150. Pteridines

Part LXXXVII[1])

Synthesis and Properties of 8-Substituted 2-Thiolumazines

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Various 8-substituted 2,8-dihydro-2-thioxopteridin-4(3*H*)-ones (**14–21**) and 2-(methylthio)pteridin-4(8*H*)-ones (**27–32**) have been synthesized by condensation of the appropriate 5-amino-6-(substituted amino)-1,2-dihydro-2-thioxopyrimidin-4(3*H*)-ones (**22–34**) and 5-amino-6-(substituted amino)-2-(methylthio)pyrimidin-4(3*H*)-ones (**25, 26**), respectively, with glyoxal, biacetyl, and benzil. The presence of a quinonoid cross-conjugated π-electron system makes this type of compounds susceptible to nucleophilic additions in position 7, which leads to intramolecular (**43, 45**) and intermolecular (**44**) covalent adducts. The newly synthesized compounds have been characterized by elemental analyses, pK_a determinations, ^{1}H-NMR and UV spectra. UV-Spectral changes in dependence of the pH are associated with the most appropriate molecular species including the monocations, neutral forms, covalent adducts, mono- and dianions.

1. Introduction. – Interest in 8-substituted lumazines [2–7] has been encountered when 6,7-dimethyl-8-(D-ribityl)lumazine was isolated from bacteria [8] and proven to be an important intermediate in riboflavin biosynthesis [9] [10]. No attention has so far been given to the 8-substituted 2-thiolumazines [11] [12] as structural analogs and potential inhibitors of riboflavin synthase. This new type of pteridine derivatives can be regarded as an extension of our research in the field of 2-thiolumazines [13–18] in general.

2. Synthesis. – The synthetic approach to the 8-substituted 2-thiolumazines is based in the first step upon a transamidation reaction [19] [20] with various amines starting from 6-amino-2-thiouracil (**1**). Conversion on **1** into 6-(methylamino)-2-thiouracil (**2**) worked best (66% yield) with $MeNH_2/MeNH_3Cl$ in *N*-methylformamide at elevated temperature. The 6-(2-hydroxyethyl)amino derivative **3** was obtained with (2-hydroxyethyl)ammonium acetate at 170° in 48% yield, and an aromatic amine like aniline (mixture of the free base and its hydrochloride salt) afforded at 170°, the anilino derivative **4** in 78% yield. Introduction of a N-function into the 5-position is usually achieved by nitrosation which, surprisingly, did not work with **2**. Instead, 6-(methylamino)-5-nitrosouracil (**7**) was obtained, and we assume that the primary electrophilic attack of the nitrosonium ion takes place at the S-atom forming a thionitrite derivative which is hydrolysed to the OH derivative and then subsequently nitrosated in the usual manner. This is surprising inasmuch as **1** can be nitrosated under the same conditions to give the

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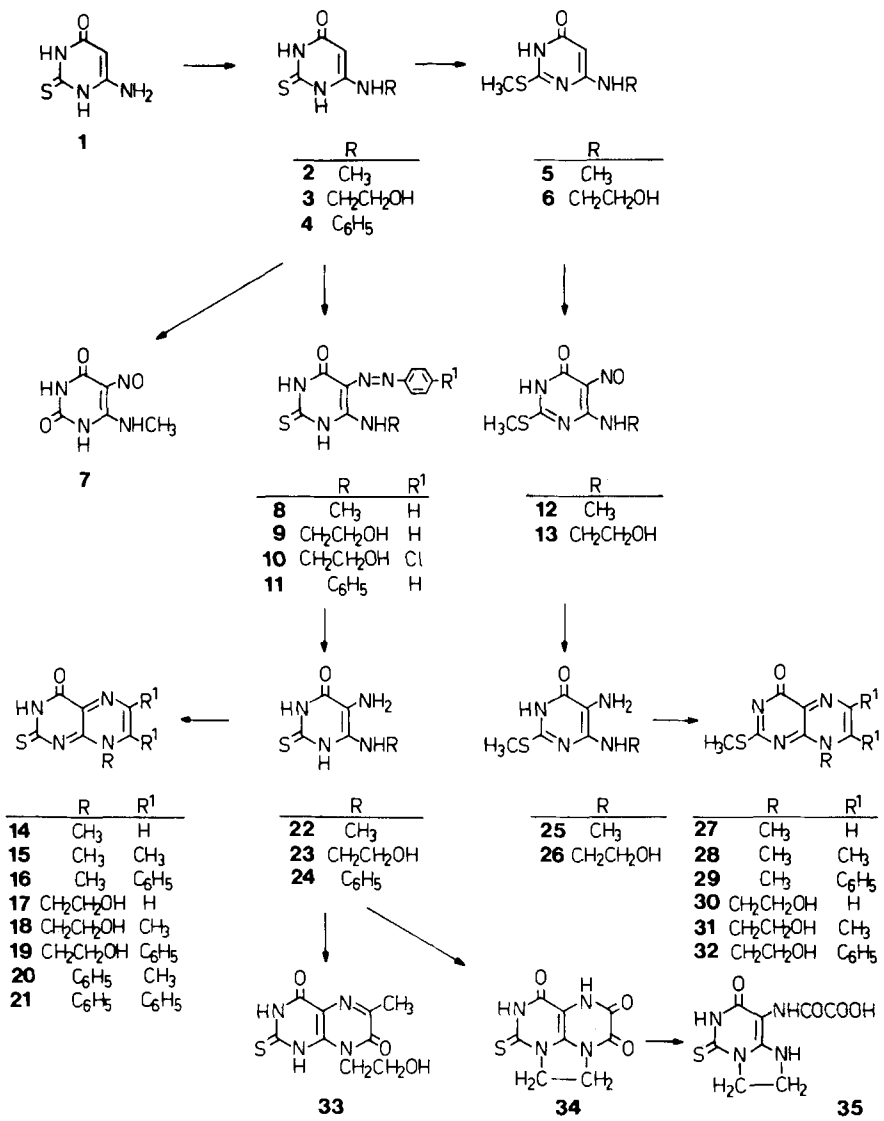
6-amino-5-nitroso-2-thiouracil in 90% yield [29]. Conversion of the 6-(methylamino)- (**2**) and 6-[(2-hydroxyethyl)amino]-2-thiouracil (**3**) into their methylthio derivatives **5** and **6**, respectively, overcame the difficulties. The latter compounds could easily be nitrosated by treatment with HNO_2 at room temperature to form **12** and **13**, respectively, in almost quantitative yields.

In the 6-(substituted amino)-2-thiouracil series, coupling with the phenyldiazonium cation in alkaline solution was, however, successful and gave in good yields the corresponding 5-(phenylazo) derivatives **8**, **9**, and **11**. Moreover, 6-[(2-hydroxyethyl)amino]-2-

Scheme 1



thiouracil (**3**) was coupled with 4-chlorophenyldiazonium chloride to give **10** in almost quantitative yield.

The reduction of the phenylazo group in **8**, **9**, and **11** to the corresponding 5-amino group was achieved by sodium-dithionite treatment in alkaline medium yielding **22** and **24** as crystalline solids, whereas **23** was too soluble in the reaction solution and used directly in solution for the subsequent condensation (**23** was also obtained by $(NH_4)_2S$ reduction). The conversion of the 5-nitroso-uracils **12** and **13** into 5-amino-6-(methylamino)- (**25**) and 5-amino-6-[(2-hydroxyethyl)amino]-2-(methylthio)pyrimidin-4(3*H*)-one (**26**), respectively, worked best with $(NH_4)_2S$ reduction to give almost colourless materials in excellent yields.

In the next step, the 8-substituted 2-thiolumazines **14**–**21** and the *S*-methyl derivatives **27**–**32** were formed *via* a *Gabriel-Isay* condensation [21–23] using 1,2-dicarbonyl compounds in an acid-catalysed reaction. The condensations of **22** and **23** with glyoxal created some problems in the 2-thioxo series and gave relatively low yields of the anticipated compounds **14** and **17**, respectively, whereas the 8-phenyl-2-thiolumazine could not be obtained at all from **24** due to the formation of many side products [24–27] as seen by TLC. In the 2-methylthio series, both **25** and **26** reacted well with glyoxal forming 8-methyl- (**27**) and 8-(2-hydroxyethyl)-2-(methylthio)pteridin-4(8*H*)-one (**30**) in good yields. Analogous condensations with biacetyl and benzil led to the corresponding 8-substituted 6,7-dimethyl- (**15**, **18**, **20**, **28**, and **31**) and 6,7-diphenyl-2-thiolumazine derivatives (**16**, **19**, **21**, **29**, and **32**). Furthermore, **23** was also condensed with ethyl pyruvate to 1,2-dihydro-8-(2-hydroxyethyl)-6-methyl-2-thioxopteridine-4,7(3*H*,8*H*)-dione (**33**), and with oxalic acid in DMF, the 2-thioxo-1,8-ethanopteridinetrione **34** was formed from **23** *via* the intermediary 8-(2-hydroxyethyl)-2-thioxopteridinetrione after intramolecular alkylation at N(1) by the side-chain [7]. The relatively base-labile compound **34** was easily hydrolysed to 2,3,4,5-tetrahydro-8-(oxaloamino)-5-thioxoimidazo[1,2-*c*]pyrimidin-7(6*H*)-one (**35**).

3. Physical Data. – The newly synthesized compounds have been characterized by elemental analysis, determination of the pK_a values, and UV/VIS and NMR spectra for further structural proof *(Table)*.

The 8-substituted 2-thiolumazines which can be considered as vinylogous thioamides of a merocyanine-type structure correlate nicely in their spectrophotometric properties with the well documented 8-substituted lumazines [5], whereby the S-atom causes a general red shift of the spectrum due to its easier polarizability. The cation species show a hypsochromic shift of the long-wavelength absorption band indicating protonation at N(1), and the neutral forms exhibit a strong absorption band in the VIS region. Anion formation, however, is again associated with more distinct structural changes depending especially upon the nature of the C(7) as well as the N(8) substituents.

In the case of 8-methyl-2-thiolumazine (**14**), the monoanion is derived mainly from nucleophilic addition of OH^- to C(7) forming a pseudobase-type molecule **37** which has the spectral properties of a 7,8-dihydrolumazine derivative as seen from the new absorption band at 332 nm *(Scheme 2)*. The long-wavelength maximum at 432 nm of low extinction has to be attributed to the 'real' monoanion **36** which is still present in a small concentration in the mixture. At higher pH, the dianion is formed which exists predominantly in the pseudobase form **39**.

Table. *Physical Data of 8-Substituted 2-Thiolumazines*

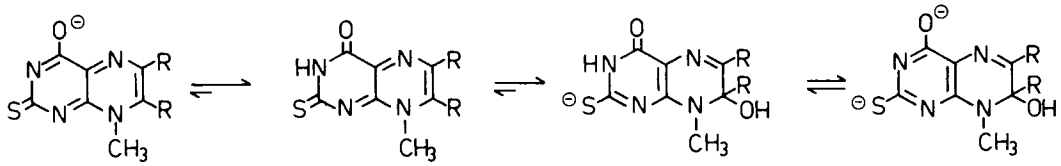
	pK_a in H_2O	UV/VIS Spectra λ_{max} [nm][a])				lg ε				pH	Molecular Form	^{1}H-NMR Spectra in (D_6)DMSO NH CH_3S	R^1–C(6)	R^1–C(7)	R–C(8)
14	–0.82		254	291	387		3.85	4.11	4.03	–2.7	+	12.36 (*s*, 1 H)	8.30 (*d*, 1 H)	8.61 (*d*, 1 H)	3.88 (*s*, 3 H)
	7.77	239		315	433	3.78		4.34	4.02	2.0	○		9.0 (*m*, 1 H)[b])	9.20 (*m*, 1 H)[b])	4.61 (*s*, 3 H)[b])
	12.53	224	264	332	432	4.35	4.22	4.23	2.91	10.0	–				
		224	264	331		4.34	4.36	4.14		14.0	– –				
15	–0.57	227	(260)	291	390	3.71	(3.90)	4.17	4.16	–2.3	+	12.4 (*s*, 1 H)	2.57 (*s*, 3 H)	2.68 (*s*, 3 H)	4.00 (*s*, 3 H)
	8.23	238	257	318	433	3.81	3.85	4.36	4.11	2.0	○		2.95 (*s*, 3 H)[b])	3.10 (*s*, 3 H)[b])	4.55 (*s*, 3 H)[b])
	13.21	(246)	287	318	(350)	(4.07)	4.43	4.27	(3.74)						
		(3.70)	383	(398)	(423)	(3.84)	3.87	(3.80)	(3.49)	11.0	–				
		251	(282)	(306)	(344)	4.37	(4.17)	(4.11)	(3.82)						
		(362)	379	(396)		(3.88)	3.93	(3.88)		2N KOH	– –				
16	–0.72		261	311	432		4.03	4.30	4.25	–3.0	+	12.51 (*s*, 1 H)	7.22 (*m*, 5 H)	7.49 (*s*, 5 H)	3.65 (*s*, 3 H)
	7.83	(248)		333	463	(4.02)		4.43	4.26	2.0	○		7.0 –	7.3 (*m*, 10 H)[b])	4.40 (*s*, 3 H)[b])
	12.80	229	274	373		4.43	4.31	4.25		10.0	–				
			273	369			4.40	4.21		14.0	– –				
17	–1.57		256	291	386		3.94	4.10	4.03	–4.0	+	12.4 (*s*, 1 H)	8.32 (*d*, 1 H)	8.48 (*d*, 1 H)	3.80 (*t*, CH_2)
	7.67	238		315	437	3.88		4.34	4.02	2.0	○				4.45 (*m*, CH_2)
	12.48	224	263	332	(340)	4.34	4.23	4.24	(4.20)	10.0	–				5.04 (*t*, OH)
18	–0.79	(233)	261	291	392	(3.75)	3.99	4.14	4.11	–2.7	+	12.2 (br. *s*, 1 H)	2.57 (*s*, 3 H)	2.77 (*s*, 3 H)	3.84 (*m*, 2 H)
	7.49	240	259	319	437	3.83	3.88	4.34	4.11	2.0	○				4.67 (*t*, 2 H)
	13.10	224	271	(285)	319	4.20	4.29	(4.19)	4.14						5.07 (*t*, 1 H, OH)
		337	385	(401)	(425)	4.00	3.53	(3.44)	(3.18)	10.0	–				
19	–0.78		260	311	435		4.08	4.28	4.21	–2.5	+	12.5 (br. *s*, 1 H)	7.2 (*m*, 5 H)	7.5 (*s*, 5 H)	3.75 (*m*, CH_2)
	5.87	(246)		331	465	(4.07)		4.39	4.21	2.0	○				4.32 (*m*, CH_2)
	13.02	234	271	383		4.39	4.30	4.32		9.0	–				4.98 (*t*, OH)
			274	372			4.36	4.23		14.0	– –				

20	–0.05		(263)	293	398		(3.94)	4.19	4.17	–3.0	+				
	6.86		258	320	445		3.78	4.40	4.13	3.0	○		2.68 (*s*, 3 H)[b]	2.98 (*s*, 3 H)[b]	7.50 (*m*, 5 H)[b]
	13.16	(270)	290	(296)	316	(4.25)	4.35	(4.35)	4.25						
			(344)	390	(405)		(3.85)	3.78	(3.71)	10.0	–				
21	–0.47	(222)	263	311	441	(4.26)	4.10	4.32	4.22	–3.0	+	12.6 (br. *s*, 1 H)	7.30 (*s*, 5 H)	7.35 (*s*, 5 H)	7.40 (*s*, 5 H)
	5.89		(250)	335	477		(4.09)	4.37	4.17	3.0	○				
	12.98	227	276	370		4.46	4.29	4.35		10.0	–				
27	3.81	240	288		380	3.73	4.28		4.16	1.0	+	2.49 (*s*, 3 H)	8.62 (*d*, 1 H)	8.76 (*d*, 1 H)	4.02 (*s*, 3 H)
	9.90	249	284	(347)	406	4.00	4.24	(3.75)	4.06	7.0	○	2.92 (*s*, 3 H)[b]	9.1 (*d*, 1 H)[b]	9.22 (*d*, 1 H)[b]	4.61 (*s*, 3 H)[b]
		239	(281)	321		4.41	(3.68)	4.03		13.0	–				
28	4.31	251	288	(297)	383	3.85	4.25	(4.18)	4.21	1.0	+				
	9.80	257	284	(322)	407	4.05	4.30	(3.58)	4.13	7.0	○	2.75 (*s*, 3 H)[b]	2.85 (*s*, 3 H)[b]	2.95 (*s*, 3 H)[b]	4.40 (*s*, 3 H)[b]
		241	273	(300)	378	4.41	4.22	(4.13)	3.86	13.0	–				
29	3.59	(223)	299		417	(4.12)	4.34		4.31	1.0	+	2.51 (*s*, 3 H)	7.23 (*m*, 5 H)	7.51 (*s*, 5 H)	3.78 (*s*, 3 H)
	9.78		299	(365)	436		4.40	(3.75)	4.25	6.0	○	2.90 (*s*, 3 H)[b]	7.0 –	7.3 (*m*, 10 H)[b]	4.41 (*s*, 3 H)[b]
		249		364		4.41		4.16		13.0	–				
303.61		240	289		383	3.76	4.25		4.16	1.0	+	2.48 (*s*, 3 H)	8.65 (*s*, 1 H)	8.65 (*s*, 1 H)	3.84 (*t*, CH_2)
	9.40	249	284	(351)	409	4.03	4.18	(3.70)	4.05	7.0	○				4.57 (*m*, CH_2)
															5.07 (*t*, OH)
		240	(280)	319		4.36	(3.66)	4.00		12.0	–	2.90 (*s*, 3 H)[b]	9.10 (*d*, 1 H)[b]	9.21 (*d*, 1 H)[b]	4.50 (*m*, 2 H)[b]
															5.25 (*m*, 2 H)[b]
31	4.18	256	290	(299)	387	3.89	4.22	(4.14)	4.22	1.0	+				
	9.35	260	285	317	411	4.06	4.25	3.57	4.10	7.0	○	2.85 (*s*, 3 H)[b]	3.00 (*s*, 3 H)[b]	3.25 (*s*, 3 H)[b]	4.50 (*m*, 2 H)[b]
		239	268	300	380	4.36	4.11	3.99	3.66	12.0	–				5.41 (*m*, 2 H)[b]
32	3.18	(224)	299		419	(4.10)	4.34		4.29	1.0	+				
	8.72	259	286	374	438	4.42	3.97	4.14	3.39	5.0	○	2.90 (*s*, 3 H)[b]	7.0 –	7.35 (*m*, 10 H)[b]	4.40 (*m*, 2 H)[b]
		254		377		4.35		4.19		11.0	–				5.52 (*m*, 2 H)[b]

[a]) Values in parentheses refer to shoulders.

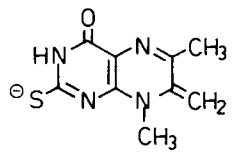
[b]) In CF_3COOH.

Scheme 2



R		R		R		R	
36	H	**14**	H	**37**	H	**39**	H
41	CH_3	**15**	CH_3	**38**	C_6H_5	**40**	C_6H_5
		16	C_6H_5				

15 ⇌



42

The spectral behaviour of 8-methyl-6,7-diphenyl-2-thiolumazine (**16**) resembles that of **14**, but pseudobase formation in the monoanion **38** is even more pronounced due to an obvious release of internal strain caused by the adjacent phenyl substituents at the sp^2-hybridized C-atoms *(Scheme 2)*. Expectedly, dianion formation (→**40**) causes again little further spectral change in this series.

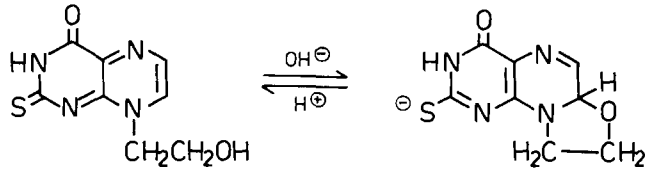
A new situation is encountered with the 6,7,8-trimethyl-2-thiolumazine (**15**) since the thioxo function activates the 7-methyl group. The monoanion **42** is, therefore, derived in this series by deprotonation from the 7-methyl group forming a 7,8-dihydro-7-methylidene structure which is associated also with a hypsochromic shift of *ca.* 50 nm *(Scheme 2)*. The presence of a shoulder in the VIS region of this spectrum indicates, furthermore, that the monoanion is again a mixture of at least two species, namely **42** and the most probable structure **41**.

A change of the 8-methyl against the 8-(2-hydroxyethyl) group reveals an analogous spectral pattern, but we have to assume that in this series in alkaline medium, a nucleophilic attack at C(7) is achieved intramolecularly by the terminal OH group of the N(8) substituent rather than by the OH^- ion. An indication of this effect is seen in the clean monoanion spectrum of **17** which is in full agreement with structure **43**.

The UV spectra of the various molecular species of the 8-substituted 2-(methylthio)pteridin-4(8*H*)-ones **27**–**32** can be interpreted in a similar manner. The interconversion of the 2-thioxo function into the 2-(methylthio) group is, thereby, mainly reflected in an increase of the base strength of the molecules by 4–5 pK_a units. Cation and anion formation causes again a blue shift of the spectra in comparison to the neutral species indicating that the same molecular features are responsible for the spectral properties as in the 8-substituted 2-thiolumazine series. The absence of an acidic amide proton gives rise to uniform monoanion spectra of the pseudobase and 7-methylidene type, respectively.

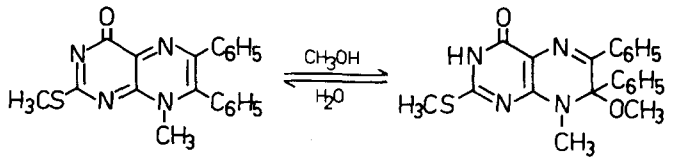
Furthermore, it is noteworthy that especially 8-methyl-2-(methylthio)-6,7-diphenylpteridin-4(8*H*)-one (**29**) shows, even as a neutral species, a high tendency for covalent

Scheme 3



17 **43**

Scheme 4



29 **44**

addition of nucleophiles. The spectrum in MeOH changes slowly, and within 4 h, the long-wavelength band at 436 nm has disappeared under build-up of a new maximum at 375 nm which is consistent with the MeOH adduct **44** *(Scheme 4)*. Dilution of this solution with buffer (pH 6) reverses the covalent binding of MeOH *(Fig. 1)*.

The 8-(2-hydroxyethyl)-2-(methylthio)-6,7-diphenylpteridin-4(8*H*)-one (**32**) exists, even in aqueous solution in the neutral form, partly as cyclic adduct since the long-wave-

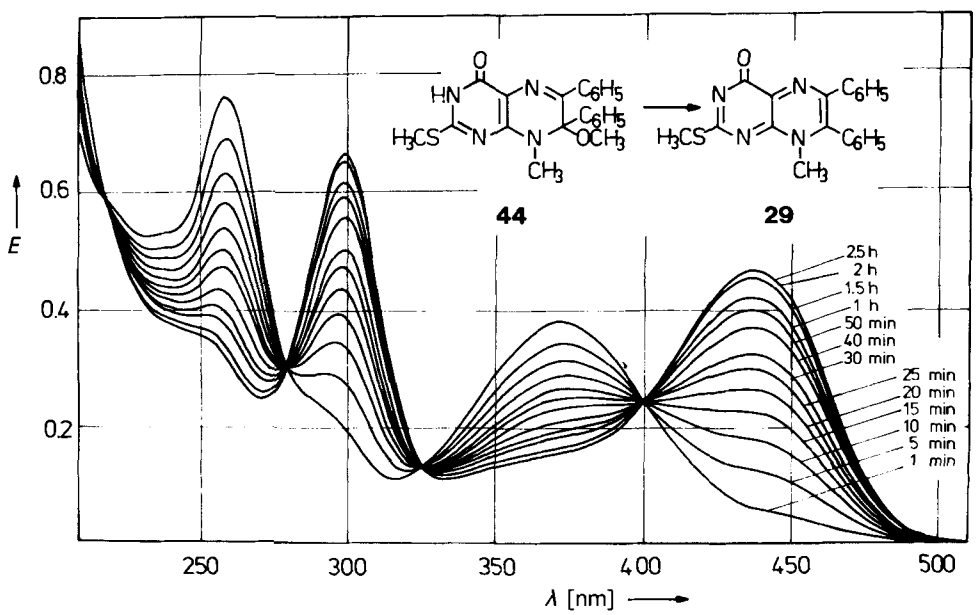


Fig. 1. *UV/VIS-Spectral change of 7,8-dihydro-7-methoxy-8-methyl-2-(methylthio)-6,7-diphenylpteridin-4(3H)-one* (**44**) *in MeCN after addition of buffer pH 6*

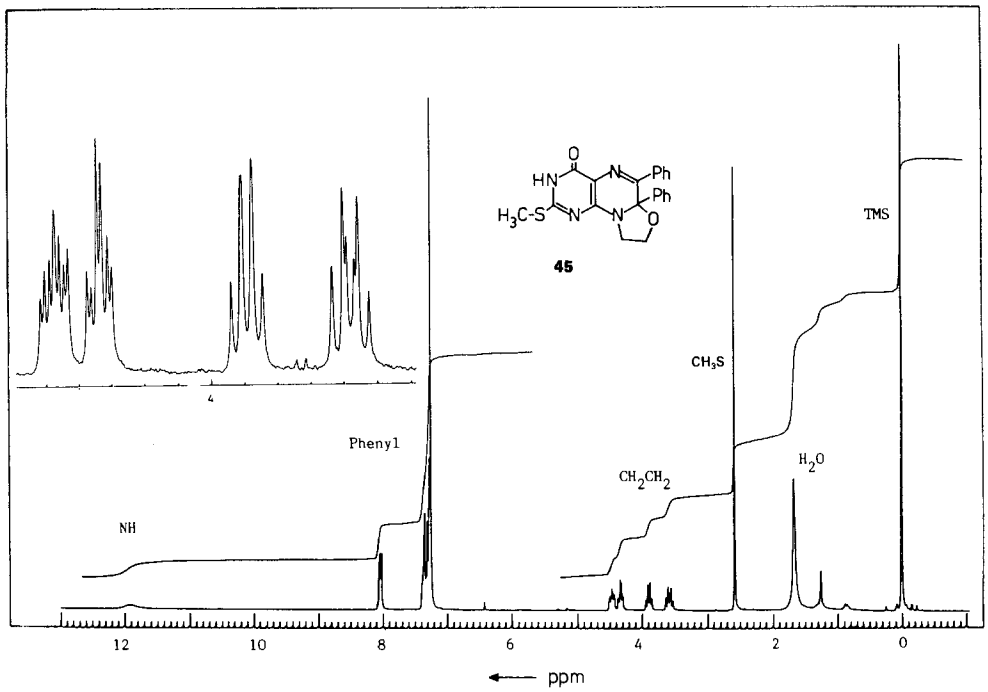


Fig. 2. *^{1}H-NMR spectrum of* **32** *in $CDCl_3$ to form* **45**

length absorption band is drastically decreased on account of the 374-nm absorption. The ^{1}H-NMR spectrum of **32** in $CDCl_3$ reveals this effect also very nicely, since adduct formation (**45**) creates a new chiral center at C(7), which is reflected in the complex coupling pattern of the diastereotopic CH_2 groups *(Fig. 2)*.

We thank the *Fond der Chemischen Industrie* for financial support and Mrs. *M. Bischler* for the determination of the p*K* values and the measurements of the UV/VIS spectra.

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.* Prep. TLC: silica gel *60 PF_{254} (Merck).* Prep. column chromatography: silica gel *Merck 60* (0.063–0.2 mm). M.p.: *Büchi* apparatus, model Dr. *Tottoli;* no corrections. UV/VIS: *Cary* recording spectrometer, model *118, Applied Phys. Corp.*, and *Uvikon 820, Kontron;* λ_{max} in nm (lg ε). ^{1}H-NMR: *Bruker WP-80 CW, Jeol JNM-MH 100,* and *Bruker WM-250* in δ (ppm) relative to TMS.

1. *1,2-Dihydro-6-(methylamino)-2-thioxopyrimidin-4(3*H*)-one* (**2**). In 200 ml of *N*-methylformamide, 60 g (0.42 mol) of 6-amino-1,2-dihydro-2-thioxopyrimidin-4(3*H*)-one (**1**) [28] [29] and 30 g of $MeNH_3Cl$ are heated under reflux for 2 h. A slow stream of $MeNH_2$ is bubbled through the soln. during the heating period. After 30 min, a clear soln. is obtained from which a precipitate separates later. The mixture is diluted with 300 ml of H_2O and cooled in the ice-box. The precipitate (49.9 g, 76%) is purified by reprecipitation from dil. NaOH/AcOH with charcoal or recrystallization from a large volume of H_2O: 43.6 g (66%) of yellowish crystals. M.p. 299–300° (dec.). pK_a 6.85. UV (pH 4): 253 (sh, 4.08), 273 (4.31). ^{1}H-NMR ((D_6)DMSO): 11.5 (br. *s*, NH); 11.4 (br. *s*, NH); 6.1 (br.

q, NH–C(6)); 4.7 (*s*, H–C(5)); 2.7 (*s*, CH_3N). Anal. calc. for $C_5H_7N_3OS$ (157.2): C 38.21, H 4.49, N 26.73, S 20.40; found: C 38.16, H 4.40, N 26.60, S 20.53.

2. *1,2-Dihydro-6-[(2-hydroxyethyl)amino]-2-thioxopyrimidin-4(3H)-one* (**3**). A mixture of 58 g (1 mol) of AcOH and 50 ml of EtOH is cooled with ice, and then 61 g (1 mol) of 2-aminoethanol are added slowly with stirring. The soln. is evaporated and then coevaporated twice with abs. EtOH to give a sirup of *(2-hydroxyethyl)ammonium acetate*. A mixture of 14.3 g (0.1 mol) of **1** and 80 g of (2-hydroxyethyl)ammonium acetate is heated in an oil bath to 170° for 2.5 h. The soln. is diluted with 400 ml of H_2O and cooled in the ice-box over night. The precipitate is dried at 100° to give 13.1 g of crude material which is treated again with 80 g of (2-hydroxyethyl)ammonium acetate at 170° for 3 h. After dilution with 350 ml of H_2O and cooling, 8.41 g (45%) of chromatographically pure crystals are obtained. M.p. 261° (dec.). This material is pure enough for further reactions. For analysis, 2 g of the crude material is recrystallized from 130 ml of H_2O with charcoal: 1.4 g of colourless crystals. M.p. 266–267° (dec.). pK_a 6.63. UV (pH 4): 253 (sh, 4.10), 275 (4.34). ^{1}H-NMR ((D_6)DMSO): 11.5 (br. *s*, NH); 11.3 (br. *s*, NH); 6.2 (br. *t*, NH–C(6); 4.8 (br. *s*, OH); 4.7 (*s*, H–C(5)); 3.5 (*m*, CH_2); 3.1 (*m*, CH_2). Anal. calc. for $C_6H_9N_3OS$ (187.2): C 38.49, H 4.85, N 22.44, S 17.13; found: C 38.62, H 4.99, N 22.46, S 17.02.

3. *6-Anilino-1,2-dihydro-2-thioxopyrimidin-4(3H)-one* (**4**). A mixture of 14.3 g (0.1 mol) of **1**, 13.0 g (0.1 mol) of anilinium chloride, and 18.6 g (0.2 mol) of aniline is heated in an oil bath to 170° for 7.5 h with stirring. The warm soln. is diluted with 200 ml of EtOH/H_2O 2:1 and cooled several h. The precipitate is dried at 100°: 17.4 g (78%) of colourless crystalline powder of m.p. 281–282° (dec.). The product can be recrystallized from DMF/H_2O or a large volume of MeOH to give colourless crystals. M.p. 287–288° (dec.). pK_a −1.22, 6.12. UV (pH 4.0): 279 (4.44). ^{1}H-NMR ((D_6)DMSO): 11.9 (br. *s*, NH); 11.6 (br. *s*, NH); 8.3 (*s*, NH–C(6)); 7.4 (*m*, 5 H); 5.0 (*s*, H–C(5)). Anal. calc. for $C_{10}H_9N_3OS$ (219.3): C 54.78, H 4.14, N 19.16, S 14.62; found: C 54.68, H 4.09, N 19.08, S 14.54.

4. *6-(Methylamino)-2-(methylthio)pyrimidin-4(3H)-one* (**5**). To a soln. of 5.0 g (31.8 mmol) of **2** in 100 ml of H_2O containing 2.1 g (37.5 mmol) of KOH are added dropwise with stirring 4.7 g (37 mmol) of dimethylsulfate. After 2 h, the precipitate is collected, washed with H_2O, and dried at 100°: 4.46 g (83%) of colourless crystals of m.p. 235–237°. Further purification can be achieved by reprecipitation from dil. NaOH/AcOH or by recrystallization from H_2O to give anal. pure crystals. M.p. 239–240°. UV (pH 5): 232 (4.18), 270 (3.89). ^{1}H-NMR ((D_6)DMSO): 11.2 (br. *s*, NH); 6.8 (*m*, NH–C(6)); 4.8 (s, H–C(5)); 2.7 (br. *d*, CH_3N); 2.4 (*s*, CH_3S). Anal. calc. for $C_6H_9N_3OS$ (171.2): C 42.09, H 5.30, N 24.54, S 18.73; found: C 42.12, H 5.23, N 24.38, S 18.75.

5. *6-[(2-Hydroxyethyl)amino]-2-(methylthio)pyrimidin-4(3H)-one* (**6**). To a soln. of 10.1 g (54 mmol) of **3** in 140 ml of 0.5N NaOH, 7.8 g (62 mmol) of dimethylsulfate are added dropwise with stirring. After 4 h, the precipitate is washed with H_2O and dried at 100°: 7.1 g (65%) of colourless crystals. Evaporation of the filtrate to ½ its volume and acidification by AcOH give another 2.4 g (22%). Recrystallization from H_2O yields 8.1 g (75%) of colourless crystals. M.p. 260–261°. UV (pH 13): 218 (4.60), 265 (3.96). ^{1}H-NMR ((D_6)DMSO): 11.2 (br. *s*, NH); 6.7 (*m*, NH–C(6)); 4.85 (*s*, H–C(5)); 4.6 (br. *s*, OH); 3.5 (*m*, CH_2); 3.2 (*m*, CH_2); 2.4 (*s*, CH_3S). Anal. calc. for $C_7H_{11}N_3O_2S$ (201.3): C 41.78, H 5.51, N 20.88, S 15.93; found: C 41.64, H 5.63, N 20.60, S 16.09.

6. *6-(Methylamino)-5-nitrosopyridine-2,4(1H,3H)-dione* (**7**) [30]. In 50 ml of H_2O and 4 ml of AcOH are suspended 3.0 g (19 mmol) of **2**. At 15°, a soln. of 3 g of $NaNO_2$ in 30 ml of H_2O is added dropwise within 4 h, and stirring is continued overnight. The brown-red precipitate (2.6 g) is purified by reprecipitation from dil. NaOH/AcOH to remove the insoluble sulfur: 2.35 g (73%) of red crystals. M.p. > 280° (dec.). The compound is spectroscopically and chromatographically identical with an authentic sample.

7. *1,2-Dihydro-6-(methylamino)-5-(phenylazo)-2-thioxopyrimidin-4(3H)-one* (**8**). A phenyldiazonium-salt soln. is prepared from 4.65 g (50 mmol) of aniline in 30 ml of 5N HCl by dropwise addition of 3.45 g (50 mmol) of $NaNO_2$ in 20 ml of H_2O at 0–5°. This soln. is added to a cold mixture of 7.85 g (50 mmol) of **2** and 350 ml of 0.35N NaOH with stirring. After 30 min, the mixture is warmed to r.t., and acidified with AcOH to pH 4. The orange-red precipitate is heated in 500 ml of H_2O to boiling and then filtered hot to give 8.6 g (65%) of an orange-red powder of m.p. 232–234° (dec.). Further purification can be achieved by reprecipitation from dil. NaOH/AcOH or recrystallization from AcOH with charcoal: orange-red crystals. M.p. 238–239°. UV (pH 13): 237 (4.29), 390 (4.30). Anal. calc. for $C_{11}H_{11}N_5OS$ (261.3): C 50.56, H 4.24, N 26.80; found: C 50.48, H 4.21, N 26.63.

8. *1,2-Dihydro-6-[(2-hydroxyethyl)amino]-5-(phenylazo)-2-thioxopyrimidin-4(3H)-one* (**9**). A phenyldiazonium-salt soln. prepared as in *Exper. 7* is added to 9.35 g (50 mmol) of **3** in 400 ml of 0.35N NaOH at 0–5° with stirring. After 1 h, the mixture is acidified with AcOH and heated to boiling and then the precipitate filtered off, washed, and dried: 9.27 g (67%) of orange-red crystals of m.p. 226–228° (dec.). This product is pure enough for

further reaction. An anal. pure sample is obtained by recrystallization from dil. AcOH: orange-red crystals. M.p. 228–229° (dec.). Anal. calc. for $C_{12}H_{13}N_5O_2S$ (291.3): C 49.47, H 4.50, N 24.04; found: C 49.64, H 4.44, N 23.84.

9. *5-(4-Chlorophenylazo)-1,2-dihydro-6-[(2-hydroxyethyl)amino]-2-thioxopyrimidin-4(3H)-one* (**10**). To a soln. of 3.74 g (20 mmol) of **3** in 200 ml of 0.5N NaOH, 24 ml of a 1M soln. of 4-chlorophenyldiazonium salt are added slowly at 0–5° with stirring. If the pH is dropping below 10, more NaOH is added simultaneously to keep the pH at *ca.* 10. After 1 h, the mixture is warmed to 60°, then acidified with AcOH. The red precipitate (5.9 g, 95%) is pure enough for further reactions. A pure anal. sample is obtained by silica-gel column chromatography with $CHCl_3$/MeOH 97:3→85:15: orange-red powder. M.p. 224–227° (dec.). Anal. calc. for $C_{12}H_{12}ClN_5O_2S$ (325.8): C 44.24, H 3.71, N 21.50; found: C 44.05, H 3.56, N 21.28.

10. *6-Anilino-1,2-dihydro-5-(phenylazo)-2-thioxopyrimidin-4(3H)-one* (**11**). A phenyldiazonium-chloride soln. prepared from 7.1 g (76 mmol) of aniline is added at 5° with stirring to a soln. of 13.5 g (62 mmol) of **4** in 300 ml of 1N NaOH/EtOH 1:1. After 1 h, the mixture is heated to 60° and then acidified with 5N HCl, to pH 2. On cooling, the precipitate is collected, washed with H_2O, and dried: 17.8 g (89%) of a red solid, pure enough for further reactions. A pure sample is obtained by recrystallization from AcOH with charcoal: red crystals. M.p. 249° (dec.). Anal. calc. for $C_{16}H_{13}N_5OS$ (324.4): C 59.43, H 4.05, N 21.66; found: C 59.65, H 4.06, N 21.35.

11. *6-(Methylamino)-2-(methylthio)-5-nitrosopyrimidin-4(3H)-one* (**12**). In 130 ml of 1N NaOH/H_2O 3:10, 4.13 g (24 mmol) of **5** and 2.2 g (32 mmol) of $NaNO_2$ are dissolved. Then, 5 ml of AcOH are added dropwise at r.t. The mixture is stirred for 3 h and the blue precipitate washed with H_2O and MeOH and dried at 100°: 4.5 g (93%) of a blue crystal powder of m.p. 247° (dec.). An anal. pure sample is obtained by recrystallization from a large volume of H_2O: blue crystals. M.p. 254° (dec.). Anal. calc. for $C_6H_8N_4O_2S$ (200.2): C 35.99, H 4.03, N 27.98; found: C 36.07, H 3.84, N 27.52.

12. *6-[(2-Hydroxyethyl)amino]-2-(methylthio)-5-nitrosopyrimidin-4(3H)-one* (**13**). In 7 ml of 5N NaOH and 150 ml of H_2O, 6.7 g (33 mmol) of **6** and 2.5 g (36 mmol) of $NaNO_2$ are dissolved. At r.t., 6 ml of AcOH are added dropwise with stirring. After 4 h, the blue-green precipitate is washed and dried to yield 7.3 g (85%) of a crystal powder of m.p. 201–202° (dec.). Recrystallization from MeOH gave 6.1 g (80%) of blue-green crystals. M.p. 207° (dec.). Anal. calc. for $C_7H_{10}N_4O_3S$ (230.3): C 36.52, H 4.38, N 24.33; found: C 36.56, H 4.40, N 24.31.

13. *2,8-Dihydro-8-methyl-2-thioxopteridin-4(3H)-one* (**14**). To a boiling soln. of 0.3 g of trimeric glyoxal dihydrate in 20 ml of EtOH, a soln. of 0.5 g (1.9 mmol) of **22** in 20 ml of 0.5N AcOH added dropwise. After boiling for 10 min, the mixture is cooled overnight and the precipitate washed and dried: 0.16 g (27%) of orange-red crystals. M.p. > 225° (dec.). Anal. calc. for $C_7H_6N_4OS \cdot 0.5\ H_2O$ (203.2): C 41.37, H 3.47, N 27.57, S 15.78; found: C 41.53, H 3.37, N 27.39, S 16.01.

14. *2,8-Dihydro-6,7,8-trimethyl-2-thioxopteridin-4(3H)-one* (**15**). In 20 ml of 0.1N HCl, 0.31 g (1.8 mmol) of **22** and 0.6 ml of biacetyl are dissolved. The mixture is heated to 80° for 30 min and then neutralized by ammonia. After cooling, the precipitate is collected, washed, and dried in a vacuum dessicator: 0.3 g (75%) of orange-red crystals. M.p. 250° (dec.). Anal. calc. for $C_9H_{10}N_4OS$ (222.3): C 48.63, H 4.53, N 25.21, S 14.43; found: C 48.40, H 4.60, N 25.11, S 14.63.

15. *2,8-Dihydro-8-methyl-6,7-diphenyl-2-thioxopteridin-4(3H)-one* (**16**). To a boiling soln. of 0.73 g (3.5 mmol) of benzil in 30 ml of EtOH, a soln. of 0.5 g (2.9 mmol) of **22** in 20 ml of 1N AcOH is added and the mixture refluxed for 40 min. After standing in the ice-box overnight, the precipitate is collected: 0.65 g (65%) of crude material. Reprecipitation from hot dil. NaOH/EtOH with AcOH yields 0.44 g (44%) of glissering red crystals. M.p. > 260° (dec.). Anal. calc. for $C_{19}H_{14}N_4OS$ (346.4): C 65.88, H 4.07, N 16.17, S 9.26; found: C 65.75, H 4.10, N 16.13, S 9.51.

16. *2,8-Dihydro-8-(2-hydroxyethyl)-2-thioxopteridin-4(3H)-one* (**17**). In 25 ml of conc. ammonia, 1.2 g (4.1 mmol) of **9** are dissolved by heating and then 80 ml of 20% $(NH_4)_2S$ soln. added. The mixture is refluxed for 3 h, treated with charcoal, and filtered. The filtrate is evaporated, the residue dissolved in 100 ml of 1N AcOH, the mixture filtered to separate from sulfur, and the filtrate concentrated to 20 ml. If more sulfur has precipitated, the mixture is filtered again. The soln. containing **23** is treated with 0.5 g of trimeric glyoxal dihydrate in 40 ml of H_2O/EtOH 1:3 by refluxing for 40 min. On cooling, a red precipitate separated out: 0.17 g (18%) of red crystals of m.p. 273° (dec.). Recrystallization from H_2O/EtOH gave an anal. pure sample. M.p. 276° (dec.). Anal. calc. for $C_8H_8N_4O_2S$ (224.2): C 42.85, H 3.60, N 24.99, S 14.30; found: C 43.13, H 3.70, N 25.04, S 14.08.

17. *2,8-Dihydro-8-(2-hydroxyethyl)-6,7-dimethyl-2-thioxopteridin-4(3H)-one* (**18**). To 10 ml of a soln. of **23** (see *Exper. 14*), 0.5 ml of biacetyl and 3 ml of AcOH are added. The mixture is heated to 80° for 1 h. After cooling,

the collected precipitate (0.29 g) is reprecipitated from dil. NaOH/AcOH: 0.19 g (30%) of orange-red crystals. M.p. 288° (dec.). Anal. calc. for $C_{10}H_{12}N_4O_2S$ (252.3): C 47.61, H 4.79, N 22.21, S 12.71; found: C 47.41, H 4.74, N 22.19, S 12.53.

18. *2,8-Dihydro-8-(2-hydroxyethyl)-6,7-diphenyl-2-thioxopteridin-4(3H)-one* (**19**). To 20 ml of a soln. of **23** (see *Exper. 14*), 1.05 g of benzil, 30 ml of EtOH, and 5 ml of AcOH are added. The mixture is refluxed for 30 min and, after cooling, the red precipitate collected (1.05 g) and recrystallized from DMF/H_2O 1:1: 0.58 g (27%) of red crystals. M.p. 237° (dec.). Anal. calc. for $C_{20}H_{16}N_4O_2S \cdot C_3H_7NO$ (249.5): C 61.45, H 5.16, N 15.58, S 7.13; found: C 61.24, H 5.26, N 15.58, S 6.90.

19. *2,8-Dihydro-6,7-dimethyl-8-phenyl-2-thioxopteridin-4(3H)-one* (**20**). To a hot mixture of 18 ml of EtOH, 12 ml of H_2O, and 1 ml of biacetyl, a soln. of 1.0 g (4.3 mmol) of **24** in 30 ml of AcOH/1N HCl 5:1 is added. Reflux is continued for 1 h and then the mixture cooled overnight. The precipitate is washed with EtOH and dried to yield 0.46 g (38%) of red crystals. M.p. 317° (dec.). Anal. calc. for $C_{14}H_{12}N_4OS$ (284.3): C 59.14, H 4.25, N 19.70, S 11.28; found: C 59.10, H 4.24, N 19.64, S 11.22.

20. *2,8-Dihydro-6,7,8-triphenyl-2-thioxopteridin-4(3H)-one* (**21**). In 110 ml of EtOH/1N HCl 10:1 1.01 g (4.3 mmol) of **24** and 1.2 g (5.7 mmol) of benzil are refluxed for 1 h. From the dark-red soln., a red precipitate separates which is collected after cooling, washed with EtOH, and dried: 0.68 g (38%) of red crystals. M.p. 299–303° (dec.). Recrystallization can be achieved from EtOH. Anal. calc. for $C_{24}H_{16}N_4OS$ (408.5): C 70.57, H 3.95, N 13.72; found: C 70.59, H 4.17, N 13.56.

21. *5-Amino-1,2-dihydro-6-(methylamino)-2-thioxopyrimidin-4(3H)-one* (**22**). In 120 ml of H_2O and 35 ml of 5N NaOH are suspended 6.0 g (23 mmol) of **8**. After heating to 100°, 15 g of $Na_2S_2O_4$ are added in small portions within 20 min, whereby the red solid dissolves and the colour of the soln. changes to yellow. After treatment with charcoal, filtration, and neutralization with AcOH to pH 6–7, the soln. is concentrated to a smaller volume till a precipitate starts to separate. The solid is collected after cooling: 1.15 g (29%) of slightly brownish crystals of m.p. 233–234° (dec.). The reaction filtrate is then evaporated and the residue recrystallized from 120 ml of H_2O with charcoal to give another 2.15 g (54%) of yellowish crystals of m.p. 234–235° (dec.). Both crops are chromatographically identical and pure enough for further reactions. Anal. calc. for $C_5H_8N_4OS$ (172.1): C 34.89, H 4.69, N 32.56; found: C 34.72, H 4.51, N 32.35.

22. *5-Amino-1,2-dihydro-6-[(2-hydroxyethyl)amino]-2-thioxopyrimidin-4(3H)-one* (**23**). As in *Exper. 13* with 120 ml of H_2O, 25 ml of 5N NaOH, 7.4 g (25 mmol) of **9**, and 10 g of $Na_2S_2O_4$. After treatment with charcoal, the soln. is concentrated to 100 ml. This soln. is used for the condensations without isolation of **23**.

23. *5-Amino-6-anilino-1,2-dihydro-2-thioxopyrimidin-4(3H)-one* (**24**). As in *Exper. 13* with 200 ml of H_2O, 50 ml of EtOH, 100 ml of 5N NaOH, 17.8 g (55 mmol) of **11**, and 30 g of $Na_2S_2O_4$. The hot soln. is treated with charcoal and the filtrate diluted with a hot mixture of 300 ml of H_2O and 25 ml of AcOH. After cooling, the precipitate is collected, washed with H_2O, and dried: 9.15 g (71%) of yellowish crystals. M.p. 255–260° (dec.). UV (pH 1): 283 (4.38). Anal. calc. for $C_{14}H_{10}N_4OS$ (234.2): C 51.28, H 4.30, N 23.92; found: C 51.05, H 4.18, N 23.74.

24. *5-Amino-6-(methylamino)-2-(methylthio)pyrimidin-4(3H)-one* (**25**). In an oil bath 120 ml of 20% $(NH_4)_2S$ soln. are heated to 90–100° and then 3.7 g (18.5 mmol) of **12** added in small portions with stirring. The mixture is heated under reflux for 40 min and afterwards cooled overnight in the ice-box. The precipitate is washed with H_2O and dried in a vacuum desiccator: 3.1 g (90%) of slightly yellowish crystals. M.p. 273° (dec.). UV (pH 13): 231 (4.29), 308 (3.94). Anal. calc. for $C_6H_{10}N_4OS$ (186.2): C 38.70, H 5.41, N 30.08; found: C 38.29, H 5.38, N 29.73.

25. *5-Amino-6-[(2-hydroxyethyl)amino]-2-(methylthio)pyrimidin-4(3H)-one* (**26**). As in *Exper. 16* with 200 ml of 20% $(NH_4)_2S$ soln. and 6.35 g (27.6 mmol) of **13**. The precipitate is dissolved in 120 ml of 1N AcOH to remove sulfur by filtration. The filtrate is neutralized with ammonia and the precipitate filtered off, after cooling, to yield 3.5 g (59%) of slightly yellowish crystals. M.p. 226–228° (dec.). Anal. calc. for $C_7H_{12}N_4O_2S$ (216.3): C 38.88, H 5.59, N 25.91; found: C 38.98, H 5.44, N 24.99.

26. *8-Methyl-2-(methylthio)pteridin-4(8H)-one* (**27**). To a boiling soln. of 0.4 g of trimeric glyoxal dihydrate in 15 ml of H_2O, a soln. of 0.7 g (3.76 mmol) of **25** in 15 ml of 0.5N HCl is added dropwise. After 15 min, the soln. is neutralized with ammonia to pH 8, concentrated to ½ the volume, and cooled. The precipitate (0.57 g) is recrystallized from H_2O with charcoal: 0.384 g (49%) of yellow crystals. M.p. > 270° (dec.). Anal. calc. for $C_8H_8N_4OS$ (208.2): C 46.14, H 3.87, N 26.90, S 15.40; found: C 46.11, H 3.82, N 26.99, S 15.57.

27. *6,7,8-Trimethyl-2-(methylthio)pteridin-4(8H)-one* (**28**). In 16 ml of 0.25N HCl, 0.7 g (3.76 mmol) of **25** and 0.7 ml of biacetyl are heated under reflux for 3 min. The soln. is evaporated and the residue dissolved in 20 ml of EtOH and then chilled overnight in the ice-box. The precipitate (0.7 g) is purified by recrystallization from 30 ml of H_2O with charcoal and neutralization to pH 6. On cooling, 0.6 g (67%) of yellow needles are obtained. M.p. 259–260° (dec.). Anal. calc. for $C_{10}H_{12}N_4OS$ (236.3): C 50.83, H 5.12, N 23.71, S 13.57; found: C 50.60, H 5.20, N 23.68, S 13.28.

28. *8-Methyl-2-(methylthio)-6,7-diphenylpteridin-4(8H)-one* (**29**). a) A soln. of 0.4 g (2.16 mol) of **25** and 0.46 g of benzil in 35 ml of 0.25N HCl/EtOH 4:3 is heated under reflux for 30 min. The soln. is treated with charcoal, filtered, and cooled. The precipitate is dried: 0.38 g (44%) of yellow crystals. M.p. 325–326°. Anal. calc. for $C_{20}H_{16}N_4OS \cdot HCl$ (396.9): C 60.52, H 4.32, N 14.12, S 8.08, Cl 8.93; found: C 60.61, H 4.40, N 14.17, S 8.10, Cl 9.19.

b) The hot reaction soln. is neutralized with ammonia to pH 7 and cooled. The precipitate is recrystallized from EtOH: 0.42 g (51%) of yellow crystals. M.p. 249–250° (dec.). Anal. calc. for $C_{20}H_{16}N_4OS \cdot H_2O$ (378.4): C 63.47, H 4.79, N 14.80, S 8.47; found: C 63.56, H 4.82, N 14.80, S 8.12.

29. *8-(2-Hydroxyethyl)-2-(methylthio)pteridin-4(8H)-one* (**30**). To a soln. of 1.2 g of trimeric glyoxal dihydrate in 15 ml of H_2O, a soln. of 1.05 g (4.85 mmol) of **26** in 20 ml of 0.25N HCl is added dropwise under reflux. The soln. is treated with charcoal and the filtrate neutralized with ammonia and cooled. The precipitate is collected: 0.76 g (66%) of yellow crystals. M.p. > 235° (dec.). Anal. calc. for $C_9H_{10}N_4O_2S$ (238.3): C 45.37, H 4.23, N 23.51, S 13.46; found: C 45.30, H 4.23, N 23.25, S 13.31.

30. *8-(2-Hydroxyethyl)-6,7-dimethyl-2-(methylthio)pteridin-4(8H)-one* (**31**). To a soln. of 1 ml of biacetyl in 13 ml of H_2O/EtOH 10:3 heated to 80° in an oil bath, 1.0 g (4.63 mmol) of **26** in 20 ml of 0.25N HCl is added. After heating to 80° for 15 min, the soln. is treated with charcoal and the filtrate neutralized with ammonia and cooled. The precipitate is reprecipitated from dil. HCl/dil. ammonia: 0.73 g (59%) of yellow crystals. M.p. 229° (dec.). Anal. calc. for $C_{11}H_{14}N_4O_2S$ (266.3): C 49.61, H 5.30, N 21.04, S 12.04; found: C 49.37, H 5.37, N 20.88, S 12.22.

31. *8-(2-Hydroxyethyl)-2-(methylthio)-6,7-diphenylpteridin-4(8H)-one* (**32**). To a soln. of 1.05 g of benzil in 15 ml of EtOH, a soln. of 1.0 g (4.63 mmol) of **26** in 25 ml of 0.2N HCl is added under reflux. The mixture is refluxed for 40 min, then treated with charcoal and the filtrate neutralized with ammonia and cooled. The yellow solid (0.9 g) is treated with Et_2O to remove excess of benzil and the residue recrystallized from EtOH/H_2O: 0.23 g (13%) of yellow crystals. M.p. 255–257° (dec.). Anal. calc. for $C_{21}H_{18}N_4O_2S \cdot H_2O$ (408.5): C 61.75, H 4.94, N 13.72, S 7.85; found: C 61.42, H 4.75, N 13.59, S 7.60.

32. *1,2-Dihydro-8-(2-hydroxyethyl)-6-methyl-2-thioxopteridine-4,7(3H,8H)-dione* (**33**). In 8 ml of 20% $(NH_4)_2S$ soln., 0.5 g (1.54 mmol) of **10** are heated for 1 h to 120° in a sealed tube and then evaporated. The residue (containing **23**) is dissolved in 15 ml of 0.1N HCl, the sulfur filtered off, and the filtrate treated with 0.7 ml of ethyl pyruvate under reflux for 45 min. The precipitate is recrystallized from H_2O: 0.18 g (46%) of yellow crystals. M.p. > 300°. pK_a 2.26, 12.36. UV (pH 0): 215 (4.26), 271 (3.96), 304 (sh, 4.02), 333 (sh, 4.29), 345 (4.34), 355 (sh, 4.27). UV (pH 7.0): 223 (4.30), 228 (sh, 4.29), 255 (4.11), 317 (sh, 4.09), 356 (4.30). Anal. calc. for $C_9H_{10}N_4O_3S$ (254.3): C 42.51, H 3.96, N 22.04, S 12.61; found: C 42.35, H 3.85, N 21.88, S 12.75.

33. *1,2-Dihydro-2-thioxo-1,8-ethanopteridine-4,6,7(3H,5H,8H)-trione* (**34**). In 12 ml of 20% $(NH_4)_2S$ soln., 0.8 g (2.75 mmol) of **9** are heated under reflux for 1 h in a sealed vessel. After evaporation, the precipitate (containing **23**) is dissolved in 20 ml of 1N HCl, the sulfur filtered off, and the filtrate evaporated. To the residue in 5 ml of DMF, 1.5 g (12 mmol) of oxalic acid dihydrate is added and heated under reflux for 1 h. The yellow precipitate is washed with H_2O and recrystallized from HCOOH: 0.26 g (40%) of a yellow solid. M.p. > 350°. pK_a 6.35, 9.38. UV (pH 2.0): 215 (4.26), 236 (sh, 4.04), 280 (sh, 4.07), 309 (4.28), 345 (sh, 3.91). UV (pH 7.8): 215 (4.26), 241 (4.08), 288 (sh, 3.99), 328 (4.23), 340 (sh, 4.20), 358 (sh, 4.03). UV (pH 12): 216 (4.24), 255 (4.19), 292 (4.02), 303 (4.02), 339 (sh, 4.14), 348 (4.16), 363 (sh, 4.02). Anal. calc. for $C_8H_6N_4O_3S$ (238.2): C 40.33, H 2.54, N 23.52; found: C 39.77, H 2.75, N 23.41.

34. *2,3,4,5-Tetrahydro-8-(oxaloamino)-5-thioxoimidazo[1,2-c]pyrimidin-7(6H)-one* (**35**). In 20 ml of hot 1N NaOH, 0.7 g (2.94 mmol) of **34** are dissolved, and after 5 min, the soln. is acidified with 5N HCl to pH 0–1 and cooled. The precipitate is recrystallized from H_2O: 0.08 g (10%) of yellowish crystals. M.p. > 300°. pK_a 9.70. UV (pH 1): 217 (4.37), 252 (4.11), 278 (4.26). Anal. calc. for $C_8H_8N_4O_4S \cdot 0.5\ H_2O$ (265.3): C 36.23, H 3.42, N 21.12; found: C 36.40, H 3.16, N 21.26.

REFERENCES

[1] W. Pfleiderer, *Tetrahedron* **1988,** *44,* 3373.
[2] W. Pfleiderer, G. Nübel, *Chem. Ber.* **1960,** *93,* 1406.
[3] R.M. Cresswell, H.C.S. Wood, *J. Chem. Soc.* **1960,** 4768.
[4] C.H. Winestock, T. Aogaichi, G.W.E. Plaut, *J. Biol. Chem.* **1963,** *238,* 2866.
[5] W. Pfleiderer, J.W. Bunting, D.D. Perrin, G. Nübel, *Chem. Ber.* **1966,** *99,* 3503.
[6] V.J. Ram, W.R. Knappe, W. Pfleiderer, *Liebigs Ann. Chem.* **1982,** 762.
[7] E. Uhlman, W. Pfleiderer, *Heterocycles* **1981,** *15,* 437.
[8] T. Masuda, T. Kishi, M. Asai, *Chem. Pharm. Bull.* **1958,** *6,* 291.
[9] G.W.E. Plaut, C.M. Smith, W.L. Alworth, *Annu. Rev. Biochem.* **1974,** *43,* 899.
[10] G.M. Brown, J.H. Williamson, *Adv. Enzymol.* **1982,** *53,* 345.
[11] W. Hübsch, W. Pfleiderer, in 'Chemistry and Biology of Pteridines', Ed. J.A. Blair, W. de Gruyter, Berlin, 1983, p.499.
[12] W. Hübsch, W. Pfleiderer, in 'Biochemical and Clinical Aspects of Pteridines', Eds. W. Pfleiderer, H. Wachter, and J.A. Blair, W. de Gruyter, Berlin, 1987, Vol. 5, p. 23.
[13] H.J. Schneider, W. Pfleiderer, *Chem. Ber.* **1974,** *107,* 3377.
[14] I.W. Southon, W. Pfleiderer, *Chem. Ber.* **1978,** *111,* 971.
[15] Z. Kazimierczuk, W. Pfleiderer, *Chem. Ber.* **1979,** *112,* 1499.
[16] A. Heckel, W. Pfleiderer, *Helv. Chim. Acta* **1986,** *69,* 704, 708, 1088, 1095.
[17] M. Bartke, Ph.D. Dissertation, University of Konstanz, 1982.
[18] M. Bartke, W. Pfleiderer, 'Pteridines', in preparation.
[19] C.W. Whitehead, J.J. Traverso, *J. Am. Chem. Soc.* **1960,** *82,* 3971.
[20] W.V. Curran, R.B. Angier, *J. Org. Chem.* **1963,** *28,* 2672.
[21] S. Gabriel, J. Colman, *Ber. Dtsch. Chem. Ges.* **1901,** *34,* 1234.
[22] O. Isay, *Ber. Dtsch. Chem. Ges.* **1906,** *39,* 205.
[23] W. Pfleiderer, in 'Comprehensive Heterocyclic Chemistry', Ed. A.R. Katritzky and C.W. Rees, Pergamon Press, Oxford, 1984, Vol. 3, Part 2B, p. 263.
[24] D.J. Brown, F.S. Mason, *J. Chem. Soc.* **1956,** 3443.
[25] W.E. Fidler, H.C.S. Wood, *J. Chem. Soc.* **1956,** 3311.
[26] N.W. Jacobsen, *J. Chem. Soc.* **1966,** 1065.
[27] W. Pfleiderer, *Chem. Ber.* **1957,** *90,* 2582.
[28] W. Traube, L. Winter, *Liebigs Ann. Chem.* **1904,** *64,* 331.
[29] E.C. Taylor, C.C. Cheng, *J. Org. Chem.* **1960,** *25,* 1481.
[30] H. Bredereck, G. Kupsch, H. Wieland, *Chem. Ber.* **1959,** *92,* 583; W. Pfleiderer, G. Nübel, *Liebigs Ann. Chem.* **1960,** *631,* 168.