Anal. Calcd. for $C_{11}H_{10}N_2O_3$: C, 60.54; H, 4.62. Found: C, 60.61; H, 4.93.

8-Amino-6-methoxylepidine.—A mixture of 33 g. of the nitro compound, 25 ml. of absolute alcohol, 75 ml. of ethyl acetate and 9 g. of Raney nickel was shaken with hydrogen at 50° and 60 lb. pressure. The theoretical amount of hydrogen was absorbed in eighty minutes. The product boiled at 164–170° (3 mm.), and weighed 20.5 g. (73%). It solidified to white crystals, m. p. 86.5–87.5° after recrystallization from ligroin.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43. Found: C, 70.32; H, 6.57.

8-(6′-Diethylaminohexylamino)-6-methoxylepidine, SN-14,011.—A mixture of 28.5 g. (0.15 mole) of 8-amino-6-methoxylepidine, 57 g. (0.18 mole) of diethylaminohexyl bromide hydrobromide, 25 g. (0.3 mole) of anhydrous sodium acetate and 90 ml. of 50% alcohol was refluxed for forty-eight hours. The solution was poured into 500 ml. of water, made alkaline with potassium hydroxide and extracted with ether. Distillation of the ether extract gave 15 g. of recovered nucleus and 19.1 g. (80% based on unrecovered nucleus) of product, b. p. 190–200° (0.05 mm.). This was dissolved in 50 ml. of *n*-propanol and titrated with propanolic hydrogen chloride. The yellow dihydrochloride so obtained weighed 21 g., and melted at 176–178°. Recrystallization from propanol raised the melting point to 179–180°.

Anal. Calcd. for $C_{21}H_{35}N_3OCl_2$: C, 60.57; H, 8.47; Cl, 17.11. Found: C, 60.43; H, 8.60; Cl, 17.5.

Summary

1. Several 8 - (ω - alkylaminoalkylamino)-6-methoxyquinolines have been prepared.

2. The four isomeric 6-butylamino-1-hexanols and their corresponding bromides have been prepared.

3. The synthesis of 6-methoxy-8-nitrolepidine is described.

NOTRE DAME, INDIANA RECEIVED APRIL 5, 1946

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Studies in the Quinoline Series. IV. The Preparation of Some 5-Amino-8-(ω-dialkylaminoalkylamino)-quinolines[1]

BY KENNETH N. CAMPBELL, JAMES F. KERWIN,[2] ARMIGER H. SOMMERS[3] AND BARBARA K. CAMPBELL

It has been reported by Schönhöfer[4] that the introduction of a methoxyl group in the 5-position in compounds of the plasmochin type enhances their antimalarial activity. In this connection it was of interest to test the antimalarial properties of plasmochin-like compounds containing other susceptible groups in the 5-position, and we undertook the preparation of several 5-amino-8-(ω-dialkylaminoalkylamino)-quinolines and of 5-hydroxy- and 5-acetoxyplasmochin.

A few 5-amino-8-alkylaminoquinolines have been reported in the literature.[5,6,7,8,9] These were prepared by selective alkylation of the 5,8-diamine[5,7] or by reduction of the corresponding 5-nitro compound.[6,8,9] The products were found to be very unstable in air, and in some cases no analytical data, physical constants or salts are reported. There appears to be no record in the literature of a 5-hydroxy-8-alkylaminoquinoline, but Moness and Christiansen[10] have reported the preparation of 8-hydroxy-5-(diethylaminoethylamino)-quinoline.

(1) The work reported here was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the University of Notre Dame.

(2) Present address: Smith, Kline and French Laboratories, Philadelphia, Pa.

(3) Present address: Department of Chemistry, Columbia University.

(4) Schönhöfer, *et al.*, *Z. physiol. Chem.*, **274**, 1 (1942).

(5) Frisch and Bogert, *J. Org. Chem.*, **9**, 338 (1944).

(6) Slater, *J. Chem. Soc.*, 2104 (1932).

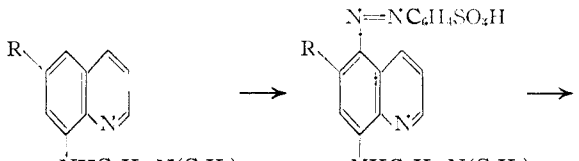
(7) Baldwin, *ibid.*, 2959 (1929).

(8) Fourneau, *et al.*, *Ann. Inst. Pasteur*, **44**, 719 (1930).

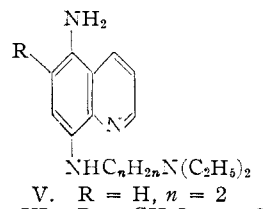
(9) Topchiev, *Compt. rend. acad. sci. U. R. S. S.*, **4**, 264 (1935); *C. A.*, **30**, 3821.

(10) Moness and Christiansen, *J. Am. Pharm. Assoc.*, **25**, 501 (1936).

Five 5 - amino - 8 - (ω - dialkylaminoalkylamino)-quinolines are described in this paper; namely, 5-aminoplasmochin, 5-amino-6-methoxy- and 5 - amino - 8 - (2′ - diethylaminoethylamino)-quinolines, and 5-amino-6-methoxy- and 5-amino - 8 - (6′ - diethylaminohexylamino)-quinolines. These were prepared easily and in good yields by a series of reactions



I. R = H, n = 2
II. R = CH_3O, n = 2
III. R = H, n = 6
IV. R = CH_3O, n = 6



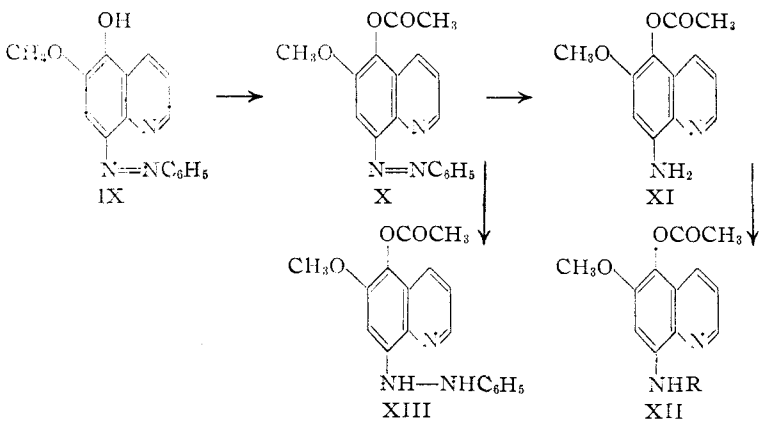
V. R = H, n = 2
VI. R = CH_3O, n = 2
VII. R = H, n = 6
VIII. R = CH_3O, n = 6

As would be expected from their analogy to *p*-phenylenediamine, the 5-amino-8-(dialkylaminoalkylamino)-quinolines were found to be extremely unstable in air. They could be distilled, however, in an atmosphere of nitrogen. Considerable difficulty was encountered in preparing suitable salts for testing; in most cases the hydro-

chlorides, sulfates and citrates darkened rapidly in air and were too hygroscopic for use. The oxalates, however, proved to be satisfactory.

Several attempts were made to prepare 5-hydroxy- and 5-acetoxyplasmochin. Jacobs and Heidelberger[11] have shown that when 5,8-diamino-6-methoxyquinoline is warmed with dilute hydrochloric acid, the 5-amino group is selectively replaced by a hydroxyl group. When we attempted to extend this reaction to 5-aminoplasmochin, the results indicated that the secondary amino group in the 8-position was attacked. This is in line with other evidence in the literature[12] that secondary amino groups on an aromatic nucleus are more easily replaced than primary. Efforts to convert 5-aminoplasmochin to the 5-hydroxy compound via diazotization led to a mixture of unstable compounds containing some nitrosamines, but none of the desired product could be isolated. A small amount of impure 5-hydroxyplasmochin was prepared by treating 8-amino-5-hydroxy-6-methoxyquinoline with Noval bromide, but the product proved to be extremely unstable and could not be purified.

The following scheme was used in attempts to prepare 5-acetoxyplasmochin, XII.



This method failed when the acetoxyazo compound X could not be reduced to the acetoxyamine, XI. Reduction of X with sodium hydrosulfite and catalytically led to a product which analyzed for the hydrazo compound, XIII. Attempts to reduce X with stannous chloride resulted in hydrolysis of the sensitive acetoxy group.

Experimental[13]

8-(2′-Diethylaminoethylamino)-6-methoxyquinoline, II.—This was prepared in 70% yield by the general procedure of Rohrmann and Shonle.[14] It boiled at 160–165° (0.15 mm.) and formed a yellow dihydrochloride melting at 182–186°, in agreement with Magidson's value.[15]

8-(2′-Diethylaminoethylamino)-quinoline, I.—8-Hydroxyquinoline and diethylaminoethylamine were reacted by Tchelintsev's procedure[16] as developed by Hartshorn[17] to give a 48% yield of compound of b. p. 135–140° (0.1 mm.). The dihydrochloride dihydrate melted at 133°.

Anal. Calcd. for $C_{15}H_{23}N_3Cl_2\cdot 2H_2O$: C, 51.15; H, 7.73; N, 11.9; Cl, 20.13. Found: C, 51.03; H, 7.79; N, 11.1; Cl, 20.1.

6-Diethylaminohexylamine.—At the time this work was done ε-aminocapronitrile was the most readily available starting material. The nitrile was ethylated with an excess of ethyl bromide, and the diethyl compound separated from primary and secondary amines by treatment with acetic anhydride. The diethylaminocapronitrile, obtained in 46% yield, had b. p. 103° (4 mm.), $n^{20}D$ 1.4433–1.4435, d^{20}_4 0.8556, MR_D obs. 52.1, MR_D calcd. 52.1. Breslow and Hauser[18] report b. p. 102–102.5° (4 mm.) for the compound prepared from ε-bromocapronitrile and diethylamine. A mixture of 37 g. of diethylaminocapronitrile, 70 ml. of absolute alcohol, 0.5 ml. of liquid ammonia and about 10 g. of Raney nickel was shaken with hydrogen at 50° and 50 lb./sq. in. The theoretical amount of hydrogen was taken up in three hours. The product weighed 27 g. (71%) and had b. p. 83–86° (4 mm.), $n^{20}D$ 1.4496, d^{20}_4 0.8312, MR_D obs. 55.6, MR_D calcd. 55.7. The dihydrochloride melted at 178–180°. This substance was used for the preparation of 8-(6′-diethylaminohexylamino)-quinoline according to Hartshorn.[17]

Anal. Calcd. for $C_{10}H_{26}N_2Cl_2$: Cl, 28.92. Found: Cl, 28.91.

5-Amino-8-(2′-diethylaminoethylamino)-6-methoxyquinoline, VI. SN-14,077.[19]—Thirty-five grams (0.128 mole) of 8-(2′-diethylaminoethylamino)-6-methoxyquinoline (II) was dissolved in 250 ml. of 1 *N* acetic acid, 250 ml. of a saturated solution of sodium acetate was added, and the mixture cooled to 5–10°. Twenty-five grams (0.143 mole) of sulfanilic acid was diazotized[20] and the slurry of diazonium salt was added to the cold aminoquinoline solution with stirring. The mixture was then stirred at 10° for thirty minutes, and the product was salted out by the addition of sodium chloride. As the azo dye tended to darken in air, it was used while still moist. A sample, dried under nitrogen, melted at 240–245°.

The moist azo dye was suspended in 500 ml. of water containing 10 g. of sodium hydroxide, and heated to 50°. Solid sodium hydrosulfite (40 g., 0.23 mole) was added with stirring in the course of twenty minutes, and the mixture was stirred at 60° for an additional thirty minutes. Reduction occurred rapidly. The cooled mixture was made strongly alkaline and extracted with ether. The ether extract, after drying over potassium carbonate, was distilled in an atmosphere of nitrogen. The material so obtained was a viscous red oil, b. p. 190–195° (0.3 mm.), it weighed 18.5 g. (50%). Since the free base turned black in air almost instantly, it was converted to the oxalate immediately after distillation. The amine (18.5 g., 0.064 mole) was dissolved in 50 ml. of absolute alcohol, and a solution of 12 g. (0.133 mole) of anhydrous oxalic acid in 50 ml. of hot absolute alcohol was added. The dioxalate started to precipitate almost at once. The mixture was chilled, the product collected and washed with a little cold alcohol. The salt was a light green, and this color was not removed by recrystallization.

(11) Jacobs and Heidelberger, THIS JOURNAL, **44**, 1077 (1922).

(12) Bucherer, *J. prakt. Chem.*, [2] **70**, 345 (1904).

(13) Most of the carbon and hydrogen, and some of the nitrogen analyses reported here were carried out at Northwestern University.

(14) Rohrmann and Shonle, THIS JOURNAL, **66**, 1640 (1944).

(15) Magidson, *Arch. Pharm.*, **272**, 74 (1934).

(16) Tchelintsev and Dubinin, *J. Gen. Chem. U. S. S. R.*, **10**, 1395 (1940); *C. A.*, **35**, 3641 (1941).

(17) Hartshorn and Baird, THIS JOURNAL, **68**, 1562 (1946).

(18) Breslow and Hauser, *ibid.*, **67**, 686 (1945).

(19) The numbers are those assigned by the Survey of Antimalarial Drugs to identify the drugs in their records. The antimalarial activities of these compounds will be tabulated in a forthcoming monograph.

(20) Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., New York, N. Y., 1941, p. 208.

It weighed 22.5 g., m. p. 127–131°. It was soluble in water, slightly soluble in alcohol, and insoluble in ether.

Anal. Calcd. for $C_{20}H_{28}N_4O_9 \cdot {}^1/_2H_2O$: C, 50.3; H, 6.1; N, 11.7: Found: C, 50.2; H, 6.5; N, 11.7.

5-Amino-8-(6′-diethylaminohexylamino)-6-methoxyquinoline, VIII, SN-14,074.—This was prepared from 8-(6′-diethylaminohexylamino)-6-methoxyquinoline[21] as described above, except that the reduction was carried out in the absence of sodium hydroxide. The 5,8-diamine was obtained in 66% yield as a red oil, b. p. 210–218° (0.5 mm.). The oxalate was a bluish-green crystalline solid, m. p. 123–125°. It had essentially the same solubilities as its lower homolog. The aqueous solution was slightly acid to congo red.

Anal. Calcd. for $C_{24}H_{36}N_4O_9$: C, 54.9; H, 6.92; N, 10.67; oxalic acid, 34.3. Found: C, 55.1; H, 6.67; N, 9.83; oxalic acid, 33.6.[22]

5-Amino-8-(2′-diethylaminoethylamino)-quinoline, V. SN-14,075.—The azo dye, m. p. 236–237°, was prepared as described for the 6-methoxy compound, and was reduced as the sodium salt with sodium hydrosulfite. The product, obtained in 70% yield, was a viscous red oil, b. p. 174–177° (0.06 mm.), which solidified on rubbing to an orange-yellow solid, m. p. 82–84° (dec.).

Anal. Calcd. for $C_{15}H_{22}N_4$: C, 69.7; H, 8.6; N, 21.7. Found: C, 69.8; H, 8.4; N, 21.2.

The free base was very unstable in air and darkened rapidly. It was converted to the trihydrochloride in ether solution; the salt was obtained as an orange-crystalline solid, m. p. 240–245°. It was extremely soluble in water to give a solution that was acid to congo red, but only slightly soluble in alcohol.

Anal. Calcd. for $C_{15}H_{25}N_4Cl_3$: C, 48.99; H, 6.85; Cl, 28.93. Found: C, 48.87; H, 6.93; Cl, 28.4.

5-Amino-8-(6′-diethylaminohexylamino)-quinoline, VII. SN-14,076.—The azo sulfonic acid, m. p. 225°, prepared from 8-(6′-diethylaminohexylamino)-quinoline[17] was reduced in aqueous alkaline solution with sodium hydrosulfite to give a 71% yield of product, a red viscous oil, b. p. 220° (0.06 mm.). The trihydrochloride was too hygroscopic for use, and the dioxalate was therefore prepared. After recrystallization from alcohol–ethyl acetate mixture it was obtained as light green crystals, m. p. 116–118°. The oxalate was very soluble in water, less soluble in alcohol and insoluble in ether.

Anal. Calcd. for $C_{28}H_{34}N_4O_8$: C, 55.85; H, 6.9; N 11.3. Found: C, 56.3; H, 7.1; N, 10.6.

5-Aminoplasmochin.—Plasmochin (31.5 g., 0.1 mole) was treated in acetic acid–sodium acetate solution with the diazonium salt from 21 g. of sulfanilic acid. The azo dye weighed 46 g. (95%) and melted at 165–167°. It was reduced in dilute aqueous alkali with sodium hydrosulfite to give a 73% yield of 5-aminoplasmochin, a viscous red oil, b. p. 190–200° (0.3 mm.), Topchiev[9] who prepared the compound by reduction of 5-nitroplasmochin, reported the boiling point as 250° (3 mm.). The salts were all extremely hygroscopic and difficult to handle, except the one with 1-methylene-bis-(2-hydroxy-3-naphthoic acid), which melted at 167°.[9] Attempts to hydrolyze the 5-aminoplasmochin with 10% hydrochloric acid[11] yielded no 5-hydroxyplasmochin. Treatment of 5-aminoplasmochin with nitrous acid gave some nitrosamine, but no 5-hydroxyplasmochin could be isolated.

5,8-Diamino-6-methoxyquinoline.—8-Amino-6-methoxyquinoline was coupled with diazotized sulfanilic acid in dilute acetic acid–sodium acetate solution. The moist crude azo compound was reduced in dilute aqueous alkali with sodium hydrosulfite to 5,8-diamino-6-methoxyquinoline in 65–80% over-all yield. The diamine melted at 161–163° after recrystallization from toluene. Jacobs and Heidelberger[11] reported the m. p. as 163–164° for the compound obtained from 5-amino-6-methoxy-8-(*p*-sulfophenylazo)-quinoline.

8-Amino-5-hydroxy-6-methoxyquinoline.—A solution of 11.5 g. of 5,8-diamino-6-methoxyquinoline in 100 g. of 10% hydrochloric acid was heated at 85° for one hour while a stream of carbon dioxide was passed through the solution. The solution was cooled under carbon dioxide and neutralized with sodium carbonate. The greenish-yellow precipitate was dried under nitrogen, as it darkened rapidly in air. The yield of compound of m. p. 180–182° was 9 g., 73%. Jacobs and Heidelberger[11] reported the melting point as 180–182°.

5-Hydroxyplasmochin, SN-12,227.—Nineteen grams of 5-hydroxy-8-amino-6-methoxyquinoline was heated with 33 g. of Noval bromide hydrobromide and 60 ml. of absolute alcohol at 95–100° for forty-eight hours in an atmosphere of nitrogen. The alcohol was evaporated, the residue diluted with water, made basic with potassium carbonate and extracted with chloroform. The dried chloroform solution was treated with ethereal hydrogen chloride, and the brown precipitate (6 g.) recrystallized several times from alcohol. It melted at 195–199° after softening at 170°. It was very hygroscopic and darkened in air; attempts to purify it further were fruitless.

Anal. Calcd. for $C_{19}H_{32}N_3O_2Cl_3 \cdot C_2H_5OH$: Cl, 21.8. Found: Cl, 20.8.

6-Methoxy-5-nitroquinoline.—The following procedure was found to be more satisfactory than that of Decker and Engler.[23] Fifty grams of 6-methoxyquinoline was added dropwise with stirring to 150 g. of fuming nitric acid (d. 1.52) kept at −5 to +3°. The addition required about one and one-half hours. The reaction mixture was allowed to stand at room temperature for one-half hour, and was then warmed gradually to 70° and kept there for one hour. It was poured onto ice, and the precipitated nitrate salt pressed as dry as possible. This was suspended in water, excess sodium hydroxide solution was added gradually, and the mixture was stirred for two hours. The 6-methoxy-5-nitroquinoline so obtained melted at 90° and was used without purification. The yield was 70–75%.

5-Amino-6-methoxyquinoline.—6-Methoxy-5-nitroquinoline was reduced with stannous chloride by the procedure of Jacobs and Heidelberger[24] to give an 80% yield of the amine. The crude product was recrystallized from benzene–hexane mixture, giving lustrous yellow needles, m. p. 150°.

5-Acetoxy-6-methoxy-8-phenylazoquinoline, X.—5-Amino-6-methoxyquinoline was coupled with diazotized aniline, and the product hydrolyzed to 5-hydroxy-6-methoxy-8-phenylazoquinoline (IX) by the method of Jacobs and Heidelberger.[24] A mixture of 35 g. of the hydroxy compound (m. p. 172–173°), 400 ml. of acetic anhydride and 35 g. of anhydrous sodium acetate was refluxed for three hours. The cooled solution was poured into ice water and stirred at 5–10° for two hours. The product was recrystallized from benzene–hexane mixture to give 18 g. of light red crystals, m. p. 153–157°.

Anal. Calcd. for $C_{18}H_{15}N_3O_3$: C, 67.3; H, 4.69. Found: C, 66.9; H, 4.72.

1-Phenyl-2-(5′-acetoxy-6′-methoxy-8-quinolyl)-hydrazine, XIII.—(a) The acetoxyazo compound (X) was hydrogenated in absolute alcohol over Raney nickel at room temperature and 60 lb. pressure. One mole of hydrogen was absorbed, and absorption then ceased. The product melted at 118–120° and did not depress the melting point of the material obtained from sodium hydrosulfite reduction.

(b) Eighteen grams of the acetoxyazo compound (X) was suspended in 150 ml. of alcohol and 150 ml. of water, and the mixture heated to boiling. Solid sodium hydrosulfite (34 g.) was added in the course of ten minutes; the red color of the mixture disappeared almost immediately. The hot mixture was stirred for an additional twenty minutes, and was poured into ice water. There was obtained 13 g. of a tan solid, m. p. 121–122°. After recrystallization from benzene–hexane and from alcohol it formed tan crystals, m. p. 124.5–125°. Analyses showed that the material

(21) Drake, *et al.*, THIS JOURNAL, **68**, 1536 (1946).

(22) Elderfield, *et al. ibid.*, **68**, 1524 (1946).

(23) Decker and Engler, *Ber.*, **42**, 1740 (1909).

(24) Jacobs and Heidelberger, THIS JOURNAL, **42**, 2278 (1920).

was the hydrazo compound and not the expected amine.

Anal. Calcd. for $C_{12}H_{12}N_2O_3$: C, 62.1; H, 5.21. Calcd. for $C_{18}H_{17}N_3O_3$: C, 66.84; H, 5.30. Found: C, 66.92; H, 5.56.

Summary

1. The preparation of several new 5-amino- 8-(ω-dialkylaminoalkylamino)-quinolines is described.

2. Attempts to prepare 5-hydroxyplasmochin and 5-acetoxyplasmochin are described.

NOTRE DAME, INDIANA RECEIVED APRIL 5, 1946

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DARTMOUTH COLLEGE]

Some N-Substituted Aminoquinolines[1]

BY ELDEN B. HARTSHORN AND SPENCER L. BAIRD, JR.

With the finding that 8-(4-diethylamino-1-methylbutylamino)-quinoline possessed significant antimalarial activity[2] interest was awakened in derivatives of quinoline containing only aliphatic polyamine side chains with no other substituents. The present paper records the synthesis of several of these substances. The compounds prepared fall into two general groups: namely, those in which the conventional Plasmochin side chain has been attached in the 2-, 5-, 6-, 7- and 8-positions of quinoline, and those compounds derived from 8-aminoquinoline in which other side chains have been introduced.

With one exception all of the substances here reported were prepared by the method of Chelintsev and Dubinin.[3]

Experimental

Intermediates.—2-Chloroquinoline was prepared from N-methyl-2-quinolone (38%)[4] and reaction of the latter with phosphorus oxychloride (70%); m. p. 35–37°; literature, 37–38°.

5-Quinolinol was obtained by stannous chloride reduction of 5-nitroquinoline and a reverse Bucherer[5] reaction on the amine (47%), m. p. 224° dec.

6- and 7-quinolinols resulted from Skraup[6] reactions on technical 4- and 3-anisidines (54, 44%), the methoxyquinolines then being cleaved with constant boiling hydrobromic acid (80–90%). The products melted 190–193° and 238–240°, respectively;[7] literature, 193° and 235–238°, respectively.

Commercial 1-diethylamino-4-aminopentane was purified by the method of Jones.[8] 1-Diethylamino-3-aminopropane and 1-diethylamino-6-aminohexane were from the Universities of Wisconsin and Columbia, respectively.

The Bucherer Reaction.[3]—This synthesis was carried out by boiling a solution of 0.28 mole of a polyamine, such as 1-diethylamino-4-aminopentane, in 100 ml. of water in which 0.2 mole of sulfur dioxide had been dissolved, with 0.1 mole of the quinolinol for thirty or more hours under a pressure exceeding that of the atmosphere by 10 cm. of mercury. Generally the quinolinol dissolved at the boiling point of the mixture and a layer of insoluble oil formed on the surface of the solution as the reaction proceeded. When the separated oil no longer increased in volume, sodium hydroxide (20+ g.) was added, and the mixture subjected to steam distillation to remove excess of the reagent amine. The remaining insoluble, non-volatile oil was then extracted with ether, the ethereal solution was dried over anhydrous potassium carbonate, and the oil distilled *in vacuo* under nitrogen. In general, the yellow oils, so obtained, darkened in air and were therefore at once transformed into suitable salts.

Quinolines with the Plasmochin Side Chain as the Only Substituent.—The above method was used to prepare the four quinolines having the Plasmochin side chain in the 5-, 6-, 7- and 8-positions, respectively. The corresponding 2-derivative was necessarily prepared in another manner.[9] Details pertinent to these (4-diethylamino-1-methylbutylamino)-quinolines are given in Table I.

Before finding that citric acid formed satisfactory salts with many bases of this type, the above oils were stored in hydrochloric acid solution. Later, a solid monocitrate of no. 5 was prepared; yellow powder, m. p. 107–108°.

Anal. Calcd. for $C_{18}H_{27}N_3 \cdot C_6H_8O_7$: C, 60.36; H, 7.39; N, 8.30. Found: C, 60.06; H, 7.08; N, 8.89.

Other N-Substituted 8-Aminoquinolines.—The following drug bases were prepared by the standard Bucherer procedure outlined above, slight modifications of the procedure being made in some cases.

8-(3-Diethylaminopropylamino)-quinoline Monocitrate (SN-13,457).—The base was obtained in 41% and 58% yields (1.0 mole of 8-quinolinol used in second run), as a yellow oil, b. p. 156–159° (0.5 mm.). The yellow citrate turned white upon drying *in vacuo* and then decomposed at 94.3–95.0°.

Anal.[10] Calcd. for $C_{16}H_{23}N_3 \cdot C_6H_8O_7 \cdot {}^1/_2C_2H_5OH$: C, 58.47; H, 7.24; N, 8.81. Found: C, 58.43; H, 6.98; N, 8.67, 8.80.

8-(6′-Diethylaminohexylamino)-quinoline Monocitrate (SN-13,458).—The yellow oily base was prepared in 33% yield using 8-quinolinol (0.43 mole) rather than 1-diethylamino-6-aminohexane (0.2 mole) in excess. It boiled at 172.5–175° (0.3 mm.). The monocitrate, a pale yellow powder, melted at 91.4–92.5° dec.

Anal.[10] Calcd. for $C_{19}H_{29}N_3 \cdot C_6H_8O_7$: C, 61.08; H, 7.59; N, 8.55. Found: C, 61.30; H, 7.80; N, 8.42.

8-[3-(4′-Diethylamino-1′-methylbutylamino)-propylamino]-quinoline (SN-14,064).—Since the excess of 1-diethylamino-4-(3′-aminopropyl)-aminopentane[11] was non-volatile with steam, the reaction mixture was saturated with sodium hydroxide, extracted with ether and the drug obtained by fractional distillation of the dried ether solution. It boiled at 200–210° (0.4 mm.) when redistilled in a Hickman still. The yield was 30%.

Anal. Calcd. for $C_{21}H_{34}N_4$: C, 73.64; H, 10.00. Found: C, 73.31; H, 10.31.

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(1) The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Dartmouth College.

(2) Antimalarial Drugs 1941–1945, published by the Survey of Antimalarial Drugs, in press.

(3) *C. A.*, **35**, 3641 (1941).

(4) Perkin and Robinson, *J. Chem. Soc.*, **103**, 1977 (1913).

(5) Kogan and Nikolaeva. *C. A.*, **32**, 7031 (1938).

(6) Elderfield, *et al.*, THIS JOURNAL, **68**, 1584 (1946).

(7) Mr. R. G. Nelb prepared the 6- and 7-quinolinols. Dr. W. R. Vaughan investigated ring closures to produce 7-quinolinol and prepared some N-methylquinolone.

(8) Jones, *Ind. Eng. Chem., Anal. Ed.*, **16**, 431 (1944).

(9) Bachmann and Cooper, *J. Org. Chem.*, **9**, 309 (1944).

(10) Analyses by courtesy of Dr. Byron Riegel.

(11) Kindly furnished by Dr. J. E. Kirby of du Pont.