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

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Dedicated to Professor Harri Lönnberg 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/$HgBr_2$, BF_3-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. ^{1}H-NMR-spectra functioned as additional structural proof.

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

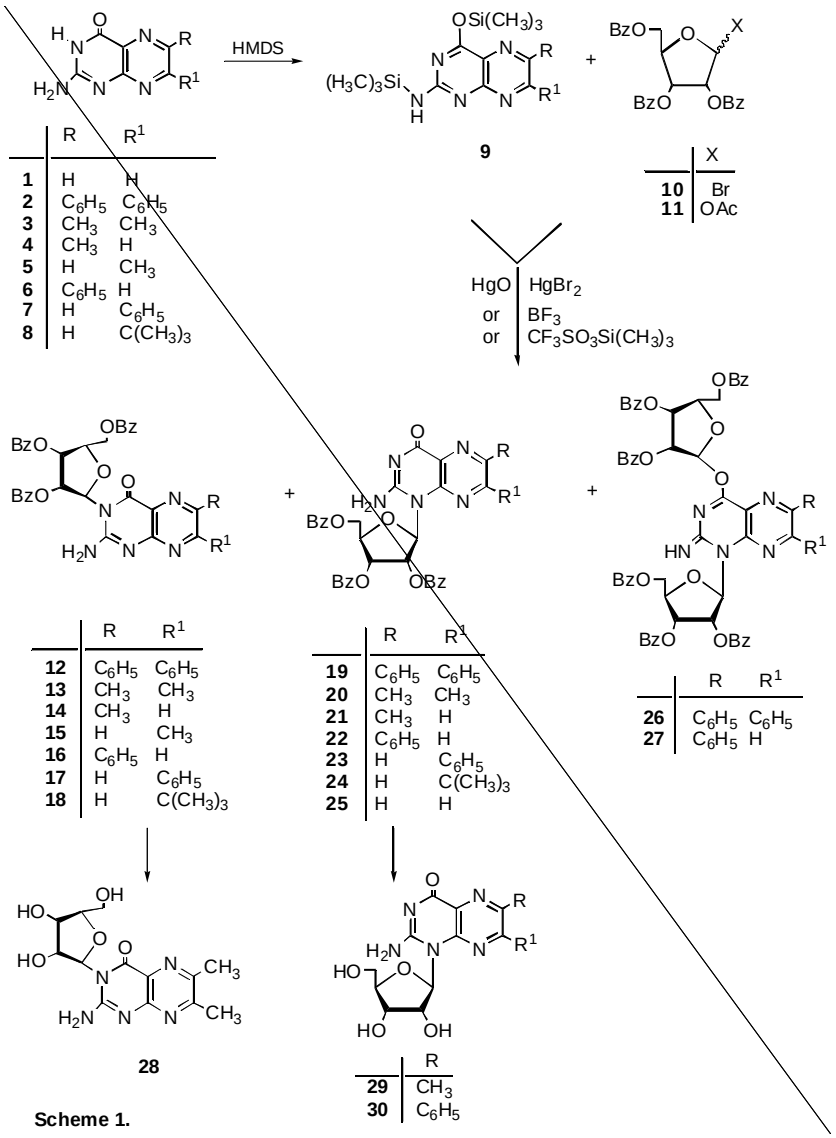
Introduction

The synthesis of pteridine nucleosides has been a major subject in our laboratory for many years. Lumazine[2-11] and isopterin nucleosides[12] can be regarded as structural analogs of the pyrimidine nucleosides whereas the many pteridin-7-one N_8-nucleosides[13-23] are structurally related to the purine nucleosides. The syntheses could be achieved either by a classical Hilbert-Johnson reaction[24], the mercury salt method by Fox and Davoll[25], the Hilbert-Johnson-Birkofer silyl procedure[26, 27] or the silyl variant by Vorbrüggen[28].

Pterin (2-amino-4(3H)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 $HgBr_2$ in analogy to the conditions of Wittenburg[29]. 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-ß-D-ribofuranosyl)-4(3H)-pteridone (**12**), the corresponding N^1-riboside (**19**) and the 2-imino-6,7-diphenyl-N^1,O^4-bis-(2,3,5-tri-*O*-benzoyl-ß-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-ß-D-ribofuranose (**11**) and BF_3- etherate as a catalyst gave predominately 2-amino-6,7-diphenyl-1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-4(3H)pteridone (**19**) in 50% yield whereas the isomeric **12** was obtained in only 1% yield.

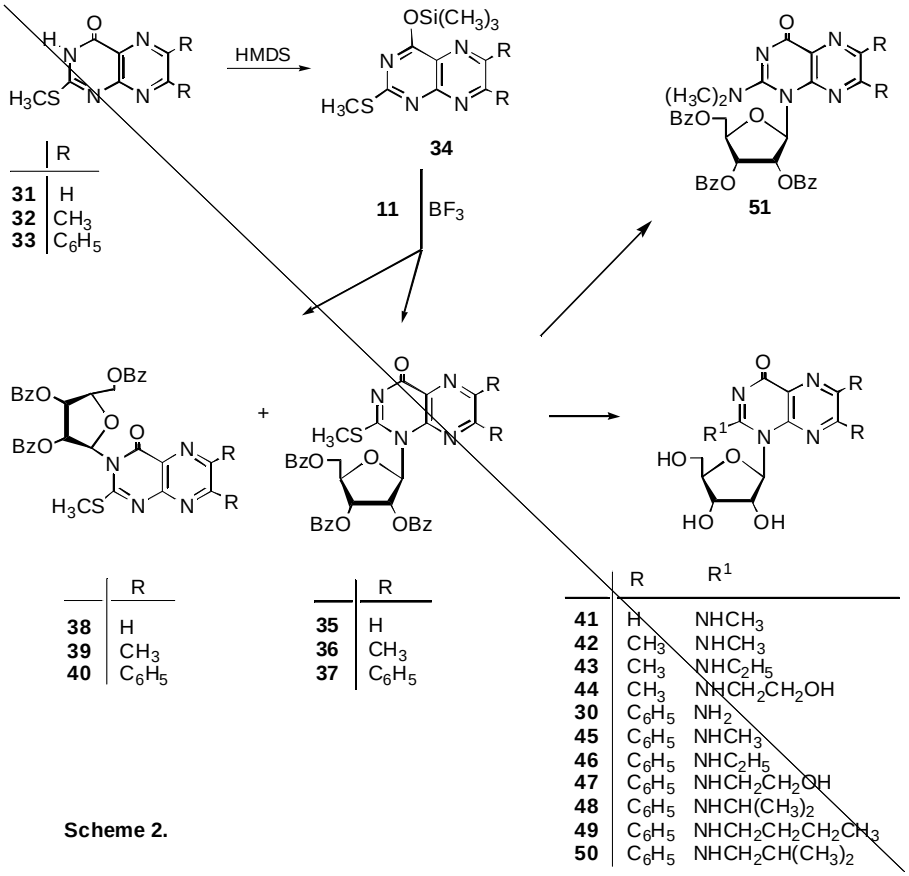


Scheme 1.

Analogously, BF_3-catalysis of 7-phenylpterin (**7**) and **11** gave small amounts of the N_1- (**23**) and N_3-nucleoside (**17**). Similarly 6-phenylpterin (**6**) and **11** in presence of trimethyl-silyl trifluorosulfonate gave three components N_1-(**22**), N_3-monoriboside (**16**) and the N_1,O^4-diriboside (**27**) that were separated from the complex reaction mixture. Ribosylations of 6,7-dimethylpterin (**3**) led with the halosugar **10** and $HgO/HgBr_2$ to 3-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6,7-dimethylpterin (**13**) in 14% yield whereas the use of **11** and BF_3-catalysis formed the N_1-riboside (**20)** in 14% as the main reaction product besides 8% of the N_3-isomer (**13)**. The ribosylation reaction have also been extended to 6-methylpterin (4) yielding with **11** and BF_3 small amounts of the N_1-(**21**) and N_3-riboside (**14**), with 7-methyl-pterin (**5**) the N_3-riboside ((**15**) in 6% yield and with 7-tert.butylpterin (**8**) again a mixture of N_1- (**24**) and N_3-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-ß-D-ribofuranosyl)pterin (**25**). Debenzoylations of the sugar protecting groups can be achieved by the Zemplen[30] 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 nucleophilicly. The ribosylations of **31**, **32** and **33** via their O^4-trimethylsilyl derivatives (**34**) with **11** and BF_3 catalysis led in moderate to good yields in each case to a mixture of the corresponding N_1-(**35-37)**, and N_3-ribosides (**38-40**).

Treatment of the 2-methylthio-1-(2,3,5-tri-*O*-benzoyl-ß-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-N_1-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-ß-D-ribofuranosyl)-4(3H)-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).

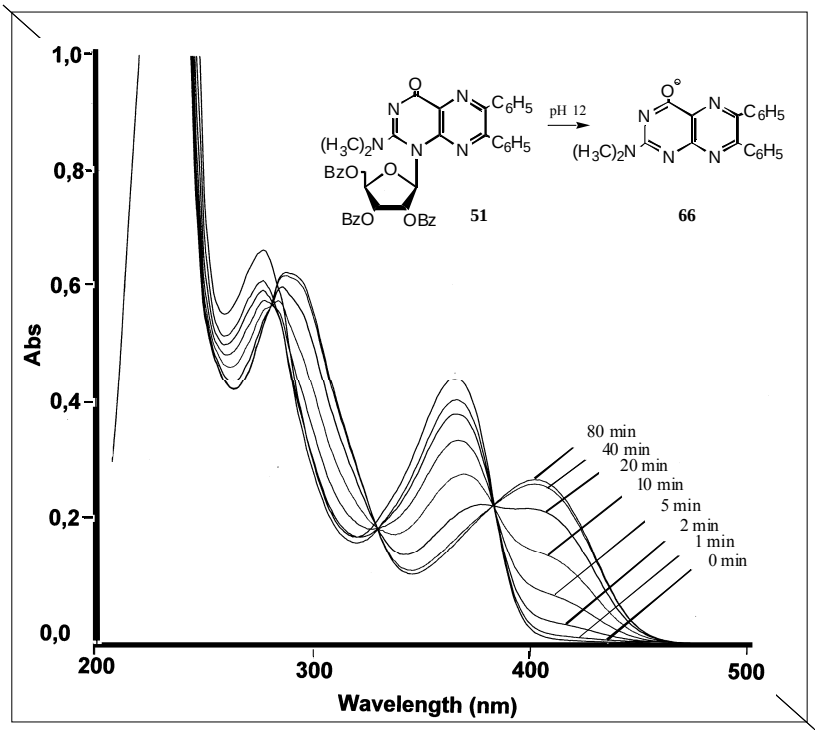


Figure 1. Cleavage of **51** at pH 12 to form **66**.

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 values[31] in order to compare the spectra of the cations and the neutral species as an additional structural proof (Tab. 1).

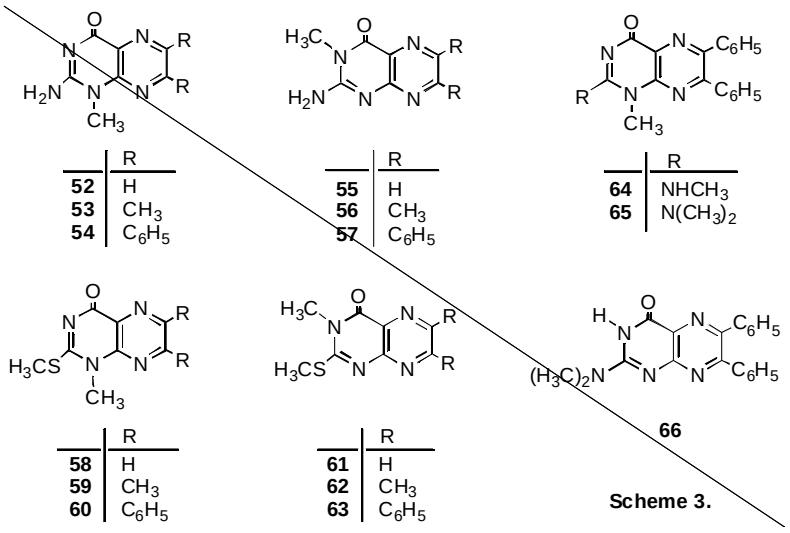


Figure 2. UV spectral comparison of **30** and **54** as well as **12** and **57**.

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-§.D-Ribofuranosyl-	2.68	218 (250) 316 (330)	4.28 (3.95) 4.00 (3.91)	0
6,7-dimethyl- (**29**)	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-§-D-Ribofuranosyl-	2.14	218 255 322 390	4.11 4.00 3.83 2.98	0
6,7-dimethyl- (**28**)		247 273 352	4.35 4.74 3.76	7
1-Methyl-6,7-diphenyl-	2.95	222 280 362	4.42 4.13 4.15	0
(**54**)[43]	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-§-D-Ribofuranosyl-	2.60	228 280 350	4.41 4.13 4.14	0
6,7-diphenyl- (**30**)	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-	2.34	229 278 362	4.46 4.13 4.18	0
(**57**)[44]	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-§-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-methyl-thio-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-methyl-thio-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 N^2-substituted pterin nucleosides

1-ß-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-§-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-§-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 ^{1}H-NMR spectra (experimental part) of the benzoyl protected ribonucleosides have not been very informative since overlapping signals make accurate assignments difficult. The free ß-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 chromatograhy (CC): silica gel 60, 70 - 230 mesh from *Merck*. Low pressure chromatography[32] (LPC): LiChroprep Si 60 from *Merck* according to [33] 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). ^{1}H-NMR: Bruker AC 250; in $CDCl_3$ or ((D_6)DMSO), δ in ppm rel. to $SiMe_4$ as internal standard. M.p.: *Büchi* apparatus, model Dr. Tottuli; no corrections. The pK_a measurements were performed by the spectrophotometric method[31]. Products were dried under high vacuum.

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

A mixture of 6,7-diphenylpterin (**2**)[34] (0.945 g, 3 mmol) and $(NH_4)_2SO_4$ (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 $HgBr_2$ were added. The mixture was refluxed for 4 h, evaporated and the residue treated with $CHCl_3$ (100 ml). The mercury salts were filtered off and the filtrate shaken with a KJ solution (15%). The organic phase was tried over Na_2SO_4, evaporated to a smaller volume, put onto a silica gel column (7 x 35 cm) and first developed with $CHCl_3$ (4 l). Evaporation of this fraction 1 gave a mixture of 3 nucleosides (1.26 g). The solvents system was changed to $CHCl_3$/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 ($CHCl_3$/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 C[30] (3 x 50 cm, silica gel Lichroprep Si 60) and a pressure of 10 atm. The eluents n-hexane/$CHCl_3$ (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 $CHCl_3$/MeOH (19:1). The main band was eluted with $CHCl_3$/MeOH (9:1) to give **12** (0.12 g, 15%). Fraction 3 gave on chromatography on thick-layer plates with $CHCl_3$/MeOH (9:1) **19** (0.165 g, 7%).

12. Yield: 0.795 g (35%). M.p. 154-158°C. ^{1}H-NMR ($CDCl_3$): 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, NH_2); 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 $C_{44}H_{33}N_5O_8$ (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. ^{1}H-NMR ($CDCl_3$): 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 $C_{70}H_{53}N_5O_{15}$ x 2 H_2O (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-ß-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 CH_2Cl_2 (30 ml), 1-*O*-acetyl-2,3,5-tri-*O*-benzoyl-ß-D-ribofuranose (**11**)[35] (2.01 g, 4.1 mmol) and BF_3-etherate (4 ml) were added and stirred at rt for 4 h. Dilution with CH_2Cl_2 (50 ml), treatment with saturated $NaHCO_3$ solution, drying of the organic layer with Na_2SO_4 and evaporation to give a crude mixture (3.2 g). Separation by CC (7 x 30 cm) first with $CHCl_3$ (1.5 l), then with $CHCl_3$/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 $CHCl_3$/MeOH (19:1). The main band was cut out, eluted with $CHCl_3$/MeOH (12:1), evaporated to give 1.535 g of **19**. Recrystallization from isopropanol/H_2O (1:1, 40 ml) gave 1.47 g (50%) of pure **19** of m.p. 152°C. ^{1}H-NMR ($CDCl_3$): 8.00-7.20 (m, 28 H, NH_2, 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 $C_{44}H_{33}N_5O_8$ x H_2O (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-ß-D-ribofuranosyl)-6,7-dimethyl-4(3H)pteridinone (13) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6,7-dimethyl-4(3H)pteridinone (20). A mixture of 6,7-dimethylpterin (**3**) (0.955 g, 5 mmo) and $(NH_4)_2SO_4$ (0.1 g) in hexa-methyldisilazane (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 CH_2Cl_2 (15 ml), **11** (2.52 g, 5.1 mmol) in CH_2Cl_2 (15 ml) and BF_3-etherate (5 ml) added. After stirring at rt for 4 h the reaction solution was treated with saturated aqueous $NaHCO_3$ solution, the organic layer separated, dried over Na_2SO_4 and evaporated to dryness. The residue was dissolved in $CHCl_3$, put onto a silica gel column (7 x 30 cm) and developed first with $CHCl_3$ (1,5 l) to give unreacted sugar and followed by $CHCl_3$/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 $CHCl_3$/MeOH (9:1). The lower band (R_f 0.28) was eluted with $CHCl_3$/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 $CHCl_3$/MeOH (19:1) to get partial separation. The band (R_f 0.51) gave after elution with $CHCl_3$/MeOH (9:1), evaporation and recrystallization from i-PrOH/H_2O (1:1)

13 (0.25 g, 8%).

20. Yield: 0.425 g, (14%).M.p. 152-154°C. ^{1}H-NMR ($CDCl_3$): 7.99-7.26 (m, 17 H, 15 arom. H, NH_2); 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 CH_3). Anal. Calc. for $C_{34}H_{29}N_5O_8$ x 0.5 H_2O (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-ß-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. C_6H_6 (35 ml), then **10** (2.27 g, 4.5 mmol), HgO (1.25 g) and $HgBr_2$ (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 $CHCl_3$ (50 ml) and then shaken several times with 15% aqueous KJ solution to remove the mercury salts. The organic layer was separated, dried over Na_2SO_4 and again evaporated. The residue was dissolved in $CHCl_3$, put onto a silica gel column (4.5 x 45 cm) and developed with $CHCl_3$/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 $CHCl_3$, MeOH (19:1). The main band was cut out, eluted by $CHCl_3$/MeOH (15:1) to give after evaporation **13** (0.425 g, 14%) of m.p. 168°C (decomp.). ^{1}H-NMR ($CDCl_3$): 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, NH_2); 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, CH_3); 2.57 (s, 3 H, CH_3), Anal. Calc. for $C_{34}H_{29}N_5O_8$ x 0.5 H_2O (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-ß-D-ribofuranosyl)-6-methyl-4(3H)pteridinone (14) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6-methyl-4(3H)pteridinone (21). A mixture of 6-methylpterin (**4**)[36] (0.709 g, 4 mmol) and $(NH_4)_2SO_4$ (0.1 g) in HMDS (30 ml) was refluxed for 24 h, then evaporate, the residue dissolved in CH_2Cl_2 (40 ml), **11** (2.01 g, 4 mmol) and BF_3-etherate (4 ml) added and then stirred at rt for 4 h. The reaction solution was treated with saturated aqueous $NaHCO_3$ solution, the organic phase separated and dried over Na_2SO_4 and evaporated. The residue was dissolved in $CHCl_3$, put onto a silica gel column (8 x 30 cm) and developed first with $CHCl_3$ (2 l) to give unreacted sugar. Extended elution with $CHCl_3$/MeOH (19:1, 2.5 l) and $CHCl_3$/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 $CHCl_3$/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: ^{1}H-NMR ($CDCl_3$): 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, NH_2); 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, CH_3). Anal. Calc. for $C_{33}H_{27}N_5O_8$ x 0.5 H_2O (630.6): C, 62.85; H, 4.32; N, 11.10. Found: C, 62.85; H, 4.31; N, 10.57.

21: ^{1}H-NMR ($CDCl_3$): 8.53 (s, 1 H, H-C(7)); 8.10-7.20 (m, 17 H, 15 arom. H, NH_2); 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, CH_3). Anal. Calc. for $C_{33}H_{27}N_5O_8$ x 0.5 H_2O (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-ß-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 BF_3-etherate (4 ml). The reaction product was purified by short column chromatography with $CHCl_3$/n-hexane (4:1). The main fraction was collected, evaporated and the residue recrystallized from EtOH/H_2O to give 0.186 g (6%) of **15**. M.p. 122-124°C.
^{1}H-NMR ($CDCl_3$): 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, NH_2); 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, CH_3). Anal. Calc. for $C_{33}H_{27}N_5O_8$ (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-ß-D-ribofuranosyl)-6-phenyl-4(3H)pteridinone (16), 2-Amino-1-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-6-phenyl-4(3H)pteridinone (22) and 2-Imino-1,*O*^{4}-bis-(2,3,5-tri-*O*-benzoyl-ß-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 trifluormethanesulfonate (2.6 g, 1.2 mmol) as catalyst. After stirring at rt for 24 h was diluted with CH_2Cl_2 (20 ml) , treated with cold aqueous Na_2HPO_4 solution, the organic phase separated, dried with Na_2SO_4 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 $CHCl_3$ (3 l, 1. fraction, unreacted sugar), then with $CHCl_3$/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 $CHCl_3$/MeOH (19:1) to give 3 main bands which were cut out and eluted separately with $CHCl_3$(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. ^{1}H-NMR ($CDCl_3$): 9.14 (s, 1 H, H-C(7)); 8.20-7.20 (m, 22 H, 20 arom. H, NH_2); 7.18 (d, 1 H, H-C(1')); 6.24 (bs, 2 H, NH_2); 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 $C_{38}H_{29}N_5O_8$ (683.7): C, 66.76; H, 4.28; N, 10.24. Found: C, 66.53; H, 4.28; N, 10.00.
22. ^{1}H-NMR ($CDCl_3$): 8.96 (s, 1 H, H-C(7)); 8.20-7.20 (m, 22 H, 20 arom. H, NH_2); 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 $C_{38}H_{29}N_5O_8$ x H_2O (701.7):C, 64.47; H, 4.45; N, 9.98. Found: C, 64.47; H, 4.23; N, 9.91.
27: ^{1}H-NMR ($CDCl_3$): 8.51 (s, 1 H, H-C(7)); 8.20-7.20 (m, 37 H, 35 arom. H, NH_2); 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 $C_{64}H_{49}N_5O_{15}$ (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-ß-D-ribofuranosyl)-7-phenyl-4(3H)pteridinone(17) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl-ß-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 BF_3-etherate (4 ml) as catalyst. After stirring at rt for 4 h was diluted with CH_2Cl_2 (20 ml) , treated with cold aqueous Na_2HPO_4 solution, the organic phase separated, dried with Na_2SO_4 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 $CHCl_3$ (3 l, 1. fraction, unreacted sugar), then with $CHCl_3$/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 $CHCl_3$. The faster moving main band was cut out, eluted with $CHCl_3$, MeOH (9:1) to give 60 mg (2%) of **17**. The slower moving band gave 0.12 g (4%) of **23**.

17. ^{1}H-NMR ($CDCl_3$): 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, NH_2); 4.75(m, 2 H, H-C(5')); 4.88 (m, 1 H, H-C(4')). Anal. Calc. for $C_{38}H_{29}N_5O_8$ x H_2O (701.7): C, 65.04; H, 4.45; N, 9.98. Found: C, 64.85; H, 3.97; N, 9.96.

23. ^{1}H-NMR ($CDCl_3$): 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, NH_2); 6.17 (m, 1 H, H-C(2')); 5.99 (m, 1 H, H-C(3')); 6.04 (bs, 2 H, NH_2); 5.00-4.70 (m, 3 H, H-C(4',5')). Anal. Calc. for $C_{38}H_{29}N_5O_8$ x 0.5 H_2O (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-ß-D-ribofuranosyl)-7-*tert.*butyl-4(3H)pteridinone (18) and 2-Amino-1-(2,3,5-tri-*O*-benzoyl-ß-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 BF_3-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 $CHCl_3$/MeOH (11:1) to give two main bands. The faster moving band gave after elution, evaporation and recrystallization from i-PrOH/H_2O 0.24 g (10%) of **18** and from the slower moving band were 0.363 g (14%) of **24** isolated.

18. ^{1}H-NMR ($CDCl_3$): 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, NH_2); 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, $(CH_3)_3$). Anal. Calc. for $C_{36}H_{33}N_5O_8$ (663.7): C, 65.15; H, 5.01; N, 10.55. Found: C, 65.24; H, 5.00; N, 10.19.

24. ^{1}H-NMR ($CDCl_3$): 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, NH_2); 4.93-4.44 (m, 3 H, H-C(4', 5')); 1.39 (s, 9 H, $(CH_3)_3$). Anal. Calc. for $C_{36}H_{33}N_5O_8$ x 0.5 H_2O (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-ß-D-ribofuranosyl)-4(3H)pteridinone (25). A mixture of pterin (**1**) (1.63 g, 10 mmol) and $(NH_4)_2SO_4$ (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. CH_2Cl_2 (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 CH_2Cl_2 (30 ml), treated with saturated aqueous $NaHCO_3$, the layers separated and the organic phase dried over Na_2SO_4. After evaporated the resulting residue was dissolved in $CHCl_3$ and put onto a silica gel column (3.5 x 29 cm) for elution first with $CHCl_3$ (1 l), followed by $CHCl_3$/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/H_2O gave 1.2 g (24%) of **25**. ^{1}H-NMR ($CDCl_3$): 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, NH_2); 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 $C_{32}H_{25}N_5O_8$ (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-ß-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% CH_3ONa solution (2 ml) with stirring for 18 h. Little DOWEX 50 x 4 (H^+-form, 200-400 mesh) and H_2O (5 ml) was added to bring the pH to 5. After filtration was evaporated, the residue dissolved in $CHCl_3$/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.).

^{1}H-NMR ((D_6)DMSO): 7.49 (bs, 2 H, NH_2); 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 CH_3). Anal. Calc. for $C_{13}H_{17}N_5O_5$ x 2 H_2O (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-ß-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 CH_3ONa (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/H_2O (4:1, 15 ml) to give 53 mg (69%) of **29**. M.p. 170°C (decomp.). ^{1}H-NMR ((D_6)DMSO): 7.70 (bs, 2 H, NH_2); 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 CH_3). Anal. Calc. for $C_{13}H_{17}N_5O_5$ x 0.5 H_2O (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-ß-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, H_2O (3 ml) was added and the pH adjusted to 5 by AcOH. The precipitate was collected after cooling and recrystallized from i-PrOH/H_2O (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-ß-D-ribofuranosyl)-4(3H)pteridinone (**37**) (0.158 g, 0.2 mmol) in abs. dioxane (5 ml) was treated with conc. NH_3 (5 ml) for 3 days stirring in a closed flask. After evaporation the residue was dissolved in little H_2O and acidified by AcOH. On cooling the precipitate was collected and recrystallized from EtOH/H_2O (1:1) to give 60 mg (70%) of **30**. M.p. 180°C. ^{1}H-NMR ((D_6)DMSO): 7.90 (bs, 2 H, NH_2); 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 $C_{23}H_{21}N_5O_5$ x 0.5 H_2O (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-ß-D-ribofuranosyl)-4(3H)pteridinone (35) and
2-Methylthio-3-(2,3,5-tri-*O*-benzoyl-ß-D-ribofuranosyl)-4(3H)pteridinone (38). A mixture of 2-methylthio-4(3H)pteridinone (**31**)[40] (1.36 g, 7 mmol) and $(NH_4)_2SO_4$ (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 CH_2Cl_2 (20 ml)**,** then **11** (3.52 g, 7 mmol) and BF_3-etherate (7 ml) added. The reaction solution was stirred at rt for 1 day, then treated with a mixture of $CHCl_3$/H_2O/NEt_3 (5:5:1, 40 ml), the organic phase separated, dried over Na_2SO_4 and evaporated to give 3.3 g crude product. The mixture was separated by short column

chromatography (SCC)[41] with $CHCl_3$/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/H_2O.

38. Yield: 1.95 g (44%). M.p. 105-108°C. ^{1}H-NMR ($CDCl_3$): 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-CH_3). Anal. Calc. for $C_{33}H_{26}N_4O_8S$ (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. ^{1}H-NMR ($CDCl_3$): 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-CH_3).Anal. Calc. for $C_{33}H_{26}N_4O_8S$ x 0.5 H_2O (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-ß-D-ribofuranosyl)-4(3H)pteridinone (36) and 6,7-Dimethyl-2-methylthio-3-(2,3,5-tri-*O*-benzoyl-ß-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 BF_3-etherate (6 ml) for 3 days. After work-up the crude material (3.85 g) was separated and purified by SSC with $CHCl_3$/n-hexane (4:1). The first main fraction gave **39** followed by **36**. Recrystallizsation from EtOH/H_2O.

39. Yield: 1.82 g (42%). M.p. 113°C. ^{1}H-NMR ($CDCl_3$): 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-CH_3); 2.75 (s, 3 H, CH_3(7)); 2.73 (s, 3 H, CH_3(6)). Anal. Calc. for $C_{35}H_{30}N_4O_8S$ (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. ^{1}H-NMR ($CDCl_3$): 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, H, S-CH_3); 2.68 (2 s, 6 H, 2 CH_3). Anal. Calc. for $C_{35}H_{30}N_4O_8S$ (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-ß-D-ribofuranosyl)-4(3H)pteridinone (37) and 2-Methylthio-6,7-diphenyl-1-(2,3,5-tri-*O*-benzoyl-ß-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 CH_2Cl_2 (10 ml) **11** (2.01 g, 4 mmol) and BF_3-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 $CHCl_3$/n-hexane (3:2). The first main fraction gave **39** followed by **37**. Recrystallizsation from EtOH/H_2O.

40. Yield: 1.636 g (52%). M.p. 213°C. ^{1}H-NMR ($CDCl_3$): 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-CH_3). Anal. Calc. for $C_{45}H_{34}N_4O_8S$ (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. ^{1}H-NMR ($CDCl_3$): 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, H, S-CH_3). Anal. Calc. for $C_{45}H_{34}N_4O_8S$ (790.8): C, 68.35; H, 4.33; N, 7.08. Found: C, 68.17; H, 4.41; N, 7.04.

2-Methylamino-1-ß-D-ribofuranosyl-4(3H)pteridinone (41). A solution of **35** (0.128 g, 0.2 mmol) in abs. tetrahydrofurane (THF) (5 ml) was treated with methanolic CH_3NH_2-solution (20%, 3 ml) in a closed flask for 2 days. It was evaporated, the residue dissolved in abs. MeOH (5 ml), 1 N-CH_3ONa (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 $CHCl_3$/MeOH (4:1) to give after recrystallization from EtOH/H_2O 46 mg (74%) of **41**. M.p. 170°C (decomp.). ^{1}H-NMR ((D$_6$)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, *H$_3$C*-NH). Anal. Calc. for $C_{12}H_{15}N_5O_5$ x H_2O (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-ß-D-ribofuranosyl-4(3H)pteridinone (42). Analogous to the preceding procedure with **36** (0.133 g, 0.2 nmmol) to give after recrystallization from EtOH/H_2O (7:3) 59 mg (88%) of **42**. M.p. 205°C. ^{1}H-NMR ((D$_6$)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, *H$_3$C*-NH); 2.55, 2.53 (2 s, 6 H, 2 CH_3). Anal. Calc. for $C_{14}H_{19}N_5O_5$ x 0.5 H_2O (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-ß-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 $C_2H_5NH_2$-gas and kept in the icebox for 2 days. It was evaporated, the residue dissolved in abs. MeOH (10 ml), 1 N CH_3ONa (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 $CHCl_3$/MeOH (4:1). The main band was cut out, eluted, evaporated and the residue recrystallized from little from H_2O to give 64 mg (91%) of **43**. M.p. 167-168°C. ^{1}H-NMR ((D$_6$)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, HN*C*H$_2$CH$_3$); 2.55 (2 s, 6 H, 2 CH_3); 1.18 (t, 3 H, *C*H$_3$CH$_2$NH). Anal. Calc. for $C_{15}H_{21}N_5O_5$ (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-ß-D-ribofuranosyl-4(3H)pteridinone (44). Analogous to the preceding procedure with **36** (0.133 g, 0.2 nmmol) 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 CH_3ONa (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 $CHCl_3$, MeOH (4:1) to give 25 mg (34%) of **44**. M.p. 161°C. ^{1}H-NMR ((D$_6$)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, CH$_2$CH$_2$*OH*); 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. CH$_2$*CH$_2$*OH); 3.40 (m, 2 H, HOCH$_2$*CH$_2$*NH); 2.55, 2.53 (2 s, 6 H, 2 CH_3). Anal. Calc. for $C_{15}H_{21}N_5O_6$ x H_2O (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-ß-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 $CHCl_3$/MeOH (4:1) to give after recrystallization from EtOH/H_2O (2:3) 62 mg (70%) of **45**. M.p. 189°C (decomp.). ^{1}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, *H$_3$C*-NH). Anal. Calc. for $C_{24}H_{23}N_5O_5$ x 0.5 H_2O (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-ß-D-ribofuranosyl-4(3H)pteridinone (46). Analogous to the preceding procedure with **37** (0.158 g, 0.2 mmol) and $C_2H_5NH_2$-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}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, N*CH$_2$*CH$_3$);); 1.29 (t, 3 H, NCH$_2$*CH$_3$*). Anal. Calc. for $C_{25}H_{25}N_5O_5$ x H_2O (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-ß-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}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, CH$_2$CH$_2$*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, CH$_2$*CH$_2$*OH); 3.41 (m, 2 H, HOCH$_2$*CH$_2$*N). Anal. Calc. for $C_{25}H_{25}N_5O_6$ (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-ß-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}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$_2$C*H*); 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, (*H$_3$C*)$_2$CH). Anal. Calc. for $C_{26}H_{27}N_5O_5$ x H_2O (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-ß-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/H_2O (3:7) 68 mg (68%) of **49**. M.p. 193°. ^{1}H-NMR ((D$_6$)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, $CH_3CH_2CH_2$*CH_2*NH); 1.60 (m, 2H, CH_3CH_2*CH_2*CH_2NH); 1.35 (m, 2H, CH_3*CH_2*CH_2CH_2NH); 0.95 (t, 3 H, *CH_3*$CH_2CH_2CH_2$NH). Anal. Calc. for $C_{27}H_{29}N_5O_5$ (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-ß-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 CH_3ONa and purification on a silica gel plate gave after recrystallization from EtOH/H_2O (3:7) 63 mg (63%) of **50**. M.p. 140-143°. ^{1}H-NMR ((D$_6$)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, HN*CH_2*); 2.05 (m, 1 H, Me_2*CH*); 0.92 (HC(*CH_3*)$_2$). Anal. Calc. for $C_{27}H_{29}N_5O_5$ x C_2H_5OH (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-ß-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 $CHCl_3$/MeOH (19:1). The main band was eluted, evaporated and the residue recrystallized from EtOH/H_2O (1:1) to give 0.135 g (86%) of **51**. M.p. 130°C. ^{1}H-NMR ($CDCl_3$): 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(CH_3)$_2$). Anal. Calc. for $C_{46}H_{37}N_5O_8$ x 0.5 H_2O (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-methyltio-6.7-diphenyl-4(3H)pteridone (**61**)[40] (0.12 g, 0.33 mmol) and the mixture stirred for 1 h and then evaportated. The residue was purified by preparative thick layer chromatography on a silica gel plate (40 x 20 x 02 cm) with $CHCl_3$/MeOH (9:1), The main band was eluted, evaporated and the solid recry-stallized from EtOH/H_2O to give 98 mg (86%) of **65**. M.p. 299°C. Anal. Calc. for $C_{20}H_{17}N_5O$ x C_2H_5OH (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/H_2O gave 57 mg (71%) of **66**. M.p. 229°C. Anal. Calc. for $C_{21}H_{19}N_5O$ (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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