11. *Pteridine Studies. Part IV.* 4 : 6- and 4 : 7-Dihydroxypteridine.*

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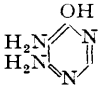
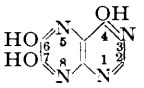
4 : 6-Dihydroxypteridine has been prepared from 4 : 6 : 7-trihydroxypteridine (II) by sodium amalgam, a reagent specific for the removal of a 7-hydroxy-group. The dihydroxypteridine produced by the action of ethyl glyoxylate on 4 : 5-diamino-6-hydroxypyrimidine (I) is shown to be the 4 : 6-derivative. 4 : 7-Dihydroxypteridine has been prepared by degrading 6-carbethoxymethyl-4 : 7-dihydroxypteridine obtained by condensing (I) with ethyl oxaloacetate.

Studies of the solubility and stability of pteridines (Part III*) necessitated the synthesis of 4 : 6- and 4 : 7-dihydroxy- and 4 : 6 : 7-trihydroxy-pteridine. The last-named (II) was readily prepared by condensation of 4 : 5-diamino-6-hydroxypyrimidine (I) and oxalic acid.


(I)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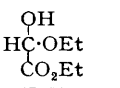
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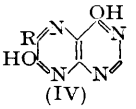
(IV)

The action of sodium amalgam in water on (II) gave 7 : 8-dihydro-4 : 6-dihydroxypteridine which was readily oxidized to 4 : 6-dihydroxypteridine. The orientation follows from analogy with 6 : 7-dihydroxypteridine from which sodium amalgam specifically removes the 7-hydroxy-group (Part II, *J.*, 1952, 1620). 4 : 6-Dihydroxypteridine was the

* Part III, *J.*, 1952, 4219.

sole product isolated from the reaction of (I) with ethyl glyoxylate hemiacetal (III) at pH 7, 6, 5, or 0, despite the fact that 4 : 5-diaminopyrimidine gave mainly 7-hydroxypteridine at pH 6, and 6-hydroxypteridine at pH 0 (Part II). Moreover, the use of ethyl glyoxylate, as such, produced no 4 : 7-dihydroxypteridine.

Potentiometric titration of the more acidic of the two hydroxyl groups in 4 : 6-dihydroxypteridine gave a hysteresis loop similar to that of 6-hydroxypteridine (illustrated

Pteridine derivative	pK_a (in H_2O) and concn. (20°)		R_F [c]	Spectrosopy in H_2O $\lambda_{max.}$ (mμ)	log $\varepsilon_{max.}$ (mol.)	pH
4 : 6 : 7-Trihydroxy-	—	—	0·05 [d]	—	—	—
(polyanion)	—	—	—	225; 319 + 330	4·45; 4·10 + 4·11	13·0
4 : 6-Dihydroxy- (+1H_2O)	—	—	0·50 [e]	<220; 270; 356	>4·14; 4·02; 3·38 [i]	4·0
(monoanion)	6·08[a] (±0·02)	(M/1000)	—	<220; 241; 280; 359	<3·9; 3·88; 4·03; 3·83 [j]	7·90
(dianion)	9·73 (±0·04)	(M/1000)	—	<220; 254; 367	>3·9; 4·18; 3·84 [j]	13·0
4 : 7-Dihydroxy-	—	—	0·30	<220; 285; 328	>4·6; 3·82; 3·94	4·0
(monoanion)	6·08 (±0·02)	(M/750)	—	227; 289; 326	4·38; 3·79; 3·95	7·9
(dianion)	9·62 (±0·03)	(M/750)	—	231; 329	4·41; 4·00	13·0
4 : 7-Dihydroxy-6-methyl- (+1H_2O)	—	—	0·45	<220; 285; 321	>4·25; 3·95; 4·00	4·50
(monoanion)	6·82 (±0·01)	(M/150)	—	225; 324	4·40; 4·04	8·44
(dianion)	10·02 (±0·06)	(M/150)	—	— [h]	—	—
6-Formyl-4 : 7-dihydroxy- (+0·9H_2O)	—	—	0·50	<220; 285; 329	>4·2; 3·80; 3·98	3·9
(monoanion)	5·93 (±0·02)	(M/100)	—	—	—	—
(dianion)	9·31 (±0·03)	(M/100)	—	—	—	—
oxime	—	—	0·20	—	—	—
4 : 7-Dihydroxy-6-carboxylic acid (+1H_2O)	—	—	0·07 [f]	—	—	—
(monoanion)	*ca.* 3 [b]	(M/750)	—	224; 288; 336	4·15; 3·78; 4·02	4·85
(dianion)	6·69 (±0·01)	(M/750)	—	226; 293; 331	4·40; 3·82; 4·01	8·37
(trianion)	10·05 (±0·05)	(M/750)	—	—	—	—
6-Carbethoxymethyl-4 : 7-dihydroxy-	—	—	0·70	<220; 287; 327; 385 [g]	>4·1; 3·84; 4·03; 2·38	4·00
(monoanion)	6·23 (±0·08)	(M/500)	—	—	—	—
(dianion)	9·62 (±0·06)	(M/500)	—	—	—	—
6-Carboxymethyl-5 : 6-dihydro-4 : 7-dihydroxy-	—	—	0·45	—	—	—
(monoanion)	4·49 (±0·07)	(M/500)	—	<220; 276; 325	>4·0; 3·80; 3·73	6·52
(dianion)	8·59 (±0·07)	(M/500)	—	—	—	—
(trianion)	*ca.* 11	(M/500)	—	—	—	—
5 : 6-Dihydro-4 : 7-dihydroxy-6-methyl-	—	—	0·65	<220; 274; 323	>4·2; 3·79; 3·71	6·0
(monoanion)	8·43 (±0·03)	(M/500)	—	—	—	—
(dianion)	11·40 (±0·04)	(M/500)	—	—	—	—

[a] Rapid back-titration (to forestall formation of pseudo-acid). [b] Back-titration (to forestall precipitation). [c] In butanol–5N-acetic acid (2 : 1) by descending method, 4-hydroxypteridine (R_F 0·50) and picric acid (R_F 0·80) being used as controls. Papers viewed in light of 254 mμ. [d] Applied as the Na salt. [e] Also a small spot at 0·05. [f] Applied as the NH_4 salt. This is a strong acid; hence the spot consists of two zones, (*a*) the violet-fluorescing neutral molecule (which is photostable) and (*b*) the darkly-absorbing anion (which becomes yellow on irradiation). When the paper was sprayed with 0·1N-HCl before exposure to ultra-violet light, only (*a*) appeared. Likewise, this substance gave two spots in 3% aq. NH_4Cl, but only one if HCl were also present. [g] Shoulder. [h] Landauer (*loc. cit.*) obtained for the dianion: 227, 327 mμ (4·36; 4·05) at pH 13. [i] Change in ε at any part of the curve not more than 3% after 24 hours at 20°. [j] No significant change in ε at any part of the curve after 24 hours at 20°.

in Part II). Because 4- and 7-hydroxypteridine do not show hysteresis, this phenomenon confirms the 4 : 6- (as opposed to the 4 : 7-)orientation. 4 : 6-Dihydroxypteridine has no evident basic properties (it is no more soluble in boiling N-mineral acids than in water); this supports the explanation of the origin of basic properties in 6-hydroxypteridine, given in Part II.

On paper chromatography, this dihydroxypteridine gives a single spot in dimethyl-

formamide (90% aqueous) but two spots (see Table, p. 75) in butanol–acetic acid. These two appeared even when sodium sulphide was added to the solvent (to prevent formation of complexes with metals possibly present in the paper, see Table 3 of Part III). When both spots were cut out and sewn, side by side, on a new piece of paper and re-run in butanol–acetic acid, each produced *two* spots corresponding in R_F and fluorescence to the original two spots. It would appear that the tautomers of 4 : 6-dihydroxypteridine are separated during paper chromatography in this solvent.

Ethyl sodio-oxaloacetate gave 6-carbethoxymethyl-4 : 7-dihydroxypteridine (IV; R = $CH_2 \cdot CO_2Et$) when heated with (I) in acetic acid. The hydroxy-group was assigned to the 7- (rather than the 6-)position because 7-hydroxypteridines are exclusively formed when other 4 : 5-diaminopyrimidines are condensed with ethyl oxaloacetate in the absence of mineral acid (Tschesche, Köhncke, and Korte, *Z. Naturforsch.*, 1950, **5***b*, 132; Elion, Hitchings, and Russell, *J. Amer. Chem. Soc.*, 1950, **72**, 78), and this was confirmed by degradation to a dihydroxypteridine different from 4 : 6-dihydroxypteridine.

Alkaline hydrolysis of the ester gave 6-carboxymethyl-4 : 7-dihydroxypteridine, isolated by acidification at about 0°. Acidification at higher temperatures brought about decarboxylation to 4 : 7-dihydroxy-6-methylpteridine (IV; R = Me) (Landauer, Thesis, London, 1951; Rydon and Landauer, in preparation). It was hoped to remove the 7-hydroxyl group from this substance by sodium amalgam; instead, 5 : 6-dihydro-4 : 7-dihydroxy-6-methylpteridine was formed. The hydrogen atoms are assigned positions 5 and 6 from analogy with the alkaline reduction of 7-hydroxypteridine (Albert, Brown, and Cheeseman, *J.*, 1952, 1620). Clearly, the 7-position is not hydrogenated because *two* acidic groups are demonstrable (see Table 1). Similarly, the action of sodium amalgam on (IV; R = $CH_2 \cdot CO_2Et$) gave 6-carboxymethyl-5 : 6-dihydro-4 : 7-dihydroxypteridine. Both these dihydro-compounds were transformed into 4 : 7-dihydroxy-6-methylpteridine by cold potassium permanganate solution. The three known examples of pteridines which have lost the hydroxy-group from the 7-position on treatment with sodium amalgam have all borne a further hydroxy-group in the 6-position and this may prove to be a necessary condition.

Attempts to oxidize the 6-methyl group with selenium dioxide or potassium permanganate resulted in destruction of the entire molecule, even under conditions satisfactory for other 6-methylpteridines (Tschesche, Köhncke, and Korte, *loc. cit.*; Cain, Mallette, and Taylor, *J. Amer. Chem. Soc.*, 1948, **70**, 3026). Moreover, the methyl group did not combine with benzaldehyde at 155° in acetic anhydride. However, no difficulty was experienced in brominating (IV; R = Me) to 6-dibromomethyl-4 : 7-dihydroxypteridine, which was readily hydrolysed to 6-formyl-4 : 7-dihydroxypteridine. The rather high solubility of this aldehyde in water (in spite of the presence of three hydrogen-bonding groups) may be due to internal hydrogen-bonding (see Part III for a discussion of the factors governing solubility in this series). The aldehyde was oxidized to the carboxylic acid by cold aqueous potassium permanganate.

This acid is rapidly decarboxylated at 260° to 4 : 7-dihydroxypteridine, which is stable and shows no hysteresis during titration. The acid can be readily decomposed in two other ways: by exposure to daylight, whereupon it rapidly becomes brown; and by boiling it with water for 15 minutes, whereupon a colourless substance is formed having an intense violet fluorescence, visible in daylight. This fluorescent substance could not be separated from the acid and is known only through its characteristic spot on the paper chromatogram (R_F 0·30 in butanol–acetic acid). It is also formed when the acid is warmed with N-sodium hydroxide, but boiling N-hydrochloric acid or cold N-ammonia have no effect. When the acid was heated for 7 hours with water at 200°, two new spots appeared (R_F 0·65 and 0·80), both fluorescing strongly. Such intense violet fluorescence is common among pyrazines, rare among pteridines, and unknown in the pyrimidine series. The pattern of ring-opening in 4-hydroxypteridines (see Part III) suggests that these three substances may be derivatives of 2-aminopyrazine-3-carboxylic acid : this will be further investigated.

Physical properties of the substances described in this paper are listed in the Table (p. 75). The ionization constants of 4 : 6- and 4 : 7-dihydroxypteridine are unusually

close for isomerides in this series, but the behaviour during titration is different (see above). The spectra of substances containing both a 4- and a 7-hydroxy-group are very similar, a variety of substituents in the 6-position having little effect. Unlike the four monohydroxypteridines and the two dihydroxypteridines previously described (*J.*, 1951, 474; 1952, 1620), 4 : 7-dihydroxypteridine does not considerably increase the wave-length of maximum absorption in passing from the neutral molecule to the monoanion, or again upon passing from the monoanion to the dianion.

The spectra of 4 : 6-dihydroxypteridine are entirely different from those of these 4 : 7-dihydroxy-derivatives. The neutral molecule, as measured, is substantially at equilibrium because little change occurred during 24 hours. The same spectrum was obtained when the substance was dissolved in 2 equivalents of alkali and added to pH 4 buffer, or when a solution (pH 5) in boiling water was added to the buffer; in the former case tautomerization must have been practically complete in less than 15 minutes.

Experimental

M. p.s are uncorrected. In the case of substances that have no definite m. p., the yield refers to the stage at which they became chromatographically homogeneous (on paper). Microanalyses were by Mr. P. R. W. Baker, Beckenham.

4 : 6 : 7-*Trihydroxypteridine* (II).—4 : 5-Diamino-6-hydroxypyrimidine (I) (2·5 g.; *J.*, 1951, 474) and oxalic acid dihydrate (17·6 g., 7 equiv.) were finely powdered and heated to 165° during 0·5 hour, and kept at 165° for 2 hours. The product was boiled with water (180 ml.) containing 6N-sodium hydroxide (40 ml.) and filtered. The filtrate was brought to pH 2 with 10N-hydrochloric acid (about 20 ml.). The white crystals were washed with boiling water, dried at 110° (yield 3·45 g. 95%), and recrystallized as the potassium salt from 40 parts of water containing 7 equivs. of potassium carbonate. 4 : 6 : 7-*Trihydroxypteridine* (90%). recovered from a hot solution of the crystals by acidification, was unchanged at 350°, not appreciably soluble in boiling dimethylformamide, 2-methoxyethanol, pyridine, formic acid, or 5N-hydrochloric acid, but soluble in 400 parts of formamide at 170° and in 7000 parts of boiling water (Found : C, 40·0; H, 2·3; N, 31·8. $C_6H_4O_3N_4$ requires C, 40·0; H, 2·2; N, 31·1%).

7 : 8-*Dihydro*-4 : 6-*dihydroxypteridine*.—4 : 6 : 7-Trihydroxypteridine (1·8 g.), finely powdered, was gently shaken with water (25 ml.) while sodium amalgam (24 g.; 4%) was added during 15 minutes at 50°. The liquid was adjusted to pH 4·5 with acetic acid (3 ml.) and 5N-sulphuric acid, then brought to the boil and filtered at once. The residue (90%) was recrystallized from about 2000 parts of boiling water, giving 7 : 8-*dihydro*-4 : 6-*dihydroxypteridine*, almost insoluble in boiling dimethylformamide, other organic solvents, or boiling N-hydrochloric acid (Found : N, 33·3. $C_6H_6O_2N_4$ requires N, 33·7%).

4 : 6-*Dihydroxypteridine*.—(a) *By oxidation of the above dihydropteridine.* To 7 : 8-dihydro-4 : 6-dihydroxypteridine (1·2 g.) and sodium hydroxide (0·52 g.) in cold water (65 ml.) was added 0·1M-potassium permanganate (46 ml., 1 equiv.) during 10 minutes. The mixture was centrifuged and the residue boiled with water (15 ml.). The combined liquids were adjusted to pH 4, giving 4 : 6-dihydroxypteridine (70%). It was purified as was the following specimen and had identical properties.

(b) *Direct synthesis.* 4 : 5-Diamino-6-hydroxypyrimidine (I) (5 g., 0·04 mole) was dissolved in boiling 2N-sulphuric acid (80 ml.). Ethyl glyoxylate hemiacetal (9 g., 0·06 mole; Rigby, *J.*, 1950, 1912) was added. The mixture was kept in boiling water for 1 hour, then cooled and filtered after 4 hours. The solid was recrystallized from boiling water (300 parts), giving yellow crystals (3·6 g.), which were dissolved in boiling water (18 ml.) containing potassium carbonate (10·8 g.). The solution was refrigerated, and the potassium salt filtered off and dissolved in boiling water (40 ml.). The solution, brought to pH 4 with acetic acid, gave pale yellow 4 : 6-*dihydroxypteridine* (52%), recrystallized from 300 parts of water, soluble in about 500 parts of boiling butanol, very soluble in formylmorpholine, and almost insoluble in pyridine acetic acid, dimethylformamide; it darkens at 320° but is unmelted at 350° (Found, for material dried at 110° : C, 39·7; H, 3·4; N, 30·9. $C_6H_4O_2N_4,H_2O$ requires C, 39·6; H, 3·3; N, 30·8%). The yellow colour (and spectrum) persists after chromatography on an alumina column in 0·5N-ammonia (cf. the 4 : 7-isomer below). A solution in borate buffer (pH 8·0) gives a reddish-orange colour with ferrous sulphate.

6-*Carbethoxymethyl*-4 : 7-*dihydroxypteridine*.—Ethyl sodio-oxaloacetate (22·5 g.), 4 : 5-diamino-6-hydroxypyrimidine (12·6 g.), and acetic acid (100 ml.) were heated at 100° for an

hour, with vigorous shaking until a clear solution was obtained (5 minutes). Water (100 ml.) was added and the mixture was chilled for an hour. The solid was washed with water (100 ml.), then with alcohol (50 ml.), and dried at 120° (yield, 70%). *6-Carbethoxymethyl-4 : 7-dihydroxypteridine* crystallized from 18 parts of pyridine (75% recovery after 24 hours' chilling) as yellow needles, decomp. *ca.* 250°. It requires more than 250 parts of boiling water for dissolution (Found : C, 48·4; H, 4·1; N, 22·3. $C_{10}H_{10}O_4N_4$ requires C, 48·0; H, 4·0; N, 22·4%).

6-Carboxymethyl-4 : 7-dihydroxypteridine.—6-Carbethoxymethyl-4 : 7-dihydroxypteridine (0·5 g.) was refluxed with 2·5N-sodium hydroxide (5 ml., 6 equiv.) for 1 hour. The solution was cooled in ice and adjusted to pH 1·5 (metanil yellow) with N-sulphuric acid. The precipitate was filtered off after 3 hours and dried at 20° ($CaCl_2$), giving the acid as a canary-yellow powder (80%) which was decarboxylated at once by warm water and other solvents, and on attempted drying at 110° (Found, for material dried at 20°/0·01 mm. : C, 43·4; H, 2·8; N, 25·1. $C_8H_6O_4N_4$ requires C, 43·2; H, 2·7; N, 25·2%). The R_F is 0·60. The sodium and the potassium salt are very soluble in water.

4 : 7-Dihydroxy-6-methylpteridine.—6-Carbethoxymethyl-4 : 7-dihydroxypteridine (10 g.) was refluxed for 1 hour with 2·5N-sodium hydroxide (100 ml.), then treated with 5N-sulphuric acid (80 ml.) and refluxed for 5 minutes. The suspension, kept at room-temperature overnight, was filtered and the crystals were rubbed in a mortar with water (10 ml.), filtered off, and dried at 110° (in a large dish because they puff up), giving 4 : 7-dihydroxy-6-methylpteridine monohydrate (90%), which from 65 parts of boiling water gave colourless crystals which darkened at 340° but did not melt at 350° (Found, for material dried at 110° : C, 43·2; H, 3·9; N, 28·4. Calc. for $C_7H_6O_2N_4,H_2O$: C, 42·85; H, 4·1; N, 28·6%). It is soluble in 55 parts of boiling acetic acid with good temperature gradient, but only moderately soluble in butanol or dry pyridine, very soluble in cold 10N-(but not in N-)hydrochloric acid.

5 : 6-Dihydro-4 : 7-dihydroxy-6-methylpteridine.—4 : 7-Dihydroxy-6-methylpteridine monohydrate (0·98 g.,) water (6 ml.), and 4% sodium amalgam (12 g.) were gently stirred at 50—60° for 15 minutes. The liquid was taken to pH 5 with acetic acid and refrigerated overnight. The solid, recrystallized from 200 parts of boiling water and dried at 110°, gave *5 : 6-dihydro-4 : 7-dihydroxy-6-methylpteridine* (90%), decomp. > 300°, poorly soluble in boiling N-hydrochloric acid, pyridine, or butanol, but readily soluble in boiling 5N-hydrochloric acid, acetic acid, dimethylformamide, and cold N-sodium hydroxide (Found : C, 46·9; H, 4·5; N, 31·0. $C_7H_8O_2N_4$ requires C, 46·7; H, 4·5; N, 31·1%). To this substance (0·45 g.), in cold N-sodium hydroxide (6 ml.), was added 0·1M-potassium permanganate (17 ml.) during 10 minutes. The mixture was centrifuged, and the manganese dioxide boiled with 0·1N-sodium hydroxide (6 ml.). The combined supernatant liquids were taken to pH 5 with acetic acid, and then deposited 4 : 7-dihydroxy-6-methylpteridine (85%).

6-Carboxymethyl-5 : 6-dihydro-4 : 7-dihydroxypteridine.—The ester (IV; R = $CH_2{\cdot}CO_2Et$) (1 g.) was suspended in water (6 ml.); sodium amalgam (12 g.; 4%) was added with gentle shaking, the temperature being kept at 50—60°. The liquid was acidified to pH 4 with acetic acid. The solid, recrystallized from water, gave *6-carboxymethyl-5 : 6-dihydro-4 : 7-dihydroxypteridine* (80%), soluble in 200 parts of boiling water, m. p. 320° (with effervescence) (Found : C, 43·1; H, 3·6. $C_8H_8O_4N_4$ requires C, 42·9; H, 3·6%). Potassium permanganate (as above) gave 4 : 7-dihydroxy-6-methylpteridine (85%).

6-Dibromomethyl-4 : 7-dihydroxypteridine.—To 4 : 7-dihydroxy-6-methylpteridine monohydrate (0·98 g.) in boiling acetic acid (55 ml.), bromine (2·1 g.) in acetic acid (5 ml.) was added and boiling was continued for 15 minutes. Next day, the *6-dibromomethyl-4 : 7-dihydroxypteridine hydrobromide* was filtered off and washed wel lwith acetic acid (yield, 1·87 g., 90%). It darkens at 215°, but is unmelted at 250° (Found : C, 20·3; H, 1·4; N, 13·5; Br, 56·7. $C_7H_4O_2N_4Br_2,HBr$ requires C, 20·2; H, 1·2; N, 13·4; Br, 57·5%).

6-Formyl-4 : 7-dihydroxypteridine.—The above hydrobromide (1·8 g.) was boiled with water (40 ml.) for 20 minutes. The solution was decolorized with carbon and kept at 0° for 2 hours, giving *4 : 7-dihydroxypteridine-6-aldehyde monohydrate* (85%), pale yellow crystals (decomp. about 320°) (from 33 parts of boiling water). It is only slightly soluble in boiling acetic acid, or dry pyridine and darkens if dried in air at 110° (Found, for material dried at 20°/0·1 mm. : C, 40·4; H, 2·95; N, 27·1. $C_7H_4O_3N_4,0{\cdot}9H_2O$ requires C, 40·4; H, 2·8; N, 26·9%). It does not reduce Fehling's solution, but blackens warm ammoniacal silver nitrate. The oxime (0·2 g.), prepared in the usual way, was recrystallized from pyridine trihydrate (15 ml.) as the pyridine salt which was dissolved in hot water (50 ml.). This solution was concentrated to half-volume in order to hydrolyse the salt and expel the pyridine. After cooling, 0·15 g. of *oxime* was obtained as yellow crystals which darken at 320° without melting. It is almost

insoluble in water and neutral organic solvents (Found, for material dried at 110°/0·01 mm.: C, 37·3; H, 2·8; N, 31·4. $C_7H_5O_3N_5,H_2O$ requires C, 37·3; H, 3·1; N, 31·1%).

4 : 7-*Dihydroxypteridine-6-carboxylic Acid*.—The finely powdered aldehyde (3·15 g.) was stirred with cold water (150 ml.), and dissolved by slow addition of N-sodium hydroxide (15 ml.). Kieselguhr (1 g.; Filter-Cel brand) was added, then 0·1M-potassium permanganate (100 ml., 1 equiv.) during 15 minutes. The mixture was centrifuged, and the sediment stirred with cold water (100 ml.) and recentrifuged. The combined supernatant liquids were taken to pH 2 (metanil-yellow) with 5N-sulphuric acid. After 1 day at 0°, the precipitate was washed, and dried at 110°, yielding pale yellow 4 : 7-*dihydroxypteridine-6-carboxylic acid monohydrate* (75%). This was purified by dissolution in cold water (200 ml.) with the aid of 6N-ammonia (2·4 ml.) and passage through aluminium oxide (10 × 2·5 cm.), followed by 0·1N-ammonia (200 + 200 ml.). The united percolates were brought to pH 4 with acetic acid, then (after clarification) to pH 2 with hydrochloric acid. The precipitate was washed and dried at 110°. The substance becomes faintly brown at about 260°. It is moderately soluble in dimethylformamide and in formylmorpholine but sparingly soluble in other organic solvents (Found, for material dried at 110°/0·01 mm.: C, 37·1; H, 2·6; N, 24·7. $C_7H_4O_4N_4,H_2O$ requires C, 37·2; H, 2·7; N, 24·8%). It is only slightly soluble in boiling 5N-sulphuric acid.

4 : 7-*Dihydroxypteridine*.—The foregoing acid (2·5 g.) was finely powdered and heated under nitrogen for an hour in a bath pre-heated to (and kept at) 265°. The residue was stirred with N-ammonia (30 ml.). The mixture was filtered, diluted to 75 ml., and poured on aluminium oxide (10 × 2·5 cm.), being followed by water (50 + 50 ml.). The alumina retained a yellow impurity of low R_F. The united percolates were acidified to pH 4·5 with acetic acid, giving 4 : 7-*dihydroxypteridine* (70%)., which recrystallized from 600 parts of boiling water. It remains almost unchanged at 350°, is almost insoluble in boiling acetic acid, pyridine, and dimethylformamide. It can be recrystallized from formylmorpholine (Found : C, 44·0; H, 2·5; N, 33·9. $C_6H_4O_2N_4$ requires C, 43·9; H, 2·45; N, 34·2%). It is no more soluble in boiling N-hydrochloric acid than in water. A solution in borate buffer (pH 8·0) gives an intense orange colour with ferrous sulphate.

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