835. *Pteridine Derivatives. Part V.* The Synthesis of 2 : 8-Dihydro-2-imino-8-alkylpteridines.*

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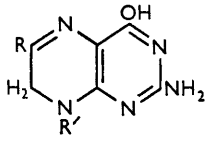
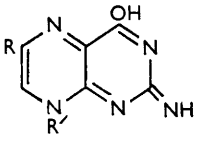
Condensation of several 2 : 5-diamino-4-alkyl(and aryl)aminopyrimidines with 1 : 2-diketones to give 2 : 8-dihydro-2-imino-8-alkyl(and aryl)pteridines is described. The structures assigned to a pteridine isolated from the eyes of *Drosophila melanogaster*, and to luciferesceine, are discussed in the light of the properties of these synthetic compounds.

Forrest and Mitchell [1] recently reported the isolation of a pteridine from the eyes of the fruit fly, *Drosophila melanogaster*. They assigned structure (I; R = CO_2H, R′ = CO·CHMe·OH) to this compound. A modified structure (II; R = CO_2H, R′ = CO·CHMe·OH) has been suggested [2] by one of us which helps to explain the similarity of the ultraviolet absorption spectrum of this pigment to that of riboflavin.

The evidence for these structures, however, is not conclusive. Forrest and Mitchell report the formation of an oxime and a 2 : 4-dinitrophenylhydrazone from the pigment, and they consider the carbonyl group which gives rise to these derivatives to be that attached at position 8. This carbonyl function is, however, part of an amide group and is not likely to form normal carbonyl derivatives.



(I)



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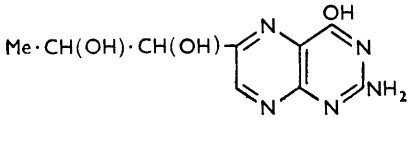


(III)

Alkaline hydrolysis of either the oxime or the dinitrophenylhydrazone of the pigment gave 2-amino-4-hydroxypteridine-6-carboxylic acid, and Forrest and Mitchell assume that the carboxyl group exists as such in the pigment. 6-Formylpteridines are known, however, to disproportionate in alkali to the acid and the more soluble hydroxymethyl compound.[3] The carboxyl group in the hydrolysis product could thus be formed from either a formyl group or a lactoyl group at position 6 in the original substance. This suggests one or other of the alternative structures (I; R = CHO, R′ = CO·CHMe·OH, and *vice versa*) for the pigment. We prefer the latter structure on grounds of biogenetic theory because of the similarity to a second pteridine which has been isolated from *Drosophila* and identified [4] as 2-amino-4-hydroxy-6-(1 : 2-dihydroxypropyl)pteridine (III). The ultraviolet absorption spectrum [1] of the pigment differs from that of known 7 : 8-dihydropteridines [5] and from that of 2-amino-7 : 8-dihydro-4-hydroxy-8-methyl-6 : 7-diphenylpteridine, prepared by condensation of benzoin with 2 : 5-diamino-4-hydroxy-6-methylaminopyrimidine. We suggest that a structure (II; R = CO·CHMe·OH, R′ = CHO or more probably CH_2·OH), which has a *para*-quinonoid type of structure similar to that found in riboflavin, is in better agreement with the published data, and we retract our previous structure (II; R = CO_2H, R′ = CO·CHMe·OH).

We now report the synthesis of 2 : 8-dihydro-4-hydroxy-2-imino-6 : 7 : 8-trimethylpteridine (IV; R = R′ = Me, R″ = H) which has a chromophoric system similar to that

* Part IV, *J.*, 1957, 3980.

[1] Forrest and Mitchell, *J. Amer. Chem. Soc.*, 1954, **76**, 5658.

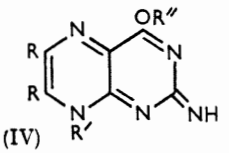
[2] Wood, Ciba Symposium on the "Chemistry and Biology of Pteridines," Churchill, London, 1954, p. 154.

[3] Waller, Goldman, Angier, Boothe, Hutchings, Mowat, and Semb, *J. Amer. Chem. Soc.*, 1950, **72**, 4630.

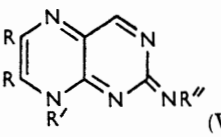
[4] Forrest and Mitchell, *ibid.*, 1955, **77**, 4865.

[5] Boothe *et al.*, *ibid.*, 1948, **70**, 27.

proposed above for the *Drosophila* pigment. 2-Amino-4-chloro-6-hydroxypyrimidine with methylamine at 120° gave 2-amino-4-hydroxy-6-methylaminopyrimidine. The derived 5-nitrosopyrimidine was reduced with sodium dithionite to 2 : 5-diamino-4-hydroxy-6-methylaminopyrimidine. Condensation with diacetyl gave 2 : 8-dihydro-4-hydroxy-2-imino-6 : 7 : 8-trimethylpteridine (IV; R = R′ = Me, R″ = H), the ultraviolet absorption spectrum of which bears no formal resemblance to that of the *Drosophila* pigment but has similar long-wavelength absorption (395 mμ at pH 1). Since few pteridines (the exceptions being mercaptopteridines) exhibit such absorption, some similarity in structure between the two compounds is indicated. The 6 : 7-diphenyl analogue (IV; R = Ph, R′ = Me, R″ = H) was synthesised by condensation of 2 : 5-diamino-4-hydroxy-6-methylaminopyrimidine with benzil.

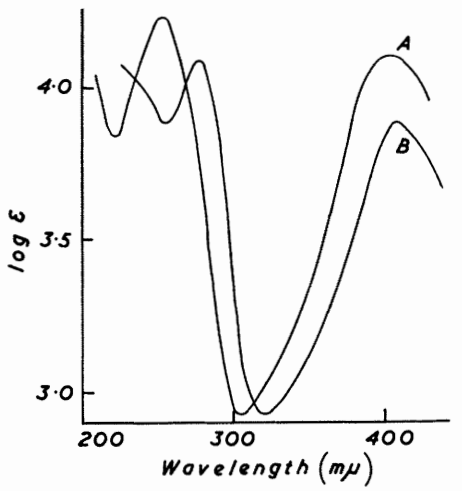


(IV)



(V)

The synthesis of 4-ethoxy-2 : 8-dihydro-2-imino-6 : 7 : 8-trimethylpteridine (IV; R = R′ = Me, R″ = Et) was also undertaken. Treatment of 2-amino-4-chloro-6-methylaminopyrimidine with sodium ethoxide in dry ethanol gave 2-amino-4-ethoxy-6-methylaminopyrimidine. The ethoxy-compound was coupled with *p*-chlorobenzenediazonium



Absorption spectra in 0·1N-*hydrochloric acid of* (*A*) 4-*ethoxy*-2 : 8-*dihydro*-2-*imino*-6 : 7 : 8-*trimethylpteridine and* (*B*) Drosophila *pigment*.[1]

chloride and then reduced, to give the unstable 2 : 5-diamino-4-ethoxy-6-methylaminopyrimidine. This was condensed directly with diacetyl to give the iminopteridine (IV; R = R′ = Me, R″ = Et). The last compound shows ultraviolet absorption at much longer wavelength in acid solution than does the 4-hydroxy-analogue (IV; R = R′ = Me, R″ = H), and we attribute this to the true *para*-quinonoid structure of the ethoxy-compound: the 4-hydroxy-compound in acid solution probably exists in the cyclic amide form [6] with consequent reduction of the chromophoric system. The spectrum of the ethoxyiminopteridine (IV; R = R′ = Me, R″ = Et) is so similar to that [1] of the *Drosophila* pigment (see Figure) that we consider that the latter must also have this true *para*-quinonoid structure.

The conversion of the naturally occurring purines into 8-substituted pteridines, *via* the intermediate 4-alkylamino-5-aminopyrimidines, has been discussed by Albert.[7] As

[6] Cf. Part IV, *J.*, 1957, 3980.
[7] Brown and Mason, *J.*, 1956, 3443.

the naturally occurring pteridines invariably have a 2-amino-group we now describe the condensation of several 2 : 5-diamino-4-alkyl(and aryl)aminopyrimidines with 1 : 2-diketones to give pteridines of structure (V).

2 : 8-Dihydro-2-imino-6 : 7 : 8-trimethylpteridine (V; R = R′ = Me, R″ = H) was synthesised by condensation of diacetyl with 2 : 5-diamino-4-methylaminopyrimidine. The latter was prepared from the known 2-amino-4-chloro-6-methylaminopyrimidine which was dechlorinated to give 2-amino-4-methylaminopyrimidine. Condensation with *p*-chlorobenzenediazonium chloride followed by catalytic hydrogenation gave the required pyrimidine. The ultraviolet absorption spectrum of the neutral molecule of the 2-iminopteridine (V; R = R′ = Me, R″ = H) closely resembles those of the 8-alkyl-2-pteridones (Part IV [6] and Table). Unlike the pteridones the imino-compound has no tendency to hydration in the solid state. The pK_a value (5·60) is higher than any previously recorded for a simple aminopteridine; the corresponding value for 2-aminopteridine is 4·2. This agrees with Angyal and Angyal's observation [8] that amino-groups kept in the imino-form by alkylation of a ring nitrogen atom have a high pK_a value.

The 2-iminopteridine gave a monoacetyl derivative which absorbs at a longer wavelength in the ultraviolet region than the parent iminopteridine. This is contrary to previous observations on the spectra of acetylated aminopteridines where acetylation decreases the wavelength of maximum absorption.[9] The anomaly is due to the increase in conjugation provided by the acetyl group of the acetyliminopteridine; no such increase in conjugation is conferred by the acetyl group in an acetamidopteridine.

A cream-coloured substance, luciferesceine, has been isolated by Strehler [10] from the head of the firefly *Photinus pyralis*. Albert [11] suggests that it may be the iminoribitylpteridine (V; R = R″ = H, R′ = ribityl) and points out the analogy with riboflavin.

Absorption spectra (in water).

Substance	$\lambda_{max.}$ (mμ)	ε	pH
2 : 8-Dihydro-4-hydroxy-2-imino-6 : 7 : 8-trimethylpteridine	223; 268; 306; 365	18,500; 8,950; 11,000; 6,800	13
	254; 284; 395	12,100; 13,150; 12,500	1
2 : 8-Dihydro-4-hydroxy-2-imino-8-methyl-6 : 7-diphenylpteridine	218; 267; 380	39,000; 24,000; 13,700	13
2-Amino-7 : 8-dihydro-4-hydroxy-8-methyl-6 : 7-diphenylpteridine	260; 398	9,700; 6,700	13
4-Ethoxy-2 : 8-dihydro-2-imino-6 : 7 : 8-trimethylpteridine	<220; 255; 405	>10,000; 17,600; 13,000	1
	234; 301; 361 [a]	24,350; 14,100; 10,200	—
2 : 8-Dihydro-2-imino-6 : 7 : 8-trimethylpteridine	235; 328	20,400; 9,900	1
	238; 340	18,900; 12,200	7
2-Acetylimino-2 : 8-dihydro-6 : 7 : 8-trimethylpteridine	226; 250 [b]; 318; 364 [a]	25,500; 9,400; 7,150; 6,100	—
2 : 8-Dihydro-6 : 7 : 8-trimethyl-2-methyliminopteridine	248; 352 [a]	23,000; 17,350	—
2 : 8-Dihydro-6 : 7 : 8-triphenyl-2-phenyliminopteridine	<220; 360 [a]	>30,000; 23,200	—
2 : 8-Dihydro-6 : 7-dimethyl-8-phenyl-2-phenyliminopteridine	245; 269; 370 [a]	15,700; 18,850; 16,150	—

[a] In EtOH. [b] Shoulder.

Comparison of the ultraviolet absorption spectrum of luciferesceine with that of 2 : 8-dihydro-2-imino-6 : 7 : 8-trimethylpteridine (V; R = R′ = Me, R″ = H) shows no similarity. The pK_a (5·60) of (V; R = R′ = Me, R″ = H) is also much lower than that quoted for luciferesceine. We thus consider the structure suggested by Albert is unlikely to be correct.

[8] Angyal and Angyal, *J.*, 1952, 1463.
[9] Albert, Brown, and Wood, *J.*, 1954, 3832.
[10] Strehler, *Arch. Biochem. Biophys.*, 1951, **32**, 397.
[11] Albert, "Fortschritte der Chemie Organischer Naturstoffe," Springer-Verlag, Vienna, 1954, p. 387.

A series of 2-alkylimino- and 2-arylimino-pteridines was synthesised by a common method. Reaction of 2 : 4-dichloro-5-nitropyrimidine with methylamine, aniline, and benzylamine gave the 2 : 4-dialkylamino(or diarylamino)-5-nitropyrimidine. Catalytic hydrogenation of these nitropyrimidines gave the 5-aminopyrimidines which were condensed directly with one or more of the dicarbonyl compounds, glyoxal, diacetyl, and benzil. The products were 2 : 8-dihydro-2-iminopteridines of general structure (V), which exhibit ultraviolet absorption characteristic of the *para*-quinonoid system of double bonds (Table and Part IV [6]). The pK_a value of the methyliminopteridine (VII; R = R′ = R″ = Me) is 6·1, in agreement with the observation [12] that methylation of an amino-group raises the pK_a value by about 0·3 unit.

Experimental

For general instructions see Part IV [6].

2-Amino-4-hydroxy-6-methylaminopyrimidine.—2-Amino-4-chloro-6-hydroxypyrimidine [13] (8·5 g.) and ethanolic methylamine (33% w/w; 25 c.c.) were heated in a sealed tube at 120° for 4 hr. The solution was cooled, and the precipitate was collected and dissolved in hot dilute hydrochloric acid (30 c.c.). The acid solution was treated with charcoal, and sodium hydrogen carbonate was added to give *2-amino-4-hydroxy-6-methylaminopyrimidine* (3·7 g.). Recrystallisation from ethanol gave light brown plates, m. p. 255—257° (Found: C, 43·1; H, 5·6; N, 39·6. $C_5H_8ON_4$ requires C, 42·9; H, 5·8; N, 40·0%).

2-Amino-4-hydroxy-6-methylamino-5-nitrosopyrimidine.—2-Amino-4-hydroxy-6-methylaminopyrimidine (2·5 g.) in 2N-hydrochloric acid (45 c.c.) was treated dropwise at 0° with sodium nitrite (2 g.) in water (25 c.c.). After being chilled overnight, the precipitate was collected, and recrystallised from water (160 parts) to give the *5-nitrosopyrimidine* (2·3 g.) as red needles, m. p. >300° (Found: C, 35·6; H, 4·1; N, 41·1. $C_5H_7O_2N_5$ requires C, 35·5; H, 4·2; N, 41·4%).

2 : 5-Diamino-4-hydroxy-6-methylaminopyrimidine.—2-Amino-4-hydroxy-6-methylamino-5-nitrosopyrimidine (0·5 g.) in hot sodium hydroxide solution (0·72 g. in 8 c.c. water) was heated to 80° on the water-bath, and a vigorous stream of nitrogen was bubbled through the solution. Sodium dithionite (2 g.) was added during 5 min., the colour of the solution changing from deep red to yellow. Heating under nitrogen was continued for a further 20 min., concentrated hydrochloric acid was added to pH 9·5, and the solution was chilled. The rather unstable *2 : 5-diamino-4-hydroxy-6-methylaminopyrimidine* (0·35 g.) was collected. The compound, m. p. 204—210° (decomp.), decomposed rapidly on attempted recrystallisation (Found: C, 38·0; H, 6·1. $C_5H_9ON_5$ requires C, 38·75; H, 5·8%).

2 : 8-Dihydro-4-hydroxy-2-imino-6 : 7 : 8-trimethylpteridine.—2 : 5-Diamino-4-hydroxy-6-methylaminopyrimidine (0·31 g.), acetic acid (3 c.c.), and water (20 c.c.) were warmed gently on the steam-bath under nitrogen, diacetyl (0·16 g.) was added, and the solution was heated at 60—70° for 30 min. The solution was neutralised with potassium hydrogen carbonate and chilled overnight. The product (0·35 g.) which separated was collected, washed with water, and recrystallised from boiling water, to give *2 : 8-dihydro-4-hydroxy-2-imino-6 : 7 : 8-trimethylpteridine* as yellow needles, decomp. >270°, pK_a 5·85 (imino-group) and 8·90 (hydroxyl group) (Found: C, 53·2; H, 5·0; N, 34·4. $C_9H_{11}ON_5$ requires C, 52·8; H, 5·4; N, 34·2%).

2 : 8-Dihydro-4-hydroxy-2-imino-8-methyl-6 : 7-diphenylpteridine.—2 : 5-Diamino-4-hydroxy-6-methylaminopyrimidine (0·3 g.), acetic acid (3 c.c.), and water (20 c.c.) were heated on the steam-bath, and a solution of benzil (0·42 g.) in ethanol (12 c.c.) was added. The solution was refluxed for 8 hr. during which a bright yellow precipitate slowly separated. This was collected, and recrystallised from dimethylformamide (7 c.c.) to give *2 : 8-dihydro-4-hydroxy-2-imino-8-methyl-6 : 7-diphenylpteridine* (0·04 g.) as yellow prisms, m. p. >300° (Found: C, 66·0; H, 4·3. $C_{19}H_{15}ON_5,H_2O$ requires C, 65·7; H, 4·9%). The infrared spectrum of this material was identical with that of a sample prepared from pyrazine intermediates.[14]

2-Amino-7 : 8-dihydro-4-hydroxy-8-methyl-6 : 7-diphenylpteridine.—2 : 5-Diamino-4-hydroxy-6-methylaminopyrimidine (0·25 g.), benzoin (0·4 g.), acetic acid (2 c.c.), and ethanol (3 c.c.) were

[12] Albert and Goldacre, *J.*, 1946, 706.
[13] Forrest, Hull, Rodda, and Todd, *J.*, 1951, 3.
[14] Dick, Fidler, and Wood, *Chem. and Ind.*, 1956, 1424.

refluxed for 2 hr., during which a heavy yellow precipitate separated. This was collected and recrystallised from dimethylformamide, to give the 7 : 8-*dihydropteridine* (0·29 g.) as yellow plates, m. p. >300° (Found: C, 68·2; H, 5·2; N, 21·2. $C_{19}H_{17}ON_5$ requires C, 68·8; H, 5·1; N, 21·2%).

2-*Amino*-4-*ethoxy*-6-*methylaminopyrimidine*.—2-Amino-4-chloro-6-methylaminopyrimidine (6·7 g.) [15] and a solution from sodium (1·05 g.) in dry ethanol (60 c.c.) were heated in an autoclave at 130° for 3 hr. The resulting solution was evaporated to dryness *in vacuo*, and the residue crystallised from water (60 c.c.) to give 2-*amino*-4-*ethoxy*-6-*methylaminopyrimidine* as colourless prisms, m. p. 123—126° (Found: C, 49·9; H, 7·2; N, 33·8. $C_7H_{12}ON_4$ requires C, 50·0; H, 7·2; N, 33·3%).

2-*Amino*-5-p-*chlorophenylazo*-4-*ethoxy*-6-*methylaminopyrimidine*.—2-Amino-4-ethoxy-6-methylaminopyrimidine (0·6 g.) in water (8 c.c.), was treated at 0° dropwise with diazotised *p*-chloroaniline (1·1 g.) in N-hydrochloric acid (20 c.c.), then kept at 0° for 5 min., and sodium carbonate (3·5 g.) was added slowly. The product which separated was collected and recrystallised from aqueous acetone to give 2-*amino*-5-p-*chlorophenylazo*-4-*ethoxy*-6-*methylaminopyrimidine* (0·8 g.) as orange needles, m. p. 169—172° (Found: C, 50·9; H, 4·5: N, 27·4. $C_{13}H_{15}ON_6Cl$ requires C, 50·9; H, 4·9; N, 27·4%).

4-*Ethoxy*-2 : 8-*dihydro*-2-*imino*-6 : 7 : 8-*trimethylpteridine*.—The above 5-*p*-chlorophenylazopyrimidine (0·6 g.) was reduced in ethanol (50 c.c.) over Raney nickel in the usual way. The solution was filtered, and acetic acid (2 drops) and diacetyl (0·3 c.c.) were added. The solution was refluxed for 20 min., concentrated *in vacuo* to 5 c.c., and neutralised by saturated potassium hydrogen carbonate solution. The product was collected, and recrystallised from aqueous ethanol (charcoal), to give 4-*ethoxy*-2 : 8-*dihydro*-2-*imino*-6 : 7 : 8-*trimethylpteridine* as red needles, m. p. 178—180° (Found: C, 56·7; H, 6·3; N, 30·4. $C_{11}H_{15}ON_5$ requires C, 56·6; H, 6·5; N, 30·0%). This was not hydrolysed by acid or alkali.

2-*Amino*-4-*methylaminopyrimidine*.—2-Amino-4-chloro-6-methylaminopyrimidine [15] (1·24 g.) was hydrogenated in water (100 c.c.) at room temperature and pressure over freshly hydrogenated 2·5% palladium–charcoal (0·6 g.) in the presence of magnesium oxide (0·9 g.). Theoretical absorption of hydrogen occurred in 12 hr., and no more took place. The mixture was heated to boiling, and the solids were filtered off and washed thoroughly with acetone. 2N-Sodium carbonate (6 c.c.) was added to the combined filtrate and washings, and the mixture was taken to dryness *in vacuo*. The residue was extracted with boiling *iso*butyl methyl ketone (150 c.c.) from which 2-*amino*-4-*methylaminopyrimidine* (0·94 g.) crystallised as colourless needles, m. p. 161—163·5° (Found: C, 48·3; H, 6·5; N, 45·0. $C_5H_8N_4$ requires C, 48·4; H, 6·5; N, 45·2%).

2-*Amino*-5-p-*chlorophenylazo*-4-*methylaminopyrimidine*.—*p*-Chloroaniline (1·4 g.) was diazotised with N-hydrochloric acid (28 c.c.) and sodium nitrite (0·81 g.), and was added to a suspension of 2-amino-4-methylaminopyrimidine (0·94 g.) in water (11 c.c.) at 0°. After 5 min. sodium carbonate (3·5 g.) was added, and the mixture was set aside for 2 hr. at 20°; solid rapidly separated. This was collected and recrystallised from ethanol (30 parts) to give 2-*amino*-5-p-*chlorophenylazo*-4-*methylaminopyrimidine* (2·25 g.) as deep red twisted needles, m. p. 227—229° (Found: C, 50·0; H, 4·3; N, 31·9. $C_{11}H_{11}N_6Cl$ requires C, 50·3; H, 4·2; N, 32·1%).

2 : 8-*Dihydro*-2-*imino*-6 : 7 : 8-*trimethylpteridine*.—2-Amino-5-*p*-chlorophenylazo-4-methylaminopyrimidine (3 g.) in warm methanol (100 c.c.) was hydrogenated over Raney nickel at 4 atm. for 16 hr. The solution was filtered, and used directly for the preparation of the pteridine. Diacetyl (1 c.c.) was added and the solution was refluxed for 30 min., concentrated *in vacuo* to *ca.* 5 c.c., and chilled overnight. The solid (0·5 g.) was collected and recrystallised from methanol (10 parts) to give 2 : 8-*dihydro*-2-*imino*-6 : 7 : 8-*trimethylpteridine* as pale yellow needles, m. p. 235—240° (decomp.), pK_a 5·60 ± 0·1 (Found: C, 57·5; H, 5·4; N, 37·5. $C_9H_{11}N_5$ requires C, 57·2; H, 5·8; N, 37·1%). Ammonia was liberated when the imino-pteridine was heated with concentrated potassium hydroxide solution.

2-*Acetylimino*-2 : 8-*dihydro*-6 : 7 : 8-*trimethylpteridine*.—The above imino-pteridine (0·1 g.) and acetic anhydride (3 c.c.) were heated on the steam-bath for 1 hr., then poured into water (15 c.c.), stirred slowly for 1 hr., and neutralised with sodium hydrogen carbonate solution. The resulting suspension was extracted with chloroform (3 × 50 c.c.), and the extracts, after being washed with water, were taken to dryness *in vacuo*. The residue, crystallised from methanol–ethyl acetate, gave the *acetyl derivative* (0·07 g.) as colourless needles, m. p. 165—170° (Found: N, 30·7. $C_{11}H_{13}ON_5$ requires N, 30·3%).

[15] Imperial Chemical Industries Ltd., B.P. 658,202/1951.

2 : 8-*Dihydro*-6 : 7 : 8-*trimethyl*-2-*methyliminopteridine*.—2 : 4-Bismethylamino-5-nitropyrimidine (0·6 g.) [16] in ethanol (150 c.c.) was reduced over Raney nickel as above, and to the filtered solution was added diacetyl (0·5 c.c.). The solution was refluxed for 10 min., concentrated to 2 c.c. *in vacuo*, and chilled overnight. The material which separated was recrystallised from methanol–water (10 : 1; 10 parts), to give 2 : 8-*dihydro*-6 : 7 : 8-*trimethyl*-2-*methyliminopteridine* (0·4 g.) as pale buff needles, m. p. 197—198° (decomp.), pK_a 6·1 ± 0·2 (Found: C, 58·9; H, 6·2; N, 34·3. $C_{10}H_{13}N_5$ requires C, 59·2; H, 6·4; N, 34·5%). Methylamine was liberated when the methyliminopteridine was heated with concentrated potassium hydroxide solution.

2 : 4-*Dianilino*-5-*nitropyrimidine*.—2 : 4-Dichloro-5-nitropyrimidine (0·5 g.) [17] in dry benzene (10 c.c.) was added dropwise to a vigorously stirred solution of aniline (4 c.c.) in benzene (10 c.c.). The mixture was stirred for 30 min., and the bright yellow product (1·3 g.) was collected and recrystallised from ethanol (200 parts), to give 2 : 4-*dianilino*-5-*nitropyrimidine* as yellow needles, m. p. 198—202° (Found: C, 63·0; H, 3·99; N, 23·2. $C_{16}H_{13}O_2N_5$ requires C, 62·6; H, 4·25; N, 22·8%).

2 : 8-*Dihydro*-6 : 7 : 8-*triphenyl*-2-*phenyliminopteridine*.—2 : 4-Dianilino-5-nitropyrimidine (0·3 g.) in ethanol (200 c.c.) was reduced over Raney nickel in the usual way. To the filtered solution were added benzil (0·3 g.), acetic acid (0·3 c.c.), and water (3 c.c.). The solution was heated on the steam-bath for 20 min. and then concentrated *in vacuo* to 10 c.c. and chilled overnight. The product which separated was collected and recrystallised from ethanol (100 parts), to give 2 : 8-*dihydro*-6 : 7 : 8-*triphenyl*-2-*phenyliminopteridine* (0·25 g.) as pale green plates, m. p. 225—227° (decomp.) (Found: C, 78·1; H, 4·9; N, 15·3. $C_{30}H_{21}N_5$ requires C, 79·8; H, 4·6; N, 15·5%). This gave a deep green colour in concentrated sulphuric acid.

2 : 8-*Dihydro*-6 : 7-*dimethyl*-8-*phenyl*-2-*phenyliminopteridine*.—2 : 4-Dianilino-5-nitropyrimidine (0·4 g.) was reduced and condensed with diacetyl as above to give 2 : 8-*dihydro*-6 : 7-*dimethyl*-8-*phenyl*-2-*phenyliminopteridine* (0·15 g.) as pale pink needles (from ethanol), m. p. 241—242° (decomp.) (Found: C, 73·9; H, 5·3; N, 21·8. $C_{20}H_{17}N_5$ requires C, 73·4; H, 5·2; N, 21·5%).

Potentiometric Titrations.—Weighed quantities of the pteridines (approx. M/1000; 5 mg.) were dissolved in 25 c.c. of distilled water and titrated with 0·1M-hydrochloric acid or -sodium hydroxide in a cell containing a glass electrode calibrated by means of phthalate and borate buffers. The reference electrode was a calomel half-cell immersed in the solution. A Cambridge pH meter was used for measurement of pH values. The solution was stirred by a current of nitrogen, and the titrant was added from a micrometer syringe, about fifteen small additions being made. The pK_a values were calculated according to the equation $pK_a = pH - \log\{([B] + [H^+])/([BH^+] - [H^+])\}$ where [B], [BH$^+$], and [H$^+$] are the calculated concentrations of the base, conjugate acid, and hydrogen ion, corrected for the dilution caused by addition of acid or alkali.

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