411. *Pteridines. Part IV.* Derivatives of 2 : 4-Diaminopteridine and Related Compounds.*

By W. R. Boon.

A series of derivatives of 2 : 4-diaminopteridine having one or both amino-groups substituted, has been prepared by condensation of the appropriate tetra-aminopyrimidines and α-diketones. Substances with different substituents in positions 6 and 7 have been prepared from 5-arylazo-6-(α-pyrimidylamino)-ketones. Recorded preparations of disubstituted aminopteridines from aminohydroxy- and aminomercapto-pteridines are, in some cases, shown to be erroneous.

The coupling of pyrimidine derivatives with aryldiazonium salts is shown to be a reaction more widely applicable than is generally known.

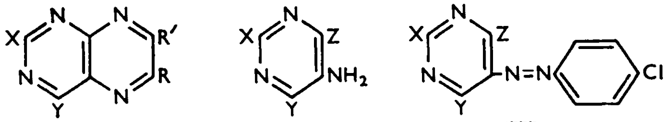
Several derivatives of 2 : 4-diaminopteridine are known to possess antimalarial activity (for a summary see Potter and Henshall [1]). It was considered of interest to prepare a series of related derivatives of 2 : 4-diamino-6 : 7-diphenylpteridine (I; $X = Y = NH_2$, $R = R' = Ph$) in which the primary amino-groups were progressively substituted by methyl. Antimalarial activity was immediately lost, but the compounds were active against experimental schistosomiasis in mice. Further modifications of the substituents X, Y, R, and R′ always lowered the activity. The only other substances examined showing appreciable activity were those in which X = Y = NHMe, R = R′ = *p*-MeO·C_6H_4 and *m*- or *p*-C_6H_4Cl.

Substances (I) in which R = R′ are most conveniently prepared by condensing a tetra-aminopyrimidine with an α-diketone, the 2- and 4-amino-groups being substituted as required. The tetra-aminopyrimidines are obtained by reducing a substance (II) in which X and Y are amino- or substituted amino-groups and Z is, *e.g.*, arylazo, nitro or nitroso.

* Part III, *J.*, 1951, 1497.

[1] Potter and Henshall, *J.*, 1956, 2000.

4 : 5 : 6-Triamino-2-dimethylaminopyrimidine was the only known substance required[2,3] but the methods by which it was obtained are not suitable for the preparation of compounds where the 4-amino-group also is substituted.



(I) (II) (III)

For the preparation of 2-dimethylamino-derivatives, 2-dimethylamino-4 : 6-dihydroxy-5-nitropyrimidine was readily obtained by nitration of 2-dimethylamino-4 : 6-dihydroxy-pyrimidine,[4] but, although it readily gave the 4 : 6-dichloro-compound, stepwise replacement of the chlorine atoms by amino-groups proved difficult, so that approach was abandoned.

When a 2-amino-group was required, 2 : 6-diamino-4-chloro-5-*p*-chlorophenylazo-pyrimidine proved a convenient starting material.[5] 2-Amino-4-chloro-5-*p*-chlorophenylazo-6-methylamino- and 4-amino-6-chloro-5-*p*-chlorophenylazo-2-methylamino-pyrimidine were also readily obtained. Lythgoe, Todd, and Topham[6] state that only those pyrimidine compounds which contain tautomerisable hydrogen atoms on at least two of the substituents in positions 2, 4, and 6 can be caused to couple with diazonium salts. Polonovski and Pesson,[7] however, state that for coupling to occur with a 4-amino- or 4-hydroxy-pyrimidine there must be a second polar group in position 2; they describe, *inter alia*, the coupling, in alkaline solution, of 2-dimethylamino-4-hydroxy-6-methylpyrimidine with benzenediazonium chloride. This procedure has now been used for the preparation of 4-chloro-5-*p*-chloro-phenylazo-2-dimethylamino-6-hydroxypyrimidine (III; X = NMe_2, Y = Cl, Z = OH) and the corresponding 2-methylamino-compound. On the other hand, coupling of 4-amino-6-chloro-2-dimethylamino- and 2-amino-4-chloro-6-dimethylamino-pyrimidine with *p*-chloro-benzenediazonium chloride occurred most readily under mildly acid conditions, giving the 5-*p*-chlorophenylazo-compounds. Coupling was also satisfactory with a number of other diazonium salts (see Table 1 and B.P. 763,041). 4-Chloro-5-*p*-chlorophenylazo-2 : 6-bisdi-methylaminopyrimidine and 5-*p*-chlorophenylazo-2-dimethylamino-4-hydroxy-6-methyl-pyrimidine were obtained similarly.

The 4-chlorine was readily replaced when 2 : 6-diamino-5-arylazopyrimidines were heated with ammonia or an amine. In preliminary experiments, because of the low solubility of the starting materials in more conventional solvents, dimethylformamide was used as an additional solvent in reaction with alcoholic ammonia, but the ammonia then reacted preferentially with the amide so that the chlorine atom was replaced by a dimethylamino-group; thus, the compounds (III; X = NHMe, Y = NH_2, Z = Cl; X = Y = NHMe, Z = Cl; X = NH_2, Y = NHMe, Z = Cl) gave the products in which Z = NMe_2, identical with those obtained by the direct action of alcoholic dimethylamine on the starting materials.

Reduction of the azo-compounds by hydrogen in presence of Raney nickel was smooth in every case. Condensation of the products with symmetrical α-diketones proceeded as expected. The amine (II; X = Z = NH_2, Y = NHMe) with benzil gave 2-amino-4-methylamino-6 : 7-diphenylpteridine (I; X = NH_2, Y = NHMe, R = R′ = Ph), m. p. 272°, which Paget[8] has shown to be preferentially absorbed on cardiac muscle. Cain, Taylor, and Daniel[9] state that this substance has m. p. 237—238°; they heated under reflux a mixture of 2-amino-4-hydroxy-6 : 7-diphenylpteridine, phosphorus oxychloride, and

[2] Roth, Smith, and Hultquist, *J. Amer. Chem. Soc.*, 1951, **73**, 2864.
[3] Andrews, Anand, Todd, and Topham, *J.*, 1949, 2490.
[4] Boon, *J.*, 1952, 1532.
[5] B.P. 677,342.
[6] Lythgoe, Todd, and Topham, *J.*, 1944, 315.
[7] Polonovski and Pesson, *Bull. Soc. chim. France*, 1948, **15**, 688.
[8] Paget, *J. Path. Bact.*, in the press.
[9] Cain, Taylor, and Daniel, *J. Amer. Chem. Soc.*, 1949, **71**, 892.

phosphorus pentachloride and heated the crude product at 150° with alcoholic methylamine; repetition of this work gave a product of m. p. 253—259°, depressed on admixture with a sample prepared as above, and shown by fractional extraction with acid to be a mixture of 2 : 4-bismethylamino-6 : 7-diphenylpteridine (I; X = Y = NHMe, R = R′ = Ph) and the methylamide of 3-amino-5 : 6-diphenylpyrazine-2-carboxylic acid. However, reaction with alcoholic methylamine at <120° gave the expected 2-amino-4-methylamino-6 : 7-diphenylpteridine.

Likewise 4-amino-2-methylamino-6 : 7-diphenylpteridine (I; X = NHMe, Y = NH_2, R = R′ = Ph) obtained from (II; X = NHMe, Y = Z = NH_2) and benzil had m. p. 307° although Taylor and Cain [10] state that the substance obtained from the action of methylamine on 4-amino-2-mercapto-6 : 7-diphenylpteridine (I; X = SH, Y = NH_2, R = R′ = Ph) has m. p. 264—265°. Repetition showed that their substance was 2 : 4-bismethylamino-6 : 7-diphenylpteridine. Further, the product, m. p. 192—195°, described by these authors as (I; X = Me_2N, Y = NH_2, R = R′ = Ph) is a mixture of this substance which has m. p. 239° and (I; X = Y = NMe_2, R = R′ = Ph), m. p. 210°, both of which have been prepared by unambiguous methods during the present work.

For the preparation of substances containing only one substituent at position 6 or 7, or with different substituents in these positions, reductive cyclisation of an α-(5-arylazo-4-pyrimidylamino)-ketone appeared the most satisfactory unambiguous method. The condensation of (III; X = Y = NH_2, Z = Cl) with glycine ethyl ester has already been recorded.[5] Analogous condensations were slower as the amino-groups were progressively substituted, and still slower when the second reactant was an α-amino-ketone so that the use of a protected derivative such as a semicarbazone or acetal was essential. In contrast, a 4-hydroxyl group increased the reactivity of the 6-chlorine atom, so that the hydroxy-compound (III; X = NMe_2, Y = OH, Z = Cl) condensed more readily than the primary diamine (III; X = Y = NH_2, Z = Cl). 4-Chloro-5-*p*-chlorophenylazo-2-dimethylamino-6-hydroxypyrimidine (III; X = NMe_2, Y = OH, Z = Cl) with ω-aminoacetophenone semicarbazone and α-amino-α-phenylacetaldehyde dimethyl acetal gave products which on hydrolysis afforded the ketone and aldehyde (III; X = NMe_2, Y = OH, Z = $NH{\cdot}CH_2{\cdot}COPh$ and NH·CHPh·CHO). These were reduced to 2-dimethylamino-7 : 8-dihydro-4-hydroxy-6- and -7-phenylpteridines (IV; R = Ph, R′ = H; R = H, R′ = Ph) respectively which were oxidised to the pteridines with alkaline permanganate. The last two compounds were also obtained by condensing 4 : 5-diamino-2-dimethylamino-6-hydroxypyrimidine with phenylglyoxal at pH 1 (6-phenyl compound) or 4 (7-phenyl compound). In the latter case, 4-amino-2-dimethylamino-6-hydroxy-5-phenacylideneaminopyrimidine (II; X = NMe_2, Y = OH, Z = N:CH·COPh) was first obtained and then cyclised to the pteridine by heating it with sodium hydroxide.

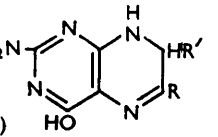
The 6- and the 7-phenyl compound were converted into the 2 : 4-bisdimethylamino-pteridines (III; X = Y = NMe_2, R = Ph, R′ = H; X = Y = NMe_2, R = H, R′ = Ph) by phosphorus oxychloride under reflux, the crude chloro-compounds being treated with alcoholic dimethylamine. From the 6-phenylpteridine some 4-ethoxy-compound (I; X = NMe_2, Y = EtO, R = Ph, R′ = H) was obtained also. The same bisdimethylamino-pteridines were obtained by condensing 4 : 5-diamino-2 : 6-bisdimethylaminopyrimidine (II; X = Y = NMe_2, Z = NH_2) with phenylglyoxal under the conditions used for the corresponding hydroxy-compounds; in this case though, the intermediate substance corresponding to the 7-phenyl compound was not isolated. As a further check on the identity of the products both 2 : 4-bisdimethylamino-compounds were converted into the corresponding 2-dimethylamino-4-hydroxy-compounds by hydrolysis with hydrochloric acid.

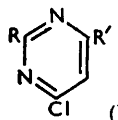
Although this series of transformations showed that condensation of phenylglyoxal could be directed to give predominantly one or the other of the two possible pteridines, it was considered unlikely that this would be possible with an α-diketone in which there is a

[10] Taylor and Cain, *J. Amer. Chem. Soc.*, 1952, **74**, 1644.

smaller difference in the reactivity of the keto-groups. The stepwise synthesis of such pteridines appeared essential in these cases.

Although both 4 : 6-dichloro-2-methylamino- and -2-dimethylamino-pyrimidine condensed smoothly with glycine ethyl ester to give the amines (V; R = NHMe or NMe_2, R′ = $NH{\cdot}CH_2{\cdot}CO_2Et$), no satisfactory products could be obtained with α-aminodeoxybenzoin.

(IV) 

 (V)

Because of the greater reactivity of the chlorine atoms in trichloropyrimidine, reaction of this substance with an α-amino-ketone appeared to offer a suitable starting point provided the two products could be separated. Trichloropyrimidine with ω-amino-ω-*p*-chlorophenyl-acetophenone gave a mixture which could not readily be separated but with alcoholic dimethylamine gave a readily separable mixture of amines (V; R = NMe_2, R′ = *p*-$C_6H_4Cl{\cdot}CHBz{\cdot}NH$ and *vice versa*). The subsequent stages in the conversion of the former into the diamine (I; X = Y = NMe_2, R = Ph, R′ = *p*-C_6H_4Cl) proceeded smoothly. In the reaction between trichloropyrimidine and aminodeoxybenzoin, the product (V; R = Cl, R′ = $Ph{\cdot}CHBz{\cdot}NH$) separated directly from the reaction mixture.

Experimental

2-*Dimethylamino*-4 : 6-*dihydroxy*-5-*nitropyrimidine*.—2-Dimethylamino-4 : 6-dihydroxy-pyrimidine (70 g.),[4] ground to pass a 30-mesh sieve, was added with stirring during 45 min. to a mixture of glacial acetic acid (280 c.c.) and nitric acid (*d* 1·5; 65 c.c.) at 20—25°. After a further 45 minutes' stirring the mixture was poured into water (1350 c.c.). The solid was separated, washed free from acid, and dried (81 g.). No suitable solvent could be found for crystallisation and the *nitro-compound* was analysed directly (Found: C, 36·1; H, 4·4; N, 27·7. $C_6H_8O_4N_4$ requires C, 36·0; H, 4·0; N, 28·0%).

4 : 6-*Dichloro*-2-*dimethylamino*-5-*nitropyrimidine*.—2-Dimethylamino-4 : 6-dihydroxy-5-nitropyrimidine (20 g.), phosphorus oxychloride (60 c.c.), and dimethylaniline (20 c.c.) were heated to 105° (bath-temperature) whereupon a vigorous reaction set in. When this had moderated heating was continued for 1 hr. After removal of the excess of phosphorus oxychloride under reduced pressure the residue was treated with ice (200 g.), then the suspension was extracted with ether (4 × 50 c.c.). The extract was dried ($MgSO_4$), filtered, and evaporated. The residue, crystallised from light petroleum (b. p. 60—80°) (yield, 3·7 g.), had m. p. 117—120°. The *compound* was purified for analysis by sublimation at 150°/19 mm. (Found: C, 30·6; H, 2·5; N, 23·6; Cl, 29·9. $C_6H_6O_2N_4Cl_2$ requires C, 30·4; H, 2·5; N, 23·6; Cl, 29·9%).

4-*Amino*-6-*chloro*-2-*dimethylamino*-5-*nitropyrimidine and* 4 : 6-*Diamino*-2-*dimethylamino*-5-*nitropyrimidine*.—4 : 6-Dichloro-2-dimethylamino-5-nitropyrimidine (14 g.), benzene (90 c.c.), and ammonia (*d* 0·880) (10 c.c.) were shaken overnight and filtered. The residue of the *diamine* (4·2 g.), after two crystallisations from dioxan, had m. p. 249—250° (Found: C, 36·6; H, 5·1; N, 42·5. $C_6H_{10}O_2N_6$ requires C, 36·6; H, 5·2; N, 42·75%). Evaporation of the filtrate gave a residue of indefinite m. p. from which the *monoamino-compound* (0·5 g.) was obtained by chromatography on alumina (120 g.) in benzene (30 c.c.) and crystallisation from ethyl acetate–light petroleum (b. p. 60—80°) and had m. p. 132° (Found: C, 33·0; H, 3·9; N, 32·6; Cl, 15·9. $C_6H_8O_2N_5Cl$ requires C, 33·1; H, 3·7; N, 32·2; Cl, 16·4%).

4 : 6-*Dihydroxy*-2-*methylaminopyrimidine*.—To a solution of sodium (91 g.) in methanol (2 l.) methylguanidine sulphate (509 g.) was added and the mixture heated under reflux for 30 min. with stirring. Ethyl malonate was then added and heating was continued for 6 hr. After cooling, the mixture was diluted with water (5 l.), treated with carbon, and filtered. Acidification to litmus with acetic acid precipitated the dihydroxypyrimidine (183 g.) immediately. After this had been collected the mother-liquors deposited a second product (15 g.), presumably 2-*amino*-1 : 4 : 5 : 6-*tetrahydro*-1-*methyl*-4 : 6-*dioxopyrimidine*, m. p. >360°, purified for analysis by dissolution in aqueous sodium hydroxide, treatment with charcoal, and reprecipitation with acetic acid (Found: C, 42·3; H, 5·3; N, 28·7. $C_5H_7O_2N_3$ requires C, 42·5; H, 5·0; N, 29·8%).

4 : 6-*Dichloro*-2-*methylaminopyrimidine*.—4 : 6-Dihydroxy-2-methylaminopyrimidine (93 g.)

and phosphorus oxychloride (510 c.c.) were heated under reflux for 1 hr. After filtration through sintered-glass the solution was poured on 32% aqueous sodium hydroxide (2250 c.c.) and ice. The solid which separated was washed with water and crystallised from methanol. The product (88 g.) had m. p. 164° undepressed on admixture with an authentic sample.[11]

4-Chloro-6-methoxy-2-methylaminopyrimidine.—4 : 6-Dichloro-2-methylaminopyrimidine (130 g.) was heated in a solution of sodium (168 g.) in methanol (570 c.c.) for 12 hr. The *ether* which separated on cooling was collected, washed with water, and crystallised from methanol; it (95 g.) had m. p. 153° (Found : C, 41·8; H, 4·7; N, 24·2; Cl, 20·3. $C_6H_8ON_3Cl$ requires C, 41·5; H, 4·6; N, 24·2; Cl, 20·5%).

4-Chloro-2-dimethylamino-6-methoxypyrimidine, m. p. 62° after sublimation (55°/0·1 mm.), was obtained similarly (81%) from 4 : 6-dichloro-2-dimethylaminopyrimidine at room temperature (Found : C, 44·7; H, 5·4; N, 22·5; Cl, 19·2. $C_7H_{10}ON_3Cl$ requires C, 44·8; H, 5·3; N, 22·4; Cl, 18·9%).

4-Chloro-6-hydroxy-2-methylaminopyrimidine.—4-Chloro-6-methoxy-2-methylaminopyrimidine (10 g.) was heated on the steam-bath for 30 min. with concentrated hydrochloric acid (50 c.c.). The *hydroxy-compound* which separated on cooling was collected and purified by dissolution in alkali, etc., as above, and had m. p. 265° (decomp.) (5·5 g.) (Found : C, 38·3; H, 4·1; N, 26·2. $C_5H_6ON_3Cl$ requires C, 37·6; H, 3·8; N, 26·3%).

4-Chloro-2-dimethylamino-6-hydroxypyrimidine, m. p. 217°, was obtained similarly (95%) from 4-chloro-2-dimethylamino-6-methoxypyrimidine (Found : C, 41·9; H, 4·9; N, 23·9; Cl, 21·0. $C_6H_8ON_3Cl$ requires C, 41·5; H, 4·6; N, 24·2; Cl, 20·5%).

2-Amino-4-dimethylamino-6-methylpyrimidine.—2-Amino-4-chloro-6-methylpyrimidine (28·7 g.) and dimethylamine (78 c.c. of a 19·5% w/v solution in ethanol) were heated at 110—120° for 17 hr. The diamine, crystallised from benzene, had m. p. 172° (16·5 g.) (Found : C, 55·8; H, 8·4; N, 37·1. $C_7H_{12}N_4$ requires C, 55·3; H, 7·9; N, 36·8%).

α-(2 : *4-Dichloro-6-pyrimidylamino*)*deoxybenzoin.*—α-Aminodeoxybenzoin hydrochloride (47 g.), dissolved in water (750 c.c.), was basified with ammonia at 0°. The precipitated base was collected, drained as dry as possible, added to trichloropyrimidine (35 g.) in ethanol (750 c.c.) and set aside at room temperature for 2 days. The *ketone* (12 g.) was collected and crystallised from ethanol; it had m. p. 165° (Found : C, 60·1; H, 3·8; N, 11·8; Cl, 19·9. $C_{18}H_{13}ON_3Cl_2$ requires C, 60·4; H, 3·6; N, 11·7; Cl, 19·85%).

ω-(*4-Chloro-2-dimethylamino-6-pyrimidylamino*)-ω-p-*chlorophenylacetophenone and* ω-(*4-Chloro-6-dimethylamino-2-pyrimidylamino*)-ω-p-*chlorophenylacetophenone.*—ω-Amino-ω-*p*-chlorophenylacetophenone hydrochloride (28·5 g.) was converted into the base and caused to react with trichloropyrimidine (9 g.) under the conditions given above. The crude product which could not be purified readily was heated under reflux for 3 hr. with dimethylamine in ethanol (10 c.c. of 19·5% w/v solution) and ethanol (10 c.c.). On evaporation of the solution to half its volume a solid, m. p. 75—95°, was obtained. Crystallisation and recrystallisation from methanol gave the *2-dimethylaminopyrimidine*, m. p. 151—152° (Found : C, 60·3; H, 4·8; N, 13·9; Cl, 17·5. $C_{20}H_{18}ON_4Cl_2$ requires C, 59·8; H, 4·5; N, 13·9; Cl, 17·7%). The *6-dimethylaminopyrimidine*, m. p. 181—182° (Found : C, 60·1; H, 4·7; N, 14·0%), was obtained by concentration of the mother-liquors and recrystallisation from ethanol. A small quantity of another substance, m. p. 239—240°, believed to be 2 : 5-di-*p*-chlorophenyl-3 : 6-diphenylpyrazine, was also obtained.

Derivatives of 2 : *4-Diamino-6-chloropyrimidine.*—(a) *From 2-amino*(*or substituted amino*)-*4* : *6-dichloropyrimidine. 2-Amino-4-chloro-6-dimethylaminopyrimidine.* 2-Amino-4 : 6-dichloropyrimidine (33 g.) was heated with dimethylamine in ethanol (175 c.c. of 19·5% w/v solution) for 3 hr. after the initial reaction had subsided. The *diamino-compound* (24 g.) which separated on cooling was collected, crystallised from methanol and then from benzene, and had m. p. 164—165° (Found : C, 41·9; H, 5·0; N, 32·5; Cl, 20·8. $C_6H_9N_4Cl$ requires C, 41·7; H, 5·2; N, 32·5; Cl, 20·5%).

The following were obtained similarly (in 70% yield) from the appropriate derivative of 2-amino-4 : 6-dichloropyrimidine and an ethanol solution of glycine ethyl ester :

Ethyl 4-chloro-2-methylamino-6-pyrimidylaminoacetate, m. p. 167° (Found : C, 43·6; H, 4·9; N, 22·8; Cl, 14·7. $C_9H_{13}O_2N_4Cl$ requires C, 44·2; H, 5·3; N, 22·9; Cl, 14·5%).

Ethyl 4-chloro-2-dimethylamino-6-pyrimidylaminoacetate, m. p. 121° (Found : C, 46·5; H, 5·6; N, 21·0; Cl, 14·2. $C_{10}H_{15}O_2N_4Cl$ requires C, 46·4; H, 5·8; N, 21·6; Cl, 13·7%).

[11] Winkelmann, *J. prakt. Chem.*, 1927, **115**, 292.

(b) *From* 2 : 4-*dichloro*-6-*methylaminopyrimidine*. 4-*Chloro*-2-*ethylamino*-6-*methylamino*-*pyrimidine*. 2 : 4-Dichloro-6-methylaminopyrimidine (36 g.), ethanol (200 c.c.), and aqueous ethylamine (50 g. of 70% w/w solution) were heated under reflux for 6 hr. After removal of the ethanol the mixture was diluted with water and extracted with ether. After drying, the ether was removed and the residue was dissolved in absolute ethanol (70 c.c.). Concentrated sulphuric acid (9 c.c.) was added until the mixture was acid to Congo-red; dry ether was then added to produce a permanent turbidity, the *diamine sulphate* separating (34 g.). After recrystallisation from ethanol-ether it had m. p. 148° (Found: C, 29·9; H, 5·0; N, 19·4; Cl, 12·5; S, 11·2. $C_7H_{11}N_4Cl,H_2SO_4$ requires C, 29·5; H, 4·6; N, 19·7; Cl, 12·45; S, 11·25%).

The following were obtained similarly: 4-*chloro*-2-*dimethylamino*-6-*methylaminopyrimidine*, m. p. 78° (from light petroleum) (Found: C, 45·5; H, 6·2; N, 30·6; Cl, 19·0. $C_7H_{11}N_4Cl$ requires C, 45·1; H, 5·9; N, 30·0; Cl, 19·0%); 4-*chloro*-2-*diethylamino*-6-*methylaminopyrimidine sulphate*, m. p. 148—149° (from ethanol-ether) (Found: C, 34·5; H, 5·6; N, 18·1; Cl, 11·6; S, 10·1. $C_9H_{15}N_4Cl,H_2SO_4$ requires C, 34·6; H, 5·4; N, 17·9; Cl, 11·4; S, 10·2%); 4-*chloro*-6-*methylamino*-2-*piperidinopyrimidine*, m. p. 118° (from methanol) (Found: C, 53·3; H, 6·8; N, 24·1; Cl, 15·5. $C_{10}H_{15}N_4Cl$ requires C, 53·0; H, 6·6; N, 24·7; Cl, 15·7%); 4-*chloro*-2-2'-*dimethylaminoethylamino*-6-*methylaminopyrimidine*, m. p. 99° (from ethyl acetate-light petroleum) (Found: C, 47·1; H, 6·9; N, 29·6; Cl, 15·5. $C_9H_{16}N_5Cl$ requires C, 47·1; H, 6·9; N, 30·5; Cl, 15·5%).

4-*Chloro*-5-p-*chlorophenylazo*-2-*dimethylamino*-6-*hydroxypyrimidine*.—To a solution of 4-chloro-2-dimethylamino-6-hydroxypyrimidine (17·5 g.) dissolved in water (500 c.c.) containing 2N-sodium hydroxide (60 c.c.) and sodium hydrogen carbonate (12·6 g.), a solution of *p*-chlorobenzenediazonium chloride (from 12·75 g. of *p*-chloroaniline) was added. After overnight stirring the *azo-compound* was collected, washed with water, ethanol, and ether, and crystallised from dioxan; it had m. p. 220—222° (decomp.) (20 g.) (Found: C, 46·4; H, 3·5; N, 22·7; Cl, 22·6. $C_{12}H_{11}ON_5Cl_2$ requires C, 46·2; H, 3·5; N, 22·5; Cl, 22·8%). 4-Chloro-5-*p*-chlorophenylazo-6-hydroxy-2-methylaminopyrimidine was obtained similarly but could not be purified without decomposition. The washed crude material was satisfactory for further use.

5-p-*Chlorophenylazo*-2-*dimethylamino*-4-*hydroxy*-6-*methylpyrimidine*.—M/40-*p*-Chlorobenzenediazonium chloride solution (500 c.c.) and crystalline sodium acetate (46 g.) were added with stirring to a solution of 2-dimethylamino-4-hydroxy-6-methylpyrimidine (3·8 g.) in water (500 c.c.). After 16 hr. the *azo-compound* was collected, washed, dried in air, and recrystallised from butanol, then having m. p. 216—217° (5·5 g.) (Found: C, 53·4; H, 4·7; N, 24·2. $C_{13}H_{14}ON_5Cl$ requires C, 53·5; H, 4·8; N, 24·1%).

2 : 6-*Diamino*-5-*arylazo*-4-*chloropyrimidines*.—The preparation of 4-*chloro*-5-p-*chlorophenylazo*-2 : 6-*bisdimethylaminopyrimidine* is typical. M/40-*p*-Chlorophenyldiazonium chloride (50 c.c.) and crystalline sodium acetate (40 g.) were added with stirring to a solution of 4-chloro-2 : 6-bisdimethylaminopyrimidine (5·0 g.) in acetic acid (70 c.c.) diluted with water (200 c.c.). The dark red oil which separated changed to a granular solid after 48 hours' stirring. The azo-compound was then collected, washed with water, and crystallised twice from ethanol; it (5 g.) had m. p. 91° (Found: C, 49·7; H, 4·6; N, 24·7; Cl, 20·9. $C_{14}H_{16}N_6Cl_2$ requires C, 49·6; H, 4·7; N, 24·8; Cl, 20·9%). Details of other compounds in this series are given in Table 1 and in B.P. 763,041.

2 : 4 : 6-*Triamino*-5-*arylazopyrimidine Derivatives*.—The preparation of 4 : 6-*diamino*-5-p-*chlorophenylazo*-2-*dimethylaminopyrimidine* is typical. 4-Amino-6-chloro-5-*p*-chlorophenylazo-2-dimethylaminopyrimidine (2 g.) and saturated alcoholic ammonia (40 c.c.) were heated at 150—160° for 36 hr. The triamino-compound (1·75 g.) which separated on cooling was crystallised from butanol; it had m. p. 272—273° (Found: C, 49·1; H, 4·8; Cl, 12·2. $C_{12}H_{14}N_7Cl$ requires C, 49·4; H, 4·8; Cl, 12·2%). The *hydrochloride* was obtained as follows: *p*-chlorobenzenediazonium chloride [from *p*-chloroaniline (6·5 g.), water (60 c.c.), concentrated hydrochloric acid (11 c.c.), and sodium nitrite (3·5 g.)] was added with stirring to 4 : 6-diamino-2-dimethylaminopyrimidine (7·5 g.) in glacial acetic acid (70 c.c.). The product separated rapidly and sufficient 50% acetic acid was added to keep the mixture mobile. The hydrochloride (14·1 g.) was collected after 4 hr., washed with water and ethanol; it had m. p. 301° (decomp.) when crystallised from 80% formic acid (Found: C, 44·6; H, 4·4; N, 29·9; Cl, 21·6. $C_{12}H_{14}N_7Cl,HCl$ requires C, 44·0; H, 4·6; N, 29·9; Cl, 21·5%). The free base identical with the above was obtained by trituration with ammonia.

Table 2 gives details of substances containing an unsubstituted 4-amino-group prepared by reaction of the corresponding 4-chloro-compounds (I) with ammonia or the appropriate amine. Further examples are given in B.P. 763,042.

5-p-*Chlorophenylazo-4-dimethylamino-2 : 6-bismethylaminopyrimidine.*—4-Chloro-5-*p*-chlorophenylazo-2 : 4-bismethylaminopyrimidine (5 g.), dimethylformamide (100 c.c.), and 10% ethanolic ammonia (20 c.c.) were heated at 60° for 64 hr. The *amine* which separated on addition of water crystallised from ethanol and had m. p. 145° (4 g.) (Found : C, 52·4; H, 5·5. $C_{14}H_{18}N_7Cl$ requires C, 52·6; H, 5·5%). The same product (m. p. and mixed m. p.) was obtained by reaction between 4-chloro-5-*p*-chlorophenylazo-2 : 6-bismethylaminopyrimidine and methanolic dimethylamine under standard conditions.

2-*Amino*-5-p-*chlorophenylazo-4-dimethylamino-6-methylaminopyrimidine*, m. p. 192° (Found : C, 51·4; H, 5·5. $C_{13}H_{16}N_7Cl$ requires C, 51·1; H, 5·2%), was obtained by reaction between 2-amino-4-chloro-5-*p*-chlorophenylazo-6-methylaminopyrimidine and alcoholic ammonia in dimethylformamide.

5-p-*Chlorophenylazo-2 : 4 : 6-trismethylaminopyrimidine*, m. p. 155° (Found : C, 51·4; H, 5·3; N, 31·3; Cl, 11·6. $C_{13}H_{16}N_7Cl$ requires C, 51·1; H, 5·3; N, 31·1; Cl, 11·6%), was obtained from 4-chloro-5-*p*-chlorophenylazo-2 : 6-bismethylaminopyrimidine and methylamine in dimethylformamide.

Tetra-aminopyrimidines.—The following procedure for the preparation of 2 : 4 : 5-*triamino-4-methylaminopyrimidine* is typical: 2 : 4-Diamino-5-*p*-chlorophenylazo-6-methylaminopyrimidine (5 g.) in ethanol (75 c.c.) was reduced by hydrogen in presence of Raney nickel (initial pressure 47 atm.) at 90—95° for 5 hr. The mixture was then acidified with acetic acid (4 c.c.) and filtered through Hyflo Supercel, and the residue washed with water. The combined filtrate and washings were evaporated to dryness under reduced pressure in an atmosphere of nitrogen. The brown residue was triturated with ether, filtered, washed with more ether to remove *p*-chloroaniline, dissolved in water (10 c.c.), and acidified to Congo-red with sulphuric acid. The *sulphate* was precipitated by addition of ethanol and crystallised from water.

No satisfactory analytical results could be obtained for 2 : 5-diamino-6-diethylamino-4-dimethylaminopyrimidine oxalate, m. p. 221° (decomp.), although it condensed normally with benzil to give the corresponding diphenylpteridine.

Details of other compounds prepared by this method are given in Table 3 and in B.P. 763,120.

5-*Arylazopyrimidylamino-aldehydes and -ketones and Derivatives.*—5-p-*Chlorophenylazo-2-dimethylamino-4-methylamino-6-pyrimidylaminoacetaldehyde diethyl acetal.* Aminoacetaldehyde diethyl acetal (15 g.) and 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-4-methylaminopyrimidine (17·5 g.) were heated under reflux for 24 hr. in dioxan (250 c.c.). The residue obtained on evaporation was triturated with ethanol and filtered. The *acetal* (10 g.), crystallised from light petroleum (b. p. 60—80°), had m. p. 95° (Found : C, 54·3; H, 6·4; N, 24·0; Cl, 8·0. $C_{19}H_{28}O_2N_7Cl$ requires C, 54·1; H, 6·7; N, 23·3; Cl, 8·4%).

α-5-p-*Chlorophenylazo-2 : 4-bisdimethylamino-6-pyrimidylamino-α-phenylacetaldehyde Dimethyl Acetal.*—α-Aminophenylacetaldehyde dimethyl acetal (11 g.) and 4-chloro-5-*p*-chlorophenylazo-2 : 6-bisdimethylaminopyrimidine in dioxan (250 c.c.) were heated under reflux for 4 hr. After removal of the solvent, the *acetal* (1·9 g.) was crystallised from butanol; it had m. p. 151° (Found : C, 59·5; H, 6·3; Cl, 7·7. $C_{24}H_{30}O_2N_7Cl$ requires C, 59·6; H, 6·2; Cl, 7·4%).

α-(5-p-*Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)-α-phenylacetaldehyde dimethyl acetal*, m. p. 242° (from butanol), was obtained similarly from 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-6-hydroxypyrimidine (Found : C, 58·0; H, 5·6; N, 18·4; Cl, 7·8. $C_{22}H_{25}O_3N_6Cl$ requires C, 57·8; H, 5·5; N, 18·4; Cl, 7·8%).

5-p-*Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylaminoacetone.*—Aminoacetone semicarbazone hydrochloride (11 g.) was stirred for 2 hr. with a solution of cold sodium ethoxide (from sodium, 1·5 g., and ethanol, 60 c.c.), 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-6-hydroxypyrimidine (9·3 g.) in dimethylformamide (140 c.c.) was then added, and stirring was continued for a further 15 hr. The semicarbazone (11 g.), m. p. 243°, was collected, washed well with water and ethanol, and dissolved in glacial acetic acid (25 c.c.) and 2N-hydrochloric acid (150 c.c.). After being kept overnight the mixture was filtered and evaporated to dryness. The *hydrochloride* (6·6 g.), crystallised from ethanol, had m. p. 217° (Found : C, 46·6; H, 4·9; N, 21·3. $C_{15}H_{17}O_2N_6Cl,HCl$ requires C, 46·8; H, 4·7; N, 21·8%).

The following were obtained similarly :

ω-(5-p-*Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)acetophenone hydrochloride monohydrate*, m. p. 229° (from ethanol) (Found: C, 51·4; H, 4·7; N, 18·0; Cl, 15·4. $C_{20}H_{19}O_2N_6Cl,HCl,H_2O$ requires C, 51·6; H, 4·7; N, 18·0; Cl, 15·3%); *semicarbazone*, m. p. 263° (decomp.) (from dimethylformamide–ethanol) (Found: C, 53·5; H, 4·9; N, 28·0; Cl, 7·7. $C_{21}H_{22}O_2N_9Cl$ requires C, 53·9; H, 4·7; N, 27·0; Cl, 7·6%).

4-*Chloro*-ω-(5-p-*chlorophenylazo-4-hydroxy-2-methylamino-6-pyrimidylamino)acetophenone hydrochloride*, m. p. 258° (decomp.) (Found: C, 48·8; H, 3·8; N, 17·1. $C_{19}H_{16}O_2N_6Cl_2,HCl$ requires C, 48·8; H, 3·6; N, 17·9%); *semicarbazone*, m. p. 264° (from dimethylformamide) (Found: C, 49·3; H, 3·9. $C_{20}H_{19}O_2N_9Cl_2$ requires C, 49·2; H, 3·9%).

4-*Chloro*-ω-(5-p-*chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)acetophenone*, m. p. 244° (decomp.) (from dimethylformamide–ethanol) (Found: C, 54·2; H, 4·0; N, 18·8; Cl, 16·0. $C_{20}H_{18}O_2N_6Cl_2$ requires C, 53·9; H, 4·0; N, 18·9; Cl, 16·0%); *semicarbazone*, m. p. 255° (decomp.) (from dimethylformamide–ethanol) (Found: C, 50·7; H, 4·3; N, 24·7; Cl, 14·6. $C_{21}H_{21}O_2N_9Cl_2$ requires C, 50·2; H, 4·2; N, 25·1; Cl, 14·1%).

α-(4-*Chloro*-5-p-*chlorophenylazo-2-dimethylamino-6-pyrimidylamino)deoxybenzoin*.—α-(2 : 4-Dichloro-6-pyrimidylamino)deoxybenzoin (17·5 g.) and 2·5M-ethanolic dimethylamine (60 c.c.) were heated under reflux for 3 hr., and the solid which separated on cooling (17 g.; m. p. 178—183°) was collected and dissolved in acetic acid (200 c.c.) together with crystalline sodium acetate (19 g.). To this solution *p*-chlorobenzenediazonium chloride [from *p*-chloroaniline (6 g.), sodium nitrate (3·4 g.), concentrated hydrochloric acid (10 c.c.), and water (34 c.c.)] was added. After four days' stirring the *azo-compound* was collected, washed with water and ethanol, and crystallised from butanol, then having m. p. 254° (decomp.) (10 g.) (Found: C, 61·8; H, 4·1; N, 16·9; Cl, 14·5. $C_{26}H_{22}ON_6Cl_2$ requires C, 61·8; H, 4·4; N, 16·7; Cl, 14·1%).

α-(5-p-*Chlorophenylazo*-2 : 4-*bisdimethylamino-6-pyrimidylamino)deoxybenzoin*.—The above chloropyrimidine (10 g.) was heated under reflux for 20 hr. with 2·5M-ethanolic dimethylamine (340 c.c.). The *diamino-compound* (5·5 g.) which separated on cooling crystallised from ethanol and had m. p. 179° (Found: C, 65·7; H, 5·4; N, 19·2; Cl, 7·4. $C_{28}H_{28}ON_7Cl$ requires C, 65·4; H, 5·5; N, 19·1; Cl, 6·9%).

The following were obtained similarly: ω-p-*chlorophenyl*-ω-(4-*chloro*-5-p-*chlorophenylazo-2-dimethylamino-6-pyrimidylamino)acetophenone*, m. p. 248° (decomp.) (from butanol) (Found: C, 58·0; H, 3·7; Cl, 19·8. $C_{26}H_{21}ON_6Cl_3$ requires C, 57·8; Cl, 3·9; H, 19·8%), and ω-p-*chlorophenyl*-ω-(5-p-*chlorophenylazo-2-dimethylamino-6-pyrimidylamino)acetophenone*, m. p. 196° (from butanol) (Found: C, 60·5; H, 5·1; N, 19·0. $C_{27}H_{25}ON_7Cl_2$ requires C, 60·7; H, 4·7; N, 18·4%).

4-*Chloro*-ω-(5-p-*chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)-ω-phenylacetophenone*.—4-Chloro-ω-phenylacetophenone hydrochloride (14·1 g.) was dissolved in water (800 c.c.) and basified with ammonia. The free amino-ketone was collected, dried over phosphoric oxide, and added to a solution of 4-chloro-5-*p*-chlorophenylazo-2-dimethylamino-4-hydroxypyrimidine (7·8 g.) in dimethylformamide (400 c.c.). After 24 hours' stirring at room temperature the separated solid was collected and crystallised from dimethylformamide–ethanol. The *ketone* (7 g.) had m. p. 239° (Found: C, 60·0; H, 4·8; N, 16·4; Cl, 13·5. $C_{26}H_{22}O_2N_6Cl_2$ requires C, 59·9; H, 4·2; N, 16·1; Cl, 13·6%).

Ethyl 4-*Amino*-5-p-*chlorophenylazo-2-dimethylamino-6-pyrimidylaminoacetate*.—To a solution of glycine ethyl ester (5·6 g.) in ethanol (100 c.c.), 4-amino-6-chloro-5-*p*-chlorophenylazo-2-dimethylaminopyrimidine (5·5 g.) in dioxan (150 c.c.) was added and the whole heated under reflux for 8 hr. Unchanged pyrimidine which separated on cooling was filtered off and the filtrate diluted with water. The precipitated solid was collected, crystallised from ethyl acetate–light petroleum (b. p. 60—80°), and recrystallised from ethanol, to give the *ester* (2 g.), m. p. 139° (Found: C, 50·9; H, 5·0; N, 26·1. $C_{16}H_{20}O_2N_7Cl$ requires C, 50·9; H, 5·3; N, 26·0%). Further examples of compounds of this type are given in B.P. 763,043. *Ethyl* 5-p-*chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylaminoacetate*, m. p. 218° (Found: C, 50·7; H, 5·2; N, 22·6; Cl, 9·6. $C_{16}H_{19}O_3N_6Cl$ requires C, 50·7; H, 5·0; N, 22·1; Cl, 9·4%), was prepared similarly.

Ethyl 4-*Chloro*-5-p-*chlorophenylazo-2-methylamino-6-pyrimidylaminoacetate*.—*p*-Chlorobenzenediazonium chloride (17 c.c. of 0·01M-solution) was added to a solution of ethyl 4-chloro-2-methylamino-6-pyrimidylaminoacetate (2·5 g.) in 50% acetic acid (160 c.c.) containing crystalline sodium acetate (10 g.). After 12 hours' stirring the *azo-compound* was collected and crystallised from butanol; it (2 g.) had m. p. 218° (Found: C, 46·7; H, 4·4; N, 22·6.

$C_{15}H_{16}O_2N_6Cl_2$ requires C, 47·0; H, 4·2; N, 21·9%). *Ethyl 4-chloro-5-p-chlorophenylazo-2-dimethylamino-6-pyrimidylaminoacetate*, m. p. 214° (from dioxan) (Found: C, 48·4; H, 4·5; N, 20·7; Cl, 18·4. $C_{16}H_{18}O_2N_6Cl_2$ requires C, 48·3; H, 4·6; N, 21·1; Cl, 17·9%), was obtained similarly.

7 : 8-*Dihydropteridines*.—2-*Dimethylamino*-7 : 8-*dihydro-4-hydroxy-6-phenylpteridine*. ω-(5-*p*-Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)acetophenone (1·2 g.) in glacial acetic acid (60 c.c.) was treated at the b. p. in an atmosphere of nitrogen with zinc dust (1·1 g.). The mixture was heated for a further 1 hr., then filtered hot. Removal of the solvent under reduced pressure gave an oil which was triturated with ether and filtered. The residue after being washed with ether was dissolved in dilute hydrochloric acid, and the solution evaporated under reduced pressure. The hydrochloride was triturated with ethyl acetate, collected, and dissolved in water. Basification of this solution with ammonia gave the base (0·1 g.) which after crystallisation from ethanol as the *hemihydrate* had m. p. 311° (Found: C, 60·1; H, 5·9; N, 25·0. $C_{14}H_{15}ON_5,\frac{1}{2}H_2O$ requires C, 60·4; H, 5·8; N, 25·2%), $\lambda_{max.}$ 270 mμ ($E^{1\%}_{1\,cm.}$ 750 in N-HCl). The following were made similarly: 2 : 4-*bisdimethylamino*-7 : 8-*dihydro*-6 : 7-*diphenylpteridine*, m. p. 278° (Found: N, 20·0; Cl, 8·8. $C_{22}H_{25}N_6Cl$ requires N, 20·6; Cl, 8·7%); 7-*p*-chlorophenyl-2-dimethylamino-7 : 8-dihydro-4-methylamino-6-phenylpteridine, m. p. 267—269° (although not obtained analytically pure it was oxidised satisfactorily to the pteridine, see below); 6-p-*chlorophenyl-2-dimethylamino*-7 : 8-*dihydro-4-hydroxy-7-phenylpteridine hydrochloride*, m. p. 346° (Found: C, 57·4; H, 5·0. $C_{20}H_{19}ON_5Cl,HCl$ requires C, 57·7; H, 4·6%).

6-p-*Chlorophenyl-2-dimethylamino*-7 : 8-*dihydro-4-hydroxypteridine*. 4-Chloro-ω-(5-*p*-chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)acetophenone (2·95 g.) in dimethylformamide (300 c.c.) was shaken in hydrogen (initial presssure 2 atm.) for 2 hr. in presence of Raney nickel (5 g.). After removal of the catalyst and solvent the residue was triturated with ether and the solid collected. Crystallisation and recrystallisation from aqueous dimethylformamide gave the *pteridine* (1·8 g.), m. p. 370° (Found: C, 55·0; H, 4·3; N, 22·5; Cl, 11·8. $C_{14}H_{14}ON_5Cl$ requires C, 55·4; H, 4·6; N, 23·1; Cl, 11·8%).

In the following case the dihydro-compound was oxidised during manipulation:

2-*Dimethylamino-4-hydroxy-7-phenylpteridine*. α-(5-*p*-Chlorophenylazo-2-dimethylamino-4-hydroxy-6-pyrimidylamino)-α-phenylacetaldehyde dimethyl acetal (5 g.) was treated in glacial acetic acid (100 c.c.) with concentrated hydrochloric acid (10 c.c.). After 1 hr. at room temperature water was added and the precipitate collected. The crude aldehyde was reduced directly with hydrogen in the presence of Raney nickel as above. After removal of the catalyst and solvent the oily residue was mixed with glacial acetic acid (10 c.c.) and triturated twice with ether. The oil remaining was dissolved in 2N-hydrochloric acid; the white solid which separated after a short while was suspended in water and treated with dilute ammonia until the mixture was just alkaline to Brilliant Yellow. The *pteridine* (2·3 g.) was collected and crystallised from aqueous dimethylformamide, having m. p. 326° (decomp.) (Found: C, 62·9; H, 4·9; N, 25·8. $C_{14}H_{13}ON_5$ requires C, 62·9; H, 4·9; N, 26·2%). $\lambda_{max.}$ 355 mμ ($E^{1\%}_{1\,cm.}$ 800 in N-HCl).

4-*Amino-2-dimethylamino-6-hydroxy-5-phenacylideneaminopyrimidine*.—4 : 5-Diamino-2-dimethylamino-6-hydroxypyrimidine sulphate (10·7 g.), phenylglyoxal monohydrate (6·1 g.), crystalline sodium acetate (27 g.), and 50% (v/v) ethanol (400 c.c.) were heated under reflux for 15 min. The solid which separated on cooling was collected and crystallised from ethanol, to give the *aldimine* (7·5 g.), m. p. 267° (decomp.) (Found: C, 59·1; H, 5·5; N, 24·2. $C_{14}H_{15}O_2N_5$ requires C, 59·0; H, 5·3; N, 24·5%).

2-*Amino*-3-N-*methylcarbamoyl*-5 : 6-*diphenylpyrazine*.—Methyl 3-amino-5 : 6-diphenylpyrazine-2-carboxylate (1 g.) was heated for 16 hr. at 160° with methylamine (10 g.) in ethanol (55 c.c.). After removal of the solvent the residue was crystallised from ethanol, to give the *amide* (0·5 g.), m. p. 197—198° (Found: C, 71·0; H, 5·4; N, 18·5. $C_{18}H_{16}ON_4$ requires C, 71·1; H, 5·3; N, 18·4%).

2 : 4-*Disubstituted Pteridines*.—These have been made by a number of methods of which the examples given are typical; details of other compounds are given in Table 4; additional examples are recorded in B.P. 763,044.

(1) *Oxidation of a* 7 : 8-*dihydropteridine*. 2-*Dimethylamino-4-hydroxy-6-phenylpteridine*. To 2-dimethylamino-7 : 8-dihydro-4-hydroxy-6-phenylpteridine (0·2 g.) in 0·5N-sodium hydroxide (50 c.c.), potassium permanganate (0·1 g.) in water (15 c.c.) was added with stirring during 15 min. After a further 1·5 hr., ethanol was added to destroy excess of permanganate, and the manganese dioxide was removed by filtration and washed. The filtrate and washings were

TABLE 1. 2 : 6-*Diamino-5-arylazo-4-chloropyrimidines* (as III; Z = Cl).

X	Y	Ar	M. p.	Solvent *	Yield (%)	Found (%) C	H	N	Cl	Formula	Required (%) C	H	N	Cl
NH_2	NHMe	p-C_6H_4Cl	255°	DMF	47	44·4	3·3	28·0	—	$C_{11}H_{10}N_6Cl_2$	44·4	3·4	28·3	—
NH_2	NMe_2	,,	204	DMF–EtOH	65	46·3	3·8	27·4	—	$C_{12}H_{12}N_6Cl_2$	46·3	3·9	27·0	—
NHMe	NH_2	,,	272 d	DMF	90	44·4	3·5	—	24·1	$C_{11}H_{10}N_6Cl_2$	44·4	3·4	—	23·9
NHMe	NHMe	,,	272	DMF–MeOH	95	46·4	3·8	27·4	22·9	$C_{12}H_{12}N_6Cl_2$	46·3	3·9	27·0	22·8
NHEt	NHMe	,,	214	BuOH	75	48·0	3·8	25·9	21·1	$C_{13}H_{14}N_6Cl_2$	48·0	4·3	25·8	21·9
NMe_2	NH_2	,,	229	BuOH	90	45·9	3·7	27·2	22·6	$C_{12}H_{12}N_6Cl_2$	46·3	3·9	27·0	22·8
NMe_2	NHMe	Ph	163	EtOH	78	53·7	5·2	28·9	—	$C_{13}H_{15}N_6Cl$	54·0	5·1	28·2	—
NMe_2	NHMe	p-C_6H_4Cl	183	BuOH	90	47·8	4·2	26·0	21·7	$C_{13}H_{14}N_6Cl_2$	48·0	4·3	25·8	21·9
$Me_2N{\cdot}[CH_2]_2{\cdot}NH$	NHMe	,,	158	EtOH	50	49·6	5·3	26·1	19·0	$C_{15}H_{19}N_7Cl_2$	49·1	4·9	26·7	19·3

* DMF = dimethylformamide.

TABLE 2. 2 : 4 : 6-*Triamino-5-*p*-chlorophenylazopyrimidines* (III; Z = NH_2).

X	Y	M. p.	Solvent *	Starting material: I; Y =	Yield (%)	Found (%) C	H	N	Cl	Formula	Required (%) C	H	N	Cl
NH_2	NHMe	213°	BuOH	NH_2, NHMe	40, 80	47·9	4·1	34·4	—	$C_{11}H_{12}N_7Cl$	47·6	4·3	35·3	—
NH_2	NMe_2	205	DMF–H_2O	NH_2	96	49·9	5·0	33·5	11·7	$C_{12}H_{14}N_7Cl$	49·5	4·8	33·6	12·2
NH_2	$Et_2N{\cdot}[CH_2]_3{\cdot}NH$	139	EtOH–H_2O	NH_2	44	54·8	6·9	29·4	9·0	$C_{17}H_{26}N_8Cl$	54·5	7·0	29·9	9·5
NHMe	NH_2	241	BuOH	NH_2	70	47·7	4·6	35·2	—	$C_{11}H_{12}N_7Cl$	47·6	4·3	35·3	—
NHMe	NHMe	197	EtAc	NH_2, NHMe	85, 92	49·8	4·8	33·6	12·5	$C_{12}H_{14}N_7Cl$	49·5	4·8	33·6	12·2
NHMe	NMe_2	184	DMF–H_2O	NH_2 †	90, 79 †	51·6	5·5	32·0	—	$C_{13}H_{16}N_7Cl$	51·1	5·2	32·1	—
NHEt	NHMe	161	BuOH	NHMe	80	51·1	5·2	31·7	11·9	$C_{13}H_{16}N_7Cl$	51·1	5·2	32·1	11·6
NMe_2	NHMe	193	BuOH	NMHe	90	51·6	5·1	32·3	11·8	$C_{13}H_{16}N_7Cl$	51·1	5·2	32·1	11·6
NMe_2	NMe_2	203	BuOH	NH_2, NMe_2	95, 93	52·7	6·0	30·1	11·3	$C_{14}H_{18}N_7Cl$	52·6	5·6	30·7	11·1
NMe_2	$[CH_2]_5{>}N$	175	BuOH	NH_2	86	56·7	5·5	27·7	10·4	$C_{17}H_{22}N_7Cl$	56·7	6·1	27·3	9·9
NMe_2	$O{<}[CH_2]_4{>}N$	183	BuOH	NH_2	91	52·9	5·5	27·4	9·8	$C_{16}H_{20}ON_7Cl$	53·1	5·5	27·1	9·8
NMe_2	$Et_2N{\cdot}[CH_2]_2{\cdot}NH$	150	60—80° Pet	NH_2	44	55·5	6·7	28·8	9·1	$C_{18}H_{27}N_8Cl$	55·3	6·9	28·7	9·1
$Me_2N{\cdot}[CH_2]_2{\cdot}NH$	NHMe	144	100—120° Pet	NHMe	90	52·4	6·3	31·9	10·3	$C_{15}H_{21}N_8Cl$	51·7	6·0	32·1	10·2

* DMF = dimethylformamide; Pet = light petroleum of stated b. p. † Prepared by direct reaction of (I; Y = NH_2) with alcoholic dimethylamine and also from (I; Y = NH_2) and ammonia in dimethylformamide.

TABLE 3. *Tetra-aminopyrimidines* (II; Z = NH_2).

X	Y	M. p.*	Solvent	Yield (%)	Found (%) C	H	N	S	Formula	Required (%) C	H	N	S
NH_2	NHMe	250°d	H_2O	89	27·2	6·0	37·3	7·2	$C_5H_{10}N_6,\frac{1}{2}H_2OSO_4,H_2O$	27·2	5·9	38·0	7·2
NH_2	NMe_2	209	H_2O–EtOH	48	26·3	5·5	—	11·1	$C_6H_{12}N_6,H_2SO_4,\frac{1}{2}H_2O$	26·2	5·5	—	11·6
NHMe	NH_2	255d	H_2O	75	23·7	4·8	31·8	12·3	$C_5H_{10}N_6,H_2SO_4$	23·8	4·8	33·3	12·7
NHMe	NHMe	259	H_2O–EtOH	80	26·3	5·9	30·4	11·0	$C_6H_{12}N_6,H_2SO_4,\frac{1}{2}H_2O$	26·2	5·5	30·5	11·6
NHMe	NMe_2	193	H_2O–EtOH	65	29·1	5·8	28·6	10·5	$C_7H_{14}N_6,H_2SO_4,\frac{1}{2}H_2O$	29·1	5·9	29·1	11·1
NHEt	NHMe	293d	H_2O–EtOH	49	28·4	6·1	28·4	—	$C_7H_{14}N_6,H_2SO_4,H_2O$	28·2	6·0	28·2	—
NMe_2	NH_2	314d	H_2O	58	27·3	5·4	31·2	11·9	$C_6H_{12}N_6,H_2SO_4$	27·1	5·3	31·6	12·1
NMe_2	NHMe	273d	H_2O	64	29·7	5·8	30·5	11·6	$C_7H_{14}N_6,H_2SO_4$	30·0	5·7	30·0	11·4
NMe_2	NMe_2	182d	EtOH	38	29·6	6·3	27·0	9·6	$C_8H_{16}N_6,H_2SO_4,\frac{1}{2}H_2O$	29·9	6·5	26·2	10·0
NMe_2	$[CH_2]_5{>}N$	208d	H_2O–EtOH	33	35·0	6·2	22·2	12·0	$C_{11}H_{20}N_6,1{\cdot}5H_2SO_4$	34·5	6·0	21·9	12·5
NMe_2	$O{<}[CH_2]_4{>}N$	194d	H_2O–EtOH	57	35·7	5·7	—	9·3	$C_{10}H_{18}ON_6,H_2SO_4$	35·7	6·0	—	9·5

* d = with decomp.

TABLE 4. 2 : 4-*Disubstituted pteridines* (I).

X	Y	R	R′	M. p.*	Solvent †	Prep.	Yield (%)	Found (%) C	H	N	Cl	Formula	Required (%) C	H	N	Cl
NH_2	NHMe	H	H	248°	H_2O	2*c*	26	47·8	4·2	47·5	—	$C_7H_8N_6$	47·7	4·5	47·7	—
NH_2	NHMe	Ph	Ph	272	EtOH	2*c*, 3	73, 5	69·4	4·9	24·8	—	$C_{19}H_{16}N_6$	69·5	4·9	25·6	—
NH_2	NMe_2	Ph	Ph	322 d	DMF	2*c*	63	69·4	5·5	24·3	—	$C_{20}H_{18}N_6$	70·1	5·5	24·6	—
NH_2	$Et_2N{\cdot}[CH_2]_3{\cdot}NH$	Ph	Ph	201 ‡	EtOH	2*c*	50	70·1	6·5	23·6	—	$C_{25}H_{29}N_7$	70·3	6·8	23·0	—
NHMe	OH	Ph	H	356 d [1]	DMF	2*b*	75	61·0	4·6	28·0	—	$C_{13}H_{11}ON_5$	61·7	4·4	27·7	—
NHMe	OH	H	Ph	387 d	DMF	2*a*, 4	80, 52	61·7	4·4	27·3	—	$C_{13}H_{11}ON_5$	61·7	4·4	27·7	—
NHMe	OH	*p*-C_6H_4Cl	H	370 d	DMF–EtOH	1, 2*b*	50, 26	54·7	3·6	23·6	13·2	$C_{13}H_{10}ON_5Cl$	54·3	3·5	24·1	12·4
NHMe	OH	H	*p*-C_6H_4Cl	363 d	DMF	2*a*, 4	65, 80	53·9	3·8	23·2	11·7	$C_{13}H_{10}ON_5Cl$	54·3	3·5	24·1	12·4
NHMe	OH	Ph	Ph	365 d	DMF	4	80	69·4	4·7	22·0	—	$C_{19}H_{15}ON_5$	69·3	4·6	22·0	—
NHMe	NH_2	H	H	242	H_2O	2*c*	72	47·4	4·4	47·7	—	$C_7H_8N_6$	47·7	4·5	47·7	—
NHMe	NH_2	Me	Me	281	EtOH	2*c*	51	53·1	6·1	41·3	—	$C_9H_{12}N_6$	52·9	5·9	41·2	—
NHMe	NH_2	Ph	Ph	307	DMF	2*c*	75	69·3	5·5	25·8	—	$C_{19}H_{16}N_6$	69·5	4·9	25·6	—
NHMe	NHMe	H	H	214	EtOH	2*c*	50	50·8	5·6	44·0	—	$C_8H_{10}N_6$	50·5	5·3	44·2	—
NHMe	NHMe	Me	Me	266	EtOH	2*c*	28	54·9	6·9	38·2	—	$C_{10}H_{14}N_6$	55·1	6·4	38·5	—
NHMe	NHMe	Ph	H	264	DMF	3	32	63·3	5·4	31·4	—	$C_{14}H_{14}N_6$	63·2	5·2	31·6	—
NHMe	NHMe	H	Ph	256 [2]	MeOH	2*b*	30	63·3	5·5	31·2	—	$C_{14}H_{14}N_6$	63·2	5·2	31·6	—
NHMe	NHMe	H	*p*-C_6H_4Cl	294 [3]	DMF	2*b*	25	55·6	4·4	27·9	11·5	$C_{14}H_{13}N_6Cl$	55·9	4·3	28·0	11·8
NHMe	NHMe	Ph	Ph	262	DMF–EtOH	2*c*	49	70·3	5·3	24·6	—	$C_{20}H_{18}N_6$	70·1	5·3	24·6	—
NHMe	NHMe	*o*-C_6H_4Cl	*o*-C_6H_4Cl	265	BuOH	2*c*	22	58·8	3·2	—	—	$C_{20}H_{16}N_6Cl_2$	58·4	3·9	20·4	17·3
NHMe	NHMe	*m*-C_6H_4Cl	*m*-C_6H_4Cl	256	MeOH	2*c*	31	58·3	3·8	20·1	17·1	$C_{20}H_{16}N_6Cl_2$				
NHMe	NHMe	*p*-C_6H_4Cl	*p*-C_6H_4Cl	323	DMF	2*c*	63	58·5	4·0	20·6	17·2	$C_{20}H_{16}N_6Cl_2$				
NHMe	NHMe	*p*-$MeO{\cdot}C_6H_4$	*p*-$MeO{\cdot}C_6H_4$	259	EtOH	2*c*	24	65·1	5·4	20·9	—	$C_{22}H_{22}O_2N_6$	65·7	5·5	20·9	—
NHMe	NHMe	3 : 4-$CH_2O_2{:}C_6H_3$	3 : 4-$CH_2O_2{:}C_6H_3$	297	EtOH–DMF	2*c*	28	60·9	4·3	19·5	—	$C_{22}H_{18}O_4N_6$	61·4	4·2	19·5	—
NHMe	NHMe	9 : 10-Phenanthrylene		311	DMF	2*c*	66	70·5	4·7	24·4	—	$C_{20}H_{16}N_6$	70·6	4·7	24·7	—
NHMe	NHMe	7 : 8-Acenaphthylene		307	DMF	2*c*	40	65·9	5·0	25·9	—	$C_{18}H_{14}N_6,H_2O$	65·1	4·8	25·3	—
NHMe	NHMe	2-Furyl	2-Furyl	218	EtOAc	2*c*	24	59·6	4·2	25·7	—	$C_{16}H_{14}O_2N_6$	59·6	4·4	26·1	—
NHMe	NHMe	2 : 3-Indolo		338	DMF	2*c*	75	58·7	5·0	33·9	—	$C_{14}H_{13}N_7,\frac{1}{2}H_2O$	58·3	4·9	34·0	—
NHMe	NMe_2	Ph	Ph	306	DMF	2*c*	60	70·4	5·6	24·1	—	$C_{21}H_{20}N_6$	70·8	5·6	23·6	—
NHEt	NHMe	Ph	Ph	249	EtOH	2*c*	21	70·7	6·1	23·3	—	$C_{21}H_{20}N_6$	70·8	5·6	23·6	—
NMe_2	OH	Ph	H	336 d	EtOH	1, 2*a*, 4	15, 90	62·5	4·8	26·6	—	$C_{14}H_{13}ON_5$	62·9	4·4	26·4	—
NMe_2	OH	H	Ph	325 d	DMF–EtOH	1, 2*b*, 4	65, 90, 90	63·0	4·8	26·0	—	$C_{14}H_{13}ON_5$	62·9	4·4	26·4	—
NMe_2	OH	*p*-C_6H_4Cl	H	377 d	DMF–EtOH	1	85	55·8	4·0	23·9	11·7	$C_{14}H_{12}ON_5Cl$	55·7	4·0	23·2	11·8
NMe_2	OH	Ph	Ph	361	DMF–EtOH	2*c*	33	69·9	5·0	20·6	—	$C_{20}H_{17}ON_5$	70·0	5·0	20·4	—
NMe_2	OH	*p*-C_6H_4Cl	Ph	350	BuOH	1	85	63·9	4·3	18·6	9·4	$C_{20}H_{16}ON_5Cl$	63·5	4·2	18·5	9·4
NMe_2	OEt	Ph	H	200	MeOH	EtOH on 4-Cl-compound	30	65·3	6·1	23·7	—	$C_{16}H_{17}ON_5$	65·1	5·8	23·7	—
NMe_2	NH_2	Ph	Ph	239	BuOH	2*c*	63	69·9	5·1	25·0	—	$C_{20}H_{18}N_6$	70·2	5·3	24·6	—
NMe_2	NHMe	Ph	Ph	205	EtOAc	2*c*	43	69·1	5·9	23·7	—	$C_{21}H_{20}N_6$	70·8	5·6	23·6	—
NMe_2	NHMe	Ph	*p*-C_6H_4Cl	239	EtOH	1	70	64·0	4·9	21·5	9·2	$C_{21}H_{12}N_6Cl$	64·6	4·9	21·5	9·1
NMe_2	NMe_2	Pr^i	Pr^i	150	EtOH–H_2O	2*c*	30	63·7	8·1	28·2	—	$C_{16}H_{26}N_6$	63·6	8·6	27·8	—
NMe_2	NMe_2	Ph	H	188	EtOH	2*a*, 3	29, 40	65·7	6·4	28·1	—	$C_{16}H_{18}N_6$	65·3	6·1	28·6	—
NMe_2	NMe_2	H	Ph	191	EtOH	2*b*, 3	37, 80	65·4	6·4	28·5	—	$C_{16}H_{16}N_6$	65·3	6·1	28·6	—
NMe_2	NMe_2	Ph	Ph	211	EtOAc	2*c*	55	71·3	6·2	23·2	—	$C_{22}H_{22}N_6$	71·4	5·9	22·7	—
NMe_2	$[CH_2]_5{>}N$	Ph	Ph	207	EtOH–H_2O	2*c*	75	73·6	6·4	21·0	—	$C_{25}H_{26}N_6$	73·3	6·3	20·5	—
NMe_2	$O{<}[CH_2]_4{>}N$	Ph	Ph	216	EtOH	2*c*	71	69·5	6·0	20·4	—	$C_{24}H_{24}ON_6$	69·9	5·8	20·4	—

* d = with decomp. † DMF = dimethylformamide. ‡ Potter and Henshall record m. p. 195—196° for this substance prepared by a different route.

[1] $\lambda_{max.}$ 280 ($E^{1\%}_{1 cm.}$ 966), 350 mμ ($E^{1\%}_{1 cm.}$ 566). [2] $\lambda_{max.}$ 365 mμ ($E^{1\%}_{1 cm.}$ 950). [3] $\lambda_{max.}$ 365 mμ ($E^{1\%}_{1 cm.}$ 925).

concentrated to about 50 c.c., acidified to Congo-red with hydrochloric acid and then neutralised with ammonia. The *pteridine*, crystallised from ethanol, had m. p. 322° (decomp.) (Found: C, 62·5; H, 4·8; N, 25·5. $C_{14}H_{13}ON_5$ requires C, 62·9; H, 4·9; N, 26·2%), $\lambda_{max.}$ 280 ($E_{1\,cm.}^{1\%}$ 910), 355 mμ ($E_{1\,cm.}^{1\%}$ 395).

(2) *Condensation of a 4 : 5-diaminopyrimidine with an α-diketone.* (*a*) With phenylglyoxal at pH >4. 2-Dimethylamino-4-hydroxy-7-phenylpteridine, identical in m. p. and mixed m. p. with the product obtained by reduction, was obtained by warming 4-amino-2-dimethylamino-6-hydroxy-5-phenacylideneaminopyrimidine with dilute sodium hydroxide. Acidification of the mixture with acetic acid gave the pteridine.

The preparation of 2 : 4-bisdimethylamino-7-phenylpteridine is typical of those cases in which the intermediate compound is not isolated: 4 : 5-Diamino-2 : 6-bisdimethylamino-pyrimidine sulphate (2·94 g.), crystalline sodium acetate (6·8 g.), phenylglyoxal monohydrate (1·5 g.), and 50% v/v ethanol were heated under reflux for 15 min. The solid which separated on cooling was collected, dissolved in 2N-acetic acid, and the solution filtered (charcoal). The *pteridine* was precipitated from the filtrate with ammonia and, crystallised from butanol and then from ethanol, had m. p. 191° (Found: C, 65·4; H, 6·4; N, 28·5. $C_{16}H_{18}N_6$ requires C, 65·3; H, 6·1; N, 28·6%).

(*b*) With phenylglyoxal at pH < 1. 2-Dimethylamino-4-hydroxy-6-phenylpteridine. 4 : 5-Diamino-2-dimethylamino-6-hydroxypyrimidine sulphate (7·43 g.), 6N-sulphuric acid (250 c.c.), phenylglyoxal monohydrate (3·7 g.), and ethanol (250 c.c.) were heated under reflux for 2 hr. After removal of the ethanol under reduced pressure the solution was cooled in ice, basified with ammonia, and separated from a small flocculent precipitate. The *pteridine* which separated on acidification to litmus with dilute acetic acid was collected and crystallised from dimethylformamide–ethanol. It had m. p. 332° (Found: C, 62·5; H, 4·8; N, 27·0. $C_{14}H_{13}ON_5$ requires C, 62·9; H, 4·4; N, 26·4%).

(*c*) With a symmetrically substituted α-diketone. 4-Methylamino-2 : 5 : 6-triaminopyrimidine sulphate (10·8 g.), benzil (14·8 g.), crystalline sodium acetate (24 g.), ethanol (400 c.c.), and water (100 c.c.) were heated under reflux for 5 hr. The product which separated on cooling was collected and extracted with 0·5N-hydrochloric acid. Basification of the extract with ammonia gave *2-amino-4-methylamino-6 : 7-diphenylpteridine* which, crystallised from ethanol, had m. p. 272° (Found: C, 69·4; H, 4·9; N, 25·8. $C_{19}H_{16}N_6$ requires C, 69·5; H, 4·9; N, 25·6%).

(3) *Replacement of a 4-hydroxy- by a 4-amino(or substituted amino)-group* via *the chloro-compound.* 2-Amino-4-methylamino-6 : 7-diphenylpteridine, identical (m. p. and mixed m. p.) with the above, was obtained as follows: 2-Amino-4-hydroxy-6 : 7-diphenylpteridine (2 g.) and redistilled phosphorus oxychloride (120 c.c.) were heated under reflux for 2 hr. After removal of excess of phosphorus oxychloride under reduced pressure, the residual glass was heated with 2·5M-ethanolic methylamine (100 c.c.) for 1 hr. The dark red oily solid which remained after removal of the solvent was extracted with 0·5N-hydrochloric acid. The pteridine was isolated from this extract as above.

In a similar sequence of reactions with 2-dimethylamino-4-hydroxy-6-phenylpteridine and alcoholic dimethylamine, in addition to *2 : 4-bisdimethylamino-6-phenylpteridine* (m. p. 190°; from methanol) (Found: C, 65·7; H, 6·4; N, 28·1. $C_{16}H_{18}N_6$ requires C, 65·3; H, 6·1; N, 28·6%), which was extracted from the crude dimethylamination product with 2N-acetic acid, there was also obtained *2-dimethylamino-4-ethoxy-6-phenylpteridine*, m. p. 200° (from ethanol) (Found: C, 65·3; H, 6·1; N, 23·7. $C_{16}H_{17}ON_5$ requires C, 65·1; H, 5·8; N, 23·7%). By using the conditions of Cain *et al.*[9] there was obtained from 2-amino-4-hydroxy-6 : 7-diphenyl pteridine a product, m. p. 253—259°. Extraction of this with 1·5N-acetic acid left 2-amino-3-*N*-methylcarbamoyl-5 : 6-diphenylpyrazine, m. p. and mixed m. p. 197—198° with an authentic sample (after crystallisation from ethanol). Basification of the extract with ammonia and crystallisation of the precipitate from ethanol gave *2 : 4-bismethylamino-6 : 7-diphenylpteridine*, m. p. 266—267°, undepressed on admixture with an authentic sample obtained by condensation of 4 : 5-diamino-2 : 6-bismethylaminopyrimidine with benzil (Found: C, 70·3; H, 5·3; N, 24·6. $C_{20}H_{18}N_6$ requires C, 70·1; H, 5·3; N, 24·6%). The same product was obtained by reaction between 4-amino-2-mercapto-6 : 7-diphenylpteridine and alcoholic methylamine under the conditions described by Taylor and Cain.[10] Repetition of the similar reaction between 4-amino-2-mercapto-6 : 7-diphenylpteridine and alcoholic dimethylamine gave a product, m. p. 186—215° (Taylor and Cain give m. p. 192—195°): trituration of this with cold 0·5N-acetic acid left a residue which on repeated crystallisation from methanol had m. p. 211° undepressed on admixture with an authentic sample of 2 : 4-*bisdimethylamino*-6 : 7-*diphenylpteridine* (Found : C, 71·3; H, 6·2; N, 23·2. $C_{22}H_{22}N_6$ requires C, 71·4; H, 5·9; N, 22·7%) obtained by condensation of 4 : 5-diamino-2 : 6-bisdimethylaminopyrimidine and benzil. Basification of the acetic acid extract with ammonia gave a substance, m. p. 221—228° raised to 236° by crystallisation from butanol and undepressed on admixture with an authentic sample of 4-*amino*-2-*dimethylamino*-6 : 7-*diphenylpteridine* (Found : C, 69·9; H, 5·1; N, 25·0. $C_{20}H_{18}N_6$ requires C, 70·2; H, 5·3; N, 24·6%), obtained by condensation of 4 : 5 : 6-triamino-2-dimethylaminopyrimidine and benzil.

(4) *Hydrolysis of a 4-amino(or substituted amino)pteridine.* 2 : 4-Bismethylamino-7-phenylpteridine (0·3 g.) and 6N-hydrochloric acid (50 c.c.) were heated under reflux for 20 hr. After cooling to about 50°, the solution was made faintly alkaline to Brilliant Yellow by ammonia. 4-*Hydroxy*-2-*methylamino*-7-*phenylpteridine* was collected, washed with water, dried, and crystallised from dimethylformamide; it had m. p. 387° (decomp.) undepressed on admixture with a sample prepared by method 2*a* (Found : C, 61·7; H, 4·4; N, 27·3. $C_{13}H_{11}ON_5$ requires C, 61·7; H, 4·4; N, 27·6%); $\lambda_{max.}$ 250 mμ ($E^{1\%}_{1\,cm.}$ 700).

*α-Bromo-α-phenylacetaldehyde Dimethyl Acetal.**—To a solution of styryl acetate [12] in carbon tetrachloride (290 c.c.), bromine (39 c.c.) in carbon tetrachloride (40 c.c.) was added with stirring below 10° during 1½ hr. Methanol (290 c.c.) was then added and stirring continued for a further 12 hr. at this temperature. After a further 48 hr. the mixture was poured into ice-water. The oil which separated was collected, washed with 5% w/w sodium hydrogen carbonate solution, dried ($MgSO_4$), and distilled in presence of a little anhydrous sodium carbonate. The *acetal* (122 g.) had b. p. 138—140°/14 mm.

*α-Benzylamino-α-phenylacetaldehyde Dimethyl Acetal.**—α-Bromo-α-phenylacetaldehyde dimethyl acetal (122 g.), benzylamine (183 g.), and a trace of sodium iodide were heated to 140° during 1 hr. When the reaction had moderated heating was continued at 160° for a further 2 hr. After cooling, the mixture was poured into water, and the product collected with ether, dried ($MgSO_4$), and distilled. The *base* (89 g.) had b. p. 121—148°/0·2 mm. (Found : N, 5·7. $C_{17}H_{21}O_2N$ requires N, 5·2%).

*α-Amino-α-phenylacetaldehyde Dimethyl Acetal.**—The above benzylamino-compound was hydrogenated in methanol (300 c.c.) over 5% palladised charcoal (25 g.) at 100—105° with an initial hydrogen pressure of 95 atm. After removal of the catalyst the *aminoacetal* (47 g.), b. p. 134—136°/18 mm., was isolated by distillation (Found : C, 65·6; H, 8·2; N, 7·8. $C_{10}H_{15}O_2N$ requires C, 66·3; H, 8·3; N, 7·7%).

*ω-Aminoacetophenone Semicarbazone.**—ω-Aminoacetophenone hydrochloride (56 g.) was dissolved in ethanol (350 c.c.) with gentle warming and the solution cooled rapidly to room temperature. Semicarbazide (25 g.) was added and the mixture set aside for several hours. The prismatic crystals were filtered off and, crystallised from ethanol, had m. p. 107—108°.

α-Amino-4-chlorodeoxybenzoin.—To 4-chlorobenzyl phenyl ketone (28 g.) in dry ether (500 c.c.) saturated with hydrogen chloride at 0° butyl nitrite (7·5 g.) in ether (50 c.c.) was added. The hydroxyimino-compound which separated immediately was collected and crystallised from aqueous methanol. It had m. p. 121—123° and was reduced at room temperature and pressure in ethanol (350 c.c.) containing concentrated hydrochloric acid (12 c.c.) in presence of palladised charcoal. After removal of the catalyst and solvent the *amino-ketone hydrochloride* (6 g.) was crystallised from 2N-hydrochloric acid and then from methanol–ether; it had m. p. 248° (decomp.) (Found : C, 59·8; H, 4·5; N, 5·1; Cl, 26·0. $C_{14}H_{13}ONCl_2$ requires C, 59·6; H, 4·6; N, 5·0; Cl, 25·2%).

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[12] Semmler, *Ber.*, 1909, **42**, 584.