Nucleotides

Part LXIX[1])

Synthesis of Phosphoramidite Building Blocks of Isoxanthopterin N^8-(2′-Deoxy-β-D-ribonucleosides): New Fluorescence Markers for Oligonucleotide Synthesis

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The chemical synthesis of isoxanthopterin and 6-phenylisoxanthopterin N^8-(2′-deoxy-β-D-ribofuranosyl nucleosides) is described as well as their conversion into suitably protected 3′-phosphoramidite building blocks to be used as marker molecules for DNA synthesis. Applying the npe/npeoc (=2-(4-nitrophenyl)ethyl/[2-(4-nitrophenyl)ethoxy]carbonyl) strategy, we used the new building blocks in the preparation of oligonucleotides by an automated solid-support approach. The hybridization properties of a series of labelled oligomers were studied by UV-melting techniques. It was found that the newly synthesized markers only slightly interfered with the abilities of the labelled oligomers to form stable duplexes with complementary oligonucleotides.

1. Introduction. – Fluorescence has proved to be a valuable and versatile tool to study molecular interactions and biochemical processes. In our efforts to provide a set of pteridine-based marker molecules for the labelling of oligonucleotides, we have previously synthesized a wide variety of pteridine 2′-deoxyribonucleosides and their corresponding 3′-phosphoramidite derivatives [2–7]. These molecules can be integrated site-specifically into oligonucleotide strands by conventional synthetic techniques as fluorescent substitutes for the natural four bases of DNA.

The isoxanthopterin (=2-aminopteridine-4,7(3*H*,8*H*)-dione; **1**) system as a structural homologue to guanine (**2**) was chosen due to its reported high quantum yield in combination with other interesting fluorescence properties. A marker system based on the 3-methylisoxanthopterin (**3**) has already been tested successfully in a real-time assay for HIV-1 integrase [8]. Unfortunately, the steric bulk of the 3-methyl group led to a decrease in the abilities of the labelled oligonucleotides to form double-stranded DNA. To overcome this problem, we chose isoxanthopterin (**1**) itself and its 6-phenyl derivative as further target molecules bearing a guanine-like pyrimidine-ring substitutions. Our synthetic aim was, therefore, to prepare, according to our npe-npeoc (=2-(4-nitrophenyl)ethyl/[2-(4-nitrophenyl)ethoxy]carbonyl) strategy [9][10], the protected phosphoramidite building blocks **4** and **5** containing these two heterocyclic bases.

Since isoxanthopterin (**1**) itself possesses low solubility in organic solvents and various positions of similar but comparatively low reactivity, direct glycosylation reactions are infeasible. In this paper, we describe two different approaches involving 2-amino- and 2-(methylthio)-substituted pteridines, respectively, to overcome these

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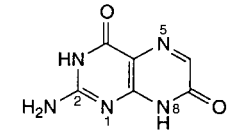

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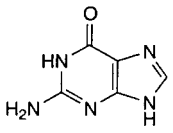

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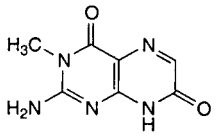

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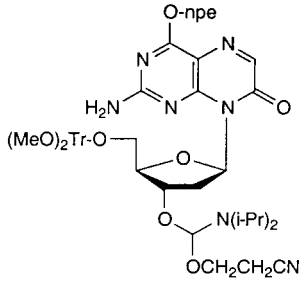

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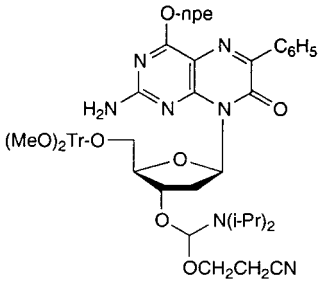

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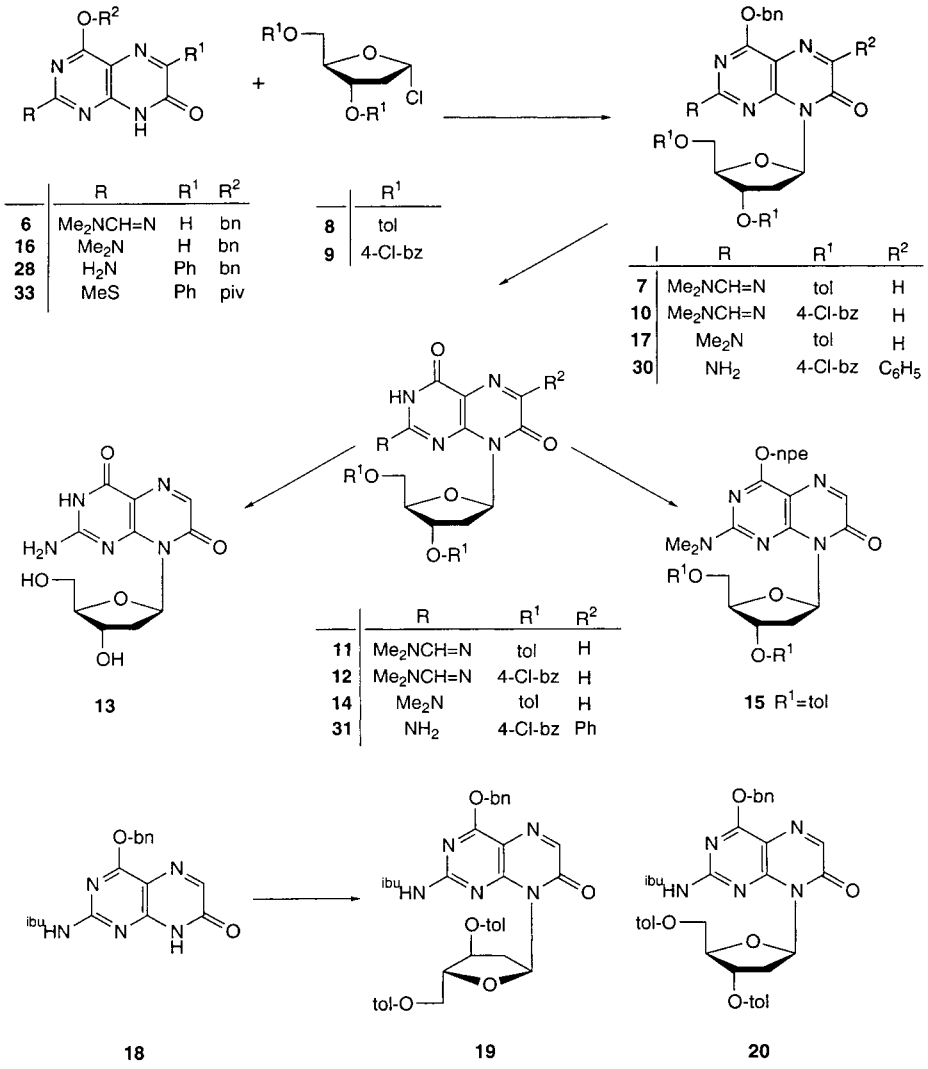
problems. It has been reported that introduction of a 2-(methylthio) group enhances the solubility of pteridine derivatives [8][11]. Since this function is stable under normal synthetic conditions and can be easily exchanged by nucleophiles after its oxidation to the methylsulfonyl stage, it offers a good way to transiently mask an isoxanthopterin. For the glycosylation step, we used a procedure developed by *Jungmann* and *Pfleiderer* [12], which allows the formation of the N^8-(β-D-nucleosides) in a highly regio- and stereoselective manner.

2. Synthesis of the Monomeric Building Blocks. – The first attempts to prepare an isoxanthopterin-containing building block were made starting with 2-amino-4-(benzyloxy)pteridin-7(8*H*)-one [13]. To carry out the glycosylation at the N^8-position selectively, this compound was further protected at the 2-amino function to increase its solubility. Treatment with *N*,*N*-dimethylformamide diethyl acetal in DMF gave the protected amidine **6** in 96% yield (*Scheme 1*). By the general procedure of *Jungmann* and *Pfleiderer* this compound was converted into its N^8-(2′-deoxy-β-D-riboside) **7** on reaction with 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-α-D-ribofuranosyl chloride (**8**) [14] in MeCN in the presence of DBU (=1,8-diazabicyclo[5.4.0]undec-7-ene), in 49% yield after chromatography. With the (4-chlorobenzoyl)-protected sugar chloride **9** [8] instead of **8**, the product precipitated during the reaction and was purified by recrystallization, to separate the β-D-anomer from a small amount of the α-D-anomer, yielding 48% of the corresponding nucleoside **10**. Hydrogenolysis of both **7** and **10** with Pd/H_2 led to the two debenzylated species **11** and **12** in 97 and 96% yield, respectively, which could be further deprotected by treatment with conc. aqueous ammonia at 50° to give the isoxanthopterin N^8-(2′-deoxy-β-D-riboside) **13** in 47–49% yield.

All attempts to introduce a 2-(4-nitrophenyl)ethyl (npe) protecting group at O–C(4) by *Mitsunobu* chemistry at the debenzylated stage **11** or **12** failed, despite the fact that the same reaction with the 2-(dimethylamino)-substituted model compound

Scheme 1



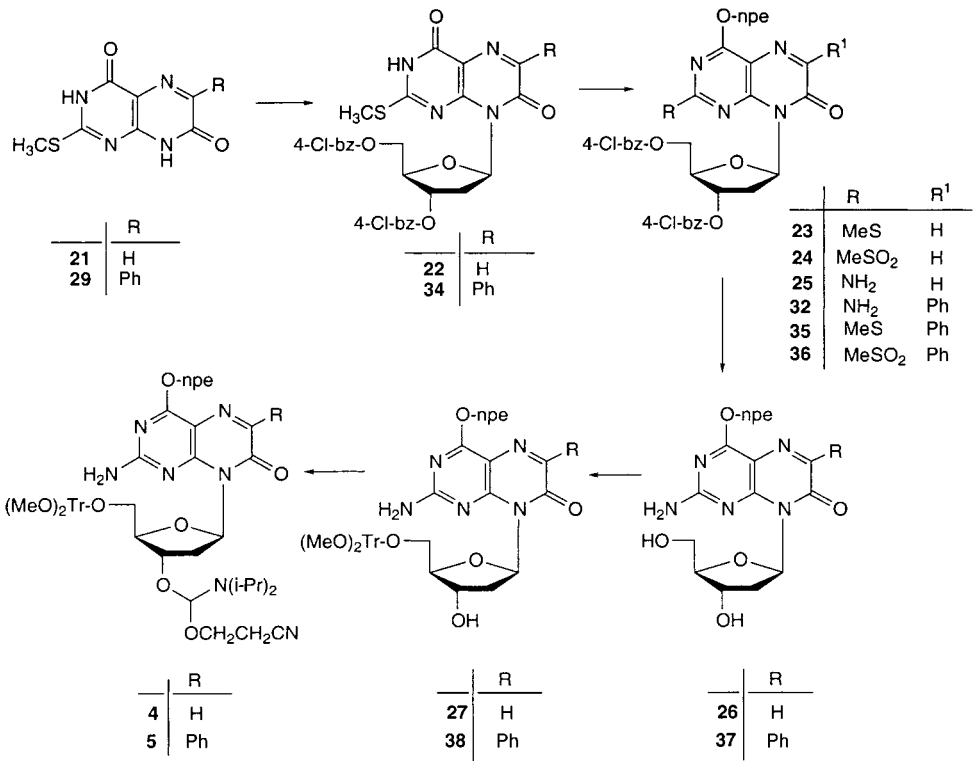
14 gave the desired 4-*O*-npe-protected product **15** in 82% yield. Compound **14** was prepared in an analogous way to **11** and **12**, starting with the glycosylation of 4-(benzyloxy)-2-(dimethylamino)pteridin-7(8*H*)-one (**16**) [15]. Due to poor separation of the anomers, the β-D-nucleoside **17** could be isolated in only 45% yield. Finally, debenzylation of **17** with Pd/H_2 afforded nucleoside **14** in 84%.

In a second attempt, the 2-amino group was protected by treatment with isobutyric anhydride/*N*,*N*-dimethylpyridin-4-amine (DMAP) in DMF to give the 4-(benzyloxy)-2-isobutyramidopteridin-7(8*H*)-one (**18**) in 53% yield (*Scheme 1*). The glycosylation of **18** afforded both the α-D- and the β-D-anomers **19** and **20** in 15 and 57%, respectively.

All attempts to selectively debenzylate **20** failed due to partial loss of the isobutyryl group during the reaction, giving an inseparable mixture.

Since the 2-amino-substituted pteridines proved to be too unreactive for further derivatization towards **4**, we decided to follow a second approach (*Scheme 2*) starting with 2-(methylthio)pteridine-4,7(3*H*,8*H*)-dione (**21**) [16]. Glycosylation of **21** in the presence of DBU afforded the corresponding N^8-(β-D-glycoside) **22** in 33–35% yield, after chromatography. Introduction of the 2-(4-nitrophenyl)ethyl group by a *Mitsunobu* reaction led to **23** in 78% yield. The crucial step in this synthetic pathway was the oxidation of the 2-(methylthio) substituent, due to a reported simultaneous oxidation at C(6) by common oxidizing agents leading to a leucopterin system [11]. After a series of attempts, the only efficient reagent found to lead selectively to a methylsulfonyl group was dimethyldioxirane. Thus, treatment of **23** in CH_2Cl_2 with this oxidant at room temperature afforded pure **24** in quantitative yield. The methylsulfonyl group was subsequently displaced by ammonia in CH_2Cl_2 to give the protected isoxanthopterin nucleoside **25** (89%). In the next step, the sugar-protecting groups were removed by treatment with NaCN in MeOH affording **26** (65%). Dimethoxytritylation of the 5′-OH function gave **27** in a poor yield of only 32%, which was due to cleavage of the npe function during chromatographic purification. Finally, phosphitylation at the 3′-OH group of **27** led to the targeted isoxanthopterin building block **4** in 71% yield.

Scheme 2



For the preparation of the 6-phenylisoxanthopterin building block **5**, we used the same general approach starting with 2-amino-4-(benzyloxy)-6-phenylpteridin-7(8*H*)-one (**28**) and 2-(methylthio)-6-phenylpteridine-4,7(3*H*,8*H*)-dione (**29**). Due to its greater solubility in organic solvents, **28** required no further protection for the glycosylation, and the corresponding N^8-(β-D-nucleoside) **30** was obtained in 31% yield (*Scheme 1*). Exchange of the O^4-protection was carried out *via* debenzylation with Pd/H_2 to give **31** in 96% yield and subsequent introduction of the 2-(4-nitrophenyl)ethyl group by *Mitsunobu* chemistry affording the fully protected nucleoside **32** (*Scheme 2*) in 84% yield.

A second approach to **32** started with 2-(methylthio)-6-phenylpteridine-4,7(3*H*,8*H*)-dione (**29**) (*Scheme 2*). The steric bulk of the 6-phenyl group allowed selective protection at the O^4-position with pivaloyl chloride/Et_3N in pyridine to give **33** (*Scheme 1*) in 62% yield. Glycosylation of **33** in the presence of DBU in MeCN followed by treatment with ammonia in MeOH afforded the desired N^8-(β-D-nucleoside) **34** (52%; *Scheme 2*). Alternatively, **34** could also be prepared by direct glycosylation of **29** (30%). Introduction of the 2-(4-nitrophenyl)ethyl protecting group gave **35** (86%). Oxidation of the methylthio function with 3-chloroperbenzoic acid (*m*CPBA) afforded the methylsulfonyl derivative **36** (85%). The presence of a substituent at C(6) prevents further oxidation at this position, so *m*CPBA could be used instead of dimethyldioxirane. Subsequently, **36** was treated with ammonia in CH_2Cl_2, to give the 2-amino-substituted compound **32** in 95% yield. All data for **32** formed by this route were consistent with those for **32** produced by the former route. Deblocking of the sugar was again accomplished by treatment with NaCN in MeOH in 86% yield, and the resulting 2-amino-8-(2-deoxy-β-D-ribofuranosyl)-4-*O*-[2-(4-nitrophenyl)ethyl]-6-phenylpteridin-7(8*H*)-one (**37**) was derivatized as its 5′-*O*-(dimethoxytrityl) ether **38** and its corresponding 3′-phophoramidite **5** in 65 and 68% yield, respectively.

3. Oligonucleotide Synthesis and Hybridization Experiments. – The monomeric building blocks **4** and **5** were incorporated directly into oligonculeotides by means of an *Applied Biosystems* DNA synthesizer model *392 B*, by standard procedures of the phosphoramidite chemistry modified according to the npe/npeoc strategy [9][10]. Due to solubility problems, **4** was dissolved in $MeCN/CH_2Cl_2$, whereas **5** was treated like the standard building blocks. For the preparation of oligonucleotides, we used conditions developed for the incorporation of pteridine nucleotides by *Charubala* [17], which included a second condensation step in each synthetic cycle. The reagents and reaction times are shown in the *Exper. Part* (*Exper. 31*).

To compare our new building blocks with 3-methylisoxanthopterin, we choose a 21-mer from the U5 terminus of the HIV genome with the sequence 5′-d(GTG TGG AAA ATC TCT AGC AGT)-3′ (**39**) as a synthetic target. The same sequence had been used in the real-time assay for HIV-I integrase [8]. A total of 13 labelled sequences, *i.e.* **40**–**52** (see *Table*), were synthesized in which one or two guanosine residues in different positions were substituted with isoxanthopterin ($\mathbf{F^H}$) or its 6-phenyl derivative $\mathbf{F^P}$. The synthesis of the oligomers was successful, with good coupling yields and only minor occurrence of failure sequences, except in the case of **40** and **46**, in which the marker was incorporated at the 5′-end. The products were purified by HPLC, if necessary, and the ability of the newly synthesized labelled oligomers to

Table. *Oligonucleotides and Differences in* T_m *Values*

Sequence (5′-3′)								ΔT_m [°]
d(GTG	TGG	AAA	ATC	TCT	AGC	AGT)	(**39**)[a]	reference
d(**F^H**TG	TGG	AAA	ATC	TCT	AGC	AGT)	(**40**)	−1.6
d(GT**F^H**	TGG	AAA	ATC	TCT	AGC	AGT)	(**41**)	−1.6
d(GTG	T**F^H**G	AAA	ATC	TCT	AGC	AGT)	(**42**)	−1.9
d(GTG	TG**F^H**	AAA	ATC	TCT	AGC	AGT)	(**43**)	0
d(GTG	TGG	AAA	ATC	TCT	A**F^H**C	AGT)	(**44**)	−1.0
d(GTG	TGG	AAA	ATC	TCT	AGC	A**F^H**T)	(**45**)	−1.6
d(**F^P**TG	TGG	AAA	ATC	TCT	AGC	AGT)	(**46**)	−1.7
d(GT**F^P**	TGG	AAA	ATC	TCT	AGC	AGT)	(**47**)	−0.7
d(GTG	T**F^P**G	AAA	ATC	TCT	AGC	AGT)	(**48**)	−1.0
d(GTG	TG**F^P**	AAA	ATC	TCT	AGC	AGT)	(**49**)	−0.4
d(GTG	TGG	AAA	ATC	TCT	A**F^P**C	ACT)	(**50**)	−1.3
d(GTG	TGG	AAA	ATC	TCT	AGC	A**F^P**T)	(**51**)	−0.4
d(GTG	T**F^{P}F^P**	AAA	ATC	TCT	AGC	AGT)	(**52**)	−1.3

[a]) $T_m = 59°$.

form stable DNA dimers with a complementary oligonucleotide was tested by determination of the melting profiles of the respective duplexes. The experiments were carried out in phosphate buffer at pH 7.4 and a Na^+ concentration of 0.15M at a concentration of oligonucleotide corresponding to 0.5 OD_{260}. The *Table* shows the sites of incorporation of isoxanthopterin (**F^H**) and 6-phenylisoxanthopterin (**F^P**) and the observed difference of the melting points compared to an unlabelled sequence (ΔT_m).

The results clearly indicate that the incorporation of isoxanthopterins with an unmodified pyrimidine moiety only slightly interferes with the hybridization abilities of the marked oligonucleotide. All measured melting temperatures compared with that of **39** lay in a range of less than $-2°$ under the conditions used, whereas the loss of a G·C base pair usually leads to a higher deviation.

4. Conclusions. – The phosphoramidite building blocks **4** of isoxanthopterin and **5** of 6-phenylisoxanthopterin have been synthesized successfully. Both monomers were used in the machine-aided synthesis of oligonucleotides according to the npe/npeoc strategy. The pteridine-containing oligomers **40**–**52** showed, besides their intense fluorescence, only a small disturbance of their hybridization properties. These results demonstrate that **4** and **5** would be favorable candidates for labelling experiments since they can be incorporated into specific positions within oligonucleotide probes. Because of the sensitivity of fluorophores for their immediate environments, this positioning might even allow the differentiation of hybridized and single-stranded probes.

5. Physical Data. – All newly synthesized compounds were characterized by elemental analysis, UV, ^{1}H-NMR, and ^{31}P-NMR spectra.

Experimental Part

General. Products were dried under high vacuum at r.t. over $CaCl_2$, unless otherwise stated. TLC: precoated silica-gel (Sil) thin-layer sheets *F 1500 LS 254* or cellulose (Cel) thin-layer sheets *C 1440 LS 254* (*Schleicher & Schüll*). Flash chromatography (FC): silica gel (*Baker*, 30–60 μm); 0.2–0.4 bar. M.p.:

Gallenkamp MDP 350; uncorrected. UV/VIS: *Perkin-Elmer Lambda-5*; λ_{max} in nm ($\log \varepsilon$). Melting curves: *Perkin-Elmer Lambda-2*; temp. control by a *Peltier* element; programmer *PTP-6* and software *PETEMP* and *PECSS*. ^{1}H-NMR: *Bruker AC-250*; δ in ppm rel. to deuterated solvent. ^{31}P-NMR: *Joel GX-400*; δ in ppm rel. to H_3PO_4. DNA Synthesis: *Applied Biosystems ABI 392B* (see *Exper. 31*). HPLC: *Merck-Hitachi L 6200*; detector *Merck-Hitachi L-4000*; column *Merck Lichrospher-100* (*RP-18*), 0.1N (Et_3NH)OAc/MeCN gradient.

1. *2-Amino-8-[2-deoxy-5-*O*-(4,4′-dimethoxytrityl)-β-*D*-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]pteridin-7(8*H*)-one 3′-(2-Cyanoethyl Diisopropylphosphoramidite)* (**4**). To a soln. of 2-amino-8-[2-deoxy-5-*O*-(4,4′-dimethoxytrityl)-β-D-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]pteridin-7(8*H*)-one (**27**; 300 mg, 402 μmol) in dry MeCN (10 ml) under Ar, 2-cyanoethyl tetraisopropylphosphorodiamidte (133 mg, 442 μmol) was added. The reaction was started by addition of 1*H*-tetrazole (14 mg, 200 μmol) and stirred for 12 h at r.t. The soln. was then diluted with CH_2Cl_2 (40 ml) and washed with 1M brine (10 ml), the aq. layer re-extracted with CH_2Cl_2 (20 ml), and the combined org. layer dried (Na_2SO_4) and evaporated. Purification by a short FC (toluene + 0.4% Et_3N) → toluene/AcOEt 10:3 + 0.4% Et_3N yielded 270 mg (71%) of **4**. Colorless foam. M.p. 68–73° (dec.). TLC (Sil, toluene/AcOEt 10:1): R_f 0.27. UV (MeOH): 205 (4.90), 238 (4.52), 272 (4.21), 348 (4.15). ^{1}H-NMR ($CDCl_3$): 8.17–8.14 (*d*, 2 H *o* to NO_2); 7.78 (*d*, H–C(6)); 7.48–7.41 (*m*, 4 H, 2 H *m* to NO_2, $(MeO)_2$*Tr*); 7.35–7.31 (*m*, 12 H, H–C(1′), arom. H); 6.78–6.71 (*m*, 4 H, $(MeO)_2$*Tr*); 5.06 (br. *d*, NH_2–C(2)); 4.80 (*m*, H–C(3′)); 4.68 (2*t*, 2 H, $NO_2C_6H_4CH_2$); 4.22 (*m*, H–C(4′)); 3.74 (*s*, 2 MeO); 3.63–3.41 (*m*, 2 H–C(5′), OCH_2CH_2CN); 3.27 (*t*, 4 CH_2O); 2.99 (*m*, 1 H–C(2′)); 2.62–2.25 (*m*, 5 H, 2 Me_2CH, OCH_2CH_2CN, 1 H–C(2′)); 1.17–1.03 (*m*, 2 Me_2CH). ^{31}P-NMR ($CDCl_3$): 149.05; 148.97. Anal. calc. for $C_{49}H_{55}N_8O_{10}P$ (947.0): C 62.15, H 5.85, N 11.83; found: C 61.84, H 5.62, N 11.63.

2. *2-Amino-8-[2-deoxy-5-*O*-(4,4′-dimethoxytrityl)-β-*D*-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-7(8*H*)-one 3′-(2-Cyanoethyl Diisopropylphophoramidite)* (**5**). As described for **4**, with 2-amino-8-[2-deoxy-5-*O*-(4,4′-dimethoxytrityl)-β-D-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-7(8*H*)-one (**38**; 822 mg, 1.0 mmol), dry MeCN (10 ml), 2-cyanoethyl tetraisopropylphosphorodiamidite (331 mg, 1.1 mmol), and 1*H*-tetrazole (35 mg, 500 μmol). Workup with CH_2Cl_2 (40 ml), 1M brine (10 ml), and CH_2Cl_2 (20 ml), a short FC (toluene + 0.4% Et_3N) → toluene/AcOEt 10:1 + 0.4% Et_3N), and drying under high vacuum yielded 695 mg (68%) of **5**. Yellow foam. M.p. 65–72° (dec.). TLC (Sil, toluene/AcOEt 10:1): R_f 0.42. UV (MeOH): 205 (4.80), 238 (4.42), (271 (4.19)), 374 (4.22). ^{1}H-NMR ($CDCl_3$): 8.21–8.15 (*d*, 2 H *o* to NO_2); 8.09–7.97 (*m*, 2 H, Ph); 7.59–7.49 (*d*, 2 H *m* to NO_2); 7.46–7.10 (*m*, 12 H, H–C(1′), 11 arom. H); 6.75–6.65 (*m*, 4 H, $(MeO)_2$*Tr*); 5.10–5.04 (br. *s*, NH_2–C(2)); 4.68–4.62 (*t*, $NO_2C_6H_4CH_2$); 4.30–4.21 (*m*, H–C(3′)); 3.78–3.72 (*t*, OCH_2CH_2CN); 3.72–3.64 (*m*, 2 MeO); 3.68–3.35 (*m*, H–C(4′), 2 H–C(5′)); 3.24–3.20 (*t*, 4 CH_2O); 3.05–2.93 (*m*, 1 H–C(2′)); 2.60–2.52 (*t*, OCH_2CH_2CN); 2.39–2.26 (*m*, 1 H–C(2′)); 2.35–2.33 (*m*, 2 Me_2CH); 1.21–1.09 (*m*, 2 Me_2CH). ^{31}P-NMR ($CDCl_3$): 149.19; 149.14. Anal. calc. for $C_{55}H_{59}N_8O_{10}P$ (1023.1): C 64.57, H 5.81, N 10.95; found: C 64.16, H 5.72, N 10.52.

3. *4-(Benzyloxy)-2-{[(dimethylamino)methylene]amino}pteridin-7(8*H*)-one* (**6**). A slurry of 2-amino-4-(benzyloxy)pteridin-7(8*H*)-one (2.90 g, 10.8 mmol) [13] in dry DMF (100 ml) was treated with dimethylformamide diethyl acetal (1.92 ml, 1.05 equiv.) at 40° for 3 h. The mixture was then concentrated to 5 ml and treated with MeOH/Et_2O 1:50 (50 ml). The precipitate was collected by filtration. The filtrate was concentrated to 2 ml and treated a 2nd time in the same manner. The product fractions were combined and dried at 40° under high vacuum to yield 3.42 g (98%) of **6**. Cream-colored powder. M.p. 330°. TLC (Cel; toluene/AcOEt 1:3): R_f 0.40. UV (pH 0): 221 (4.53), 331 (4.26). UV (MeOH): 209 (4.43), 228 (4.35), (259 (4.05)), 350 (4.39). ^{1}H-NMR ((D_6)DMSO): 11.80 (br. *s*, H–N(8)); 8.75 (*s*, H–C(7)); 7.75 (*s*, H–C(6)); 7.55–7.30 (*m*, 5 arom. H); 5.50 (*s*, CH_2O); 3.19 (*d*, Me_2N). Anal. calc. for $C_{16}H_{16}N_6O_2 \cdot H_2O$ (332.3): C 57.82, H 4.85, N 25.29; found: C 57.71, H 5.08, N 25.82.

4. *4-(Benzyloxy)-8-[2-deoxy-3,5-di-*O*-(*p*-toluoyl)-β-*D*-ribofuranosyl]-2-{[(dimethylamino)methylene]amino}pteridin-7(8*H*)-one* (**7**). Pteridinone **6** (3.24 g, 10.0 mmol) was dissolved in dry MeCN (100 ml) by adding DBU (1.87 ml, 12.5 mmol). After stirring for 10 min at r.t., a clear soln. was obtained, and 2-deoxy-3,5-di-*O*-(*p*-toluoyl)-α-D-ribofuranosyl chloride (**8**; 4.5 g, 11.0 mmol) [14] was added in 3 portions. Stirring was continued for 30 min. The precipitate (2.43 g of anomer mixture) was removed by filtration, and the filtrate was evaporated. The residue was dissolved in CH_2Cl_2, washed with H_2O (2 × 50 ml), dried (Na_2SO_4), and evaporated. FC (toluene/AcOEt 3:1) of the residue gave another 1.67 g of anomer mixture. The two product fractions were combined and recrystallized from AcOEt/MeOH 20:1: 3.29 g (49%) of **7**. Fine colorless needles. M.p. 145–149°. TLC (Sil, toluene/AcOEt 9:1): R_f 0.47. UV (MeOH): 221 (4.62), (234 (4.59)), 356 (4.28). ^{1}H-NMR ($CDCl_3$): 8.55 (*s*, 2 N=CH); 7.84 (*m*, 5 H, H–C(6), arom. H); 7.48–7.23 (2*m*, 6 H, H–C(1′), bn); 7.21–7.03 (*dd*, 4 H, tol); 5.99 (*m*, H–C(3′)); 5.54 (*s*, 4 CH_2O); 4.75 (*m*, H–C(4′)); 4.68–4.48 (*m*, 2 H–C(5′)); 3.29

(*m*, 1 H–C(2′)); 3.10 (*d*, Me_2N); 2.43 (*m*, 1 H–C(2′)); 2.35–2.29 (2*s*, Me(tol)). Anal. calc. for $C_{37}H_{36}N_6O_7$ (672.7): C 61.80, H 3.96, N 9.48; found: C 61.46, H 4.07, N 9.23.

5. *4-(Benzyloxy)-8-[3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-2-{[(dimethylamino)methylene]amino}pteridin-7(8*H*)-one* (**10**). A suspension of **6** (3.01 g, 9.3 mmol) in dry MeCN (100 ml) was stirred in the presence of DBU (1.67 ml, 1.2 equiv.) for 15 min. Then 3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-α-D-ribofuranosyl chloride (**9**; 4.0 g, 9.3 mmol) [8] was added in three equal portions. After a few minutes, the product started to crystallize, and the reaction was allowed to proceed for 1 h. The product was collected by filtration, washed with MeCN and Et_2O, and dried: 1.43 g (48%) of **10**. Colorless needles. M.p. 147–151°. TLC (Sil, toluene/AcOEt 1:9): R_f 0.46. UV (MeOH): 202 (4.73), 239 (4.68), 356 (4.39). ^{1}H-NMR ($CDCl_3$): 8.67 (*s*, 2 N=CH); 7.99–7.92 (*m*, 5 H, H–C(6), 4-Cl-bz); 7.58–7.50 (*m*, H–C(1′)); 7.50–7.30 (*m*, 9 H, bn, 4-Cl-bz); 6.13–6.06 (*m*, H–C(3′)); 5.62 (*s*, 4 CH_2O); 4.87–4.49 (*m*, H–C(4′), 2 H–C(5′)); 3.41–3.30 (*m*, 1 H–C(2′)); 3.22–3.20 (*d*, Me_2N); 2.58–2.47 (*m*, 1 H–C(2′)). Anal. calc. for $C_{35}H_{30}Cl_2N_6O_7$ (717.6): C 58.58, H 4.21, N 11.71; found: C 59.22, H 4.53, N 11.24.

6. *8-[2-Deoxy-3,5-di-*O*-(*p*-toluoyl)-β-*D*-ribofuranosyl]-2-{[(dimethylamino)methylene]amino}pteridine-4,7(3*H*,8*H*)-dione* (**11**). A soln. of **7** (1.54 g, 2.3 mmol) in MeOH/CH_2Cl_2 2:1 (100 ml) was hydrogenated overnight over 5% Pd/$BaCO_3$ (117 mg), consuming 50 ml of H_2 (calc.: 51 ml). The mixture was diluted with CH_2Cl_2 (100 ml) and filtered and the yellow filtrate evaporated: 1.28 g (97%) of **11**. Yellow, amorphous solid. M.p. 164–170°. TLC (Sil, toluene/AcOEt/MeOH 5:4:2): R_f 0.51. UV (MeOH): 203 (4.72), 239 (4.66), 360 (4.33). ^{1}H-NMR ($CDCl_3$): 9.23 (*s*, H–N(3)); 8.64 (*s*, N=CH(2)); 7.92–7.87 (*m*, 5 H, H–C(6), tol); 7.45–7.35 (*m*, H–C(1′)); 7.24–7.20 (*d*, 2 H, tol); 7.15–7.12 (*d*, 2 H, tol); 6.0–5.85 (*m*, H–C(3′)); 4.8–4.55 (*m*, H–C(4′), 2 H–C(5′)); 3.45–3.33 (*m*, 1 H–C(2′)); 3.25 (*s*, MeN); 3.10 (*s*, MeN); 2.55–2.45 (*m*, 1 H–C(2′)); 2.45 (*s*, Me(tol)); 2.35 (*s*, Me(tol)). Anal. calc. for $C_{30}H_{30}N_6O_7 \cdot H_2O$ (604.6): C 59.60, H 5.33, N 13.90; found: C 59.92, H 5.24, N 13.80.

7. *8-[3,5-Bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-2-{[(dimethylamino)methylene]amino}-pteridine-4,7(3*H*,8*H*)-dione* (**12**). A soln. of **10** (1.07 g, 1.5 mmol) in MeOH/CH_2Cl_2 1:2 (100 ml) was hydrogenated for 24 h after addition of 5% Pd/C (200 mg). The mixture was then diluted with CH_2Cl_2 (100 ml) and filtered and the yellow filtrate evaporated: 898 mg (96%) of **12**. Light-yellow, amorphous solid, which was used without further purification. M.p. 158–165°. TLC (Sil, toluene/AcOEt/MeOH 5:4:2): R_f 0.49. ^{1}H-NMR ($CDCl_3$): 9.74 (br. *s*, H–N(3)); 8.65 (*s*, N=CH(2)); 7.98–7.91 (*m*, 5 H, Cl-bz, H–C(6)); 7.44–7.31 (*m*, 5 H, Cl-bz, H–C(1′)); 6.04 (*m*, H–C(3′)); 4.84–4.55 (3*m*, H–C(4′), 2 H–C(5′)); 3.36 (*m*, 1 H–C(2′)); 3.27 (*s*, MeN); 3.16 (*s*, MeN); 2.54 (*m*, 1 H–C(2′)).

8. *2-Amino-8-[2-deoxy-β-*D*-ribofuranosyl]pteridine-4,7(3*H*,8*H*)-dione* (**13**). A soln. of **11** (1.17 g, 2.0 mmol) in conc. aq. ammonia (100 ml) was stirred for 12 h at 50°. The mixture was concentrated to 20 ml and cooled to r.t. The precipitate was collected by filtration and washed with H_2O (5 × 20 ml), EtOH (10 ml), and Et_2O (10 ml). Concentration of the filtrate to 10 ml afforded a second product fraction. The two fractions were combined and dried: 288 mg (49%) of **13**. Colorless solid. M.p. >300°. TL (Cel, 4% sodium citrate soln./MeOH 1:1): R_f 0.65. UV (pH 12): 258 (4.07), 279 (sh, 3.65), 356 (4.13). ^{1}H-NMR ((D_6)DMSO): 11.25 (br. *s*, H–N(3)); 7.53 (*s*, H–C(6)); 7.12 (*t*, H–C(1′)); 5.14 (*d*, OH–C(3′)); 4.63 (*t*, OH–C(5′)); 4.92 (*m*, H–C(3′)); 3.75–3.40 (*m*, H–C(4′), 2 H–C(5′)); 2.88 (*m*, 1 H–C(2′)); 1.95 (*m*, 1 H–C(2′)). Anal. calc. for $C_{11}H_{13}N_5O_5 \cdot H_2O$ (304.3): C 43.42, H 4.64, N 23.02; found: C 43.57, H 4.55, N 23.53.

The same procedure starting from **12** led to **13** in 47% yield.

9. *8-[2-Deoxy-3,5-di-*O*-(*p*-toluoyl)-β-*D*-ribofuranosyl]-2-(dimethylamino)pteridine-4,7(3*H*,8*H*)-dione* (**14**). A soln. of 4-(benzyloxy)-8-[2-deoxy-3,5-di-*O*-(*p*-toluoyl)-β-D-ribofuranosyl]-2-(dimethylamino)-pteridin-7(8*H*)-one (**17**; 3.08 g, 4.7 mmol) in MeOH/CH_2Cl_2 1:1 (150 ml) was hydrogenated for 40 h over 5% Pd/C (30 mg). The reaction ceased after consuming 100 ml of H_2 (calc.: 106 ml). Filtration and removal of the solvent afforded 2.59 g of crude material which was recrystallized from EtOH (200 ml) to give 1.92 g of greenish crystals. Concentration of the mother-liquor gave another 310 mg. Overall yield: 2.23 g (84%) of **14**. M.p. 142–146°. TLC (Sil, CH_2Cl_2/MeOH 50:1): R_f 0.10. UV (MeOH): 202 (4.69), 236 (4.63), 297 (3.94), 357 (4.12). ^{1}H-NMR ($CDCl_3$): 11.37 (br. *s*, H–N(3)); 7.93–7.85 (*dd*, 4 H, tol); 7.76 (*s*, H–C(6)); 7.35 (*m*, H–C(1′)); 7.24–7.12 (*dd*, 4 H, tol); 5.93 (*m*, H–C(3′)); 4.83–4.52 (*m*, H–C(4′), 2 H–C(5′)); 3.42–3.28 (*m*, 1 H–C(2′), Me_2N); 2.53–2.35 (*m*, 1 H–C(2′), 2 Me(tol)). Anal. calc. for $C_{29}H_{29}N_5O_7 \cdot 0.5\ H_2O$ (568.6): C 61.74, H 5.27, N 12.42; found: C 61.52, H 5.26, N 12.18.

10. *8-[2-Deoxy-3,5-di-*O*-(*p*-toluoyl)-β-*D*-ribofuranosyl]-2-(dimethylamino)-4-[2-(4-nitrophenyl)ethoxy]-pteridin-7(8*H*)-one* (**15**). A mixture of **14** (140 mg, 250 μmol), PPh_3 (72 mg, 275 μmol), and 2-(4-nitrophenyl)ethanol (46 mg, 275 μmol) in dry dioxane (5 ml) was stirred for 30 min. Diisopropyl azodicarboxylate (= bis(1-methylethyl) diazenedicarboxylate; 55 μl, 275 μmol) was added, and stirring was continued for 14 h.

The mixture was evaporated and the residue purified by FC (toluene/AcOEt 100:1 → 10:1): 146 mg (82%) of **15**. Colorless solid. M.p. 116–119°. TLC (Sil, CH_2Cl_2/MeOH 50:1): R_f 0.62. UV (MeOH): 202 (4.79), 212 (sh, 4.62), 240 (4.67), 268 (sh, 4.16), 362 (4.19). ^{1}H-NMR ($CDCl_3$): 8.20–8.16 (*d*, 2 H *o* to NO_2); 7.94–7.90 (*m*, 4 H, tol); 7.78 (*s*, H–C(6)); 7.48–7.40 (*m*, H–C(1′), 2 H *m* to NO_2); 7.24–7.12 (*m*, 4 H, tol); 5.98–5.92 (*m*, H–C(3′)); 4.80–4.53 (*m*, H–C(4′), 2 H–C(5′), OCH_2CH_2); 3.45–3.28 (*m*, 1 H–C(2′), OCH_2CH_2); 3.25 (*s*, Me_2N); 2.52–2.34 (*m*, 1 H–C(2′), 2 Me(tol)). Anal. calc. for $C_{37}H_{36}N_6O_9$ (708.7): C 62.70, H 5.12, N 11.86; found: C 62.76, H 5.17, N 11.30.

11. *4-(Benzyloxy)-[2-deoxy-3,5-di*-O-(p-*toluoyl)-β*-D-*ribofuranosyl]-2-(dimethylamino)pteridin-7(8*H*)-one* (**17**). As described for **7**, with 4-(benzyloxy)-2-(dimethylamino)pteridin-7(8*H*)-one (**16**; 3.27 g, 11.0 mmol), MeCN (100 ml), DBU (2.06 ml, 13.75 mmol), and **8** (4.7 g, 12.1 mmol) [13]. After 30 min at r.t., the reaction was quenched by the addition of AcOH (735 µl) in MeOH/H_2O 9:1 (50 ml). The mixture was evaporated, the residue redissolved in CH_2Cl_2 (250 ml), the soln. washed with H_2O (2 × 50 ml), dried (Na_2SO_4), and evaporated, and the residue purified by FC (toluene/AcOEt 20:1 → 4:1): 3.22 g (4.95 mmol, 45%) of **17**. Colorless solid. M.p. 127–132°. TLC (Sil, toluene/AcOEt 4:1): R_f 0.76. UV (MeOH): 202 (4.79), 214 (sh, 4.59), 239 (4.68), 282 (3.73), 362 (4.23). ^{1}H-NMR ($CDCl_3$): 7.92 (*d*, 4 H, tol); 7.77 (*s*, H–C(6)); 7.51–7.11 (*m*, 10 H, H–C(1′), tol, bn); 5.94 (*m*, H–C(3′)); 5.56 (*s*, CH_2O); 4.79–4.52 (*m*, H–C(4′), 2 H–C(5′)); 3.39 (*m*, 1 H–C(2′)); 3.22 (*s*, Me_2N); 2.51–2.35 (*m*, 2 Me(tol), 1 H–C(2′)). Anal. calc. for $C_{36}H_{35}N_5O_7$ (649.7): C 66.55, H 5.43, N 10.78; found: C 66.24, H 5.43, N 10.53.

12. *4-(Benzyloxy)-2-isobutyramidopteridin-7(8*H*)-one* (**18**). A mixture of 2-amino-4-(benzyloxy)pteridin-7(8*H*)-one (**6**; 1.71 g, 6.4 mmol), isobutyric anhydride (5.08 ml, 30.0 mmol), and *N*,*N*-dimethylpyridin-4-amine (DMAP; 30 mg, 245 µmol) in dry DMF (50 ml) was heated under reflux for 60 min. The mixture was cooled to r.t., stirred for an additional 5 min after the addition of MeOH (3 ml), and then evaporated. The residue was dissolved in hot DMF (100 ml) and treated with charcoal. H_2O (70 ml) was added to the hot filtrate, and the mixture was allowed to cool down. The resulting colorless crystals were collected after 12 h, washed with Et_2O, and dried: 970 mg (45%) of **18**. M.p. 252–257°. TLC (Sil, toluene/AcOEt 4:1): R_f 0.53. UV (MeOH): 216 (4.60), 229 (sh, 4.41), 322 (4.19), 332 (4.20), 349 (sh, 4.05). ^{1}H-NMR ((D$_6$)DMSO): 10.60 (br. *s*, NH); 7.90 (*s*, H–C(6)); 7.61–7.29 (*m*, 5 H, bn); 5.55 (*s*, CH_2O); 3.10–2.91 (*m*, Me_2CH); 1.15 (*d*, Me_2CH). Anal. calc. for $C_{17}H_{17}N_5O_3$ (339.4): C 60.17, H 5.05, N 20.64; found: C 59.92, H 5.06, N 20.37.

13. *4-(Benzyloxy)-8-[2-deoxy-3,5-di*-O-(p-*toluoyl)-α*-D-*ribofuranosyl]-2-isobutyramidopteridin-7(8*H*)-one* (**19**). Pteridinone **18** (2.83 g, 7.29 mmol) was dissolved in dry MeCN by adding 2.2 equiv. of DBU (2.46 ml, 16.0 mmol). The clear soln. was cooled to 0°, and **8** (3.12 g, 8.0 mmol) [13] was added in 3 equal portions. After 15 min, the external cooling was removed, and stirring was continued for 2 h. The mixture was evaporated, the residue redissolved in CH_2Cl_2 (300 ml), the soln. washed with 1M $NaHCO_3$ (100 ml) and H_2O (2 × 100 ml), dried (Na_2SO_4), and evaporated, and the residue submitted to FC (toluene/AcOEt 20:1 → 5:2): 750 mg (15%) of **19** (with toluene/AcOEt 7:1). M.p. 129–137°. TLC (Sil, toluene/AcOEt 5:1): R_f 0.41. UV (MeOH): 202 (4.71), 217 (4.49), 238 (4.66), 323 (4.14). ^{1}H-NMR ($CDCl_3$): 8.12 (*s*, H–C(6)); 8.05 (*s*, NH); 7.94–7.90 (*d*, 4 H, tol); 7.57–7.53 (*d*, 2 H, bn); 7.42–7.34 (*m*, 3 H, bn); 7.28–7.15 (*d*, 4 H, tol); 7.06–7.02 (*dd*, H–C(1′)); 5.78–5.70 (*m*, H–C(3′), CH_2O); 4.73–4.47 (*m*, H–C(4′), 2 H–C(5′)); 3.15–3.01 (*m*, Me_2CH); 2.98–2.72 (*m*, 2 H–C(2′)); 2.46–2.35 (2*s*, 2 Me(tol)); 1.29–1.23 (2*d*, Me_2CH). ^{1}H-NMR ((D$_6$)DMSO): 10.7 (*s*, NH); 8.08 (*s*, H–C(6)); 7.93–7.88 (2*d*, 2 H, tol); 7.77–7.72 (*d*, 2 H, tol); 7.65–7.55 (*m*, 2 H, bn); 7.45–7.27 (*m*, 5 H, bn, tol); 7.25–7.21 (*d*, 2 H, bn); 6.85 (*m*, H–C(1′)); 5.70–5.54 (*m*, H–C(3′), CH_2O); 4.70–4.38 (*m*, H–C(4′), 2 H–C(5′)); 2.98–2.75 (*m*, 2 H–C(2′), Me_2CH); 2.46–2.30 (2*s*, 2 Me(tol)); 1.19–1.10 (2*d*, Me_2CH).

14. *4-(Benzyloxy)-8-[2-deoxy-3,5-di*-O-(p-*toluoyl)-β*-D-*ribofuranosyl]-2-isobutyramidopteridin-7(8*H*)-one* (**20**). As described in *Exper. 13*. After the isolation of the α-D-anomer **19** by FC, further elution with toluene/AcOEt 5:1 afforded the β-D-anomer **20** (2.88 g, 57%). M.p. 136–142°. TLC (Sil, toluene/AcOEt 5:1): R_f 0.27. UV (MeOH): 202 (4.69), 217 (4.50), 238 (4.66), 323 (4.15). ^{1}H-NMR ($CDCl_3$): 8.29 (*s*, NH); 8.02 (*s*, H–C(6)); 7.94–7.80 (2*d*, 4 H, tol); 7.53–7.46 (*m*, 2 H, bn); 7.39–7.33 (*m*, 3 H, bn); 7.32–7.10 (*m*, 5 H, tol, H–C(1′)); 6.08–6.03 (*m*, H–C(3′)); 5.63 (*s*, CH_2O); 4.81–4.74 (*m*, H–C(4′)); 4.61–4.46 (*m*, 2 H–C(5′)); 3.58–3.47 (*m*, 1 H–C(2′)); 3.01–2.92 (*m*, Me_2CH); 2.51–2.34 (*m*, 1 H–C(2′), 2 Me(tol)); 1.29–1.20 (2*d*, Me_2CH). Anal. calc. for $C_{38}H_{37}N_5O_8 \cdot 0.5\ H_2O$ (700.7): C 65.13, H 5.47, N 10.00; found: C 65.68, H 5.38, N 9.59.

15. *8-[3,5-Bis*-O-*(4-chlorobenzoyl)-2-deoxy-β*-D-*ribofuranosyl]-2-(methylthio)pteridine-4,7(3*H*,8*H*)-dione* (**22**). The 2-(methylthio)pteridine-4,7(3*H*,8*H*)-dione (**21**; 1.5 g, 5.0 mmol) [16] was dissolved in dry MeCN (100 ml) by the addition of DBU (1.87 ml, 12.5 mmol). The resulting soln. was cooled to 0°, and 3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-α-D-ribofuranosyl chloride (**9**) (1.93 g, 4.5 mmol) [8] was added in 3 equal portions. After 1 h, the reaction was quenched by addition of AcOH (200 µl) in MeOH/H_2O 9:1 (20 ml). The clear soln. was stirred for 30 min and evaporated. The residue was dissolved in CH_2Cl_2 (150 ml) and washed with H_2O (2 ×

50 ml), the org. layer dried (Na_2SO_4) and evaporated, and the residue submitted to FC (CH_2Cl_2/MeOH 99:1 → 95:5): 870 mg (32%) of **22**. Cream-colored foam. An anal. sample was obtained by recrystallization from toluene. M.p. 165–168°. TLC (Sil, CH_2Cl_2/MeOH 9:1): R_f 0.38. UV (MeOH): 202 (4.70), 239 (4.64), 352 (4.06) ^{1}H-NMR ($CDCl_3$): 8.04 (*s*, H–C(6)); 7.99–7.93 (*m*, 4 H, Cl-bz); 7.48–7.73 (*m*, 5 H, H–C(1′), Cl-bz); 5.99 (*m*, H–C(3′)); 4.83–4.54 (*m*, H–C(4′), 2 H–C(5′)); 3.35 (*m*, 1 H–C(2′)); 2.67 (*s*, MeS); 2.55 (*m*, 1 H–C(2′)). Anal. calc. for $C_{26}H_{20}Cl_2N_4O_7S$ (603.4): C 51.75, H 3.34, N 9.28; found: C 51.24, H 3.28, N 9.28.

16. *8-[3,5-Bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-2-(methylthio)-4-[2-(4-nitrophenyl)ethoxy]pteridin-7(8*H*)-one* (**23**). As described for **15**, with PPh_3 (1.20 g, 4.6 mmol), 2-(4-nitrophenyl)ethanol (762 mg, 4.6 mg), **22** (2.20 g, 3.6 mmol), and dioxane (100 ml) for 15 min, then with diisopropyl azodicarboxylate (0.9 ml, 4.6 mmol) for 4 h. FC (toluene, toluene/AcOEt 10:1) gave 2.15 g (78%) of **23**. Colorless solid. An anal. sample was recrystallized from toluene. M.p. 129–133°. TLC (Sil, toluene/AcOEt 5:1): R_f 0.44. UV (MeOH): 202 (4.75), 221 (4.60), 241 (4.69), 267 (sh, 4.23), 336 (4.18). ^{1}H-NMR ((D_6)DMSO): 8.16 (*d*, 2 H *o* to NO_2); 8.03 (*s*, H–C(6)); 7.98–7.88 (*m*, 4 H, Cl-bz); 7.64–7.55 (*m*, 4 H, 2 H *m* to NO_2, Cl-bz); 7.54–7.48 (*m*, 2 H, Cl-bz); 7.28 (*m*, H–C(1′)); 5.89 (*m*, H–C(3′)); 4.76 (*t*, OCH_2CH_2); 4.71–4.53 (*m*, H–C(4′), 2 H–C(5′)); 3.31–3.25 (*t*, OCH_2CH_2); 3.13 (*m*, 1 H–C(2′)); 2.67–2.55 (*m*, MeS, 1 H–C(2′)). Anal. calc. for $C_{34}H_{27}Cl_2N_5O_9S$ (752.6): C 54.26, H 3.62, N 9.31; found: C 54.45, H 3.86, N 9.48.

17. *8-[3,5-Bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-2-(methylsulfonyl)-4-[2-(4-nitrophenyl)-ethoxy]pteridin-7(8*H*)-one* (**24**). A soln. of dimethyldioxirane in acetone (7.15 ml, 500 μmol; *ca.* 0.07M), freshly prepared according to the procedure of *Adam et al.* [18], was added at r.t. to a soln. of **23** (188 mg, 250 μmol) in dry CH_2Cl_2 (20 ml). TLC (Sil, AcOEt) showed 2 products with R_f 0.42 and 0.82 after 10 min. Addition of more dimethyldioxirane (1.8 ml, 125 μmol) gave a single product (R_f 0.82). The mixture was filtered and evaporated: 190 mg (97%) of **24**. Colorless foam. M.p. 175–179°. TLC (Sil, AcOEt): R_f 0.82. UV (MeOH): 202 (4.76), 217 (4.52), 240 (4.64), 278 (4.21), 292 (sh, 4.18). ^{1}H-NMR ($CDCl_3$): 8.29 (*s*, H–C(6)); 8.17 (*d*, 2 H *o* to NO_2); 7.96–7.88 (*dd*, 4 H, Cl-bz); 7.50–7.28 (*m*, 7 H, 2 H *m* to NO_2, Cl-bz, H–C(1′)); 6.12–6.05 (*m*, H–C(3′)); 4.90 (*t*, OCH_2CH_2); 4.75–4.48 (*m*, H–C(4′), 2 H–C(5′)); 3.38–3.20 (*m*, $MeSO_2$, OCH_2CH_2, 1 H–C(2′)); 2.65–2.50 (*m*, 1 H–C(2′)). Anal. calc. for $C_{34}H_{27}Cl_2N_5O_{11}S \cdot 1.5\ H_2O$ (811.6): C 50.32, H 3.72, N 8.62; found: C 50.12, H 3.63, N 8.52.

18. *2-Amino-8-[3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]pteridin-7(8*H*)-one* (**25**). Gaseous ammonia was bubbled slowly through a soln. of **24** (79 mg, 100 μmol) in CH_2Cl_2 until TLC showed only a single product (60 min). The mixture was washed with H_2O (2 × 20 ml), dried (Na_2SO_4), and evaporated. Recrystallization from AcOEt (2.5 ml) afforded 64 mg (89%) of yellow crystals. M.p. 163–166°. TLC (Sil, toluene/AcOEt 2:1): R_f 0.71. UV (MeOH): 203 (4.78), 239 (4.64), 269 (sh, 4.19), 348 (4.13). ^{1}H-NMR ($CDCl_3$): 8.14 (*d*, 2 H *o* to NO_2); 7.97–7.90 (*m*, 4 H, Cl-bz); 7.85 (*s*, H–C(6)); 7.50–7.05 (*m*, 7 H, 2 H *m* to NO_2, Cl-bz, H–C(1′)); 6.06 (*m*, H–C(3′)); 5.53 (br. *s*, NH_2); 5.02–4.93 (*m*, H–C(4′)); 4.67 (*t*, OCH_2CH_2); 4.55 (*m*, 2 H–C(5′)); 3.37 (*m*, 1 H–C(2′)); 3.28 (*t*, OCH_2CH_2); 2.52–2.42 (*m*, 1 H–C(2′)). Anal. calc. for $C_{33}H_{26}Cl_2N_6O_9 \cdot H_2O$ (739.5): C 53.60, H 3.81, N 11.36; found: C 53.90, H 4.13, N 11.03.

19. *2-Amino-8-(2-deoxy-β-*D*-ribofuranosyl)-4-[2-(4-nitrophenyl)ethoxy]-pteridin-7(8*H*)-one* (**26**). A mixture of **25** (721 mg, 1.0 mmol) and NaCN (245 mg, 5.0 mmol) was stirred in dry MeOH (30 ml) for 12 h. The precipitate was collected by filtration, washed with H_2O and CH_2Cl_2, and dried at 40° over $CaCl_2$: 381 mg (86%) of **26**. Colorless solid. M.p. 228–242° (dec.). UV (MeOH): 210 (4.57), 229 (sh, 4.11), 267 (sh, 4.01), 278 (4.02), 347 (4.18). ^{1}H-NMR ((D_6)DMSO): 8.16 (*d*, 2 H *o* to NO_2); 7.61 (*d*, 3 H, 2 H *m* to NO_2, H–C(6)); 7.40 (br. *s*, NH_2); 7.10 (*m*, H–C(1′)); 5.15 (*d*, OH–C(3′)); 4.62 (*m*, OCH_2CH_2, H–C(3′)); 4.40 (*m*, OH–C(5′)); 3.72–3.21 (*m*, H–C(4′), 2 H–C(5′), OCH_2CH_2); 2.85 (*m*, 1 H–C(2′)); 1.93 (*m*, 1 H–C(2′)). Anal. calc. for $C_{19}H_{20}N_6O_7$ (444.4): C 51.35, H 4.54, N 18.91; found: C 51.04, H 4.42, N 18.62.

20. *2-Amino-8-[2-deoxy-5-*O*-(4,4′-dimethoxytrityl)-β-*D*-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]pteridin-7(8*H*)-one* (**27**). Pteridinone **26** (600 mg, 1.35 mmol) was co-evaporated twice with dry pyridine (2 × 5 ml) and then dissolved in dry pyridine (10 ml). The soln. was treated with 4,4′-dimethoxytrityl chloride (501 mg, 1.48 mmol) and stirred at r.t. overnight. The mixture was then evaporated and the residue purified by FC (toluene + 1% Et_3N → toluene/AcOEt 3:1 + 1% Et_3N): 323 mg (32%) of **27**. Colorless foam. M.p. 68–79° (dec.). TLC (Sil, toluene/AcOEt 2:1): R_f 0.58. UV (MeOH): 205 (4.94), 237 (4.56), 272 (4.25), 348 (4.15). ^{1}H-NMR ($CDCl_3$): 8.08 (*d*, 2 H *o* to NO_2); 7.70 (*s*, H–C(6)); 7.39–7.06 (*m*, 14 H, H–C(1′), 2 H *m* to NO_2, $(MeO)_2Tr$); 6.74–6.69 (*m*, 4 H *o* to MeO); 5.00 (br. *s*, NH_2); 4.77 (*m*, H–C(3′)); 4.62 (*t*, OCH_2CH_2); 3.89 (*m*, H–C(4′)); 3.72 (*s*, 2 MO); 3.49 (*m*, 1 H–C(5′)); 3.38 (*m*, 1 H–C(5′)); 3.29 (*t*, OCH_2CH_2); 2.93 (*m*, 1 H–C(2′)); 2.32–2.20 (*m*, 1 H–C(2′)); 2.09 (br. *d*, OH–C(3′)). Anal. calc. for $C_{40}H_{38}N_6O_9$ (746.8): C 64.33, H 5.13, N 11.25; found: C 64.31, H 5.05, N 10.92.

21. *2-Amino-4-(benzyloxy)-6-phenylpteridin-7(8*H*)-one* (**28**). To a soln. of 4-(benzyloxy)pyrimidine-2,4,6-triamine (578 mg, 2.5 mmol) [11] in 20% aq. AcOH soln. (50 ml), methyl phenylpyruvate (= methyl 2-oxo-3-phenylpropanoate; 360 µl, 1.1 equiv.) was added, and the soln. was stirred for 45 min at r.t. and then for 16 h at 60–70°. The mixture was cooled and the yellow precipitate collected by filtration, washed with H_2O (2 × 20 ml) and Et_2O (2 × 20 ml), and dried at 100° under high vacuum: 605 mg (75%) of **28**. Colorless foam. M.p. >330°. UV (MeOH): 209 (4.60), 239 (4.14), 288 (3.85), 370 (4.34). ^{1}H-NMR ((D$_6$)DMSO): 12.56 (br. *s*, H–N(8)); 8.13–8.08 (*dd*, Ph); 7.59–7.33 (*m*, 8 arom. H); 7.28 (br. *s*, NH_2); 5.52 (*s*, CH_2O). Anal. calc. for $C_{19}H_{15}N_5O_2$ (345.4): C 66.08, H 4.38, N 20.28; found: C 65.99, H 4.40, N 20.35.

22. *2-(Methylthio)-6-phenylpteridine-4,7(3*H*,8*H*)-dione* (**29**). A slurry of 5,6-diamino-2-(methylthio)pyrimidin-4(3*H*)-one (4.31 g, 25.0 mmol) [16] in AcOH (25 ml) at 15° was treated with methyl phenylglyoxylate (4.25 ml, 30.0 mmol). The orange precipitate was collected after 30 min and washed with cold H_2O and Et_2O. The obtained 6-amino-5-[(2-methoxy-2-oxo-1-phenylethylidene)amino]-2-(methylthio)pyrimidin-4(3*H*)-one was treated with 0.1N NaOH (25 ml) in MeOH (250 ml) for 10 min at r.t. to give an almost colorless soln. from which the product was precipitated by adjusting the pH to 4.5 with AcOH. After 4 h, the product was collected by filtration, thoroughly washed with H_2O, and dried at 40° under high vacuum over $CaCl_2$: 4.61 g (64%) of **29**. Yellow powder. M.p. >300°. pK_a = 6.42 ± 0.2, 8.99 ± 0.17. UV (pH 13): 234 (4.55), 257 (sh, 4.21), 358 (4.29). UV (MeOH): 211 (4.50), 237 (sh, 4.11), 289 (4.04), 352 (4.23). ^{1}H-NMR ((D$_6$)DMSO): 12.94 (br. *s*, H–N(8), H–N(3)); 8.24 (*m*, 2 H, Ph); 7.44 (*m*, 3 H, Ph); 2.57 (*s*, MeS). Anal. calc. for $C_{13}H_{10}N_4O_2S \cdot H_2O$ (304.3): C 51.31, H 3.97, N 18.41; found: C 51.12, H 3.34, N 17.88.

23. *2-Amino-4-(benzyloxy)-8-[3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-6-phenylpteridin-7(8*H*)-one* (**30**). Pteridinone **28** (2.59 g, 7.5 mmol) was dissolved in dry MeCN (200 ml) by the addition of DBU (1.39 ml, 9.0 mmol). Then **9** [8] was added to the yellow soln. After 60 min, the mixture was evaporated, the residue dissolved in CH_2Cl_2 (250 ml), the soln. washed with H_2O (50 ml), dried (Na_2SO_4), and evaporated, and the residue submitted to FC (toluene/AcOEt 100:1 → 5:1): 1.67 g (30%) of **30**. Yellow solid. M.p. 142–147°. TLC (Sil, toluene/AcOEt 10:1): R_f 0.42. UV (MeOH): 202 (4.57), 242 (4.49), 372 (4.12). ^{1}H-NMR ($CDCl_3$): 8.16 (*m*, 2 H, Ph); 7.93 (*m*, 4 H, Cl-bz); 7.50–7.15 (*m*, 13 H, H–C(1′), Cl-bz, arom. H); 6.11 (*m*, H–C(3′)); 5.57 (*s*, OCH_2CH_2); 5.39 (br. *s*, NH_2); 4.98 (*m*, H–C(4′)); 4.57 (*m*, 2 H–C(5′)); 3.41 (*m*, 1 H–C(2′)); 2.50 (*m*, 1 H–C(2′)). Anal. calc. for $C_{38}H_{29}Cl_2N_5O_7$ (738.6): C 61.80, H 3.96, N 9.48; found: C 61.46, H 4.07, N 9.23.

24. *2-Amino-[3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-6-phenyl-8-pteridine-4,7(3*H*,8*H*)-dione* (**31**). A soln. of **30** (1.5 g, 2.0 mmol) in CH_2Cl_2/MeOH 2:1 (150 ml) was hydrogenated over 5% Pd/C (50 mg), consuming 50 ml of H_2 (calc.: 45 ml). The mixture was evaporated. *Soxhlet* extraction of the residue with CH_2Cl_2 (500 ml, 24 h) afforded 1.26 g (96%) of **31**. M.p. 166–171°. TLC (Sil, toluene/AcOEt 3:1): R_f 0.48. UV (MeOH): 202 (4.62), 242 (4.52), 359 (4.06). ^{1}H-NMR ($CDCl_3$): 12.9 (br. *s*, H–N(3)); 8.16 (*m*, 2 H, Ph); 7.93 (*m*, 4 H, Cl-bz); 7.50–7.15 (*m*, 8 H, H–C(1′), Ph, Cl-bz); 6.11 (*m*, H–C(3′)); 5.39 (br. *s*, NH_2); 4.98 (*m*, H–C(4′)); 4.57 (*m*, H–C(5′)); 3.40 (*m*, 1 H–C(2′)); 2.50 (*m*, 1 H–C(2′)). Anal. calc. for $C_{31}H_{23}Cl_2N_5O_7$ (648.5): C 57.42, H 3.58, N 10.80; found: C 56.92, H 3.69, N 10.32.

25. *2-Amino-8-[3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-7(8*H*)-one* (**32**). *Method A:* As described for **15**, with **31** (1.25 g, 1.9 mmol), PPh_3 (632 mg, 2.4 mmol), 2-(4-nitrophenyl)ethanol (403 mg, 2.4 mmol), and dioxane (50 ml); for 15 min. Then with diisoproyl azodicarboxylate (464 µl, 2.4 mmol); for 3 h. FC (toluene, toluene/AcOEt 10:1) and further purification by reprecipitation from CH_2Cl_2 with hexane gave 1.23 g (86%) of **32**. M.p. 106–109°. TLC (Sil, toluene/AcOEt 3:1): R_f 0.92. UV (MeOH): 202 (4.61), 241 (4.50), 373 (4.14). ^{1}H-NMR ($CDCl_3$): 8.16 (*m*, 4 H, Ph, 2 H *o* to NO_2); 7.93 (*m*, 4 H, Cl-bz); 7.55–7.23 (*m*, 10 H, H–C(1′), Ph, Cl-bz, 2 H *m* to NO_2); 6.14 (*m*, H–C(3′)); 5.39 (br. *s*, NH_2); 4.92 (*m*, H–C(4′)); 4.70 (*t*, OCH_2CH_2); 4.57 (*m*, 2 H–C(5′)); 3.48–3.35 (*m*, 1 H–C(2′)); 3.28 (*t*, OCH_2CH_2); 2.50 (*m*, 1 H–C(2′)). Anal. calc. for $C_{39}H_{30}Cl_2N_6O_9$ (797.6): C 58.72, H 3.79, N 10.54; found: C 58.87, H 4.18, N 10.43.

Method B: To a soln. of 8-[3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-D-ribofuranosyl]-2-(methylthio)-4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-7(8*H*)-one (**35**; 1.50 g, 1.8 mmol) in dry CH_2Cl_2 (100 ml), 55% *m*-CPBA (1.20 g, 3.80 mmol) was added, and the yellow soln. was stirred at r.t. for 18 h. The mixture was evaporated and the residue purified by FC (toluene → toluene/AcOEt 3:1): 1.33 g (85%) of *8-[3,5-bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-2-(methylsulfonyl)-4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-7(8*H*)-one* (**36**). Colorless foam. TLC (Sil, $CHCl_3$/MeOH 19:1): R_f 0.74. UV (MeOH): 202 (4.76), 217 (4.52), 240 (4.64), 278 (4.21), 292 (sh, 4.18). ^{1}H-NMR ((D$_6$)DMSO): 8.15 (*m*, ph, 2 *H o* to NO_2); 7.92 (*m*, 2 H, Cl-bz); 7.23 (*m*, 10 H, 2 H *m* to NO_2, Cl-bz, H–C(1′)); 6.05 (*m*, H–C(3′)); 4.91 (*t*, OCH_2CH_2); 4.74–4.53 (*m*, H–C(4′), 2 H–C(5′)); 3.50 (*s*, $MeSO_2$); 3.43–3.20 (*m*, 1 H–C(2′)); 2.96 (*t*, OCH_2CH_2); 2.65 (*m*, 1 H–C(2′)).

Gaseous ammonia was bubbled slowly through a soln. of **36** (900 mg, 1.0 mmol) in dry CH_2Cl_2 (100 ml) for 90 min. The mixture was washed with H_2O (2 × 50 ml) and dried (Na_2SO_4). Evaporation afforded 792 mg (95%) of **32**.

26. *4-[(2,2-Dimethylpropanoyl)oxy]-2-(methylthio)-6-phenylpteridin-7(8*H*)-one* (**33**). Pivaloyl chloride (= 2,2-dimethylpropanoyl chloride; 1.23 ml, 10.0 mmol) was added dropwise to a suspension of 2-(methylthio)-6-phenylpteridine-4,7(3*H*,8*H*)-dione (**29**; 2.86 g, 10.0 mmol) in dry pyridine (50 ml) and Et_3N (2 ml) at 0°. The external cooling was removed, and the mixture was stirred for 45 min before being evaporated. The residue was dissolved in CH_2Cl_2 (700 ml) and washed with 0.5M $(Et_3NH)CH_3COO$ buffer (200 ml, pH 7). The org. layer was dried and evaporated. The product was purified by FC (toluene/AcOEt 10:1 → 3:1); 2.29 g (62%) of **33**. Yellow solid. M.p. > 300°. TLC (Sil, CH_2Cl_2/MeOH 19:1): R_f 0.43. UV (MeOH): 203 (4.39), 212 (sh, 4.35), 239 (sh, 4.18), 283 (3.99), 363 (4.33). ^{1}H-NMR ((D$_6$)DMSO): 13.35 (br. *s*, H–N(8)); 8.14 (*m*, 2 H, Ph); 7.52 (*m*, 3 H, ph); 2.66 (*s*, MeS); 1.35 (*s*, Me_3C). Anal. calc. for $C_{18}H_{18}N_4O_3S$ (370.4): C 58.36, H 4.90, N 15.12; found: C 58.94, H 5.16, N 14.85.

27. *8-[3,5-Bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-2-(methylthio)-6-phenylpteridine-4,7(3*H*,8*H*)-dione* (**34**). *Method A:* A suspension of **29** (1.43 g, 5.0 mmol) in dry MeCN (100 ml) was treated with DBU (1.7 ml, 11.0 mmol). To the yellow soln. **9** (1.94 g, 4.5 mmol) [8] was added in 3 equal portions. The mixture was evaporated after 60 min, the residue dissolved in CH_2Cl_2 (200 ml), the soln. washed twice with H_2O (50 ml) and evaporated, and the product isolated by FC (toluene/AcOEt 20:1 → 5:1): 911 mg (30%) of **34**.

Method B: Pteridinone **33** (1.85 g, 5.0 mmol) was dissolved in dry MeCN (200 ml) by adding DBU (771 µl, 5.0 mmol). To this soln. **9** (2.15 g, 5.0 mmol) [8] was added in 2 equal portions. The mixture was evaporated after 60 min and the residue dissolved in CH_2Cl_2 (250 ml) and treated with sat. methanolic ammonia (25 ml) for 10 min. The mixture was evaporated and the product isolated by FC (toluene/AcOEt 20.1 → 8:1): 1.84 mg (54%) of **34**. M.p. 184–189°. TLC (Sil, toluene/AcOEt 5:1): R_f 0.53. $pK_a = 8.71 \pm 0.17$. UV (MeOH): 202 (4.68), 221 (sh, 4.49), 240 (4.63), 267 (sh, 4.09), 378 (4.31). ^{1}H-NMR ($CDCl_3$): 8.25–8.17 (*m*, 2 H, Ph); 7.96 (*m*, 4 H, Cl-bz); 7.50–7.44 (*m*, H–C(1′)); 7.40–7.12 (*m*, 7 H, Cl-bz, Ph); 6.12 (*m*, H–C(3′)); 4.90–4.56 (*m*, H–C(4′), 2 H–C(5′)); 3.39 (*m*, 1 H–C(2′)); 2.54 (*s*, MeS, 1 H–C(2′)). Anal. calc. for $C_{32}H_{24}Cl_2N_4O_7S$ (679.5): C 56.56, H 3.56, N 8.24; found: C 56.41, H 3.64, N 8.11.

28. *8-[3,5-Bis-*O*-(4-chlorobenzoyl)-2-deoxy-β-*D*-ribofuranosyl]-2-(methylthio)-4-[2-(4-nitrophenyl)-ethoxy]-6-phenylpteridin-7(8*H*)-one* (**35**). As described for **15**, with **34** (1.50 g, 2.2 mmol), PPh_3 (724 mg, 2.8 mmol), 2-(4-nitrophenyl)ethanol (461 mg, 2.8 mmol), and dioxane (150 ml); for 15 min. Then with diisopropyl azodicarboxylate (545 µl, 2.8 mmol; for 5 h). FC (toluene, toluene/AcOEt 10:1) and recrystallization from toluene/AcOEt 1:1 gave 1.58 g (86%) of **35**. M.p. 98–102°. TLC (Sil, toluene/AcOEt 10:1): R_f 0.45. UV (MeOH): 203 (4.65), 221 (4.46), 242 (4.55), 364 (3.90). ^{1}H-NMR ($CDCl_3$): 8.19 (*m*, 4 H, 2 H *o* to NO_2, Cl-bz); 7.97 (*m*, 4 H, Ph, Cl-bz); 7.54–7.15 (*m*, 10 H, 2 H *m* to NO_2, Cl-bz, Ph, H–C(1′)); 6.12 (*m*, H–C(3′)); 4.85–4.53 (*m*, OCH_2CH_2, H–C(4′), 2 H–C(5′)); 3.41–3.18 (*m*, OCH_2CH_2, 1 H–C(2′)); 2.57 (*m*, MeS, 1 H–C(2′)). Anal. calc. for $C_{40}H_{31}Cl_2N_5O_9S$ (828.7): C 57.97, H 3.77, N 8.45; found: C 57.61, H 3.67, N 8.09.

29. *2-Amino-8-[2-deoxy-β-*D*-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-7(8*H*)-one* (**37**). As described for **26**, with **32** (1.20 g, 1.50 mmol), MeOH (50 ml), and NaCN (370 mg, 7.5 mmol); for 14 h. Drying at 50°/high vacuum gave 554 mg (71%) **37**. Yellow powder. M.p. 197–202°. UV (MeOH): 211 (4.59), 248 (4.22), 373 (4.29). ^{1}H-NMR ((D$_6$)DMSO): 8.19–8.15 (*d*, 2 H *o* to NO_2); 8.07–8.00 (*m*, 2 H, Ph); 7.63 (*d*, 2 H *m* to NO_2); 7.44 (*m*, 5 H, Ph, NH_2); 7.15 (*t*, H–C(1′)); 5.13 (br. *s*, OH–C(3′)); 4.66–4.60 (*t*, OCH_2CH_2); 4.43 (br. *s*, OH–C(5′)); 3.76–3.35 (*m*, H–C(3′), H–C(4′), 2 H–C(5′)); 3.22 (*t*, OCH_2CH_2); 2.93–2.81 (*m*, 1 H–C(2′)); 1.95 (*m*, 1 H–C(2′)). Anal. calc. for $C_{25}H_{24}N_6O_7$ (520.5): C 57.69, H 4.65, N 16.15; found: C 57.23, H 4.72, N 15.80.

30. *2-Amino-8-[2-deoxy-5-*O*-(4,4′-dimethoxytrityl)-β-*D*-ribofuranosyl]-4-[2-(4-nitrophenyl)ethoxy]-6-phenylpteridin-7(8*H*)-one* (**38**). As described for **27**, with **37** (520 mg, 1.0 mmol), pyridine (2 × 5 ml), then pyridine (10 ml), and 4,4′-dimethoxytrityl chloride (373 mg, 1.1 mmol). FC (toluene + 1% Et_3N → toluene/AcOEt 4:1 + 1% Et_3N) gave 534 mg (65%) of **38**. Yellow foam. M.p. 60–70° (dec.). TLC (Sil, toluene/AcOEt 4:1): R_f 0.51. UV (MeOH): 205 (4.81), 237 (4.43), 271 (sh, 4.19), 374 (4.23). ^{1}H-NMR ((D$_6$)DMSO): 8.17 (*d*, 2 H *o* to NO_2); 8.09–7.97 (*m*, 2 H, Ph); 7.63 (*d*, 2 H *m* to NO_2); 7.41-7.14 (*m*, 14 H, Ph, $(MeO)_2Tr$, NH_2); 7.08 (*m*, H–C(1′)); 5.62 (*d*, OH–C(3′)); 4.66–4.60 (*t*, OCH_2CH_2); 4.12 (*m*, H–C(3′)); 3.72–3.35 (*m*, 9 H, H–C(4′), 2 H–C(5′), 2 MeO); 3.22 (*t*, OCH_2CH_2); 2.93–2.81 (*m*, 1 H–C(2′)); 1.99–1.88 (*m*, 1 H–C(2′)). Anal. calc. for $C_{46}H_{42}N_6O_9$ (822.9): C 67.14, H 5.14, N 10.21; found: C 66.82, H 5.22, N 9.96.

31. *Oligonucleotide Synthesis:* **40–52**. Syntheses were carried out by means of an *Applied-Biosystems 392B DNA* synthesizer on a 0.2–0.4-µmol scale. LCMAA-CPG material [9][10], functionalized with dT, was used as starting material and packed into a small *ABI* column. Chain elongation was carried out by a programmed cycle

of reagent and solvent washes, based on a procedure of *Charubala* [17] under the following conditions (all times include reagent delivery and wait steps): *1*) 5′-*O* deprotection: 3% CCl_3COOH/CH_2Cl_2 for 130 s. The eluate was collected, and the absorbance 498 nm was determined to monitor the coupling yields. *2*) Coupling: 0.1M phosphoramidite and 0.5M 1*H*-tetrazole in MeCN, carried out twice with 65 s each. *3*) Capping: Ac_2O/2,6-lutidine (=2,6-dimethylpyridine)/THF 1:1:8 and 1-methyl-1*H*-imidazole/THF 16:84 for 20 s. *4*) Oxidation: 0.05M I_2 in THF/pyridine/H_2O 7:2:1 for 35 s. After the last cycle, an additional 5′-*O* deprotection step was carried out, and the oligomer was then fully deprotected and subsequently cleaved off the solid support by the following sequence. *1*) Deblocking: npe, npeoc, and cyanoethyl groups were removed by treatment with 1M DBU in MeCN for 12 h. *2*) Cleavage from the solid support: conc. aq. NH_3 soln. for 60 min. The eluate was collected, and the amount of oligomer was determined from the absorbance at 260 nm. Finally, the product was isolated as its ammonium salt by lyophilization.

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