417. *Pteridine Derivatives. Part II.* Methylation of 2 : 4-Dihydroxy-6- and -7-phenylpteridine, and Related Topics.*

By G. P. G. Dick, H. C. S. Wood, and (in part) W. R. Logan.

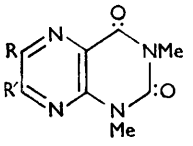
Unequivocal syntheses of 1 : 2 : 3 : 4-tetrahydro-1 : 3-dimethyl-2 : 4-dioxo-6-phenylpteridine (I; R = Ph, R′ = H) and the 7-phenyl isomer (I; R = H, R′ = Ph) have been carried out. Alkaline degradation of these *N*-alkylpteridones leads to pyrazine derivatives. The condensation of 5 : 6-diaminouracil and phenylglyoxal has been re-investigated, and the nature of the products obtained by Ganapati [1] and by Weijlard, Tishler, and Erikson [2] has been established. The methylation of these substances has been studied. The condensation of aminomalonamide and phenylglyoxal has been re-investigated and the product, m. p. 252—253°, has been identified as 3-hydroxy-5-phenylpyrazine-2-carboxyamide. Unambiguous structures have been established for the pteridines obtained by condensation of 2 : 4 : 5-triamino-6-hydroxypyrimidine with ωω-dichloroacetophenone, with phenylglyoxal, and with ω-nitroacetophenone.

The structures which have been assigned [1,2,3] to certain derivatives of 6- and 7-phenylpteridine are not completely unambiguous. This paper presents evidence leading to unequivocal structures for these compounds. Condensation of an *o*-aminonitrosopyrimidine with carbonyl compounds possessing a reactive α-methylene group has been

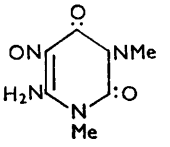
* Part I, *J.*, 1955, 1379.

[1] Ganapati, *J. Indian Chem. Soc.*, 1937, **14**, 627.
[2] Weijlard, Tishler, and Erikson, *J. Amer. Chem. Soc.*, 1945, **67**, 802.
[3] King and Spensley, *J.*, 1952, 2144.

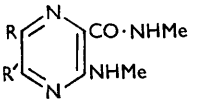
shown to give pteridines of unambiguous structure.[4] Addition of 4-amino-1 : 3-dimethyl-5-nitrosouracil (II) to excess of refluxing phenylacetaldehyde gave 1 : 2 : 3 : 4-tetrahydro-1 : 3-dimethyl-2 : 4-dioxo-6-phenylpteridine (I; R = Ph, R′ = H), m. p. 251—253°. Similar condensation of acetophenone gave the 7-phenyl isomer (I; R = H, R′ = Ph), m. p. 298—300°. The latter material was identical with that obtained from condensation of phenylglyoxal and 5 : 6-diamino-1 : 3-dimethyluracil in the presence of sodium hydrogen sulphite. This compound was also obtained by diazomethylation of 2 : 4-dihydroxy-7-phenylpteridine, which was prepared by condensation of phenylglyoxal and 5 : 6-diaminouracil in ammoniacal solution,[2] or (better) in the presence of sodium hydrogen sulphite. Hitherto, it has been generally accepted that when these aldehyde-binding reagents are used the alkyl or aryl group will be in the 6-position. One exception to this rule has already been reported.[5]



(I)



(II)



(III)

Ganapati [1] has described the condensation of phenylglyoxal with 5 : 6-diaminouracil in dilute acetic acid, followed by diazomethylation of the product to give a dimethyl derivative, m. p. 278°. Repetition of this experiment gave an apparently homogeneous product, m. p. 237—238°. This material was also obtained by condensation of phenylglyoxal with 5 : 6-diamino-1 : 3-dimethyluracil in 10% hydrochloric acid, thus establishing the *NN*-methylation. A mixture of 1 : 2 : 3 : 4-tetrahydro-1 : 3-dimethyl-2 : 4-dioxo-6-phenylpteridine (2 parts) and the 7-phenyl isomer (1 part) formed a complex, m. p. 236—238°. A similar complex, m. p. 278°, was obtained by mixing the 6-phenyl compound (1 part) and the 7-phenyl isomer (2 parts). We believe the materials obtained by Ganapati [1] and by us to be of this nature.

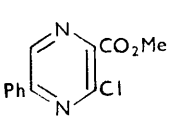
The constant solubility, ultraviolet absorption spectrum, and m. p. of the mixed dimethyl derivatives, through successive recrystallisation, together with the failure of routine paper chromatography to separate these isomers, is worthy of note in a series where much reliance is placed upon these criteria.[6]

The ease with which *N*-alkylpteridones can be degraded with dilute alkali is well known.[7,8] 1 : 2 : 3 : 4-Tetrahydro-1 : 3-dimethyl-2 : 4-dioxo-6-phenylpteridine (I; R = Ph, R′ = H) showed surprising stability to aqueous alkali, but gave a quantitative yield of 3-methylamino-6-phenylpyrazine-2-carboxymethylamide (III; R = Ph, R′ = H) when refluxed with ethanolic 0·1N-potassium hydroxide. Similar treatment of the 7-phenyl isomer (I; R = H, R′ = Ph) gave 3-methylamino-5-phenylpyrazine-2-carboxymethylamide (III; R = H, R′ = Ph). More drastic hydrolysis of the pteridones (I) or the methylamides (III) gave the corresponding 3-methylamino-5- and -6-phenylpyrazine-2-carboxylic acid.

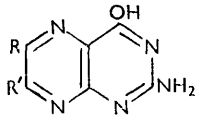
Condensation of aminomalonamide with phenylglyoxal has been shown [9] to give 3-hydroxy-5(or 6)-phenylpyrazine-2-carboxyamide, m. p. 213—216° (decomp.). We obtained from this reaction a compound, m. p. 252—253° (decomp.), in poor yield, and this has been identified (see below) as 3-hydroxy-5-phenylpyrazine-2-carboxyamide. The material obtained by Jones is presumably the 6-phenyl isomer. A similar condensation between aminomalonamide and methylglyoxal [10] gave 3-hydroxy-5-methylpyrazine-2-carboxyamide, whereas earlier work by Jones [9] had given the 6-methyl compound. The use of

[4] Timmis, *Nature*, 1949, **164**, 139.
[5] Albert, *Quart. Reviews*, 1952, **6**, 227; Albert, Brown, and Wood, *J.*, 1954, 3832.
[6] Albert, Brown, and Cheeseman, *J.*, 1951, 474.
[7] Wood, "Ciba Symposium on the Chemistry and Biology of Pteridines," Churchill, London, 1954, p. 35; Albert, Brown, and Wood, *J.*, 1956, 2066.
[8] Taylor, *J. Amer. Chem. Soc.*, 1952, **74**, 2380.
[9] Jones, *ibid.*, 1949, **71**, 80.
[10] Dick and Wood, *J.*, 1955, 1379.

aldehyde-binding reagents in this type of condensation has already been reported,[10] and, as expected, sodium hydrogen sulphite facilitated the reaction between aminomalonamide and phenylglyoxal, and 3-hydroxy-5-phenylpyrazine-2-carboxyamide was obtained in the absence of the usual basic catalyst.



(IV)



(V)

3-Hydroxy-5-phenylpyrazine-2-carboxyamide was hydrolysed to the acid, m. p. 217° (decomp.), the methyl ester of which with phosphorus oxychloride gave 3-chloro-2-methoxycarbonyl-5-phenylpyrazine (IV). Reaction of the chloro-ester with alcoholic methylamine at 140° gave 3-methylamino-5-phenylpyrazine-2-carboxymethylamide (III; R = H, R = Ph). This material was identical with that obtained by alkali degradation of 1 : 2 : 3 : 4-tetrahydro-1 : 3-dimethyl-2 : 4-dioxo-7-phenylpteridine (I; R = H, R′ = Ph). This establishes the position of the phenyl group in the above pyrazine derivatives.

King and Spensley [3] reported the synthesis of 2-amino-4-hydroxy-6-phenylpteridine (V; R = Ph, R′ = H) from 2 : 4 : 5-triamino-6-hydroxypyrimidine and ωω-dichloroacetophenone, and of the 7-phenyl isomer (V; R = H, R′ = Ph) from the triaminohydroxypyrimidine and either phenylglyoxal or ω-nitroacetophenone. The structure of these pteridines was not conclusively proved, and rests upon the characteristic colour given by 5-aminopyrimidine derivatives with the Folin–Denis reagent. Alkaline degradation of these pteridines gave 3-hydroxy-6-phenylpyrazine-2-carboxylic acid, m. p. 200° (ethyl ester, m. p. 158—159°), and the 5-phenyl isomer, m. p. 208—209° (ethyl ester, m. p. 112).[3] The latter acid appears to be identical with that, m. p. 217° (ethyl ester, m. p. 112—114°), obtained by us from 3-hydroxy-5-phenylpyrazine-2-carboxyamide.

We have repeated the condensation of 2 : 4 : 5-triamino-6-hydroxypyrimidine with ωω-dichloroacetophenone, with phenylglyoxal, and with ω-nitroacetophenone, and we find the product in each case to be 2-amino-4-hydroxy-6-phenylpteridine (V; R = Ph, R′ = H). The infrared spectra of these products were identical and different from that of the 7-phenyl isomer (V; R = H, R′ = Ph) prepared by condensation of 3-chloro-2-methoxycarbonyl-5-phenylpyrazine (IV) and guanidine carbonate (cf. ref. 10). The infrared spectrum of a specimen of " 2-amino-4-hydroxy-7-phenylpteridine " kindly supplied by Dr. P. C. Spensley was identical with that of our 6-phenyl isomer (V; R = Ph, R′ = H) and different from that of the authentic 7-phenyl compound. The Schiff's base formed by condensation of the triaminohydroxypyrimidine and ω-nitroacetophenone gave no colour with the Folin–Denis reagent. Cyclisation of the anil with sodium dithionite, followed by alkaline degradation of the pteridine, gave 3-hydroxy-6-phenylpyrazine-2-carboxylic acid, m. p. 200° (ethyl ester, m. p. 158—159°).

Experimental

Paper Chromatography.—Chromatograms were prepared by the ascending method with (separately) aqueous ammonium chloride (3%) and butanol–5N-acetic acid (7 : 3), and viewed in ultraviolet light of wavelengths 254 and 365 mμ.

Mixed Dimethyl Compounds (I), *M. p.* 237—238°.—(*a*) Phenylglyoxal was condensed with 5 : 6-diaminouracil [11] in acetic acid as described by Ganapati.[1] The product was recrystallised from aqueous ethanol or (better) *NN*-dimethylformamide to give orange-yellow needles, m. p. >300°. The solubility in these solvents, and the ultraviolet spectrum (in 0·1N-sodium hydroxide) were constant. Only one spot was obtained on paper chromatography in the above solvent systems.

This material was treated with diazomethane (8 equivs.) in ether,[1] methanol being added to initiate the reaction. The product was recrystallised from 80% formic acid, giving pale yellow needles, m. p. 237—238° (Ganapati [1] gives m. p. 278°) (Found: C, 62·4; H, 4·5; N, 20·7%).

[11] Bogert and Davidson, *J. Amer. Chem. Soc.*, 1933, **55**, 1668.

(*b*) 5 : 6-Diamino-1 : 3-dimethyluracil [12] (1 g.) was dissolved in a mixture of 10% hydrochloric acid (25 c.c.) and ethanol (15 c.c.), and phenylglyoxal hydrate (1 g.) was added. The solution was refluxed for 1 hr., then cooled, and the product collected. Recrystallisation from 80% formic acid (15 c.c.) gave pale yellow needles (1·3 g., 83%), m. p. 237—238°.

1 : 2 : 3 : 4-*Tetrahydro*-1 : 3-*dimethyl*-2 : 4-*dioxo*-7-*phenylpteridine*.—(*a*) Acetophenone (10 g.) and 4-amino-1 : 3-dimethyl-5-nitrosouracil [13] (1 g.) were refluxed gently for 30 min. During this period an acetophenone–water mixture was allowed to distil off, and the volume was restored with fresh acetophenone (*ca.* 3 c.c.). The dark mixture was cooled, and ether (50 c.c.) added. Next morning the solid was collected, washed with ether, and dried, to give a tan powder (0·5 g., 35%). Recrystallisation from 80% formic acid (charcoal) gave 1 : 2 : 3 : 4-*tetrahydro*-1 : 3-*dimethyl*-2 : 4-*dioxo*-7-*phenylpteridine* as yellow needles, m. p. 298—300° (Found : C, 62·6; H, 4·3; N, 20·5. $C_{14}H_{12}O_2N_4$ requires C, 62·7; H, 4·5; N, 20·9%).

(*b*) To phenylglyoxal hydrate (2 g.) in water (25 c.c.) was added a solution of sodium hydrogen sulphite (*d* 1·34; 15 c.c.), and the mixture was set aside for 1 hr. 5 : 6-Diamino-1 : 3-dimethyluracil (2 g.) and sodium sulphite (hydrated; 8 g.) in water (100 c.c.) were added, and the solution was refluxed for 40 min. On cooling, the dimethylpteridone crystallised rapidly. Recrystallisation from 80% formic acid gave pale yellow needles, m. p. and mixed m. p. 299—300°.

(*c*) A similar condensation was carried out with 5 : 6-diaminouracil sulphate (2 g.), the solution being refluxed for 1 hr. Acetic acid was added to pH 4—5; 2 : 4-dihydroxy-7-phenylpteridine (2·5 g., 87%) crystallised as cream needles, m. p. >300°.

This material (2 g.) was stirred for 1 hr. with 8 equivs. of diazomethane (from 21 g. of toluene-*p*-sulphonylmethylnitrosamide [14]) in ether–methanol; vigorous evolution of nitrogen took place. Next morning the product was collected and recrystallised from 80% formic acid, to give the pteridone (2 g., 90%), m. p. and mixed m. p. 299—300°.

(*d*) Phenylglyoxal was condensed with 5 : 6-diaminouracil in ammoniacal solution as described by Weijlard, Tishler, and Erikson.[2] The crude product was treated with diazomethane as above, to give the dimethylpteridone (from 80% formic acid), m. p. and mixed m. p. 299—300°.

1 : 2 : 3 : 4-*Tetrahydro*-1 : 3-*dimethyl*-2 : 4-*dioxo*-6-*phenylpteridine*.—Phenylacetaldehyde (5 g.) was refluxed gently and 4-amino-1 : 3-dimethyl-5-nitrosouracil (0·5 g.) was added slowly. After refluxing for 25 min., the mixture, which was dark red, was cooled and ether was added. The orange-yellow solid (0·32 g., 41%) which separated was collected next morning and washed with ether. Recrystallisation from 80% formic acid gave 1 : 2 : 3 : 4-*tetrahydro*-1 : 3-*dimethyl*-2 : 4-*dioxo*-6-*phenylpteridine* as lemon-yellow needles, m. p. 251—253° (Found : C, 62·9; H, 4·3; N, 20·8%).

Hydrolysis of 1 : 2 : 3 : 4-*Tetrahydro*-1 : 3-*dimethyl*-2 : 4-*dioxo*-7-*phenylpteridine*.—(*a*) The dimethylpteridone (0·2 g.) was dissolved in boiling ethanol (200 c.c.) and warm 0·3N-ethanolic potassium hydroxide (100 c.c.) was added with shaking. After refluxing for 15 min., the solution was cooled and neutralised by acetic acid (1·7 c.c.). The ethanol was removed *in vacuo*, and the yellow residue suspended in water and extracted with chloroform (3 × 50 c.c.). The combined extracts were dried ($MgSO_4$) and evaporated to give a yellow solid. Crystallisation from light petroleum (b. p. 60—80°) gave yellow needles of 3-*methylamino*-5-*phenylpyrazine*-2-*carboxymethylamide* (99%), m. p. 112—114° (Found : C, 64·7; H, 5·7; N, 23·1. $C_{13}H_{14}ON_4$ requires C, 64·4; H, 5·8; N, 23·1%).

(*b*) The pteridone (1·05 g.) and sodium hydroxide (1 g.) in ethanol (35 c.c.) were heated in a steel bomb at 200° for 16 hr. After cooling, water (50 c.c.) was added, and the ethanol evaporated. The hot solution was filtered, concentrated hydrochloric acid was added to pH 4, and the yellow precipitate was collected after chilling. 3-*Methylamino*-5-*phenylpyrazine*-2-*carboxylic acid* (0·76 g., 80%) recrystallised from ethanol as needles, m. p. 178—179° (decomp.) (methyl ester, m. p. 134—135°) (Found : C, 62·7; H, 4·5; N, 18·2. $C_{12}H_{11}O_2N_3$ requires C, 62·9; H, 4·8; N, 18·3%).

This acid was also obtained in 85% yield on similar hydrolysis of 3-methylamino-5-phenylpyrazine-2-carboxymethylamide.

Hydrolysis of 1 : 2 : 3 : 4-*Tetrahydro*-1 : 3-*dimethyl*-2 : 4-*dioxo*-6-*phenylpteridine*.—(*a*) The dimethylpteridone was hydrolysed with 0·1N-ethanolic potassium hydroxide as above, to give 3-*methylamino*-6-*phenylpyrazine*-2-*carboxymethylamide* (98%) as yellow needles (from light petroleum), m. p. 92—94° (Found : C, 64·5; H, 5·8; N, 23·3%).

[12] Speer and Raymond, *ibid.*, 1953, **75**, 114.
[13] Traube, *Ber.*, 1900, **33**, 3035.
[14] Boer and Backer, *Rec. Trav. chim.*, 1954, **73**, 229.

(*b*) Hydrolysis of the pteridone or of the methylamide with ethanolic sodium hydroxide at 140° gave 3-*methylamino*-6-*phenylpyrazine*-2-*carboxylic acid* (100%) as yellow needles (from methanol), m. p. 173—174° (methyl ester, m. p. 140—141°) (Found: C, 63·2; H, 4·6; N, 18·5%).

3-*Hydroxy*-5-*phenylpyrazine*-2-*carboxyamide*.—Phenylglyoxal hydrate (5·4 g.) in water (25 c.c.) was treated with aqueous sodium hydrogen sulphite (*d* 1·34; 50 c.c.), and the mixture was kept at room temperature for 45 min. Aminomalonamide [10] (3·9 g.) in water (30 c.c.) was added, and the cloudy solution was heated on the steam-bath for 2·5 hr., during which a yellow crystalline precipitate separated. This was collected, washed with water and ethanol, and dried. Recrystallisation from ethanol gave 3-*hydroxy*-5-*phenylpyrazine*-2-*carboxyamide* (4·81 g., 62%) as yellow needles, m. p. 252—253° (decomp.) (Found: C, 61·7; H, 4·3; N, 19·3. $C_{11}H_9O_2N_3$ requires C, 61·4; H, 4·2; N, 19·5%).

The same product, in much smaller yield, was obtained when the condensation was carried out as described by Jones.[9]

3-*Hydroxy*-5-*phenylpyrazine*-2-*carboxylic Acid*.—3-Hydroxy-5-phenylpyrazine-2-carboxyamide was hydrolysed with ethanolic sodium hydroxide at 150° for 16 hr. as described above for the degradation of 1 : 2 : 3 : 4-tetrahydro-1 : 3-dimethyl-2 : 4-dioxo-7-phenylpteridine. 3-Hydroxy-5-phenylpyrazine-2-carboxylic acid (93%) was isolated in the usual way and recrystallised from ethanol as yellow needles, m. p. 217° (decomp.) (Found: C, 60·9; H, 3·5; N, 13·0. Calc. for $C_{11}H_8O_3N_2$: C, 61·1; H, 3·7; N, 13·0%). This acid gave a mid-blue fluorescence in ultraviolet light. King and Spensley [3] report a similar fluorescence and m. p. 208—209° (decomp.).

The acid was converted into the ethyl ester which was obtained as prisms, m. p. 112—114° (Found: C, 63·5; H, 4·7; N, 11·7. Calc. for $C_{13}H_{12}O_3N_2$: C, 63·9; H, 5·0; N, 11·5%). King and Spensley [3] report m. p. 112°.

3-*Hydroxy*-2-*methoxycarbonyl*-5-*phenylpyrazine*.—3-Hydroxy-5-phenylpyrazine-2-carboxylic acid (2·75 g.) in dry boiling methanol (150 c.c.) was treated with dry hydrogen chloride until it had completely dissolved (about 20 min.), and the clear orange solution was refluxed for a further 2 hr. When the mixture was cooled, the *ester* was deposited as white prismatic needles. The acidic mother-liquors were concentrated *in vacuo* to *ca.* 75 c.c., water (75 c.c.) was added, and the solution was neutralised with ammonia (*d* 0·88), the temperature being kept below 10°. The solution was extracted with chloroform (4 × 100 c.c.) and the combined extracts after drying (sodium sulphate) were evaporated *in vacuo* to give a yellow solid. Crystallisation from methanol (charcoal) gave a second crop of the *ester* (total yield 2·7 g., 92%). A sample recrystallised from chloroform–methanol had m. p. 172—173° (Found: C, 62·7; H, 4·3; N, 12·4. $C_{12}H_{10}O_3N_2$ requires C, 62·6; H, 4·4; N, 12·2%).

3-*Chloro*-2-*methoxycarbonyl*-5-*phenylpyrazine*.—3-Hydroxy-2-methoxycarbonyl-5-phenylpyrazine (1 g.) and redistilled phosphorus oxychloride (14 c.c.) containing one drop of concentrated sulphuric acid were mixed in a Carius tube. The mixture was heated at 115° (bath) for 30 min.; evolution of hydrogen chloride had then ceased. The tube was sealed and heated at 155° for 6 hr. The cooled mixture was poured on cracked ice (150 g.) and stirred for 30 min. The product which separated was collected, washed with water, and dried (0·94 g., 87%). Recrystallisation from chloroform–methanol and finally from methanol gave the *chloro-ester* as prisms, m. p. 81—83° (Found: C, 57·5; H, 3·5; N, 11·4; Cl, 13·9. $C_{12}H_9O_2N_2Cl$ requires C, 57·9; H, 3·6; N, 11·3; Cl, 14·3%).

3-*Methylamino*-5-*phenylpyrazine*-2-*carboxymethylamide*.—3-Chloro-2-methoxycarbonyl-5-phenylpyrazine (0·1 g.) and 33% ethanolic methylamine (2 c.c.) were heated in a Carius tube at 140° for 6 hr. The yellow solution was evaporated to dryness *in vacuo*, absolute methanol was added, and the solution again taken to dryness, leaving a yellow residue which was extracted with chloroform (3 × 10 c.c.). The combined extracts were concentrated and, on the addition of light petroleum (b. p. 60—80°), 3-methylamino-5-phenylpyrazine-2-carboxymethylamide (65 mg., 67%) crystallised as yellow needles, m. p. 112—113°. A mixed m. p. with the methylamide obtained by degradation of 1 : 2 : 3 : 4-tetrahydro-1 : 3-dimethyl-2 : 4-dioxo-7-phenylpteridine showed no depression.

2-*Amino*-4-*hydroxy*-7-*phenylpteridine*.—An intimate mixture of 3-chloro-2-methoxycarbonyl-5-phenylpyrazine (0·2 g.) and guanidine carbonate (0·5 g.) was heated at 170—180° for 30 min. with occasional stirring. The yellow mixture was cooled, and warm water (40 c.c.) was added. The resulting suspension was heated to 95°, and acetic acid was added to pH 4—5, further precipitation taking place. The pale yellow solid was collected at 90—100°, washed with water, ethanol and ether, and dried, to give 2-amino-4-hydroxy-7-phenylpteridine (170 mg., 88%), m. p. >300°. The material was purified by dissolving it in hot 2N-sodium hydroxide, and

reprecipitating it with acetic acid at 95—100°, and was dried at 135° (Found: C, 59·9; H, 3·8; N, 29·4. Calc. for $C_{12}H_9ON_5$: C, 60·2; H, 3·8; N, 29·3%).

2-Amino-4-hydroxy-6-phenylpteridine.—(*a*) 2 : 4 : 5-Triamino-6-hydroxypyrimidine reacted with ωω-dichloroacetophenone as described by King and Spensley,[3] to give 2-amino-4-hydroxy-6-phenylpteridine.

(*b*) 2 : 4 : 5-Triamino-6-hydroxypyrimidine was condensed with phenylglyoxal as described by King and Spensley [3] for the preparation of the 7-phenyl isomer. The infrared spectrum of the purified product was identical with that of the material prepared from ωω-dichloroacetophenone, and different from the spectrum of the authentic 2-amino-4-hydroxy-7-phenylpteridine prepared as above.

(*c*) 2 : 4 : 5-Triamino-6-hydroxypyrimidine dihydrochloride (5 g.) was treated with ω-nitroacetophenone (4 g.) in aqueous buffer, giving an orange solid (4·52 g., 63%).[3] 2 : 4-*Diamino*-6-*hydroxy*-5-(2-*nitro*-1-*phenylethylideneamino*)*pyrimidine* was obtained from 50% ethanol as orange needles, m. p. >300°, which gave no colour in ammoniacal solution with the Folin–Denis reagent (Found: C, 47·2; H, 4·4; N, 27·8. $C_{12}H_{12}O_3N_6,H_2O$ requires C, 47·1; H, 4·6; N, 27·5%).

The Schiff's base was cyclised by treatment with sodium dithionite as described by King and Spensley, to give 2-amino-4-hydroxy-6-phenylpteridine, identical with the material prepared as in (*a*) and (*b*).

Degradation of this pteridine with 4N-sodium hydroxide at 170° for 24 hr. gave 3-hydroxy-6-phenylpyrazine-2-carboxylic acid, m. p. 200° (decomp.) (ethyl ester, m. p. 158—159°). In dilute acid solution this acid gave a brilliant pale green ultraviolet fluorescence, distinct from that of the isomeric phenylpyrazine; the mixed m. p. with the latter was 187—190°.

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