175. Pteridines

Part XCVII[1])

Synthesis and Properties of 6-Thioxanthopterin and 7-Thioisoxanthopterin

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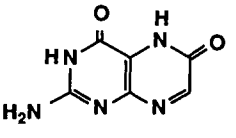
6-Thioxanthopterin (**13**) was synthesized in four steps starting from 2-amino-4-(penthyloxy)pteridine (**3**) *via* the 8-oxide **4**, its subsequent interconversion to the 6-chloro (**7**) and 6-thio derivative (**12**) and final hydrolysis of the pentyloxy group. 7-Thioisoxanthopterin (**15**) was derived analogously from 2-amino-4-(pentyloxy)pteridine-7(8*H*)-thione (**14**) by alkaline hydrolysis. The various 6- and 7-thiopteridines were methylated to give the corresponding 6- (**10**, **11**) and 7-(methylthio) derivatives (**16**, **17**). The newly synthesized compounds have been characterized by elemental analyses, their UV spectra, and the determination of the acidic and basic pK_a values. The spectral relationships are discussed in detail.

1. Introduction. – Xanthopterin (**1**) and isoxanthopterin (**2**) belong to the classical butterfly pigments which have helped with their structural elucidation in 1940 by *Purrmann* [2] to substantiate the pteridine nucleus as an important new naturally occurring heterocyclic ring system and to initiate synthetic chemistry in this field on a broad basis [3].



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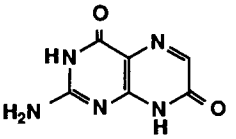

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However, little chemistry has been performed with **1** [4] and **2** [5] due to their insolubility in most common solvents caused by intermolecular H-bonding and aggregation [6]. As an extension of our work on thiopteridines [7–14], we have been interested in the synthesis and characterization of 6-thioxanthopterin (**13**) and 7-thioisoxanthopterin (**15**). All attempts to introduce the thioxo groups by direct thiation reactions with P_4S_{10} or the *Lawesson* reagent in a broad variety of solvents were so far unsuccessful and forced us to solve this problem by new indirect approaches.

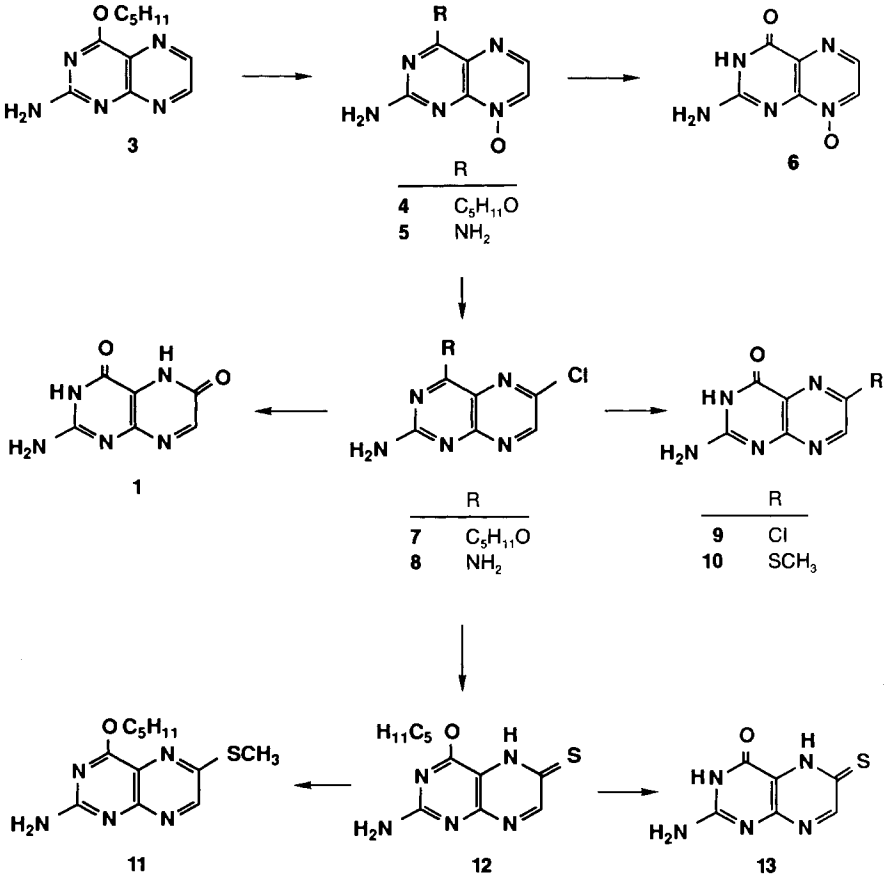
2. Results and Discussion. – Based upon earlier findings [15] [16] that conversion of the amide function in pterins into 4-alkoxy-2-aminopteridine derivatives improves solubility in organic solvents dramatically, we decided to start the synthesis of 6-thioxan-

[1]) Part XCVI: [1].

thopterin (**13**) from 2-amino-4-(pentyloxy)pteridine (**3**; *Scheme 1*). This starting material was obtained by a *Gabriel-Isay* reaction [17] between 2,5,6-triamino-4-(pentyloxy)pyrimidine [18] and glyoxal in 69% yield. Oxidation of **3** in CF_3COOH with 30% H_2O_2 proceeded analogously to pterin [19] and afforded 2-amino-4-(pentyloxy)pteridine *N(8)*-oxide (**4**) in 42% yield accompanied by the formation of 18% of pterin *N(8)*-oxide **6** as a by-product. The yield of **4** could not be improved by varying the reaction conditions, neither was the use of glacial AcOH or HCOOH successful. The structure of **4** was established by hydrolysis to the known pterin *N(8)*-oxide **6** [19–24] and ammonolysis to 2,4-diaminopteridine *N(8)*-oxide **5** [19] [22]. In the next step, a *Katada*-type rearrangement with $AcCl/CF_3COOH$ at −40° was achieved to afford analogous to the reaction with pterin *N(8)*-oxide [23], under tele-substitution 2-amino-6-chloro-4-(pentyloxy)pteridine (**7**) in 80% yield. AcBr did not react in the same manner and formed under deoxygenation 2-amino-4-(pentyloxy)pteridine (**3**).

Hydrolysis studies with **7** proved its structure, since 0.1N NaOH afforded at room temperature 6-chloropterin (**9**) [23], and prolonged heating under reflux in 1N NaOH led

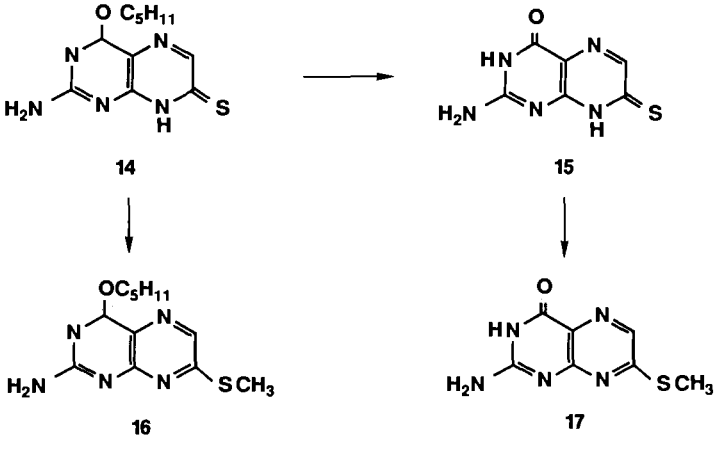
Scheme 1



to xanthopterin (**1**). Furthermore, conc. NH_3 converted **7** in a smooth reaction at room temperature into 6-chloro-2,4-diaminopteridine (**8**) [24] in excellent yield. In contrast to these results, **7** showed with NaSH in $CHCl_3$/MeOH at room temperature a selective nucleophilic displacement reaction of the 6-Cl atom, leading to the sodium salt of 2-amino-4-(pentyloxy)pteridine-6-thione (**12**), which could easily be isolated and recrystallized from i-PrOH or converted by acidification into the free compound **12**. Hydrolysis of **12** by 0.1N NaOH in dioxane gave rise to 6-thioxanthopterin (**13**), which was best purified as its disodium salt by recrystallization. Methylation of **12** and **13** in aqueous base with MeI gave the corresponding 6-(methylthio) derivatives **11** and **10**, respectively, of which the latter one has already been synthesized by a different route [23].

The chemical synthesis of 7-thioisoxanthopterin (**15**; *Scheme 2*) was achieved by a similar series of reactions, of which the interconversion of 2-amino-4-(pentyloxy)pteridin-7-one [18] *via* 2-amino-7-chloro-4-(pentyloxy)pteridine into 2-amino-4-(pentyloxy)-pteridine-7-thione (**14**) [24] was already described earlier. Base hydrolysis of **14** led to 7-thioisoxanthopterin (**15**) in 90% yield, and methylation of the thioxo groups in **14** and **15** afforded the corresponding 7-(methylthio) derivatives **16** and **17**, respectively.

Scheme 2



3. Physical Properties. – To characterize the newly synthesized compounds more thoroughly and to discuss several fine-structural features, the pK_a values and the UV spectra of the various molecular forms were determined (*Table*).

It is noted that conversion of 2-amino-4-(pentyloxy)pteridine (**3**) into its *N(8)*-oxide **4** causes a drop of basicity of *ca.* 3 pK_a units as well as a bathochromic shift of the long-wavelength absorption band analogously to the features in the pterin series [19]. Introduction of a Cl-atom at C(6) does not alter the basicity much as seen from the comparisons of **3** and **7**, pterin [26] and (**9**), and 2,4-diaminopteridine [27] and (**8**), respectively.

The presence of a 6-thioxo group is associated with more dramatic changes of the physical properties. In comparison to xanthopterin (**1**), 6-thioxanthopterin (**13**) is a somewhat weaker base expressed by the basic pK_a of 0.97. On the other hand, **13** is a much stronger acid than **1**, which is in agreement with the general features of amide-thioamide

Table. *Physical Data of Pteridine Derivatives*[a])

Compound	pK_a in H_2O	UV-Absorption spectra												pH	Molecular form
		λ_{max} [nm]						lg ε							
3		233	263			361		4.28	3.95			3.82		MeOH	○
	3.48	218			[324]	332	[342]	4.29			[3.99]	4.03	[3.93]	1.0	+
		232	[260]			359		4.30	[3.93]			3.89		6.0	○
7		241	271			374		4.31	4.13			3.88		MeOH	○
	2.96	230				345	[356]	4.35				4.08	[4.01]	1.0	+
		241	267			374		4.31	4.11			3.92		6.0	○
4	0.51		251	288	[340]	357	[367]		4.39	3.84	[3.77]	3.89	[3.80]	–1.0	+
		225	268	[292]		389	[405]	4.19	4.34	[3.87]		3.89	[3.84]	4.0	○
6	–0.63		252	[273]	342		[390]		4.29	[3.87]	3.71		[3.84]	–2.0	+
	6.94	242	268	291		376		4.05	4.33	4.01		3.87		4.0	○
			259	[285]		383			4.50	[3.78]		3.95		10.0	–
5	2.17		250	279	351	365			4.55	4.10	4.04	4.00		0.0	+
		[224]	261	290		390		[4.09]	4.63	3.94		4.07		6.0	○
9	1.75	236	252		333			4.08	4.10		3.92			–1.0	+
	7.56	241		278		356		4.03		4.22		3.75		4.0	○
			259	[280]		372			4.36	[3.84]		3.83		10.0	–
8	4.36		248	[287]	344	[352]			4.21	[3.62]	4.00	[3.96]		2.0	+
			262	[284]		378			4.33	[3.76]		3.83		7.0	○
12	2.21		257	310			453		4.06	4.13			3.74	0.0	+
	4.68		250	305			447		4.08	4.24			3.80	3.5	○
			246	299			425		4.15	4.36			3.85	7.0	–
11	3.44	205	247	275		391		4.03	4.25	4.23		3.99		1.0	+
		[222]	245	286		401		[4.08]	4.19	4.31		3.95		6.0	○
1	1.6	232	259		356	[390]		4.06	4.06		3.71	[3.43]		–1.0	+
	6.3			275	[305]	385				4.15	[3.74]	3.39		4.0	○
	9.23		238	275		389			4.07	4.12		3.75		7.8	–
			255			392			4.26			3.83		12.0	– –

Table (cont.)

Compound	pK_a in H_2O	UV-Absorption spectra												pH	Molecular form
		λ_{max} [nm]						lg ε							
13	0.97			277	315	375	445			3.87	4.14	3.42	3.61	–1.0	+
	4.70	218	[244]		316		451	3.98	[3.74]		4.29		3.74	3.0	○
	9.23	213	[246]		306		420	4.14	[3.83]		4.31		3.68	7.0	–
		215	256		299		417	4.07	4.06		4.26		3.79	12.0	– –
10	2.37	[228]		284		381		[3.92]		4.24		3.75		0.0	+
	8.14	213		292		390		4.08		4.28		3.75		5.0	○
		210	269			390		4.06	4.21			3.84		11.0	–
14	0.15	220			314	368	396	4.29			3.87	4.15	4.17	–2.0	+
	6.18	234		298			412	4.44		3.82			4.31	4.0	○
		233	253	286			387	4.36	4.28	3.82			4.28	10.0	–
16	3.53	222		271		362	372	4.46		3.69		4.37	4.36	1.0	+
		237		271		368		4.46		3.91		4.24		6.0	○
2	–0.5			266	320					3.82	4.04			–3.0	+
	7.34	210		286	340			4.48		4.00	4.14			4.0	○
	10.06	229		280	332			4.46		3.81	4.11			8.7	–
		221	253		339			4.58	4.05		4.14			13.0	– –
15	–0.92	224	255		348		397	4.29	3.85		4.05		3.75	–3.0	+
	5.82	239	253		306		408	4.26	4.25		3.94		4.27	3.0	○
	9.40	226	255	288		380		4.24	4.28	3.85		4.23		8.0	–
		239				382		4.40				4.22		13.0	– –
17	2.49	227		283		354		4.36		3.79		4.28		0.0	+
	8.14		243	280		363			4.32	4.06		4.18		6.0	○
		237				370		4.39				4.17		12.0	–

[a]) [ ] = Shoulder; + = cation; ○ = neutral form; – = monoanion; – – = dianion.

relationships. The second acidic pK_a of **1** and **13** are identical due to the ionization of the H–N(3), which is little influenced by the electronic arrangement in the annellated pyrazine ring. Even more striking differences between **1** and **13** can be seen from the UV/VIS spectra. The S-atom causes a strong bathochromic shift of almost 70 nm, and cation formation shows only a small hypsochromic shift in comparison to the findings with xanthopterin (**1**). It is, furthermore, notable that monoanion formation gives rise to a small bathochromic shift for **1**, whereas ionization of the thioamide function shows the typical pronounced hypsochromic affect of the long-wavelength band. The nature of tautomerism of the thioamide group can also be depticted from the spectra of the neutral forms of 6-thioxanthopterin (**13**) and its *S*-methyl derivative **10**, which reveals an entirely different spectral shape and absorbs at much lower wavelength, indicating a high preference for the thioxo form in the tautomeric equilibrium (*Fig. 1*).

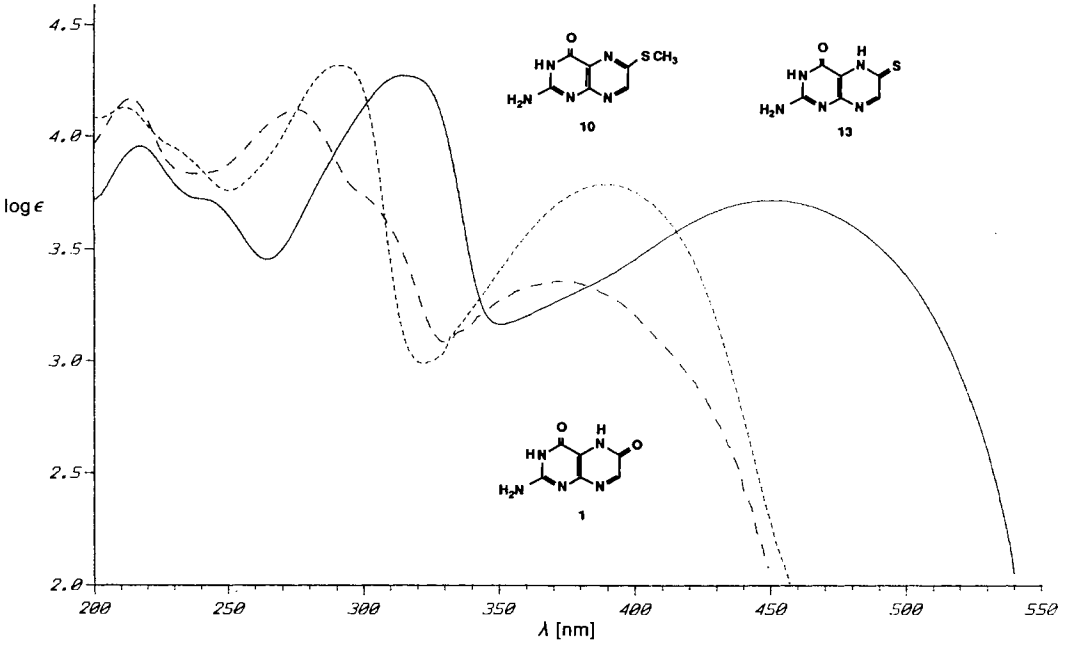


Fig. 1. *UV-Absorption spectra of the neutral species of xanthopterin* (**1**; pH 4.0; ----), *6-thioxanthopterin* (**13**; pH 3.0; ——), *and 6-(methylthio)pterin* (**10**; pH 5.0; · · · ·)

Finally, the characteristic feature of covalent hydration, which affects the neutral form of **1** to *ca.* 40% and is responsible for the low extinction of the long-wavelength band, does not play any role in **13** due to its normal UV/VIS spectrum (*Fig. 1*).

An analogous discussion of the physical properties can be considered for the pair isoxanthopterin (**2**) and 7-thioisoxanthopterin (**15**). Compound **15** is again the weaker base and consequently also the stronger acid compared to **2**. The thioxo group causes in this series also a strong bathochromic shift of almost 70 nm, monoanion formation results in a blue shift, and the thioxo tautomer as the predominant neutral species in aqueous medium is derived from the spectral comparison of **15** and its 7-(methylthio) derivative **17** (*Fig. 2*).

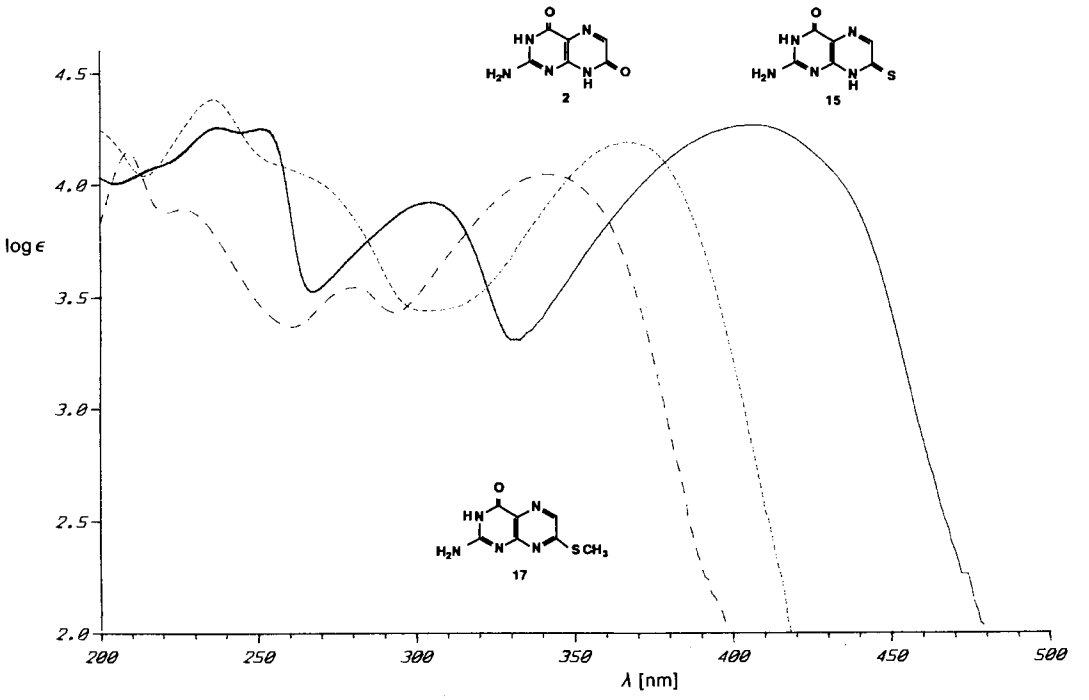


Fig. 2. *UV-Absorption spectra of the neutral species of isoxanthopterin* (**2**; pH 4.0; ----), *7-thioisoxanthopterin* (**15**; pH 3.0; ——), *and 7-(methylthio)pterin* (**17**; pH 6.0; · · · ·)

Compounds **14** and **16** behave similarly, since conversion of the amide group into an imidoester function does, in general, not affect the basic properties severely.

Experimental Part

General. TLC: precoated silica gel thin-layer sheets *F 1500 LS 254* and cellulose thin-layer sheets *F 1440 LS 254* from *Schleicher & Schüll.* M.p.: *Büchi* apparatus, model Dr. *Tottoli*; no corrections. p*K*: the determination were done by the spectrophotometric method [28]. UV/VIS: *Uvikon 820*, *Kontron*, and *Lambda 5* (*Perkin-Elmer*); λ_{max} (log ε). ^{1}H-NMR: *Bruker-WN-250*; in δ (ppm) relative to TMS.

1. *Xanthopterin* (**1**). In a soln. of 10 ml of 1N NaOH and 5 ml of dioxan, 0.2 g (0.75 mmol) of *2-amino-6-chloro-4-(pentyloxy)pteridine* (**7**) were heated under reflux for 18 h. The mixture was then treated with a little charcoal, filtered, and the filtrate added dropwise to 20 ml of boiling 0.5N HCl. The yellow precipitate was collected after cooling, washed with H_2O and EtOH, and dried at 100° to give 0.111 g (83%) of a yellow-to-orange-coloured powder. M.p. > 300°. The material is chromatographically and spectrophotometrically identical with an authentic sample.

2. *2,5,6-Triamino-4-(pentyloxy)pyrimidine* [18]. To a mixture of 220 ml of an aq. 20% ammonium sulfide soln. and 65 ml of EtOH were added gradually at 80° 24 g (0.1 mol) of 2,6-diamino-5-nitroso-4-(pentyloxy)pyrimidine [18], and then stirring was continued for 15 min. After cooling, the EtOH was removed in a flash evaporator and the resulting suspension chilled in ice. The precipitate was collected, washed with H_2O, and dried in a vacuum desiccator to give 22 g (98%) crude, but homogenous material. A sample was recrystallized from H_2O with charcoal to give colorless crystals. M.p. 76–78°. UV (MeOH): 242 (3.90), 287 (3.29). Anal. calc. for $C_9H_{17}N_5O$ (211.3): C 51.17, H 8.11, N 33.15; found: C 50.86, H 8.05, N 32.73.

3. *2-Amino-4-(pentyloxy)pteridine* (**3**). A mixture of 5.0 g (0.024 mol) of 2,5,6-triamino-4-(pentyloxy)pyrimidine in 150 ml of DMF and 1.65 g of glyoxal-hydrate trimer in 150 ml of DMF was stirred at r.t. for 3 days under N_2. Some insoluble material was filtered off and the filtrate diluted with 300 ml of H_2O. The soln. was extracted (3 × 200 ml) with $CHCl_3$, then the org. layer was washed twice with H_2O, dried (Na_2SO_4), filtered, and evaporated to dryness (4.6 g). Recrystallization from 80 ml of MeOH/H_2O 1:1 gave 3.8 g (69%) of yellowish crystals. M.p. 128–129°. Anal. calc. for $C_{11}H_{15}N_5O$ (233.3): C 56.64, H 6.48, N 30.02; found: C 56.54, H 6.43, N 30.30.

4. *2-Amino-4-(pentyloxy)pteridine* N(8)-*Oxide* (**4**). A soln. of 5.0 g (0.021 mol) of **3** in 85 ml of CF_3COOH was cooled to 6°, and then 5 ml of 30% H_2O_2 were slowly added with stirring. The mixture was kept at 6° for 60 h, whereby another 2 ml of 30% H_2O_2 were added after 30 h. The soln. was concentrated in vacuum to 1/3 of its volume, then diluted with 20 ml of H_2O, and the resulting precipitate was collected. The solid was suspended in 100 ml of H_2O, then neutralized by NH_3, the precipitate was filtered off and dried to give 2.2 g (43%) of yellowish, chromatographically pure material. M.p. 209–211°. Recrystallization of a sample from EtOH/H_2O 1:1 gave yellowish crystals. M.p. 210–211°. Anal. calc. for $C_{11}H_{15}N_5O_2$ (249.3): C 53.00, H 6.06, N 28.09; found: C 52.95, H 6.04, N 28.18.

5. *2,4-Diaminopteridine* N(8)-*Oxide* (**5**) [19]. Conc. NH_3 (40 ml) and 0.1 g (0.4 mmol) of **4** were heated to 80° for 30 min. The starting suspension soon became a clear soln., and some time later a yellow precipitate separated. The mixture was finally refluxed for 15 min, cooled, and the precipitate collected, washed with H_2O, and dried at 100° to give 0.055 g (78%) of a yellow powder. M.p. 327–329° (dec.) ([19]: m.p. 328–330° (dec.)). The material was chromatographically and spectrophotometrically identical with an authentic sample.

6. *Pterin* N(8)-*Oxide* (**6**) [19]. For 1 h, 10 ml of 0.1N HCl and 0.1 g (0.4 mmol) of **4** were heated under reflux. After cooling, the precipitate was collected, washed with H_2O and EtOH, and then dried at 100° to give 0.067 g (93%) of a yellow powder. M.p. > 300°. The UV spectrum of this product is identical with that of an authentic sample.

7. *2-Amino-6-chloro-4-(pentyloxy)pteridine* (**7**). At −40°, 1 g (4 mmol) of **4** was suspended in 10 ml of freshly distilled AcCl, and then with stirring 3 ml of CF_3COOH were slowly added. The soln. was warmed to 0°, stirred for 3 h, and then the reaction was stopped by addition of 30 g of ice. The mixture was neutralized with conc. NH_3 to pH 4, then extracted with $CHCl_3$ (6 × 50 ml), the org. layer washed with H_2O, dried (Na_2SO_4), and evaporated to a small volume. The residue was purified by chromatography on a silica-gel column with $CHCl_3$. The product fraction was evaporated to dryness and the residue recystallized from i-PrOH to give 0.75 g (70%) of colorless crystals. M.p. 211° (dec.). Anal. calc. for $C_{11}H_{14}Cl\,N_5O$ (267.7): C 49.35, H 5.27, N 26.16; found: C 49.36, H 5.19, N 26.31.

8. *2,4-Diamino-6-chloropteridine* (**8**) [24]. A mixture of 20 ml of conc. NH_3, 20 ml of dioxan, and 0.1 g (0.37 mmol) of **7** were stirred at r.t. for 24 h. The precipitate was collected, washed with H_2O, and dried in a vacuum desiccator to give 0.066 g (90%) of a yellowish powder. M.p. > 300°. Anal. calc. for $C_6H_5Cl\,N_6$ (196.6): C 36.66, H 2.56, N 42.75; found: C 36.66, H 2.77, N 42.57.

9. *6-Chloropterin* (**9**) [23]. A mixture of 20 ml of 1N NaOH/dioxan 1:1 and 0.1 g (0.37 mmol) of **7** were stirred at r.t. for 6 h. The mixture was neutralized with AcOH to form a colorless precipitate, which was collected, washed with H_2O, and dried at 100° to give 0.065 g (89%) of a colorless powder. M.p. > 300°. Anal. calc. for $C_6H_4ClN_5O$ (197.6): C 36.47, H 2.04, N 35.45; found: C 36.38, H 2.11, N 35.28.

10. *6-(Methylthio)pterin* (**10**). A soln. of 0.6 g (3.1 mmol) of *6-thioxanthopterin* (**13**) in 100 ml of 0.4N NaOH was treated with 0.5 ml of MeI at r.t. for 3 h with stirring. The resulting gelatinous precipitate was centrifuged, washed three times with H_2O and EtOH, and then the solid was dried at 100° to give 0.06 g (90%) of a yellow, chromatographically pure powder. M.p. > 300°. Anal. calc. for $C_7H_7N_5OS \times H_2O$ (227.2): C 37.01, H 3.99, N 30.83; found: C 37.19, H 3.87, N 30.59.

11. *2-Amino-6-(methylthio)-4-(pentyloxy)pteridine* (**11**). A soln. of 0.1 g (0.38 mmol) of **12** in 10 ml of 0.2N NaOH was treated with 0.25 ml of MeI at r.t. for 2.5 h with stirring. The precipitate was collected, washed with dilute AcOH and H_2O, and gave, on recrystallization from 6 ml of EtOH/H_2O 1:1, 0.057 g (54%) of yellow crystals. M.p. 164°. ^{1}H-NMR ($CDCl_3$): 8.85 (*s*, H–C(7)); 5.27 (*s*, NH_2); 4.51 (*t*, CH_2O); 2.68 (*s*, CH_3S); 1.92 (*m*, CH_2); 1.46 (*m*, CH_2CH_2); 0.96 (*m*, CH_3). Anal. calc. for $C_{12}H_{17}N_5O_5$ (279.3): C 51.60, H 6.14, N 25.08; found: C 51.56, H 5.94, N 25.00.

12. *2-Amino-4-(pentyloxy)pteridine-6(5H)-thione* (**12**). *a*) Compound **7** (0.1 g, 0.3 mmol) was dissolved in a mixture of 10 ml of $CHCl_3$/MeOH 1:1, and 0.11 g NaSH in 2 ml of H_2O were added and then stirred at r.t. for 15 h.

The orange colored soln. was evaporated to dryness, the residue was dissolved in little H_2O and acidified with AcOH. The precipitate was collected, then dissolved in little $CHCl_3$, placed onto a preparative silica-gel plate (40 × 20 × 0.2 cm), and developed with $CHCl_3$/MeOH 9:1. The required band was cut out, eluted with $CHCl_3$/MeOH 4:1, evaporated, and the residue was recrystallized from EtOH to give 0.03 g (30%) of a yellow powder. M.p. 235° (dec.). Anal. calc. for $C_{11}H_{15}N_5O_5$ (265.3): C 49.79, H 4.70, N 26.40; found: C 49.71, H 5.43, N 26.27.

b) 2-Amino-4-(pentyloxy)-6-thiopteridine Monosodium Salt. Analogously to the preceding procedure, 0.1 g (0.3 mmol) of 7 was treated with NaSH. The orange colored soln. was evaporated to dryness, and the residue was recrystallized from 12 ml of i-PrOH to give 0.06 g (67%) of orange crystalline plates. M.p. 195–220° (dec.). Anal. calc. for $C_{11}H_{14}N_5O_5Na \times H_2O$ (305.3): C 43.28, H 5.28, N 22.93; found: C 43.43, H 5.28, N 22.86.

13. *6-Thioxanthopterin* (**13**). *a)* In a mixture of 60 ml of 1N NaOH and 12 ml of dioxane were dissolved 0.531 g (2 mmol) of **12** and then refluxed for 20 min. The soln. was treated with a little charcoal, filtered, and the hot filtrate was added dropwise to a boiling soln. of 10 ml of AcOH in 60 ml H_2O. After cooling, the precipitate was collected, washed with H_2O, and dried at 100° to give 0.342 g (88%) of dark red crystals. M.p. > 300°. Reprecipitation from 0.1N NaOH into excess of hot 0.1N HCl gave an anal. pure sample. Anal. calc. for $C_6H_5N_5OS$ (195.2): C 36.92, H 2.58, N 35.88; found: C 36.87, H 2.78, N 35.61.

b) Thioxanthopterin Disodium Salt. Compound **12** (0.15 g, 0.57 mmol) in 30 ml of 1N NaOH was heated to 80° for 30 min and then co-evaporated several times with H_2O, until all pentanol has been removed. After final co-evaporation to dryness, the remaining residue was recrystallized from 15 ml of EtOH/H_2O 9:1 to give 0.128 g (88%) of a yellow crystal powder. M.p. > 300°. Anal. calc. for $C_6H_3N_5Na_2OS \cdot H_2O$ (258.2): C 27.91, H 1.95, N 27.13; found: C 28.16, H 2.07, N 27.26.

14. *7-Thioisoxanthopterin* (**15**). Compound **14** (0.5 g, 1.9 mmol) [25] in 20 ml of 1N NaOH was heated in boiling H_2O for 1 h. After treatment with a little charcoal and filtration, the hot filtrate was added dropwise to boiling dil. AcOH. The yellow precipitate was collected and then again reprecipitated from dil. NaOH by addition into hot dil. AcOH to give 0.33 g (90%) of a yellow-to-orange-colored powder. M.p. > 300°. Anal. calc. for $C_6H_5N_5OS$ (195.2): C 36.93, H 2.58, N 35.89, S 16.42; found: C 37.05, H 2.68, N 36.06, S 16.31.

15. *2-Amino-7-(methylthio)-4-(pentyloxy)pteridine* (**16**). A soln. of 0.76 g (2.86 mmol) of **14** [25] in 25 ml of 1N KOH was treated by 0.3 ml of MeI at r.t. for 2 h with stirring. The yellow precipitate was filtered off, washed with H_2O, and gave, on recrystallization from MeOH, 0.45 g (56%) of yellow needles. M.p. 185–186°. Anal. calc. for $C_{12}H_{17}N_5OS$ (279.3): C 51.60, H 6.14, N 25.08; found: C 51.43, H 6.07, N 24.86.

16. *7-(Methylthio)pterin* (**17**). A soln. of 1.95 g (10 mmol) of **15** in 200 ml of 0.2N NaOH was treated dropwise with 0.6 ml of MeI at r.t. with stirring for 3 h. The soln. was neutralized by AcOH, the precipitate was collected, washed with H_2O, and dried at 100° to give 2.0 g (96%) of chromatographically pure material. A sample was recrystallized from EtOH/H_2O 1:1 to give a yellow crystalline powder. M.p. > 300°. Anal. calc. for $C_7H_7N_5OS$ (209.2): C 40.19, H 3.38, N 33.48, S 15.30; found: C 40.04, H 3.31, N 33.34, S 15.27.

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