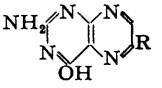
344. *Pteridines. Part III.* Unambiguous Syntheses of Xanthopterin and 2-Amino-4-hydroxy-6-methylpteridine.*

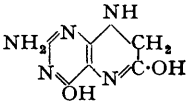
By W. R. Boon and T. Leigh.

Reduction of ethyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (V; R = OEt) gives dihydroxanthopterin (II). Similarly, reduction of 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetone (V; R = Me) and 2-amino-6-hydroxy-4-(ω-phenoxyacetonylamino)-5-phenylazopyrimidine (V; R = CH_2·OPh) gives 2-amino-7 : 8-dihydro-4-hydroxy-6-methylpteridine. The dihydro-compounds are readily oxidised to the parent pteridines.

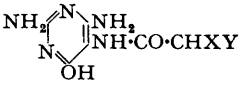
Two of the key compounds in the study of pteridine derivatives of natural origin are xanthopterin (I; R = OH) and 2-amino-4-hydroxy-6-methylpteridine (I; R = Me). Although the structures of these two substances have been established, beyond any reasonable doubt, by degradative methods they have not hitherto been obtained synthetically by completely unequivocal methods.



(I.)



(II.)



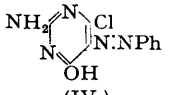
(III.)

Xanthopterin has been synthesised by Purrmann (*Annalen*, 1941, **546**, 98), who condensed 2 : 4 : 5-triamino-6-hydroxypyrimidine with dichloroacetic acid to obtain the amide (III; X = Y = Cl), which when heated with silver oxide gave xanthopterin in poor yield. Koschara (*Z. physiol. Chem.*, 1943, **277**, 159) obtained a better yield by condensing the same pyrimidine with the bisulphite compound of barium glyoxylate in concentrated sulphuric acid. Both of these syntheses, at least in their structure-determining aspect, require that the initial acylation occurs on the 5-amino-group of the pyrimidine. Although this has been one of the accepted principles of pyrimidine chemistry since 1900 (Traube, *Ber.*, **33**, 3035), there was no direct proof that it was so until Wilson (*J.*, 1948, 1157) obtained 5-acetamido-2 : 4-diamino-6-hydroxypyrimidine (III; X = Y = H) by condensation of ethyl acetamidocyanoacetate with guanidine, identical with the product obtained by direct acetylation of 2 : 4 : 5-triamino-6-hydroxypyrimidine. Xanthopterin has also been obtained by oxidation of dihydroxanthopterin, to which O'Dell, Vandenbelt, Bloom, and Pfiffner (*J. Amer. Chem. Soc.*, 1947, **69**, 250) assigned the structure (II). They obtained this substance by reduction of xanthopterin; it has similarly been obtained from leucopterin (Totter, *J. Biol. Chem.*, 1944, **154**, 105; Elion, Light, and Hitchings, *J. Amer. Chem. Soc.*, 1949, **71**, 741) and xanthopterincarboxylic acid (Purrmann, *Annalen*, 1941, **548**, 284). Hitchings and Elion (*J. Amer. Chem. Soc.*, 1949, **71**, 467) have cast doubt on the assignment of structure (II) to dihydroxanthopterin by showing that the product obtained by reaction of 2 : 4-diamino-5-chloroacetamido-6-hydroxypyrimidine (III; X = H, Y = Cl) with sodium hydrogen carbonate is different from dihydroxanthopterin. Whatever may be the constitution of the substance prepared by Hitchings and Elion, we have now shown, by an extension of the methods described in Part I (Boon, Jones, and Ramage, *J.*, 1950, 96), that dihydroxanthopterin has the structure (II).

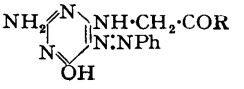
The most direct method for the preparation of dihydroxanthopterin by the above procedure would involve, initially, condensation of a glycine ester with 2-amino-4 : 6-dichloro-5-nitropyrimidine. Unfortunately, the preparation of this substance proved unexpectedly difficult and recourse was had to the use of a 4-chloro-5-phenylazopyrimidine, the phenylazo-residue serving both as a precursor of the 5-amino-group and to activate the adjacent chlorine atom. No identifiable product was isolated from the reaction of 2-amino-4 : 6-dihydroxy-5-phenylazopyrimidine with phosphorus oxychloride in dimethylaniline. The sodium salt of the pyrimidine when heated with phosphorus oxychloride gave 2-amino-6-hydroxy-5-phenylazo-4-pyrimidyl dihydrogen phosphate. Addition of phosphorus pentachloride to the reaction mixture led to formation of a product containing, in addition to phosphorus, chlorine so labile that it was readily lost on exposure to moist air.

* Part II, *J.*, 1951, 591.

In view of the failure to prepare a 4-chloro-5-phenylazopyrimidine directly from the 4-hydroxy-compound, the possibility of preparing it by coupling a suitable chloropyrimidine with a diazo-compound remained to be explored. Lythgoe, Todd, and Topham (*J.*, 1944, 315) have shown that 5-arylazopyrimidines are only obtainable when the pyrimidine is substituted at positions 2 or 4 and 6 by such groups as amino and hydroxy. 2-Amino-4-chloro-6-hydroxypyrimidine was readily obtained by acid hydrolysis of 2-amino-4-chloro-6-methoxypyrimidine (Rose and Tuey, *J.*, 1946, 81); it coupled rather slowly with benzenediazonium chloride to give 2-amino-4-chloro-6-hydroxy-5-phenylazopyrimidine (IV). This condensed readily with glycine ethyl ester in formodimethylamide solution to give ethyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (V; R = OEt), readily reduced by zinc and acetic acid to dihydroxanthopterin identical in ultra-violet absorption spectrum and *X*-ray powder photograph with an authentic specimen prepared from leucopterin (Elion *et al.*, *loc. cit.*). Oxidation with alkaline potassium permanganate by the method of Elion *et al.* converted the dihydroxanthopterin into xanthopterin.



(IV.)



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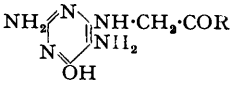

(VI.)

By hydrolysis of their " β-dihydroxanthopterin," prepared by reaction of 2 : 4-diamino-5-chloroacetamido-6-hydroxypyrimidine with sodium hydrogen carbonate, Hitchings and Elion (*loc. cit.*) obtained a substance to which they assigned the structure (VI; R = OH) and from which they prepared a methyl ester (VI; R = OMe). Both the acid and the ester were readily reconverted into β-dihydroxanthopterin. There is no doubt that the acid obtained by the above authors does not possess the structure (VI), since the ethyl ester of the acid of the above structure is shown by the present series of reactions to cyclise to dihydroxanthopterin. In an attempt to isolate a substance having the structure (VI), *iso*propyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (V; R = OPr^i) was prepared by condensation of (IV) with glycine *iso*propyl ester, since Abderhalden and Suzuki (*Z. physiol. Chem.*, 1928, **176**, 103) have shown that the latter substance only takes part sluggishly in amide-forming reactions as judged by its rate of conversion into diketopiperazine. No trace of (VI; R = OPr^i), could be isolated after reduction of (V; R = OPr^i) either in *NN*-dimethylformamide solution over Raney nickel or in *iso*propyl-alcoholic hydrochloric acid over palladised charcoal; the only product identified was dihydroxanthopterin.

2-Amino-4-hydroxy-6-methylpteridine was first obtained by Boothe, Waller, Stokstad, Hutchings, Mowat, Angier, Semb, SubbaRow, Cosulich, Fahrenbach, Hultquist, Kuh, Northey, Seeger, Sickels, and Smith (*J. Amer. Chem. Soc.*, 1948, **70**, 27) by reduction of 2-amino-4-hydroxy-6-pteridylmethylpyridinium iodide followed by oxidation of the dihydropteridine. It has since been prepared by a number of authors by condensation of 2 : 4 : 5-triamino-6-hydroxypyrimidine with suitable three-carbon compounds (cf. Angier, Waller, Boothe, Mowat, Semb, Hutchings, Stokstad, and SubbaRow, *ibid.*, p. 3029; Karrer and Schwyzer, *Helv. Chim. Acta*, 1949, **32**, 423; 1950, **33**, 39; King and Spensley, *Nature*, 1949, **164**, 574; Forrest and Waller, *J.*, 1949, 2077; Weygand, Wacker, and Schmied-Kowarzik, *Experientia*, 1950, **6**, 184). By their nature, these syntheses contain an element of uncertainty in the determination of the structure of the final product; Weygand *et al.* (*loc. cit.*) state that mixed products are always obtained, though some improvement has been claimed by Forrest and Walker (*loc. cit.*) if condensation of the pyrimidine with α-ketols is effected in presence of hydrazine.

Aminoacetone did not condense satisfactorily with (IV), but aminoacetone semicarbazone readily condensed with it in *NN*-dimethylformamide to give the semicarbazone of 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetone (V; R = Me); this substance was readily hydrolysed, without previous purification, with cold dilute hydrochloric acid to the parent ketone, which was reduced with zinc and acetic acid to 2-amino-7 : 8-dihydro-4-hydroxy-6-methylpteridine, which on oxidation with alkaline potassium permanganate gave 2-amino-4-hydroxy-6-methylpteridine.

Boothe *et al.* (*loc. cit.*) converted the last substance into 2-amino-6-bromomethyl-4-hydroxypteridine in poor yield by heating it with bromine in hydrobromic acid. It was thought that a substance such as 2-amino-4-hydroxy-6-phenoxymethylpteridine would offer a more suitable starting point for the preparation of this bromo-compound. Condensation of (IV) with the semicarbazone of 1-amino-3-phenoxypropan-2-one proceeded smoothly to give the semicarb-

azone of 2-amino-6-hydroxy-4-(ω-phenoxyacetonylamino)-5-phenylazopyrimidine (V; R = CH_2·OPh). Reduction of the parent ketone under a variety of conditions led invariably to 2-amino-7 : 8-dihydro-4-hydroxy-6-methylpteridine as the sole product. This result is almost certainly due to the splitting off of phenol from 2-amino-7 : 8-dihydro-4-hydroxy-6-phenoxymethylpteridine first formed, followed by reduction of the resultant 2-amino-4-hydroxy-6-methylpteridine. Angier *et al.* (*loc. cit.*), Weygand, Wacker, and Schmied-Kowarzik (*Experientia*, 1948, **4**, 427), and Weygand and Schmied-Kowarzik (*Ber.*, 1949, **82**, 333) have already produced evidence suggesting that 7 : 8-dihydropteridines containing the group CH_2X, where X = OH, NHR, etc., in the 6-position are unstable and capable of only a transitory existence.

1-Ethoxy- and 1-phenoxy-3-phthalimidopropan-2-ol were obtained readily by reaction of the appropriate glycidyl ethers with phthalimide. Oxidation to the ketones, with chromium trioxide in acetic acid, proceeded smoothly, but hydrolysis of the phthalimido-groups was not possible without simultaneous hydrolysis of the ether group. 1-Phenoxy-3-succinimidopropan-2-one was made by a similar series of reactions and could not be hydrolysed any more readily. The semicarbazone of 1-phenoxy-3-phthalimidopropan-2-one, however, was hydrolysed by a two-stage procedure to the semicarbazone of the amino-ketone, by use of dilute sodium hydroxide to convert the phthalimide into the phthalamic acid, which was then further hydrolysed with dilute acid.

The condensation of a 5-arylazo-4-chloropyrimidine with α-amino-ketones and esters forms the subject matter of B.P. Appl. 21,615/1949, Boon, Leigh, and Imperial Chemical Industries Limited.

Experimental.

(Microanalyses are by Drs. Weiler and Strauss.)

2-Amino-4 : 6-dihydroxy-5-phenylazopyrimidine.—To a solution of 2-amino-4 : 6-dihydroxypyrimidine (23 g.) and sodium hydrogen carbonate (45 g.) in sodium hydroxide (0·2N.; 1 l.), benzenediazonium chloride [from aniline (14 g.) and 5N-hydrochloric acid (80 c.c.)] was added during 30 minutes. After 1 hour the yellow solid was filtered off and washed with water. The filter cake was dissolved in hot N-sodium hydroxide (200 c.c.), 10N-sodium hydroxide (50 c.c.) was added, and the crystalline sodium salt which separated was collected, washed with 0·5N-sodium hydroxide, and dried *in vacuo* at 100° (33 g.). For analysis the *pyrimidine* was recrystallised from hot 2N-sodium carbonate to give a microcrystalline yellow solid, m. p. above 300° (Found: C, 51·6; H, 4·1; N, 30·1. $C_{10}H_9O_2N_5$ requires C, 52·0; H, 3·9; N, 30·3%).

2-Amino-6-hydroxy-5-phenylazo-4-pyrimidyl Dihydrogen Phosphate.—The sodium salt of 2-amino-4 : 6-dihydroxy-5-phenylazopyrimidine (5 g.) and phosphorus oxychloride were heated on a steam-bath for 4 hours. The precipitated solid was collected, washed with hot phosphorus oxychloride, and dissolved in 2% sodium hydrogen carbonate solution (100 c.c.). The pale yellow *phosphate* precipitated by addition of acetic acid had m. p. above 300° (Found: C, 38·6; H, 3·3; N, 23·0; P, 10·8. $C_{10}H_{10}O_5N_5P$ requires C, 38·6; H, 3·2; N, 22·5; P, 10·0%).

2-Amino-4-chloro-6-hydroxypyrimidine.—2-Amino-4-chloro-6-methoxypyrimidine (32 g.) and concentrated hydrochloric acid (130 c.c.) were heated on the steam-bath for 30 minutes, and the resulting suspension poured into cold water (500 c.c.). The *chloro*-compound was collected, washed with water, dried, and recrystallised from methanol; the yield was 28·5 g., 98%, and the m. p. 261° (Found: C, 32·9; H, 3·2; N, 28·7; Cl, 23·8. $C_4H_4ON_3Cl$ requires C, 33·0; H, 2·8; N, 28·9; Cl, 24·4%).

2-Amino-4-chloro-6-hydroxy-5-phenylazopyrimidine.—To a solution of the foregoing compound (87 g.) and anhydrous sodium carbonate (120 g.) in 0·2N-sodium hydroxide (3·6 l.), there was added during 1 hour a solution of benzenediazonium chloride [from aniline (56 g.) and 5N-hydrochloric acid (320 c.c.)]. After a further 12 hours' stirring, the brown precipitate was collected and washed successively with water, ethanol, and ether; the yield was 101 g., 67%. Purification of this substance for analysis proved difficult, attempts at crystallisation leading to decomposition. The *diethylamine* salt was prepared by adding diethylamine (1·0 c.c.) to a solution of the azo-compound (0·5 g.) in *NN*-dimethylformamide (8·0 c.c.); after 5 minutes the salt (m. p. 118°, decomp.) was filtered off and washed with acetone (Found: C, 51·5; H, 6·0; N, 25·0; Cl, 10·5. $C_{10}H_8ON_5Cl,C_4H_{11}N$ requires C, 52·1; H, 5·9; N, 26·1; Cl, 11·0%). This substance likewise could not be purified further without decomposition. If the salt is not removed rapidly from the reaction mixture, it redissolves with the formation of *2-amino-4-diethylamino-6-hydroxy-5-phenylazopyrimidine*, m. p. 206°, isolated by addition of water and recrystallised from ethanol (Found: C, 59·0; H, 6·4; N, 29·9. $C_{14}H_{18}ON_6$ requires C, 58·7; H, 6·3; N, 29·4%).

Ethyl 2-Amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate.—To 2-amino-6-chloro-4-hydroxy-5-phenylazopyrimidine (1 g.) in dimethylformamide (5 c.c.), glycine ethyl ester (0·9 g.) in ethanol (10 c.c.) was added. Next day, the *ester* was filtered off, washed with ethanol and water, dried, and recrystallised from *n*-butanol; it had m. p. 238° (1·1 g.; 85%) (Found: C, 53·4; H, 5·2; N, 27·0. $C_{14}H_{16}O_3N_6$ requires C, 53·2; H, 5·1; N, 26·6%). The corresponding iso*propyl* ester (Found: C, 54·1; H, 5·4; N, 25·4. $C_{15}H_{18}O_3N_6$ requires C, 54·5; H, 5·5; N, 25·4%) was obtained similarly by using an *iso*propanol solution of glycine *iso*propyl ester; recrystallised from *iso*propanol, it had m. p. 222°.

Dihydroxanthopterin.—To ethyl 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetate (1·0 g.) in glacial acetic acid (10 c.c.), heated to 90°, zinc dust (1 g.) was added with stirring during 10 minutes. After being decanted from most of the unused zinc dust, the reaction mixture was centrifuged, and the solid crystallised from 0·25N-sulphuric acid as the *sulphate dihydrate* (0·6 g.) [Found, on sample dried at

90°/0·5 mm.: C, 29·4; H, 3·9; N, 28·4; S, 6·4. $(C_6H_7O_2N_5)_2,H_2SO_4,2H_2O$ requires C, 29·0; H, 4·0; N, 28·2; S, 6·5%]. The ultra-violet absorption in 0·1N-hydrochloric acid and the *X*-ray powder photograph of the free base were identical with those of an authentic sample prepared by reduction of leucopterin (Elion *et al.*, *loc. cit.*). It was readily converted into xanthopterin by oxidation with alkaline potassium permanganate as described by Elion *et al.*

Aminoacetone Semicarbazone.—To aminoacetone hydrochloride (38 g.) in ethanol (250 c.c.), semicarbazide hydrochloride (48 g.) in water (100 c.c.) was added. After 2 hours, *aminoacetone semicarbazone hydrochloride* (53 g., 87%) was collected, washed with ethanol, and crystallised from aqueous ethanol; it had m. p. 212° (Found: C, 29·1; H, 6·7; N, 34·1; Cl, 21·9. $C_4H_{11}ON_4Cl$ requires C, 28·8; H, 6·6; N, 33·6; Cl, 21·3%).

1-*Ethoxy*-3-*phthalimidopropan*-2-*ol.*—Glycidyl ethyl ether (Fairbourne, Gibson, and Stephens *J.*, 1932, 1965) (262 g.) and phthalimide (370 g.) were heated at 150° for 24 hours. After distillation of unchanged ether (71 g.), benzene (1 l.) was added, and phthalimide (99 g.) removed by filtration. Concentration of the filtrate gave 1-*ethoxy*-3-*phthalimidopropan*-2-*ol* (350 g., 75%), m. p. 68° (Found: C, 63·0; H, 6·1; N, 6·0. $C_{13}H_{15}O_4N$ requires C, 62·7; H, 6·0; N, 5·6%).

1-*Phenoxy*-3-*phthalimidopropan*-2-*ol*, m. p. 117°, from ethanol (Found: C, 68·7; H, 5·1; N, 4·4. $C_{17}H_{15}O_4N$ requires C, 68·6; H, 5·0; N, 4·7%), and 1-*phenoxy*-3-*succinimidopropan*-2-*ol*, m. p. 132°, from ethanol (Found: C, 62·4; H, 5·8; N, 5·4. $C_{13}H_{15}O_4N$ requires C, 62·5; H, 6·0; N, 5·6%), were obtained similarly.

1-*Ethoxy*-3-*phthalimidopropan*-2-*one.*—To a solution of 1-ethoxy-3-phthalimidopropan-2-ol (25 g.) in glacial acetic acid (100 c.c.) warmed to 30°, 21 c.c. of a 5·75M-solution of chromium trioxide in 50% acetic acid were added in portions during 45 minutes. After a further 30 minutes' heating on the steam-bath, the acetic acid was removed under reduced pressure, and the residue was triturated with water and extracted with ether. The ethereal solution was washed with sodium hydrogen carbonate solution and dried ($MgSO_4$), and the ether removed by distillation. The semi-solid residue was twice crystallised from aqueous methanol, and 1-*ethoxy*-3-*phthalimidopropan*-2-*one* was obtained, having m. p. 75° (Found: C, 62·9; H, 5·2; N, 5·4. $C_{13}H_{13}O_4N$ requires C, 63·1; H, 5·3; N, 5·7%); the 2:4-*dinitrophenylhydrazone* had m. p. 224° (Found: C, 52·8; H, 3·8; N, 16·3. $C_{19}H_{17}O_7N_5$ requires C, 53·4; H, 4·0; N, 16·4%). 1-*Phenoxy*-3-*phthalimidopropan*-2-*one*, recrystallised from ethanol, had m. p. 164° (Found: C, 69·0; H, 4·4; N, 4·7. $C_{17}H_{13}O_4N$ requires C, 69·1; H, 4·4; N, 4·7%) [*semicarbazone* (from *n*-butanol), m. p. 193° (Found: C, 61·6; H, 4·9. $C_{18}H_{16}O_4N_4$ requires C, 61·4; H, 4·6%], and 1-*phenoxy*-3-*succinimidopropan*-2-*one*, m. p. 112° (from methanol) (Found: C, 63·2; H, 5·4; N, 5·9. $C_{13}H_{13}O_4N$ requires C, 63·1; H, 5·3; N, 5·7%), were obtained similarly.

1-*Amino*-3-*phenoxypropan*-2-*one Semicarbazone.*—Sodium hydroxide (13 g.) in water (200 c.c.) was added during 15 minutes with stirring to a suspension of 1-phenoxy-3-phthalimidopropan-2-one semicarbazone (98 g.) in ethanol (500 c.c.). After 1 hour, the solution was filtered, and the bulk of the ethanol removed by distillation under reduced pressure. The solution was cooled to 5°, concentrated hydrochloric acid (40 c.c.) added, and the *phthalamic acid* (1-o-*carboxybenzamido*-3-*phenoxypropan*-2-*one semicarbazone*) filtered off, washed with water, and air-dried. A sample, redissolved in sodium hydroxide, treated with charcoal, filtered, and reprecipitated, had m. p. 135° (Found: N, 14·5. $C_{18}H_{18}O_5N_4$ requires N, 15·1%). The phthalamic acid (87 g.), ethanol (250 c.c.), and 0·33N-hydrochloric acid (120 c.c.) were heated on the steam-bath for 30 minutes. The syrupy residue, obtained on evaporation to dryness under reduced pressure, was lixiviated with water (200 c.c.), filtered to remove phthalic acid, and the filtrate again evaporated to dryness. The residue was dissolved in hot ethanol (250 c.c.) from which on cooling there was obtained 1-*amino*-3-*phenoxypropan*-2-*one semicarbazone hydrochloride* (23 g., 31%), m. p. 194°, raised to 201° by recrystallisation from ethanol (Found: C, 45·9; H, 6·3; N, 22·0. $C_{10}H_{15}O_2N_4Cl$ requires C, 46·4; H, 5·8; N, 21·7%).

2-*Amino*-6-*hydroxy*-5-*phenylazo*-4-*pyrimidylaminoacetone.*—Aminoacetone semicarbazone hydrochloride (107 g.) was added to a cold solution of sodium ethoxide [from sodium (14·8 g.) and ethanol (600 c.c.)]. After 2 hours the mixture was added to 2-amino-4-chloro-6-hydroxy-5-phenylazopyrimidine (75 g.) in dimethylformamide (400 c.c.). Next day, the solid was collected, washed successively with ethanol and water, and dried in air. The semicarbazone (88 g.) was dissolved in glacial acetic acid (250 c.c.), and 2N-hydrochloric acid (1500 c.c.) added. 2-*Amino*-6-*hydroxy*-4-*acetonylamino*-5-*phenylazopyrimidine hydrochloride* (75 g., 76%), m. p. >300°, separated in a few minutes; it was filtered off, and washed with 0·5N-hydrochloric acid and then with acetone (Found: C, 48·4; H, 5·1; N, 25·4; Cl, 10·8. $C_{13}H_{15}O_2N_6Cl$ requires C, 48·4; H, 4·7; N, 26·0; Cl, 11·0%). The free base (from ethanol) had m. p. 183°.

2-*Amino*-6-*hydroxy*-4-(ω-*phenoxyacetonylamino*)-5-*phenylazopyrimidine hydrochloride*, m. p. 192° (from methanol) (Found: C, 54·9; H, 4·7; N, 20·1; Cl, 8·5. $C_{19}H_{19}O_3N_6Cl$ requires C, 55·0; H, 4·6; N, 20·3; Cl, 8·6%), and its *semicarbazone*, m. p. 265° (decomp.) (from dimethylformamide–ethanol) (Found: C, 54·9; H, 4·7; N, 29·0. $C_{20}H_{21}O_3N_9$ requires C, 55·2; H, 4·8; N, 29·0%), were obtained similarly.

2-*Amino*-7:8-*dihydro*-4-*hydroxy*-6-*methylpteridine.*—To a stirred solution of 2-amino-6-hydroxy-5-phenylazo-4-pyrimidylaminoacetone hydrochloride (51 g.) i glacial acetic acid (250 c.c.) at 90°, zinc dust (40 g.) was added during 30 minutes. The mixture was filtered hot, and 5N-hydrochloric acid (500 c.c.) added to the filtrate. The solid which separated was collected after 30 minutes, washed with 2N-hydrochloric acid, and dissolved in 0·25N-sodium hydroxide (1 l.) at 60°, and the solution filtered. Concentrated hydrochloric acid (150 c.c.) was added to the filtrate to give 2-amino-7:8-dihydro-4-hydroxy-6-methylpteridine hydrochloride (25 g.), m. p. >300°. A sample for analysis was dried over phosphoric oxide at 100°/0·5 mm. (Found: C, 35·7; H, 5·1; N, 30·4; Cl, 15·2. Calc. for $C_7H_9ON_5,HCl,H_2O$: C, 36·0; H, 5·1; N, 30·0; Cl, 15·3%). The ultra-violet absorption in 0·1N-sodium hydroxide and an *X*-ray powder photograph were identical with those of a sample prepared by the

method of Boothe *et al.* (*loc. cit.*). Oxidation with alkaline permanganate readily converted the product into 2-amino-4-hydroxy-6-methylpteridine. The dihydro-compound was also obtained by reduction of 2-amino-6-hydroxy-4-(ω-phenoxyacetonylamino)-5-phenylazopyrimidine hydrochloride with zinc dust in acetic acid at room temperature, of the free base (i) similarly at 90°, (ii) with hydrogen and Raney nickel in ethanol at 50°, or (iii) with boiling sodium dithionite solution.

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