A New Synthesis of Pteridines Substituted with Branched and Linear Alkenyl Groups at C(6). The Nitroso-Ene Reaction of 4-(Alkenoylamino)-5-nitrosopyrimidines

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Pteridines substituted with a 1,1-, 1,2-, or 1,1,3-substituted alkenyl group (mostly (*E*)-configured) at C(6) were synthesized in high yields by the intramolecular nitroso-ene reaction of 4-(alkenoylamino)-2-amino-6-benzyloxy-5-nitroso- and 4-(alkenoylamino)-2,6-diamino-5-nitrosopyrimidines. Thus, the *N*-alkenoyl nitrosopyrimidines **4** and **5** provided the pteridines **6** and **7**, respectively, characterized by a 1,2-disubstituted (*E*)-alkenyl substituent, the *C(4)*-(*E*)-geranoyl amide **13** led regio- and stereoselectively to the (*E*)-1,1,2-trisubstituted alkenyl-pteridine **16**, and the *C(4)*-(*Z*) isomer **14** led to **17** possessing a 1,1-disubstituted alkenyl group. The trifluoromethylated butenoyl amide **15** possessing a less highly nucleophilic alkenoyl group reacted more slowly to give the trifluoromethylated vinylpteridine **18**. Also the 4-(alkenoylamino)-2,6-diamino-5-nitrosopyrimidine **20** reacted more slowly than **4** and **5**, and provided the pteridines **23**; introduction of additional *N*-acyl groups as in **21** and **22** led to a considerably faster ene reaction.

The X-ray crystal structure analysis of the nitroso amide **15** shows eight symmetrically independent molecules in the unit cell. In the crystalline state, the *N*,*N*-dimethylformamidine derivative **9** of **6** forms a centrosymmetric dimer with the 7,8-lactam group connected by intermolecular hydrogen bonds.

Introduction. – The nitroso-ene reaction [1] is a valuable method for the regio- and stereoselective introduction of allylic nitrogen substituents, notwithstanding the debate about its precise reaction mechanism [2]. The most useful applications of the nitroso-ene reaction involve electron-deficient nitroso compounds, such as *N*-acylnitroso derivatives [3], α-chloronitroso ethers [4], and 4-nitro-nitrosobenzene [5]. To the best of our knowledge, nitroso-ene reactions of pyrimidines are not known, while *Wanner* and *Koomen* [6] used the ene reaction of 2-nitrosoadenosine triacetate with cyclohexene to demonstrate that the nitroso-ene reaction might be involved in the direct damage of DNA.

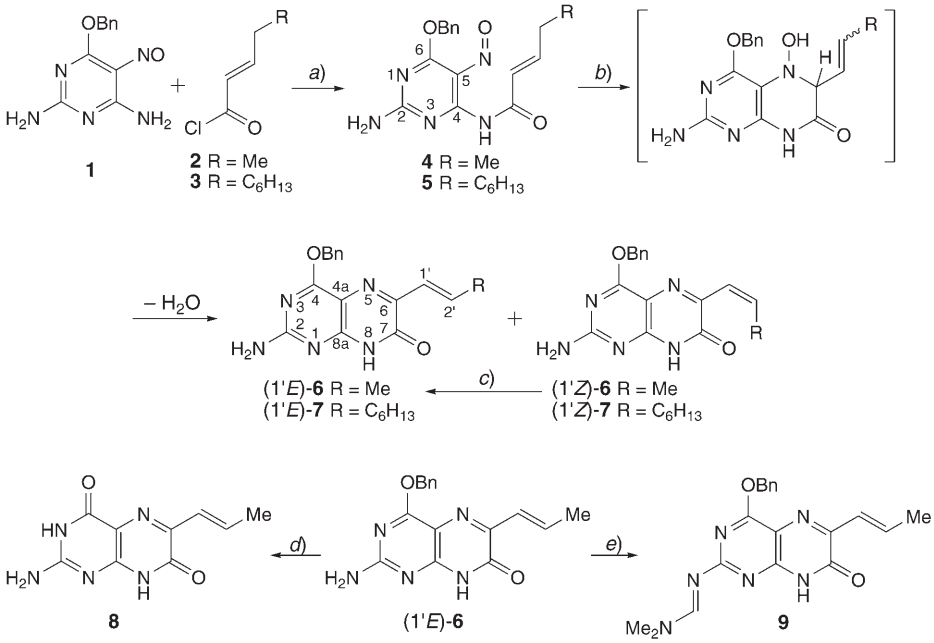
We have recently described a new method for the synthesis of pteridines substituted with a (*Z*)-3-hydroxyalk-1-enyl group at C(6), based on a high-yielding intramolecular [4 + 2] cycloaddition of *N*-(alka-2,4-dienoyl)-4-amino-5-nitrosopyrimidines [7]. In a similar way, the intramolecular nitroso-ene reaction of *N*-(alk-2-enoyl)-4-amino-5-nitrosopyrimidines should lead regioselectively to pteridines substituted with an alkenyl group at C(6), with the structure of the alkenyl substituent depending on the starting material and on the regioselectivity of the nitroso-ene reaction. We were interested in exploring these reactions in view of the configurational complementarity of the *C(6)*-1,2-disubstituted alkenyl substituents resulting from the ene reaction and

the [4 + 2] cycloaddition, respectively, and considering the large number of naturally occurring *C(6)*-substituted pteridines [8].

We planned to first evaluate the nitroso-ene reaction of unsaturated amides derived from 2,4-diamino-6-(benzyloxy)-5-nitrosopyrimidine (**1**) [9] (*Schemes 1* and *2*) and of 2,4,6-triamino-5-nitrosopyrimidine (**19**) [10] (*Scheme 3*). The desired amides should be obtained by acylation with (*E*)-pent-2-enoyl chloride (**2**), dec-2-enoyl chloride (**3**), the acid chlorides **10** and **11** derived from (*E*)- and (*Z*)-geranic acid[1]), respectively, and (*E*)-4,4,4-trifluoro-3-methylbut-2-enoyl chloride (**12**).

Results and Discussion. – The 4-(alkenoylamino)-5-nitrosopyrimidines **4** and **5** were obtained in a yield of 63 and 77%, respectively, by acylating a suspension of **1** in THF with (*E*)-pent-2-enoyl chloride (**2**) and (*E*)-dec-2-enoyl chloride (**3**), respectively, in the presence of K_2CO_3 (*cf.* [12]; *Scheme 1*). Purification of the amides by silica-gel chromatography was accompanied by the progressive formation of one or several polar, yellow, strongly blue-fluorescent products (*ca.* 10%), suggesting a facile ene

Scheme 1



a) 1.3 equiv. **2** or **3**, 8 equiv. K_2CO_3, −18°, THF; 63% of **4**, 77% of **5**. *b*) Suspension in toluene, 11 mM, 100°, 3 h; *ca.* 98% of **6** or **7**. *c*) 10% I_2 in benzene, reflux; or 1% AcOH in toluene, reflux, 36 h; *ca.* 98%. *d*) 1.5 equiv. Me_3SiCl, 1.3 equiv. LiBr, MeCN, 23°; 90%. *e*) 1.1 equiv. *t*-BuOCH(NMe_2)$_2$, DMF, 23°; 95%

[1]) We thank Dr. *Markus Gautschi*, *Givaudan AG*, Dübendorf, for a generous gift of the two geranic acids. For the combination of heterocycles with terpenes, see [11].

reaction leading to pteridines. In keeping with this interpretation, the nitrosopyrimidines **4** and **5** reacted already at room temperature, either in the solid state or in solution, as judged by a slow progressive colour change from blue to yellow, and the formation of a new spot on TLC. All acylated nitrosopyrimidines, therefore, had to be stored at a temperature below 5°.

On a preparative scale, suspensions of the blue nitrosopyrimidines **4** and **5** in toluene went into solution upon heating to 100°, and were progressively transformed into a yellow precipitate within *ca.* 3 h. Similarly to the facile cleavage of the N,O bond in the primary products of the nitroso *Diels–Alder* reaction [7], a N,O bond cleavage of the product of the ene reaction led in high yields to *ca.* 8:2 (*E*/*Z*)-mixtures[2]) of the pteridin-7(8*H*)-ones **6** and **7**, respectively (*Scheme 1*). The pure (*E*/*Z*)-pteridinones **6** (from **4**) and **7** (from **5**) were obtained by filtration, followed by washing the solid with H_2O and Et_2O. The structure of the products was confirmed by their spectroscopic data. Thus, the constitution of (*E*/*Z*)-**6** is evidenced by a high-resolution MALDI-MS, by IR bands at 3359 and 3192 cm^{-1} (NH), a comparison of the UV spectra with those of closely related pteridinones [7], by *J*(1′,2′) of the alkenyl H-atoms (15.6 Hz for (*E*)-**6** and 12.3 Hz for (*Z*)-**6**; *Table 1* in the *Exper. Part*), and by the ^{13}C-NMR data (*Table 2* in the *Exper. Part*).

Treating a suspension of (*E*/*Z*)-**6** in toluene with I_2 [13] or with AcOH resulted in the pure (*E*)-**6** isomer that was debenzylated to the poorly soluble *C(6)*-(*E*)-prop-1-enyl-isoxanthopterin **8**[3]) by treatment with Me_3SiBr generated *in situ* (90%; *Scheme 1*). As expected, the amidine **9** obtained by treating (*E*)-**6** with *Bredereck*'s reagent [16] proved much more soluble in a range of apolar solvents than **6** [17]. Crystals of **9** suitable for X-ray analysis[4]) were obtained by slowly concentrating a solution in MeCN. The crystals were multiple twins with loosely bound MeCN, showing heavy and uncorrectable overlapping of intensities reflected in a bad agreement factor (*Fig. 1*).

The (*E*)- and (*Z*)-geranylamides **13** and **14** and the (trifluoromethyl)butenoylamide **15** were prepared similarly as **4** and **5** to explore the regioselectivity of this nitroso-ene reaction and the effect of the nucleophilicity of the alkene (*Scheme 2*). The required (*E*)- and (*Z*)-geranoyl chlorides, **10** and **11** were obtained from the corresponding sodium salt and oxalyl chloride in the presence of pyridine[5]).

Beautifully blue, but poorly diffracting single crystals of **15** for X-ray analysis[4]) were obtained by slow evaporation of a solution of **15** in $CHCl_3$ (*Fig. 2*). The unit cell

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[2]) The nitroso-ene reaction of **4** at room temperature led exclusively to the (*E*)-isomer, suggesting an (*E*/*Z*) isomerisation at higher temperature. About 5% of **4** remained after two weeks.

[3]) For references about isoxanthopterin, see [14][15].

[4]) To the best of our knowledge, this is the first crystal structure of an isoxanthopterin derivative. The crystallographic data have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-617876 for **9** and No. CCDC-617875 for **15**. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB21EZ (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

[5]) The preparation of **10** from (*E*)-geranic acid and oxalyl chloride has been described, the ^{1}H-NMR data indicating a purity of 90% [18]. In our hands, this procedure led to substantial addition of HCl to the dimethylethylene moiety of (*E*)- and (*Z*)-geranic acid. For the preparation of acid chlorides from the corresponding sodium carboxylates, see [19][20].

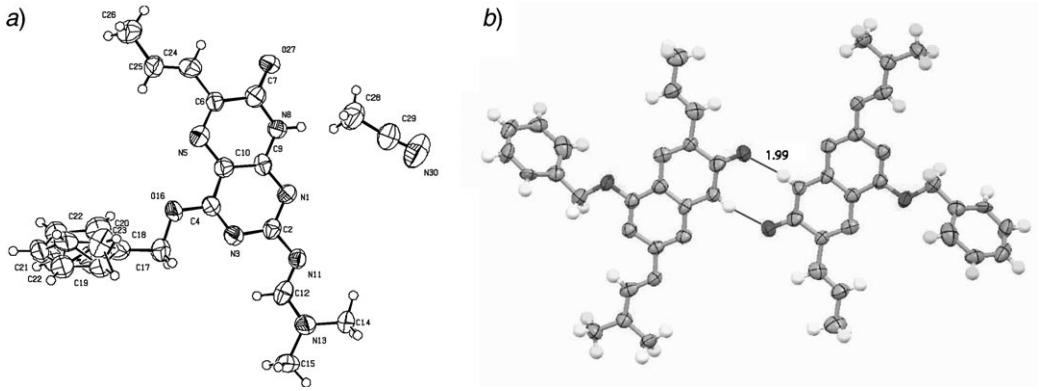
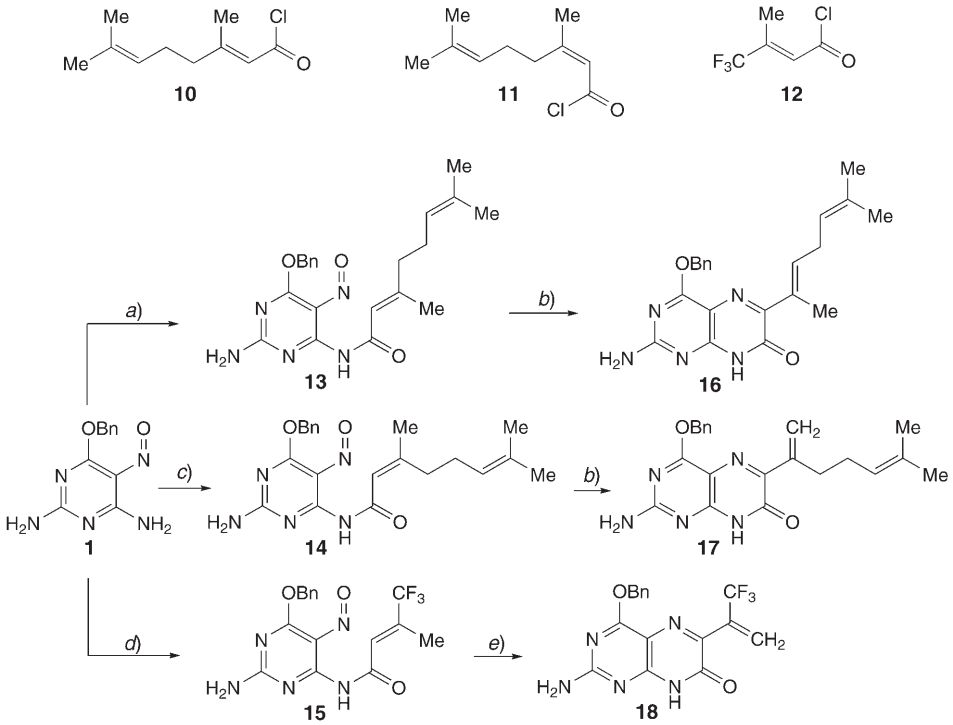


Fig. 1. *Crystal structure of* **9**·*MeCN. a*) ORTEP Drawing of a single molecule with co-crystallizing MeCN (ellipsoids at the 50% level, Ph group disordered over two equally occupied positions). *b*) Centrosymmetric H-bonded dimers (N···O 2.84 Å, H···O 1.99 Å). Only one position of the Ph group is shown for clarity.

Scheme 2



a) 1.3 equiv. **10**, 8 equiv. K_2CO_3, −18°, THF; 72% of **13**. *b*) Soln. in CH_2Cl_2, 6 mM, 23°, 4 d; *ca.* 98% of **16** or **17**. *c*) 1.3 equiv. **11**, 8 equiv. K_2CO_3, −18°, THF; 80% of **14**. *d*) 1.3 equiv. **12**, 8 equiv. K_2CO_3, −18°, THF; 68% of **15**. *e*) Suspension in toluene, 11 mM, 150°, 8 h in a sealed V-vial; *ca.* 98% of **18**.

parameters and the pattern of weak, but systematic reflections indicated a pseudosymmetric arrangement of independent molecules in the crystal structure. The angles differ by 3.9°, 0.4°, and 0.8° from 90° that would be required for crystallographic symmetry other than an inversion centre. The structure was solved in $P\bar{1}$ with eight molecules in the asymmetric unit. There are no crystallographic glide planes and translations between the molecules, mainly differing significantly by the conformation of the Ph ring. In all molecules, the *C(4)*-amido N–H form intramolecular H-bonds to the *C(5)*-nitroso O-atom (8 N···O distances in the range of 2.61 to 2.91 Å, H···O 1.78 to 1.95 Å). This is consistent with the unusual ^{1}H-NMR chemical shift (12–13 ppm) of the *C(4)*-amido NH group in **4**, **5** and **13**–**15**.

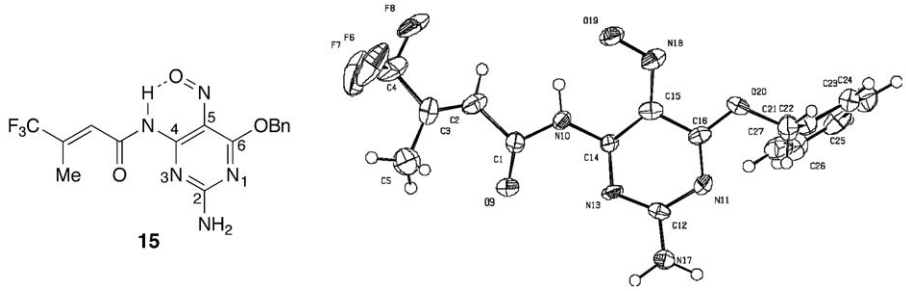


Fig. 2. *Crystal structure of* **15**. ORTEP Drawing of a single molecule (ellipsoids at the 50% level).

The nitroso-amido groups of two molecules of **15** are related by a pseudo twofold axis and in close contact (*Fig. 3*), with typical N=O···N=O distances around 2.8 Å. No intermolecular H-bond is observed.

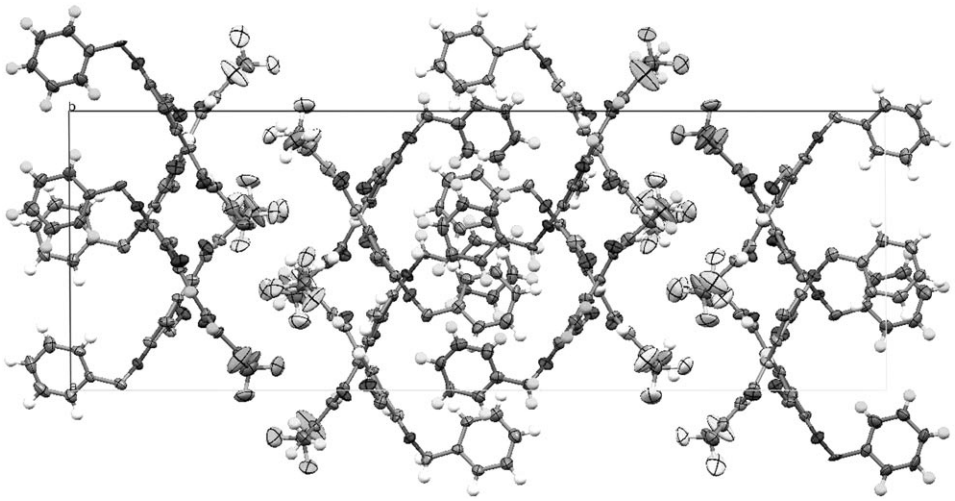


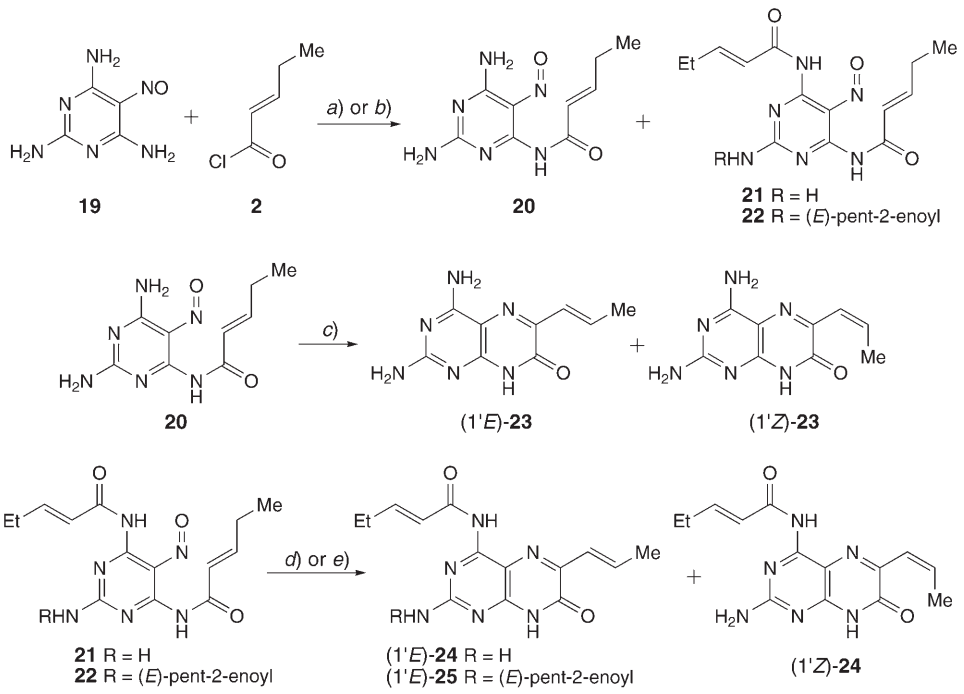
Fig. 3. *Crystal structure of* **15** *showing the pseudosymmetric arrangement of eight independent molecules in the unit cell.* Note that the cell angle β is 89.6°.

The ene reactions of the (*E*)-configured geranoyl amide **13** led diastereoselectively to the (*E*)-configured pteridinone **16**. A similar regioselective H abstraction of the (*Z*)-geranoyl amide **14** led to the pteridinone **17** characterized by a newly formed 1,1-disubstituted alkenyl group (*Scheme 2*). Performing the ene reaction of **13** and **14** under the same conditions as the one of **4** and **5** resulted in some side-products that were no longer formed at a lower temperature and concentration. As expected, the strongly electron-withdrawing CF_3 group of **15** led to a slower reaction. The much higher temperature (150°) required for this ene reaction, did not, however, decrease the yield of the resulting pteridinone **18**.

The pteridinones **16** and **17** were easily distinguished by their ^{1}H-NMR spectra. Thus, **16** shows a *triplet* for $H-C(2')$ and signals of three olefinically bound Me groups, while **17** is characterized by two *doublet*s for the *exo*-methylidene group $CH_2=C(1')$ and the signals of two Me groups. The *exo*-methylidene group $CH_2=C(1')$ of the pteridinone **18** resonates as a *doublet* and a broad *singlet*.

Considering the importance of 4-amino-pteridines [14], we also explored the nitroso-ene reaction of amides derived from 2,4,6-triamino-5-nitrosopyrimidine (**19**; *Scheme 3*), expecting a lower reactivity of the less electrophilic NO group. Mono-

Scheme 3



a) 2.5 equiv. **2**, 8 equiv. K_2CO_3, −18°, DMF; 42% of **20** and 13% of **21**. *b*) 3.5 equiv. **2**, 10 equiv. K_2CO_3, 0°, THF, crude **22**. *c*) Suspension in toluene, 11 mM, 100°, 24 h; *ca*. 98% of **23**. *d*) Suspension of **21** in toluene, 11 mM, 100°, 3 h; *ca*. 98% of **24**. *e*) Flash chromatography of crude **22** gave **25**; 78% of **25** from **19**.

acylation of **19** to **20** proved difficult, and some **21** was always formed, even when the (*E*)-pent-2-enoyl chloride (**2**) was slowly added using a syringe pump. The lowered electrophilicity of the diamino-nitrosopyrimidine **20** resulted in a considerably longer reaction time, *viz*. 24 h at 100°, as compared to 3 h at 100° for **4** and **5**. A second *N*-acyl group, as in the 4,6-diacylated nitroso compound **21**, increases the electrophilic properties of the NO group sufficiently to perform the ene reaction under the same conditions as for **4** and **5**, leading to the pteridinones **24** in high yield (98%) as *ca*. 8:2 (*E*/*Z*)-mixtures. The 2,4,6-triacylated nitrosopyrimidine **22** was formed when the acylation was run at 0° and proved even more highly reactive; flash chromatography of crude **22** at ambient temperature transformed most of the nitrosopyrimidine into the (*E*)-configured *C(6)*-prop-1-enyl-pteridinone **25** that was isolated in a yield of 78% after keeping the suspension of **22** and **25** overnight at ambient temperature.

The NMR spectra of the amino-nitroso amide **20** show two sets of signals in a 7:3 ratio, evidencing a mixture of two isomers, differing by the nature of their intramolecular H-bonds (*Fig. 4*). The major isomer is characterized by a NO···H_2N–C(6′) H-bond and the minor one by a NO···HN–C(4′) H-bond, suggesting the dominant influence of the stronger conjugation between the NH_2 and the NO group as compared to the formally more pronounced H-bond donor ability of the amido group. A similar observation was reported by *Tumkevicius* and co-workers [21]. The constitution of the 4-aminopteridinone **23** is evidenced by a high-resolution MALDI-MS, by broad NH bands at 3330 and 3213 cm^{-1} in the ATR-IR spectra, a comparison of the UV spectra with those of closely related pteridinones [22], by *J*(1′,2′) of the alkenyl H-atoms (15.8 Hz for (*E*)-**23** and 11.7 Hz for (*Z*)-**23**), and by the ^{13}C-NMR data (*Table 2* in the *Exper. Part*).

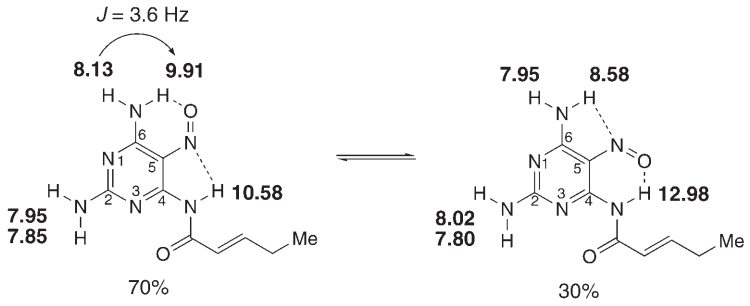


Fig. 4. *Two H-bonded isomers of* **20** *and the relevant chemical shift values* [ppm] *of their N*H *groups in (*D_6*)DMSO*

The conjugative interaction between either the *N*-acylamino or NH_2, and the NO substituents, and the ensuing intramolecular H-bonds also explains the observation that the C(2) and/or C(5) signals in the ^{13}C-NMR spectra of the nitroso amides **4**, **5**, and **13**–**15**[6]) were either missing, or, at best, very weak and broad in the spectra registered at

[6]) The expected weak concentration dependence of the chemical shift of *C(4)*–NH group involved in an intramolecular H-bond, and the moderate dependence of the chemical shift of the *C(2)*–NH_2 group involved in an intermolecular H-bond was confirmed for the ^{1}H-NMR spectra ($CDCl_3$) of the nitroso amide **5**.

room temperature, but visible at $-30°$. This observation is rationalized by a hindered rotation about the C(2)–NH_2 and C(5)–NO bonds due to a vinylogous amide-like interaction of the NH_2 and NO groups. All ^{13}C-NMR signals of the diamines **1** [12] and **20** are visible in the spectra obtained at room temperature. The conjugative interaction between the NO and the *ortho*-amino group leads to a particularly favourable intramolecularly H-bonded species.

We thank the *ETH Zürich* and *F. Hoffmann-La Roche AG*, Basel, for generous support, and Dr. *Bruno Bernet* for checking the analytical data.

Experimental Part

General. See [23]. Flash chromatography (FC): *Merck* silica gel *60* (0.063–0.200 mm). UV Spectra: MeOH, λ_{max} (log ε). FT-IR Spectra: neat (ATR), absorption in cm^{-1}. HR-MALDI-MS: in 3-hydroxypicolinic acid (3-HPA) matrix.

*(*E*)-Pent-2-enoyl Chloride* (**2**) *and (*E*)-Dec-2-enoyl Chloride* (**3**). Oxalyl chloride (21.2 ml, 0.25 mol) was added dropwise to a soln. of the corresponding acid (0.1 mol) in toluene (40 ml) at 0°. The resulting soln. was allowed to warm to r.t. and stirred for 5 h. Distillation of the residue afforded 8.9 g (74%) of **2** (65°/25 Torr) or 16.0 g (85%) of **3** (88°/0.3 Torr).

*(*E*)- and (Z)-Geranoyl Chlorides* (**10** and **11**, resp.). An emulsion of (*E*)- or (*Z*)-geranic acid in a 5% excess of 0.2N NaOH was stirred for 10 min at r.t, the resulting soln. was evaporated (45°/15 Torr) to dryness. The resulting off-white powder was then dried at 0.1 Torr (12 h at 40°, then 2 h at 105°). A suspension of the sodium salt of (*E*)- or (*Z*)-geranic acid (0.78 g, 4.0 mmol) in toluene (20 ml) was treated with pyridine (49 µl, 0.6 mmol), cooled to *ca.* −5°, and treated dropwise with oxalyl chloride (0.8 ml, 9.2 mmol) within 0.5 h. The ice-bath was removed, and stirring was continued for 20 min. After filtration, the filtrate was evaporated (<20°/0.5 Torr), affording **10** (0.65 g, 87%) or **11** (0.6 g, 80%).

Data of **10**. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.05 (*s*, H–C(2)); 5.07 (br. *t*, *J* = 5.7, H–C(6)); 2.24 (br. *s*, 2 H–C(4), 2 H–C(5)); 2.16 (*s*, Me–C(3)); 1.73, 1.64 (2*s*, Me_2C).

Data of **11**. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.03 (*s*, H–C(2)); 5.10 (br. *t*, *J* = 7.2, H–C(6)); 2.56 (*t*, *J* ≈ 7.8, 2 H–C(4)); 2.16 (*q*, *J* ≈ 7.5, 2 H–C(5)); 1.97 (*s*, Me–C(3)); 1.70, 1.62 (2*s*, Me_2C).

*(*E*)-4,4,4-Trifluoro-3-methylbut-2-enoyl Chloride* (**12**). A mixture of the corresponding acid (4.6 g, 30 mmol) and $SOCl_2$ (3.3 ml, 45 mmol) was refluxed for 3 d. Distillation (110°/760 Torr) afforded 3.2 g (63%) of **12**.

General Procedure for the Preparation of the Amides **4**, **5**, *and* **13**–**15**. A suspension of **1** (368 mg, 1.5 mmol) in THF (60 ml) was treated with K_2CO_3 (1.7 g, 12 mmol), cooled to −18°, and treated with a soln. of the acyl chloride (1.75 mmol) in THF (5 ml) within 2 h (addition *via* a syringe pump), stirred for 0.5 h, diluted with CH_2Cl_2 (100 ml), washed with cold H_2O (2 × 50 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH 200:1 or 100:1) of the green residue gave **4** (309 mg, 63%), **5** (460 mg, 77%), **13** (427 mg, 72%), **14** (474 mg, 80%), **15** (389 mg, 68%), resp., each as a blue powder.

*Data of (*E*)-N-[2-Amino-6-(benzyloxy)-5-nitrosopyrimidin-4-yl]pent-2-enamide* (**4**)[7]. UV: 204 (4.33), 263 (4.06), 351 (4.22), 650 (2.04, of a 10^{-3} M soln.). IR (ATR): 3372*m*, 3064*w*, 2930*w*, 2872*w*, 1708*m*, 1640*s*, 1601*s*, 1533*s*, 1498*m*, 1485*m*, 1461*s*, 1442*s*, 1386*m*, 1347*s*, 1310*m*, 1276*s*, 1248*m*, 1213*s*, 1167*s*, 1144*m*, 1112*s*, 1093*s*, 1031*m*, 977*w*, 901*w*, 865*w*, 834*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 12.80 (br. *s*, NH); 7.53–7.32 (*m*, 5 arom. H); 7.17 (*dt*, *J* = 15.0, 6.0, H–C(3)); 6.88, 5.95 (2 br. *s*, NH_2); 6.09 (*dt*, *J* = 15.0, 1.5, H–C(2)); 5.70 (*s*, PhCH_2); 2.38–2.28 (*m*, 2 H–C(4)); 1.14 (*t*, *J* = 7.5, Me). ^{13}C-NMR (75 MHz, $CDCl_3$, 298 K): 165.01 (*s*, C=O); 164.21 (*s*, C(6′)); 151.46 (*d*, C(3)); 145.36 (br. weak *s*, C(2′)); 139.08 (*s*, C(4′)); 135.13 (*s*); 128.52 (2*d*); 128.37 (*d*); 128.19 (2*d*); 123.54 (*d*, C(2)); 69.57 (*t*, PhCH_2); 25.66 (*t*, C(4)); 12.19

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[7]) The pteridinones **6**, **7**, **16**–**18**, and **23**–**25** show a range of decomposition temperatures between *ca.* 250 and 300°, whereas the nitroso compounds **4**, **5**, **13**, **14**, **20**, and **21** undergo the ene reaction, with the exception of **15**.

(*q*, Me); signal of C(5′) not visibile due to coalescence. HR-MALDI-MS: 328.1404 (5, $[M+H]^+$, $C_{16}H_{18}N_5O_3^+$; calc. 328.1404), 350.1218 (17, $[M+Na]^+$, $C_{16}H_{17}N_5NaO_3^+$; calc. 350.1224); low intensity of desired peaks due to the occurence of ene reaction during measurement.

*Data of (*E*)-*N*-[2-Amino-6-(benzyloxy)-5-nitrosopyrimidin-4-yl]dec-2-enamide* (**5**). UV: 208 (4.34), 263 (4.16), 352 (4.32), 648 (1.28, of a 10^{-3} M soln.). IR (ATR): 3329*w*, 3208*w*, 3164*w*, 2953*w*, 2924*m*, 2854*m*, 1721*m*, 1654*m*, 1639*s*, 1593*s*, 1581*s*, 1522*s*, 1497*m*, 1451*s*, 1390*m*, 1344*s*, 1286*m*, 1259*m*, 1212*s*, 1151*s*, 1112*s*, 1064*s*, 1030*m*, 976*m*, 915*w*, 846*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 12.96 (br. *s*, NH); 7.76 (br. *d*, $J=5.4$, NH); 7.52–7.25 (*m*, 5 arom. H); 7.09 (*dt*, $J=15.3$, 6.9, H–C(3)); 6.34 (br. *d*, $J=3.6$, NH); 6.05 (br. *d*, $J=15.6$, H–C(2)); 5.66 (*s*, PhCH_2); 2.30–2.10 (*m*, 2 H–C(4)); 1.52–1.29 (*m*, 5 CH_2); 0.91–0.86 (*m*, Me). ^{1}H-NMR titration (300 MHz, $CDCl_3$): 7.61, 6.35 (25 mM), 7.91, 6.49 (10 mM), 7.71, 6.32 (5 mM) for C(2)–NH_2; 12.91 (25 mM), 12.89 (10 mM), 12.85 (5 mM), 12.81 (1 mM) for C(4)–NH. ^{13}C-NMR (75 MHz, $CDCl_3$, 298 K): 165.08 (*s*, C=O); 164.31 (*s*, C(6′)); 150.54 (*d*, C(3)); 139.03 (*s*, C(4′)); 135.18 (*s*); 128.52 (2*d*); 128.37 (*d*); 128.25 (2*d*); 124.34 (*d*, C(2)); 69.42 (*t*, Ph*C*H_2); 32.39, 31.62, 29.06, 28.95, 27.86, 22.53 (6*t*); 13.99 (*q*, Me); signals of C(2′) and C(5′) not visibile due to coalescence. ^{13}C-NMR (75 MHz, $CDCl_3$, 243 K): 171.04 (*s*, C(5′)); 165.39 (*s*, C=O); 164.01 (*s*, C(6′)); 151.59 (*d*, C(3)); 145.78 (*s*, C(2′)); 138.71 (*s*, C(4′)); 134.86 (*s*); 128.70 (5*d*, 5 C of Ph); 123.95 (*d*, C(2)); 69.84 (*t*, Ph*C*H_2), 32.84 (*t*); 32.01 (*t*); 29.44 (2*t*); 27.97 (*t*); 23.00 (*t*); 14.61 (*q*, Me). HR-MALDI-MS: 398.2180 (84, $[M+H]^+$, $C_{21}H_{28}N_5O_3^+$; calc. 398.2187), 420.1995 (8, $[M+Na]^+$, $C_{21}H_{27}N_5NaO_3^+$; calc. 420.2006).

*Data of (*E*)-*N*-[2-Amino-6-(benzyloxy)-5-nitrosopyrimidin-4-yl]-3,7-dimethylocta-2,6-dienamide* (**13**). UV: 202 (4.21), 233 (4.11), 264 (4.19), 350 (4.36). IR (ATR): 3326*w*, 3155*m*, 2912*w*, 1714*w*, 1655*m*, 1628*m*, 1593*s*, 1581*s*, 1520*s*, 1496*m*, 1450*s*, 1388*m*, 1342*s*, 1290*m*, 1259*m*, 1219*s*, 1197*s*, 1148*s*, 1115*s*, 1061*s*, 1031*m*, 1003*w*, 969*w*, 933*w*, 891*w*, 864*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 12.33 (br. *s*, NH); 8.67 (br. *s*, NH_2); 7.55–7.33 (*m*, 5 arom. H); 6.49 (*s*, H–C(2)); 5.61 (*s*, PhCH_2); 5.10 (br. *t*, $J=6.8$, H–C(6)); 2.26–2.16 (*m*, 2 H–C(4), 2 H–C(5)); 2.10 (*s*, Me–C(3)); 1.65, 1.60 (2*s*, Me_2C). ^{13}C-NMR (300 MHz, (D_6)DMSO, 298 K): 165.26 (*s*, C=O); 163.48 (*s*, C(6′)); 160.35 (*s*, C(3)); 138.57 (*s*, C(4′)); 135.49 (*s*); 131.39 (*s*, C(7)); 128.33 (2*d*); 128.27 (2*d*); 128.10 (*d*); 123.14 (*d*, C(2)); 118.89 (*d*, C(6)); 68.37 (*t*, Ph*C*H_2); 40.46 (*t*, C(4)); 25.73 (*t*, C(5)); 25.46 (*q*, *Me*–C(3)); 19.02, 17.61 (2*q*, *Me*$_2$C); signals of C(2′) and C(5′) not visibile due to coalescence. HR-MALDI-MS: 396.2025 (51, $[M+H]^+$, $C_{21}H_{26}N_5O_3^+$; calc. 396.2030), 418.1855 (7, $[M+Na]^+$, $C_{21}H_{25}N_5NaO_3^+$; calc. 418.1850).

*Data of (*Z*)-*N*-[2-Amino-6-(benzyloxy)-5-nitrosopyrimidin-4-yl]-3,7-dimethylocta-2,6-dienamide* (**14**). UV: 202 (4.34), 232 (4.17), 262 (4.23), 350 (4.39). IR (ATR): 3333*w*, 3215*m*, 2973*w*, 1718*w*, 1656*s*, 1626*m*, 1584*s*, 1513*s*, 1479*m*, 1441*s*, 1389*m*, 1330*s*, 1292*w*, 1271*m*, 1232*s*, 1200*s*, 1175*s*, 1111*s*, 1079*s*, 1061*s*, 1037*s*, 1000*w*, 972*w*, 961*w*, 938*w*, 909*m*, 874*w*, 855*w*, 845*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 12.35 (br. *s*, NH); 8.71, 8.68 (2 br. *s*, NH_2); 7.56–7.38 (*m*, 5 arom. H); 6.56 (*s*, H–C(2)); 5.62 (*s*, PhCH_2); 5.10 (*t*, $J=6.9$, H–C(6)); 2.55 (br. *t*, $J=7.2$, 2 H–C(4)); 2.11 (br. *q*, $J\approx7.2$, 2 H–C(5)); 1.97 (*s*, Me–C(3)); 1.62, 1.57 (2*s*, Me_2C). ^{13}C-NMR (300 MHz, (D_6)DMSO, 298 K): 165.17 (*s*, C=O); 163.73 (*s*, C(6′)); 161.18 (*s*, C(3)); 138.75 (*s*, C(4′)); 135.70 (*s*); 131.47 (*s*, C(7)); 128.49 (2*d*); 128.46 (2*d*); 128.27 (*d*); 123.65 (*d*, C(2)); 119.54 (*d*, C(6)); 68.45 (*t*, Ph*C*H_2); 33.56 (*t*, C(4)); 26.21 (*t*, C(5)); 25.40 (*q*, *Me*–C(3)); 25.25, 17.47 (2*q*, *Me*$_2$C); signals of C(2′) and C(5′) not visibile due to coalescence. HR-MALDI-MS: 396.2029 (54, $[M+H]^+$, $C_{21}H_{26}N_5O_3^+$; calc. 396.2030), 418.1855 (7, $[M+Na]^+$, $C_{21}H_{25}N_5NaO_3^+$; calc. 418.1850).

*Data of (*E*)-*N*-[2-Amino-6-(benzyloxy)-5-nitrosopyrimidin-4-yl]-4,4,4-trifluoro-3-methylbut-2-enamide* (**15**). M.p. 148.9–149.2°. UV: 206 (4.39), 267 (4.14), 353 (4.36). IR (ATR): 3354*w*, 3321*w*, 3167*w*, 2949*w*, 1732*w*, 1653*m*, 1594*m*, 1581*m*, 1527*m*, 1496*w*, 1460*m*, 1390*m*, 1344*s*, 1299*s*, 1260*w*, 1214*s*, 1187*m*, 1149*s*, 1126*s*, 1103*m*, 1059*s*, 948*w*, 895*w*, 812*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 12.61 (br. *s*, NH); 7.53–7.31 (*m*, 5 arom. H); 6.73 (br. *quint.*, $J\approx1.5$, H–C(2)); 6.63, 6.05 (2 br. *s*, NH_2); 5.70 (*s*, PhCH_2); 2.24 (*d*, $J=1.5$, Me). ^{13}C-NMR (75 MHz, $CDCl_3$, 298 K): 164.66 (*s*, C=O); 164.18 (*s*, C(6′)); 144.85 (br. weak *s*, C(2′)); 142.09 (*q*, ^2J(C,F) = 30.3, C(3)); 138.96 (*s*, C(4′)); 135.25 (*s*); 128.86 (2*d*); 128.78 (*d*); 128.50 (2*d*); 124.11 (*q*, ^3J(C,F) = 5.5, C(2)); 123.29 (*q*, ^1J(C,F) = 272.4, CF_3); 70.00 (*t*, Ph*C*H_2); 12.84 (*q*, Me); signal of C(5′) not visibile due to coalescence. ^{19}F-NMR (282 MHz, $CDCl_3$): –70.93. HR-MALDI-MS: 382.1116 (100, $[M+H]^+$, $C_{16}H_{15}F_3N_5O_3^+$; calc. 382.1122), 404.0941 (18, $[M+Na]^+$, $C_{16}H_{14}F_3N_5NaO_3^+$; calc. 404.0941). Anal. calc. for $C_{16}H_{14}F_3N_5O_3$ (381.31): C 50.40, H 3.70, N 18.37, F 14.95; found: C 50.24, H 3.89, N 18.17, F 15.11.

X-Ray Analysis of **15**[4]). Slow evaporation of a soln. of **15** in $CHCl_3$ gave suitable single crystals for X-ray analysis (dimensions: $0.24 \times 0.2 \times 0.04$ mm; colour: dark blue). $C_{16}H_{14}F_3N_5O_3$, M_r 381.314, triclinic, $P\bar{1}$, $a = 13.1447(2)$, $b = 13.4048(2)$, $c = 38.5360(5)$ Å, $\alpha = 86.0982(6)$, $\beta = 89.5773(5)$, $\gamma = 89.2288(5)^\circ$, $V = 6773.6(2)$ Å^3; $Z = 16$, $Z' = 8$, $D_{calc.} = 1.496$ Mg/m^3. Intensities were measured on a *Nonius Kappa CCD* diffractometer, with MoK_α radiation $\lambda = 0.71073$ Å, Cell parameters from 38829 reflections, $\theta = 0.998 - 26.373^\circ$, $\mu = 0.128$ mm^{-1}, $T = 223$ K. 38829 measured reflections, 25068 independent reflections, 8976 observed reflections ($> 2\sigma(I)$). Refinement on F^2: Full-matrix least-squares refinement, $R(\text{all}) = 0.2165$, $R(\text{gt}) = 0.0860$. Pseudo α-centering and pseudo-inversion centre at 0.0, 0.25, 0.25 with relatively week $k + l =$ odd reflections but refinement in monoclinic space group does not give satisfactory results. All diagrams and calculations were performed using maXus (*Bruker Nonius*, *Delft & MacScience*, Japan). The programme SIR97 was used to solve the structure and the programme SHELXL-97 to refine it.

*Preparation of the Pteridin-7(8*H*)-ones* **6**, **7**, *and* **18**. A suspension of **4** (72 mg, 0.22 mmol), **5** (87.5 mg, 0.22 mmol), or **15** (84 mg, 0.22 mmol) in toluene (20 ml) was heated at the indicated temp. and time, affording a blue soln. upon heating and the desired product as yellow precipitate. **4**, **5** (100°, 3 h), **15** (150°, 8 h). The suspension was concentrated, followed by filtration, to give a yellow powder, which was successively washed with H_2O and Et_2O. Drying *i.v.* gave (*E/Z*)-**6** (67 mg), (*E/Z*)-**7** (82 mg), and **18** (78.5 mg) in a yield of *ca.* 98%, resp. Heating (*E/Z*)-**6** under reflux in benzene containing 10% I_2 for 36 h, or in toluene with 1% AcOH for 36 h, gave pure (*E*)-**6**.

*Preparation of the Pteridin-7(8*H*)-ones* **16** *and* **17**. A soln. of **13** or **14** (43.5 mg, 0.11 mmol) in CH_2Cl_2 (10 ml) was stirred at 23° for 4 d. The suspension of the resulting precipitate was concentrated to a small volume. Filtration gave **16** as yellow powder and **17** as light-brown powder. Drying *i.v.* gave **16** (40 mg) and **17** (41 mg) in a yield of *ca.* 98%, resp.

*Data of 2-Amino-6-[(*E/Z*)-prop-1-enyl]-4-(benzyloxy)pteridin-7(8*H*)-one* (**6**). UV: 211 (4.21), 291 (3.57), 370 (3.90). IR (ATR): 3359*m*, 3192*m*, 2905*w*, 2844*w*, 2778*w*, 1652*s*, 1614*s*, 1560*s*, 1532*s*, 1495*s*, 1446*s*, 1391*s*, 1348*s*, 1310*m*, 1293*m*, 1220*w*, 1186*m*, 1104*w*, 1082*m*, 1068*m*, 1028*w*, 1005*w*, 978*m*, 956*m*, 937*w*, 913*m*, 898*m*, 852*m*, 832*w*, 815*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO; (*E*)/(*Z*) 83 : 17): see *Table 1*; additionally, 7.00 – 6.88 (*m*, 0.83 H), 6.10 – 6.04 (*m*, 0.17 H) (H–C(2′)); 6.71 (*d*, $J = 12.3$, 0.17 H), 6.64 (*d*, $J = 15.6$, 0.83 H) (H–C(1′)); 2.17 (*d*, $J = 7.8$, 0.51 H), 1.87 (*d*, $J = 6.9$, 2.49 H) (Me(3′)). ^{13}C-NMR (125 MHz, (D_6)DMSO; only signals of the the (*E*)-isomer observed): see *Table 2*; additionally, 136.36 (*s*); 133.58 (*d*); 128.47 (2*d*); 128.41 (2*d*); 128.06 (*d*, C(1′)); 125.93 (*d*, C(2′)); 67.38 (*t*, Ph*C*H$_2$); 18.66 (*q*, Me). HR-MALDI-MS: 310.1297 (82, $[M + H]^+$, $C_{16}H_{16}N_5O_2^+$; calc. 310.1299), 332.1113 (100, $[M + Na]^+$, $C_{16}H_{15}N_5NaO_2^+$; calc. 332.1118).

*Data of 2-Amino-6-[(*E/Z*)-oct-1-enyl]-4-(benzyloxy)pteridin-7(8*H*)-one* (**7**). UV: 210 (4.21), 288 (3.77), 375 (3.94). IR (ATR): 3360*w*, 3189*m*, 3065*w*, 3032*w*, 2951*w*, 2919*m*, 2848*m*, 2767*w*, 1791*w*, 1650*s*, 1614*s*, 1557*s*, 1529*s*, 1496*s*, 1480*m*, 1443*s*, 1390*m*, 1342*s*, 1306*m*, 1216*w*, 1179*m*, 1086*m*, 1068*m*, 1029*w*,

Table 1. *Selected ^{1}H-NMR Chemical Shifts* [ppm] *and Coupling Constants* [Hz] *of the Pteridin-7(8*H*)-ones* **6**, **7**, *and* **16** – **18** *in (D_6)DMSO*

	6	**7**	**16**	**17**	**18**
H–N(8)	12.37	12.37	12.30	12.36	12.68
H_2N–C(2)	7.18, 7.16	7.14, 7.11	7.13	7.22	7.44
Ph	7.50 – 7.33	7.52 – 7.34	7.51 – 7.33	7.51 – 7.31	7.51 – 7.31
H_E–C(1′)	6.64	6.61	–	–	–
H_Z–C(1′)	6.71	6.68	–	–	–
H_E–C(2′)	7.00 – 6.88	7.00 – 6.92	6.97	–	–
H_Z–C(2′)	6.10 – 6.04	5.99 – 5.93	–	–	–
H_2C=C(1′)	–	–	–	6.48, 5.51	7.01, 6.39
PhCH_2	5.48	5.48	5.50	5.49	5.51
$J(1',2')_E$	15.6	15.8	–	–	–
$J(1',2')_Z$	12.3	11.8	–	–	–

Table 2. *Selected ^{13}C-NMR Chemical Shifts* [ppm] *of the Pteridin-7(8*H*)-ones* **6**, **7**, **16**–**18**, *and* **23**–**25** *in (D$_6$)DMSO*

	6	**7**	**16**[a])	**17**[a])	**18**	**23**	**24**	**25**
C(2)	150.73	150.75	150.56	150.80	150.90	148.61	149.74	151.45
C(4)	164.39	164.38	164.47	164.68	164.66	161.80	163.50	161.38
C(4a)	107.58	107.62	107.07	107.21	107.43	106.44	108.02	113.78
C(6)	145.73	145.33	147.90	144.12	139.47	142.59	145.02	147.07
C(7)	156.83	156.87	156.71	156.77	156.14	157.32	156.96	156.56
C(8a)	161.08	161.07	161.27	161.60	161.91	160.49	161.17	157.25

[a]) Assignments based on a HSQC and a HMBC spectrum.

976*m*, 949*m*, 913*s*, 848*m*, 815*w*. ^{1}H-NMR (500 MHz, (D$_6$)DMSO; (*E*)/(*Z*) 78:22): see *Table 1*; additionally, 7.00–6.92 (*m*, 0.78 H), 5.99–5.93 (*m*, 0.22 H) (H–C(2′)); 6.68 (*d*, *J* = 11.8, 0.22 H), 6.61 (*d*, *J* = 15.8, 0.78 H) (H–C(1′)); 2.73 (*q*, *J* = 7.6, 0.44 H), 2.21 (*q*, *J* = 6.5, 1.56 H) (CH$_2$(3′)); 1.45–1.15 (*m*, 4 CH$_2$); 0.86 (*t*, *J* = 6.8, 2.34 H), 0.80 (*t*, *J* = 6.8, 0.66 H) (Me(8′)). ^{13}C-NMR (125 MHz, (D$_6$)DMSO; only signals of the (*E*)-isomer observed): see *Table 2*; additionally, 138.50 (*s*); 136.38 (*d*, C(1′)); 128.46 (2*d*); 128.39 (2*d*); 128.06 (*d*); 124.59 (*d*, C(2′)); 67.35 (*t*, PhCH$_2$); 32.67 (*t*, C(3′)); 31.06 (*t*, C(4′)); 28.31 (2*t*, C(5′), C(6′)); 22.02 (*t*, C(7′)); 13.91 (*q*, C(8′)). HR-MALDI-MS: 380.2075 (100, $[M+H]^+$, $C_{21}H_{26}N_5O_2^+$; calc. 380.2081), 402.1906 (6, $[M+Na]^+$, $C_{21}H_{25}N_5NaO_2^+$; calc. 402.1900).

*Data of 2-Amino-4-(benzyloxy)-6-[(*E*)-1,5-dimethylhexa-1,4-dienyl]pteridin-7(8*H*)-one* (**16**). UV: 211 (4.32), 256 (3.57), 293 (3.60), 363 (4.10). IR (ATR): 3461*m*, 3298*w*, 3282*w*, 3184*m*, 2962*w*, 2908*w*, 2761*w*, 1797*w*, 1654*s*, 1631*s*, 1619*s*, 1560*s*, 1531*s*, 1489*m*, 1470*m*, 1457*m*, 1439*s*, 1398*m*, 1349*s*, 1323*m*, 1295*m*, 1218*w*, 1177*m*, 1110*w*, 1087*m*, 1044*m*, 978*w*, 950*m*, 915*s*, 862*w*, 833*m*, 800*m*. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): see *Table 1*; additionally, 6.97 (br. *t*, *J* ≈ 6.8, H–C(2′)); 5.15 (br. *t*, *J* ≈ 6.4, H–C(4′)); 2.90 (br. *t*, *J* ≈ 7.1, CH$_2$(3′)); 1.97 (*s*, Me–C(1)); 1.67, 1.63 (2*s*, Me$_2$C). ^{13}C-NMR (100 MHz, (D$_6$)DMSO): see *Table 2*; additionally: 136.54 (*s*); 134.47 (*d*, C(2′)); 132.20 (*s*, C(1′)); 131.61 (*s*, C(5′)); 128.40 (2*d*); 128.05 (2*d*); 127.96 (*d*); 121.88 (*d*, C(4′)); 67.17 (*t*, PhCH$_2$); 27.81 (*t*, C(3′)); 25.42 (*q*, *Me*–C(1)); 17.66, 14.22 (2*q*, *Me*$_2$C). HR-MALDI-MS: 378.1917 (100, $[M+H]^+$, $C_{21}H_{24}N_5O_2^+$; calc. 378.1925), 400.1739 (5, $[M+Na]^+$, $C_{21}H_{23}N_5NaO_2^+$; calc. 400.1744).

*Data of 2-Amino-4-(benzyloxy)-6-[5-methyl-1-methylidenehex-4-enyl]pteridin-7(8*H*)-one* (**17**). UV: 211 (4.57), 292 (3.70), 363 (4.31). IR (ATR): 3338*m*, 3190*m*, 2965*w*, 2910*m*, 2850*m*, 2778*m*, 1647*s*, 1620*s*, 1607*s*, 1561*s*, 1531*s*, 1480*s*, 1454*m*, 1438*s*, 1387*s*, 1345*s*, 1304*m*, 1218*w*, 1188*s*, 1102*m*, 1083*m*, 1046*m*, 1027*m*, 982*m*, 962*m*, 929*m*, 909*m*, 893*m*, 842*m*, 827*m*, 812*w*. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): see *Table 1*; additionally, 6.48 (*d*, *J* = 2.7, CH=C(1′)); 5.51 (CH′=C(1′), overlapping with the PhC*H*$_2$ signal); 5.10 (br. *t*, *J* ≈ 7.1, H–C(4′)); 2.48 (CH$_2$(2′), overlapping with the DMSO signal); 2.12 (br. *q*, *J* ≈ 6.9, CH$_2$(3′)); 1.59, 1.46 (2*s*, Me$_2$C). ^{13}C-NMR (125 MHz, (D$_6$)DMSO): see *Table 2*; additionally, 145.85 (*s*, C(1′)); 136.52 (*s*); 130.89 (*s*, C(5′)); 128.34 (2*d*); 127.89 (*d*); 127.79 (2*d*); 124.19 (*d*, C(4′)); 120.05 (*t*, *C*H$_2$=C(1′)); 67.19 (*t*, PhCH$_2$); 34.81 (*t*, C(2′)); 27.30 (*t*, C(3′)); 25.45, 17.42 (2*q*, *Me*$_2$C). HR-MALDI-MS: 378.1916 (100, $[M+H]^+$, $C_{21}H_{24}N_5O_2^+$; calc. 378.1925), 400.1744 (10, $[M+Na]^+$, $C_{21}H_{23}N_5NaO_2^+$; calc. 400.1744).

*Data of 2-Amino-4-(benzyloxy)-6-[1-(trifluoromethyl)ethenyl]pteridin-7(8*H*)-one* (**18**). UV: 211 (4.44), 287 (3.52), 366 (4.19). IR (ATR): 3464*w*, 3319*w*, 3198*w*, 3144*w*, 2836*w*, 2732*w*, 1969*w*, 1813*w*, 1662*w*, 1611*s*, 1567*s*, 1542*m*, 1490*m*, 1465*m*, 1449*m*, 1430*s*, 1394*m*, 1370*m*, 1353*s*, 1318*m*, 1308*m*, 1251*w*, 1187*m*, 1163*s*, 1137*s*, 1094*m*, 1078*m*, 1030*m*, 983*m*, 926*m*, 875*w*, 834*w*, 822*w*, 813*w*. ^{1}H-NMR (300 MHz, (D$_6$)DMSO): see *Table 1*; additionally, 7.01 (*d*, *J* = 1.5, CH=C(1′)); 6.39 (br. *s*, CH′=C(1′)). ^{13}C-NMR (75 MHz, (D$_6$)DMSO): see *Table 2*; additionally, 136.16 (*s*); 133.08 (*q*, ^2J(C,F) = 27.9, C(1′)); 128.20 (2*d*); 127.74 (*d*); 127.48 (2*d*); 126.44 (*d*, ^3J(C,F) = 6.0, C(2′)); 122.44 (*q*, ^1J(C,F) = 272.3, CF$_3$); 67.23 (*t*, PhCH$_2$). ^{19}F-NMR (282 MHz, (D$_6$)DMSO): –61.85. HR-MALDI-MS: 364.1011 (100, $[M+H]^+$, $C_{16}H_{13}F_3N_5O_2^+$; calc. 364.1016), 386.0837 (33, $[M+Na]^+$, $C_{16}H_{12}F_3N_5NaO_2^+$; calc. 386.0835).

*2-Amino-6-[(*E*)-prop-1-enyl]pteridine-4,7(3*H*,8*H*)-dione* (**8**). A soln. of anh. LiBr (7.3 mg, 0.083 mmol) in MeCN (1 ml) was treated with Me_3SiCl (12.5 µl, 0.1 mmol), stirred at 23° under Ar for 5 min, and treated with dry (*E*)-**6** (20 mg, 0.064 mmol). The resulting suspension was stirred at 23° for 12 h, cooled to 0°, and treated with MeOH (0.5 ml). The suspension was filtered. The solid was washed with H_2O and dried *i.v.* to afford **8** (12.7 mg, 90%). Light yellow powder. UV: 214 (4.22), 302 (3.73), 369 (3.99). IR (ATR): 3323*w*, 3122*m*, 2961*w*, 2912*w*, 2849*w*, 2770*w*, 1697*m*, 1666*s*, 1641*s*, 1601*s*, 1581*s*, 1518*m*, 1474*m*, 1443*m*, 1374*m*, 1342*m*, 1317*w*, 1287*w*, 1252*w*, 1186*w*, 1156*w*, 1111*w*, 966*m*, 937*w*, 901*m*, 819*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 12.29, 10.96 (2 br. *s*, 2 NH); 6.97 (br. *s*, NH_2); 6.97–6.85 (*m*, H–C(2′)); 6.60 (*dq*, *J* = 15.0, 1.8, H–C(1′)); 1.88 (*dd*, *J* = 6.9, 1.8, Me). ^{13}C-NMR (125 MHz, (D_6)DMSO): 158.55 (*s*, C(6)); 156.57 (*s*, C(4)); 154.45 (*s*, C(8a)); 150.26 (*s*, C(7)); 143.89 (*s*, C(2)); 132.09 (*d*, C(2′)); 125.97 (*d*, C(1′)); 110.80 (*s*, C(4a)); 18.54 (*q*, Me). HR-MALDI-MS: 220.0833 (35, $[M+H]^+$, $C_9H_{10}N_5O_2^+$; calc. 220.0829), 242.0645 (24, $[M+Na]^+$, $C_9H_9N_5NaO_2^+$; calc. 242.0648).

*4-(Benzyloxy)-2-{[(dimethylamino)methylidene]amino}-6-[(*E*)-prop-2-enyl]pteridin-7(8*H*)-one* (**9**). A suspension of (*E*)-**6** (110 mg, 0.36 mmol) in DMF (15 ml) was treated at 23° with *Bredereck*'s reagent (83.2 µl, 0.4 mmol) and stirred for 3 h, leading progressively to a red-brown soln. DMF was distilled off at 25°/0.3 Torr. Drying of the residue *i.v.* gave **9** (124.3 mg, 95%). Red-brown solid. UV: 209 (4.42), 267 (4.04), 378 (4.43). IR (ATR): 3500–2000*w* (br.), 3038*w*, 2925*m*, 1660*m*, 1625*m*, 1579*s*, 1550*s*, 1515*m*, 1498*m*, 1484*m*, 1433*s*, 1420*s*, 1381*s*, 1351*s*, 1336*s*, 1321*s*, 1278*s*, 1234*m*, 1215*m*, 1153*m*, 1114*s*, 1048*m*, 998*w*, 974*m*, 944*m*, 913*m*, 895*m*, 849*m*, 832*w*, 803*m*. ^{1}H-NMR (300 MHz, (D_6)DMSO): 12.56 (br. *s*, NH); 8.70 (*s*, HC=N); 7.52–7.33 (*m*, 5 arom. H); 7.09–6.89 (*m*, H–C(2′)); 6.71 (*dq*, *J* = 15.6, 1.8, H–C(1′)); 5.56 (*s*, PhCH_2); 3.17, 3.06 (2s, Me_2N); 1.91 (br. *d*, *J* = 6.9, Me). ^{13}C-NMR (75 MHz, CD_2Cl_2): 164.53 (*s*, C(8a)); 164.46 (*s*, C(4)); 159.46 (*d*, HC=N); 157.17 (*s*, C(2)); 149.86 (*s*, C(7)); 149.20 (*s*, C(6)); 136.96 (*d*, C(2′)); 136.73 (*s*); 128.72 (2*d*); 128.50 (*d*); 128.23 (2*d*); 125.83 (*d*, C(1′)); 111.14 (*s*, C(4a)); 68.94 (*t*, Ph*C*H_2); 41.64, 35.45 (2*q*, Me_2N); 19.35 (*q*, Me). HR-MALDI-MS: 365.1717 (100, $[M+H]^+$, $C_{19}H_{21}N_6O_2^+$; calc. 365.1721), 387.1533 (52, $[M+Na]^+$, $C_{19}H_{20}N_6NaO_2^+$; calc. 387.1540).

X-Ray Analysis of **9**[4]). Slow evaporation of a soln. of **9** in MeCN gave crystals suitable for X-ray analysis (dimensions: cube 0.4 × 0.2 × 0.06 mm; color: amber). $C_{19}H_{20}N_6O_2 \cdot MeCN$, M_r 405.462, triclinic, $P\bar{1}$, *a* = 4.6804 (5), *b* = 13.789 (2), *c* = 17.642(2) Å, α = 79.920 (6), β = 87.846 (6), γ = 83.811 (6)°, *V* = 1114.3 (2) Å^3, *Z* = 2, $D_{calc.}$ = 1.208 Mg/m^3, Intensities were measured on a *Nonius Kappa CCD* diffractometer, with MoK_α radiation λ = 0.71073 Å, cell parameters from 5500 reflections, θ = 2.910–22.986°, μ = 0.082 mm^{-1}, *T* = 213 K, 5500 measured reflections, 3019 independent reflections, 2176 observed reflections. Refinement on F^2: full-matrix least-squares refinement, *R*(all) = 0.2525, *R*(gt) = 0.2237. Crystals lose solvent rapidly at r.t. Crystals composed of multiple twins (>4). Cell selection manually. Overlap correction for twinning not possible leading to bad agreement factors. All calculations were performed using maXus (*Bruker Nonius, Delft & MacScience*, Japan). The programme SIR97 was used to solve the structure and the programme SHELXL-97 to refine it.

Acylation of **19**. A soln. of **19** (308 mg, 2.0 mmol) in DMF (30 ml) was treated with K_2CO_3 (2.2 g, 16.0 mmol), cooled to −18°, treated with a soln. of **2** (0.57 ml, 5.0 mmol) in THF (5 ml) within 4 h (addition *via* a syringe pump), and stirred for 0.5 h. DMF was distilled off at 25°/0.3 Torr. A soln. of the residue in CH_2Cl_2 (100 ml) was washed with cold H_2O (2 × 50 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/MeOH 100:1 → 50:1) gave **20** (200 mg, 42%) as a green powder and **21** (81 mg, 13%) as a blue powder.

Data of (E)-N-*(2,6-Diamino-5-nitrosopyrimidin-4-yl)pent-2-enamide* (**20**). UV: 220 (4.32), 265 (4.14), 341 (4.36), 562 (1.87, of a 10^{-3} M soln.). IR (ATR): 3333*m*, 3186*w*, 2974*w*, 2940*w*, 2887*w*, 1688*m*, 1663*m*, 1616*s*, 1511*m*, 1486*s*, 1462*s*, 1392*w*, 1347*m*, 1321*m*, 1288*s*, 1256*m*, 1183*s*, 1128*s*, 1087*m*, 1055*m*, 1001*w*, 979*m*, 969*m*, 885*w*, 856*w*, 821*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 7:3 mixture): 12.98 (*s*, 0.3 H), 10.58 (*s*, 0.7 H) (NH–C(4′); 9.91, 8.13 (2 br. *d*, *J* = 3.6, 1.4 H), 8.58, 7.95 (2 br. *s*, 0.6 H) (NH_2–C(6′)); 7.95, 7.85 (2 br. *s*, 1.4 H), 8.02, 7.80 (2 br. *s*, 0.6 H) (NH_2–C(2′)); 7.01–6.93 (*m*, H–C(3)); 6.83 (br. *d*, *J* = 15.9, H–C(2)); 2.25 (*q*, *J* = 7.5, CH_2(4)); 1.05 (*t*, *J* = 7.5, Me). ^{13}C-NMR (100 MHz, (D_6)DMSO; 7:3 mixture): 165.99, 163.85 (2*s*, C=O); 165.93, 163.51 (2*s*, C(5′)); 164.41, 162.43 (2*s*, C(4′)); 150.23, 145.44 (2*s*, C(2′)); 150.18, 149.31 (2*d*, C(3)); 138.24, 136.57 (2*s*, C(6′)); 124.34, 123.64 (2*d*, C(2)); 24.95, 24.79 (2*t*, C(4)); 12.27, 12.18 (2*q*, Me). HR-MALDI-MS: 237.1091 (100, $[M+H]^+$, $C_9H_{13}N_6O_2^+$; calc. 237.1095), 259.0916 (33, $[M+Na]^+$, $C_9H_{12}N_6NaO_2^+$; calc. 259.0914).

*Data of 5-Nitroso-4,6-bis{[(*E*)-pent-2-enoyl]amino}pyrimidine* (**21**). UV: not measured, due to the rapid ene reaction in solution. IR (ATR): 3331*w*, 3188*m*, 2966*w*, 2933*w*, 2872*w*, 1722*w*, 1682*m*, 1663*s*, 1632*s*, 1610*s*, 1528*s*, 1464*s*, 1419*m*, 1386*w*, 1334*m*, 1310*s*, 1282*s*, 1245*m*, 1172*s*, 1114*s*, 1090*m*, 1066*m*, 1014*m*, 977*m*, 919*w*, 887*w*, 857*w*, 842*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 12.64 (br. *s*, NH); 10.23 (br. *s*, NH); 7.24–7.15 (*m*, H–C(3′), H–C(3″)); 7.08, 6.95 (2 br. *s*, NH_2); 6.35 (*d*, J = 15.3, H–C(2′)); 6.14 (*d*, J = 16.2, H–C(2″)); 2.34 (br. *s*, 2 CH_2); 1.14 (*d*, J = 6.3, 2 Me). ^{13}C-NMR (75 MHz, (D_6)DMSO): the rapid ene reaction of a sat. soln. of **21** in DMSO prevented the measurement of a ^{13}C-NMR spectrum. HR-MALDI-MS (low intensity of the desired peaks): 319.1523 (14, $[M+H]^+$, $C_{14}H_{19}N_6O_3^+$; calc. 319.1513), 341.1340 (45, $[M+Na]^+$, $C_{14}H_{18}N_6NaO_3^+$; calc. 341.1333).

*Preparation of the Pteridin-7(8*H*)-ones* **23** *and* **24**. A suspension of **20** (52 mg, 0.22 mmol) or **21** (70 mg, 0.22 mmol) in toluene (20 ml) was heated at 100° for the indicated time, to afford a greenish-blue soln. upon heating and the desired product as yellow precipitate. The suspension was concetrated to a small volume and filtered to give a yellow powder, which was successively washed with H_2O and Et_2O. Drying of the residue *i.v.* gave (*E/Z*)-**23** (24 h, 48 mg, 98%) and (*E/Z*)-**24** (3 h, 65 mg, 98%), resp.

*Data of 2,4-Diamino-6-[(*E/Z*)-prop-1-enyl]pteridin-7(8*H*)-one* (**23**). UV: 211 (4.36), 245 (4.03), 267 (4.04), 299 (3.68), 382 (4.21). IR (ATR): 3438*w*, 3330*w*, 3213*w*, 2843*w*, 2766*w*, 2720*w*, 1834*w*, 1611*s*, 1562*s*, 1530*m*, 1476*m*, 1458*s*, 1397*m*, 1374*w*, 1329*m*, 1298*w*, 1251*w*, 1198*w*, 1172*w*, 1154*w*, 1065*w*, 1016*w*, 966*w*, 937*m*, 856*w*, 818*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO; (*E*)/(*Z*) 81:19): 11.94 (br. *s*, NH); 7.06–6.95 (*dq*, J = 15.8, 6.9, 0.81 H), 6.07–6.01 (*dq*, J = 11.7, 7.2, 0.19 H) (H–C(2′)); 6.88 (br. *s*, NH_2); 6.67 (br. *dq*, J = 15.6, 1.5, H–C(1′), relative signal of (*Z*)-isomer not observed due to overlapping); 6.40, 6.35 (2 br. *s*, NH_2); 2.13 (*d*, J = 7.2, 0.57 H), 1.89 (*d*, J = 6.9, 2.43 H) (Me). ^{13}C-NMR (75 MHz, (D_6)DMSO; only signals of the (*E*)-isomer observed): see *Table 2*; additionally, 131.89 (*d*, C(2′)); 124.98 (*d*, C(1′)); 18.67 (*q*, Me). HR-MALDI-MS: 219.0983 (100, $[M+H]^+$, $C_9H_{11}N_6O^+$; calc. 219.0989), 241.0804 (1, $[M+Na]^+$, $C_9H_{10}N_6NaO^+$; calc. 241.0808).

*Data of 2-Amino-4-{[(*E*)-pent-2-enoyl]amino}-6-[(*E/Z*)-prop-1-enyl]pteridin-7(8*H*)-one* (**24**). UV: 213 (4.35), 251 (4.18), 319 (3.76), 381 (4.19). IR (ATR): 3317*m*, 3201*m*, 2965*w*, 2931*w*, 2904*w*, 2880*w*, 2847*w*, 2764*w*, 2726*w*, 1668*s*, 1626*s*, 1561*s*, 1473*s*, 1389*m*, 1346*m*, 1288*m*, 1246*m*, 1193*m*, 1119*m*, 1073*w*, 1051*w*, 972*m*, 933*w*, 904*w*, 855*w*, 828*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO; (*E*)/(*Z*) 78:22): 12.44, 9.65 (2 br. *s*, 2 NH); 7.14 (br. *s*, NH_2); 7.15 (*dq*, J = 15.6, 6.9, 0.78 H), 6.17 (*dq*, J = 11.7, 7.5, 0.22 H) (CH=C*H*Me); 6.97 (*dt*, J = 15.3, 6.0, CH=C*H*Et); 6.87 (*dt*, J = 15.3, 1.5, C*H*=CHEt); 6.70 (*dq*, J = 15.6, 1.8, 0.78 H, C*H*=CHMe; the signals of the (*Z*)-isomer hidden due to overlapping); 2.26 (*quint.*, J = 6.0, CH_2); 2.13 (*dd*, J = 7.5, 1.8, 2.34 H), 1.92 (*dd*, J = 6.9, 1.8, 0.66 H) (=CH*Me*); 1.05 (*t*, J = 7.5, Me). ^{13}C-NMR (75 MHz, (D_6)DMSO; only signals of the (*E*)-isomer were observed): see *Table 2*; additionally, 154.77 (*s*, C=O); 148.84 (*d*, CH=*C*HEt); 134.58 (*d*, CH=*C*HMe); 124.75 (*d*, *C*H=CHMe); 123.23 (*d*, *C*H=CHEt); 24.88 (*t*, CH_2); 18.78 (*q*, CH=CH*Me*); 12.40 (*q*, CH_2*Me*). HR-MALDI-MS: 301.1406 (100, $[M+H]^+$, $C_{14}H_{17}N_6O_2^+$; calc. 301.1408), 323.1230 (15, $[M+Na]^+$, $C_{14}H_{16}N_6NaO_2^+$; calc. 323.1227). Anal. calc. for $C_{14}H_{16}N_6O_2 \cdot 0.5\ H_2O$ (309.32): C 54.36, H 5.54, N 27.17; found: C 54.87, H 5.51, N 27.14.

*Preparation of 2,4-Bis{[(*E*)-pent-2-enoyl]amino}-6-[(*E*)-prop-1-enyl]pteridin-7(8*H*)-one* (**25**). A suspension of **19** (154 mg, 1.0 mmol) in THF (30 ml) was treated with K_2CO_3 (1.4 g, 10 mmol), cooled to 0°, treated with the a soln. of **2** (0.4 ml, 3.5 mmol) in THF (5 ml) within 2 h (addition *via* a syringe pump), stirred for 10 h at 0–5°, diluted with CH_2Cl_2 (100 ml), washed with cold H_2O (2 × 50 ml) and brine (50 ml), dried ($MgSO_4$), and evaporated. FC (CH_2Cl_2/AcOEt 1:2) gave a yellowish-green soln., which was concentrated to *ca.* 10 ml, whereupon **25** precipitated. Upon stirring at 23° overnight, the colour of the supernatant liquor disappeared almost completely. Filtration and drying of the solid gave **25** (296 mg, 78%). Yellow powder. UV: 217 (4.53), 239 (4.47), 315 (3.97), 380 (4.25). IR (ATR): 3372*w*, 3310*w*, 3206*w*, 2964*w*, 2912*w*, 2880*w*, 2835*w*, 2768*w*, 1718*m*, 1670*s*, 1638*s*, 1614*s*, 1552*s*, 1538*s*, 1499*m*, 1463*w*, 1418*s*, 1393*m*, 1336*m*, 1294*m*, 1245*m*, 1186*s*, 1156*m*, 1109*m*, 1060*w*, 1020*w*, 966*m*, 918*w*, 846*w*. ^{1}H-NMR (300 MHz, (D_6)DMSO, 333 K): 12.52 (br. *s*, NH); 7.26 (2 br. *s*, 2 NH); 6.95 (*dt*, J = 15.3, 6.9, 2 =C*H*Et); 6.82 (*dq*, J = 15.6, 6.9, =C*H*Me); 6.67 (*dq*, J = 15.6, 1.5, C*H*=CHMe); 6.17 (*dt*, J = 15.3, 1.5, 2 C*H*=CHEt); 2.20 (*dq*, J = 1.5, 7.2, 2 CH_2); 1.88 (*dd*, J = 1.5, 6.9, =CH*Me*); 0.98 (*t*, J = 7.2, 2 CH_2*Me*). ^{13}C-NMR (75 MHz, (D_6)DMSO): see *Table 2*; additionally, 167.43 (*s*, 2 C=O); 150.41 (*d*, 2 CH=*C*HEt); 135.10 (*d*, CH=*C*HMe); 124.24 (*d*, *C*H=CHMe); 122.85 (*d*, 2 *C*H=CHEt); 24.85 (*t*, 2 *C*H_2Me); 18.60 (*q*,

Me); 12.31 (*q*, 2 CH_2*Me*). HR-MALDI-MS: 383.1821 (38, $[M+H]^+$, $C_{19}H_{23}N_6O_3^+$; calc. 383.1826), 405.1641 (34, $[M+Na]^+$, $C_{19}H_{22}N_6NaO_3^+$; calc. 405.1646).

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