Acylation of a 6-(Methylamino)-5-nitrosopyrimidine and 1,3-Dipolar Cycloaddition of an 8-Methylisoxanthopterin *N(5)*-Oxide. Synthesis of *C(6)*,*N(8)*-Disubstituted Isoxanthopterins

by **Thomas Steinlin** and **Andrea Vasella***

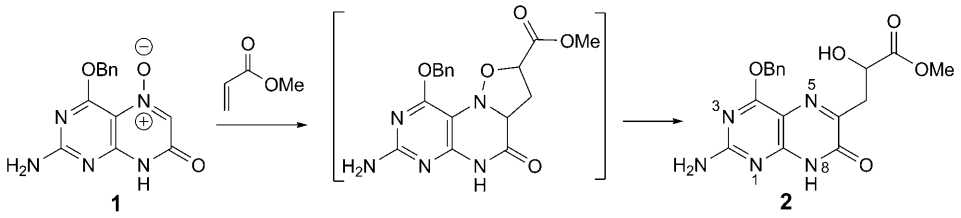
Laboratorium für Organische Chemie, Departement Chemie und Angewandte Biowissenschaften, ETH Zürich, HCI, CH-8093 Zürich
(e-mail: vasella@org.chem.ethz.ch)

Acylation of 2-amino-4-(benzyloxy)-6-(methylamino)-5-nitrosopyrimidine (**5**) with acetic anhydride or chloroacetic anhydride in the presence of 4-(dimethylamino)pyridine (DMAP) led to the *C(2)*-acylamino derivatives **6** and **7**, respectively. In the absence of a base, acetylation did not lead to a product, while chloroacetylation led to the 6-chloropteridine **11**. Chloroacetylation in the presence of *Hünig*'s base provided the pteridinone *N(5)*-oxide **10**, suggesting that acylation of **5** is readily reversible, and that the unfavourable equilibrium must be displaced by a follow-up reaction to trap the acylation product. Acylation of **5** with hexadienoyl chloride, followed by intramolecular *Diels–Alder* reaction, provided the pteridinone **12**. A high yielding 1,3-dipolar cycloaddition of the acylnitrone **10** to electron-poor and electron-rich dipolarophiles, followed by spontaneous N,O-bond cleavage, gave the *C(6)*-substituted pteridinones **19a**–**19e** that were deprotected to the pteridine-4,7(3*H*,8*H*)-diones **20a**–**20e**. Substitution of the 6-chloropterin **11** provided the 6-morpholinopteridine **25**. *Sonogashira* coupling yielded the fluorescent [(pteridin-6-yl)ethynyl]-glucopyranoside **26**, 6-ethynylpteridine **28**, and 6,6′-(ethynediyl)-bispteridine **29**. The alkyne **28** reacted with Me_3SiCl and LiBr in MeCN to produce the bromoalkene **31**.

Introduction. – We described new routes to 6-substituted pteridines based on intramolecular *Diels–Alder* cycloadditions, ene-reactions, and condensations of *N(6)*-acylated or *N(6)*-alkylated 6-amino-5-nitrosopyrimidines [1–4]. We also showed that the pteridinone *N(5)*-oxides, resulting from the condensation of 6-amino-5-nitrosopyrimidines with chloroacetic acid anhydride ($(ClCH_2CO)_2O$) react as acylnitrones. The course of their [3+2] cycloaddition to acceptor-substituted dipolarophiles is illustrated in *Scheme 1* by the addition of **1** to methyl acrylate. This reaction provides **2**, resulting from a spontaneous eliminative cleavage of the N,O bond of the initially formed isoxazolidine, and thus constitutes a new, high-yielding access to isoxanthopterins **2** possessing a functionalised side chain at C(6) [5]. The poor solubility of these isoxanthopterins was assumed to result from a favourable intermolecular H-bonding of the DADA motif involving HN(2′), N(1′), HN(8′) and O=C(7′) of the products of type **2**. This hypothesis prompts to investigate the formation and 1,3-dipolar cycloaddition of *N(8)*-alkyl derivatives of **1**. The simplest ones, *N(8)*-methylpteridinone *N(5)*-oxides, should be obtained by an intramolecular condensation of 6-[(chloroacetyl)(methyl)-amino]-5-nitrosopyrimidines. We were thus interested in the cycloaddition of *N(8)*-alkylated pteridinone *N(5)*-oxides and the solubility of the resulting products, in the formation of the pteridinone *N*-oxides by condensation of 6-[(alkyl)(chloroacetyl)-amino]-5-nitrosopyrimidines, and in the *N*-acylation leading to these amides. As we had

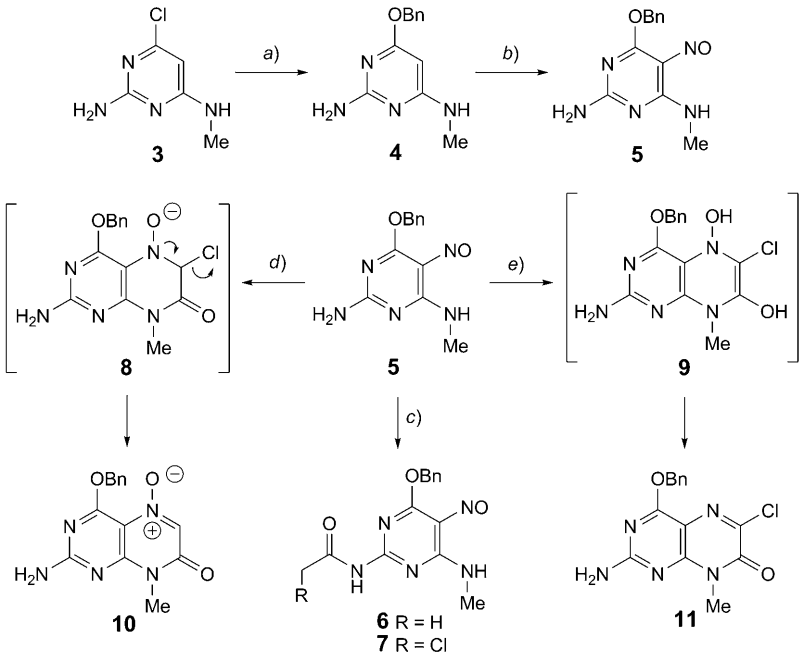
assumed that the C(6)–*N*-acylation of 6-amino-5-nitrosopyrimidines proceeds *via O*-acylation of the NO group and intramolecular acyl transfer, we had to consider that it may be affected by C(6)–*N*-alkylation.

Scheme 1



Results and Discussion. – The synthesis of the desired *N*(8)-methylisoxanthopterin *N(5)*-oxide **10** started by transforming the known 2-amino-6-chloro-4-(methylamino)-pyrimidine (**3**) [6] into the benzyl ether **4** by treatment with benzyl alcoholate in DMSO (*Scheme 2*). Nitrosation of **4** provided the 6-(methylamino)-5-nitrosopyrimidine **5** that was thus obtained in a yield of 81% from 2-amino-4,6-dichloropyrimidine.

Scheme 2

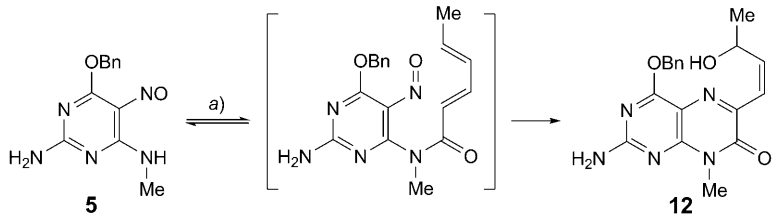


a) Benzyl alcohol (BnOH), NaH, DMSO; 90%. *b*) $NaNO_2$, $AcOH/H_2O$ 3:7; 90%. *c*) Ac_2O, 4-(dimethylamino)pyridine (DMAP), THF; 88% of **6**. Chloroacetic anhydride ($(ClCH_2CO)_2O$), DMAP, THF; 71% of **7**. *d*) $(ClCH_2CO)_2O$, $^iPr_2EtN$, THF; 78%. *e*) $(ClCH_2CO)_2O$, THF; 82%.

Acylation of **5** required a more subtle control of reaction conditions than we had anticipated. While Ac_2O in THF did not appear to react with **5**, addition of 4-(dimethylamino)pyridine (DMAP) led to the acetamide **6**. A similar DMAP promoted treatment of **5** with $(ClCH_2CO)_2O$ gave the 2-chloroacetamide **7** (77%), while replacing DMAP by *Hünig*'s base resulted in the desired 8-methylpteridin-7-one *N(5)*-oxide **10** (78%). In contradistinction to the treatment of **5** with Ac_2O, treatment with $(ClCH_2CO)_2O$ in THF (in the absence of an added base) gave rise to the 6-chloropteridin-7-one **11** (82%).

That acetylation of **5** with Ac_2O did not lead to the *C(4)*-acetamido derivative, while the analogous chloroacetylation provided **11** is rationalised by postulating an unfavourable equilibrium between the *C(4)*-acetamide or chloroacetamide and the starting material **5** that can be shifted for the chloroacetamide by intramolecular addition of the enolised chloroacetamide to the NO group, enolisation to generate **9**, and irreversible β-elimination to cleave the N,O bond. *Hünig*'s base is assumed to similarly shift the equilibrium by deprotonating the hydroxylamino group and, thus, *via* **8**, promote the elimination of chloride to generate the nitrone **10**. It is not clear if DMAP acts by deprotonating the C(2)–NH_2 group and/or by generating an intermediate (chloro)ketene, (chloro)acetylation of C(2)–NH_2 being irreversible. Acylation of **5** at the C(4)–*N*HMe group differs from the one of analogous nitrosopyrimidines possessing a C(4)–NH_2 group that leads to amides that are sufficiently stable to be isolated in spite of their activation by conjugation with the NO group. This difference is explained by pointing out that the *N*-acyl-*N*-methyl amino group can no longer form a favourable intramolecular H-bond from the acylamino NH to the NO group [7][4]. To substantiate the hypothesis that the C(4)–*N*HMe group is reversibly acylated, and that the amide can be trapped by an irreversible follow-up reaction, we treated **5** with hexadienoyl chloride (*Scheme 3*).

Scheme 3



a) Hexa-2,4-dienoyl chloride, $^iPr_2EtN$, THF; 84%.

Similarly as reported in [4], the intermediate amide reacted by a hetero-*Diels–Alder* reaction and eliminative N,O bond cleavage to provide the pteridinone **12** that was isolated in a yield of 84%.

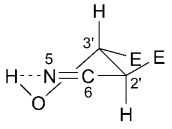
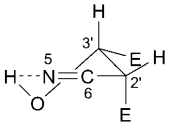
The 4-(benzyloxy)-6-(methylamino)pyrimidine **4** is characterised by the H–C(5) *s* at 5.06 ppm, the *q* at 6.47 ppm ($J = 4.9$ Hz) and *d* at 2.67 ppm ($J = 4.8$ Hz) of the MeNH group, and by the IR NH bands at 3428, 3344, and 3201 cm^{-1}. The nitrosation of **4** to **5** was accompanied by a change from colourless to dark purple and by a change of the chemical shift for the *q* ($J = 5.1$ Hz) of the MeNH group from 6.47 to 11.12 ppm.

The shift to lower field is due to a strong H-bond from the NH to the N=O group. C(2)–NH_2 resonate as two *s*, at 8.02 and 8.00 ppm. The regioselectivity of the acylation of **5** to the C(2)–*N*-acyl derivatives **6** and **7** is evidenced by the unchanged H,H-coupling of the MeNH group and by a signal for HN–C(2) at 10.80 and 11.22 ppm, respectively. The structure of the nitrone **10** is evidenced by a HR-MALDI mass spectrum, elemental analysis, NH bands at 3425, 3339, and 3225 cm^{-1}, the signal of the H–C(6) at 7.40 ppm, and the one of C(6) at 124.05 ppm. This signal is shifted to higher fields by *ca.* 25 ppm, as compared to those of **19a**–**19e** due to its increased electron density at C(6). The structure of the 6-chloropterin **11** is supported by a UV maximum at 359 nm ($\log \varepsilon = 4.24$), the HR-EI-MS signal at *m*/*z* 319.0656 for M^+(^{37}Cl) with 30% intensity of the parent signal at *m*/*z* 317.0673, and by elemental analysis. The ^{1}H-NMR spectrum of the (*Z*)-allylic alcohol **12** shows a *dd* at 6.66 ppm for H–C(1′) ($J = 12.0$ and 1.5 Hz) and a *dd* for H–C(2′) at 5.97 ppm ($J = 12.0$ and 4.2 Hz), a *m* for H–C(3′) between 5.19 and 5.13 ppm, a *d* ($J = 6.3$ Hz) at 1.20 ppm for the Me group, and a *d* ($J =$ 4.2 Hz) for the OH group at 4.88 ppm. In the UV spectrum, the conjugation of the pteridine ring system and the alkenyl group is evidenced by a maximum at 376 nm ($\log \varepsilon = 4.17$).

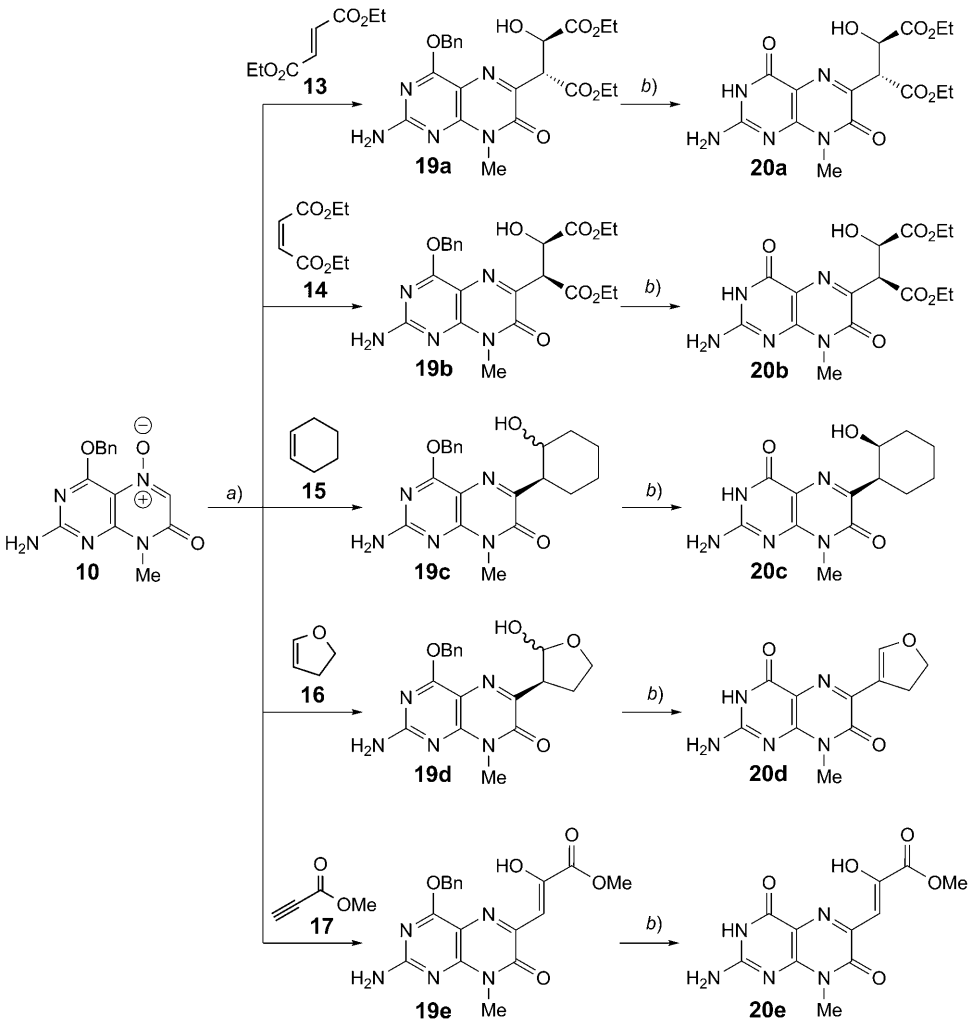
The 1,3-dipolar cycloadditions of the nitrone **10** were performed by heating in toluene, proceeded in yields between 79 and 90%, and yielded essentially a single regioisomer [8] (*Scheme 4*). To demonstrate the expected stereoselectivity of the 1,3-dipolar cycloaddition, we determined the configuration of the cycloadducts to diethyl fumarate and diethyl maleate (**13** and **14**, resp.). The ^{1}H-NMR spectra of **19a** and **19b** in $CDCl_3$ show considerable differences (*Table 1*). Presumably, the OH group in both products forms a persistent H-bond to N(5), leading to a six-membered ring. The coupling constant between H–C(3′) and the OH group is 3.3 Hz for both compounds, as expected for a *gauche* configuration, suggesting that H–C(3′) occupies a pseudoaxial position in both **19a** and **19b**. The coupling constant of 10.5 Hz between H–C(2′) and H–C(3′) of **19a** indicates a *trans*-diaxial configuration and the one of 5.3 Hz for **19b** a *cis* configuration, evidencing the stereoselective cycloaddition of the nitrone **10**.

The reaction of cyclohexene (**15**) with **10** yielded 89% of the *cis*-(2-hydroxycyclohexyl)pteridine **19c** in 89% yield. The OH group resonates at 4.48 ppm as a *dd* ($J = 3.3$, 1.0 Hz), coupling with H–C(2′) (4.21 ppm, br. *s*) and H_{ax}–C(3). H–C(1′) gives rise to

Table 1. *Configuration and Conformation of the Diesters* **19a** *and* **19b**, *Relevant Chemical Shifts, and Coupling Constants in* $CDCl_3$

Substituent	 **19a**		 **19b**	
	δ(H)	J_{vic}	δ(H)	J_{vic}
HO	4.68	3.3	4.78	3.3
H–C(2′)	4.91	10.6	4.16	5.3
H–C(3′)	4.97	10.5, 3.3	4.92	5.3, 3.3

Scheme 4



a) Dipolarophile, toluene, reflux; 90% of **19a**, 89% of **19b**, 89% of **19c**, 79 of **19d**; 85% of **19e**. *b*) Me_3SiCl, LiBr, MeCN; 93% of **20a**, 93% of **20b**, 89% of **20c**, 77% of **20a**, 97% of **20a**.

a *ddd* ($J = 12.3$, 3.3, 2.2 Hz) at 3.05 ppm. Cycloaddition to 2,3-dihydrofuran (**16**) resulted in the formation a 1:1 mixture (79%) of *cis*/*trans*-isomers of the (2-hydroxytetrahydrofuran-3-yl)pteridinone **19d**. The reaction of **10** with methyl propiolate led to the fully enolized α-ketoester **19e** (85%) that was crystallised from hot (D_6)DMSO. The crystal structure (*Fig. 1*) shows a strong intramolecular H-bond (N⋯O distance 2.58 Å) that is evidenced in solution by a *s* at 13.76 ppm for OH. The structure of **19e** is further evidenced by a *s* at 6.87 ppm for H–C(2), a *d* resonating at 98.47 ppm for C(3), and a *s* for C(2) at 153.64 ppm. Similar to the crystal structure of

the pteridine dimer **29** (compare *Fig. 2*), two molecules of **19e** are bridged *via* H-bonds to two DMSO molecules[1]).

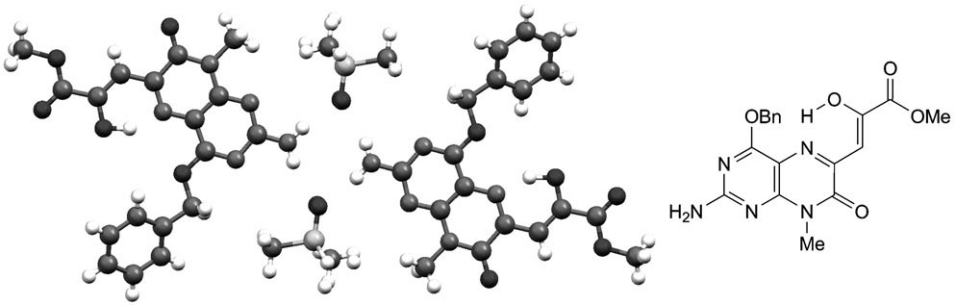


Fig. 1. *Crystal structure of* **19e** · *DMSO*[1]) *showing the intra- and intermolecular H-bonds between two molecules of* **19e** *and two molecules of DMSO*

As expected, the solubility of *N(8)*-methylpteridines improved dramatically: whereas the *N(8)*-unsubstituted pteridines are only soluble in DMSO, their *N*-Me analogues are well soluble in CH_2Cl_2, $CHCl_3$, MeOH, AcOEt, THF, and dioxane.

The pteridinones **19a**–**19e** were debenzylated with *in situ* generated Me_3SiBr to yield 89–96% of the pteridine-4,7(3*H*,8*H*)-diones **20a**–**20e**. Their structures were established on the basis of their IR, ^{13}C- and ^1H-NMR, and HR-MALDI mass spectra, and by the similarity of the UV spectra to those of **19a**–**19e** (except **19d**).

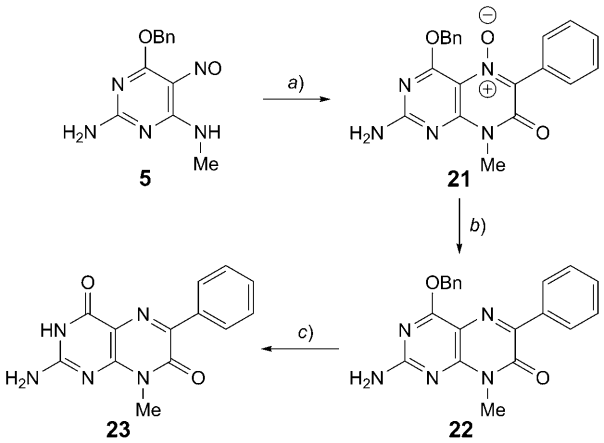
Deprotection of **19d** by *in situ* generated Me_3SiBr was accompanied by dehydration and led to the 6-(2,3-dihydrofuranyl)pteridine **20d**. The structure of **20d** is characterised by a bathochromic shift (from 341 to 379 nm) in the UV spectrum compared to **19d**, a t ($J = 1.6$ Hz) at 7.87 ppm for H–C(5′) showing the allylic coupling, and corresponding resonances at 140.90 and 114.93 ppm for C(5′) and C(4′), respectively. The pteridinediones **20a**–**20e** are well soluble in MeOH and in aqueous MeOH, but not in H_2O. The diethyl esters **20a** and **20b** are well soluble in CH_2Cl_2, $CHCl_3$, and AcOEt.

To test whether also 6-substituted pteridine 5-oxides undergo 1,3-dipolar cycloadditions, we synthesized the 6-phenylpteridinedione **21** (*Scheme 5*). Treating **5** with 2-chloro-2-phenylacetyl chloride in the presence of *Hünig*'s base yielded 82% of **21**. Heating of **21** in the presence of dipolarophiles, such as phenylmaleimide, diethyl fumarate, or *N*-(cyclopent-1-enyl)morpholine led to a single strongly fluorescent compound. In contrast to 2-phenyl-3*H*-indol-3-one 1-oxide that reacts with dipolarophiles by forming 1,3-dipolar addition products [9], **21** reacted by only forming the deoxygenated product **22** in 82% yield; products resulting from the dipolarophiles were not analysed. Debenzylation of **22** by *in situ* generated Me_3SiBr gave 6-phenylpteridine-4,7-dione **23** in 96% yield.

---

[1]) The crystallographic data have been deposited with the *Cambridge Christallographic Data Centre* as deposition No. CCDC-715315 for **19e** and CCDC-715316 for **29**. Copies of the data can be obtained free of charge *via* http://www.ccdc.cam.ac.uk/data_request/cif (or from the *Cambridge Christallographic Data Centre*, 12 Union Road, Cambridge CB21EZ (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

Scheme 5



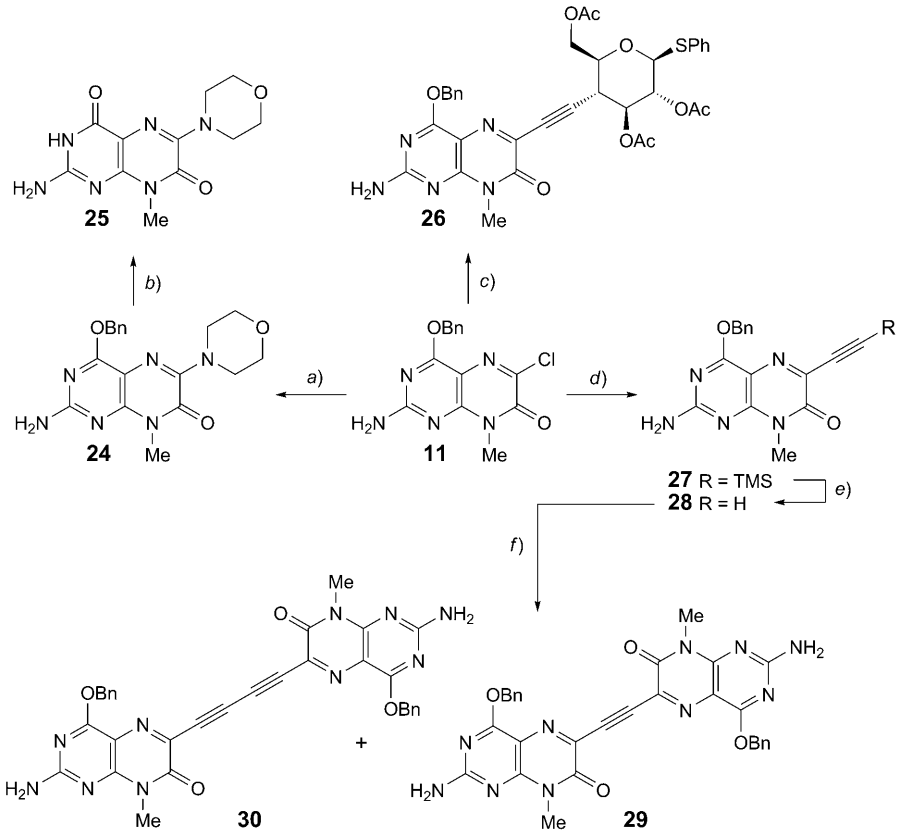
a) 2-Chloro-2-phenylacetyl chloride, $^{i}Pr_2EtN$, THF, 0–23°, 1 h, 82%. *b*) Phenylmaleimide, toluene, reflux, 0.5 h, 82%. *c*) Me_3SiCl, LiBr, MeCN, 0° – r.t.; 96%.

The pteridines **21**–**23** were characterised by elemental analysis, IR, ^{1}H- and ^{13}C-NMR, UV, and HR-mass spectra. The UV spectra show maxima at 366, 370, and 369 nm for **21**, **22**, and **23**, respectively, evidencing the conjugation between the heterocycle and the Ph substituent. Similarly to **10**, the ^{13}C-NMR spectra show a *s* at 129.50 ppm for C(6) of the pteridine 5-oxide **21** and a *s* at 144.12 ppm for the pteridine **22**, while **23** is characterised by a NH *s* at 11.19 ppm, a br. NH_2 *s* at 7.22 ppm, and a *s* for the *N*-Me group at 3.52 ppm.

6-Chloropterin and 2,4-diamino-6-chloropteridine were synthesised by treating pterin 8-oxide and 2,4-diaminopteridine 8-oxide, respectively, with AcCl or phosphorous oxychloride [10]. The chloride was substituted by a variety of oxo- and thionucleophiles. Treatment with amines resulted in decomposition of the starting material. In their studies towards the synthesis of the molybdenum cofactor, *Taylor et al.* used 6-chloropterin in *Sonogashira* cross-couplings [11–14]. As 6-Cl derivatives of isoxanthopterins were not known, we subject the more highly electrophilic 6-chloropteridine **11** to a few substitution reactions.

Heating **11** in the presence of morpholine in toluene yielded 97% of 6-morpholinopteridine **24** (*Scheme 6*). The same product was obtained when the nitrone **10** was heated in the presence of morpholine. Under these conditions, the reaction time could be reduced from 4.5 to 1.5 h. Deprotection with *in situ* generated Me_3SiBr in MeCN gave pteridinedione **25**. Treating **11** with phenyl 2,3,6-tri-*O*-acetyl-4-deoxy-4-ethynyl-1-thio-*β*-D-glucopyranoside [15][16] under conditions of the *Sonogashira* reaction gave the 6-ethynylpteridine **26**. It was isolated in 89% yield by silica-gel chromatography. Recrystallisation in $^{i}PrOH$ and toluene gave an analytically pure sample of a strongly fluorescent product. The strong fluorescence of **26** suggested to also prepare an ethynediyl-bridged dimer, and (trimethylsilyl)acetylene was coupled to the 6-chloropteridine **11** to provide **27** in 92% yield. Desilylation with wet Bu_4NF in THF [17] gave the monosubstituted alkyne **28** that was treated with 6-chloropterin **11**

Scheme 6



a) Morpholine, toluene; 97%. *b*) Me_3SiCl, LiBr, MeCN; 93%. *c*) Phenyl 2,3,6-tri-*O*-acetyl-4-deoxy-4-ethynyl-1-thio-β-D-glucopyranoside, $Pd(AcO)_2$, Ph_3P, CuI, MeCN/Et_3N 2:3; 89%. *d*) (Trimethylsilyl)-acetylene, $Pd(AcO)_2$, Ph_3P, CuI, MeCN/Et_3N 2:3; 92%. *e*) $Bu_3NF \cdot 3\,H_2O$, THF; 98% [19]. *f*) **11**, $Pd(AcO)_2$, Ph_3P, CuI, MeCN/Et_3N 2:3; 49% of **29**, 32% of **30**.

under *Sonogashira* conditions to yield 49% of the ethynediyl-bridged dimer **29** besides the homodimer **30** (32%) resulting from of a *Glaser* coupling. The oxidative dimerisation was avoided by effecting the transformation of **11** to **29** in one pot. Subjecting the 6-chloropterin **11** to (trimethylsilyl)acetylene, $Bu_4NF \cdot 3\,H_2O$, and again to **11** in the presence of CuI and Pd^0 yielded exclusively the desired bispteridine **29** in an overall yield of 47%. Crystals suitable for X-ray crystallography were obtained by allowing a hot solution of **29** in DMSO to cool to room temperature. In the crystal structure (*Fig. 2*), the two pteridine moieties are only 1.6° out of a common plane. Similar to the crystal structure of the pteridine **19e**, two molecules of **29** are bridged by H-bonding from NH_2 to two molecules of DMSO, to form bands that are stacked at a distance of 3.51 Å.

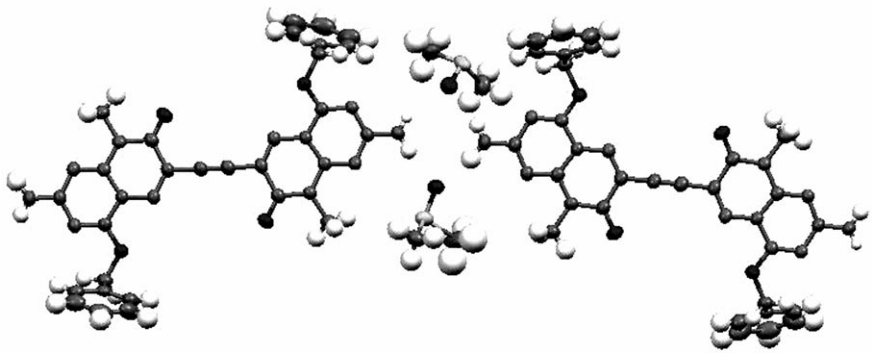
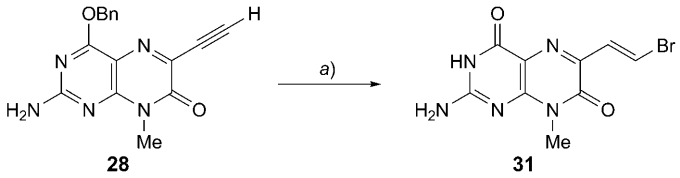


Fig. 2. *Crystal structure of* **29**·*3 DMSO* (ORTEP drawing of two H-bonded molecules of **29** and two molecules of DMSO)[1])

Debenzylation of **28** in the presence of Me_3SiBr was accompanied by the addition of HBr to the C≡C bond (*Scheme 7*), illustrating the strongly electrophilic character of the ethynyl derivative **28**. The structure of **31** is evidenced by two H *d*s ($J = 13.4$ Hz), one for H–C(1′) at 7.57 ppm, and one for H–C(2′) at 6.92 ppm, the coupling constant evidencing the (*E*)-configuration of the C=C bond. C(1′) is resonating at 130.1 ppm, C(2′) at 124.66 ppm, and the UV spectrum shows a maximum at 376 nm ($\log \varepsilon = 4.38$).

Scheme 7



a) Me_3SiCl, LiBr, MeCN; 72%.

Pteridines are used for labelling experiments in biochemistry and molecular biology [18–21], since the fluorescence maxima of pteridines are well separated from those of natural nucleosides and aromatic amino acids. The close structural relation of pteridine-*N*(1) and *N*(8) nucleosides to pyrimidine and purine nucleosides prompted *Pfleiderer* and co-workers [22] and *Hawkins et al.* [18] to introduce pteridine nucleosides as fluorescent markers into oligonucleotides to study stacking effects and oligonucleotide interactions during hybridisation and intermolecular loop formation. The quantum yields of selected pteridines in MeOH are listed In *Table 2*. The independence of the quantum yield from the presence or absence of the BnO group is shown by comparison of **22** and **23**.

The excitation and emission spectra of the monosubstituted alkyne **26** and the disubstituted analogue **28** are very similar (*Fig. 3*), indicating a weak dependence of the fluorescence on the ethynyl substituents. In the excitation and emission spectra of the (ethynediyl)bispteridine **29**, one notices a blue shift by 68 nm and a narrowing of *Stoke*'s shift by 4 nm.

Table 2. *Quantum Yield of Selected Pteridines*[a])

	19a	**19e**	**20d**	**19d**	**22**	**23**	**26**	**27**
Q	0.14	0.38	0.26	0.36	0.38	0.39	0.34	0.38
Q_R	0.25	0.65	0.45	0.62	0.66	0.68	0.59	0.66

[a]) *Q:* Absolute quantum yield. Q_R: quantum yield relative to quinine. $\lambda_{ex} = 350$ nm. Emission integrated from 380 and 520 nm. Measured in MeOH. Optical density ≈ 0.05.

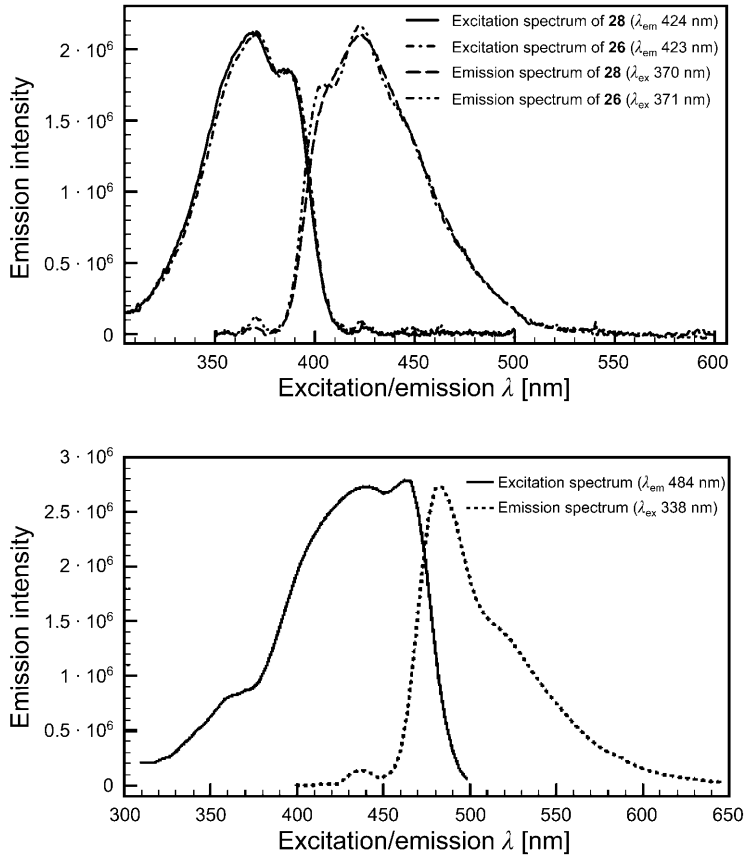


Fig. 3. *Excitation and emission spectra of* **26** *and* **28** (top), *and* **29** (bottom) *recorded in* CH_2Cl_2

We thank *Novartis AG*, Basel, for a fellowship, the *ETH-Zürich* for financial support, Dr. *Bruno Bernet* for checking the analytical data, and *Anaella Dumas* for the fluorescence data.

Experimental Part

General. Solvents were distilled before use. Reactions were carried out under N_2, unless stated otherwise. Qual. TLC: precoated silica-gel plates (*Merck* silica gel 60 F_{254}); detection under UV (254 nm). Flash chromatography (FC): silica gel *Fluka 60* (0.04 – 0.063 mm). M.p.: uncorrected. UV

Spectra: λ_{max} (log ε). FT-IR Spectra: neat (ATR), absorption in cm^{-1}. ^{1}H- and ^{13}C-NMR Spectra: chemical shifts δ in ppm rel. to Me_4Si as external standard, and coupling constants J in Hz. HR-MALDI-MS: in gentisic acid (=2,5-dihydroxybenzoic acid, DHB) or 3-hydroxypropionaldehyde (3-HPA) matrix.

4-(Benzyloxy)-6-(methylamino)pyrimidine-2,4-diamine (**4**). A soln. of BnOH (1 ml, 9.3 mmol) in DMSO (30 ml) was treated with 60% NaH in oil (242 mg, 6.07 mmol) and stirred for 20 min. To this mixture was added **3** (738 mg, 4.67 mmol) in a single portion, followed by heating to 90° for 5 h. The mixture was cooled to r.t. and poured on ice. The colourless precipitate was filtered off, and the aq. filtrate was extracted with CH_2Cl_2/MeOH 19:1 (3 × 100 ml). The combined org. layers were washed with brine (100 ml), and the solvent was evaporated to afford **4** (967 mg, 90%). A sample for analysis was obtained by sublimation at 120° and $< 10^{-3}$ mbar. R_f (AcOEt) 0.42. M.p. 150°. UV (MeOH, c = 0.09 mM): 212 (4.44), 268 (4.00). IR (ATR): 3428*m*, 3344*m*, 3201*m*, 2947*w*, 2872*w*, 2791*w*, 1650*m*, 1574*s*, 1503*m*, 1466*s*, 1453*s*, 1440*s*, 1407*m*, 1391*m*, 1353*s*, 1312*m*, 1288*m*, 1192*s*, 1093*m*, 1052*m*, 1023*m*, 968*w*, 911*w*, 873*w*, 852*w*, 833*w*, 792*s*, 765*m*, 743*m*, 700*m*, 688*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.38–7.33 (*m*, 5 arom. H); 6.47 (*q*, J = 4.9, NH); 5.96 (*s*, NH_2); 5.21 (*s*, PhCH_2); 5.06 (*s*, H–C(5)); 2.67 (*d*, J = 4.8, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 169.56 (br. *s*, C(2)); 165.78 (*s*, C(4)); 162.61 (*s*, C(6)); 137.56 (*s*); 128.24 (2*d*); 127.70 (2*d*); 127.53 (*d*); 75.09 (br. *d*, C(5)); 65.80 (*t*, Ph*C*H$_2$); 27.52 (*q*, MeN). HR-MALDI-MS: 231.1237 (100, $[M+H]^+$, $C_{12}H_{15}N_4O^+$; calc. 231.1240). Anal. calc. for $C_{12}H_{14}N_4O$ (230.27): C 62.59, H 6.13, N 24.33; found: C 62.67, H 6.39, N 24.39.

4-(Benzyloxy)-6-(methylamino)-5-nitrosopyrimidine-2,4-diamine (**5**). A suspension of **4** (1.8 g, 1.08 mmol) in AcOH/H_2O 3:7 (30 ml) was heated to 40° leading to a pale yellow soln. A soln. of $NaNO_2$ (1.08 g, 15.6 mmol) in H_2O (3.0 ml) was added dropwise leading to a purple precipitate. The formation of brown gases indicated completion of the reaction. The precipitate was filtered off, dissolved in CH_2Cl_2, and washed with sat. aq. $NaHCO_3$ soln. The org. layer was dried (Na_2SO_4) and evaporated. Recrystallisation in hexane/MeOH gave **5** (1.72 g, 90%). Purple crystals. R_f (AcOEt): 0.60. M.p. 185°. UV (MeOH, c = 0.11 mM): 207 (4.30), 232 (3.90), 329 (4.34). VIS (DMSO, c = 0.005 M): 605 (2.03). IR (ATR): 3453*m*, 3284*w*, 3238*w*, 3134*m*, 3099*m*, 3045*m*, 1641*m*, 1589*s*, 1578*s*, 1525*s*, 1495*m*, 1470*m*, 1439*s*, 1419*s*, 1385*s*, 1325*s*, 1304*s*, 1221*w*, 1177*s*, 1156*s*, 1128*s*, 1069*m*, 1052*m*, 1025*m*, 1002*s*, 965*m*, 917*m*, 860*w*, 844*m*, 793*m*, 762*s*, 731*m*, 721*s*, 704*s*, 684*m*, 620*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.12 (*q*, J = 5.1, NH); 8.02, 8.00 (2*s*, NH_2); 7.54–7.36 (*m*, 5 arom. H); 5.57 (*s*, PhCH_2); 2.86 (*d*, J = 5.1, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 170.39 (*s*, C(2)); 163.16 (*s*, C(4)); 151.08 (*s*, C(6)); 138.74 (*s*, C(5)); 136.09 (*s*); 128.39 (4*d*); 128.12 (*d*); 67.87 (*t*, Ph*C*H$_2$); 26.28 (*q*, MeN). HR-MS-MALDI: 282.0961 (29, $[M+Na]^+$, $C_{12}H_{13}NaN_5O_2^+$; calc. 282.0961), 260.1138 (100, $[M+H]^+$, $C_{12}H_{14}N_5O_2^+$; calc. 260.1142), 229.1076 (48, $[M-NO]^+$, $C_{12}H_{14}N_4O^+$; calc. 229.1084). Anal. calc. for $C_{12}H_{13}N_5O_2 \cdot 0.25$ MeOH (267.27): C 55.05, H 5.28, N 26.20; found: C 55.03, H 5.14, N 26.29.

N-*[4-(Benzyloxy)-6-(methylamino)-5-nitrosopyrimidin-2-yl]acetamide* (**6**). A soln. of **5** (520 mg, 2.01 mmol) and DMAP (268 mg, 2.2 mmol) in THF (20 ml) was cooled to 0°, treated with Ac_2O (375 ml, 4.0 mmol), stirred for 15 min at 0° and for 20 h at 23°, diluted with sat. aq. NH_4Cl soln. (20 ml), and extracted with CH_2Cl_2 (3 × 30 ml). The combined org. layers were washed with H_2O, dried (Na_2SO_4), and evaporated. Crystallisation from EtOH gave **6** (527 mg, 88%). R_f (CH_2Cl_2/MeOH 9:1) 0.68. M.p. 204°. UV (MeOH, c = 0.095 mM): 210 (4.36), 251 (3.92), 315 (4.17), 354 (4.10). VIS (DMSO, c = 0.005 M): 646 (1.96). IR (ATR): 3212*w*, 3156*w*, 3010*w*, 2933*w*, 1677*m*, 1612*m*, 1578*s*, 1542*m*, 1499*s*, 1456*m*, 1436*m*, 1390*m*, 1366*s*, 1347*m*, 1335*m*, 1293*s*, 1240*m*, 1213*m*, 1200*s*, 1161*s*, 1134*s*, 1067*w*, 1040*w*, 1006*s*, 933*w*, 906*w*, 867*w*, 849*m*, 824*w*, 795*m*, 759*m*, 738*m*, 692*m*, 615*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 10.99 (*q*, J = 4.5, NH–C(6)); 10.80 (*s*, NH–C(2)); 7.61–7.37 (*m*, 5 arom. H); 5.70 (*s*, PhCH_2); 2.92 (*d*, J = 4.8, MeN); 2.38 (*s*, AcN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 171.37 (br. *s*, C(4)); 170.79 (*s*, C=O); 158.89 (*s*, C(2)); 148.42 (br. *s*, C(6)); 139.78 (*s*, C(5)); 135.79 (*s*); 128.67 (2*d*); 128.45 (2*d*); 128.31 (*d*); 68.76 (*t*, Ph*C*H$_2$); 26.99 (*q*, MeN); 25.90 (*q*, *Me*C=O). HR-MALDI-MS: 324.1068 (73, $[M+Na]^+$, $C_{14}H_{15}N_5NaO_3^+$; calc. 324.1067), 302.1248 (100, $[M+H]^+$, $C_{14}H_{16}N_5O_3^+$; calc. 302.1248). Anal. calc. for $C_{14}H_{15}N_5O_3$ (301.30): C 55.81, H 5.02, N 23.24; found: C 55.65, H 5.09, N 23.02.

N-*[4-(Benzyloxy)-6-(methylamino)-5-nitrosopyrimidin-2-yl]-2-chloroacetamide* (**7**). A soln. of **5** (260 mg, 1.0 mmol) and DMAP (146 mg, 1.2 mmol) in THF (10 ml) was cooled to 0°, treated with $(ClCH_2CO)_2O$ (204 mg, 1.20 mmol), stirred for 30 min at 0° and for 1 h at 23°, diluted with sat. aq. NH_4Cl soln. (10 ml), and extracted with CH_2Cl_2 (3 × 20 ml). The combined org. layers were washed with H_2O

and evaporated. FC (CH_2Cl_2/AcOEt 9:1) gave **7**/**11** 90:10 (280 mg). Crystallisation from EtOH gave pure **7** (237 mg, 71%). R_f (CH_2Cl_2/MeOH 9:1) 0.73. M.p. 163°. UV (MeOH, $c = 0.088$ mM): 209 (4.37), 226 (sh, 4.21), 250 (sh, 3.91), 318 (4.21), 344 (sh, 4.14). VIS (DMSO, $c = 0.005$ M): 650 (1.94). IR (ATR): 3208*w*, 3160*w*, 3062*w*, 3014*w*, 2967*w*, 1694*m*, 1615*m*, 1576*m*, 1544*m*, 1504*s*, 1457*m*, 1441*m*, 1416*w*, 1398*m*, 1390*m*, 1370*m*, 1326*s*, 1236*m*, 1199*s*, 1154*s*, 1134*s*, 1083*w*, 1064*w*, 1001*m*, 919*w*, 901*m*, 874*w*, 858*m*, 792*s*, 772*m*, 755*m*, 737*w*, 696*s*, 622*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.22 (*s*, NH−C(2)); 10.98 (*q*, $J = 4.9$, NH−C(6)); 7.61–7.40 (*m*, 5 arom. H); 5.71 (*s*, PhCH_2); 4.82 (*s*, CH_2Cl); 2.93 (*d*, $J = 5.0$, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 166.95 (*s*, C=O); 158.48 (*s*, C(2)); 139.73 (*s*, C(5)); 135.47 (*s*); 128.66 (2*d*); 128.48 (2*d*); 128.35 (*d*); 68.94 (*t*, PhCH_2); 45.66 (*t*, C(1)); 27.12 (*q*, Me); signals of C(5) and C(2) not visible due to coalescence. HR-EI-MS: 337.0754 (5, M^+(^{37}Cl), $C_{14}H_{14}{}^{37}ClN_5O_3^+$; calc. 337.0756), 335.0779 (14, M^+(^{35}Cl), $C_{14}H_{14}{}^{35}ClN_5O_3^+$; calc. 335.0785), 91.0539 (100, $C_7H_7^+$). Anal. calc. for $C_{14}H_{14}ClN_5O_3$ (335.75): C 50.08, H 4.20, N 20.86; found: C 50.20, H 4.23, N 20.61.

*2-Amino-4-(benzyloxy)-8-methylpteridin-7(8*H*)-one 5-Oxide* (**10**). A soln. of **5** (2.59 g, 10 mmol) in THF (50 ml) was cooled to 0° and treated with EtN^iPr$_2$ (4.1 ml, 25 mmol) and ($ClCH_2CO)_2O$ (1.88 g, 11 mmol). The greenish suspension was stirred for 90 min at 0° and for 60 min at 23°, diluted with MeOH (25 ml), and cooled to 0°. The precipitate was filtered off, washed with MeOH, and dried, to afford **10** (1.990 g). The filtrate was evaporated, and FC (CH_2Cl_2/MeOH 49:1 → 9:1) gave additional **10** (340 mg; total yield 2.330 g, 78%). R_f (CH_2Cl_2/MeOH 9:1) 0.49. M.p. 228°. UV (MeOH): 216 (4.52), 230 (sh, 230), 268 (4.13), 295 (sh, 3.84), 355 (4.09). IR (ATR): 3425*w*, 3339*w*, 3225*w*, 3090*w*, 1636*m*, 1552*s*, 1494*m*, 1443*m*, 1416*m*, 1392*m*, 1354*s*, 1223*s*, 1182*m*, 1105*w*, 1078*w*, 1041*m*, 909*w*, 872*w*, 814*w*, 786*w*, 747*m*, 734*s*, 717*w*, 696*w*, 659*w*, 647*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.60–7.33 (*m*, 5 arom. H, NH_2, H−C(6)); 5.49 (*s*, PhCH_2); 3.42 (*s*, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 162.20 (*s*, C(4)); 160.55 (*s*, C(2)); 157.20 (*s*, C(7)); 153.42 (*s*, C(8a)); 136.07 (*s*); 128.28 (2*d*); 127.79 (*d*); 127.63 (2*d*); 124.05 (*d*, C(6)); 107.85 (*s*, C(4a)); 68.01 (*t*, PhCH_2); 27.70 (*q*, MeN). HR-MALDI-MS: 322.0916 (100, $[M + Na]^+$, $C_{14}H_{13}N_5NaO_3^+$; calc. 322.0911), 300.1097 (50, $[M + H]^+$, $C_{14}H_{14}N_5O_3^+$; calc. 300.1091). Anal. calc. for $C_{14}H_{13}N_5O_3$ (299.29): C 56.18, H 4.38, N 23.40; found: C 56.36, H 4.46, N 23.25.

*2-Amino-4-(benzyloxy)-6-chloro-8-methylpteridin-7(8*H*)-one* (**11**). A soln. of **5** (260 mg, 1.0 mmol) in THF (10 ml) was cooled to 0°, treated with ($ClCH_2CO)_2O$ (204 mg, 1.2 mmol), stirred for 30 min at 0° and for 1 h at 23°, diluted with sat. aq. NH_4Cl soln. (10 ml), and extracted with CH_2Cl_2 (3 × 20 ml). The combined org. layers were washed with H_2O, dried (Na_2SO_4), and evaporated. FC (CH_2Cl_2/AcOEt 9:1) gave **11** (259 mg, 82%). Colourless crystals. R_f (CH_2Cl_2/MeOH 9:1) 0.66. M.p. 211°. UV (MeOH, $c =$ 0.075 mM): 214 (4.51), 232 (4.14), 282 (3.71), 349 (4.24). IR (ATR): 3482*w*, 3348*m*, 3217*w*, 2949*w*, 1681*m*, 1613*m*, 1578*s*, 1553*s*, 1525*s*, 1490*s*, 1465*s*, 1436*s*, 1411*m*, 1355*s*, 1308*m*, 1270*w*, 1226*m*, 1172*m*, 1079*w*, 1055*m*, 1036*m*, 1023*s*, 958*m*, 914*w*, 905*w*, 852*w*, 829*w*, 793*m*, 758*w*, 733*m*, 693*m*, 673*w*, 638*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.53–7.37 (*m*, 5 arom. H, NH_2); 5.48 (*s*, PhCH_2); 3.49 (*s*, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 164.33 (*s*, C(4)); 161.22 (*s*, C(2)); 153.03 (*s*, C(7)); 151.45 (*s*, C(8a)); 138.16 (*s*, C(6)); 135.79 (*s*); 128.53 (2*d*); 128.30 (2*d*); 128.10 (*d*); 106.55 (*s*, C(4a)); 67.82 (*t*, PhCH_2); 28.52 (*q*, MeN). HR-EI-MS: 319.0656 (7, M^+(^{37}Cl), $C_{14}H_{12}{}^{37}ClN_5O_2^+$; calc. 319.0645), 317.0673 (20, M^+(^{35}Cl), $C_{14}H_{12}{}^{35}ClN_5O_2^+$; calc. 317.0674), 91.0523 (100, $C_7H_7^+$). Anal. calc. for $C_{14}H_{12}ClN_5O_2$ (317.73): C 52.92, H 3.81, N 22.04, Cl 11.16; found: C 52.69, H 3.94, N 21.77, Cl 11.34.

*2-Amino-4-(benzyloxy)-6-[(*E*)-3-hydroxybut-1-enyl]-8-methylpteridin-7(8*H*)-one* (**12**). A soln. of **5** (130 mg, 0.5 mmol) in THF (7 ml) was cooled to 0°, treated with hexa-2,4-dienoyl choride (76 µg, 0.6 mmol) and *Hünig*'s base (102 µl, 0.6 mmol), stirred for 30 min at 0° and for 2 h at 23°, diluted with sat. aq. NH_4Cl soln. (10 ml), and extracted with CH_2Cl_2 (3 × 15 ml). The combined org. layers were washed with H_2O, dried (Na_2SO_4), and evaporated. FC (CH_2Cl_2/AcOEt 9:1) gave **12** (149 mg, 84%). R_f (CH_2Cl_2/MeOH 9:1) 0.56. M.p. 158°. UV (MeOH, $c = 0.11$ mM): 219 (4.31), 235 (sh, 4.09), 291 (3.79), 376 (4.17). IR (ATR): 3569*w*, 3464*w*, 3340*w*, 3213*w*, 3031*w*, 2963*w*, 1646*m*, 1632*m*, 1558*s*, 1527*m*, 1490*s*, 1476*s*, 1432*s*, 1382*m*, 1359*s*, 1332*m*, 1308*w*, 1276*w*, 1232*m*, 1205*m*, 1112*w*, 1067*m*, 1041*s*, 1000*w*, 923*w*, 902*w*, 848*w*, 833*w*, 812*w*, 792*m*, 748*w*, 730*m*, 694*w*, 665*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.54–7.32 (*m*, 5 arom. H, NH_2); 6.66 (*dd*, $J = 12.0, 1.5$, H−C(1′)); 5.97 (*dd*, $J = 12.0, 4.2$, H−C(2′)); 5.52, 5.46 (2*d*, $J = 12.9$, PhCH_2); 5.19–5.13 (*m*, H−C(3′)); 4.88 (*d*, $J = 4.2$, OH); 1.20 (*d*, $J = 6.3$, Me). ^{13}C-NMR (100 MHz, (D_6)DMSO): 165.07 (*s*, C(4)); 161.08 (*s*, C(2)); 156.45 (*s*, C(7)); 150.61 (*s*, C(8a)); 145.84 (*d*, C(2′)); 144.12 (*s*, C(6)); 136.31(*s*); 128.29 (2*d*); 127.85 (*d*); 127.44 (2*d*); 119.13 (*d*, C(1′)); 107.85 (*s*, C(4a)); 67.57 (*t*, PhCH_2); 63.49 (*d*, C(3′));

27.43 (*q*, MeN); 22.33 (*q*, Me). HR-MALDI-MS: 376.1381 (29, $[M+Na]^+$, $C_{18}H_{17}N_5NaO_2^+$; calc. 376.1381), 354.1562 (86, $[M+H]^+$, $C_{18}H_{18}N_5O_2^+$; calc. 354.1561), 353.1484 (100, M^+, $C_{18}H_{17}N_5O_2^+$; calc. 353.1482), 352.1405 (55, $[M-H]^+$, $C_{18}H_{16}N_5O_2^+$; calc. 352.1405), 336.1456 (51, $[M-OH]^+$, $C_{18}H_{17}N_5O^+$; calc. 336.1455), 310.1295 (83, $[M-43]^+$).

*Diethyl (2*RS,*3*RS*)-2-[2-Amino-4-(benzyloxy)-7,8-dihydro-8-methyl-7-oxopteridin-6-yl]-3-hydroxybutanedioate* (**19a**). A suspension of **10** (300 mg, 1.0 mmol) and *diethyl (*E*)-but-2-enedioate* (**13**; 0.5 ml) in toluene (10 ml) was heated to reflux for 1.5 h and cooled to r.t. FC (AcOEt/hexane 1:1) gave **19a** (241 mg, 89%). Colourless amorphous solid. R_f (CH_2Cl_2/MeOH 9:1) 0.51. UV (MeOH, $c=$ 0.084 mM): 215 (4.37), 229 (sh, 4.04), 282 (3.60), 348 (4.16). IR (ATR): 3456*w*, 3346*w*, 3229*w*, 2981*w*, 2953*w*, 2937*w*, 2872*w*, 1731*m*, 1668*m*, 1616*m*, 1582*s*, 1553*s*, 1495*m*, 1463*m*, 1437*s*, 1392*w*, 1356*m*, 1222*s*, 1177*m*, 1093*m*, 1065*m*, 1022*s*, 913*w*, 859*w*, 801*m*, 737*m*, 698*m*, 671*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.59–7.41 (*m*, 5 arom. H, NH_2); 5.84 (*d*, $J=7.0$, exch. OH); 5.57 (s, PhCH_2); 4.76 (*dd*, $J=8.8$, 7.0, H–C(3)); 4.34 (*d*, $J=8.8$, H–C(2)); 4.18–4.05 (*m*, 2 MeCH_2O); 3.53 (*s*, MeN); 1.21, 1.12 (2*t*, $J=7.1$, 2 Me). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.49–7.30 (*m*, 5 arom. H); 5.51 (*s*, PhCH_2); 5.23 (*s*, NH_2); 4.97 (*dd*, $J=10.5$, 3.3, H–C(3)); 4.91 (*d*, $J=10.6$, H–C(2)); 4.68 (*d*, $J=3.3$, OH); 4.25, 4.08 (2*q*, $J=7.1$, 2 MeCH_2O); 3.59 (*s*, MeN); 1.26, 1.08 (2*t*, $J=7.1$, 2 Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): 171.54, 168.97 (2*s*, 2 C=O); 165.11 (*s*, C(4′)); 161.27 (*s*, C(2′)); 155.97 (*s*, C(7′)); 151.35 (*s*, C(8′a)); 145.56 (*s*, C(6′)); 136.20 (*s*); 128.43 (2*d*); 128.41 (2*d*); 128.13 (*d*); 107.43 (*s*, C(4′a)); 69.14 (*d*, C(3)); 67.71 (*t*, Ph*C*H$_2$); 60.52, 60.29 (2*t*, 2 MeCH_2O); 52.81 (*d*, C(2)); 27.49 (*q*, MeN); 13.87, 13.81 (2*q*, 2 Me). HR-MALDI-MS: 510.397 (28, $[M+K]^+$, $C_{22}H_{25}KN_5O_7^+$; calc. 510.1386), 494.1639 (100, $[M+Na]^+$, $C_{22}H_{25}N_5NaO_7^+$; calc. 494.1646).

*Diethyl (2*RS,*3*SR*)-2-[2-Amino-4-(benzyloxy)-7,8-dihydro-8-methyl-7-oxopteridin-6-yl]-3-hydroxybutanedioate* (**19b**). A suspension of **10** (600 mg, 2.01 mmol) and *diethyl (Z)-but-2-enedioat*e (**14**; 0.5 ml) in toluene (10 ml) was heated to reflux for 1.5 h and cooled to r.t. FC (AcOEt/hexane 1:1) gave **19b** (846 mg, 90%). Colourless, amorphous solid. R_f (CH_2Cl_2/MeOH 9:1) 0.44. UV (MeOH, $c=$ 0.075 mM): 215 (4.41), 229 (sh, 4.05), 283 (3.61), 347 (4.16). IR (ATR): 3464*w*, 3343*w*, 3228*w*, 2982*w*, 1729*m*, 1666*m*, 1615*m*, 1582*s*, 1552*s*, 1495*m*, 1463*m*, 1439*s*, 1391*w*, 1356*m*, 1224*s*, 1178*m*, 1094*m*, 1063*m*, 1025*s*, 860*w*, 801*m*, 739*w*, 698*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.54–7.33 (*m*, 5 arom. H, NH_2); 5.86 (*d*, $J=6.9$, OH); 5.51, 5.49 (2*d*, $J=12.6$, PhCH_2); 4.70 (*dd*, $J=7.8$, 6.9, H–C(3)); 4.34 (*d*, $J=7.8$, H–C(2)); 4.09–4.01 (*m*, MeCH_2O); 3.96–3.82 (*m*, MeCH_2O); 3.47 (*s*, MeN); 1.13, 0.95 (2*t*, $J=7.1$, 2 Me). ^{1}H-NMR (400 MHz, $CDCl_3$): 7.47–7.32 (*m*, 5 arom. H); 5.54, 5.44 (2*d*, $J=12.4$, PhCH_2); 5.25 (*s*, NH_2); 4.92 (*dd*, $J=5.3$, 3.3, H–C(3)); 4.78 (*d*, $J=3.3$, OH); 4.23–4.15 (*m*, 2 MeCH_2O); 4.16 (*d*, $J=5.3$, H–C(2)); 3.60 (*s*, MeN); 1.22, 1.21 (2*t*, $J=7.1$, 2 Me). ^{13}C-NMR (100 MHz, (D_6)DMSO): 171.35, 168.97 (2*s*, 2 C=O); 165.07 (*s*, C(4′)); 161.26 (*s*, C(2′)); 155.91 (*s*, C(7′)); 151.19 (*s*, C(8′a)); 145.02 (*s*, C(6′)); 136.22 (*s*); 128.32 (2*d*); 128.07 (2*d*); 127.99 (*d*); 107.16 (*s*, C(4′a)); 69.69 (*d*, C(3)); 67.58 (*t*, Ph*C*H$_2$); 60.44, 60.10 (2*t*, 2 Me*C*H$_2$O); 51.84 (*d*, C(2)); 27.48 (*q*, MeN); 13.92, 13.68 (2*q*, 2 Me).

*2-Amino-4-(benzyloxy)-6-(*cis*-2-hydroxycyclohexyl)-8-methylpteridin-7(8*H*)-one* (**19c**). A suspension of **10** (300 mg, 1.0 mmol) and *cyclohexene* (**15**; 3 ml) in toluene (20 ml) was boiled under reflux for 43 h and evaporated. FC (AcOEt) gave **19c** (339 mg, 89%). A sample for analysis was sublimed at 180°, $<10^{-3}$ mbar. R_f (CH_2Cl_2/MeOH 9:1) 0.57. M.p. 204°. UV (MeOH, $c=0.14$ mM): 218 (4.30), 229 (sh, 4.16), 285 (3.80), 345 (4.25). IR (ATR): 3455*w*, 3292*w*, 3201*w*, 2925*w*, 2853*w*, 1663*m*, 1631*m*, 1590*s*, 1556*s*, 1495*m*, 1467*m*, 1443*s*, 1429*s*, 1351*s*, 1297*w*, 1251*m*, 1233*m*, 1218*m*, 1194*m*, 1109*w*, 1067*m*, 1024*m*, 1011*m*, 974*m*, 911*w*, 896*w*, 879*w*, 846*w*, 815*w*, 801*w*, 782*w*, 754*m*, 733*m*, 698*m*, 676*m*, 666*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.52–7.32 (*m*, 5 arom. H); 7.23 (*s*, NH_2); 5.52, 5.50 (2*d*, $J=12.6$, PhCH_2); 4.48 (*dd*, $J=3.3$, 1.0, exch. OH); 4.21 (br. *s*, H–C(2′)); 3.46 (*s*, MeN); 3.05 (*ddd*, $J=12.3$, 3.3, 2.2, H–C(1′)); 1.86 (*qd*, $J=$ 12.8, 3.4, H_{ax}–C(6′)); 1.78–1.70 (*m*, H_{eq}–C(3′), H_{eq}–C(5′)); 1.61 (*dtd*, $J=17.6$, 9.5, 4.0, H_{ax}–C(4′)); 1.51–1.48 (*m*, H_{ax}–C(3′), H_{eq}–C(6′)); 1.40–1.34 (*m*, H_{eq}–C(4′)); 1.30 (*qt*, $J=12.8$, 3.5, H_{ax}–C(5′)). ^{13}C-NMR (100 MHz; (D_6)DMSO): 164.74 (*s*, C(4)); 160.71 (*s*, C(2)); 155.93 (*s*, C(7)); 153.34 (*s*, C(8a)); 150.92 (*s*, C(6)); 136.39 (*s*); 128.34 (2*d*); 127.97 (2*d*); 127.91 (*d*); 106.96 (*s*, C(4a)); 67.31 (*t*, Ph*C*H$_2$); 65.53 (*d*, C(2′)); 43.45 (*d*, C(1′)); 32.54 (*t*, C(3′)); 27.26 (*q*, MeN); 25.28 (*t*, C(6′)); 23.39 (*t*, C(4′)); 19.35 (*t*, C(5′)). HR-MALDI-MS: 404.1700 (33, $[M+Na]^+$, $C_{20}H_{23}N_5NaO_3^+$; calc. 404.1693), 382.1878 (100, $[M+H]^+$, $C_{20}H_{24}N_5O_3^+$; calc. 383.1874), 364.1772 (71, $[M-OH]^+$, $C_{20}H_{22}N_5O_2^+$; calc. 364.1768). Anal. calc. for $C_{20}H_{23}N_5O_3$ (381.43): C 62.98, H 6.08, N 18.36; found: C 62.73, H 6.17, N 18.30.

*2-Amino-4-(benzyloxy)-6-(*cis/trans*-2-hydroxytetrahydrofuran-3-yl)-8-methylpteridin-7(8*H*)-one* (**19d**). A suspension of **10** (300 mg, 1.0 mmol) and *2,3-dihydrofuran* (**16**; 0.8 ml) in toluene (20 ml) was stirred at reflux for 2 h and adsorbed on silica gel. FC (AcOEt) gave **19d** (290 mg, 79%). Colourless solid. A sample for analysis was recrystallised in ^{i}PrOH. R_f (CH_2Cl_2/MeOH 9:1) 0.45. M.p. 185°. UV (MeOH, $c = 0.086$ mM): 214 (4.49), 229 (sh, 4.17), 286 (3.81), 341 (4.26). IR (ATR): 3505*w*, 3342*w*, 3231*w*, 3055*w*, 3030*w*, 2947*w*, 2888*w*, 1661*m*, 1635*m*, 1581*s*, 1552*s*, 1498*m*, 1447*s*, 1392*w*, 1353*m*, 1290*w*, 1275*w*, 1236*m*, 1219*m*, 1111*w*, 1071*w*, 1025*m*, 1001*m*, 957*w*, 923*m*, 912*m*, 893*w*, 849*w*, 806*m*, 792*w*, 757*m*, 704*m*, 665*w*, 620*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO; *cis*/*trans* 1:1; assignment based on a DQFCOSY spectrum): 7.53–7.32 (*m*, 5 arom. H); 7.27, 7.24 (2*s*, NH_2); 5.53, 5.52, 5.51, 5.50 (4*d*, $J = 12.5$, PhCH_2); 3.48, 3.47 (2*s*, MeN); data for *trans*-**19d**: 6.14 (*d*, $J = 5.1$, OH); 5.43 (*dd*, $J = 5.1$, 2.3, H–C(1′)); 3.99–3.88 (*m*, 2 H–C(4′)); 3.56 (*ddd*, $J = 8.1$, 5.7, 2.3, H–C(2′)); 2.25–2.08 (*m*, 2 H–C(3′)); data for *cis*-**19d**: 5.85 (*dd*, $J = 4.5$, 0.9, OH); 5.71 (*t*, $J = 4.5$, 0.5, H–C(1′)); 3.99–3.88 (*m*, H_a–C(4′)); 3.77 (*q*, $J = 8.0$, H_b–C(4′)); 3.50–3.44 (*m*, H–C(2′)); 2.71–2.61 (*m*, H_a–C(3′)); 1.91 (*dtd*, $J = 12.1$, 8.0, 4.1, H_b–C(3′)). ^{13}C-NMR (100 MHz, (D_6)DMSO; *cis*/*trans* 1:1; assignment based on a HSQC spectrum): 164.96 (*s*, C(4)); 160.96, 160.82 (2*s*, C(2)); 156.63, 156.25 (2*s*, C(7)); 151.18, 151.14 (2*s*, C(8a)); 149.63, 148.55 (2*s*, C(6)); 136.52, 136.50 (2*s*); 128.42–127.95 (several *d*); 107.18, 107.02 (2*s*, C(4a)); 67.39, 67.34 (2*t*, Ph*C*H_2); 27.42, 27.28 (2*q*, MeN); data for *trans*-**22d**: 100.05 (*d*, C(1′)); 66.22 (*t*, C(4′)); 49.31 (*d*, C(2′)); 28.43 (*t*, C(3′)); data for *cis*-**22d**: 96.32 (*d*, C(1′)); 65.28 (*t*, C(4′)); 48.01 (*d*, C(2′)); 24.18 (*t*, C(3′)). HR-MALDI-MS: 392.1332 (100, $[M + Na]^+$, $C_{18}H_{19}N_5NaO_4^+$; calc. 392.1329). Anal. calc. for $C_{18}H_{19}N_5O_4$ (369.38): C 58.53, H 5.18, N 18.96; found: C 58.27, H 5.34, N 18.51.

*Methyl (*Z*)-3-[2-Amino-4-(benzyloxy)-7,8-dihydro-8-methyl-7-oxopteridin-6-yl]-2-hydroxyprop-2-enoate* (**19e**). A suspension of **10** (300 mg, 1.0 mmol) and *methyl prop-2-ynoate* (**17**; 0.8 ml) in toluene (10 ml) was stirred at 100° for 1 h and then cooled to 0°. The orange precipitate (200 mg of **19e**) was filtered off. Evaporation of the filtrate, and FC (CH_2Cl_2/AcOEt 9:1) gave additional **19e** (127 mg, total yield: 85%). Orange solid. R_f (CH_2Cl_2/MeOH 9:1) 0.68. M.p. 227° (dec.). UV (MeOH, $c = 0.096$ mM): 216 (4.34), 246 (3.84), 289 (3.75), 409 (4.18), 426 (4.18), 490 (sh, 3.39). IR (ATR): 3537*w*, 3505*w*, 3369*m*, 3221*w*, 3119*w*, 2954*w*, 1727*m*, 1670*m*, 1625*m*, 1585*s*, 1564*s*, 1487*s*, 1472*s*, 1453*s*, 1347*m*, 1287*m*, 1232*s*, 1113*w*, 1069*w*, 1038*m*, 994*m*, 975*m*, 919*w*, 888*w*, 874*w*, 794*m*, 782*w*, 760*m*, 723*w*, 706*m*, 672*w*, 646*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 13.76 (*s*, OH); 7.54–7.37 (*m*, 5 arom. H, NH_2); 6.87 (*s*, H–C(2)); 5.53 (*s*, PhCH_2); 3.79 (*s*, MeO); 3.50 (*s*, MeN). ^{13}C-NMR (100 MHz, (D_6)DMSO): 163.01, 162.86 (2*s*, OC=O, C(4′)); 160.98 (*s*, C(2′)); 156.04 (*s*, C(7′)); 153.64 (*s*, C(2)); 150.79 (*s*, C(8a)); 145.10 (*s*, C(6)); 136.02 (*s*); 128.51 (2*d*); 128.18 (*d*); 127.94 (2*d*); 104.79 (*s*, C(4′a)); 98.47 (*d*, C(3)); 67.99 (*t*, Ph*C*H_2); 52.42 (*q*, MeO); 27.80 (*q*, MeN). HR-MALDI-MS: 406.1118 (44, $[M + Na]^+$, $C_{18}H_{17}N_5NaO_5^+$; calc. 406.1122), 384.1303 (100, $[M + H]^+$, $C_{18}H_{18}N_5O_5^+$; calc. 384.1303), 324.1091 (59, $[M - C_2H_4O_2 + H]^+$, $C_{16}H_{14}N_5O_3^+$; calc. 324.1091).

X-Ray Crystal-Structure Analysis of **19e** · *DMSO*. Cooling a hot soln. of **19e** in DMSO gave yellow single crystals of **19e** · DMSO. $C_{18}H_{17}N_5O_5 \cdot C_2H_6OS$, $M_r = 461.497$, monoclinic, $P2_1/n$, $a = 14.7687(3)$, $b = 7.2892(2)$, $c = 20.7070(5)$ Å, $\beta = 98.5485(11)°$, $V = 2204.39(9)$ Å^3, $Z = 4$, $D_{calc} = 1.391$ Mg/m^3. Intensities were measured on a *Nonius Kappa CCD* diffractometer, with MoK_α radiation ($\lambda = 0.71073$ Å). Cell parameters from 16871 reflections, $\theta = 2.425–27.485°$, $\mu = 0.194$ mm^{-1}, $T = 223$ K. 9817 measured reflections, 5031 independent reflections, 3347 observed reflections ($> 2\sigma(I)$). Refinement on F^2: Full-matrix least squares refinement, $R(\text{all}) = 0.0989$, $R(\text{gt}) = 0.0639$. All diagrams and calculations were performed using maXus (*Bruker Nonius*, Delft, *MacScience*, Japan). The program SIR97 was used to solve the structure and the program SHELXL-97 to refine it.

*Diethyl (2*RS*,3*RS*)-2-[2-Amino-3,4,7,8-tetrahydro-8-methyl-4,7-dioxopteridin-6-yl]-3-hydroxybutanedioate* (**20a**). A suspension of **19a** (150 mg, 0.32 mmol) and LiBr (69 mg, 0.80 mmol) in MeCN (5 ml) was cooled to 0°, treated with Me_3SiCl (122 ml, 0.95 mmol), stirred for 15 min at 0° and for 3.5 h at r.t., cooled to 0°, diluted with MeOH (2 ml), and stored over night at −20°. The precipitate was filtered off, washed with CH_2Cl_2, and dried *in vacuo* to afford **20a** (112 mg, 93%). Amorphous solid. UV (MeOH, $c = 0.094$ mM): 218 (4.36), 294 (3.83), 343 (4.03). IR (ATR): 3492*w*, 3294*w*, 3136*w*, 2980*w*, 1732*m*, 1718*m*, 1685*w*, 1636*s*, 1587*m*, 1540*s*, 1524*s*, 1469*w*, 1445*w*, 1370*m*, 1342*w*, 1269*m*, 1242*m*, 1200*w*, 1180*m*, 1116*m*, 1067*w*, 1016*m*, 924*w*, 885*w*, 858*w*, 797*m*, 738*w*, 724*w*, 684*w*, 627*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 11.24 (*s*, NH); 7.22 (br. *s*, NH_2); 5.83 (*d*, $J = 7.2$, OH); 4.68 (*dd*, $J = 9.0$, 7.2, H–C(3)); 4.31 (*d*, $J = 9.3$, H–C(2));

4.10, 4.01 (2*q*, *J* = 6.9, 2 MeC*H*$_2$O); 3.43 (*s*, MeN); 1.19, 1.08 (2*t*, *J* = 6.9, 2 Me). ^{13}C-NMR (100 MHz, (D$_6$)DMSO): 171.69, 169.19 (2*s*, 2 C=O); 158.69 (*s*, C(2′)); 156.00 (*s*, C(7′)); 154.59 (*s*, C(4′)); 151.14 (*s*, C(8′a)); 143.50 (*s*, C(6′)); 110.83 (*s*, C(4′a)); 69.34 (*d*, C(3)); 60.45, 60.26 (2*t*, MeCH$_2$O); 51.96 (*d*, C(2)); 27.95 (*q*, MeN); 13.89, 13.85 (2*q*, 2 Me). HR-MALDI-MS: 404.1170 (22, $[M+Na]^+$, $C_{15}H_{19}N_5NaO_7^+$; calc. 404.1177), 388.1431 (100, $[M+Li]^+$, $C_{15}H_{19}LiN_5O_7^+$; calc. 388.1431), 382.1349 (17, $[M+H]^+$, $C_{15}H_{20}N_5O_7^+$; calc. 382.1357).

*Diethyl (2*RS*,3*SR*)-2-[2-Amino-3,4,7,8-tetrahydro-8-methyl-4,7-dioxopteridin-6-yl]-3-hydroxybutanedioate* (**20b**). A suspension of **19b** (300 mg, 0.64 mmol) and LiBr (138 mg, 1.59 mmol) in MeCN (10 ml) was cooled to 0°, treated with Me$_3$SiCl (241 µl, 1.91 mmol), stirred for 15 min at 0° and 3 h at r.t., and cooled to 0°. The precipitate was filtered off, washed with cold MeCN, and dried *in vacuo* to afford **20b** (225 mg, 93%). Amorphous solid. UV (MeOH, *c* = 1.0 mM): 219 (4.33), 294 (3.86), 342 (4.08). IR (ATR): 3347*w*, 3332*w*, 3193*w*, 3159*w*, 2982*w*, 2940*w*, 2903*w*, 1744*m*, 1721*m*, 1633*s*, 1587*m*, 1545*s*, 1522*s*, 1466*m*, 1445*m*, 1404*m*, 1364*m*, 1274*m*, 1263*m*, 1219*s*, 1195*m*, 1180*m*, 1116*m*, 1093*m*, 1082*m*, 1026*s*, 853*m*, 802*m*, 729*m*, 629*s*. ^{1}H-NMR (400 MHz, (D$_6$)DMSO): 11.26 (*s*, NH); 7.35 (br. *s*, NH$_2$); 5.83 (*d*, *J* = 6.7, OH); 4.71 (*dd*, *J* = 7.9, 6.7, H–(3)); 4.29 (*d*, *J* = 8.0, H–C(2)); 4.06 (*qd*, *J* = 7.1, 1.0, MeC*H*$_2$O); 4.00 (*qd*, *J* = 7.0, 2.3, MeC*H*$_2$O); 3.43 (*s*, MeN); 1.14, 1.06 (2*t*, *J* = 7.1, 2 Me). ^{13}C-NMR (100 MHz, (D$_6$)DMSO): 171.49, 169.04 (2*s*, 2 C=O); 158.50 (*s*, C(2′)); 155.84 (*s*, C(7′)); 154.58 (*s*, C(4′)); 151.03 (*s*, C(8′a)); 143.02 (*s*, C(6′)); 110.59 (*s*, C(4′a)); 69.80 (*d*, C(3)); 60.33, 60.17 (2*t*, 2 MeCH$_2$O); 51.67 (*d*, C(2)); 27.92 (*q*, MeN); 13.96, 13.70 (2*q*, 2 Me). HR-MALDI-MS: 404.1175 (30, $[M+Na]^+$, $C_{15}H_{19}N_5NaO_7^+$; calc. 404.1177), 388.1438 (100, $[M+Li]^+$, $C_{15}H_{19}LiN_5O_7^+$; calc. 388.1431), 382.1349 (20, $[M+H]^+$, $C_{15}H_{20}N_5O_7^+$; calc. 382.1357).

*2-Amino-6-(*cis*-2-hydroxycyclohexyl)-8-methylpteridin-4,7(3*H*,8*H*)-dione* (**20c**). A suspension of **19c** (227 mg, 0.60 mmol) and LiBr (129 mg, 1.49 mmol) in MeCN (7 ml) was cooled to 0°, treated with Me$_3$SiCl (227 µl, 1.79 mmol), stirred for 15 min at 0° and for 6 h at r.t., cooled to 0°, diluted with MeOH (2 ml), and stirred for 15 min. The precipitate was filtered off. Crystallization from H$_2$O/PrOH 1:1 gave **20c** (154 mg, 89%). UV (MeOH, *c* = 0.070 mM): 218 (4.38), 296 (3.91), 343 (4.07). IR (ATR): 3367*w*, 3295*w*, 3200*w*, 3152*w*, 2927*w*, 2850*w*, 1682*m*, 1629*s*, 1584*m*, 1537*s*, 1514*s*, 1445*m*, 1359*m*, 1297*w*, 1273*w*, 1226*w*, 1196*w*, 1136*w*, 1111*w*, 1071*w*, 1056*w*, 1028*w*, 1010*w*, 972*w*, 948*w*, 920*w*, 893*w*, 848*w*, 821*w*, 802*m*, 788*w*, 726*w*, 712*w*, 659*w*, 622*w*. ^{1}H-NMR (400 MHz; (D$_6$)DMSO): 11.13 (*s*, NH); 7.07 (*s*, NH$_2$); 4.64 (*dd*, *J* = 2.7, 1.0, OH); 4.18 (br. *s*, H–C(2′)); 3.43 (*s*, MeN); 3.00 (*ddd*, *J* = 12.3, 3.4, 2.1, H–C(1′)); 1.84 (*qd*, *J* = 12.8, 3.4, H$_{ax}$–C(6′)); 1.78–1.72 (*m*, H$_{eq}$–C(3′), H$_{eq}$–C(5′)); 1.64 (*qt*, *J* = 12.7, 3.4, H$_{ax}$–C(4′)); 1.52–1.47 (*m*, H$_{ax}$–C(3′), H$_{eq}$–C(6′)); 1.44–1.35 (*m*, H$_{eq}$–C(4′)); 1.31 (*qt*, *J* = 12.8, 3.6, H$_{ax}$–C(5′)). ^{13}C-NMR (100 MHz, (D$_6$)DMSO): 158.85 (*s*, C(2)); 155.93 (*s*, C(7)); 154.15 (*s*, C(4)); 151.51 (*s*, C(8a)); 150.50 (*s*, C(6)); 110.18 (*s*, C(4a)); 65.69 (*d*, C(2′)); 43.02 (*d*, C(1′)); 32.62 (*t*, C(3′)); 27.80 (*q*, MeN); 25.49 (*t*, C(6′)); 23.49 (*t*, C(4′)); 19.43 (*t*, C(5′)). HR-MALDI-MS: 314.1225 (100, $[M+Na]^+$, $C_{13}H_{17}N_5NaO_3^+$; calc. 314.1224), 292.1404 (70, $[M+H]^+$, $C_{13}H_{18}N_5O_3^+$; calc. 292.1404), 274.1298 (93, $[M-OH]^+$, $C_{13}H_{16}N_5O_2^+$; calc. 274.1299).

*2-Amino-6-(2,3-dihydrofuran-4-yl)-8-methylpteridine-4,7(3*H*,8*H*)-dione* (**20d**). A suspension of **19d** (130 mg, 0.352 mmol) and LiBr (76 mg, 0.881 mmol) in MeCN (5 ml) was cooled to 0°, treated with Me$_3$SiCl (134 ml, 1.057 mmol), stirred for 15 min at 0° and for 4 h at r.t., diluted with MeOH (2 ml), and stirred for 15 min. The precipitate was filtered off, washed with CH$_2$Cl$_2$/MeOH 9:1, and dried *in vacuo* to afford **20d** (75 mg, 76%). Red-brown solid. UV (MeOH, *c* = 0.13 mM): 218 (4.24), 242 (sh, 3.71), 323 (4.73), 379 (4.09). IR (ATR): 3369*w*, 3177*m*, 3115*w*, 2908*w*, 2726*w*, 1672*m*, 1638*s*, 1588*s*, 1548*s*, 1501*s*, 1451*m*, 1383*m*, 1322*m*, 1266*m*, 1253*m*, 1171*w*, 1148*m*, 1123*s*, 1042*m*, 1011*m*, 979*w*, 933*w*, 909*m*, 890*w*, 879*m*, 867*w*, 824*w*, 796*m*, 787*w*, 775*w*, 727*w*, 625*w*. ^{1}H-NMR (400 MHz, (D$_6$)DMSO): 11.18 (*s*, NH); 7.87 (*t*, *J* = 1.6, H–C(5′)); 7.11 (*s*, NH$_2$); 4.41 (*t*, *J* = 9.6, 2 H–C(4′)); 3.50 (*s*, MeN); 2.96 (*td*, *J* = 9.6, 1.6, 2 H–C(3′)). ^{13}C-NMR (100 MHz, (D$_6$)DMSO): 158.98 (*s*, C(2)); 155.17 (*s*, C(7)); 153.63 (*s*, C(4)); 150.19 (*s*, C(8a)); 148.82 (*s*, C(6)); 140.90 (*d*, C(5′)); 114.93 (*s*, C(4′)); 111.52 (*s*, C(4a)); 69.82 (*t*, C(2′)); 29.88 (*t*, C(3′)); 27.90 (*q*, MeN). HR-MALDI-MS: 284.0749 (71, $[M+Na]^+$, $C_{11}H_{11}NaN_5O_3^+$; calc. 284.0754), 268.1017 (64, $[M+Li]^+$, $C_{11}H_{11}LiN_5O_3^+$; calc. 268.1016), 262.0933 (100, $[M+H]^+$, $C_{11}H_{12}N_5O_3^+$; calc. 268.1016).

*Methyl (*Z*)-3-[2-Amino-3,4,7,8-tetrahydro-8-methyl-4,7-dioxopteridin-6-yl]-2-hydroxyprop-2-enoate* (**20e**). A suspension of **19e** (50 mg, 0.13 mmol) and LiBr (28 mg, 0.33 mmol) in MeCN (3 ml) was cooled

to 0°, treated with Me_3SiCl (50 µl, 0.39 mmol), stirred for 15 min at 0° and for 4 h at r.t., cooled to 0°, diluted with MeOH (2 ml), and stirred for 30 min. The precipitate was filtered off, washed with CH_2Cl_2/MeOH 9:1, and dried *in vacuo* to afford **20e** (37 mg, 97%). UV (MeOH, $c = 0.13$ mM): 220 (4.34), 268 (3.71), 309 (3.78), 408 (4.21), 425 (4.20), 489 (3.43). IR (ATR): 3319*w*, (br.) 3183*m*, 2953*w*, 1718*m*, 1630*s*, 1583*s*, 1552*s*, 1504*s*, 1435*s*, 1360*m*, 1263*s*, 1212*s*, 1106*m*, 1071*w*, 985*w*, 968*w*, 924*w*, 868*w*, 828*w*, 775*m*, 758*m*, 711*m*, 619*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 13.85 (*s*, OH); 11.49 (*s*, NH); 7.40 (*s*, NH_2); 6.81 (*s*, H–C(3)); 3.79 (*s*, MeO); 3.47 (*s*, MeN). ^{13}C-NMR (100 MHz, (D_6)DMSO): 163.09 (*s*, C=O); 157.47 (*s*, C(2′)); 155.99 (*s*, C(7′)); 154.21 (*s*, C(4′)); 153.43 (*s*, C(2)); 150.25 (*s*, C(8′a)); 143.45 (*s*, C(6′)); 107.82 (*s*, C(4′a)); 98.22 (*d*, C(3)); 52.32 (*q*, MeO); 28.21 (*q*, MeN). HR-MALDI-MS: 294.0625 (100, $[M+H]^+$, $C_{11}H_{12}N_5O_5^+$; calc. 294.0833).

*2-Amino-4-(benzyloxy)-8-methyl-6-phenylpteridin-7(8*H*)-one 5-Oxide* (**21**). A soln. of **5** (520 mg, 2.01 mmol) and EtN^iPr_2 (862 µl, 5.00 mmol) in THF (20 ml) was cooled to 0°, treated with 2-chloro-2-phenylacetyl chloride (349 µl, 2.40 mmol), stirred for 30 min at 0° and for 30 min at r.t., diluted with sat. aq. $NaHCO_3$ soln., and extracted with CH_2Cl_2 (3 × 30 ml). The combined org. layers were washed with brine, dried (Na_2SO_4), and evaporated. FC (CH_2Cl_2/AcOEt 9:1) gave **21** (612 mg, 82%). Crystalisation from ^{i}PrOH gave yellow crystals. R_f (CH_2Cl_2/MeOH 9:1) 0.63. M.p. 240°. UV (MeOH): 217 (4.46), 244 (sh, 4.20), 269 (4.14), 366 (4.19). IR (ATR): 3458*w*, 3326*w*, 3210*w*, 3115*w*, *3066w*, 3014*w*, 1660*m*, 1634*m*, 1555*s*, 1499*m*, 1482*s*, 1465*m*, 1453*s*, 1441*s*, 1421*s*, 1359*s*, 1312*m*, 1288*m*, 1243*s*, 1194*m*, 1140*m*, 1107*w*, 1077*w*, 1044*m*, 1025*m*, 999*w*, 987*w*, 954*w*, 921*w*, 904*w*, 853*w*, 826*w*, 785*s*, 763*m*, 739*m*, 724*m*, 688*m*, 674*m*, 650*m*, 617*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.55–7.29 (*m*, 10 arom. H, NH_2); 5.47 (*s*, PhCH_2); 3.57 (*s*, MeN). ^{13}C-NMR (100 MHz, (D_6)DMSO): 162.34 (*s*, C(4)); 160.24 (*s*, C(2)); 156.97 (*s*, C(7)); 152.33 (*s*, C(8a)); 136.05, 134.03 (2*s*); 129.50 (*s*, C(6)); 130.55, 128.47, 28.26, 127.76, 127.68, 127.38 (several *d*); 107.88 (*s*, C(4a)); 68.14 (*t*, Ph*C*H_2); 28.39 (*q*, MeN). HR-MALDI-MS: 398.1217 (100, $[M+Na]^+$, $C_{20}H_{17}N_5NaO_3^+$; 398.1224), 376.1400 (62, $[M+H]^+$, $C_{20}H_{18}N_5O_3^+$; calc. 376.1404). Anal. calc. for $C_{20}H_{17}N_5O_3$ (375.39): C 63.99, H 4.56, N 18.66; found: C 64.11, H 4.72, N 18.51.

*2-Amino-4-(benzyloxy)-8-methyl-6-phenylpteridin-7(8*H*)-one* (**22**). A suspension of **21** (120 mg, 0.32 mmol) in toluene (5 ml) was treated with *N*-phenylmaleimide (83 mg, 0.480 mmol), kept at reflux for 1 h, and evaporated. FC (hexane/AcOEt 3:2) gave **22** (95 mg, 82%). A sample for analysis was crystallized from EtOH. R_f (CH_2Cl_2/MeOH 9:1) 0.76. M.p. 178°. UV (MeOH): 219 (4.32), 241 (4.08), 292 (3.76), 370 (4.28). IR (ATR): 3494*w*, 3455*w*, 3335*m*, 3221*w*, 3048*w*, 1663*m*, 1624*m*, 1556*s*, 1522*m*, 1478*s*, 1472*s*, 1455s, 1439*s*, 1394*m*, 1356*s*, 1315*m*, 1292*m*, 1256*m*, 1228*s*, 1184*m*, 1115*w*, 1094*m*, 1059*w*, 1037*m*, 1020*s*, 956*m*, 924*w*, 900*m*, 851*w*, 834*w*, 802*m*, 754*m*, 746*s*, 726*m*, 699*m*, 686*s*, 647*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 8.13–8.10 (*m*, 2 arom. H); 7.54–7.32 (*m*, 8 arom. H, NH_2); 5.55 (*s*, PhCH_2); 3.54 (*s*, Me). ^{13}C-NMR (100 MHz, (D_6)DMSO): 165.35 (*s*, C(4)); 161.15 (*s*, C(2)); 156.05 (*s*, C(7)); 151.21 (*s*, C(8a)); 144.12 (*s*, C(6)); 136.35, 136.12 (2*s*); 128.98, 128.54, 128.40, 128.27, 128.03, 127.72 (several *d*); 108.25 (*s*, C(4a)); 67.56 (*t*, Ph*C*H_2); 27.62 (*q*, MeN). HR-MALDI-MS: 360.1454 (100, $[M+H]^+$, $C_{20}H_{18}N_5O_2^+$; calc. 360.1455). Anal. calc. for $C_{20}H_{17}N_5O_2$ (359.39): C 66.84, H 4.77, N 19.49; found: C 67.00, H 4.90, N 19.44.

*2-Amino-8-methyl-6-phenylpteridin-4,7(3*H*,8*H*)-dione* (**23**). A suspension of **22** (160 mg, 0.45 mmol) and LiBr (50 mg, 0.58 mmol) in MeCN (7 ml) was cooled to 0°, treated with Me_3SiCl (86 µl, 0.67 mmol), stirred for 15 min at 0° and for 16 h at r.t., diluted with MeOH (2 ml), and stirred for 15 min. The precipitate was filtered off. Recrystallisation in PrOH gave **23** (117 mg, 97%). Yellow crystals. R_f (CH_2Cl_2/MeOH 9:1) 0.35. M.p. > 370° (dec.). UV (MeOH, $c = 0.12$ mM): 224 (4.35), 240 (sh, 4.12), 302 (4.00), 369 (4.33). IR (ATR): 3413*w*, 3338*w*, 3184*w*, 3106*m*, 2924*w*, 2839*w*, 2760*w*, 1678*m*, 1664*m*, 1627*s*, 1595*s*, 1555*m*, 1505*s*, 1485*s*, 1442*s*, 1397*m*, 1386*m*, 1336*m*, 1287*m*, 1252*w*, 1216*w*, 1181*w*, 1152*w*, 1105*w*, 1074*w*, 1050*w*, 1021*m*, 1010*m*, 929*w*, 913*w*, 861*w*, 838*m*, 803*m*, 748*w*, 732*m*, 686*m*, 652*w*, 625*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.19 (*s*, H–N(3)); 8.20–8.17 (*m*, 2 arom. H); 7.44–7.36 (*m*, 3 arom. H); 7.22 (br. *s*, NH_2); 3.52 (*s*, MeN). ^{13}C-NMR (100 MHz, (D_6)DMSO): 159.01 (*s*, C(2)); 155.90 (*s*, C(7)); 154.41 (*s*, C(4)); 150.98 (*s*, C(8a)); 141.85 (*s*, C(6)); 136.34 (*s*); 128.60 (*d*); 128.22 (2*d*); 127.67 (2*d*); 111.59 (*s*, C(4a)); 28.10 (*q*, MeN). HR-MALDI-MS: 308.0541 (15, $[M+K]^+$, $C_{13}H_{11}KN_5O_2^+$; calc. 308.0544), 292.0800 (49, $[M+Na]^+$, $C_{13}H_{11}N_5NaO_2^+$; calc. 292.0805), 270.0984 (100, $[M+H]^+$, $C_{13}H_{12}N_5O_2^+$; calc. 270.0984). Anal. calc. for $C_{13}H_{11}N_5O_2$ (269.26): C 57.99, H 4.12, N 26.01; found: C 57.89, H 4.25, N 25.82.

*2-Amino-4-(benzyloxy)-8-methyl-6-(morpholin-4-yl)pteridin-7(8*H*)-one* (**24**). *From* **11**. A suspension of **11** (50 mg, 0.16 mmol) in toluene (5 ml) was treated with freshly distilled morpholine (0.3 ml), kept for 4.5 h at reflux, cooled to r.t., and evaporated. FC (AcOEt/hexane 2 : 3) gave **24** (56 mg, 97%).

From **10**. A suspension of **10** (300 mg, 1.0 mmol) in toluene (10 ml) was treated with freshly distilled morpholine (1.0 ml), kept for 1.5 h at reflux, cooled to r.t., and evaporated. FC (AcOEt/hexane 2 : 3) gave **24** (359 mg, 98%). A sample for analysis was sublimed at 160°, $< 10^{-3}$ mbar. Colourless solid. R_f (CH_2Cl_2/MeOH 9 : 1) 0.60. M.p. 172°. UV (MeOH, $c = 0.10$ mM): 215 (4.33), 243 (4.06), 299 (3.95), 362 (4.21). IR (ATR): 3439*w*, 3344*m*, 3233*w*, 3031*w*, 2970*w*, 2900*w*, 2857*w*, 1661*m*, 1640*s*, 1564*s*, 1550*s*, 1497*m*, 1443*s*, 1433*s*, 1406*m*, 1393*s*, 1354*s*, 1302*m*, 1242*s*, 1225*s*, 1178*m*, 1107*s*, 1063*m*, 1037*s*, 1028*s*, 1000*m*, 965*m*, 949*w*, 893*m*, 854*m*, 789*m*, 734*m*, 694*m*, 651*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.50–7.30 (*m*, 5 arom. H); 6.84 (*s*, $H_2N-C(2)$); 5.49 (*s*, PhCH_2); 3.69 (*t*, $J = 4.5$, $H_2-C(3')$); 3.55 (*t*, $J = 4.5$, $H_2-C(2')$); 3.48 (*s*, MeN). ^{13}C-NMR (75 MHz, (D_6)DMSO): 163.42 (*s*, C(4)); 158.80 (*s*, C(2)); 153.23 (*s*, C(7)); 148.90 (*s*, C(8a)); 146.96 (*s*, C(6)); 136.83 (*s*); 128.37 (2*d*); 127.91 (2*d*); 127.82 (*d*); 105.60 (*s*, C(4a)); 66.90 (*t*, PhCH_2); 65.87 (*t*, 2 CH_2O); 47.25 (*t*, 2 CH_2N); 28.52 (*q*, MeN). HR-MALDI-MS: 369.1667 (100, $[M+H]^+$, $C_{18}H_{20}N_6O_3^+$; calc. 369.1670). Anal. calc. for $C_{18}H_{20}N_6O_3$ (368.39): C 58.69, H 5.47, N 22.81; found: C 58.96, H 5.63, N 22.59.

*2-Amino-8-methyl-6-(morpholin-4-yl)pteridin-4,7(3*H*,8*H*)-dione* (**25**). A suspension of **24** (60 mg, 0.16 mmol) and LiBr (21 mg, 0.24 mmol) in MeCN (5 ml) was cooled to 0°, treated with Me_3SiCl (41 µl, 0.36 mmol), stirred for 15 min at 0° and for 8 h at r.t., cooled to 0°, diluted with MeOH (2 ml), and stirred for 15 min. The precipitate was filtered, washed with CH_2Cl_2/MeOH 9 : 1, and dried *in vacuo* to give **25** (42 mg, 93%). Colourless solid. UV (MeOH, $c = 0.13$ mM): 213 (4.40), 318 (4.12), 357 (4.15). IR (ATR): 3576*w*, 3446*w*, 3359*w*, 3186*m*, 2933*w*, 2896*w*, 2757*w*, 1655*s*, 1606*s*, 1561*m*, 1551s, 1519*s*, 1453*m*, 1441*m*, 1392*m*, 1366*m*, 1328*m*, 1296*w*, 1281*w*, 1248*s*, 1214*w*, 1169*w*, 1107*s*, 1070*w*, 1052*w*, 1034*w*, 1023*m*, 981*m*, 941*w*, 899*m*, 867*m*, 822*w*, 788*m*, 776*w*, 731*w*, 666*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 10.98 (*s*, H–N(3)); 6.75 (*s*, NH_2); 3.69 (br. *t*, $J = 4.7$, 2 CH_2O); 3.50 (br. *t*, $J = 4.7$, 2 CH_2N); 3.45 (*s*, MeN). ^{13}C-NMR (100 MHz, (D_6)DMSO): 158.86 (*s*, C(2)); 152.87 (*s*, C(7)); 152.27 (*s*, C(4)); 147.38 (*s*, C(8a)); 146.40 (*s*, C(6)); 108.50 (*s*, C(4a)); 65.90 (*t*, 2 CH_2O); 47.28 (*t*, 2 CH_2N); 28.16 (*q*, MeN). HR-MALDI-MS: 301.1017 (25, $[M+Na]^+$, $C_{11}H_{14}N_6NaO_3^+$; calc. 301.1020), 279.1197 (100, $[M+H]^+$, $C_{11}H_{15}N_6O_3^+$; calc. 279.1200).

*Phenyl 2,3,6-Tri-*O*-acetyl-4-{2-[2-amino-4-(benzyloxy)-7,8-dihydro-7-oxopteridin-6-yl]ethynyl}-4-deoxy-1-thio-β-*D*-glucopyranosid* (**26**). A suspension of **11** (50 mg, 0.16 mmol), phenyl 2,3,6-tri-*O*-acetyl-4-deoxy-4-ethynyl-1-thio-β-D-glucopyranoside (96 mg, 0.24 mmol), $Pd(OAc)_2$ (4.3 mg, 0.02 mmol), CuI (6.0 mg, 0.03 mmol), and Ph_3P (10 mg, 0.04 mmol) in MeCN (2 ml) was treated with Et_3N (3 ml) and stirred for 5.5 h at 23°. The soln. was diluted with $CHCl_3$ (10 ml) and filtered through a pad of *Celite*. Evaporation and FC (AcOEt/Hexane 1 : 1 → 4 : 1) gave **26** (94 mg, 87%). A sample for analysis was recrystallised in ^{i}PrOH and toluene. Cream coloured solid. R_f (CH_2Cl_2/MeOH 9 : 1) 0.56. M.p. 224°. UV (MeOH, $c = 0.088$ mM): 218 (4.48), 242 (4.23), 286 (sh, 3.67), 379 (4.38). IR (ATR): 3516*w*, 3405*m*, 3058*w*, 2949*w*, 2880*w*, 2236*w*, 1736*s*, 1666*m*, 1601*m*, 1573*s*, 1555*s*, 1522*m*, 1479*m*, 1422*m*, 1399*w*, 1369*m*, 1355*m*, 1315*w*, 1289*m*, 1226*s*, 1216*s*, 1143*w*, 1121*w*, 1071*m*, 1036*s*, 1012*s*, 913*m*, 879*w*, 856*m*, 800*m*, 754*m*, 742*m*, 722*w*, 703*m*, 689*m*, 642*w*, 621*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.60 (*s*, NH_2); 7.53–7.30 (*m*, 10 arom. H); 5.48 (*s*, PhCH_2); 5.45 (*dd*, $J = 10.8, 9.2$, H–C(3)); 5.31 (*d*, $J = 10.0$, H–C(1)); 4.78 (*dd*, $J = 10.0, 9.2$, H–C(2)); 4.41–4.36 (*m*, H_a–C(6)); 4.28–4.21 (*m*, H–C(5), H_b–C(6)); 3.44 (*s*, MeN); 3.28 (*dd*, $J = 10.8, 10.2$, H–C(4)); 2.04, 2.02, 2.01 (3*s*, AcO). ^{13}C-NMR (100 MHz, (D_6)DMSO): 170.00, 169.19, 169.17 (3*s*, 3 C=O); 164.94 (*s*, C(4′)); 161.61 (*s*, C(2′)); 156.10 (*s*, C(7′)); 151.32 (*s*, C(8′a)); 135.97 (*s*); 132.51 (*s*, C(6′)); 130.96 (*s*); 130.67 (2*d*); 129.02 (2*d*); 128.71 (2*d*); 128.43 (2*d*); 128.25 (*d*); 127.45 (*d*); 108.92 (*s*, C(4′a)); 88.03 (*s*, C≡*C*–C(4)); 83.43 (*d*, C(1)); 81.24 (*s*, *C*≡C–C(4)); 75.07 (*d*, C(5)); 72.43 (*d*, C(3)); 70.10 (*d*, C(2)); 67.99 (*t*, Ph*C*H_2); 63.84 (*t*, C(6)); 36.23 (*d*, C(4)); 27.64 (*q*, MeN); 20.52, 20.44, 20.35 (3*q*, 3 *Me*C=O). HR-MALDI-MS: 710.1897 (100, $[M+Na]^+$, $C_{34}H_{33}N_5NaO_9S^+$; calc. 710.1891), 688.2081 (65, $[M+H]^+$, $C_{34}H_{34}N_5O_9S^+$; calc. 688.2072). Anal. calc. for $C_{34}H_{33}N_5O_9S \cdot 0.1$ toluene (696.94): C 59.85, H 4.89, N 10.03; found: C 59.83, H 4.93, N 10.00.

*2-Amino-4-(benzyloxy)-8-methyl-6-[2-(trimethylsilyl)ethynyl]pteridin-7(8*H*)-one* (**27**). A suspension of **11** (500 mg, 1.58 mmol), (trimethylsilyl)acetylene (337 ml, 2.37 mmol), $Pd(OAc)_2$ (42 mg, 0.19 mmol), CuI (60 mg, 0.32 mmol), and Ph_3P (99 mg, 0.38 mmol) in MeCN (12 ml) was treated with

Et_3N (18 ml) and stirred for 8 h at 23°. The soln. was diluted with $CHCl_3$ (50 ml) and filtered through a pad of *Celite*. Evaporation and FC ($AcOEt/CH_2Cl_2$ 1:4) gave **27** (550 mg, 92%). Cream coloured solid. A sample for analysis was recrystallised in ^{i}PrOH. R_f (CH_2Cl_2/MeOH 9:1) 0.69. M.p. >300° (dec.). UV (MeOH, $c = 0.092$ mM): 220 (4.37), 242 (4.14), 260 (sh, 3.88), 290 (sh, 3.73), 384 (4.39). IR (ATR): 3520*w*, 3275*w*, 3188*w*, 3135*w*, 2955*w*, 2152*w*, 1661*m*, 1619*m*, 1597*m*, 1558*s*, 1522*m*, 1466*s*, 1439*s*, 1355*m*, 1320*m*, 1276*s*, 1249*m*, 1227*m*, 1091*w*, 1065*w*, 1037*w*, 984*w*, 910*w*, 883*w*, 838*s*, 798*m*, 759*m*, 747*m*, 736*m*, 697*m*, 624*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.45 (br. *s*, NH_2); 7.53–7.37 (*m*, 5 arom. H); 5.48 (*s*, PhCH_2); 3.34 (*s*, MeN); 0.22 (*s*, Me_3Si). ^{13}C-NMR (100 MHz, (D_6)DMSO): 164.97 (*s*, C(4)); 161.63 (*s*, C(2)); 156.07 (*s*, C(7)); 151.33 (*s*, C(8a)); 135.92 (*s*); 131.07 (*s*, C(6)); 128.81 (2*d*); 128.44 (2*d*); 128.28 (*d*); 109.07 (*s*, C(4a)); 101.51 (*s*, $C\equiv C-C(6)$); 98.66 (*s*, $C\equiv C-C(6)$); 68.02 (*t*, PhCH_2); 27.59 (*q*, MeN); −0.41 (*q*, Me_3Si). HR-MALDI-MS: 402.1348 (19, $[M+Na]^+$, $C_{19}H_{21}N_5NaO_2Si^+$; calc. 402.1357), 380.1529 (100, $[M+H]^+$, $C_{19}H_{22}N_5O_2Si^+$; calc. 380.1537). Anal. calc. for $C_{19}H_{21}N_5O_2Si$ (379.49): C 60.14, H 5.58, N 18.45; found: C 60.14, H 5.65, N 18.61.

*2-Amino-4-(benzyloxy)-6-ethynyl-8-methylpteridin-7(8*H*)-one* (**28**). A soln. of **27** (240 mg, 0.78 mmol) in THF (10 ml) was treated with $Bu_4NF\cdot 3\,H_2O$ (74 mg, 0.23 mmol), stirred for 30 min, and adsorbed on silica gel. FC ($AcOEt/CH_2Cl_2$ 1:4 → 2:3) gave **28** (233 mg, 98%). R_f (CH_2Cl_2/MeOH 9:1) 0.53. M.p. 201°. UV (MeOH, $c = 0.12$ mM): 218 (4.35), 240 (4.07), 286 (3.34), 375 (4.30). IR (ATR): 3434*m*, 3284*m*, 3181*m*, 2953*w*, 2114*w*, 1672*m*, 1626*m*, 1583*m*, 1567*s*, 1550*s*, 1479*s*, 1453*s*, 1435*s*, 1356*s*, 1326*m*, 1312*m*, 1270*m*, 1237*s*, 1215*s*, 1125*m*, 1057*m*, 1038*s*, 981*m*, 909*w*, 838*w*, 799*m*, 777*w*, 739*m*, 726*m*, 700*m*, 658*m*, 646*m*, 618*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.61 (*s*, NH_2); 7.53–7.35 (*m*, 5 arom. H); 5.48 (*s*, PhCH_2); 4.45 (*s*, $C\equiv CH$); 3.45 (*s*, MeN). ^{13}C-NMR (100 MHz, (D_6)DMSO): 164.96 (*s*, C(4)); 161.67 (*s*, C(2)); 156.24 (*s*, C(7)); 151.36 (*s*, C(8a)); 135.95 (*s*); 130.97 (*s*, C(6)); 128.63 (2*d*); 128.42 (2*d*); 128.22 (*d*); 108.97 (*s*, C(4a)); 84.44 (*s*, $C\equiv CH$); 80.32 (*d*, $C\equiv CH$); 67.98 (*t*, PhCH_2); 27.61 (*q*, MeN). HR-MALDI-MS: 330.0961 (34, $[M+Na]^+$, $C_{16}H_{13}N_5NaO_2^+$; calc. 330.0961), 308.1144 (100, $[M+H]^+$, $C_{16}H_{14}N_5O_2^+$; calc. 308.1142). Anal. calc. for $C_{16}H_{13}N_5O_2\cdot 0.46\,CH_2Cl_2$ (346.38): C 57.06, H 4.05, N 20.21; found: C 57.03, H 4.17, N 20.17.

*6,6′-(Ethyne-1,2-diyl)bis[2-amino-4-(benzyloxy)-8-methylpteridin-7(8*H*)-one]* (**29**). *From* **11** *and* **28**. A suspension of **11** (70 mg, 0.29 mmol), **28** (108 mg, 0.34 mmol), $Pd(OAc)_2$ (6 mg, 0.03 mmol), CuI (9 mg, 0.05 mmol), and Ph_3P (14 mg, 0.06 mmol) in MeCN (4 ml) was treated with Et_3N (6 ml), stirred for 7 h at 23°, diluted with $CHCl_3$ (10 ml), and filtered through a pad of *Celite*. Evaporation and FC (CH_2Cl_2/MeOH 49:1 → 9:1) gave **29** (63 mg, 47%).

From **11** *and* $Me_3Si-C\equiv CH$. A suspension of **11** (250 mg, 0.79 mmol), (trimethylsilyl)acetylene (169 µl, 1.18 mmol), $Pd(OAc)_2$ (42 mg, 0.19 mmol), CuI (60 mg, 0.32 mmol), and Ph_3P (99 mg, 0.38 mmol) in MeCN (8 ml) was treated with Et_3N (12 ml), stirred for 7 h at 23°, treated with $Bu_4NF\cdot 3\,H_2O$ (75 mg, 0.24 mmol), stirred for 30 min, treated with **11** (250 mg, 0.79 mmol), and stirred overnight. The soln. was diluted with $CHCl_3$ (20 ml), and filtered through a pad of *Celite*. Evaporation and FC (CH_2Cl_2/MeOH 49:1 → 9:1) gave **29** (253 mg, 55%). R_f (CH_2Cl_2/MeOH 9:1) 0.44. UV (MeOH, sat. soln.): 212, 237 (sh), 369 (sh), 438, 458 (sh). IR (ATR): 3462*w*, 3340*m*, 3328*m*, 3217*w*, 2953*w*, 2200*w*, 1660*m*, 1619*m*, 1567*s*, 1547*s*, 1485*s*, 1462*s*, 1429*s*, 1391*m*, 1360*m*, 1337*m*, 1305*m*, 1260*m*, 1218*s*, 1097*m*, 1060*m*, 1001*m*, 912*w*, 881*w*, 812*w*, 799*m*, 773*w*, 757*w*, 734*m*, 702*w*, 621*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 7.72 (br. *s*, NH_2); 7.55–7.39 (*m*, 5 arom. H); 5.50 (*s*, PhCH_2); 3.46 (*s*, MeN). HR-ESI-MS: 627.1626 (28, $[M+K]^+$, $C_{30}H_{24}KN_{10}O_4^+$; calc. 627.1614), 611.1884 (100, $[M+Na]^+$, $C_{30}H_{24}N_{10}NaO_4^+$; calc. 611.1874), 589.2051 (19, $[M+H]^+$, $C_{30}H_{25}N_{10}O_4^+$; calc. 589.2055).

X-Ray Crystal Structure Analysis of **29**·*3 DMSO*. Cooling a hot soln. of **29** in DMSO gave single crystals. $C_{30}H_{30}N_{10}O_4\cdot 3\,C_2H_6OS$, $M_r = 822.987$, monoclinic, *P*2/*c*, $a = 18.2346(7)$, $b = 14.4849(6)$, $c = 15.0548(5)$ Å, $\beta = 90.801(2)°$, $V = 3976.0(3)$ Å^3, $Z = 4$, $D_{calc} = 1.375$ Mg/m^3. Intensities were measured on a *Nonius Kappa CCD* diffractometer, with MoK_α radiation ($\lambda = 0.71073$ Å). Cell parameters from 55443 reflections, $\theta = 2.425–27.028°$, $\mu = 0.247$ mm^{-1}, $T = 203$ K. 23841 measured reflections, 6996 independent reflections, 4579 observed reflections ($>2\sigma(I)$). Refinement on F^2: full-matrix least squares refinement, $R(\text{all}) = 0.1105$, $R(\text{gt}) = 0.0673$. All diagrams and calculations were performed using maXus (*Bruker Nonius*, Delft, *MacScience*, Japan). The program SIR97 was used to solve the structure and the program SHELXL-97 to refine it.

*2-Amino-6-[(*E*)-2-bromoethenyl]-8-methylpteridin-4,7(3*H,*8*H*)-dione* (**31**). A suspension of **28** (100 mg, 0.33 mmol) and LiBr (42 mg, 0.489 mmol) in MeCN (5ml) was cooled to 0°, treated with Me_3SiCl (83 µl, 0.641 mmol), stirred for 15 min at 0° and for 13 h at r.t., cooled to 0°, diluted with MeOH (2 ml), and stirred for 15 min. The precipitate was filtered off, washed with cold MeCN, and dried *in vacuo* to afford **31** (70 mg, 72%). UV (MeOH, $c = 0.099$ mM): 222 (4.42), 238 (sh, 4.22), 303 (4.01), 376 (4.38). IR (ATR): 3551*w*, 3341*w*, 3184*m*, 3118*m*, 2931*w*, 2756*w*, 1655*s*, 1643*s*, 1602*s*, 1551*m*, 1519*s*, 1458*m*, 11392*m*, 1386*m*, 1335*m*, 1277*m*, 1227*w*, 1202*w*, 1071*m*, 971*w*, 943*m*, 873*m*, 846*m*, 818*m*, 788*m*, 764*w*, 743*w*, 729*w*, 678*w*, 626*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.25 (*s*, NH); 8–6.5 (br. *s*, NH_2); 7.57 (*d*, $J = 13.4$, H–C(2′)); 6.92 (*d*, $J = 13.4$, H–C(1′)); 3.46 (*s*, MeN). ^{13}C-NMR (100 MHz, (D_6)DMSO; assignment based on a HMBC spectrum): 158.72 (*s*, C(2)); 155.57 (*s*, C(7)); 154.50 (*s*, C(4)); 150.76 (*s*, C(8a)); 138.95 (*s*, C(6)); 130.10 (*d*, C(1′)); 124.66 (*d*, C(2′)); 111.94 (*s*, C(4a)); 27.80 (*q*, MeN).

REFERENCES

[1] M. Xu, A. Vasella, *Helv. Chim. Acta* **2006**, *89*, 1140.
[2] F.-L. Zhang, W. B. Schweizer, M. Xu, A. Vasella, *Helv. Chim. Acta* **2007**, *90*, 521.
[3] F.-L. Zhang, A. Vasella, *Helv. Chim. Acta* **2007**, *90*, 2315.
[4] T. Steinlin, A. Vasella, *Helv. Chim. Acta* **2008**, *91*, 435.
[5] T. Steinlin, T. Sonati, A. Vasella, *Helv. Chim. Acta* **2008**, *91*, 1879.
[6] C. W. Noell, R. K. Robins, *J. Med. Pharm. Chem.* **1962**, *5*, 558.
[7] F.-L. Zhang, A. Vasella, *Helv. Chim. Acta* **2008**, *91*, 2351.
[8] R. Huisgen, H. Seidl, I. Brüning, *Chem. Ber.* **1969**, *102*, 1102.
[9] R. Huisgen, H. Hauck, H. Seidl, M. Burger, *Chem. Ber.* **1969**, *102*, 1117.
[10] E. C. Taylor, R. Kobylecki, *J. Org. Chem.* **1978**, *43*, 680.
[11] E. C. Taylor, P. S. Ray, *J. Org. Chem.* **1987**, *52*, 3997.
[12] E. C. Taylor, P. S. Ray, *J. Org. Chem.* **1988**, *53*, 35.
[13] E. C. Taylor, P. S. Ray, I. S. Darwish, J. L. Johnson, K. V. Rajagopalan, *J. Am. Chem. Soc.* **1989**, *111*, 7664.
[14] E. C. Taylor, R. Doetzer, *J. Org. Chem.* **1991**, *56*, 1816.
[15] A. Ernst, A. Vasella, *Helv. Chim. Acta* **1996**, *79*, 1279.
[16] Z. Miao, M. Xu, B. Hoffmann, B. Bernet, A. Vasella, *Helv. Chim. Acta* **2005**, *88*, 1885.
[17] C. Cai, A. Vasella, *Helv. Chim. Acta* **1995**, *78*, 732.
[18] M. E. Hawkins, W. Pfleiderer, F. M. Balis, D. Porter, J. R. Knutson, *Anal Biochem.* **1997**, *244*, 86.
[19] R. Charubala, J. Maurinsh, A. Rösler, M. Melguizo, O. Jungmann, M. Gottlieb, J. Lehbauer, M. Hawkins, W. Pfleiderer, *Nucleosides Nucleotides* **1997**, *16*, 1369.
[20] S. L. Driscoll, M. E. Hawkins, F. M. Balis, W. Pfleiderer, W. R. Laws, *Biophys. J.* **1997**, *73*, 3277.
[21] M. E. Hawkins, W. Pfleiderer, O. Jungmann, F. M. Balis, *Anal. Biochem.* **2001**, *298*, 231.
[22] M. Melguizo, M. Gottlieb, W. Pfleiderer, *Pteridines* **1995**, *6*, 85.

Received January 9, 2009