Pteridines

Part CXIII[1])

Protection of Pteridines

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The low solubility of pterins can drastically be improved by N^2-acylation or formation of the N^2-[(dimethylamino)methylene] derivatives. Both types of compounds can be alkylated under *Mitsunobu* conditions to form from N^2-acylpterins (see **2** and **3**) and their derivatives (see **5**, **6**, **8**, **9**, **11**, **13**, **15**, and **17**) selectively the O^4-alkyl derivatives **22**–**31**, whereas the electron-donating [(dimethylamino)methyleneamino function in **46**–**51** gives, in a selective reaction, the N(3)-substitution (→ **52**–**61**). N^2,N^2-Dimethylpterins and **18** and **19** and N^2-methylpterins **20** and **21** direct alkylation also to the O^4-position (→ **32**–**35**, **38** and **39**). Deacylation can be achieved under very mild conditions by solvolysis with MeOH (**22** → **40**, **26** → **41**), and displacement of the O^4-[2-(4-nitrophenyl)ethyl] group proceeds with ammonia at room temperature to the corresponding pteridin-2,4-diamines **42**–**45**. Cleavage of the N^2-[(dimethylamino)methylene] group works well with ammonia (→ **62**–**67**). The advantage of applying the 2-(4-nitrophenyl)ethyl (npe) group as blocking group is seen in its selective removal by 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) under aprotic conditions without harming the other substituents.

1. Introduction. – Pteridines are a synonym for high-melting, insoluble compounds, as noticed already during the isolation [2–4] and structural elucidation [4–6] of the butterfly pigments xanthopterin, isoxanthopterin, and leucopterin. These unexpected properties are due to strong intermolecular interactions to form aggregates by H-bonding, especially between amide functions and amino groups. It has been shown [7][8] that introduction of one, two, three, or four hydroxy or mercapto groups into the various positions of the pteridine molecule itself, which is very soluble in H_2O, decreases solubility in this solvent systematically. The same is true for amino groups, which form intermolecular H-bonds to the ring N-atoms. The worst combination in this respect is the presence of an amide function and an amino group due to the fact that these functions show weak acidic and basic properties, respectively, themselves promoting favorably the intermolecular interaction. Consequently, protection of the N- or O-atom of the amide function, even by the hydrophobic Me group, increases solubility in H_2O and organic solvents drastically. Similarly, acylation of the amino group affects solubility to a large extent. Pterin (= 2-aminopteridine-4(3*H*)-one; **1**), for example, shows a solubility in H_2O at room temperature of 1:57000, whereas the N(3)-methyl derivative shows a proportion of 1:100 and the 2-(acetylamino) derivative one of 1:450. Successive substitution of the NH_2 group in pteridine-2-amine by one and two Me groups increases the solubility again from 1:1350 to 1:320, and 1:2.5, respectively.

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[1]) Part CXII: [1].

To provide more-soluble pteridines in general, we developed new protection strategies that allow the easy introduction of such protecting groups cleavable under mild conditions back to the parent molecules. Based on our excellent results in protecting nucleobases in nucleosides and nucleotides [9][10], we chose again the 2-(4-nitrophenylethyl) (npe) group for pteridine protection, since its cleavage can be effectively performed under aprotic conditions with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a base.

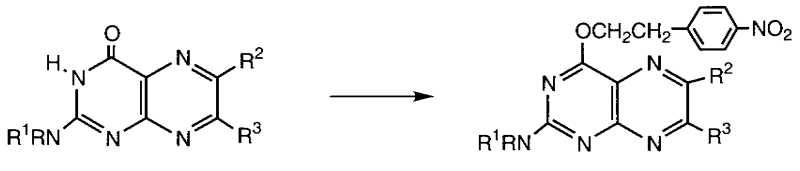
2. Synthesis. – To study the reactivity of the amido group of pterin (**1**) in the *Mitsunobu* reaction [11], we protected first the NH_2 group by acylation with Ac_2O ($\rightarrow$**2**) and isobutyryl anhydride ($\rightarrow$**3**), respectively (*Scheme 1*), or by treatment with dimethylformamide dimethyl acetal to form the N^2-[(dimethylamino)methylene] derivative (see below). Similarly, the N^2-acylated starting materials **5** and **6** were obtained from **4**, **8** and **9** from **7**, **11** from **10**, **13** from **12**, **15** from **14**, and **17** from **16**. These starting materials possess enough solubility in organic solvents to react in dioxane with ethyl azodicarboxylate, triphenylphosphine, and 2-(4-nitrophenyl)ethanol under *Mitsunobu* conditions. The reagents were applied in 1.5M excess, and the reaction time was generally 24 h. The highly selective alkylation to the corresponding O^4-2-(4-nitrophenyl)ethyl derivatives **22**–**31** gave yields in the range of 60–90%. Prolonged reaction times may increase the yield, as shown with N^2-isobutyrylpterin (**3**), which formed **23** after 24 h in 68% and after 36 h in 89% yield. In the case of N^2-acetyl-6,7-diphenylpterin (**17**), the *Mitsunobu* reaction required higher temperatures of 75–80° for solubility reasons and led to a mixture of the expected N^2-ac-O^4-npe-protected 6,7-diphenylpterin **31** in 69% yield and N^2-ac-N^2-npe-substituted 6,7-diphenylpterin **37** as a by-product in 6% yield. N^2-Ac-protected 6-phenylpterin **11** also formed two products **28** and **36** in 68 and 7% yield at room temperature and in 38 and 53% yield, respectively, at 75–80°.

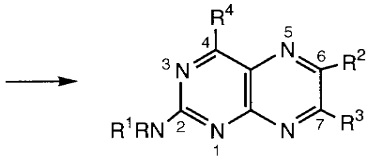
N^2,N^2-Dimethylpterin (**18**) and its 6,7-dimethyl derivative **19** as well as N^2-methylpterin (**20**) and its 6-methyl derivative **21** showed the same reaction behavior, forming, under O^4-alkylation, **32**–**35** in good yields. The *Mitsunobu* reaction is of general use for O^4-alkylations in the pterin series, as shown with **18** and **19**, which formed with MeOH instead of npe-OH the corresponding O^4-methyl derivatives **38** and **39** in 69 and 63% yield, respectively.

The new pteridine derivatives can be used as starting materials for various chemical interconversions. Treatment of **22** or **26** with MeOH for 18 h at 50° or 3 d at room temperature cleaved the labile *N*-acetyl group to form O^4-npe-pterin **40** or its corresponding 6-(acetyloxy)methyl derivative **41**, respectively. Acetylation of **40** regenerated compound **22**. The O^4-npe group is also prone to mild nucleophilic displacement reactions as seen from the treatment of **22**, **26**, **31**, and **36**, respectively, with aqueous ammonia in MeOH at room temperature for 1–10 d to form the corresponding 4-aminopteridine derivatives **42**–**45** under simultaneous cleavage of the acetyl group.

An entirely different result was obtained when N^2-[(dimethylamino)methylene]-pterins **46**–**51** were treated under the same *Mitsunobu* conditions (*Scheme 2*). Alkylations now led selectively to N^3-substitution to form the 3-npe-substituted (see **52**, **54**, **55**, **57**, and **60**), the 3-methyl-substituted (see **53**, **56**, **58**, and **61**), or the 3-ethyl-

Scheme 1

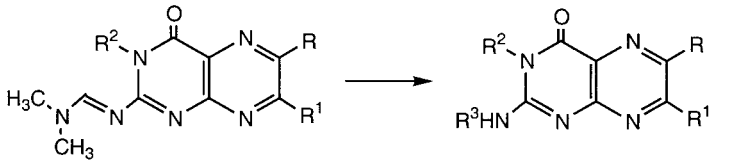




	R	R^1	R^2	R^3	
1	H	H	H	H	
2	ac	H	H	H	**22**
3	ibu	H	H	H	**23**
4	H	H	Me	H	
5	ac	H	Me	H	**24**
6	ibu	H	Me	H	**25**
7	H	H	CH_2OH	H	
8	ac	H	CH_2Oac	H	**26**
9	ibu	H	CH_2Oibu	H	**27**
10	H	H	Ph	H	
11	ac	H	Ph	H	**28**
12	H	H	H	Me	
13	ac	H	H	Me	**29**
14	H	H	Me	Me	
15	ac	H	Me	Me	**30**
16	H	H	Ph	Ph	
17	ac	H	Ph	Ph	**31**
18	Me	Me	H	H	**32**
19	Me	Me	Me	Me	**33**
20	Me	H	H	H	**34**
21	Me	H	H	Me	**35**
	ac	npe	Ph	H	**36**
37	ac	npe	Ph	Ph	

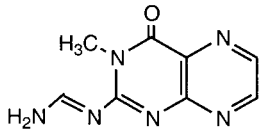
	R	R^1	R^2	R^3	R^4
38	Me	Me	H	H	MeO
39	Me	Me	Me	Me	MeO
40	H	H	H	H	npeO
41	H	H	CH_2Oac	H	npeO
42	H	H	H	H	NH_2
43	H	H	CH_2OH	H	NH_2
44	H	H	Ph	Ph	NH_2
45	H	npe	Ph	H	NH_2

Scheme 2



	R	R^1	R^2
46	H	H	H
47	CH_2OH	H	H
48	CH_2Oac	H	H
49	Me	H	H
50	Ph	H	H
51	Ph	Ph	H
52	H	H	npe
53	H	H	Me
54	CH_2Oac	H	npe
55	Me	H	npe
56	Me	H	Me
57	Ph	H	npe
58	Ph	H	Me
59	Ph	H	Et
60	Ph	Ph	npe
61	Ph	Ph	Me

	R	R^1	R^2	R^3
62	H	H	npe	H
63	CH_2OH	H	npe	H
64	Ph	H	npe	H
65	H	H	Me	H
66	Me	H	Me	H
67	H	H	npe	ac



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substituted derivative (see **59**), depending on the alcohol applied, in yields of 62–91%. Treatment of **52**, **54**, **57**, **53** and **56** with aqueous ammonia/MeOH 1:1 at room temperature cleaved the (dimethylamino)methylene and the acetyl group to give the 3-substituted pterins **62**–**66**, respectively, without harming the N(3) substituent, as expected. Acetylation converted 3-[2-(4-nitrophenyl)ethyl]pterin (**62**) to its N^2-acetyl derivative **67**, which could not be obtained under *Mitsunobu* condition starting from N^2-acetylpterin (**2**).

The advantage of the use of the npe group for pterin protection becomes obvious by the fact that its cleavage could be achieved with DBU in aprotic solvents without harming other protecting groups present. The O^4-npe-protected pterin **40** could be converted into pterin (**1**) by treatment with 0.25M DBU in DMF at room temperature for 4 h in 89% isolated yield. The N(3)-npe-protected pterin **62** is, as expected for an *N*-alkyl derivative, somewhat more stable, but cleavage could also be achieved with 0.5M DBU in DMF for 24 h at room temperature to give 92% of **1**. Treatment of N^2-[(dimethylamino)methylene]-3-npe-protected pterin (**52**), under similar conditions, showed very slow cleavage since 0.25M DBU in MeCN gave, after 4 d, only 19%, and in DMF, after 10 d, 32% of N^2-[(dimethylamino)methylene]pterin (**46**). During the deprotection of **53** with ammonia in MeOH, a precipitate separated out after 5–10 min, showing that the N^2-[(dimethylamino)methylene] group was converted to the N^2-(aminomethylene) function (see **68**); longer reaction times yielded, as expected, 3-methylpterin (**65**).

3. Physical Data. – During the experimental studies, several characteristic differences in the physical properties of the N(3)- and the O^4-alkylated pterin derivatives allowed easy structural assignment from TLC and UV and ^{1}H-NMR spectra. As a qualitative measure, the R_f values on TLC (silica-gel sheet, $CHCl_3$/MeOH 9:1) gave good information, since the R_f of an O^4-npe-pterin is always higher than that of the corresponding N(3)-npe-pterin. Also, the color of the fluorescence is changing from the dark blue of the former compounds to the light blue of the latter ones. More convincing are, however, the UV spectra in MeOH, which show distinct differences in the overall shapes and shifts to longer-wavelength absorption bands for the O^4- as compared with the corresponding N(3)-alkylpterins (*Table 1*).

The ^{1}H-NMR spectra are of special value since differentiation between the N(3)- and the O^4-[2-(4-nitrophenyl)ethyl]pterins can easily be achieved by comparing the chemical shifts of the CH_2(1) and CH_2(2) signals of the npe group. Some typical comparisons are listed in *Table 2*.

Experimental Part

General. TLC: precoated cellulose thin-layer sheets *F 1440 LS 254* and silica-gel thin-layer sheets *F 1500 LS 254* from *Schleicher & Schüll*. Column (CC) or flash chromatography (FC): silica gel (*Baker*, 30–60 mm); 0.2–0.3 bar. M.p.: *Büchi* apparatus, model, *Dr. Tottoli*; no corrections. UV/VIS: *Perkin-Elmer Lambda 5*; λ_{max} (log ε). ^{1}H-NMR: *Bruker WN-250*; δ in ppm rel. to $SiMe_4$, J in Hz.

1. *2-Aminopteridin-4(3*H*)-one* (**1**). 1.1. To a suspension of 3-npe-pterin **62** (see below; 63 mg, 0.2 mmol) in dry DMF (2.4 ml) was added DBU (92 mg, 0.6 mmol), and the mixture was stirred at r.t. for 24 h. After neutralization with 1M AcOH to pH 5–6, the precipitate was collected, washed with $CHCl_3$ and H_2O, and dried: 30 mg (92%) of **1**. Colorless powder. M.p. >330°.

1.2. Analogously to *Exper. 1.1*, O^4-npe-pterin **40** gave (see below), after 4 h treatment, 89% of **1**. Both substances are chromatographically and UV-spectroscopically identical with authentic material.

2. N-*{6-[(Acetyloxy)methyl]-3,4-dihydro-4-oxopteridin-2-yl}acetamide* (**8**). A suspension of 6-(hydroxymethyl)pterin (**7**; 0.65 g, 3.4 mmol) in Ac_2O (100 ml) and AcOH (28 ml) was refluxed for 3 h until a clear soln. was obtained. After cooling, the mixture was evaporated to 1/3 of the volume and kept in the icebox overnight. The resulting precipitate was washed with EtOH, AcOEt, and Et_2O to give, after drying at 100°, 0.724 g (78%) of **8**. Yellow powder. M.p. 224–226° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.56. ^{1}H-NMR ((D$_6$)DMSO): 12.29 (br. *s*, 1 NH); 11.98 (br. *s*, 1 NH); 8.94 (*s*, 1 H, H–C(7)); 5.27 (*s*, CH_2); 2.22 (*s*, AcN); 2.12 (*s*, AcO). Anal. calc. for $C_{11}H_{11}N_5O_4$ (277.6): C 47.66, H 4.00, N 25.34; found: C 47.30, H 4.04, N 25.07.

3. N-*{6-[(Isobutyryloxy)methyl]-3,4-dihydro-4-oxopteridin-2-yl}isobutyramide* (**9**). A suspension of **7** (0.65 g, 3.4 mmol) in dry pyridine (30 ml) and isobutyric anhydride (8 ml) was heated under reflux for 4 h, and then the soln. was evaporated and co-evaporated twice with toluene. The resulting residue was treated with hexane/MeOH 10:1 and filtered. The solid (0.993 g) was recrystallized from $CHCl_3$/hexane: 0.87 g (78%) of **9**. Colorless crystals. M.p. 193–194° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.58. ^{1}H-NMR ($CDCl_3$): 12.51 (br. *s*, 1 NH); 9.19 (br. *s*, 1 NH); 8.90 (*s*, 1 H, H–C(7)); 5.27 (*s*, CH_2); 2.80 (*sept.*, 1 Me_2CH); 2.67 (*sept.*, 1 Me_2CH); 1.28 (*d*, Me_2CH); 1.21(*d*, 1 Me_2CH). Anal. calc. for $C_{14}H_{15}N_5O_2$ (281.3): C 59.78, H 3.94, N 24.90; found: C 59.52, H 4.10, N 24.61.

4. N-*(3,4-Dihydro-4-oxo-6-phenylpteridin-2-yl)acetamide* (**11**). As described for **8**, with 6-phenylpterin (**10**; 0.5 g, 2.09 mmol), Ac_2O (80 ml) and AcOH (20 ml) till a clear soln. was obtained: 0.522 g (89%) of **11**. Yellow powder. M.p. >330° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.55. ^{1}H-NMR ((D$_6$)DMSO): 12.35 (br. *s*, 1 NH); 12.00 (br. *s*, 1 NH); 9.43 (*s*, H–C(7)); 8.17 (*d*, 2 arom. H); 7.56–7.47–7.27 (*m*, 3 arom. H); 2.20 (*s*, Ac). Anal. calc. for $C_{11}H_{11}N_5O_4$ (277.6): C 47.66, H 4.00, N 25.34; found: C 47.30, H 4.04, N 25.07.

5. N-*(3,4-Dihydro-6,7-dimethyl-4-oxopteridin-2-yl)acetamide* (**15**). A suspension of 6,7-dimethylpterin (**14**; 0.5 g, 2.62 mmol) in Ac_2O (50 ml) was refluxed for 4 h. The resulting soln. was concentrated to 1/4 of its volume and then cooled in the icebox, the precipitate collected and washed with AcOEt and Et_2O, and the residue recrystallized from dioxane: 0.536 g (88%) of **15**. Colorless crystal powder. M.p. 304–305° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.35. ^{1}H-NMR ((D$_6$)DMSO): 12.21 (br. *s*, 1 NH); 11.82 (br. *s*, 1 NH); 2.58 (*s*, 2 Me); 2.19 (*s*, Ac). Anal. calc. for $C_{10}H_{11}N_5O_2 \cdot 0.5\ H_2O$ (242.3): C 49.56, H 4.99, N 28.89; found: C 49.33, H 4.80, N 28.60.

Table 1. *UV-Absorption Spectra of* O^4*- and N(3)-Alkylated Pterin Derivatives in MeOH*[a])

	λ_{max} [nm]				log ε_{max}			
2	(232)		278	327	(4.11)		4.14	3.86
5	(222)		279	332	(4.47)		4.32	3.81
8	(232)		281	333	(4.40)		4.20	3.87
11	(216)		302	358	(4.09)		4.21	3.90
15	(224)		281	332	(4.10)		4.13	3.91
17	224	256	296	362	4.41	4.25	4.27	4.14
22		241	(261)	331		4.47	(4.27)	3.95
24		241	(263)	330		4.41	(4.26)	3.86
25	(217)	242	(263)	330	(4.21)	4.45	(4.32)	3.94
26		242	(267)	333		4.33	(4.16)	3.79
27	(217)	244	(264)	334	(4.23)	4.55	(4.39)	4.02
28	(218)	254	281	359	(4.22)	4.35	4.40	4.03
29	(218)	242	(262)	328	(4.20)	4.50	(4.29)	4.04
30	(218)	241	263	330	(4.15)	4.44	4.27	3.98
31	(218)	249	(274)	366	(4.47)	4.52	(4.45)	3.95
32		238	274	389		4.31	4.36	3.77
33		242	276	383		4.45	4.41	3.88
34		233	269	373		4.57	4.61	4.09
35		237	270	368		4.41	4.32	3.95
36	(214)	(264)	279	363	(4.37)	(4.50)	4.51	3.88
37	(218)	264	(288)	371	(4.73)	4.53	(4.47)	3.95
38		237	277	388		4.37	4.24	3.87
39		240	278	383		4.43	4.25	3.93
40		229	264	360		4.06	3.99	3.51
41	(219)	240	268	361	(4.19)	4.27	4.21	3.63
44	(217)	283	(310)	397	(4.15)	4.36	(4.12)	3.82
45	(224)		274	389	(4.42)		4.41	4.13
47		234	302	345		4.03	4.48	4.03
48		236	305	351		3.95	4.43	3.99
49		237	302	350		4.09	4.51	4.01
50	(221)	254	321	374	(4.13)	4.10	4.54	4.25
51	(222)	(274)	317	377	(4.38)	(4.12)	4.51	4.24
52	(241)	(279)	303	(347)	(4.18)	(4.37)	4.42	(4.00)
53	(241)	(270)	304	(350)	(4.12)	(4.28)	4.59	(3.89)
54	(242)	(280)	307	(353)	(4.27)	(4.40)	4.43	(4.13)
55	(241)	(270)	304	(350)	(4.12)	(4.28)	4.59	(3.89)
56	240	(268)	306	(354)	4.09	(4.04)	4.44	(3.98)
57	(213)	270	324	377	(4.62)	4.60	4.77	4.48
58		261	323	377		4.16	4.50	4.19
59		261	324	377		4.14	4.50	4.19
60	(221)	274	320	379	(4.39)	4.36	4.44	4.16
61	(222)	(274)	320	379	(4.33)	(4.21)	4.55	4.25
62	(215)	(249)	274	353	(4.34)	(4.17)	4.32	3.72
63	(213)	(253)	278	358	(4.18)	(4.16)	4.31	3.65
64	(211)	(262)	299	376	(4.41)	(4.31)	4.51	4.01
65		239	276	354		4.07	4.07	3.71
66	(223)	242	277	358	(3.96)	4.07	4.11	3.68
67	(214)		267	(323)	(4.03)		4.25	(3.75)

[a]) Values in parentheses refer to shoulders.

Table 2. *^{1}H-NMR-Data of N(3)- and O^4-Substituted Pterins*

Pterin[a])		npe Group				Solvent
		H_o to NO_2	H_m to NO_2	$CH_2(1)$	$CH_2(2)$	
O^4-npe-	**40**	8.15 (*d*)	7.62 (*d*)	4.72 (*t*)	3.30 (*t*)	(D_6)DMSO
6-CH_2Oac-O^4-npe-	**41**	8.15 (*d*)	7.64 (*d*)	4.85 (*t*)	3.37 (*t*)	(D_6)DMSO
N(3)-npe-	**62**	8.15 (*d*)	7.57 (*d*)	4.24 (*t*)	3.04 (*t*)	(D_6)DMSO
6-CH_2OH-N(3)-npe-	**63**	8.16 (*d*)	7.55 (*d*)	4.25 (*t*)	3.04 (*t*)	(D_6)DMS
N^2-ac-O^4-npe-	**22**	8.15 (*d*)	7.49 (*d*)	4.87 (*t*)	3.37 (*t*)	$CDCl_3$
N^2-ibu-O^4-npe-	**23**	8.15 (*d*)	7.49 (*d*)	4.87 (*t*)	3.37 (*t*)	$CDCl_3$
N^2-ac-N(3)-npe-	**67**	8.17 (*d*)	7.48 (*d*)	4.53 (*t*)	3.15 (*t*)	$CDCl_3$
N^2-dmam-N(3)-npe-	**52**	8.13 (*d*)	7.42 (*d*)	4.61 (*t*)	3.18 (*t*)	$CDCl_3$
N^2-ac-6-Me-O^4-npe-	**24**	8.19 (*d*)	7.53 (*d*)	4.90 (*t*)	3.42 (*t*)	$CDCl_3$
N^2-ac-6-CH_2Oac-O^4-npe-	**26**	8.15 (*d*)	7.64 (*d*)	4.85 (*t*)	3.37 (*t*)	$CDCl_3$
N^2-ibu-6-Me-O^4-npe-	**25**	8.19 (*d*)	7.56 (*d*)	4.95 (*t*)	3.42 (*t*)	$CDCl_3$
N^2-dmam-6-Me-N(3)-npe-	**55**	8.13 (*d*)	7.42 (*d*)	4.61 (*t*)	3.18 (*t*)	$CDCl_3$
N^2-ac-7-Me-O^4-npe-	**29**	8.19 (*d*)	7.52 (*d*)	4.88 (*t*)	3.49 (*t*)	$CDCl_3$
N^2-ac-6-Ph-O^4-npe-	**28**	8.22 (*d*)	7.61 (*d*)	4.88 (*t*)	3.41 (*t*)	$CDCl_3$
N^2-dmam-6-Ph-N(3)-npe-	**57**	8.15 (*d*)	7.44 (*d*)	4.63 (*t*)	3.20 (*t*)	$CDCl_3$
N^2-dmam-6,7-diPh-N(3)-npe-	**60**	8.15 (*d*)	7.44 (*d*)	4.63 (*t*)	3.20 (*t*)	$CDCl_3$
6-Ph-N(3)-npe-	**64**	8.14 (*d*)	7.62 (*d*)	4.27 (*t*)	3.08 (*t*)	(D_6)DMSO
N^2-ac-6,7-diMe-O^4-npe-	**30**	8.19 (*d*)	7.52 (*d*)	4.88 (*t*)	3.39 (*t*)	$CDCl_3$
N^2-ac-6,7-diPh-O^4-npe-	**31**	8.19 (*d*)	7.52 (*d*)	4.88 (*t*)	3.49 (*t*)	$CDCl_3$
N^2,N^2-diMe-O^4-npe-	**32**	8.15 (*d*)	7.46 (*d*)	4.80 (*t*)	3.36 (*t*)	$CDCl_3$
N^2,N^2,6,7-tetraMe-O^4-npe-	**33**	8.15 (*d*)	7.45 (*d*)	4.80 (*t*)	3.34 (*t*)	$CDCl_3$

[a]) npe = 2-(4-nitrophenyl)ethyl; dmam = (dimethylamino)methylene.

6. N-*(3,4-Dihydro-4-oxo-6,7-diphenylpteridin-2-yl)acetamide* (**17**). A mixture of 6,7-diphenylpterin (**16**) and Ac_2O (120 ml) was refluxed for 3 h. The resulting clear soln. was concentrated to 1/5 of the volume and then cooled overnight in the icebox. The precipitate was washed with AcOEt and Et_2O and dried: 1.245 g (94%) of **17** · AcOH. Colorless needles. M.p. 264–266°. R_f ($CHCl_3$/MeOH 9:1) 0.57. ^{1}H-NMR ((D_6)DMSO): 12.33 (br. *s*, 1 NH); 11.98 (br. *s*, 1 NH, AcOH); 7.46–7.33 (*m*, 10 arom. H); 2.23 (*s*, AcN); 1.89 (*s*, AcO). Anal. calc. for $C_{20}H_{15}N_5O_2 \cdot CH_3COOH$ (417.4): C 63.30, H 4.59, N 16.78; found: C 62.93, H 4.63, N 16.63.

Recrystallization from dioxane gave a dioxane adduct. Colorless crystal powder. M.p. 276–277°. ^{1}H-NMR ($CDCl_3$): 12.55 (br. *s*, 1 NH); 10.91 (br. *s*, 1 NH); 7.52–7.29 (*m*, 10 arom. H); 3.71 (*s*, 8 H, dioxane); 2.25 (*s*, AcN). Anal. calc. for $C_{20}H_{15}N_5O_2 \cdot C_4H_8O_2$ (445.5): C 64.71, H 5.20, N 15.72; found: C 64.64, H 5.17, N 15.69.

7. N-*{4-[2-(4-Nitrophenyl)ethoxy]pteridin-2-yl}acetamide* (**22**). 7.1. To a suspension of N^2-acetylpterin (**2**; 0.205 g, 1 mmol), npe-OH (0.25 g, 1.5 mmol), and Ph_3P (0.393 g, 1.5 mmol) in dry dioxane (25 ml) was added diisopropyl azodicarboxylate (0.303 g, 1.5 mmol). The mixture was stirred at r.t. for 24 h and then evaporated. The residue was separated by column chromatography (CC; silica gel, AcOEt/$CHCl_3$ 1:1, then $CHCl_3$/MeOH 95:5). The residue of the product fraction was recrystallized from Ac_2O: 0.219 g (62%) of **22**. Colorless crystals. M.p. 186–188°. R_f ($CHCl_3$/MeOH 9:1) 0.53. ^{1}H-NMR ($CDCl_3$): 8.99 (*d*, H–C(7)); 8.76 (*d*, H–C(6)); 8.28 (br. *s*, 1 NH); 8.17 (*d*, 2 H_o to NO_2); 7.51 (*d*, 2 H_m to NO_2); 4.87 (*t*, OCH_2CH_2); 3.37 (*t*, OCH_2CH_2); 2.66 (*s*, Ac).

7.2. A suspension of **40** (0.1 g, 0.32 mmol) in Ac_2O (20 ml) and AcOH (10 ml) was refluxed for 4 h. Then the soln. was concentrated to 1/3 of its volume and cooled and the precipitate collected. Washing with AcOEt and Et_2O and drying gave 0.076 g (66%) of **22**. Colorless crystals. M.p. 186–189°. Anal. calc. for $C_{16}H_{14}N_5O_4 \cdot 0.5\ H_2O$ (363.3): C 52.89, H 4.16, N 23.13; found: C 52.69, H 4.20, N 22.86.

8. N-*{4-[2-(4-Nitrophenyl)ethoxy]pteridin-2-yl}isobutyramide* (**23**). As described in *Exper. 7.1*, with N^2-isobutyrylpterin (**3**; 0.234 g, 1 mmol). The main fraction from CC yielded, after recrystallization from $CHCl_3$/hexane, 0.260 g (68%) of **23**. Extension of the reaction time to 36 h yielded 89% of **23**. Yellowish crystals. M.p. 173–175°. R_f ($CHCl_3$/MeOH 9:1) 0.67. ^{1}H-NMR ($CDCl_3$): 8.99 (*d*, H–C(7)); 8.75 (*d*, H–C(6)); 8.16 (*d*, 2 H_o to NO_2); 8.07 (br. *s*, NH); 7.53 (*d*, 2 H_m to NO_2); 4.93 (*t*, OCH_2CH_2); 3.39 (*t*, OCH_2CH_2); 3.24 (*sept.*, Me_2CH); 1.29

(*d*, *Me*$_2$CH). Anal. calc. for $C_{18}H_{18}N_6O_4 \cdot 0.5\ H_2O$ (391.4): C 55.24, H 4.89, N 21.47; found: C 55.38, H 5.00, N 21.40.

9. N-*{6-Methyl-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-yl}acetamide* (**24**). As described in *Exper. 7.1* with N^2-acetyl-6-methylpterin (**5**; 0.219 g, 1 mmol): 0.17 mg (46%) of **24**. Colorless crystals. M.p. 217–218° (AcOEt/MeOH 1:1). R_f ($CHCl_3$/MeOH 9:1) 0.51. ^{1}H-NMR ($CDCl_3$): 8.91 (*d*, H–C(7)); 8.21 (*d*, 2 H_o to NO_2); 8.18 (br. *s*, NH); 7.55 (*d*, 2 H_m to NO_2); 4.90 (*t*, OCH_2CH$_2$); 3.42 (*t*, OCH$_2$CH_2); 2.81 (*s*, Me–C(6)); 2.68 (*s*, Ac). Anal. calc. for $C_{17}H_{16}N_6O_4$ (368.4): C 55.43, H 4.38, N 22.81; found: C 55.07, H 4.42, N 22.80.

10. N-*{6-Methyl-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-yl}isobutyramide* (**25**). As described in *Exper. 7.1*, with N^2-isobutyryl-6-methylpterin (**6**; 0.248 g, 1 mmol): 0.17 mg (48%) of **25**. Colorless crystals. M.p. 200–202° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.69. ^{1}H-NMR ($CDCl_3$): 8.90 (*d*, H–C(7)); 8.21 (*d*, 2 H_o NO_2); 8.07 (br. *s*, NH); 7.58 (*d*, 2 H_m to NO_2); 4.95 (*t*, OCH_2CH$_2$); 3.42 (*t*, OCH$_2$CH_2); 3.21 (*sept.*, Me$_2$C*H*); 2.80 (*s*, Ac); 1.30 (*d*, *Me*$_2$CH). Anal. calc. for $C_{19}H_{20}N_6O_4 \cdot 0.5\ H_2O$ (405.4): C 56.29, H 5.21, N 20.92; found: C 56.31, H 5.12, N 20.52.

11. N-*{[(Acetyloxy)methyl]-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-yl}acetamide* (**26**). As described in *Exper. 7.1*, with **8** (0.28 g, 1 mmol): 0.308 g (70%) of **26**. Colorless crystals. M.p. 175–177°. R_f ($CHCl_3$/MeOH 9:1) 0.45. ^{1}H-NMR ($CDCl_3$): 9.06 (*d*, H–C(7)); 8.17 (*d*, 2 H_o to NO_2); 8.03 (br. *s*, NH); 7.53 (*d*, 2 H_m to NO_2); 5.40 (*s*, CH_2–C(6)); 4.85 (*t*, OCH_2CH$_2$); 3.37 (*t*, OCH$_2$CH_2); 2.66 (*s*, AcN); 2.18 (*s*, AcO). Anal. calc. for $C_{19}H_{18}N_6O_6 \cdot 0.5\ H_2O$ (435.4): C 52.58, H 4.40, N 19.30; found: C 52.58, H 4.43, N 19.21.

12. N-*{6-[(Isobutyryloxy)methyl]-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-yl}isobutyramide* (**27**). As described in *Exper. 7.1*, with **9** (0.336 g, 1 mmol): 0.2 g (41%) of **27**. Colorless crystals. M.p. 137–138°. R_f ($CHCl_3$/MeOH 9:1) 0.73. ^{1}H-NMR ($CDCl_3$): 9.07 (*d*, H–C(7)); 8.18 (*d*, 2 H_o to NO_2); 8.14 (br. *s*, NH); 7.56 (*d*, 2 $_m$ to NO_2); 5.44 (*t*, CH_2–C(6)); 4.94 (*t*, OCH_2CH$_2$); 3.37 (*t*, OCH$_2$CH_2); 3.22 (*sept.*, 1 Me$_2$C*H*); 2.71 (*s*, 1 Me$_2$C*H*); 1.31 (*d*, 1 *Me*$_2$CH); 1.25 (*d*, 1 *Me*$_2$CH) . Anal. calc. for $C_{23}H_{26}N_6O_6$ (482.5): C 57.25, H 5.43, N 17.42; found: C 56.83, H 5.47, N 16.96.

13. N-*{4-[2-(4-Nitrophenyl)ethoxy]-6-phenylpteridin-2-yl}acetamide* (**28**). As described in *Exper. 7.1*, with **11** (0.282 g, 1 mmol): 0.29 g (68%) of **28**. Colorless crystals. M.p. 242–244°. R_f ($CHCl_3$/MeOH 9:1) 0.66. ^{1}H-NMR ($CDCl_3$): 9.48 (*d*, H–C(7)); 8.22 (*d*, 2 H_o to NO_2); 8.17 (*d*, 2 arom. H); 8.12 (br. *s*, 1 NH); 7.62 (*d*, 2 H_m to NO_2); 7.62–7.47 (*m*, 3 arom. H); 4.88 (*t*, OCH_2CH$_2$); 3.41 (*t*, OCH$_2$CH_2); 2.71 (*s*, Ac). Anal. calc. for $C_{22}H_{18}N_6O_4$ (430.4): C 61.39, H 4.21, N 19.52; found: C 61.07, H 4.27, N 19.64.

14. N-*{Methyl-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-yl}acetamide* (**29**). As described in *Exper. 7.1*, with N^2-acetyl-7-methylpterin (**13**; 0.22 g, 1 mmol): 0.252 g (86%) of **29**. Colorless crystals. M.p. 213–215°. R_f ($CHCl_3$/MeOH 9:1) 0.72. ^{1}H-NMR ($CDCl_3$): 8.65 (*d*, H–C(6)); 8.21 (*d*, 2 H_o to NO_2); 8.17 (br. *s*, NH); 7.54 (*d*, 2 H_m to NO_2); 4.88 (*t*, OCH_2CH$_2$); 3.40 (*t*, OCH$_2$CH_2); 2.81 (*s*, Me–C(7)); 2.70 (*s*, Ac). Anal. calc. for $C_{17}H_{16}N_6O_4$ (368.4): C 55.43, H 4.38, N 22.81; found: C 55.33, H 4.49, N 22.39.

15. N-*{6,7-Dimethyl-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-yl}acetamide* (**30**). As described in *Exper. 7.1*, with **15** (0.232 g, 1 mmol): 0.272 g (74%) of **30**. Colorless crystals. M.p. 220–222° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.46. ^{1}H-NMR ($CDCl_3$): 8.21 (*d*, 2 H_o to NO_2); 8.05 (br. *s*, NH); 7.54 (*d*, 2 H_m to NO_2); 4.87 (*t*, OCH_2CH$_2$); 3.39 (*t*, OCH$_2$CH_2); 2.77 (*s*, Me–C(7)); 2.75 (*s*, Me–C(6)); 2.68 (*s*, Ac). Anal. calc. for $C_{18}H_{18}N_6O_4$ (382.4): C 56.54, H 4.74, N 21.98; found: C 56.04, H 4.70, N 21.55.

16. N-*{4-[2-(4-Nitrophenyl)ethoxy]-6,7-diphenylpteridin-2-yl}acetamide* (**31**). As described in *Exper. 7.1*, with **17** (0.416 g, 1 mmol) at 75–80° for 24 h. CC gave as the first fraction **37** (see *Exper. 22*) and as the second, main fraction 0.368 g (69%) of **31**. Colorless crystals. M.p. 255–257°. R_f ($CHCl_3$/MeOH 9:1) 0.75. ^{1}H-NMR ($CDCl_3$): 8.23 (*d*, 2 H_o to NO_2); 8.12 (br. *s*, NH); 7.61–7.31 (*m*, 12 H, H_m to NO_2, arom. H); 4.87 (*t*, OCH_2CH$_2$); 3.40 (*t*, OCH$_2$CH_2); 2.69 (*s*, Ac). Anal. calc. for $C_{28}H_{22}N_6O_4 \cdot 1.5\ H_2O$ (533.6): C 63.04, H 4.69, N 15.74; found: C 63.28, H 4.37, N 15.44.

17. N^2,N^2-*Dimethyl-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-amine* (**32**). As described in *Exper. 7.1*, with N^2,N^2-dimethylpterin (**18**; 0.192 g, 1 mmol). Recrystallization from MeOH gave 0.288 g (84%) of **32**. Orange crystals. M.p. 192–194°. R_f ($CHCl_3$/MeOH 9:1) 0.74. ^{1}H-NMR ($CDCl_3$): 8.73 (*d*, H–C(7)); 8.39 (*d*, H–C(6)); 8.16 (*d*, 2 H_o to NO_2); 7.47 (*d*, 2 H_m to NO_2); 4.80 (*t*, OCH_2CH$_2$); 3.36 (*t*, OCH$_2$CH_2); 3.30 (*s*, Me_2N). Anal. calc. for $C_{16}H_{16}N_6O_3$ (340.3): C 56.47, H 4.74, N 24.96; found: C 56.34, H 4.69, N 24.50.

18. N^2,N^2,*6,7-Tetramethyl-4-[2-(4-nitrophenyl)ethyoxy]pteridin-2-amine* (**33**). As described in *Exper. 7.1*, with N^2,N^2,6,7-tetramethylpterin (**19**; 0.22 g, 1 mmol): 0.222 g (60%) of **33**. Yellow crystals. M.p. 190–191°. R_f ($CHCl_3$/MeOH 9:1) 0.43. ^{1}H-NMR ($CDCl_3$): 8.15 (*d*, 2 H_o to NO_2); 7.45 (*d*, 2 H_m to NO_2); 4.80 (*t*, OCH_2CH$_2$); 3.34 (*t*, CH_2CH_2); 3.28 (*s*, Me_2N); 2.64 (*s*, Me–C(7)); 2.61 (*s*, Me–C(6)). Anal. calc. for $C_{18}H_{20}N_6O_3$ (368.4): C 58.69, H 5.47, N 22.81; found: C 58.15, H 5.35, N 22.48.

19. N^2-*Methyl-4-[2-(4-nitrophenyl)ethyoxy]pteridin-2-amine* (**34**). As described in *Exper. 7.1*, with N^2-methylpterin (**20**; 0.178 g, 1 mmol): 0.236 g (72%) of **34**. Yellow crystals. M.p. 235°. R_f ($CHCl_3$/MeOH 9:1) 0.52. ^{1}H-NMR ($CDCl_3$): 8.80 (*s*, H–C(7)); 8.47 (*s*, H–C(6)); 8.20 (*d*, 2 H_o to NO_2); 7.51 (*d*, 2 H_m to NO_2); 5.37 (*m*, NH); 4.78 (*t*, OCH_2CH_2); 3.36 (*t*, OCH_2CH_2); 3.17 (*s*, Me_2N). Anal. calc. for $C_{15}H_{14}N_6O_3 \cdot 0.5\ H_2O$ (335.3): C 53.73, H 4.47, N 25.04; found: C 53.65, H 4.25, N 24.54.

20. N^2,7-*Dimethyl-4-[2-(4-nitrophenyl)ethoxy]pteridin-2-amine* (**35**). As described for *Exper. 7.1*, with N^2,7-dimethylpterin (**21**; 0.192 g, 1 mmol): 0.236 g (72%) of **35**. Yellow crystals. M.p. 230–231°. R_f ($CHCl_3$/MeOH 9:1) 0.70. ^{1}H-NMR ($CDCl_3$): 8.36 (*s*, H–C(6)); 8.20 (*d*, H_o to NO_2); 7.49 (*d*, 2 H_m to NO_2); 5.33 (*m*, NH); 4.77 (*t*, OCH_2CH_2); 3.35 (*t*, OCH_2CH_2); 3.16 (*s*, MeN); 2.69 (*s*, Me–C(7)). Anal. calc. for $C_{16}H_{16}N_6O_3$ (340.4): C 56.47, H 4.74, N 24.69; found: C 56.46, H 4.74, N 24.71.

21. N-*{4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-2-yl}*-N-*[2-(4-nitrophenyl)ethyl]acetamide* (**36**). During chromatographic workup in *Exper. 13*, a minor first fraction was obtained that yielded on evaporation 0.04 g (7%) of **36**. Colorless solid. M.p. 179–181°. R_f ($CHCl_3$/MeOH 9:1) 0.90. ^{1}H-NMR ($CDCl_3$): 9.52 (*d*, H–C(7)); 8.23 (*d*, 2 H_o to NO_2); 8.18 (*m*, 2 arom. H); 8.12 (br. *s*, NH); 8.08 (*d*, 2 H_o to NO_2); 7.64–7.60 (*m*, 3 arom. H); 7.62 (*d*, 2 H_m to NO_2); 7.53 (*d*, 2 H_o to NO_2); 4.82 (*t*, OCH_2CH_2); 4.49 (*t*, 2 NCH_2CH_2); 3.41 (*t*, OCH_2CH_2); 3.15 (*t*, NCH_2CH_2); 2.64 (*s*, Ac). Anal. calc. for $C_{30}H_{27}N_7O_6$ (581.6): C 61.96, H 4.68, N 16.86; found: C 61.94, H 4.50, N 16.63.

22. N-*{3,4-Dihydro-4-oxo-6,7-diphenylpteridin-2-yl}*-N-*[2-(4-nitrophenyl)ethyl]acetamide* (**37**). The first CC fraction obtained in *Exper. 16* was evaporated and the residue treated with Et_2O and dried: 0.031 g (6%) of **37**. Colorless powder. M.p. 247–249° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.94. ^{1}H-NMR ($CDCl_3$): 13.59 (br. *s*, NH); 8.09 (*d*, 2 H_o to NO_2); 8.12 (br. *s*, NH); 7.55–7.31 (*m*, 2 H_m to NO_2, 10 arom. H); 4.83 (*t*, NCH_2CH_2); 3.24 (*t*, NCH_2CH_2); 2.34 (*s*, Ac). Anal. calc. for $C_{28}H_{22}N_6O_4 \cdot 0.5\ H_2O$ (515.5): C 65.23, H 4.49, N 16.30; found: C 65.21, H 4.42, N 16.17.

23. *4-Methoxy*-N^2,N^2-*dimethylpteridin-2-amine* (**38**) [11]. As described in *Exper. 7.1* with N^2,N^2-dimethylpterin (**18**; 0.192 g, 1 mmol) and MeOH (25 mg, 0.75 mmol) instead of npe-OH: 0.141 g (69%) of **38**. Yellow crystals. M.p. 159–161°. R_f ($CHCl_3$/AcOEt 1:1) 0.36. ^{1}H-NMR ($CDCl_3$): 8.75 (*d*, H–C(7)); 8.40 (*d*, H–C(6)); 4.20 (*s*, MeO); 3.35 (*s*, Me_2N). Data: identical with those of authentic material.

24. *4-Methoxy*-N^2,N^2,*6,7-tetramethylpteridin-2-amine* (**39**) [11]. As described in *Exper. 7.1*, with N^2,N^2,6,7-tetramethylpterin (**19**; 0.22 g, 1 mmol) and MeOH (25 mg, 0.75 mmol) instead of npe-OH: 0.148 g (63%) of **39**. Yellow crystals. M.p. 145–147°. R_f ($CHCl_3$/MeOH 9:1) 0.36. ^{1}H-NMR ($CDCl_3$): 4.18 (*s*, MeO); 3.32 (*s*, Me_2N); 2.66 (*s*, Me–C(7)); 2.63 (*s*, Me–C(6)). Data identical with those of authentic material.

25. *4-[2-(4-Nitrophenyl)ethoxy]pteridin-2-amine* (**40**). Acetamide **22** (50 mg, 0.14 mmol) was heated under reflux in MeOH (6 ml) for 15 h. After cooling the precipitate was collected, washed with MeOH, and dried: 36 mg (82%) of **40**. Yellow crystals. M.p. 259–260°. R_f ($CHCl_3$/MeOH 9:1) 0.51. ^{1}H-NMR ((D_6)DMSO): 8.78 (*d*, H–C(7)); 8.43 (*d*, H–C(6)); 8.17 (*d*, 2 H_o to NO_2); 7.64 (*d*, 2 H_m to NO_2); 7.37 (br. *s*, NH_2); 4.72 (*t*, OCH_2CH_2); 3.30 (*t*, OCH_2CH_2). Anal. calc. for $C_{14}H_{12}N_6O_3$ (312.3): C 53.84, H 3.87, N 26.91; found: C 53.60, H 4.01, N 26.75.

26. *2-Amino-4-[2-(4-nitrophenyl)ethoxy]pteridine-6-methanol 6-Acetate* (**41**). Acetamide **26** (80 mg, 0.19 mmol) was stirred in MeOH (10 ml) at r.t. for 3 d. The precipitate was collected and recrystallized from MeOH: 44 mg (61%) of **41**. Yellow crystals. M.p. 203–204°. R_f ($CHCl_3$/MeOH 9:1) 0.54. ^{1}H-NMR ((D_6)DMSO): 8.84 (*d*, H–C(7)); 8.17 (*d*, 2 H_o to NO_2); 7.66 (*d*, 2 H_m to NO_2); 7.36 (br. *s*, NH_2); 5.21 (*s*, CH_2(6)); 4.71 (*t*, OCH_2CH_2); 3.31 (*t*, OCH_2CH_2); 2.11 (*s*, Ac). Anal. calc. for $C_{17}H_{16}N_6O_5$ (384.4): C 53.12, H 4.20, N 21.86; found: C 52.64, H 4.24, N 21.47.

27. *Pteridine-2,4-diamine* (**42**) [12]. A mixture of **22** (0.1 g, 0.38 mmol) in MeOH (30 ml) and aq. NH_3 soln. (10 ml) was stirred at r.t. for 24 h. The residue obtained on evaporation was recrystallized from H_2O to give 26 mg (56%) of **42**. Yellow powder. M.p. 313–315°. R_f (cellulose, PrOH/1% aq. NH_3 soln. 1:1) 0.45. Data: identical with those of authentic material.

28. *2,4-Diaminopteridine-6-methanol* (**43**) [13]. As described in *Exper. 27*, with **26** (80 mg, 0.18 mmol): 20 mg (54%) of **43**. Yellow crystalline powder. M.p. >300°. ^{1}H-NMR ((D_6)DMSO): 8.74 (*d*, H–C(7)); 7.65 (br. *s*, NH_2–C(2)); 6.55 (br. *s*, NH_2–C(4)); 5.42 (*t*, OH); 4.62 (*s*, CH_2(6)). Data: identical with those of authentic material.

29. N^2-*[2-(4-Nitrophenyl)ethyl]-6-phenylpteridine-2,4-diamine* (**45**). A mixture of **36** (80 mg, 0.14 mmol) in MeOH (80 ml) and aq. NH_3 soln. (70 ml) was stirred at r.t. for 2 d and then evaporated. The residue was purified by CC (silica gel, $CHCl_3$/MeOH 20:1): 24 mg (43%) of **45**. Yellow powder. M.p. 267–269°. R_f ($CHCl_3$/MeOH 9:1) 0.48. ^{1}H-NMR ($CDCl_3$): 9.25 (*s*, H–C(7)); 8.17 (*d*, 2 H_o to NO_2); 8.04 (*d*, 2 arom. H); 7.55–7.47 (*m*, 3 arom. H); 7.43 (*d*, 2 H_m to NO_2); 6.84 (br. *s*, NH); 5.22 (br. *s*, 2 NH_2); 3.49 (*t*, NCH_2CH_2); 3.11

(*t*, NCH_2CH_2). Anal. calc. for $C_{20}H_{17}N_7O_2 \cdot 0.25\ H_2O$ (391.9): C 61.29, H 4.50, N 25.02; found: C 61.10, H 4.61, N 24.83.

30. *6,7-Diphenylpteridine-2,4-diamine* (**44**) [12]. As described in *Exper. 29*, with **31** (69 mg, 0.14 mmol) (10 days): 25 mg (58%) of **44**. Yellow powder. M.p. 302–304°. R_f ($CHCl_3$/MeOH 9:1) 0.24. ^{1}H-NMR ($CDCl_3$): 7.57–7.28 (*m*, 10 arom. H, 1 NH_2); 5.19 (br. *s*, 1 NH_2). Anal. calc. for $C_{18}H_{14}N_6$ (314.4): C 68.78, H 4.49, N 26.73; found: C 68.51, H 4.59, N 26.26.

31. *2-[[(Dimethylamino)methylene]amino]pteridin-4-(3*H*)-one* (**46**). To a suspension of **1** (1 g, 6.1 mmol) in abs. DMF (100 ml) was added dimethylformamide dimethyl acetal (5 ml, 29.2 mmol), and then the mixture was stirred at r.t. for 24 h to give an orange soln. After evaporation, the residue was purified by CC ($CHCl_3$/MeOH 95:5), the main fraction evaporated, and the solid dried at 50°/high vacuum: 1.19 g (89%) of **46**. Yellow powder. M.p. 273° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.52. ^{1}H-NMR ((D_6)DMSO): 12.0 (br. *s*, NH); 8.77 (*s*, N=CH); 8.60 (*s*, H–C(7)); 8.46 (*s*, H–C(6)); 3.21, 3.07 (2 *s*, Me_2N). Anal. calc. for $C_9H_{10}N_6O$ (218.2): C 49.54, H 4.62, N 38.57; found: C 49.72, H 4.65, N 38.60.

32. *2-[[(Dimethylamino)methylene]amino]-6-(hydroxymethyl)pteridin-4(3*H*)-one* (**47**). As described in *Exper. 31*, with 6-(hydroxymethyl)pterin (**7**; 2 g, 10.2 mmol), DMF (200 ml), and dimethylformamide dimethyl acetal (10 ml, 75.1 mmol) (2 h). The main fraction of CC (silica gel, $CHCl_3$, $CHCl_3$/MeOH 10:1) was evaporated and the resulting solid recrystallized from $CHCl_3$/MeOH 8:1: 2.13 g (85%) of **47**. Pale yellow crystalline powder. M.p. 233° (dec.). R_f ($CHCl_3$/MeOH 4:1) 0.67. ^{1}H-NMR ((D_6)DMSO): 12.01 (br. *s*, NH); 8.79 (*s*, N=CH, H–C(7)); 5.63 (*t*, OH); 4.64 (*d*, CH_2(6)); 3.21, 3.08 (2 *s*, Me_2N). Anal. calc. for $C_{10}H_{12}N_6O_2$ (248.2): C 48.35, H 4.87, N 33.85; found: C 47.92, H 4.87, N 33.67.

33. *6-[(Acetyloxy)methyl]-2-[[(dimethylamino)methylene]amino]pteridin-4(3*H*)-one* (**48**). A mixture of **47** (0.26 g, 1.05 mmol), Ac_2O (2 ml), and pyridine (4 ml) was stirred at r.t. for 18 h and then evaporated and twice co-evaporated with toluene. The resulting foam recrystallized from dioxane/AcOEt 1:1: 0.23 g (76%) of **48**. Yellow crystalline powder. M.p. 222–224°. R_f ($CHCl_3$/MeOH 9:1) 0.45. ^{1}H-NMR ($CDCl_3$): 9.69 (br. *s*, NH); 8.95 (*s*, H–C(7)); 8.80 (*s*, N=CH); 5.32 (*s*, CH_2(6)); 3.21, 3.15 (2 *s*, Me_2N); 2.12 (*s*, Ac). Anal. calc. for $C_{12}H_{14}N_6O_3$ (290.3): C 49.65, H 4.86, N 28.95; found: C 49.57, H 4.99, N 29.32.

34. *2-[[(Dimethylamino)methylene]amino]-6-methylpteridin-4(3*H*)-one* (**49**). As described in *Exper. 31*, with 6-methylpterin (**4**; 0.5 g, 2.83 mmol), DMF (40 ml), and dimethylformamide dimethyl acetal (2.5 ml, 12 mmol) (3.5 h). The main fraction of CC (silica gel, $CHCl_3$/MeOH 95:5) was evaporated, and the residue recrystallized from $CHCl_3$/hexane 1:1: 0.464 g (71%) of **49**. Yellow crystalline powder. M.p. 230–232°. R_f ($CHCl_3$/MeOH 9:1) 0.5. ^{1}H-NMR ($CDCl_3$): 9.53 (br. *s*, NH); 8.97 (*s*, H–C(7)); 8.65 (*s*, N=CH); 3.24, 3.18 (2 *s*, Me_2N); 2.70 (*s*, Me–C(6)). Anal. calc. for $C_{10}H_{12}N_5O \cdot 0.5\ H_2O$ (241.2): C 49.78, H 5.42, N 34.82; found: C 50.26, H 5.14, N 34.60.

35. *2-[[(Dimethylamino)methylene]amino]-6-phenylpteridin-4(3*H*)-one* (**50**). As described in *Exper. 31*, with 6-phenylpterin (**10**; 0.5 g, 2.09 mmol) (3.5 h): 0.476 g (77%) of **50**. Yellow crystal powder. M.p. 274–276° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.50. ^{1}H-NMR ($CDCl_3$): 9.25 (br. *s*, NH); 9.20 (*s*, H–C(7)); 8.98 (*s*, N=CH); 8.12 (*d*, 2 arom. H); 7.52–7.43 (*m*, 3 arom. H); 3.22, 3.16 (2 *s*, Me_2N). Anal. calc. for $C_{15}H_{14}N_6O \cdot 0.5\ H_2O$ (308.4): C 59.41, H 4.99, N 27.71; found: C 59.74, H 5.12, N 27.58.

36. *2-[[(Dimethylamino)methylene]amino]-6,7-diphenylpteridin-4(3*H*)-one* (**51**). As described in *Exper. 31*, with 6,7-diphenylpterin (**16**; 0.631 g, 2 mmol), DMF (33 ml), and dimethylformamide dimethyl acetal (1.14 g, 9 mmol) (2 d). The resulting precipitate was washed and dried to give 0.495 g. The filtrate was evaporated and the residue purified by CC ($CHCl_3$/MeOH 50:1). The product fraction gave as a second crop 0.196 g. Total yield: 0.691 g (91%) of **51**. Yellow needles. M.p. 327–329° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.54. ^{1}H-NMR ($CDCl_3$): 9.03 (*s*, N=CH); 8.92 (br. *s*, NH); 7.55–7.37 (*m*, 12 arom. H); 3.23, 3.18 (2 *s*, Me_2N). Anal. calc. for $C_{21}H_{18}N_6O \cdot 0.5\ H_2O$ (379.4): C 66.48, H 5.03, N 22.15; found: C 66.65, H 4.94, N 21.91.

37. *2-[[(Dimethylamino)methylene]amino]-3-[2-(4-nitrophenyl)ethyl]pteridin-4(3*H*)-one* (**52**). To a mixture of **46** (0.218 g, 1 mmol), Ph_3P (0.394 g, 1.5 mmol), and 2-(4-nitrophenyl)ethanol (0.25 g, 1.5 mmol) in dry dioxane (15 ml) was added diisopropyl azodicarboxylate (0.304 g, 1.5 mmol) and then stirred at r.t. for 24 h. The soln. was evaporated and the residue purified by CC (silica gel, $CHCl_3$/AcOEt 1:1 (→ by-products triphenylphosphine oxide and diisopropyl hydrazinedicarboxylate), then $CHCl_3$/MeOH 95:5) to give the product fraction, which was evaporated. Recrystallization of the residue from MeOH gave 0.238 g (65%) of **52**. Pale yellow powder. M.p. 232–233°. R_f ($CHCl_3$/MeOH 9:1) 0.63. ^{1}H-NMR ($CDCl_3$): 8.87 (*s*, N=CH); 8.76 (*s*, H–C(7)); 8.57 (*d*, H–C(6)); 8.15 (*d*, 2 H_o to NO_2); 7.44 (*d*, 2 H_m to NO_2); 4.61 (*t*, NCH_2CH_2); 3.18 (*t*, NCH_2CH_2); 3.26, 3.21 (2 *s*, Me_2N). Anal. calc. for $C_{17}H_{17}N_7O_3$ (367.4): C 55.58, H 4.66, N 26.69; found: C 55.80, H 4.70, N 26.37.

38. *2-{[(Dimethylamino)methylene]amine}-3-methylpteridin-4(3H)-one* (**53**). 38.1. As described in Exper. 37, with **46** (0.218 g, 1 mmol) and MeOH instead of npe-OH. Recrystallization from MeOH gave 0.186 g (80%) of **53**. Yellow powder. M.p. 253–254°. R_f ($CHCl_3$/MeOH 9:1) 0.58. ^{1}H-NMR ($CDCl_3$): 8.95 (*s*, N=CH); 8.73 (*s*, H–C(7)); 8.55 (*d*, H–C(6)); 3.72 (*s*, Me–N(3)); 3.26, 3.22 (2 *s*, Me_2N). Anal. calc. for $C_{10}H_{12}N_6O$ (232.3): C 51.77, H 5.21, N 36.18; found: C 52.13, H 5.36, N 36.28.

38.2. A mixture of **1** (0.2 g, 1.23 mmol) and dimethylformamide dimethyl acetal (0.585 g, 4.92 mmol) in dry dioxane (10 ml) was refluxed for 5 h. After evaporation, the residue was purified by CC (silica gel, $CHCl_3$/MeOH 20:1). The main fraction was evaporated and the residue dried: 0.189 g (66%) of **53**. Yellowish solid foam.

39. *6-[(Acetyloxy)methyl]-2-{[(dimethylamino)methylene]amino}-3-[2-(nitrophenyl)ethyl]pteridin-4(3H)-one* (**54**). As described in *Exper. 37*, with **48** (0.29 g, 1 mmol). Recrystallization from MeOH gave 0.312 g (71%) of **54**. Yellow crystalline powder. M.p. 198–200°. R_f ($CHCl_3$/MeOH 9:1) 0.22. ^{1}H-NMR ($CDCl_3$): 8.83 (*s*, N=CH); 8.81 (*s*, H–C(7)); 8.13 (*d*, 2 H_o to NO_2); 7.38 (*d*, 2 H_m to NO_2); 5.35 (*s*, CH_2–C(6)); 4.59 (*t*, NCH_2CH_2); 3.14 (*t*, NCH_2CH_2); 3.21, 3.16 (2 *s*, Me_2N); 2.14 (*s*, Ac). Anal. calc. for $C_{20}H_{21}N_7O_5$ (439.4): C 54.67, H 4.82, N 22.31; found: C 54.32, H 4.90, N 22.31.

40. *2-{[(Dimethylamino)methylene]amino}-6-methyl-3-[2-(4-nitrophenyl)ethyl]pteridin-4(3H)-one* (**55**). As described in *Exper. 37*, with **49** (0.232 g, 1 mmol). Recrystallization from MeOH gave 0.306 g (79%) of **55**. Yellowish powder. M.p. 247–249°. R_f ($CHCl_3$/MeOH 9:1) 0.50. ^{1}H-NMR ($CDCl_3$): 8.81 (*s*, H–C(7)); 8.65 (*s*, N=CH); 8.15 (*d*, 2 H_o to NO_2); 7.47 (*d*, 2 H_m to NO_2); 4.63 (*t*, NCH_2CH_2); 3.21 (*t*, NCH_2CH_2); 3.21, 3.17 (2 *s*, Me_2N); 2.71 (*s*, Me–C(6)). Anal. calc. for $C_{18}H_{19}N_7O_3 \cdot H_2O$ (396.4): C 54.54, H 5.08, N 24.73; found: C 54.74, H 5.03, N 24.42.

41. *2-{[(Dimethylamino)methylene]amino}-3,6-dimethylpteridin-3(4H)-one* (**56**). 41.1. As described in *Exper. 38.1*, with **49** (0.232 g, 1 mmol): 0.2 g (81%) of **56**. Yellow powder. M.p. 233–234°. R_f ($CHCl_3$/MeOH 9:1) 0.37. ^{1}H-NMR ($CDCl_3$): 8.92 (*s*, N=CH); 8.63 (*s*, H–C(7)); 3.71 (*s*, Me–N(3)); 3.24, 3.20 (2 *s*, Me_2N); 2.71 (*s*, Me–C(6)). Anal. calc. for $C_{11}H_{14}N_6O$ (246.3): C 53.65, H 5.73, N 34.12; found: C 53.46, H 5.72, N 33.56.

41.2. A mixture of 6-methylpterin (**4**; 0.177 g, 1 mmol) and dimethylformamide dimethyl acetal (0.477 g, 4 mmol) in dry dioxane (10 ml) was refluxed for 3 h. After evaporation the residue was purified by CC (silica gel, $CHCl_3$/MeOH 20:1). The main fraction was evaporated and dried: 0.18 g (74%) of **56**. Yellowish solid foam.

42. *2-{[(Dimethylamino)methylene]amino}-6-phenyl-3-[2-(4-nitrophenyl)ethyl]pteridin-3(4H)-one* (**57**). As described in *Exper. 37*, with **50** (0.294 g, 1 mmol): 0.344 g (78%) of **57**. Yellowish powder. M.p. 230–232°. R_f ($CHCl_3$/MeOH 9:1) 0.8. ^{1}H-NMR ($CDCl_3$): 9.24 (*s*, H–C(7)); 8.87 (*s*, N=CH); 8.19 (*d*, 2 arom. H); 8.16 (*d*, 2 H_o to NO_2); 7.46 (*d*, 2 H_m to NO_2); 7.52–7.45 (*m*, 3 arom. H); 4.65 (*t*, NCH_2CH_2); 3.20 (*t*, NCH_2CH_2); 3.24, 3.20 (2 *s*, Me_2N). Anal. calc. for $C_{23}H_{21}N_7O_3 \cdot H_2O$ (461.5): C 59.86, H 5.02, N 21.25; found: C 60.01, H 5.26, N 21.34.

43. *2-{[(Dimethylamino)methylene]amino}-3-methyl-6-phenylpteridin-3(4H)-one* (**58**). As described in *Exper. 38.1*, with **50** (0.294 g, 1 mmol): 0.192 g (62%) of **58**. Yellow crystals. M.p. 272–274°. R_f ($CHCl_3$/MeOH 9:1) 0.76. ^{1}H-NMR ($CDCl_3$): 9.24 (*s*, H–C(7)); 8.93 (*s*, N=CH); 8.16 (*d*, 2 arom. H); 7.52–7.43 (*m*, 3 arom. H); 3.71 (*s*, Me–N(3)); 3.23, 3.19 (2 *s*, Me_2N). Anal. calc. for $C_{16}H_{16}N_6O$ (308.4): C 62.32, H 5.23, N 27.25; found: C 62.07, H 5.44, N 26.62.

44. *2-{[(Dimethylamino)methylene]amino}-3-ethyl-6-phenylpteridin-3(4H)-one* (**59**). As described in *Exper. 37*, with **50** (0.294 g, 1 mmol) and EtOH instead of npe-OH: 0.236 g (73%) of **59**. Yellowish powder. M.p. 235–237°. R_f ($CHCl_3$/MeOH 9:1) 0.67. ^{1}H-NMR ($CDCl_3$): 9.21 (*s*, H–C(7)); 8.98 (*s*, N=CH); 8.18 (*d*, 2 arom. H); 7.54 (*m*, 3 arom. H); 4.46 (*q*, NCH_2Me); 3.25, 3.21 (2 *s*, Me_2N); 1.35 (*t*, NCH_2Me). Anal. calc. for $C_{17}H_{18}N_6O$ (322.4): C 63.34, H 5.63, N 26.07; found: C 63.30, H 5.78, N 25.67.

45. *2-{[(Dimethylamino)methylene]amino}-6,7-diphenyl-3-[2-(4-nitrophenyl)ethyl]pteridin-3(4H)-one* (**60**). As described in *Exper. 37*, with **51** (0.37 g, 1 mmol). Recrystallization from MeOH gave 0.47 g (91%) of **60**. Yellow crystals. M.p. 298–299°. R_f ($CHCl_3$/MeOH 9:1) 0.77. ^{1}H-NMR ($CDCl_3$): 8.85 (*s*, N=CH); 8.16 (*d*, 2 H_o to NO_2); 7.44 (*d*, 2 H_m to NO_2); 7.56–7.29 (*m*, 10 arom. H); 4.66 (*t*, NCH_2CH_2); 3.23 (*t*, NCH_2CH_2); 3.21, 3.17 (2 *s*, Me_2N). Anal. calc. for $C_{29}H_{25}N_7O_3$ (519.6): C 67.04, H 4.86, N 18.87; found: C 67.05, H 5.11, N 18.73.

46. *2-{[(Dimethylamino)methylene]amino}-3-methyl-6,7-diphenylpteridin-3(4H)-one* (**61**). 46.1. As described in *Exper. 38.1*, with **51** (0.37 g, 1 mmol): 0.27 g (69%) of **61**. Yellow powder. M.p. 268–270°. R_f ($CHCl_3$/MeOH 9:1) 0.75. ^{1}H-NMR ($CDCl_3$): 8.97 (*s*, N=CH); 7.54–7.29 (*m*, 10 arom. H); 3.74 (*s*, Me–N(3)); 3.23, 3.21 (2 *s*, Me_2N). Anal. calc. for $C_{22}H_{20}N_6O \cdot 0.5\ H_2O$ (393.4): C 67.16, H 5.37, N 21.35; found: C 67.43, H 5.33, N 20.85.

46.2. A mixture of 6,7-diphenylpterin (**16**) (0.2 g, 0.63 mmol) and dimethylformamide dimethyl acetal (0.258 g, 2.2 mmol) in dry dioxane (10 ml) was refluxed for 4.5 h. After evaporation, the residue was purified by CC (silica gel, $CHCl_3$/MeOH 20:1). The main fraction was evaporated and recrystallized from MeOH: 0.19 g (79%) **61**. Yellow powder.

47. *2-Amino-3-[2-(4-nitrophenyl)ethyl]pteridin-4(3*H*)-one* (**62**). 47.1. A mixture of **52** (0.1 g, 0.27 mmol), MeOH (50 ml), and conc. aq. NH_3 soln. (50 ml) was stirred at r.t. for 5 d. The precipitate was collected, washed with H_2O, and dried: 80 mg (90%) of **62**. Colorless powder. M.p. $>340°$.

47.2. Treatment of **67** (see below; 0.1 g, 0.3 mmol) with MeOH/conc. aq. NH_3 soln. at r.t. for 24 h gave 60 mg (68%) of **62**. R_f ($CHCl_3$/MeOH 9:1) 0.29. ^{1}H-NMR ((D_6)DMSO): 8.66 (*s*, H–C(7)); 8.36 (*d*, H–C(6)); 8.17 (*d*, 2 H_o to NO_2); 7.74 (br. *s*, NH_2); 7.59 (*d*, 2 H_m to NO_2); 4.24 (*t*, NCH_2CH_2); 3.04 (*t*, NCH_2CH_2). Anal. calc. for $C_{14}H_{12}N_6O_3 \cdot 0.5\ H_2O$ (321.3): C 52.35, H 4.08, N 26.15; found: C 52.68, H 4.12, N 26.06.

48. *2-Amino-6-(hydroxymethyl)-3-[2-(4-nitrophenyl)ethyl]pteridin-4(3*H*)-one* (**63**). As described in *Exper. 47.1*, with **54** (0.1 g, 0.22 mmol) (2 d): 58 mg (73%) of **63**. Yellow powder. M.p. $>320°$ (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.13. ^{1}H-NMR ((D_6)DMSO): 8.71 (*s*, H–C(7)); 8.18 (*d*, 2 H_o to NO_2); 7.64 (br. *s*, NH_2); 7.56 (*d*, 2 H_m to NO_2); 5.54 (*t*, OH); 4.60 (*d*, CH_2(6)): 4.25 (*t*, NCH_2CH_2); 3.04 (*t*, NCH_2CH_2). Anal. calc. for $C_{15}H_{14}N_6O_4 \cdot 0.5\ H_2O$ (351.3): C 51.29, H 4.30, N 23.91; found: C 51.34, H 4.29, N 23.72.

49. *2-Amino-3-[2-(4-nitrophenyl)ethyl]-6-phenylpteridin-4(3*H*)-one* (**64**). As described in *Exper. 47.1*, with **57** (80 mg, 0.18 mmol) (2 days): 62 mg (89%) of **64**. Pale yellow powder. M.p. $>340°$. R_f ($CHCl_3$/MeOH 9:1) 0.42. ^{1}H-NMR ((D_6)DMSO): 9.31 (*s*, H–C(7)); 8.19 (*d*, 2 H_o to NO_2); 8.13 (*d*, 2 arom. H); 7.66 (br. *s*, NH_2); 7.62 (*d*, 2 H_m to NO_2); 7.55–7.45 (*m*, 3 arom. H); 4.27 (*t*, NCH_2CH_2); 3.08 (*t*, NCH_2CH_2). Anal. calc. for $C_{20}H_{16}N_6O_3 \cdot H_2O$ (406.4): C 59.11, H 4.46, N 20.68; found: C 58.79, H 4.51, N 20.72.

50. *2-Amino-3-methylpteridin-4(3*H*)-one* (**65**) [14]. Treatment of **53** (0.1 g, 0.44 mmol) with MeOH (8 ml) and conc. aq. NH_3 soln. (8 ml) for 24 h with stirring, evaporation and recrystallization of the residue from MeOH gave 40 mg (52%) of **65**. Yellowish powder. M.p. 325–326°. Data: identical with those of authentic material.

51. *2-Amino-3,6-dimethylpteridin-4(3*H*)-one* (**66**). As described in *Exper. 50*, with **56** (65 mg, 0.26 mmol): 36 mg (71%) of **66**. Yellowish powder. M.p. 277–278° (dec.). R_f ($CHCl_3$/MeOH 9:1) 0.10. ^{1}H-NMR ((D_6)DMSO): 8.57 (*s*, H–C(7)); 7.43 (br. *s*, NH_2); 3.37 (*s*, Me–N(3)); 2.49 (*s*, Me–C(6)). Anal. calc. for $C_8H_9N_5O \cdot H_2O$ (209.2): C 45.93, H 5.29, N 33.48; found: C 45.85, H 5.32, N 33.69.

52. N-*{3,4-Dihydro-3-[2-(4-nitrophenyl)ethyl]-4-oxopteridin-2-yl}acetamide* (**67**). A mixture of **62** (0.1 g, 0.32 mmol), Ac_2O (10 ml), and AcOH (4 ml) was refluxed for 4 h, then concentrated to 1/3 of the volume, and cooled. The precipitate was washed with AcOEt and dried: 58 mg (51%) of **67**. Colorless crystals. M.p. 199–200°. ^{1}H-NMR ($CDCl_3$): 13.92 (br. *s*, NH); 8.68 (*s*, H–C(7)); 8.65 (*d*, H–C(6)); 8.19 (*d*, 2 H_o to NO_2); 7.50 (*d*, 2 H_m to NO_2); 4.53 (*t*, NCH_2CH_2); 3.15 (*t*, NCH_2CH_2); 2.15 (*s*, Ac). Anal. calc. for $C_{16}H_{14}N_6O_4$ (354.3): C 54.24, H 3.98, N 23.72; found: C 53.63, H 4.16, N 23.40.

53. *2-[(Aminomethylene)amino]-3-methylpteridin-4(3*H*)-one* (**68**). A soln. of **53** (0.1 g, 0.43 mmol) in MeOH (16 ml) and conc. aq. NH_3 soln. (16 ml) was stirred for 10 min. The precipitate was washed with MeOH: 40 mg (46%) of **68**. Pale brownish crystal powder. M.p. 267–268°. R_f (cellulose, 3% sodium citrate soln.) 0.37. ^{1}H-NMR ((D_6)DMSO): 8.76 (*s*, H–C(7)); 8.75–8.68 (*m*, N=CH, NH); 8.52 (*d*, H–C(6)); 8.43 (br. *s*, NH); 3.51 (*s*, Me–N(3)). Anal. calc. for $C_8H_8N_6O$ (204.2): C 47.04, H 3.95, N 41.15; found: C 47.06, H 4.11, N 40.29.

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