-3-ribofuranosides (**12-18**) which are difficult to be separated were obtained. Debenzoylation by the Zemplen method led to the free pterin-nucleosides (**28-30**). A second approach starting from 2-methylthio-4(3*H*)pteridinones (**31-33**) gave again mixtures of the N-1-(**35-37**) and N-3-ribonucleosides (**38-40**). The 2-methylthio function in **35-37** can easily be substituted by various amines leading after subsequently debenzoylation to the N-2-substituted pterin-ribonucleosides (**41-50**). The structural assignments were based on comparisons of the UV spectra with the corresponding N-methyl substituted model substances. ¹H-NMR-spectra functioned as additional structural proof.

Keywords: Pterin ribosylations, silyl methods, UV comparisons, pK -determinations

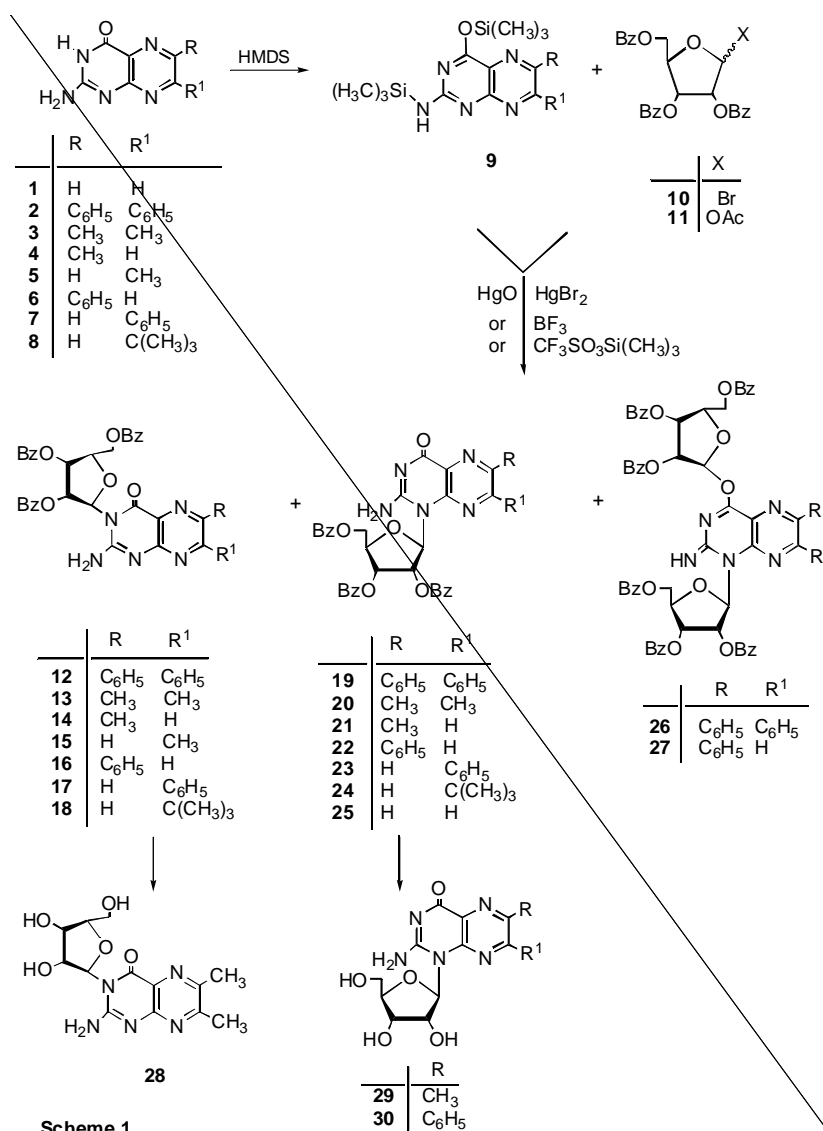
Introduction

The synthesis of pteridine nucleosides has been a major subject in our laboratory for many years. Lumazine²⁻¹¹ and isopterin nucleosides¹² can be regarded as structural analogs of the pyrimidine nucleosides whereas the many pteridin-7-one N₈-nucleosides¹³⁻²³ are structurally related to the purine nucleosides. The syntheses could be achieved either by a classical Hilbert-Johnson reaction²⁴, the mercury salt method by Fox and Davoll²⁵, the Hilbert-Johnson-Birkofer silyl procedure^{26, 27} or the silyl variant by Vorbrüggen²⁸.

Pterin (2-amino-4(3*H*)pteridone) (**1**), the basic molecule of most naturally occurring pteridine derivatives, has so far not been included in our investigations. Thin layer chromatographic analysis of the reaction mixture obtained from preliminary experiments with **1** suggested that the reaction is not straightforward; formation of a complex mixture of several reactions products was thereby indicated.

Synthesis

Starting with 6,7-diphenylpterin (**2**) silylation with hexamethyldisilazane took 6 days till all starting material had dissolved to form 2-trimethylsilylamino-4-trimethylsilyloxypteridine (**9**) which was first treated with 1-bromo-2,3,5-tri-*O*-benzoyl-D-ribofuranose (**10**) in presence of HgO and HgBr₂ in analogy to the conditions of Wittenburg²⁹. After a very tedious chromatographic separation by column, low-pressure and preparative thick layer chromatography three compounds 2-amino-6,7-diphenyl-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4(3H)-pteridone (**12**), the corresponding N¹-riboside (**19**) and the 2-imino-6,7-diphenyl-N¹,O⁴-bis-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-1,2-dihydropteridine (**26**) could be isolated in low yields. An analogous reaction with 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**11**) and BF₃-etherate as a catalyst gave predominately 2-amino-6,7-diphenyl-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4(3H)pteridone (**19**) in 50% yield whereas the isomeric **12** was obtained in only 1% yield.

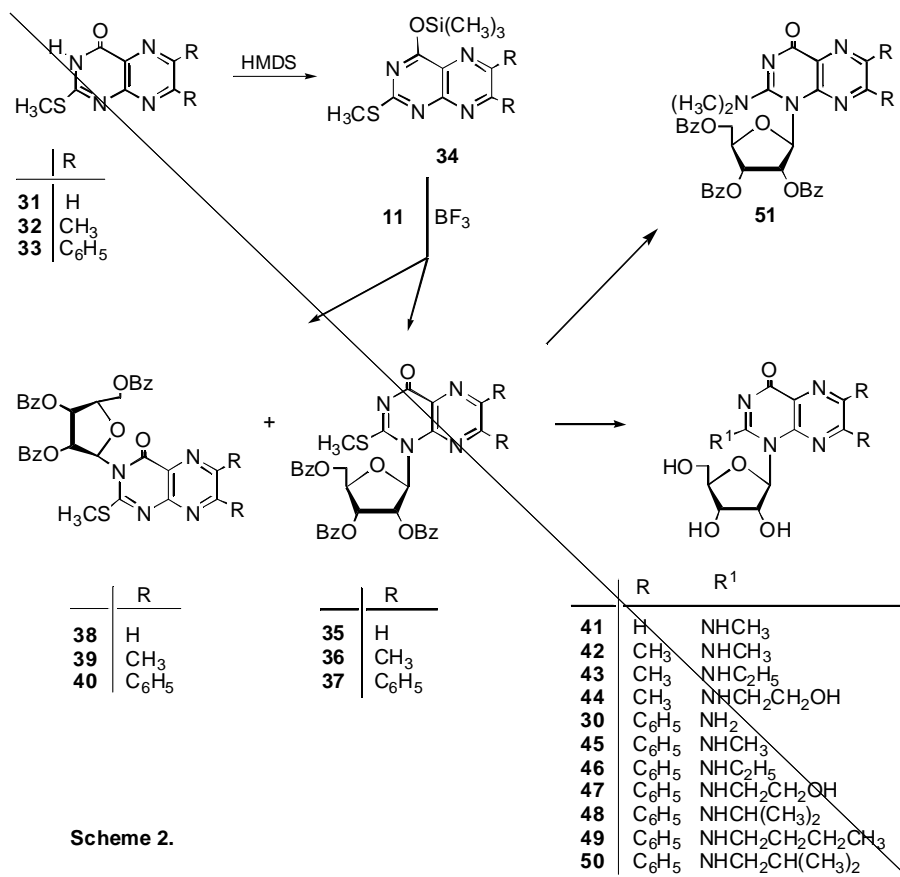


Scheme 1.

Analogously, BF₃-catalysis of 7-phenylpterin (**7**) and **11** gave small amounts of the N₁- (**23**) and N₃-nucleoside (**17**). Similarly 6-phenylpterin (**6**) and **11** in presence of trimethyl-silyl trifluorosulfonate gave three components N₁-(**22**), N₃-monoriboside (**16**) and the N₁,O⁴-diriboside (**27**) that were separated from the complex reaction mixture. Ribosylations of 6,7-dimethylpterin (**3**) led with the halosugar **10** and HgO/HgBr₂ to 3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6,7-dimethylpterin (**13**) in 14% yield whereas the use of **11** and BF₃-catalysis formed the N₁-riboside (**20**) in 14% as the main reaction product besides 8% of the N₃-isomer (**13**). The ribosylation reaction have also been extended to 6-methylpterin (**4**) yielding with **11** and BF₃ small amounts of the N₁-(**21**) and N₃-riboside (**14**), with 7-methyl-pterin (**5**) the N₃-riboside ((**15**) in 6% yield and with 7-tert.butylpterin (**8**) again a mixture of N₁- (**24**) and N₃-riboside (**18**). A highly unpleasant reaction was encountered with pterin (**1**) itself which led after a tedious isolation and purification process only to 10% yield of the 1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)pterin (**25**). Debenzoylations of the sugar protecting groups can be achieved by the Zemplen³⁰ method as demonstrated with **13**, **19** and **20**, respectively, forming the free pterin-nucleosides **28-30**.

The encountered difficulties during the ribosylations of the pterin derivatives, in general, force us to search for a more convenient synthetic pathway to this class of pteridine nucleosides. The more soluble 2-methylthio-4(3H)pteridione (**31**) and its 6,7-dimethyl-(**32**) and 6,7-diphenyl-(**33**) derivatives have been chosen as the most likely candidates due to the fact that the methylthio group can be displaced by amino functions nucleophilically. The ribosylations of **31**, **32** and **33** via their O⁴-trimethylsilyl derivatives (**34**) with **11** and BF₃ catalysis led in moderate to good yields in each case to a mixture of the corresponding N₁-(**35-37**), and N₃-ribosides (**38-40**).

Treatment of the 2-methylthio-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4(3H)-pteridones **35-37** with a great variety of amines led under displacement of the methylthio group and subsequent cleavage of the benzoyl groups by sodium methoxide to the corresponding pterin-N₁-ribofuranosides **41-51**.



Scheme 2.

Similar treatment of **37** with dimethylamine afforded first 2-dimethylamino-6,7-diphenyl-1-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-4(3*H*)-pteridone (**51**) but debenzoylation by the Zemplen method was not successful since sodium methoxide led to the cleavage of the glycosidic linkage forming 2-dimethylamino-6,7-diphenyl-4-(3*H*)-pteridone (**66**) (Fig. 1).

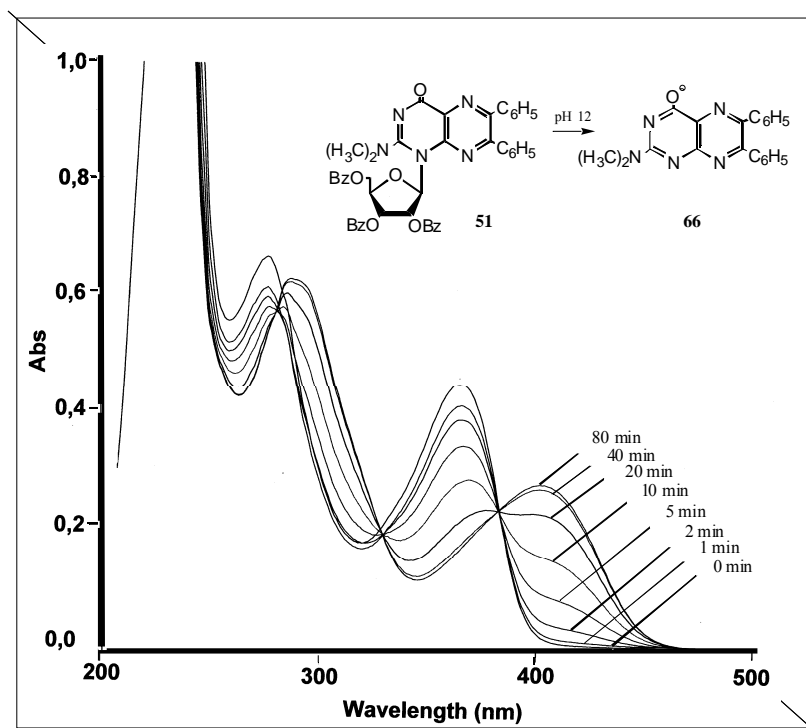


Figure 1. Cleavage of **51** at pH 12 to form **66**.

Structural assignment

The site of attachment of the sugar moiety to the pterin nucleus can best be assigned by comparison of the UV spectra with those of the corresponding model substances **52-66** most of which are already described in literature. We have determined in several cases also the pK_a values³¹ in order to compare the spectra of the cations and the neutral species as an additional structural proof (Tab. 1).

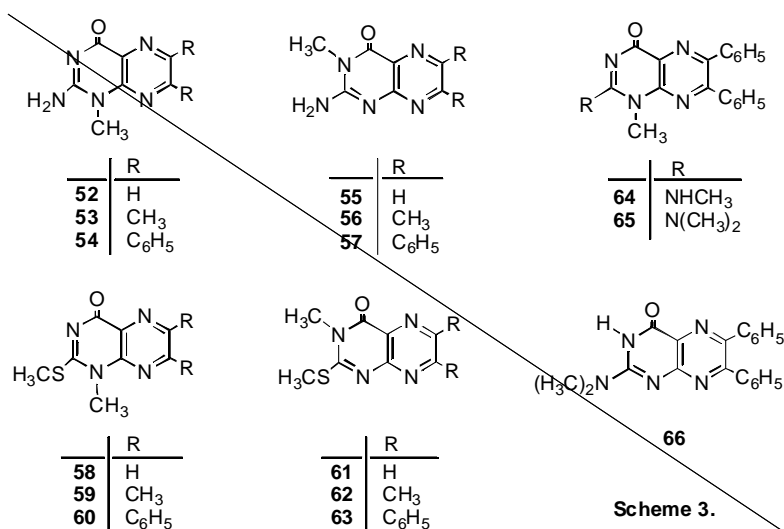


Figure 2. UV spectral comparison of **30** and **54** as well as **12** and **57**.

Table 1. UV-data of pterin nucleosides and model substances

-pterin	pK _a	λ _{max} (nm)			log ε			pH
1,6,7-Trimethyl- (53) ⁴²	3.25	217	254	320 (333)	4.28	3.95	4.00 (3.92)	0
	13.24	241	(315)	329 (342)	4.24 (3.92)	3.95	(3.98)	7
20		230	272	320 (335)	4.69	4.03	4.02 (3.93)	MeOH
1-β-D-Ribofuranosyl- 6,7-dimethyl- (29)	2.68	218 (250)	316 (330)		4.28 (3.95)	4.00 (3.91)		0
	12.58	238 (310)	322 (335)		4.23 (3.96)	4.02 (3.96)		7
21		230	275	315	4.74	4.13	3.97	MeOH
24		230	274 (282)	312	4.60	3.84 (3.82)	3.93	MeOH
25		230	272	315	4.61	3.89	3.91	MeOH
3,6,7-Trimethyl- (56) ⁴³	2.34	218	250	322 390	4.17	3.81	3.89 2.61	0
			241	276 352		4.16	4.09 3.83	5
13		(222)	242	282 355	(4.28)	4.18	4.31 3.88	MeOH
14		227	275	360	4.68	4.20	3.67	MeOH
15		228	280	350	4.80	4.31	3.91	MeOH
18		230	278	348	4.70	4.20	3.84	MeOH
3-β-D-Ribofuranosyl- 6,7-dimethyl- (28)	2.14	218	255	322 390	4.11	4.00	3.83 2.98	0
			247	273 352		4.35	4.74 3.76	7
1-Methyl-6,7-diphenyl- (54) ⁴³	2.95	222	280	362	4.42	4.13	4.15	0
		12.85	222	265 362	4.37	4.30	4.20	7
19		228	269	357	4.75	4.34	4.14	MeOH
51		228	273	363	4.81	4.37	4.20	MeOH
1-β-D-Ribofuranosyl- 6,7-diphenyl- (30)	2.60	228	280	350	4.41	4.13	4.14	0
		12.22	226	266 359	4.39	4.30	4.17	7
22		230	275 (283)	361	4.71	4.22 (4.20)	4.10	MeOH
23		228	273 (281)	345	4.76	4.12 (4.06)	4.28	MeOH
3-Methyl-6,7-diphenyl- (57) ⁴⁴	2.34	229	278	362	4.46	4.13	4.18	0
		13.02	224 (250)	292 380	4.42 (4.27)	4.35	4.10	7
12		227 (250)	297 380		4.69 (4.35)	4.35 3.98	MeOH	
16		230	305 374		4.75	4.41 3.93	MeOH	
17		227	304 375		4.76	4.48 3.95	MeOH	

Table 2. UV-data of 2-methylthio-lumazine nucleosides and model substances

- 2-methylthio-lumazine	λ_{\max} (nm)	log ϵ	pH
1-Methyl- (58) ⁴⁰	231 258 289 333 344	4.13 4.28 3.80 4.12 4.08	4
1,6,7-Trimethyl- (59) ⁴⁰	231 258 289 333 344	4.13 4.28 3.80 4.12 4.08	4
1-Methyl-6,7-diphenyl- (60) ⁴⁰	253 277 370	4.29 4.40 4.30	4
3-Methyl- (61) ⁴⁰	243 264 283 337	4.06 4.08 4.11 3.81	5
3,6,7-Trimethyl- (62) ⁴⁰	246 286 335	4.19 4.16 3.91	5
3-Methyl-6,7-diphenyl- (63) ⁴⁰	263 300 367	4.30 4.31 4.15	5
-(2,3,5-tri.O-benzoyl- β -D-ribofuranosyl)lumazine			
2-Methylthio-1- (35)	229 (252) 282 323 (340)	4.68 (4.08) 3.98 4.05 (3.80)	MeOH
6,7-Dimethyl-2-methylthio-1- (36)	228 (255) 282 324 (340)	4.70 (4.10) 3.98 4.09 (4.00)	MeOH
2-Methylthio-6,7-diphenyl-1- (37)	229 275 366	4.78 4.43 4.24	MeOH
2-Methyl-3- (38)	230 (275) 282 330	4.64 (4.15) 4.19 3.85	MeOH
6,7-Dimethyl-2-methylthio-3- (39)	228 (274) 282 (293) 330	4.72 (4.19) 4.25 (4.18) 3.92	MeOH
2-Methylthio-6,7-diphenyl-3- (40)	230 266 307 367	4.77 4.28 4.27 4.13	MeOH

Table 3. UV-data of N²-substituted pterin nucleosides

1-β-D-ribofuranosylpterin	pK _a	λ _{max} (nm)				log ε				pH
N ² -Methyl- (41)	1.34	210	239	280	324	4.25	4.11	3.68	3.86	0
	12.97	210	239		324	4.30	4.11		3.86	7
N ² ,6,7-Trimethyl- (42)	1.84	222	253		324	4.30	4.04		4.01	0
	13.78	241	280	330	(343)	4.26	3.65	4.06	(4.02)	7
N ² -Ethyl-6,7-dimethyl- (43)	1.87	222	(252)	322	(334)	4.28	(4.03)	3.99	(3.91)	0
	14.22	242	280	331	(343)	4.27	3.68	4.05	(4.00)	5
N ² -β-Hydroxyethyl-6,7-dimethyl- (44)	1.48	220	252	(293)	332	4.25	4.04	(3.68)	3.93	0
	13.59	240	278	328	(342)	4.26	3.68	4.06	(4.01)	5
6,7-Diphenyl- (30)	2.60	228		280	350	4.41		4.13	4.14	0
	12.22	226	266		359	4.39	4.30		4.17	7
N ² -Methyl-6,7-diphenyl- (45)	1.55	233		280	364	4.43		4.18	4.18	0
	13,14	225	269		364	4.37	4.34		4.23	5
N ² -Ethyl-6,7-diphenyl- (46)	1.88	236		279	364	4.43		4.17	4.17	0
	13.76		270		364		4.37		4.23	5
N ² -Isopropyl-6,7-diphenyl- (47)	1.69	233		280	364	4.43		4.18	4.18	0
	14.04	(225)	269		364	(4.46)	4.35		4.24	5
N ² -β-Hydroxyethyl-6,7-diphenyl- (48)	1.27	235		280	364	4.43		4.18	4.17	0
	12.88	(234)	270		364	(4.47)	4.34		4.24	7
N ² -n-Butyl-6,7-diphenyl. (49)	1.58	236		279	364	4.44		4.19	4.19	0
	13.98	(226)	270		364	(4.45)	4.36		4.25	5
N ² -Isobutyl-6,7-diphenyl- (50)	1.74	235		280	364	4.61		4.36	4.33	0
	14.05		270		365		4.51		4.47	5

The ¹H-NMR spectra (experimental part) of the benzoyl protected ribonucleosides have not been very informative since overlapping signals make accurate assignments difficult. The free β-D-ribofuranosylpterin nucleosides (**28-30**, **41-50**) on the other hand showed well separated proton signals of the sugar moieties which are in good agreement with the pattern of the

ribonucleosides, in general. The H-C(1') appears always as doublet at lowest field followed by the 5'-OH, 2'-OH, 3'-OH, H-C(2'), H-C(3'), H-C(4') and H-C(5') towards higher fields.

Experimental Section

General Procedures. Products were dried under high vacuum. TLC: precoated cellulose thin-layer sheets F 1440b LS 254 and silica gel thin-layer sheets F 1500 LS 254 from *Schleicher and Schüll*. Preparative TLC: plates 20 x 20 x 0.2 cm with silica gel 60 PF 254 from *Merck*. Column chromatography (CC): silica gel 60, 70 - 230 mesh from *Merck*. Low pressure chromatography³² (LPC): LiChroprep Si 60 from *Merck* according to³³ under 8-10 atm. Short column chromatography (SCC): silica gel 60 H from *Merck*. UV/VIS: Perkin-Elmer Lambda 5; λ_{\max} in nm (log ϵ). ¹H-NMR: Bruker AC 250; in CDCl₃ or ((D₆)DMSO), δ in ppm rel. to SiMe₄ as internal standard. M.p.: *Büchi* apparatus, model Dr. Tottuli; no corrections. The pK_a measurements were performed by the spectrophotometric method³¹. Products were dried under high vacuum.

2-Amino-3-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-6,7-diphenyl-4(3H)pteridinone (12), 2-Amino-1-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-6,7-diphenyl-4(3H)pteridinone (19) and 2-Imino-1,*O*⁴-bis-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)1,2-dihydropteridine (26).

A mixture of 6,7-diphenylpterin (**2**)³⁴ (0.945 g, 3 mmol) and (NH₄)₂SO₄ (0.1 g) was heated in hexamethyldisilazane (HMDS) (15 ml) 6 days under reflux till a clear solution was obtained. The excess of HMDS was removed in vacuum and the resulting **9** dissolved in abs. benzene (15 ml). A solution of 1-bromo-2,3,5-tri-*O*-benzoyl-D-ribofuranose (**10**)³⁵ (1.575 g, 3 mmol) in benzene (15 ml) and each 0.75 g of HgO and HgBr₂ were added. The mixture was refluxed for 4 h, evaporated and the residue treated with CHCl₃ (100 ml). The mercury salts were filtered off and the filtrate shaken with a KJ solution (15%). The organic phase was dried over Na₂SO₄, evaporated to a smaller volume, put onto a silica gel column (7 x 35 cm) and first developed with CHCl₃ (4 l). Evaporation of this fraction 1 gave a mixture of 3 nucleosides (1.26 g). The solvents system was changed to CHCl₃/MeOH (19:1, 1 l) followed by (9:1, 1l) and gave on evaporation fraction 2 (0.15 g). Fraction 3 resulted from the elution with (CHCl₃/MeOH 4:1 (500 ml) and (1:1, 1.5 l) to give 0.3 g.

Fraction 1 was further separated by low pressure chromatography on a column type C³⁰ (3 x 50 cm, silica gel Lichroprep Si 60) and a pressure of 10 atm. The eluents n-hexane/CHCl₃ (7/3) separated first unreacted sugar and with 6/4 next **26** (0.21 g, 9%) and followed by **12** (0.675 g, 30%). Fraction 2 was separated by preparative thick-layer chromatography on plates (40 x 20 x 0.2 cm) with CHCl₃/MeOH (19:1). The main band was eluted with CHCl₃/MeOH (9:1) to give **12** (0.12 g, 15%). Fraction 3 gave on chromatography on thick-layer plates with CHCl₃/MeOH (9:1) **19** (0.165 g, 7%).

12. Yield: 0.795 g (35%). M.p. 154-158°C. ¹H-NMR (CDCl₃): 8.08 (d, 2 H, arom. H); 7.96-7.90

(dd, 4 H, arom. H); 7.60-7.26 (m, 20 H, arom. H); 7.17 (d, 1 H, H-C(1')); 6.19 (pt, 1 H, H-C(2')); 6.12 (bs, 2 H, NH₂); 6.02 (m, 1 H, H-C(3')); 4.88 (d, 2 H, H-C(5')); 4.47 (m, 1 H, H-C(4')). Anal. Calc. for C₄₄H₃₃N₅O₈ (759.6): C, 69.57; H, 4.38; N, 9.22. Found: C, 68.99; H, 4.49; N, 9.19.

26. Yield: 0.21 g (9%). M.p. 132-136°C. ¹H-NMR (CDCl₃): 8.10-7.85 (m, 14 H, arom. H), 7.56-7.28 (m, 28 H, 26 arom. H, H-N, H-C(1')); 6.42 (d, 1 H, H-C(1')); 6.26-6.19 (m, 2 H, H-C(2')); 5.99 (m, 2 H, H-C(3')); 4.73 (m, 4 H, H-C(5')); 4.57 (m, 2 H, H-C(4')). Anal. Calc. for C₇₀H₅₃N₅O₁₅ x 2 H₂O (1240.2): C, 67.79; H, 4.63; N, 5.64. Found: C, 67.38; H, 4.87; N, 5.35.

2-Amino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6,7-diphenyl-4(3H)pteridinone (19).

Silylation analogous to the preceding procedure with **2** (1.265 g, 4 mmol). The intermediate **9** was dissolved in CH₂Cl₂ (30 ml), 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-β-D-ribofuranose (**11**)³⁵ (2.01 g, 4.1 mmol) and BF₃-etherate (4 ml) were added and stirred at rt for 4 h. Dilution with CH₂Cl₂ (50 ml), treatment with saturated NaHCO₃ solution, drying of the organic layer with Na₂SO₄ and evaporation to give a crude mixture (3.2 g). Separation by CC (7 x 30 cm) first with CHCl₃ (1.5 l), then with CHCl₃/MeOH (19:1, 500 ml; 13:1, 500 ml and 9:1, 1.5 l) to give the main fraction on evaporation. The mixture was further purified by chromatography on 10 thick-layer plates (40 x 20 x 0.2 cm) with CHCl₃/MeOH (19:1). The main band was cut out, eluted with CHCl₃/MeOH (12:1), evaporated to give 1.535 g of **19**. Recrystallization from isopropanol/H₂O (1:1, 40 ml) gave 1.47 g (50%) of pure **19** of m.p. 152°C. ¹H-NMR (CDCl₃): 8.00-7.20 (m, 28 H, NH₂, 25 arom. H, H-C(1')); 6.41 (m, 1H, H.C(2')); 5.49 (pt, 1 H, H-C(3')); 4.70-4.50 (m, 3 H, H-C(4'), H-C(5')). Anal. Calc. for C₄₄H₃₃N₅O₈ x H₂O (777.6): C, 67.96; H, 4.53; N, 9.00. Found: C, 67.82; H, 4.43; N, 8.91.

2-Amino-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6,7-dimethyl-4(3H)pteridinone (13) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6,7-dimethyl-4(3H)pteridinone (20).

A mixture of 6,7-dimethylpterin (**3**) (0.955 g, 5 mmo) and (NH₄)₂SO₄ (0.1 g) in hexamethyldisilazane (10 ml) was heated under reflux for 5 h to form a clear solution. The excess of HMDS was distilled off, the residue dissolved in CH₂Cl₂ (15 ml), **11** (2.52 g, 5.1 mmol) in CH₂Cl₂ (15 ml) and BF₃-etherate (5 ml) added. After stirring at rt for 4 h the reaction solution was treated with saturated aqueous NaHCO₃ solution, the organic layer separated, dried over Na₂SO₄ and evaporated to dryness. The residue was dissolved in CHCl₃, put onto a silica gel column (7 x 30 cm) and developed first with CHCl₃ (1,5 l) to give unreacted sugar and followed by CHCl₃/MeOH (19:1, 500 ml; 12: 1, 1000 ml and 9:1, 1000 ml) to give a mixture of 3 substances (1.1 g). This fraction was separated on preparative silica gel plates (40 x 20 x 0.2 cm) with CHCl₃/MeOH (9:1). The lower band (R_f 0.28) was eluted with CHCl₃/MeOH (9:1) and gave on evaporation pure **20** (0.425 g, 14%).

The upper band was still a mixture of two substances and had to be rechromatographed on plates with CHCl₃/MeOH (19:1) to get partial separation. The band (R_f 0.51) gave after elution with CHCl₃/MeOH (9:1), evaporation and recrystallization from *i*-PrOH/H₂O (1:1)

13 (0.25 g, 8%).

20. Yield: 0.425 g, (14%).M.p. 152-154°C. ¹H-NMR (CDCl₃): 7.99-7.26 (m, 17 H, 15 arom. H, NH₂); 7.05 (d, 1 H, H-C(1')); 6.51-6.30 (m, 2 H, H-C(2', 3')); 4.92-4.71 (d, 3 H, H-C(4', 5')); 2.61,

2.58 (2 s, 6H, 2 CH₃). Anal. Calc. for C₃₄H₂₉N₅O₈ x 0.5 H₂O (644.6): C, 63.35; H, 4.69; N, 10.86. Found: C, 63.24; H, 4.53; N, 10.27.

2-Amino-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6,7-dimethyl-4(3H)pteridinone (13).

Silylation of **3** (0.955 g, 5 mmol) was performed analogous to the preceding procedure. The silylated intermediate **9** was dissolved in abs. C₆H₆ (35 ml), then **10** (2.27 g, 4.5 mmol), HgO (1.25 g) and HgBr₂ (1.25 g) added. The mixture was heated under reflux for 4 h. After cooling MeOH (2 ml) was added, the mixture evaporated to dryness, the residue dissolved in CHCl₃ (50 ml) and then shaken several times with 15% aqueous KJ solution to remove the mercury salts. The organic layer was separated, dried over Na₂SO₄ and again evaporated. The residue was dissolved in CHCl₃, put onto a silica gel column (4.5 x 45 cm) and developed with CHCl₃/MeOH (19:1). After 1.5 l elution the next fraction (400 ml) was collected, evaporated to give 0.6 g. This mixture was further purified on 5 preparative thick layer plates (40 x 20 x 0.2 cm) with CHCl₃, MeOH (19:1). The main band was cut out, eluted by CHCl₃/MeOH (15:1) to give after evaporation **13** (0.425 g, 14%) of m.p. 168°C (decomp.). ¹H-NMR (CDCl₃): 8.06-7.92 (m, 5 H, arom. H); 7.55-7.20 (10 H, arom. H); 7.18 (d, 1 H, H-C(1')); 6.20 (bs, 2 H, NH₂); 6.18 (m, 1 H, H-C(2')); 6.08 (m, 1 H, H-C(3')); 4.91 (m, 2 H, H-C(5')); 4.72 (m, 1 H, H-C(4')); 2.61 (s, 3 H, CH₃); 2.57 (s, 3 H, CH₃). Anal. Calc. for C₃₄H₂₉N₅O₈ x 0.5 H₂O (644.6): C, 63.35; H, 4.69; N, 10.86. Found: C, 63.15; H, 4.78; N, 10.71.

2-Amino-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methyl-4(3H)pteridinone (14) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-6-methyl-4(3H)pteridinone (21).

A mixture of 6-methylpterin (**4**)³⁶ (0.709 g, 4 mmol) and (NH₄)₂SO₄ (0.1 g) in HMDS (30 ml) was refluxed for 24 h, then evaporate, the residue dissolved in CH₂Cl₂ (40 ml), **11** (2.01 g, 4 mmol) and BF₃-etherate (4 ml) added and then stirred at rt for 4 h. The reaction solution was treated with saturated aqueous NaHCO₃ solution, the organic phase separated and dried over Na₂SO₄ and evaporated. The residue was dissolved in CHCl₃, put onto a silica gel column (8 x 30 cm) and developed first with CHCl₃ (2 l) to give unreacted sugar. Extended elution with CHCl₃/MeOH (19:1, 2.5 l) and CHCl₃/MeOH (14:1, 500 ml) gave on evaporation a mixture of **14** and **21** (0.745 g). Its difficult separation was performed on preparative thick-layer silica gel plates (40 x 20 x 0.2 cm) by repeated development with CHCl₃/MeOH (19:1) to get separation of 2 main bands. Elution of the faster moving band yielded after evaporation 0.18 g (6%) of **14** and from the lower moving band 0.27 g (9%) of **21**.

14: ¹H-NMR (CDCl₃): 8.30 (s, 1 H, H-C(7)); 8.20-7.20 (m, 15 H, arom. H); 7.15 (d, 1 H, H-C(1')); 6.17 (bs, 2 H, NH₂); 6.15-5.82 (m, 2 H, H-C(2', 3')); 4.93-4.62 (m, 3 H, H-C(4', 5')); 2.65 (s, 3 H, CH₃). Anal. Calc. for C₃₃H₂₇N₅O₈ x 0.5 H₂O (630.6): C, 62.85; H, 4.32; N, 11.10. Found: C, 62.85; H, 4.31; N, 10.57.

21: ¹H-NMR (CDCl₃): 8.53 (s, 1 H, H-C(7)); 8.10-7.20 (m, 17 H, 15 arom. H, NH₂); 7.05 (d, 1 H, H-C(1')); 6.30-6.05 (m, 2 H, H-C(2', 3')); 4.93-4.44 (m, 3 H, H-C(4', 5')); 2.62 (s, 3 H, CH₃). Anal. Calc. for C₃₃H₂₇N₅O₈ x 0.5 H₂O (630.6): C, 62.85; H, 4.32; N, 11.10. Found: C, 62.63; H, 4.20; N, 11.27.

2-Amino-3-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-7-methyl-4(3H)pteridinone (15).

Analogous to the preceding procedure with 7-methylpterin (**5**)³⁷ (0.886 g, 5 mmol) and **11** (2.52 g, 5 mmol) and BF₃-etherate (4 ml). The reaction product was purified by short column chromatography with CHCl₃/n-hexane (4:1). The main fraction was collected, evaporated and the residue recrystallized from EtOH/H₂O to give 0.186 g (6%) of **15**. M.p. 122-124°C.

¹H-NMR (CDCl₃): 8.39 (s, 1 H, H-C(6)); 8.20-7.22 (m, 15 H, arom. H); 7.20 (d, 1 H, H-C(1')); 6.11 (bs, 2 H, NH₂); 6.30-5.90 (m, 2 H, H-C(2', 3')); 5.00-4.44 (m, 3 H, H-C(4', 5')); 2.62 (s, 3 H, CH₃). Anal. Calc. for C₃₃H₂₇N₅O₈ (621.6): C, 63.76; H, 4.38; N, 11.27. Found: C, 63.78; H, 4.27; N, 10.93.

2-Amino-3-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-6-phenyl-4(3H)pteridinone (16), 2-Amino-1-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-6-phenyl-4(3H)pteridinone (22) and 2-Imino-1,0⁴-bis-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)1,2-dihydropteridine (27).

Analogous to the preceding procedure with 6-phenylpterin (**6**)³⁸ (0.957 g, 4 mmol), **11** (2.01 g, 4 mmol) and trimethylsilyl trifluoromethanesulfonate (2.6 g, 1.2 mmol) as catalyst. After stirring at rt for 24 h was diluted with CH₂Cl₂ (20 ml), treated with cold aqueous Na₂HPO₄ solution, the organic phase separated, dried with Na₂SO₄ and evaporated to give a crude mixture (2.46 g). This mixture was put onto a silica gel column (9 x 15 cm) for chromatography with CHCl₃ (3 l, 1. fraction, unreacted sugar), then with CHCl₃/MeOH (19:1, 2 l, 2. fraction). The second fraction was further separated on preparative thick layer silica gel plates (40 x 20 x 0.2 cm) by repeated development with CHCl₃/MeOH (19:1) to give 3 main bands which were cut out and eluted separately with CHCl₃/MeOH (12:1). The fastest moving band (R_f 0.82) gave **27** (0.08 g, 8%), the middle band **16** (0.09 g, 6%) and the lowest band **22** (0.04 g, 2%).

16. ¹H-NMR (CDCl₃): 9.14 (s, 1 H, H-C(7)); 8.20-7.20 (m, 22 H, 20 arom. H, NH₂); 7.18 (d, 1 H, H-C(1')); 6.24 (bs, 2 H, NH₂); 6.30-6.00 (m, 2 H, H-C(2', 3')); 5.00-4.60 (m, 3 H, H-C(4', 5')). Anal. Calc. for C₃₈H₂₉N₅O₈ (683.7): C, 66.76; H, 4.28; N, 10.24. Found: C, 66.53; H, 4.28; N, 10.00.

22. ¹H-NMR (CDCl₃): 8.96 (s, 1 H, H-C(7)); 8.20-7.20 (m, 22 H, 20 arom. H, NH₂); 6.82 (d, 1 H, H-C(1')); 6.50-6.25 (m, 2 H, H-C(2', 3')); 5.40-5.00 (m, 3 H, H-C(4', 5')). Anal. Calc. for C₃₈H₂₉N₅O₈ x H₂O (701.7): C, 64.47; H, 4.45; N, 9.98. Found: C, 64.47; H, 4.23; N, 9.91.

27: ¹H-NMR (CDCl₃): 8.51 (s, 1 H, H-C(7)); 8.20-7.20 (m, 37 H, 35 arom. H, NH₂); 7.00-6.30 (m, 6 H, H-C(1', 2', 3')); 4.90-4.50 (m, 6 H, H-C(4', 5')). Anal. Calc. for C₆₄H₄₉N₅O₁₅ (1128.1): C, 68.14; H, 4.38; N, 6.21. Found: C, 67.89; H, 4.48; N, 5.89.

2-Amino-3-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-7-phenyl-4(3H)pteridinone(17) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-7-phenyl-4(3H)pteridinone (23).

Analogous to the preceding procedure with 7-phenylpterin (**7**)³⁸ (0.957 g, 4 mmol), **11** (2.01 g, 4 mmol) and BF₃-etherate (4 ml) as catalyst. After stirring at rt for 4 h was diluted with CH₂Cl₂ (20 ml), treated with cold aqueous Na₂HPO₄ solution, the organic phase separated, dried with Na₂SO₄ and evaporated to give a crude mixture (2.35 g). This mixture was put onto a silica gel column (9 x 15 cm) for chromatography with CHCl₃ (3 l, 1. fraction, unreacted sugar), then with CHCl₃/MeOH (19:1, 3.5 l). This fraction was evaporated and separated on 6 preparative thick-

layer silica gel plates (40 x 20 x 0.2 cm) by repeated development with CHCl₃. The faster moving main band was cut out, eluted with CHCl₃, MeOH (9:1) to give 60 mg (2%) of **17**. The slower moving band gave 0.12 g (4%) of **23**.

17. ¹H-NMR (CDCl₃): 9.16 (s, 1 H, H-C(7)); 8.20-7.20 (m, 21 H, 20 arom. H, H-C(1')); 6.18 (m, 1 H, H-C(2')); 6.06 (m, 1 H, H-C(3')); 6.04 (bs, 2 H, NH₂); 4.75(m, 2 H, H-C(5')); 4.88 (m, 1 H, H-C(4')). Anal. Calc. for C₃₈H₂₉N₅O₈ x H₂O (701.7): C, 65.04; H, 4.45; N, 9.98. Found: C, 64.85; H, 3.97; N, 9.96.

23. ¹H-NMR (CDCl₃): 9.14 (s, 1 H, H-C(7)); 8.20-7.20 (m, 21 H, 20 arom. H, H-C(1')); 6.42 (bs, 2 H, NH₂); 6.17 (m, 1 H, H-C(2')); 5.99 (m, 1 H, H-C(3')); 6.04 (bs, 2 H, NH₂); 5.00-4.70 (m, 3 H, H-C(4',5')). Anal. Calc. for C₃₈H₂₉N₅O₈ x 0.5 H₂O (692.7): C, 65.89; H, 4.36; N, 10.11. Found: C, 65.74; H, 4.17; N, 9.89.

2-Amino-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-7-*tert*.butyl-4(3H)pteridinone (18) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-7-*tert*.butyl-4(3H)pteridinone (24).

Silylation and ribosylation was performed analogous to the preceding procedures with 7-*tert*.butyl-pterin (**8**)³⁹ (0.877 g, 4 mmol), **11** (2.01 g, 4 mmol) and BF₃-etherate (4 ml). Work-up was done after 5 days stirring at rt. The crude product mixture was separated on 10 preparative thick-layer plates with CHCl₃/MeOH (11:1) to give two main bands. The faster moving band gave after elution, evaporation and recrystallization from *i*-PrOH/H₂O 0.24 g (10%) of **18** and from the slower moving band were 0.363 g (14%) of **24** isolated.

18. ¹H-NMR (CDCl₃): 8.62 (s, 1 H, H-C(6)); 8.20-7.20 (m, 16 H, 15 arom. H, H-C(1')); 5.95 (bs, 2 H, NH₂); 6.16 (m, 1 H, H-C(2')); 5.93 (m, 1 H, H-C(3')); 5.00-4.70 (m, 3 H, H-C(4', 5')); 1.43 (s, 9 H, (CH₃)₃). Anal. Calc. for C₃₆H₃₃N₅O₈ (663.7): C, 65.15; H, 5.01; N, 10.55. Found: C, 65.24; H, 5.00; N, 10.19.

24. ¹H-NMR (CDCl₃): 8.76 (s, 1 H, H-C(6)); 8.20-7.10 (m, 16 H, 15 arom. H, H-C(1')); 6.15 (m, 1 H, H-C(2')); 6.08 (bs, 2 H, NH₂); 4.93-4.44 (m, 3 H, H-C(4', 5')); 1.39 (s, 9 H, (CH₃)₃). Anal. Calc. for C₃₆H₃₃N₅O₈ x 0.5 H₂O (672.7): C, 64.34; H, 5.10; N, 10.41. Found: C, 64.35; H, 5.04; N, 10.26.

2-Amino-1-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)-4(3H)pteridinone (25). A mixture of pterin (**1**) (1.63 g, 10 mmol) and (NH₄)₂SO₄ (0.1 g) in HMDS (50 ml) was heated under reflux for 20 h. The excess of HMDS was distilled off under high vacuum and the residue dissolved in abs. CH₂Cl₂ (30 ml). To the solution was added **11** (5.5 g, 11 mmol) and trimethylsilyl triflate (2.6 g, 12 mmol) and then stirred at rt for 24 h. The solution was diluted with CH₂Cl₂ (30 ml), treated with saturated aqueous NaHCO₃, the layers separated and the organic phase dried over Na₂SO₄. After evaporated the resulting residue was dissolved in CHCl₃ and put onto a silica gel column (3.5 x 29 cm) for elution first with CHCl₃ (1 l), followed by CHCl₃/MeOH (100:1, 500 ml), (100:3, 500 ml), (100:4, 500 ml) and (100:5, 1 l). These 4 fractions were evaporated to give 3.2 g crude product. Recrystallization from *i*-PrOH/H₂O gave 1.2 g (24%) of **25**. ¹H-NMR (CDCl₃): 8.84-8.66 (m, 6 H, arom. H); 8.29 (d, 1 H, H-C(7)); 8.07 (d, 1 H, H-C(6)); 8.00-7.26 (m, 11 H, arom. H, NH₂); 7.05 (d, 1 H, H-C(1')); 6.11 (m, 1 H, H-C(2')); 4.99-4.58 (m, 3 H, H-C(4', 5')). Anal. Calc. for C₃₂H₂₅N₅O₈ (607.6): C, 63.26; H, 4.15; N, 11.53. Found: C, 63.11; H,

4.25; N, 11.36.

2-Amino-6,7-dimethyl-3- β -D-ribofuranosyl-4(3H)pteridinone (28). A solution of **13** (0.2 g, 0.3 mmol) in abs. MeOH (100 ml) was treated with 0.2% CH₃ONa solution (2 ml) with stirring for 18 h. Little DOWEX 50 x 4 (H⁺-form, 200-400 mesh) and H₂O (5 ml) was added to bring the pH to 5. After filtration was evaporated, the residue dissolved in CHCl₃/MeOH (4:1, 10 ml), ether (10 ml) added and after cooling for 2 h the precipitate collected by centrifugation to give 44 mg (43%) of **28**. M.p. 161°C (decomp.).

¹H-NMR ((D₆)DMSO): 7.49 (bs, 2 H, NH₂); 6.51 (d, 1 H, H-C(1')); 5.62 (t, 1 H, 5'-OH); 5.28 (d, 1 H, 2'-OH); 5.15 (d, 1 H, 3'-OH); 4.47 (dd, 1 H; H-C(2')); 4.10-3.90 (m, 2 H, H-C(3', 4')); 3.64 (m, 2 H, H-C(5')); 2.51 (2 s, 6 H, 2 CH₃). Anal. Calc. for C₁₃H₁₇N₅O₅ x 2 H₂O (359.3): C, 43.45; H, 5.89; N, 19.49. Found: C, 43.89; H, 5.82; N, 19.09.

2-Amino-6,7-dimethyl-1- β -D-ribofuranosyl-4(3H)pteridinone (29). To a solution of **20** (0.15 g, 0.24 mmol) in abs. MeOH (5 ml) was added 1 M CH₃ONa (0.25 ml) and stirred for 2 h. The pH was brought to 5 by AcOH and the solution kept overnight in the icebox. The precipitate was collected and recrystallized from i-PrOH/H₂O (4:1, 15 ml) to give 53 mg (69%) of **29**. M.p. 170°C (decomp.). ¹H-NMR ((D₆)DMSO): 7.70 (bs, 2 H, NH₂); 6.68 (d, 1 H, H-C(1')); 5.78 (t, 1 H, 5'-OH); 5.35 (d, 1 H, 2'-OH); 5.18 (d, 1 H, 3'-OH); 4.56 (dd, 1 H; H-C(2')); 4.10-3.90 (m, 2 H, H-C(3', 4')); 3.65 (m, 2 H, H-C(5')); 2.55 (2 s, 6 H, 2 CH₃). Anal. Calc. for C₁₃H₁₇N₅O₅ x 0.5 H₂O (332.3): C, 46.98; H, 5.45; N, 21.07. Found: C, 46.64; H, 5.54; N, 20.48.

2-Amino-6,7-diphenyl-1- β -D-ribofuranosyl-4(3H)pteridinone (30). (a). Analogous to the preceding procedure with **19** (0.15 g, 0.2 mmol). After stirring for 2 h, H₂O (3 ml) was added and the pH adjusted to 5 by AcOH. The precipitate was collected after cooling and recrystallized from i-PrOH/H₂O (1:1, 15 ml) to give 53 mg (60%) of **30**. M.p. 180°C (decomp.). (b). A solution of 2-methylthio-6,7-diphenyl-1-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-4(3H)pteridinone (**37**) (0.158 g, 0.2 mmol) in abs. dioxane (5 ml) was treated with conc. NH₃ (5 ml) for 3 days stirring in a closed flask. After evaporation the residue was dissolved in little H₂O and acidified by AcOH. On cooling the precipitate was collected and recrystallized from EtOH/H₂O (1:1) to give 60 mg (70%) of **30**. M.p. 180°C. ¹H-NMR ((D₆)DMSO): 7.90 (bs, 2 H, NH₂); 7.50-7.30 (m, 10 H, arom. H); 6.99 (d, 1 H, H-C(1')); 5.98 (t, 1 H, 5'-OH); 5.42 (d, 1 H, 2'-OH); 5.25 (d, 1 H, 3'-OH); 4.58 (dd, 1 H; H-C(2')); 4.12 (m, 1 H, H-C(3')); 4.00 (m, 1 NH, H-C(4')); 3.67 (m, 2 H, H-C(5')). Anal. Calc. for C₂₃H₂₁N₅O₅ x 0.5 H₂O (456.4): C, 60.52; H, 4.95; N, 15.34. Found: C, 60.75; H, 4.73; N, 15.46.

2-Methylthio-1-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-4(3H)pteridinone (35) and

2-Methylthio-3-(2,3,5-tri-*O*-benzoyl- β -D-ribofuranosyl)-4(3H)pteridinone (38). A mixture of 2-methylthio-4(3H)pteridinone (**31**)⁴⁰ (1.36 g, 7 mmol) and (NH₄)₂SO₄ (0.1 g) in hexamethyldisilazane (HMDS) (30 ml) was refluxed for 2 h. (30 ml). The excess of HMDS was distilled off, the residue dissolved in dry CH₂Cl₂ (20 ml), then **11** (3.52 g, 7 mmol) and BF₃-etherate (7 ml) added. The reaction solution was stirred at rt for 1 day, then treated with a mixture of CHCl₃/H₂O/NEt₃ (5:5:1, 40 ml), the organic phase separated, dried over Na₂SO₄ and evaporated to give 3.3 g crude product. The mixture was separated by short column

chromatography (SCC)⁴¹ with CHCl₃/n-hexane (3:2) to give as the first fraction **38** and followed by **35**. The fractions were evaporated and the residues recrystallized from EtOH/H₂O.

38. Yield: 1.95 g (44%). M.p. 105-108°C. ¹H-NMR (CDCl₃): 8.89 (d, 1 H, H-C(7)); 8.76 (d, 1 H, H-C(6)); 8.10-7.20 (m, 15 H, arom. H); 6.40 (d, 1 H, H-C(1')); 6.32-6.20 (m, 2 H, H-C(2', 3')); 4.90-4.60 (m, 3 H, H-C(4', 5')); 2.74 (s, 3 H, S-CH₃). Anal. Calc. for C₃₃H₂₆N₄O₈S (638.6): C, 62.06; H, 4.10; N, 8.77. Found: C, 61.75; H, 4.15; N, 8.62.

35. Yield: 0.95 g (24%). M.p. 135°C. ¹H-NMR (CDCl₃): 8.75 (d, 1 H, H-C(7)); 8.48 (d, 1 H, H-C(6)); 8.00-7.20 (m, 15 H, arom. H); 6.64 (d, 1 H, H-C(1')); 6.39 (m, 1 H, H-C(2')); 6.26 (m, 1 H, H-C(3')); 5.00-4.60 (m, 3 H, H-C(4', 5')); 2.68 (s, 3 H, S-CH₃). Anal. Calc. for C₃₃H₂₆N₄O₈S x 0.5 H₂O (647.6): C, 61.20; H, 4.20; N, 8.65. Found: C, 61.49; H, 3.91; N, 8.68.

6,7-Dimethyl-2-methylthio-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4(3H)pteridinone (36) and 6,7-Dimethyl-2-methylthio-3-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4(3H)pteridinone (39). Analogous to the preceding procedure with 6,7-dimethyl-2-methylthio-4(3H)pteridinone (**32**)⁴⁰ (1.11 g, 6 mmol), **11** (3.02 g, 6 mmol) and BF₃-etherate (6 ml) for 3 days. After work-up the crude material (3.85 g) was separated and purified by SSC with CHCl₃/n-hexane (4:1). The first main fraction gave **39** followed by **36**. Recrystallization from EtOH/H₂O.

39. Yield: 1.82 g (42%). M.p. 113°C. ¹H-NMR (CDCl₃): 8.10-7.20 (m, 15 H, arom. H); 6.33 (d, 1 H, H-C(1')); 6.50-6.40 (m, 2 H, H-C(2', 3')); 4.90-4.70 (m, 3 H, H-C(4', 5')); 2.69 (s, 3 H, S-CH₃); 2.75 (s, 3 H, CH₃(7)); 2.73 (s, 3 H, CH₃(6)). Anal. Calc. for C₃₅H₃₀N₄O₈S (666.7): C, 63.05; H, 4.54; N, 8.40. Found: C, 63.26; H, 4.49; N, 8.35.

36. Yield: 1.08 g (32%). M.p. 110°C. ¹H-NMR (CDCl₃): 8.00-7.20 (m, 15 H, arom. H); 6.59 (d, 1 H, H-C(1')); 6.50-6.40 (m, 2 H, H-C(2', 3')); 4.90-4.70 (m, 3 H, H-C(4', 5')); 2.69 (s, 3 H, S-CH₃); 2.68 (2 s, 6 H, 2 CH₃). Anal. Calc. for C₃₅H₃₀N₄O₈S (666.7): C, 63.05; H, 4.54; N, 8.40. Found: C, 63.01; H, 4.66; N, 8.37.

2-Methylthio-6,7-diphenyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4(3H)pteridinone (37) and 2-Methylthio-6,7-diphenyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4(3H)pteridinone (40). Analogous to the preceding procedure first silylation with 2-methylthio-6,7-diphenyl-4(3H)pteridinone (**33**)⁴⁰ (1.386 g, 4 mmol) and HMDS under reflux for 1 day. After evaporation and solution in CH₂Cl₂ (10 ml) **11** (2.01 g, 4 mmol) and BF₃-etherate (5 ml) were added and stirred for day. After work-up the crude material (3.36 g) was separated and purified by SSC with CHCl₃/n-hexane (3:2). The first main fraction gave **39** followed by **37**. Recrystallization from EtOH/H₂O.

40. Yield: 1.636 g (52%). M.p. 213°C. ¹H-NMR (CDCl₃): 8.20-7.20 (m, 25 H, arom. H); 6.50-6.30 (m, 3 H, H-C(1', 2', 3')); 5.00-4.70 (m, 3 H, H-C(4', 5')); 2.77 (s, 3 H, S-CH₃). Anal. Calc. for C₄₅H₃₄N₄O₈S (790.8): C, 68.35; H, 4.33; N, 7.08. Found: C, 68.05; H, 4.36; N, 7.02.

37. Yield: 0.81 g (26%). M.p. 169-171°C. ¹H-NMR (CDCl₃): 8.10-7.20 (m, 15 H, arom. H); 6.77 (d, 1 H, H-C(1')); 6.60 (dd, 1 H, H-C(2')); 5.97 (m, 1 H, H-C(3')); 4.72 (m, 1 H, H-C(4')); 4.35 (m, 2 H, H-C(5')); 2.69 (s, 3 H, S-CH₃). Anal. Calc. for C₄₅H₃₄N₄O₈S (790.8): C, 68.35; H, 4.33; N, 7.08. Found: C, 68.17; H, 4.41; N, 7.04.

2-Methylamino-1-β-D-ribofuranosyl-4(3H)pteridinone (41). A solution of **35** (0.128 g, 0.2 mmol) in abs. tetrahydrofuran (THF) (5 ml) was treated with methanolic CH₃NH₂-solution (20%, 3 ml) in a closed flask for 2 days. It was evaporated, the residue dissolved in abs. MeOH (5 ml), 1 N-CH₃ONa (0.2 ml) added and 1 day stirred at rt. The solution was acidified by AcOH to pH 5, evaporated and the residue purified by chromatography on a preparative thick layer plate (40 x 20 x 0.2 cm) with CHCl₃/MeOH (4:1) to give after recrystallization from EtOH/H₂O 46 mg (74%) of **41**. M.p. 170°C (decomp.). ¹H-NMR ((D₆)DMSO): 8.67 (d, 1 H, H-C(7)); 8.63 (d, 1 H, H-C(6)); 7.99 (bs, H, NH); 6.92 (d, 1 H, H-C(1')); 5.95 (bs, 1 H, 5'-OH); 5.41 (d, 1 H, 2'-OH); 5.21 (d, 1 H, 3'-OH); 4.49 (dd, 1 H; H-C(2')); 4.11 (m, 1 H, H-C(3')); 4.07 (m, 1 H, H-C(4')); 3.71 (m, 2 H, H-C(5')); 2.85 (s, 3 H, H₃C-NH). Anal. Calc. for C₁₂H₁₅N₅O₅ x H₂O (327.3): C, 44.03; H, 5.23; N, 21.40. Found: C, 44.09; H, 5.25; N, 21.29.

2-Methylamino-6,7-dimethyl-1-β-D-ribofuranosyl-4(3H)pteridinone (42). Analogous to the preceding procedure with **36** (0.133 g, 0.2 mmol) to give after recrystallization from EtOH/H₂O (7:3) 59 mg (88%) of **42**. M.p. 205°C. ¹H-NMR ((D₆)DMSO): 7.85 (bs, H, NH); 6.87 (d, 1 H, H-C(1')); 5.95 (bs, 1 H, 5'-OH); 5.45 (d, 1 H, 2'-OH); 5.30 (bs, 1 H, 3'-OH); 4.49 (dd, 1 H; H-C(2')); 4.10 (m, 1 H, H-C(3')); 4.02 (m, 1 H, H-C(4')); 3.70 (m, 2 H, H-C(5')); 2.84 (s, 3 H, H₃C-NH); 2.55, 2.53 (2 s, 6 H, 2 CH₃). Anal. Calc. for C₁₄H₁₉N₅O₅ x 0.5 H₂O (346.3): C, 48.66; H, 5.82; N, 20.22. Found: C, 48.95; H, 5.88; N, 20.30.

2-Ethylamino-6,7-dimethyl-1-β-D-ribofuranosyl-4(3H)pteridinone (43). A solution of **36** (0.133 g, 0.2 mmol) in abs. THF (5 ml) was cooled to -15°C, then saturated with C₂H₅NH₂-gas and kept in the icebox for 2 days. It was evaporated, the residue dissolved in abs. MeOH (10 ml), 1 N CH₃ONa (0.2 ml) added and stirred for 1 day. The solution was acidified by AcOH to pH 5, again evaporated and the residue purified by chromatography on a preparative thick layer silica gel plate (40 x 20 x 0.2 cm) with CHCl₃/MeOH (4:1). The main band was cut out, eluted, evaporated and the residue recrystallized from little from H₂O to give 64 mg (91%) of **43**. M.p. 167-168°C. ¹H-NMR ((D₆)DMSO): 7.85 (bs, H, NH); 6.82 (d, 1 H, H-C(1')); 5.82 (t, 3 H, 5'-OH); 5.40 (d, 1 H, 2'-OH); 5.20 (d, 1 H, 3'-OH); 4.48 (dd, 1 H; H-C(2')); 4.11 (m, 1 H, H-C(3')); 4.04 (m, 1 H, H-C(4')); 3.69 (m, 2 H, H-C(5')); 3.40 (q, 2-H, HNCH₂CH₃); 2.55 (2 s, 6 H, 2 CH₃); 1.18 (t, 3 H, CH₃CH₂NH). Anal. Calc. for C₁₅H₂₁N₅O₅ (351.4): C, 51.27; H, 6.08; N, 19.93. Found: C, 50.94; H, 5.88; N, 19.52.

2-Ethanolamino-6,7-dimethyl-1-β-D-ribofuranosyl-4(3H)pteridinone (44). Analogous to the preceding procedure with **36** (0.133 g, 0.2 mmol) and methanolic ethanolamine (10%, 3 ml) and keeping in the icebox for 1 day. It was evaporated, the residue dissolved in abs. MeOH (10 ml), 1 N CH₃ONa (0.2 ml) added and stirred at rt for 1 day. Again evaporation and purification on a preparative thick layer silica gel plate (40 x 20 x 0.2 cm) with CHCl₃, MeOH (4:1) to give 25 mg (34%) of **44**. M.p. 161°C. ¹H-NMR ((D₆)DMSO): 7.79 (bs, H, NH); 6.84 (d, 1 H, H-C(1')); 5.79 (t, 1 H, 5'-OH); 5.45 (d, 1 H, 2'-OH); 5.21 (d, 1 H, 3'-OH); 4.83 (t, 1 H, CH₂CH₂OH); 4.50 (dd, 1 H; H-C(2')); 4.12 (m, 1 H, H-C(3')); 3.98 (m, 1 H, H-C(4')); 3.71 (m, 2 H, H-C(5')); 3.55 (bs, 2 H, CH₂CH₂OH); 3.40 (m, 2 H, HOCH₂CH₂NH); 2.55, 2.53 (2 s, 6 H, 2 CH₃). Anal. Calc. for C₁₅H₂₁N₅O₆ x H₂O (385.4): C, 46.74; H, 6.02; N, 18.17. Found: C, 46.95; H, 5.63; N, 17.82.

2-Methylamino-6,7-diphenyl-1- β -D-ribofuranosyl-4(3H)pteridinone (45). A solution of **37** (0.158 mg, 0.2 mmol) in abs. THF was cooled to -15°C , then methanolic CH_3NH_2 (5%, 2 ml) added and kept in the icebox for 1 day. It was evaporated, the residue dissolved in abs. MeOH (10 ml), 1 N CH_3ONa (0.2 ml) added and stirred at rt for 1 day. The solution was acidified by AcOH to pH 5, evaporated and purified on a preparative thick layer silica gel plate (40 x 20 x 0.2 cm) with $\text{CHCl}_3/\text{MeOH}$ (4:1) to give after recrystallization from EtOH/ H_2O (2:3) 62 mg (70%) of **45**. M.p. 189°C (decomp.). $^1\text{H-NMR}$ ((D_6) DMSO): 8.02 (bs, 1 H, NH); 7.40-7.20 (m, 10 H, arom. H); 6.98 (d, 1 H, H-C(1')); 5.02 (bs, 1 H, 5'-OH); 5.40 (d, 1 H, 2'-OH); 5.21 (d, 1 H, 3'-OH); 4.52 (dd, 1 H; H-C(2')); 4.15 (m, 1 H, H-C(3')); 4.05 (m, 1 NH, H-C(4')); 3.72 (m, 2 H, H-C(5')); 2.91 (s, 3 H, $\text{H}_3\text{C-NH}$). Anal. Calc. for $\text{C}_{24}\text{H}_{23}\text{N}_5\text{O}_5 \times 0.5 \text{ H}_2\text{O}$ (470.4): C, 61.16; H, 5.14; N, 14.88. Found: C, 60.84; H, 5.02; N, 14.82.

2-Ethylamino-6,7-diphenyl-1- β -D-ribofuranosyl-4(3H)pteridinone (46). Analogous to the preceding procedure with **37** (0.158 g, 0.2 mmol) and $\text{C}_2\text{H}_5\text{NH}_2$ -gas for 3 days in the icebox. Treatment with CH_3ONa and purification on a silica gel plate to give after recrystallization from EtOH/ H_2O (2:3) 65 mg (78%) of **46**. Mp. 177°C . $^1\text{H-NMR}$ ((D_6) DMSO): 8.07 (bs, 1 H, NH); 7.50-7.30 (m, 10 H, arom. H); 6.95 (d, 1 H, H-C(1')); 5.89 (t, 1 H, 5'-OH); 5.46 (d, 1 H, 2'-OH); 5.24 (d, 1 H, 3'-OH); 4.52 (dd, 1 H; H-C(2')); 4.14 (m, 1 H, H-C(3')); 4.03 (m, 1 NH, H-C(4')); 3.71 (m, 2 H, H-C(5')); 3.45 (q, 2 H, NCH_2CH_3); 1.29 (t, 3 H, NCH_2CH_3). Anal. Calc. for $\text{C}_{25}\text{H}_{25}\text{N}_5\text{O}_5 \times \text{H}_2\text{O}$ (493.5): C, 60.84; H, 5.51; N, 14.09. Found: C, 60.58; H, 5.32; N, 13.61.

2-Ethanolamino-6,7-diphenyl-1- β -D-ribofuranosyl-4(3H)pteridinone (47). Analogous to the preceding procedure with **37** (0.158 g, 0.2 mmol) and methanolic ethanolamine (10%, 3 ml) for 2 days in the icebox. Treatment with CH_3ONa and purification on a silica gel plate gave after recrystallization from EtOH/ H_2O (2:3) 65 mg (66%) of **47**. M.p. 177° . $^1\text{H-NMR}$ ((D_6) DMSO): 7.98 (bs, 1 H, NH); 7.50-7.30 (m, 10 H, arom. H); 6.96 (d, 1 H, H-C(1')); 5.78 (t, 1 OH, 5'-OH); 5.38 (d, 1 H, 2'-OH); 5.21 (d, 1 H, 3'-OH); 4.87 (t, 1 H, $\text{CH}_2\text{CH}_2\text{OH}$); 4.56 (dd, 1 H; H-C(2')); 4.14 (m, 1 H, H-C(3')); 4.01 (m, 1 NH, H-C(4')); 3.71 (m, 2 H, H-C(5')); 3.55 (bs, 2 H, $\text{CH}_2\text{CH}_2\text{OH}$); 3.41 (m, 2 H, $\text{HOCH}_2\text{CH}_2\text{N}$). Anal. Calc. for $\text{C}_{25}\text{H}_{25}\text{N}_5\text{O}_6$ (491.5): C, 61.09; H, 5.13; N, 14.26. Found: C, 60.60; H, 5.36; N, 14.16.

2-Isopropylamino-6,7-diphenyl-1- β -D-ribofuranosyl-4(3H)pteridinone (48). Analogous to the preceding procedure with **37** (0.158 g, 0.2 mmol) and methanolic isopropylamine (10%, 3 ml) for 2 days in the icebox. Treatment with CH_3ONa and purification on a silica gel plate gave after recrystallization from EtOH/ H_2O (2:3) 31 mg (32%) of **48**. M.p. 190° . $^1\text{H-NMR}$ ((D_6) DMSO): 7.85 (bs, 1 H, NH); 7.50-7.30 (m, 10 H, arom. H); 6.93 (d, 1 H, H-C(1')); 5.75 (t, 1 H, 5'-OH); 5.45 (d, 1 H, 2'-OH); 5.23 (d, 1 H, 3'-OH); 4.46 (m, 2 H; H-C(2'), Me_2CH); 4.15 (m, 1 H, H-C(3')); 3.98 (m, 1 NH, H-C(4')); 3.71 (bs, 2 H, H-C(5')); 1.25 (d, 6 H, $(\text{H}_3\text{C})_2\text{CH}$). Anal. Calc. for $\text{C}_{26}\text{H}_{27}\text{N}_5\text{O}_5 \times \text{H}_2\text{O}$ (507.5): C, 61.43; H, 5.41; N, 13.45. Found: C, 61.04; H, 5.75; N, 13.79.

2-n-Butylamino-6,7-diphenyl-1- β -D-ribofuranosyl-4(3H)pteridinone (49). Analogous to the preceding procedure with **37** (0.158 g, 0.2 mmol) and methanolic n-butylamine (10%, 3 ml) for 2 days in the icebox. Treatment with CH_3ONa and purification on a silica gel plate gave after

recrystallization from EtOH/H₂O (3:7) 68 mg (68%) of **49**. M.p. 193°. ¹H-NMR ((D₆)DMSO): 8.03 (bs, 1 H, NH); 7.50-7.30 (m, 10 H, arom. H); 6.98 (d, 1 H, H-C(1')); 5.88 (t, 1 H, 5'-OH); 5.46 (d, 1 H, 2'-OH); 5.25 (d, 1 H, 3'-OH); 4.52 (dd, 1 H; H-C(2')); 4.14 (m, 1 H, H-C(3')); 4.03 (m, 1 NH, H-C(4')); 3.70 (m, 2 H, H-C(5')); 3.42 (m, 2 H, CH₃CH₂CH₂CH₂NH); 1.60 (m, 2H, CH₃CH₂CH₂CH₂NH); 1.35 (m, 2H, CH₃CH₂CH₂CH₂NH); 0.95 (t, 3 H, CH₃CH₂CH₂CH₂NH). Anal. Calc. for C₂₇H₂₉N₅O₅ (503.5): C, 64.40; H, 5.80; N, 13.90. Found: C, 64.21; H, 5.82; N, 13.65.

2-Isobutylamino-6,7-diphenyl-1-β-D-ribofuranosyl-4(3H)pteridinone (50). Analogous to the preceding procedure with **37** (0.158 g, 0.2 mmol) and methanolic isobutylamine (10%, 3 ml) for 3 days in the icebox. Treatment with CH₃ONa and purification on a silica gel plate gave after recrystallization from EtOH/H₂O (3:7) 63 mg (63%) of **50**. M.p. 140-143°. ¹H-NMR ((D₆)DMSO): 8.08 (bs, 1 H, NH); 7.50-7.30 (m, 10 H, arom. H); 7.03 (d, 1 H, H-C(1')); 5.85 (t, 1 H, 5'-OH); 5.51 (d, 1 H, 2'-OH); 5.23 (d, 1 H, 3'-OH); 4.56 (dd, 1 H; H-C(2')); 4.14 (m, 1 H, H-C(3')); 4.05 (m, 1 NH, H-C(4')); 3.73 (m, 2 H, H-C(5')); 3.25 (m, 2 H, HNCH₂); 2.05 (m, 1 H, Me₂CH); 0.92 (HC(CH₃)₂). Anal. Calc. for C₂₇H₂₉N₅O₅ x C₂H₅OH (549.5): C, 63.39; H, 6.20; N, 12.74. Found: C, 63.57; H, 5.70; N, 12.44.

2-Dimethylamino-6,7-diphenyl-1-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)-4(3H)-pteridinone (51). A solution of **37** (0.158 g, 0.2 mmol) in abs. THF (5 ml) was cooled to -15°C and then methanolic dimethylamine (115%, 2 ml) added. After storage in the icebox for 2 days was evaporated and the residue purified on a preparative silica gel plate with CHCl₃/MeOH (19:1). The main band was eluted, evaporated and the residue recrystallized from EtOH/H₂O (1:1) to give 0.135 g (86%) of **51**. M.p. 130°C. ¹H-NMR (CDCl₃): 7.93-7.22 (m, 25 H, arom. H); 6.70 (d, 1 H, H-C(1')); 6.11 (dd, 1 H, H-C(2')); 5.83 (m, 1 H, H-C(3')); 4.64 (m, 1 H, H-C(4')); 4.25 (m, 2 H, H-C(5')); 4.10 (s, 6 H, N(CH₃)₂). Anal. Calc. for C₄₆H₃₇N₅O₈ x 0.5 H₂O (796.8): C, 69.34; H, 4.81; N, 8.79. Found: C, 69.08; H, 5.03; N, 8.80.

1-Methyl-2-methylamino-6,7-diphenyl-4(3H)pteridinone (64). To a solution of ethanolic methylamine (50%, 30 ml) was added 1-methyl-2-methylamino-6,7-diphenyl-4(3H)pteridinone (**61**)⁴⁰ (0.12 g, 0.33 mmol) and the mixture stirred for 1 h and then evaporated. The residue was purified by preparative thick layer chromatography on a silica gel plate (40 x 20 x 0.2 cm) with CHCl₃/MeOH (9:1), The main band was eluted, evaporated and the solid recrystallized from EtOH/H₂O to give 98 mg (86%) of **65**. M.p. 299°C. Anal. Calc. for C₂₀H₁₇N₅O x C₂H₅OH (389.4): C, 67.85; H, 5.85; N, 17.98. Found: C, 67.67; H, 5.56; N, 18.28.

1-Methyl-2-dimethylamino-6,7-diphenyl-4(3H)pteridinone (65). Analogous to the preceding procedure with **61** (0.12 g, 0.33 mmol) in methanolic dimethylamine solution (20 ml) and stirring for 1 day. Work-up and recrystallization from EtOH/H₂O gave 57 mg (71%) of **66**. M.p. 229°C. Anal. Calc. for C₂₁H₁₉N₅O (357.4): C, 70.57; H, 5.36; N, 19.59. Found: C, 70.43; H, 5.29; N, 19.34.

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