5. *Pteridine Studies. Part XXVIII.*[1] *Some 6- and 7-Substituted Pteridines.*

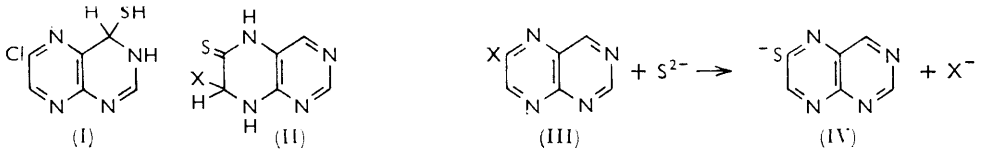
By Adrien Albert and Jim Clark.

The hitherto inaccessible compound 6-mercaptopteridine has been prepared from 6-chloropteridine under new conditions which avoid the addition reactions that frustrated earlier attempts. In aqueous solution, the neutral species and the cation of 6-mercaptopteridine are largely covalently hydrated across the 7,8-bond, but the anion is anhydrous.

The chlorine atoms of 6,7-dichloropteridine were replaced either stepwise or simultaneously to give a variety of 6,7-disubstituted pteridines. Nucleophilic reagents preferentially attacked the 7-chlorine atom. In acid conditions 6,7-diamino- and 6,7-dimercapto-pteridine were readily hydrolysed, stepwise, to 6,7-dihydroxypteridine.

The previous Paper [1] in this series showed that 6- and 7-chloropteridine react with nucleophiles in either of two ways: (i) normal nucleophilic substitution and (ii) rapid, reversible addition across the 3,4-bond. However, 6-hydroxypteridine and some of its derivatives undergo addition reactions at the 7,8-bond.[2,3]

Earlier attempts to prepare 6-mercaptopteridine from 6-chloropteridine by the action of bisulphide anion (SH^-) or thiourea or from 6-hydroxypteridine (with phosphorus pentasulphide), under a wide range of conditions, invariably led to more complex products.[4,5] Formation of these, often highly coloured, materials can now be attributed to adducts such as (I) or (II; X = SH) which can participate in further condensation or oxidation reactions. The difficulties were overcome by treating 6-chloropteridine (III; X = Cl)



(I) (II) (III) (IV)

with sulphide anion (as Na_2S) in aqueous ethanol. As was expected,[1] these conditions inhibit formation of an adduct with the chloro-compound, so that the reaction led directly to the anion of 6-mercaptopteridine (cf. IV). The wisdom of proceeding directly to this ionic species was indicated by experience with 6-hydroxypteridine, the anion of which is anhydrous [2] and has a reduced tendency to adduct formation. The anion (IV) was preferably converted into the stable, covalently monohydrated neutral species (II; X = OH) by way of the cation, since simple neutralisation of the sodium salt caused a trace of contamination through side reactions.

Ultraviolet spectra of 6-mercaptopteridine (see Table) reveal the large bathochromic shift on anion formation which is characteristic of compounds which lose a molecule of water during this ionisation.[2] Because the pK_a values and spectra of the various species closely parallel those of 6-hydroxypteridine it is concluded that this water molecule is added to the 7,8-bond in cation and neutral species. As expected,[6] the mercapto-compound is a slightly stronger acid and weaker base than the hydroxy-compound and absorbs at somewhat longer wavelengths.

The tendency for 6-mercaptopteridine to form adducts had been encountered in the following earlier attempt to prepare this compound. 6-Benzylthiopteridine [1] (III; X = S·CH_2Ph) was treated with sodium hydrogen sulphide under mild conditions to yield a

[1] Part XXVII, Clark, *J.*, 1964, 4920.
[2] Brown and Mason, *J.*, 1956, 3443.
[3] Albert and Reich, *J.*, 1961, 127.
[4] Albert, Brown, and Cheeseman, *J.*, 1952, 1620.
[5] Albert, Brown, and Wood, *J.*, 1954, 3832; Clark, unpublished observations.
[6] Albert and Barlin, *J.*, 1959, 2383.

Physical properties of pteridines.

Pteridine	Ionisation (H_2O, 20°) [a] pK_a and spread	Anal λ (mμ)	Spectroscopy in water [i] Species [b]	$\lambda_{max.}$ (mμ)	log ε	pH
6-Mercapto	3·06 ± 0·02	260	+	230, *242*, 332	3·91, *3·83*, 4·28	1·0
	5·78 ± 0·06 [c]	330	0	242, 331	3·87, 4·24	4·4
			−	237, 299, 411	4·03, 4·17, 3·83	11·0
6-Benzylthio-7,8-dihydro-6-mercapto				333 [d]	4·17	1·0
				236, 331 [d]	*4·08*, 4·22	4·4
				237, 299, 411 [e]	4·20, 4·16, 3·80	11·0
6-Methylthio	3·27 ± 0·03	300	+	Unstable—see text		1·3
			0	235, 274, 365	4·05, 4·08, 3·86	7·0
6,7-Diamino	−0·35 ± 0·05	264	++	219, 244, *324*, 337, 353	4·41, 4·00, *4·17*, 4·35, 4·28	−2·4 [f]
	3·54 ± 0·03	264	+	228, 258, 342, 352	4·38, 4·10, 4·25, 4·25	1·5
			0	221, 242, *268*, *278*, *327*, 337, 352	4·45, 4·08, *3·59*, *3·56*, *4·18*, 4·27, 4·13	7·0
6-Amino-7-hydroxy			+	212, *230*, *281*, *301*, 310, *325*	4·41, *4·02*, *4·00*, *4·18*, 4·20, *3·86*	−2·4
6,7-Dihydroxy	0·90 ± 0·04	235	+	222, *281*, 306	4·22, *3·88*, 4·16	−1·5 [f]
6-Hydroxy-7-mercapto [h]	0·98 ± 0·04	391	+	*227*, 270, *352*, 363	*4·12*, 3·62, *4·32*, 4·39	−1·5 [f]
	5·95 ± 0·05	383	0	257, *340*, 352, 369, 388	3·52, *4·09*, 4·28, 4·31, 4·05	3·5
	9·62 ± 0·04	250	—	*232*, 266, 375, *390*	*4·08*, 3·61, 4·35, *4·28*	7·8
			−−	236, 270, *362*, 377, 393	4·28, 3·74, *4·17*, 4·34, 4·29	12·0
7-Hydroxy-6-mercapto	0·76 ± 0·03	245	+	235, *260*, 327, *355*, 367	4·15, *3·78*, 3·98, *4·17*, 4·21	−1·5 [f]
	5·59 ± 0·03	258	0	246, 292, 354, 371	3·70, 3·66, 4·23, 4·27	3·2
	9·28 ± 0·03	240	—	258, 308, 367	3·89, 3·70, 4·22	7·5
			−−	218, 238, *261*, 311, 363	4·41, 4·26, *3·88*, 3·80, 4·24	12·0
6,7-Dimercapto	0·74 ± 0·05	286	+	277, 368, *382*, *410*	4·19, 4·10, *4·07*, *4·00*	−1·5 [f]
	5·16 ± 0·05	315	0	256, *290*, *378*, 394, 414, *433*	4·26, *3·81*, *4·07*, 4·14, 4·14, *3·99*	3·0
	8·01 ± 0·05	274	—	260, 298, *380*, *400*, 412, *440*	4·27, 3·91, *4·05*, *4·13*, 4·15, *3·98*	6·6
			−−	247, 271, *302*, *396*, 409, *427*	4·22, 4·32, *3·90*, *4·18*, 4·22, *4·10*	12·0

[a] Determined spectroscopically at 20° with 0·01M-buffers (Perrin, *Austral. J. Chem.*, 1963, **16**, 572). [b] ++ Di-cation, + cation, 0 neutral species, − anion, −− dianion. [c] Equilibrium pK_a. [d] Benzylthio-group probably partly or wholly exchanged for OH by the time measurement was made. [e] Toluene-α-thiol lost to give anion of 6-mercaptopteridine. [f] H_0, hydrochloric acid (Paul and Long, *Chem. Rev.*, 1957, **57**, 12. [g] From ref. 4. [h] Stock solutions for pH and spectroscopic measurements made up in 0·1N-potassium hydroxide; each measurement was made immediately after a portion had been neutralised and buffered. [i] Shoulders and inflexions in italics.

product whose empirical formula, $C_{13}H_{12}N_4S_2$, suggested that H_2S had been added to the starting material. However, ultraviolet spectra at various pH values indicated that replacement of the benzylthio-group had been achieved and that the product was a derivative of 6-mercaptopteridine. Apparently the ejected group had added to the primary product; in agreement with this interpretation the yield of adduct (II; X = S·CH_2Ph) was increased by adding toluene-α-thiol to the reaction mixture. The proposed structure, 7-benzylthio-7,8-dihydro-6-mercaptopteridine, was later confirmed by preparing the adduct from 6-mercaptopteridine and toluene-α-thiol. The reversibility of the thiol addition is clearly illustrated by the spectral data (see Table) and it was also demonstrated by the isolation of dibenzyl disulphide from an aerated alkaline solution of the adduct.

6-Benzylthiopteridine, on catalytic reduction, gave a dihydro-derivative, whereas reduction by sodium in liquid ammonia gave a mixture containing some 6-mercaptopteridine which could not be isolated conveniently.

Methylation of 6-mercaptopteridine yielded 6-methylthiopteridine (III; X = SMe), the only monomethylthiopteridine not previously synthesised.[7] The structure was confirmed

[7] Brown, Ciba Symposium on the Chemistry and Biology of Pteridines, Churchill, London, 1954, p. 63.

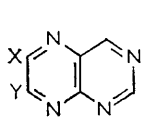
by the ready formation of methanethiol and 6-hydroxypteridine on treatment with dilute acid. At 20°, the methylthio-compound had a half-life of about 20 minutes at pH 1·3 compared with about 14 hours at pH 0·3 for 6-mercaptopteridine, which was also converted into 6-hydroxypteridine by acid (figures determined spectrophotometrically).

Disubstituted Pteridines.—The preparation of 6,7-dichloropteridine [8] has made possible the synthesis of new 6,7-disubstituted pteridines. Treatment of the dichloro-compound with ethanolic ammonia at 155° provided a route to 6,7-diaminopteridine (V; X = Y = NH_2), which could not be prepared from 4,5-diaminopyrimidine.[9] The dichloro-compound and sodium hydrogen sulphide gave 6,7-dimercaptopteridine (VI; X = Y = S).

The chlorine atoms were also replaced stepwise. Reaction with cold aqueous ammonia gave 7-amino-6-chloropteridine (V; X = Cl, Y = NH_2), the structure of which was proved by mild alkaline hydrolysis to the known 7-amino-6-hydroxypteridine.[10]

Treatment of 6,7-dichloropteridine with cold sodium carbonate gave 6-chloro-7-hydroxypteridine (V; X = Cl, Y = OH), the structure of which was assigned when it gave an aminohydroxypteridine (V; X = NH_2, Y = OH) different from that described above.

Sodium hydrogen sulphide also reacted preferentially with the 7-chlorine atom. Thus treatment of 6,7-dichloropteridine with this reagent, followed by sodium hydroxide, gave 6-hydroxy-7-mercaptopteridine (VI; X = O, Y = S). The structure followed from the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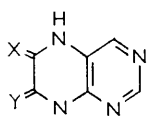
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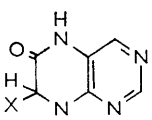
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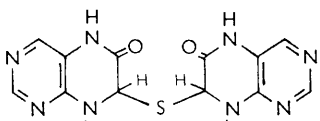
(VIII)

fact that 6-chloro-7-hydroxypteridine and sodium hydrogen sulphide gave a different hydroxymercaptopteridine (VI; X = S, Y = O) and also from the following unambiguous synthesis in which advantage was taken of the tendency of 6-hydroxypteridine to undergo addition.

Hydrogen sulphide was slowly passed through a solution of 6-hydroxypteridine in the presence of air. Equilibria under these conditions involve the hydrate (VII; X = OH), the hydrogen sulphide adduct (VII; X = SH), and apparently the dipteridinyl sulphide (VIII). Aerial oxidation of the thiol (VII; X = SH) gradually gave 6-hydroxy-7-mercaptopteridine. Formation of the dipteridinyl sulphide (VIII), which was isolated under slightly different conditions, is presumably analogous to that of the corresponding dipteridinylamine from 6-hydroxypteridine and ammonia, as reported previously.[10]

6-Hydroxy-7-mercapto- and 7-hydroxy-6-mercapto-pteridine were isolated also after treatment of 6,7-dihydroxypteridine with phosphorus pentasulphide. This is the shortest route to these compounds but instability under conditions necessary for their isolation causes low yields. 6,7-Dimercaptopteridine could not be isolated satisfactorily from similar reactions.

6,7-Dimercaptopteridine and 6-hydroxy-7-mercaptopteridine were unstable in boiling water, slightly unstable at pH 0 or 6·8 (cold), but more stable at pH 13 (cold). All the mercapto-compounds mentioned were readily converted into 6,7-dihydroxypteridine by boiling dilute hydrochloric acid. 6,7-Diaminopteridine, also unstable to acid, was shown spectroscopically to give exclusively 6-amino-7-hydroxypteridine [time for half conversion ($t_{0·5}$) ~28 minutes at H_0 −2·4 and 20°] which, in turn slowly gave 6,7-dihydroxypteridine ($t_{0·5}$, 20°, ~4 days). 7-Amino-6-hydroxypteridine is as readily hydrolysed to 6,7-dihydroxypteridine.[10]

[8] Albert and Clark, *J.*, 1964, 1666.
[9] Albert, Lister, and Pedersen, *J.*, 1956, 4621.
[10] Albert, *J.*, 1955, 2690.

Experimental

Microanalyses were carried out by Dr. J. E. Fildes and her staff.

6-*Mercaptopteridine.*—To a stirred solution of 6-chloropteridine (1·34 g.) in ethanol (80 ml.) at 35° was added during ½ hr., without further heating, a solution of sodium sulphide nonahydrate (2 g.) in water (12 ml.). The mixture was kept at −20° for 3 days and sodium 6-mercaptopteridine dihydrate (1·58 g.) was filtered off. This salt was dissolved in water (15 ml.), and N-hydrochloric acid (22 ml.) added. After filtration, the pH of the solution was adjusted to 3·5 with potassium acetate; 6-*mercaptopteridine* (84%) separated as a bright yellow solid. This was reprecipitated from N-hydrochloric acid by potassium acetate three times, to give yellow crystals, >160° (Found: C, 39·5; H, 3·5; N, 30·4; S, 17·4. $C_6H_4N_4S,H_2O$ requires C, 39·6; H, 3·3; N, 30·95; S, 17·6%).

The crude sodium salt (above) contained sodium chloride but could be purified as follows. The salt (0·05 g.) was vigorously shaken with ethanol (3·5 ml.) and filtered. The filtrate was kept at −20° for 2 days and sodium 6-*mercaptopteridine dihydrate* (0·024 g.) was collected on a chilled filter as red needles and dried *in vacuo* at 65°; it had m. p. >250° (Found: C, 32·5; H, 3·3; N, 25·45; S, 14·5. $C_6H_3N_4NaS,2H_2O$ requires C, 32·4; H, 3·2; N, 25·2; S, 14·4%).

7-*Benzylthio*-7,8-*dihydro*-6-*mercaptopteridine.*—(*a*) Sodium 6-mercaptopteridine dihydrate (0·088 g.) was shaken with ethanol (20 ml.) and the solution set aside for 3 hr. before being filtered. The filtrate was treated with toluene-α-thiol (0·4 ml.) and glacial acetic acid (5 drops) and refrigerated for 1 hr. 7-*Benzylthio*-7,8-*dihydro*-6-*mercaptopteridine* (79%) was filtered off as nearly white crystals which gradually decomposed above 200° (Found: C, 54·1; H, 4·3; N, 19·5; S, 22·1. $C_{13}H_{12}N_4S_2$ requires C, 54·1; H, 4·2; N, 19·4; S, 22·2%).

(*b*) A solution of sodium (0·075 g.) in ethanol (10 ml.) was saturated with hydrogen sulphide, and a solution of 6-benzylthiopteridine [1] (0·5 g.) in hot ethanol (10 ml.) was added. After ½ min., toluene-α-thiol (0·24 ml.) in ethanol (1 ml.) was added and the mixture refrigerated. 7-Benzylthio-7,8-dihydro-6-mercaptopteridine (0·36 g.) was filtered off and shown by comparison of infrared spectra to be identical with that prepared by method (*a*).

6-*Benzylthio*-x,y-*dihydropteridine.*—6-Benzylthiopteridine [1] (1 g.), ethanol (200 ml.), and 5% palladised charcoal were shaken with hydrogen at atmospheric pressure and 20° for 2½ hr. The mixture was heated to 80° and filtered. The volume of the filtrate was reduced to 15 ml. and 6-*benzylthio*-xy-*dihydropteridine* (0·42 g.) separated as a solid which crystallised from dioxan as needles, m. p. 195—198° (decomp.) (Found: C, 61·1; H, 4·6; N, 21·4; S, 12·8. $C_{13}H_{12}N_4S$ requires C, 60·9; H, 4·7; N, 21·9; S, 12·5%).

6-*Methylthiopteridine.*—Sodium 6-mercaptopteridine dihydrate (0·364 g.), water (5 ml.), 0·1N-sodium hydroxide (3 drops), and methyl iodide (0·2 ml.) were shaken for 30 min. A solid was filtered off and combined with a little more material obtained by benzene extraction of the filtrate. 6-*Methylthiopteridine* (77%) crystallised from ethanol as golden yellow plates, m. p. 163° (Found: C, 46·9; H, 3·35; S, 17·9. $C_7H_6N_4S$ requires C, 47·2; H, 3·4; S, 18·0%).

6,7-*Diaminopteridine.*—6,7-Dichloropteridine (1 g.) and ethanolic ammonia (20 ml. containing 0·8 g. of NH_3) were heated in a sealed tube at 155° for 2 hr. A yellow solid (0·92 g.) was filtered off and crystallised from water (2000 parts), to yield 6,7-*diaminopteridine* as flocculent needles (46%), m. p. >250° (Found: C, 44·2; H, 3·7; N, 51·8. $C_6H_6N_6$ requires C, 44·4; H, 3·7; N, 51·8%).

7-*Amino*-6-*chloropteridine.*—6,7-Dichloropteridine (0·2 g.) was added to aqueous ammonia (10 ml.; *d* 0·91) with stirring. After ½ hr. a pale-cream solid (0·16 g.) was filtered off and crystallised from γ-butyrolactone, to yield 7-*amino*-6-*chloropteridine* (71%) as off-white plates. The substance recrystallised from water (charcoal) as needles, m. p. >250° (Found: C, 39·2; H, 2·3; N, 38·3. $C_6H_4ClN_5$ requires C, 39·7; H, 2·2; N, 38·6%).

7-*Amino*-6-*hydroxypteridine.*—7-Amino-6-chloropteridine (0·1 g.), sodium carbonate (0·15 g.), and water (5 ml.) were heated under reflux for 1 hr. The solution was adjusted to pH 5·5 with citric acid and sulphuric acid and heated to the b. p.; 7-amino-6-hydroxypteridine (56%) was then filtered off; this was shown to be identical with an authentic specimen [10] by comparison of infrared spectra and paper chromatography in two solvent systems.

6-*Chloro*-7-*hydroxypteridine.*—Finely ground 6,7-dichloropteridine (0·465 g.) was shaken with 2N-sodium carbonate (10 ml.) for 1 hr. A trace of insoluble matter was filtered off and the pH value of the solution adjusted to 3·5 with citric acid and sulphuric acid. 6-*Chloro*-7-*hydroxypteridine* separated as pale yellow plates (67%) which gave one spot on paper

chromatography. Crystallisation from water gave nearly colourless plates, m. p. 232° (decomp.) (Found: C, 39·3; H, 1·7; N, 30·75. $C_6H_3ClN_4O$ requires C, 39·5; H, 1·7; N, 30·7%).

6-*Amino*-7-*hydroxypteridine*.—6-Chloro-7-hydroxypteridine (0·1 g.) and ethanolic ammonia (5 ml. containing 0·33 g. of NH_3) were heated under reflux for 1½ hr. During this time further 5-ml. portions of ethanolic ammonia were added, after ½ hr. and 1 hr., respectively. The cooled filtered mixture gave 6-*amino*-7-*hydroxypteridine* (0·044 g.) which was purified by reprecipitation from N-hydrochloric acid as a white solid, m. p. >250° (Found: C, 43·9; H, 3·2; N, 42·5. $C_6H_5N_5O$ requires C, 44·15; H, 3·1; N, 42·9%). The original filtrate was evaporated to dryness and the residue crystallised from water to yield unchanged 6-chloro-7-hydroxypteridine (0·013 g.).

7-*Hydroxy*-6-*mercaptopteridine*.—(*a*) Finely ground 6,7-dichloropteridine (0·45 g.) was shaken with 2N-sodium carbonate (20 ml.) for 1 hr. A trace of insoluble matter was filtered off, and the solution was saturated with hydrogen sulphide and set aside for 3 hr. The solution, adjusted to pH 4·5 with citric and sulphuric acid, deposited an orange solid (0·3 g.), which was shown by paper chromatography to be free from 6-hydroxy-7-mercaptopteridine. Crystallisation from water gave 7-*hydroxy*-6-*mercaptopteridine* (0·18 g.) as copper-coloured needles, m. p. >250° (Found: C, 40·0; H, 2·2; N, 31·1; S, 18·0. $C_6H_4N_4OS$ requires C, 40·0; H, 2·2; N, 31·1; S, 17·8%).

(*b*) See phosphorus pentasulphide method, below.

6-*Hydroxy*-7-*mercaptopteridine*.—(*a*) 0·1N-Sodium hydroxide (10 ml.), saturated with hydrogen sulphide, was added during 10 min. to a well-stirred solution of 6,7-dichloropteridine (0·2 g.) in ethanol (10 ml.). After a further 10 min., the ethanol was removed under reduced pressure and 2N-sodium hydroxide (10 ml.) was added. The mixture was heated on the steam-bath for 20 min.; after cooling, the pH was adjusted to 2·5 with sulphuric acid. A red-brown solid was filtered off and crystallised from dimethylformamide, to yield 6-*hydroxy*-7-*mercaptopteridine* (0·1 g.) as bronze plates containing solvent of crystallisation which was lost only slowly at 130°. A specimen was crystallised from water (2000 parts) with a minimum of heating (large loss) as an orange-brown *monohydrate* (Found: C, 36·4; H, 3·1; N, 28·3. $C_6H_4N_4OS,H_2O$ requires C, 36·4; H, 3·05; N, 28·3%) which gave a reddish anhydrous *compound* on drying at 130° (Found: C, 40·4; H, 2·4; N, 31·0. $C_6H_4N_4OS$ requires C, 40·0; H, 2·2; N, 31·1%). The anhydrous material, monohydrate, and material from dimethylformamide had different infrared spectra (Nujol mulls).

(*b*) A slow stream of hydrogen sulphide was passed through a solution of 6-hydroxypteridine hydrate [10] (50 mg.) in 0·1N-hydrochloric acid (35 ml.) contained in an open flask. A variable quantity of 6-hydroxy-7-mercaptopteridine monohydrate was gradually deposited (30—70% after 2 days). The material was shown by comparison of infrared spectra of anhydrous and hydrated forms and by paper chromatography to be identical with that prepared as described above. The filtrate from the preparation was shown, by paper chromatography in three different solvent systems, to contain 6,7-dihydroxypteridine.

(*c*) See phosphorus pentasulphide method, below.

6,7-*Dimercaptopteridine*.—6,7-Dichloropteridine (0·5 g.) was added to N-sodium hydroxide (15 ml.) which had previously been saturated with hydrogen sulphide and cooled to 10°. The mixture was stirred for 1 hr. and kept for 48 hr. The solution, adjusted to pH 3, deposited a solid which, on repeated precipitation from sodium hydroxide solution, gave 6,7-*dimercaptopteridine* (0·42 g.) as a brown hemihydrate, m. p. >250°, after drying at 120° (Found: C, 34·6; H, 2·6; N, 27·1; S, 31·6. $C_6H_4N_4S_2,\frac{1}{2}H_2O$ requires C, 35·1; H, 2·5; N, 27·3; S, 31·2%).

Bis-(7,8-*dihydro*-6-*hydroxy*-7-*pteridinyl*) *Sulphide*.—A solution of 6-hydroxypteridine hydrate (0·83 g.) in 0·5N-potassium hydroxide (20 ml.) was added to a solution of sodium sulphide nonahydrate (1·3 g.) in water (3 ml.), and the mixture was filtered. The solution, adjusted to pH 5 by the dropwise addition of 5N-sulphuric acid, deposited *bis*-(7,8-*dihydro*-6-*hydroxy*-7-*pteridinyl*) *sulphide* (0·85 g.) as a salmon-pink solid, m. p. >250° (Found: C, 43·2; H, 3·3; S, 9·2. $C_{12}H_{10}N_8O_2S$ requires C 43·6; H, 3·1; S, 9·7%).

Treatment of 6,7-*Dihydroxypteridine with Phosphorus Pentasulphide*.—6,7-Dihydroxypteridine (1 g.), phosphorus pentasulphide (3·0 g.), and dried pyridine (75 ml.) were stirred under nitrogen at 100° (bath) for 2 hr. The solvent was removed under reduced pressure and the residue treated with water (50 ml.) at 90° for 10 min. The cooled, filtered mixture gave a solid which was boiled with water (100 ml.) and filtered hot, to yield a further solid (*a*) (0·2 g.) and a solution

(*b*). Product (*a*) crystallised from dimethylformamide as bronze-like plates (0·09 g.) identical with 6-hydroxy-7-mercaptopteridine described above.

On cooling, solution (*b*) deposited a brown solid (0·45 g.) which was stirred with N-hydrochloric acid (200 ml.) for 15 min. and filtered. The refrigerated solution deposited crystals (0·23 g.) which recrystallised from water as needles with a copper lustre (0·122 g.), identical with 7-hydroxy-6-mercaptopteridine described above.

Hydrolysis of Mercapto-derivatives.—7-Hydroxy-6-mercaptopteridine (0·05 g.) and N-hydrochloric acid (2 ml.) were heated under reflux for 1 hr. The mixture, when cooled and filtered, deposited a residue which crystallised from water (charcoal) as plates (0·025 g.), which when dried at 50°/760 mm. were shown, by infrared spectroscopy, to be identical with authentic 6,7-dihydroxypteridine monohydrate. A different infrared spectrum, obtained from material dried at 130°, was identical with that of authentic anhydrous 6,7-dihydroxypteridine; the identity was confirmed by paper chromatography in four solvents and by ultraviolet spectroscopy. 6,7-*Dihydroxypteridine monohydrate*, which has not been reported previously, loses water only slowly at 80° (Found: C, 39·7; H, 3·4; N, 30·7. $C_6H_4N_4O_2$ requires C, 39·6; H, 3·3; N, 30·8%). Hydrolysis of 6-hydroxy-7-mercapto- and 6,7-dimercapto-pteridine also gave 6,7-dihydroxypteridine under these conditions.

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