218. *Attempts to find New Antimalarials. Part XVII. Derivatives of* 5 : 6 : 3′ : 2′-*Pyridoquinoline.*

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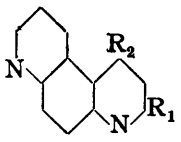
In order that they might be tested for antimalarial activity, derivatives of 5 : 6 : 3′ : 2′-pyridoquinoline, carrying basic side chains, have been prepared by condensation of the corresponding chloro-derivative with the appropriate amine. In this way, compounds such as 2-β-*diethylaminoethylamino*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline* and 4-γ-diethylaminopropylamino-2-methyl-5 : 6 : 3′ : 2′-pyridoquinoline have been obtained. Compounds have also been synthesised lacking the methyl group by the condensation of *p*-aminoacetanilide with ethyl oxaloacetate to yield *ethyl* 6-*acetamido*-4-*hydroxyquinoline*-2-*carboxylate*, which by hydrolysis and decarboxylation yields 6-amino-4-hydroxyquinoline, whence 4-*hydroxy*- and 4-*chloro*-5 : 6 : 3′ : 2′-*pyridoquinoline* have been prepared. The latter compound reacts with suitable amines to yield compounds of the desired type.

The nitration of ethyl 4-hydroxyquinoline-2-carboxylate is shown to occur in the 6-position. It is proved that the pyridoquinoline formed by the Skraup reaction from 6-amino-4-hydroxyquinoline has the angular, and not the linear, structure.

When 6-amino-2-hydroxy-4-methylquinoline (Balaban, J., 1930, 2350) is submitted to the Skraup reaction, a compound of the expected formula, $C_{13}H_{10}ON_2$, is obtained, and from the large mass of evidence which shows that angular ring systems are formed rather than linear ones, there is little doubt that the new compound is 2-*hydroxy*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline* (I; R_1 = OH, R_2 = Me). Treatment of this with phosphorus pentachloride yields 2-*chloro*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline* (I; R_1 = Cl, R_2 = Me), from which, by heating with the appropriate amines, 2-*piperidino*-, 2-*piperazino*- 2-β-*diethylaminoethylamino*-, and 2-γ-*diethylaminopropylamino*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline* are obtained.



(I.)

Advantage was taken of the availability of 6-nitro-2-hydroxy-4-methylquinoline to prepare 2-chloro-6-nitro-4-methylquinoline (Balaban, J., 1930, 2350). The latter was condensed with piperidine and with β-diethylaminoethylamine to yield 2-*piperidino*- and 2-β-*diethylaminoethylamino*-6-*nitro*-4-*methylquinoline*, respectively.

6-Amino-4-hydroxy-2-methylquinoline (Kermack and Weatherhead, J., 1939, 563) was converted into 4-*hydroxy*-2-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline* (I; $R_1 = Me$, $R_2 = OH$) and 4-*chloro*-2-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline* (I; $R_1 = Me$, $R_2 = Cl$), from which 4-*piperidino*- and 4-β-*diethylaminoethylamino*-2-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline* have been obtained.

In B.P. 481,874 (1936), which became available while the above work was in progress, the preparation of 4-β-diethylaminoethylamino-2-methyl-5 : 6 : 3′ : 2′-pyridoquinoline is described, (1) by condensation of 6-aminoquinoline and ethyl acetoacetate by the method of Conrad and Linpach, followed by replacement of the hydroxyl group by chlorine and then by β-diethylaminoethylamine, (2) from 6-amino-4-chloro-2-methylquinoline, which was condensed with β-diethylaminoethylamine to yield 6-amino-4-β-diethylaminoethylamino-2-methylquinoline, which was then submitted to the Skraup reaction.

The products obtained by these two methods are said to boil at 210—215°/1 mm. and 235—240°/0·45 mm. respectively. The difference in these two boiling points may be noticed, as well as the discrepancy between the m. p. 195° of the intermediate chloro-compound, 4-chloro-2-methyl-5 : 6 : 3′ : 2′-pyridoquinoline, given in the patent and that given above, namely, 149°. Although we made various attempts to condense 6-aminoquinoline and ethyl acetoacetate by the method of Conrad and Limpach, the only product we isolated was 2-hydroxy-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline, of which the corresponding 2-chloro-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline melts at 204°. It seems possible that this corresponds to the compound, m. p. 195°, in which case the product obtained by method (1) would have been 2-β-diethylaminoethylamino-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline. This suggestion would reconcile the discrepancies.

In view of the deleterious effect on antimalarial activity of a methyl group introduced into the 2-position of the quinoline nucleus of 4-diethylaminoalkylamino-6-methoxyquinoline (Magidson, *J. Gen. Chem. Russ.*, 1937, **7**, 1896) it was considered desirable to synthesise compounds analogous to the above but without the methyl group in position 2. The 6-amino-4-hydroxyquinoline required for this purpose was prepared in two ways: (1) The nitration of *ethyl* 4-*hydroxyquinoline*-2-*carboxylate* yielded *ethyl* 6-*nitro*-4-*hydroxyquinoline*-2-*carboxylate*, which on reduction with tin and hydrochloric acid gave 6-amino-4-hydroxyquinoline-2-carboxylic acid. (2) The position of the nitro- and the amino-group in these compounds was proved as follows: *p*-Aminoacetanilide and ethyl oxaloacetate were condensed to yield *ethyl* α-p-*acetamidoanilinofumarate*,

$$NHAc{\cdot}C_6H_4{\cdot}NH{\cdot}C(CO_2Et){:}CH{\cdot}CO_2Et,$$

which when cyclised gave *ethyl* 6-*acetamido*-4-*hydroxyquinoline*-2-*carboxylate*. This compound on hydrolysis yielded 6-amino-4-hydroxyquinoline-2-carboxylic acid identical with the acid obtained by the previous method, decarboxylation of which with the formation of 6-amino-4-hydroxyquinoline, was effected by boiling with quinoline in presence of copper bronze. The yield depended much on the quality of the copper bronze.

The application of the Skraup reaction to 6-amino-4-hydroxyquinoline presented unexpected difficulties, but by the use of the sulphate under strictly defined conditions, a good yield of 4-*hydroxy*-5 : 6 : 3′ : 2′-*pyridoquinoline* (I; $R_1 = H$, $R_2 = OH$) was obtained. When this compound was submitted to zinc dust distillation in a current of hydrogen, a white crystalline compound was immediately obtained, m. p. 177°, not depressed by 5 : 6 : 3′ : 2′-pyridoquinoline obtained from 6-aminoquinoline by the Skraup reaction. As the constitution of 5 : 6 : 3′ : 2′-pyridoquinoline (I; $R_1 = R_2 = H$) has already been established (Skraup and Vortmann, *Monatsh.*, 1883, **4**, 571), the above result proves that the 4-hydroxypyridoquinoline of melting point 298° has the constitution assigned to it, *i.e.*, the three rings have the angular and not the linear arrangement. This further justifies the angular arrangement assigned to the pyridoquinolines derived from 4-hydroxy-2-methyl- and 2-hydroxy-4-methyl-6-aminoquinoline.

4-Hydroxy-5 : 6 : 3′ : 2′-pyridoquinoline was converted into 4-*chloro*-5 : 6 : 3′ : 2′-*pyridoquinoline* (I; $R_1 = H$, $R_2 = Cl$), from which, by treatment with the corresponding

bases, 4-β-*diethylaminoethylamino-* and 4-*γ-diethylaminopropylamino*-5 : 6 : 3′ : 2′-*pyridoquinoline* were obtained.

Experimental.

2-*Hydroxy*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—6-Amino-2-hydroxy-4-methylquinoline (1·4 g.), arsenic acid (1·16 g.), concentrated sulphuric acid (2·2 g.), and glycerol (2·4 g.) were refluxed on a sand-bath for 3 hours. The cooled solution, diluted with water, was neutralised with sodium hydroxide until a brownish precipitate separated. This precipitate was dissolved in alcohol, and the hydrobromide, m. p. above 400°, precipitated by addition of alcoholic hydrobromic acid. The *base* was precipitated by addition of aqueous ammonia to a hot aqueous solution of the salt and recrystallised from alcohol; m. p. 330°, yield 1·4 g. (Found: N, 13·5. $C_{13}H_{10}ON_2$ requires N, 13·3%). It was sparingly soluble in alcohol and acetone, but insoluble in ligroin, chloroform, and benzene.

Condensation of 6-*Aminoquinoline and Ethyl Acetoacetate*.—When equimolecular quantities of 6-aminoquinoline and ethyl acetoacetate were heated together on the water-bath or at lower temperatures, with or without catalysts, no condensation appeared to take place, but when they were refluxed on the oil-bath they yielded a compound, m. p. 330°, not depressed by the 2-hydroxy-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline obtained as described above.

2-*Chloro*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—A mixture of 2-hydroxy-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·5 g.), phosphorus pentachloride (0·5 g.), and phosphorus oxychloride (4 c.c.) was heated at 130° for 5 hours. The product was decomposed by ice, and the filtered aqueous solution neutralised by sodium carbonate. The precipitated white solid, recrystallised from ethyl alcohol, formed long white needles (0·3 g.), m. p. 204° (Found: N, 12·1. $C_{13}H_9N_2Cl$ requires N, 12·3%), soluble in alcohol, ligroin, benzene and acetone, very soluble in chloroform, difficultly soluble in ether.

2-*Piperidino*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—2-Chloro-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·3 g.) and piperidine (0·5 g.) were refluxed for 2 hours. The product was treated with alcoholic hydrobromic acid, and the yellow *hydrobromide* which separated recrystallised from methyl alcohol; m. p. above 400°, yield 0·6 g. (Found: N, 9·6. $C_{18}H_{19}N_3$,2HBr requires N, 9·6%). The *base* obtained from the hydrobromide separated as an oil, which solidified and was recrystallised from aqueous alcohol; m. p. 104° (Found: C, 77·9; H, 6·4. $C_{18}H_{19}N_3$ requires C, 77·9; H, 6·8%); it was soluble in benzene, alcohol, ether and chloroform.

2-*Piperazino*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—2-Chloro-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·5 g.) and piperazine (1 g.) were heated at 140° for 5 hours. The product, a yellow-brown solid, crystallised from water in white needles, m. p. 110° (Found: N, 17·8; H_2O, 11·4. $C_{17}H_{18}N_4$,2H_2O requires N, 17·8; H_2O, 11·4%). The anhydrous compound melted at 125°.

2-β-*Diethylaminoethylamino*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—2-Chloro-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·3 g.) and β-diethylaminoethylamine (2 c.c.) were refluxed at 150° for 2 hours. After the excess of diethylaminoethylamine had been removed in a vacuum, the product was dissolved in alcoholic hydrobromic acid. The *hydrobromide* which separated crystallised from alcohol in pale yellow needles (0·5 g.), m. p. 229° (Found: N, 10·2. $C_{19}H_{24}N_4$,3HBr requires N, 10·0%), very soluble in water, sparingly soluble in methyl alcohol and ethyl alcohol, insoluble in ligroin, chloroform and acetone. The *base* obtained from the hydrobromide separated as a yellow oil, which, on scratching, solidified to a white solid, m. p. 123° after recrystallisation from aqueous alcohol (Found: C, 74·3; H, 7·8. $C_{19}H_{24}N_4$ requires C, 74·0; H, 7·8%). The base was very soluble in chloroform, ligroin, ether and alcohol, difficultly soluble in acetone and insoluble in water.

2-*γ-Diethylaminopropylamino*-4-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—2-Chloro-4-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·3 g.) and γ-diethylaminopropylamine (1 c.c.) were refluxed at 160° for 2 hours, and the product worked up as before. The *hydrobromide* was recrystallised from alcohol; m. p. 265° (Found: C, 40·0; H, 5·7; N, 9·2; Br, 39·1. $C_{20}H_{26}N_4$,3HBr,2H_2O requires C, 39·9; H, 5·5; N, 9·3; Br, 40·4%). It was soluble in water, alcohol, and methyl alcohol, insoluble in chloroform, ligroin and acetone. The free base separated as an oil from the neutralised aqueous solution of the salt and would not crystallise.

6-*Nitro*-2-*piperdino*-4-*methylquinoline*.—2-Chloro-6-nitro-4-methylquinoline (0·3 g.) and piperidine (0·5 c.c.) together with a trace of copper bronze were refluxed at 120° for 4 hours. After removal of the excess of piperidine in a vacuum, the dark brown solid product was recrystallised from aqueous alcohol, forming golden leaflets (0·4 g.), m. p. 167° (Found: N, 15·7. $C_{15}H_{17}O_2N_3$ requires N, 15·5%), readily soluble in alcohol, benzene, acetone, chloroform and ligroin, sparingly soluble in ether.

6-*Nitro*-2-β-*diethylaminoethylamino*-4-*methylquinoline*.—2-Chloro-6-nitro-4-methylquinoline (0·3 g.) and diethylaminoethylamine (1 c.c.) with a trace of copper bronze were refluxed at 140° for 4 hours, the liquid filtered, and the excess of diethylaminoethylamine removed in a vacuum. The *hydrochloride* separated in yellow needles on addition of alcoholic hydrochloric acid to the product; it was recrystallised from the minimum amount of methyl alcohol; m. p. 165° (Found: N, 16·3. $C_{16}H_{22}N_4O_2$,HCl requires N, 16·5%). The *picrate*, formed from the crude product and picric acid in alcoholic solution, crystallised from boiling water in long yellow needles, m. p. 210° (Found: C, 50·2; H, 4·8; N, 18·3. $C_{16}H_{22}O_2N_4$,$C_6H_3O_7N_3$ requires C, 50·0; H, 4·7; N, 18·5%). The free base separated as an oil from the neutralised solutions of these salts, and would not crystallise.

4-*Hydroxy*-2-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—6-Amino-4-hydroxy-2-methylquinoline (2·82 g.), arsenic acid (2·32 g.), glycerol (4·8 g.), and concentrated sulphuric acid (4·49 g.) were cautiously refluxed together for 5 hours; the cooled product, diluted with water, was neutralised with sodium hydroxide. The yellow precipitate was repeatedly crystallised from aqueous ethyl alcohol; m. p. 358°, yield 3 g. (Found: C, 73·7; H, 4·8. $C_{13}H_{10}ON_2$ requires C, 74·2; H, 4·8%). It was soluble in dilute acids and in warm dilute alkali solution, readily soluble in alcohol and ligroin, insoluble in acetone.

4-*Chloro*-2-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—4-Hydroxy-2-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·5 g.), phosphorus pentachloride (0·5 g.), and phosphorus oxychloride (4 c.c.) were refluxed at 120° for 3 hours. The resulting deep blue solution was decomposed by ice and after neutralisation with sodium carbonate the pink flocculent precipitate was crystallised from aqueous alcohol, forming small colourless needles (0·34 g.), m. p. 149° (Found: C, 68·1; H, 3·7. $C_{13}H_9N_2Cl$ requires C, 68·3; H, 3·9%), soluble in dilute acids but insoluble in alkali, readily soluble in alcohol and methyl alcohol, slightly soluble in benzene and ligroin, and insoluble in acetone.

4-*Piperidino*-2-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—4-Chloro-2-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·2 g.) and piperidine (0·5 c.c.) were heated together at 100° for 4 hours. After removal of the excess of piperidine in a vacuum the resulting crystalline mass was dissolved in alcohol, and an alcoholic solution of picric acid added. The *picrate* which separated was recrystallised from boiling water; m. p. 225° (Found: C, 57·4; H, 4·4. $C_{18}H_{19}N_3$,$C_6H_3O_7N_3$ requires C, 57·7; H, 4·6%). The free *base*, which was obtained by dissolving the crystalline mass in dilute hydrochloric acid and adding aqueous ammonia, separated as an oil, which crystallised to a white solid, m. p. 163° after recrystallisation from aqueous alcohol in needles (Found: N, 13·9. $C_{18}H_{19}N_3$,H_2O requires N, 14·2%), insoluble in water, but very soluble in alcohol, ether, ligroin, and benzene.

4-β-*Diethylaminoethylamino*-2-*methyl*-5 : 6 : 3′ : 2′-*pyridoquinoline*.—4-Chloro-2-methyl-5 : 6 : 3′ : 2′-pyridoquinoline (0·3 g.) and β-diethylaminoethylamine (0·6 c.c.) were heated together at 140 for 3 hours. The oil which remained after removal of the excess of diethylaminoethylamine in a vacuum was dissolved in dilute hydrochloric acid, and sodium hydroxide added until a cloudiness appeared. On standing, a white solid separated, which crystallised from light petroleum in long rectangular plates, m. p. 68° (Found: N, 17·2. $C_{19}H_{24}N_4$,H_2O requires N, 17·2%), soluble in benzene, ligroin, alcohol, and methyl alcohol.

Ethyl α-p-*Acetamidoanilinofumarate*.—*p*-Aminoacetanilide (2·75 g.) and ethyl oxaloacetate (3·45 g.) in alcohol containing concentrated hydrochloric acid (0·1 c.c.) were heated together on the water-bath for 15 minutes. Water was then added; a yellow oil separated which gradually solidified and then crystallised from ligroin in pale yellow plates, m. p. 122° (Found: N, 9·1. $C_{16}H_{20}O_5N_2$ requires N, 8·8%), difficultly soluble in benzene and ligroin, very soluble in alcohol and methyl alcohol.

Ethyl 6-*Acetamido*-4-*hydroxyquinoline*-2-*carboxylate*.—Ethyl α-*p*-acetamidoanilinofumarate was added to medicinal paraffin at 250—260°. The yellow solid which separated on cooling was washed with light petroleum and crystallised from methyl alcohol, forming small plates, m. p. 309° (Found: N, 10·4. $C_{14}H_{14}O_4N_2$ requires N, 10·2%), slightly soluble in alcohol and methyl alcohol, insoluble in benzene, ligroin, acetone and chloroform.

6-*Amino*-4-*hydroxyquinoline*-2-*carboxylic Acid*.—The preceding ester (10 g.) was refluxed with 3·5N-hydrochloric acid (100 c.c.) for 3 hours, and the solution evaporated to dryness. The resulting *hydrochloride* crystallised from the minimum amount of methyl alcohol in small yellow needles, m. p. above 400° (Found: N, 11·3. $C_{10}H_8O_3N_2$,HCl requires N, 11·6%). Treatment of the hydrochloride with water liberated the yellow base; the addition of sodium acetate ensured the complete dissociation of the hydrochloride. The base, m. p. 308°, was very slightly soluble in alcohol, insoluble in ligroin, water, methyl alcohol and benzene. Its solution in alcohol had a strong green fluorescence.

Ethyl 4-Hydroxyquinoline-2-carboxylate.—A mixture of aniline (1·2 g.) and ethyl oxaloacetate (2·5 g.) containing 0·02 c.c. of concentrated hydrochloric acid was kept overnight in an evacuated desiccator containing sulphuric acid. The oily product was slowly added to medicinal paraffin at 260° and the yellow crystalline solid which separated on cooling was washed with light petroleum and recrystallised from the minimum amount of methyl alcohol, forming small, pale yellow crystals (1·5 g.), m. p. 212° (Found: N, 6·6. $C_{12}H_{11}O_3N$ requires N, 6·5%), difficultly soluble in methyl alcohol, ligroin, and benzene and insoluble in chloroform.

Ethyl 6-Nitro-4-hydroxyquinoline-2-carboxylate.—Ethyl 4-hydroxyquinoline-2-carboxylate (0·65 g.), dissolved in sulphuric acid (4 c.c.), was nitrated by addition of nitric acid (0·23 c.c., *d* 1·42) and sulphuric acid (0·25 c.c.) at 0°. After 2 hours the solution was poured into ice-water. The yellow solid that separated crystallised from ethyl alcohol in small yellow needles, m. p. 286° (Found: N, 10·9. $C_{12}H_{10}O_5N_2$ requires N, 10·7%), soluble in dilute alkali solution, and insoluble in dilute acids, methyl alcohol, ether, and benzene.

Reduction. The nitro-derivative (0·2 g.) was slowly added to a boiling solution of stannous chloride (0·5 g.) in 10N-hydrochloric acid (3 c.c.), and the boiling continued for 5 hours. On cooling, the tin salt which had separated was filtered off and, after removal of the tin by hydrogen sulphide, the combined filtrates were evaporated to dryness. The residue of hydrochloride, m. p. above 400°, dissociated on addition of water to yield a yellow base, m. p. 310°, identical with the 6-amino-4-hydroxyquinoline-2-carboxylic acid already described, with which it gave no depression of the m. p.

6-Amino-4-hydroxyquinoline.—6-Amino-4-hydroxyquinoline-2-carboxylic acid (10 g.), quinoline (100 c.c.), and copper bronze (5 g.) were refluxed for 5 hours. The brown solution was filtered from the copper, the quinoline removed by distillation with steam, and the remaining pale yellow solution evaporated to dryness. The resulting brown sticky oil, treated with concentrated hydrochloric acid, formed a white *dihydrochloride*, which crystallised from water in small white needles, m. p. 305° (Found: N, 11·8; Cl, 29·5. $C_9H_8ON_2,2HCl$ requires N, 12·0; Cl, 30·0%). Its solution in alcohol had a marked yellow-green fluorescence.

The base liberated from the hydrochloride separated as an oil which would not crystalllise, showing in this respect a marked contrast to 6-amino-4-hydroxy-2-methylquinoline (J., 1939, 563).

The *sulphate* could not always be prepared by treatment of the crude base with sulphuric acid, but was obtained most readily from the hydrochloride by dissolving it in water, adding aqueous ammonia, evaporating the solution to dryness, and cautiously adding very small quantities of concentrated sulphuric acid to the residue. Recrystallised from a small quantity of boiling water, the sulphate formed long white needles, m. p. 275° (Found: N, 7·7. $C_9H_8ON_2,2H_2SO_4$ requires N, 7·8%), soluble in water and alcohol and insoluble in acetone. Its solution in alcohol had a strong green fluorescence.

4-Hydroxy-5 : 6 : 3′ : 2′-pyridoquinoline.—The sulphate of 6-amino-4-hydroxyquinoline (1·7 g.), arsenic acid (0·68 g.), glycerol (1·4 g.), and sulphuric acid (0·98 g.) were cautiously brought to the b. p. and then refluxed in a metal-bath for 3 hours, care being taken to avoid charring. The resulting thick, dark brown liquid was poured into water, and the filtered solution basified with sodium carbonate. The brownish precipitate, after crystallisation from boiling water, formed a pale yellow solid, m. p. 298° (Found: C, 70·5; H, 4·6. $C_{12}H_8ON_2,\frac{1}{2}H_2O$ requires C, 70·2; H, 4·4%), extremely soluble in dilute acids, insoluble in dilute alkali solution, and difficultly soluble in alcohol.

4-Chloro-5 : 6 : 3′ : 2′-pyridoquinoline.—4-Hydroxy-5 : 6 : 3′ : 2′-pyridoquinoline (0·3 g.), phosphorus pentachloride (0·3 g.), and phosphorus oxychloride (3 c.c.) were refluxed at 130° for 3 hours. The excess of phosphorus oxychloride was removed from the greenish solution in a vacuum, the residue decomposed with water, and the filtered solution basified with sodium carbonate. The flocculent, pale pink precipitate crystallised from boiling water in long felted needles, m. p. 147° (Found: N, 13·1. $C_{12}H_7N_2Cl$ requires N, 13·1%), soluble in alcohol and methyl alcohol and insoluble in benzene and ligroin.

4-β-Diethylaminoethylamino-5 : 6 : 3′ : 2′-pyridoquinoline.—4-Chloro-5 : 6 : 3′ : 2′-pyridoquinoline (0·5 g.) and β-diethylaminoethylamine (0·4 c.c.) were refluxed together at 140° for 3 hours. To the sticky brown oil which remained after removal of the excess of diethylaminoethylamine in a vacuum, fuming alcoholic hydrochloric acid was added. On addition of acetone and prolonged scratching, a cream-coloured solid gradually separated; recrystallised from the minimum amount of alcohol, it formed small plates, m. p. 235° (Found: C, 51·5; H, 6·3. $C_{18}H_{22}N_4,3HCl,H_2O$ requires C, 51·3; H, 6·4%).

4-γ-Diethylaminopropylamino-5 : 6 : 3′ : 2′-pyridoquinoline.—4-Chloro-5 : 6 : 3′ : 2′-pyridoquin-

oline (0·5 g.) and γ-diethylaminopropylamine (0·4 c.c.) were refluxed together at 160° for 4 hours. The excess of diethylaminopropylamine was removed in a vacuum and to the oil which remained an alcoholic solution of picric acid was added. A sticky yellow mass was formed which, on scratching, gradually solidified to a yellow solid, which was recrystallised from boiling water; m. p. 231° (Found: C, 48·3; H, 4·1. $C_{19}H_{24}N_4,2C_6H_3O_7N_3$ requires C, 48·6; H, 3·9%). The base was obtained from the *picrate* as an oil which did not crystallise. Attempts to obtain salts other than the picrate were unsuccessful.

We thank the Medical Research Council for a grant to one of us (A. P. W.) which enabled this work to be carried out.

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[*Received, May 29th,* 1940.]