92. *Some* meso-*Amino-acridines and -quinolines derived from 2-Aminodiphenyl.*

By J. H. Wilkinson.

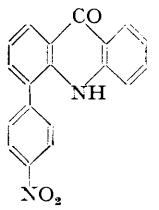
Several new derivatives of 5-aminoacridine and 4-aminoquinoline have been prepared in order to study their effects on mitosis and tissue respiration. Difficulty was experienced in the preparation of 5-*amino*-1-p-*nitrophenylacridine*; the reaction of 1-p-*nitrophenylacridone* with phosphorus oxychloride is discussed.

The observations of Dustin (*Arch. Exp. Zellforsch.*, 1939, **22**, 395; *Sang*, 1937, **12**, 677) and Bucher (*Z. Zellforsch.*, 1939, **29**, 283) that trypaflavine (acriflavine) possessed a powerful inhibitory effect on mitosis suggested that it might be profitable to study certain other acridine derivatives from this viewpoint. A preliminary report (Lasnitzki and Wilkinson, *Brit. J. Cancer*, 1948, **2**, 369) showed that several other compounds of this type inhibited mitosis in tissue cultures of chick-embryo fibroblasts, and that it would be desirable to extend the study. Recently a number of quaternary salts of heterocyclic compounds has been prepared by Hartwell and Kornberg (*J. Amer. Chem. Soc.*, 1945, **67**, 1606; 1946, **68**, 868, 1131) and some have shown activity against tumour cells (Peters, "Approaches to Tumor Chemotherapy," 1947, p. 244). In the present work therefore, the emphasis was originally placed on the preparation of quaternary salts, but the biological results (Lasnitzki and Wilkinson, *loc. cit.*) have indicated that, with acridine derivatives, quaternisation was not an essential pre-requisite for anti-mitotic activity (contrast O'Connor, *Nature*, 1949, **163**, 408; *Brit. J. Exp. Path.*, 1949, **30**, 30). Several new derivatives of 5-aminoacridine have therefore been prepared with the object of examining their effects on cell division and respiration. Similar 4-aminoquinolines have also been prepared for comparison. The biological results will be published elsewhere.

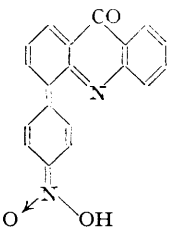
The 5-aminoacridines were prepared by standard methods from the appropriately substituted anilines which were condensed with *o*-chloro- or 2 : 4-dichloro-benzoic acid to give the corresponding diphenylamine-2-carboxylic acids. 4 : 4′-Dinitro-2-aminodiphenyl, however, failed to react under any of the conditions tried, whilst 4′-nitro-2-aminodiphenyl reacted normally to give 2′-p-*nitrophenyldiphenylamine-2-carboxylic acid*. The acids were cyclised with phosphorus oxychloride to give the corresponding 5-chloroacridines, but the 1-*p*-nitrophenyl derivative proved so sensitive to hydrolysis that it could be obtained only in minute amounts, the bulk being isolated as 1-p-*nitrophenylacridone*. Interaction with ammonium carbonate in molten phenol

by the method of Albert and Gledhill (*J. Soc. Chem. Ind.*, 1945, **64**, 169T) gave 5-amino-1-phenylacridine, 8-*chloro*-5-*amino*-1-*phenylacridine*, and 5-*amino*-1-p-*nitrophenylacridine*.

p-Nitrophenylacridone (I) proved highly resistant to phosphorus oxychloride, possibly because of the effect of the nitro-group on the ratio of the contributing resonance forms (cf.



(I.)



(II.)

Hunter, *J.*, 1945, 806). Thus it is probable that the compound exists largely as the "ψ-nitrolic acid" (II), a suggestion supported by the red colour of a solution in alcoholic sodium hydroxide. If this assumption is correct, the proton will not be available for the formation of the 5-hydroxyacridine structure presumably necessary for the promotion of reaction with phosphorus oxychloride. It must be assumed that the effect of the nitro-group is accentuated by transmission through the phenyl group, for 1-nitroacridone, though it does not react under normal conditions with phosphorus oxychloride, undergoes chlorination with phosphorus pentachloride in a high-boiling solvent (Albert and Gledhill, *loc. cit.*; cf. Hampton and Magrath, *J.*, 1949, 1008). *p*-Nitrophenylacridone failed to react with phosphorus pentachloride in xylene.

Since the principal object in preparing 5-amino-1-*p*-nitrophenylacridine was to reduce it to the corresponding diamino-compound, the very poor yields obtained led to the study of alternative methods. 2′-p-*Aminophenyldiphenylamine*-2-*carboxylic acid* and 1-p-*aminophenylacridone* were obtained by reduction of the respective nitro-compounds with stannous chloride, but neither reacted satisfactorily with phosphorus oxychloride.

The quinoline derivatives were prepared by condensing various 2-aminodiphenyls with ethoxymethylenemalonic ester (Gould and Jacobs, *J. Amer. Chem. Soc.*, 1939, **61**, 2890; Price and Roberts, *ibid.*, 1946, **68**, 1204; Duffin and Kendall, *J.*, 1948, 893). In most cases the required ethyl 4-hydroxyquinoline-3-carboxylate was obtained, but when 4 : 4′-dinitro-2-aminodiphenyl was used ring closure did not occur and *ethyl* 4′ : 5-*dinitro*-2-*phenylanilinomethylenemalonate* was isolated: several cyclising agents were tried without success. Hydrolysis and decarboxylation gave the 4-hydroxyquinolines which were converted into the 4-chloroquinolines by phosphorus oxychloride. Subsequent treatment with ammonium carbonate in phenol at 180° gave the required 4-aminoquinolines.

An attempt was made to prepare the quaternary 1-methyl derivatives of 4-*amino*-8-*phenyl*-an l-8-p-*nitrophenyl*-*quinoline* by the methods used for the acridine compounds, but this succeeded only in the latter case. The *product* was reduced to the corresponding 4 : 4′-diamino-compound (isolated as its *bromide hydrobromide*).

When 4-*acetamido*-8-*phenylquinoline* was heated with methyl sulphate in nitrobenzene solution and the product hydrolysed with hydrobromic acid, an uncrystallisable oil was obtained. However with methyl toluene-*p*-sulphonate in the absence of a solvent it gave 4-*acetamido*-8-*phenyl*-1-*methylquinolinium toluene*-p-*sulphonate*. Removal of the acetyl group proved difficult, for the compound was recovered unchanged after being heated with 2N-sulphuric acid or -hydrobromic acid at 90° for 2 hours. Boiling with 4N-hydrobromic acid, however, not only deacetylated, but also deaminated, the product.

Experimental.

(Analyses are by Drs. Weiler and Strauss, Oxford. M. p.s are uncorrected.)

5-*Chloro*-2′-*phenyldiphenylamine*-2-*carboxylic Acid*.—A solution of 2 : 4-dichlorobenzoic acid (9·55 g.) in amyl alcohol (40 c.c.) was treated with anhydrous potassium carbonate (7 g.). 2-Aminodiphenyl (8·45 g.) and copper (0·1 g.) were added, and the mixture was refluxed for 6 hours. The amyl alcohol was removed by steam-distillation, and the residue filtered. The ammonium salt of the product was precipitated by the addition of 30% ammonium chloride solution (50 c.c.). This salt was collected and dissolved in 2N-potassium hydroxide, and the free *acid* (8·2 g., 51%) liberated with 2N-hydrochloric acid. It crystallised from toluene in pale yellow prisms, m. p. 203° (Found: C, 70·7; H, 4·5; N, 4·3; Cl, 11·0. $C_{19}H_{14}O_2NCl$ requires C, 70·7; H, 4·3; N, 4·3; Cl, 11·0%).

5 : 8-*Dichloro*-1-*phenylacridine*.—The foregoing acid (2 g.) was refluxed with phosphorus oxychloride (5 c.c.) for 1 hour. Excess of the reagent was removed under reduced pressure, and the residue dissolved in chloroform (30 c.c.). The solution was stirred for 30 minutes with ammonia solution (*d* 0·88; 30 c.c.),

cooled with ice. The chloroform layer was separated and the solvent removed. The *product* (2 g.) crystallised from anhydrous benzene in bright yellow needles, m. p. 164° (Found: N, 4·6; Cl, 21·4. $C_{19}H_{11}NCl_2$ requires N, 4·3; Cl, 21·9%).

8-*Chloro*-5-*amino*-1-*phenylacridine*.—5 : 8-Dichloro-1-phenylacridine (5 g.) was dissolved in phenol (15 g.) at 80°, and ammonium carbonate (1·5 g.) added. The temperature was raised to 140° for 1 hour. Acetone (70 c.c.) was added to the cooled melt, and the precipitated 8-*chloro*-5-*amino*-1-*phenylacridine hydrochloride* (3·76 g., 71%) collected. It crystallised from 20% alcohol in bright yellow prisms, m. p. over 300°, sparingly soluble in water (Found: N, 7·25; Cl, 18·3. $C_{19}H_{13}N_2Cl,HCl,3H_2O$ requires N, 7·1; Cl, 18·0%). The *base* was obtained in yellow prisms from chlorobenzene, m. p. 189° (Found: C, 74·4; H, 4·25; N, 8·9. $C_{19}H_{13}N_2Cl$ requires C, 74·8; H, 4·25; N, 9·2%).

The *acetamido*-compound (0·94 g., 82%) was obtained by heating the amino-compound (1 g.) with acetic anhydride (4 c.c.) and acetic acid (2 c.c.) at 105° for 30 minutes, and treating the cooled mixture with benzene (30 c.c.). It crystallised from dioxan in fine pale yellow needles, m. p. 309° (Found: N, 8·35. $C_{21}H_{15}ON_2Cl$ requires N, 8·1%).

8-*Chloro*-5-*amino*-1-*phenyl*-10-*methylacridinium bromide*. The above acetyl derivative (0·7 g.) was treated with methyl sulphate (0·7 c.c.) in nitrobenzene (7 c.c.) at 140—150° for 1 hour. After treatment with benzene (15 c.c.) overnight, the precipitate was collected and hydrolysed by heating it with 48% hydrobromic acid (5 c.c.) on a water-bath for 1 hour. The *product* (0·6 g., 74%) crystallised from water in bright yellow prisms, m. p. over 300° (Found: N, 7·25. $C_{20}H_{16}N_2ClBr$ requires N, 7·0%).

2′-p-*Nitrophenyldiphenylamine*-2-*carboxylic Acid*.—*o*-Chlorobenzoic acid (1·56 g.) was dissolved in amyl alcohol (8 c.c.), and the solution treated with potassium carbonate (1·4 g.). 4′-Nitro-2-amino-diphenyl (1·91 g.) and copper (0·1 g.) were added, and the mixture was refluxed for 6 hours. The solvent was removed by steam-distillation and the residue filtered. The filtrate was acidified with acetic acid to precipitate the required *acid* (2·45 g., 81%), which crystallised from 70% alcohol in bright orange-yellow needles, m. p. 243°, sparingly soluble in most organic solvents (Found: C, 68·6; H, 4·3; N, 8·7. $C_{19}H_{14}O_4N_2$ requires C, 68·3; H, 4·2; N, 8·4%).

5-*Amino*-1-p-*nitrophenylacridine*.—2′-*p*-Nitrophenyldiphenylamine-2-carboxylic acid (0·7 g.) was treated with phosphorus oxychloride (2 c.c.) as described for 5 : 8-dichloro-1-phenylacridine. The resultant crude 5-chloro-1-*p*-nitrophenylacridine proved very susceptible to hydrolysis during isolation and it was considered advisable to attempt the conversion of this material into the corresponding 5-amino-compound without further purification. 1-p-*Nitrophenylacridone* (0·45 g.) was obtained as a by-product; this crystallised from pyridine in small pale yellow needles, m. p. 262—263° (Found: N, 8·75. $C_{19}H_{12}O_3N_2$ requires N, 8·9%). The crude 5-chloroacridine (0·25 g.) was dissolved in phenol (1 g.) at 70° and treated with ammonium carbonate (0·1 g.) at 120° for 1 hour. Acetone (10 c.c.) was added to precipitate the yellow hydrochloride, which was sparingly soluble in cold water and underwent rapid hydrolysis to the acridone when an aqueous suspension was heated. The base was obtained by suspending the hydrochloride in 90% alcohol and stirring at 20° with a small excess of 2N-sodium hydroxide. After 1 hour this was collected by filtration and crystallised from chlorobenzene. 5-*Amino*-1-p-*nitrophenylacridine* (90 mg.) was obtained as red needles, m. p. 277—278° (Found: C, 71·5; H, 4·3; N, 13·0. $C_{19}H_{13}O_2N_3$ requires C, 72·3; H, 4·15; N, 13·3%).

1-p-*Aminophenylacridone*.—1-*p*-Nitrophenylacridone (3·16 g.) was finely powdered and heated on a water-bath with stannous chloride (6·8 g.) and hydrochloric acid (50 c.c.) for 2 hours. The mixture was set aside overnight and the solid collected. It was triturated several times with 5N-sodium hydroxide and washed with water. 1-p-*Aminophenylacridone* was thus obtained as a red powder which crystallised from pyridine in irregular orange crystals, m. p. over 300° (Found: N, 9·5. $C_{19}H_{14}ON_2$ requires N, 9·8%).

2′-p-*Aminophenyldiphenylamine*-2-*carboxylic Acid*.—2′-*p*-Nitrophenyldiphenylamine-2-carboxylic acid (2·75 g.) was heated under reflux with stannous chloride (6 g.) in alcohol (25 c.c.) and hydrochloric acid (*d* 1·16; 15 c.c.) for 3 hours. During this period the solid slowly dissolved. The alcohol was removed by distillation, and the cooled residue treated with saturated sodium acetate solution (100 c.c.). The solid was collected, washed with water, and drained as completely as possible. It was then extracted with three 100 c.c. portions of boiling alcohol. The solvent was removed and the residue dissolved in N/2-sodium hydroxide. Acidification with acetic acid gave 2′-p-*aminophenyldiphenylamine*-2-*carboxylic acid* which crystallised from 90% alcohol in buff-coloured hexagonal plates, m. p. 188—189° (Found: C, 74·7; H, 5·35; N, 8·9. $C_{19}H_{16}O_2N_2$ requires C, 74·6; H, 5·25; N, 9·2%).

5-2′-*Phenylethylaminoacridine*.—5-Chloroacridine (10·67 g.) was dissolved in phenol (30 g.) at 70°; 2-phenylethylamine (6·1 g.) was added, and the mixture heated at 120° for 1 hour. A green gum was precipitated from the cooled melt by treatment with ether (100 c.c.). When kept, this hardened to a yellow solid which was washed with ether and crystallised twice from methanol. 5-2′-*Phenylethylamino-acridine hydrochloride* (11·7 g., 70%) was thus obtained as lemon-yellow rectangular prisms, m. p. 214—215°, sparingly soluble in water but readily soluble in alcohol (Found: N, 8·1; Cl, 10·9. $C_{21}H_{18}N_2,HCl$ requires N, 8·4; Cl, 10·6%). The *base* was obtained as an oil which crystallised, on treatment with benzene and light petroleum (b. p. 40—60°), in bright yellow irregular crystals, m. p. 79—80°, highly soluble in most organic solvents (Found: C, 84·6; H, 6·25; N, 9·1. $C_{21}H_{18}N_2$ requires C, 84·6; H, 6·0; N, 9·4%). The *acetyl* derivative separated from alcohol in colourless needles, m. p. 230° (Found: N, 8·3. $C_{23}H_{20}ON_2$ requires N, 8·2%).

Quinoline Derivatives.—*Ethyl* 4-*hydroxy*-8-*phenylquinoline*-3-*carboxylate*. 2-Aminodiphenyl (16·9 g.) and ethoxymethylenemalonic ester (21·6 g.) were dissolved in " Dowtherm " (70 c.c.). The temperature of the solution was gradually raised to 270°, and the alcohol eliminated during the reaction collected (10·3 c.c. Theor.: 11·5 c.c.). The *ester* (23·5 g., 80%) which separated from the cooled mixture was collected by filtration and washed successively with benzene and light petroleum (b. p. 40—60°). It crystallised from alcohol in colourless needles, m. p. 249° (Found: C, 73·7; H, 5·5; N, 4·85. $C_{18}H_{15}O_3N$ requires C, 73·7; H, 5·1; N, 4·8%).

4-*Hydroxy*-8-*phenylquinoline*-3-*carboxylic acid*. The ethyl ester (20 g.) was heated under reflux with 5N-sodium hydroxide (100 c.c.) for 1½ hours, whereby complete dissolution was obtained. After cooling,

the mixture was filtered, diluted with water (200 c.c.), and acidified with hydrochloric acid, to precipitate the *acid* (18 g.), colourless rhombs (from methyl ethyl ketone), m. p. 241—242°, sparingly soluble in alcohol (Found: C, 72·3; H, 4·3; N, 5·15. $C_{16}H_{11}O_3N$ requires C, 72·4; H, 4·2; N, 5·3%).

4-*Hydroxy*-8-*phenylquinoline*. The above acid (16·2 g.) was added during 15 minutes to "Dowtherm" (80 c.c.) maintained at 250° during the addition and for a further 30 minutes. The *base* (13·5 g.) which separated on cooling was collected and washed with light petroleum (b. p. 40—60°); it crystallised from 70% alcohol in colourless plates, m. p. 201° (Found: C, 81·6; H, 5·0; N, 6·5. $C_{15}H_{11}ON$ requires C, 81·4; H, 5·0; N, 6·35%).

4-*Chloro*-8-*phenylquinoline*. 4-Hydroxy-8-phenylquinoline (2·2 g.) was heated under reflux for 2 hours with phosphorus oxychloride (6 c.c.). The cooled solution was poured on crushed ice (30 g.) and made alkaline with aqueous ammonia. The gum which separated hardened to a white solid (2·27 g., 95%) on trituration with dilute aqueous ammonia. It was collected by filtration and dried over calcium chloride. 4-*Chloro*-8-*phenylquinoline* crystallised from alcohol in colourless needles, m. p. 93° (Found: C, 75·1; H, 4·1; N, 5·65; Cl, 15·0. $C_{15}H_{10}NCl$ requires C, 75·1; H, 4·2; N, 5·85; Cl, 14·85%).

4-*Amino*-8-*phenylquinoline*. 4-Chloro-8-phenylquinoline (2 g.) was dissolved in phenol (6 g.) at 70° and treated with powdered ammonium carbonate (1 g.). The temperature was raised to 180° for 2 hours. After cooling, the hydrochloride of the product was precipitated with acetone (50 c.c.) and converted into the *base* (1·1 g.) with aqueous sodium hydroxide. It crystallised from toluene in colourless prisms, m. p. 166° (Found: C, 81·8; H, 5·45; N, 12·8. $C_{15}H_{12}N_2$ requires C, 81·8; H, 5·45; N, 12·7%). The *acetyl* derivative separated from alcohol in colourless cubes, m. p. 206—207° (Found: C, 77·8; H, 5·45; N, 10·9. $C_{17}H_{14}ON_2$ requires C, 77·9; H, 5·35; N, 10·7%).

4-*Acetamido*-8-*phenyl*-1-*methylquinolinium toluene*-p-*sulphonate*. A mixture of 4-acetamido-8-phenylquinoline (1 g.) and methyl toluene-*p*-sulphonate (1 g.) was heated at 160° for 30 minutes. The cooled melt was crushed and triturated with hot benzene. The residual *salt* crystallised from water or alcohol in colourless needles, m. p. 254—255° (Found: C, 67·1; H, 5·4; N, 6·3; S, 7·1. $C_{25}H_{24}O_4N_2S$ requires C, 67·0; H, 5·36; N, 6·3; S, 7·1%).

Attempted Hydrolysis of 4-*Acetamido*-8-*phenyl*-1-*methylquinolinium toluene*-p-*sulphonate*. (i) The quaternary salt (0·32 g.) was heated on a steam-bath with 2N-sulphuric acid (3 c.c.) for 1 hour. The solid (0·21 g.) which separated on cooling had m. p. 254° and proved to be unchanged starting material (Found: N, 6·5; S, 7·4%). (ii) Similar treatment with 2N-hydrobromic acid also failed to hydrolyse the toluene-*p*-sulphonate. (iii) 0·5 G. of the salt was heated under reflux with 4N-hydrobromic acid (5 c.c.) for 2 hours. The oil which separated on cooling soon hardened to a solid, which was dissolved in hot water. The resulting solution was made alkaline with sodium hydroxide, and the precipitate produced was dissolved in hot 2N-hydrobromic acid. After two recrystallisations from water, the solid which separated on cooling, was obtained in colourless prisms, m. p. 155—156°. It contained no bromine, was devoid of basic properties, and evidently consisted of 4-*hydroxy*-2-*keto*-8-*phenyl*-1-*methyl*-1 : 2-*dihydroquinoline* or its tautomer (Found: C, 76·1; H, 6·1; N, 5·0. $C_{16}H_{14}O_2N$ requires C, 76·3; H, 5·55; N, 5·55%).

Ethyl 4-*hydroxy*-8-p-*nitrophenylquinoline*-3-*carboxylate*. 4′-Nitro-2-aminodiphenyl (10·7 g.) and ethoxymethylenemalonic ester (10·8 g.) were heated in "Dowtherm" (40 c.c.) as described above. The theoretical amount of alcohol was eliminated after 2 hours. The product (13·9 g., 82%), which crystallised, was washed with benzene and light petroleum (b. p. 40—60°). The *ester* was sparingly soluble in most organic solvents, and separated from aqueous pyridine in pale yellow masses, m. p. 285° (Found: C, 63·7; H, 4·2; N, 8·5. $C_{18}H_{14}O_5N_2$ requires C, 63·9; H, 4·15; N, 8·3%).

4-*Hydroxy*-8-p-*nitrophenylquinoline*. The ester (13 g.) was hydrolysed by being heated under reflux with 2N-sodium hydroxide (200 c.c.) for 1 hour. The resulting solution was filtered while still hot, and the quinoline-3-carboxylic acid (12 g.) precipitated with hydrochloric acid. It was obtained as a pale yellow powder, m. p. 280° (decomp.), very sparingly soluble in organic solvents. No suitable solvent for crystallisation was found. The acid (12 g.) was gradually added to boiling "Dowtherm" (60 c.c.), and the mixture maintained at 250—260° for 1 hour and then cooled. The product (9·85 g., 95%) was collected, washed with benzene and light petroleum (b. p. 40—60°), and dried at 100°. It crystallised from 70% aqueous pyridine in yellow irregular prisms, m. p. >300°, sparingly soluble in most organic solvents (Found: N, 10·7. $C_{15}H_{10}O_3N_2$ requires N, 10·4%).

4-*Chloro*-8-p-*nitrophenylquinoline*. 4-Hydroxy-8-*p*-nitrophenylquinoline (9·5 g.) was refluxed with phosphorus oxychloride (20 c.c.) for 2 hours. The mixture was cooled, poured on crushed ice, and neutralised with aqueous ammonia. The solid *base* (10·15 g., 100%) crystallised from 80% aqueous dioxan in fine pale yellow needles, m. p. 224° (Found: N, 9·6. $C_{15}H_9O_2N_2Cl$ requires N, 9·75%).

4-*Amino*-8-p-*nitrophenylquinoline*. 4-Chloro-8-*p*-nitrophenylquinoline (9·7 g.) was dissolved in phenol (27 g.) at 100°, and ammonium carbonate (4 g.) was added portionwise whilst the temperature was raised to 180° for 2 hours. The product (5·8 g., 65%) was isolated in the same manner as 4-amino-8-phenylquinoline. 4-*Amino*-8-p-*nitrophenylquinoline* crystallised from alcohol in lemon-yellow, squat prisms, m. p. 224—225° (Found: C, 67·6; H, 4·15; N, 16·0. $C_{15}H_{11}O_2N_3$ requires C, 67·9; H, 4·15; N, 15·8%). The *acetyl* derivative crystallised from alcohol in pale yellow needles, m. p. 242° (Found: N, 13·8. $C_{17}H_{13}O_3N_3$ requires N, 13·65%).

4-*Amino*-8-p-*nitrophenyl*-1-*methylquinolinium bromide*. 4-Acetamido-8-*p*-nitrophenylquinoline (1·9 g.) was dissolved in nitrobenzene (7 c.c.) and treated with methyl sulphate (2 c.c.) at 150° for 1 hour. The cooled mixture was treated with benzene (25 c.c.) and set aside for 4 hours. The gum was washed by decantation with benzene and hydrolysed with 48% hydrobromic acid (10 c.c.) on a steam-bath for 1 hour. The product (1·9 g., 85%) was collected and washed with water. 4-*Amino*-8-p-*nitrophenyl*-1-*methylquinolinium bromide* crystallised from water in pale yellow plates, m. p. 279—281° (decomp.) (Found: N, 11·6. $C_{16}H_{14}O_2N_3Br$ requires N, 11·7%). An aqueous solution gave no precipitate with saturated sodium hydrogen carbonate solution, but sodium hydroxide precipitated the yellow ψ-base.

4 : 4′-*Diamino*-8-*phenyl*-1-*methylquinolinium bromide hydrobromide*. The nitro-salt (1·5 g.) was suspended in 4N-hydrochloric acid (8 c.c.) and treated with stannous chloride (3 g.) under reflux for 3 hours. The cooled mixture was diluted with water (30 c.c.) and made alkaline to phenolphthalein with

5N-sodium hydroxide. The solid base was collected and washed with water. It was dissolved in hot 2N-hydrobromic acid (20 c.c.) and, on cooling, the required *bromide hydrobromide* (1·29 g., 94%) separated. It crystallised from water in buff-coloured needles, m. p. >300°, charring at *ca.* 295° (Found: N, 9·0; Br, 34·8. $C_{16}H_{16}N_3Br,HBr,3H_2O$ requires N, 9·0; Br, 34·4%).

Attempted Preparation of 4′: 5-Dinitro-4-hydroxy-8-phenylquinoline.—4 : 4′-Dinitro-2-aminodiphenyl (12·95 g.) and ethoxymethylenemalonic ester (10·8 g.) were heated with "Dowtherm" (50 c.c.) at 250° for 4 hours, after which no more alcohol distilled off. Only half of the theoretical amount was obtained. On cooling, *ethyl 4′: 5-dinitro-2-phenylanilinomethylenemalonate* (12·1 g., 56%) separated. This crystallised from alcohol in bright yellow needles, m. p. 188°, sparingly soluble in most organic solvents, but readily soluble in dioxan and *p*-tolyl methyl ether (Found: C, 55·8; H, 4·55; N, 9·8. $C_{20}H_{19}O_8N_3$ requires C, 55·9; H, 4·45; N, 9·75%). Several methods of cyclisation including heating with sulphuric and phosphoric acids were attempted, but in no case was the required ethyl 4′: 5-dinitro-8-phenyl-4-quinolone-3-carboxylate obtained.

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Department of Chemical Pathology,
Westminster Medical School (University of London),
17, Horseferry Road, London, S.W.1.

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