

Quinoline-2,4-dicarboxanilide.—The dicarbonyl chloride was dissolved in an excess of hot aniline. The dianilide crystallized out on cooling. The compound when recrystallized from aniline or nitrobenzene formed small bluish-white needles; very insoluble in hot water, slightly soluble in hot alcohol, m. p. 285–286°. The crystals turn red in cold concentrated sulfuric acid and go into solution (orange) on warming.

Anal. Calcd. for $C_{23}H_{17}N_3O_2$: N, 11.44. Found: N, 11.42, 11.41.

2,4-Dicarbamylquinoline.—The dimethyl ester (10 g.) was heated with ammoniacal methanol (100 cc.) at 85° for twenty hours. The amide, formed in quantitative yield, crystallized from water or alcohol as small white needles, m. p. 277.5–279.5°; soluble in concentrated sulfuric acid (yellow).

Anal. Calcd. for $C_{11}H_9N_3O_2$: N, 19.53. Found: N, 19.33, 19.02.

2,4-Diaminoquinoline.—Fifteen grams of the diamide was added to 725 cc. of a solution containing 50 g. of potassium hydroxide and 23 g. of bromine. The amide dissolved readily in the cold. The solution was heated on the water-bath for one hour, the small amount of dark brown precipitate filtered off, and the solution bone-blackened, filtered and cooled. The diamine slowly crystallized from the solution. More product was obtained by concentrating the solution. The diamine was recrystallized from water (tendency for supersaturation) as lustrous white needles, m. p. 197–198.5°,²³ yield, 85%. The picrate, crystallized from much hot water, melted at approximately 283° (decomp.).

Anal. Calcd. for $C_9H_9N_3$: N, 26.41. Found: N, 26.51. Calcd. for $C_{15}H_{15}N_6O_7$ (monopicrate): N, 21.64. Found: N, 21.84.

(23) The m. p. in German Patent 615,184 is given as 188–190°; the analysis reported was N, 25.3.

2-Carbamylethyl Cinchoninate.—On heating 2,4-dicarbethoxyquinoline with ammoniacal methanol at 50°, the mono amide was formed in 86% yield; slightly soluble in hot alcohol, very insoluble in water, m. p. 226–227.5° (melts to a tan liquid with a green fluorescence).

Anal. Calcd. for $C_{13}H_{13}N_2O_3$: N, 11.41. Found: N, 11.59, 11.56.

2-Aminocinchoninic Acid.—Five grams of 2-carbamylethyl cinchoninate was heated on the steam-bath for one hour with 250 cc. of water containing 10 g. of potassium hydroxide and 4.75 g. of bromine. Solution (red) was effected on warming. The solution, after being cooled, was diluted to dissolve the potassium salt and made weakly acidic with hydrochloric acid. The yellow precipitate of 2-aminocinchoninic acid was crystallized from much water as lustrous tan crystals, m. p. 362° (dec.); soluble in concentrated sulfuric acid (red), concentrated hydrochloric acid (red), and dilute sodium hydroxide; insoluble in alcohol and benzene.

Anal. Calcd. for $C_{10}H_8N_2O_3$: N, 14.9; neut. equiv., 188. Found: N, 14.3; neut. equiv., 187.

Diazotization in concentrated sulfuric acid with dry sodium nitrite and pouring into water gave the known 2-hydroxycinchoninic acid,¹⁸ m. p. 342°. Fusion with soda-lime gave 2-aminoquinoline, white plates from water, m. p. 125–127°.

Summary

Improved preparations of 3- and 4-aminoquinoline, and a new method of preparation of 2,4-diaminoquinoline and of 2-aminocinchoninic acid are described. The attempted preparation of 4-nitroquinoline from 3-aminoquinoline is discussed.

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Coupling Reactions of Aminoquinolines with Benzenediazonium Chloride. A Study of Orientation in the Quinoline Ring

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Knorr⁴ and Marekwald⁵ pointed out that the chemical properties of naphthalene and quinoline are best explained by accepting the static bond structure proposed by Erlenmeyer, while the chemical properties of benzene are better explained on the basis of Kekulé's concept of shifting double bonds. More recently Pauling⁶ has

arrived at the same conclusion from quantum mechanical studies, and Le Fèvre and Le Fèvre,⁷ from dipole studies of quinoline, favor the Erlenmeyer structure.

There are several good recent surveys of the naphthalene problem,⁸ but quinoline has been given only brief discussions.^{7,9} Therefore, a comprehensive study of the coupling reactions of the aminoquinolines was undertaken to char-

(1) This paper is being published, following the death of Professor Renshaw, by his collaborators.

(2) Present address: Pyridium Corporation, Yonkers, N. Y.

(3) Present address: General Aniline Works, Inc., Grasselli, N. J.

(4) Knorr, *Ann.*, **279**, 212 (1894).

(5) Marekwald, *Ann.*, **274**, 334 (1898); **279**, 14 (1894).

(6) Pauling in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., Chap. 22, p. 1970.

(7) Le Fèvre and Le Fèvre, *J. Chem. Soc.*, 1470 (1935).

(8) Fieser in Gilman's "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., Chap. 2, p. 81; Fieser, *This Journal*, **57**, 1459 (1935); *Ann. Repts. Chem. Soc.*, 281 ff. (1936).

(9) Mills and Smith, *J. Chem. Soc.*, 2724 (1922).

acterize the orientation and the "fixed bond" structure of quinoline, for Fieser¹⁰ has shown that the coupling reaction is indicative of bond structure.

Table I compares the actual results obtained by coupling the different aminoquinolines with benzenediazonium chloride with those to be expected from Erlenmeyer's static formula.

TABLE I

Position of NH ₂	Expected coupling	Obsd. coupling
2	2 (diazamino)	2 (diazamino)
3	4	4
4	3	Failed
2, 4	3	2(?)
5	8 or 6	8 and 6
6	5	5
7	8	(8)
8	5 or 7	5

These results indicate a good agreement with the Erlenmeyer structure. Since both the methods of preparation and of coupling of the mono-bz- and mono-py-aminoquinolines are very different, they are discussed separately below.

Results of Coupling Bz-Aminoquinolines with Benzenediazonium Chloride.—The bz-aminoquinolines were made by the reduction of the corresponding nitro compounds obtained by the appropriate Skraup reactions. The 7-nitroquinoline was also prepared by the lithium nitrate reaction.¹¹

The earlier work on the coupling of mono-bz-aminoquinolines was that of Knuepel¹² and of Jacobs and Heidelberger.¹³ The former attempted to prepare the azo derivative of 6-aminoquinoline, but obtained the intermediate diazoamino compound, which did not undergo rearrangement. The latter were successful in coupling diazotized aniline with 5-aminoquinoline in dilute acetic acid-sodium acetate solution. The authors have been successful in applying Jacobs and Heidelberger's conditions to all of the mono-bz-aminoquinolines. They have also effected coupling in dilute hydrochloric acid solutions. The former method yielded the purer product.

The structure of each resulting azo compound was determined by the following procedures. (1) Reduction of the azo compound from 8-aminoquinoline gave a diaminoquinoline which melted at 163°. It did not form a phen-

anthrenequinone condensation product (test for an ortho diamine¹⁴).

(2) Reduction of the azo compound formed by coupling 5-aminoquinoline in dilute hydrochloric acid gave two diamines. The main product was a diamine of m. p. 163° which gave no melting point depression with the diamine of (1) and gave no phenanthrene-quinone condensation product. The other diamine present could not be purified sufficiently to show a sharp melting point. It gave a condensation product with phenanthrenequinone, m. p. 294–295°, and must, therefore, have been 5,6-diaminoquinoline. Therefore, 8-aminoquinoline coupled mainly in the 8-position and to a slight extent in the 6-position. It was found that coupling of the 5-amine in dilute acetic acid-sodium acetate solution gave only the 8-phenylazo compound.

(3) Reduction of the azo compound from 6-aminoquinoline gave a diamine which yielded a phenanthrenequinone condensation product of m. p. 294–295°. This azine did not depress the melting point of the azine formed in (2), hence, the 6-aminoquinoline coupled in the 5-position.

(4) Reduction of the azo compound from 7-aminoquinoline gave a new diamine which formed a phenanthroquinone azine, showing it to be an ortho diamine. It was not possible to prove the structure of this diamine. It must be either the 7,8- or 6,7-diaminoquinoline. It is tentatively considered the 7,8-diamine.

The hydrochlorides of the phenylazo-aminoquinolines were prepared for bactericidal tests.

Results of Coupling Py-Aminoquinolines with Benzenediazonium Chloride.—The py-aminoquinolines were prepared by various new or improved methods described in a previous report.¹⁵

Since negative results were obtained in attempting coupling reactions under the same conditions as for the bz-aminoquinolines, various solvents were tried in order to effect coupling. The results of reactions with benzenediazonium chloride are in Table II.

TABLE II

Solvent	2NH ₂	3NH ₂	4NH ₂	2,4NH ₂
H ₂ O, HOAc, NaOAc	No	Diazoamino	No	Diazoamino
H ₂ O, HCl (dil.)	...	No	No	No
H ₂ O, HCl (excess)	...	No	...	No
H ₂ O, MeOH	Diazoamino	Diazoamino	No	Diazoamino
HOAc (glacial)	No	Red tar	No	Diazoamino
EtOH (abs.)	Diazoamino	Azo compound	No	No

The coupling of 2-aminoquinoline with benzenediazonium chloride gave a diazoamino compound, an expected result. No attempt was made to rearrange it, since Chichibabin¹⁶ has shown that the analogous diazoamino compound from 2-aminopyridine does not undergo rearrangement, a result confirmed by the authors.

(10) Fieser, *THIS JOURNAL*, **57**, 1459 (1935).

(11) Bacharach, Haut and Caroline, *Rec. trav. chim.*, **52**, 413 (1933).

(12) Knuepel, *Ann.*, **310**, 87 (1899).

(13) Jacobs and Heidelberger, *THIS JOURNAL*, **42**, 2284 (1920).

(14) Hinsberg, *Ann.*, **237**, 340 (1887).

(15) R. R. Renshaw and Friedman, *THIS JOURNAL*, **61**, 3320 (1939).

(16) Chichibabin and Persits, *Chem. Abstr.*, **20**, 2499 (1926).

The 3-aminoquinoline gave in small yield the desired azo compound only by coupling in absolute alcohol. Although the 3-amine is truly aromatic, it gave the diazoamino compound when coupling was effected under the conditions for the bz-aminoquinolines. The 3-diazoaminoquinoline was destroyed readily by boiling in dilute hydrochloric acid. The decomposition is characterized by the appearance of the blue fluorescence of the 3-amine. Reduction of the azo compound 3-aminoquinoline gave a new diamine, m. p. 176–177°, ¹⁷ which can be characterized by an intense blue to purple fluorescence in various solvents. This diamine gave a condensation product with phenanthrenequinone, and is, therefore, an ortho diamine. To fix the structure conclusively, 4-aminoquinoline was brominated to yield the 3-bromo derivative¹⁸ and this was converted to the 3,4-diamine with 26% ammonia water.¹⁹ The 3,4-diamine so prepared was identical with that from the reduction of the azo compound. Hence, the 3-aminoquinoline coupling occurred at the 4-position.

The 4-aminoquinoline failed to couple under any conditions tried; the unreacted amine always could be isolated at the end of the reaction. Attempted coupling in absolute alcohol with *p*-nitrobenzenediazonium chloride produced a very interesting phenomenon. A bright red solution was formed which rapidly faded. The fading was accompanied by loss of nitrogen. This effervescence was studied carefully at different temperatures, and was found to occur at as low as –10°. It was not possible to isolate the red compound, since at the temperatures at which it formed, decomposition immediately occurred. Nitrobenzene was isolated from the solution; this is the normal product obtained by the reaction of *p*-nitrobenzenediazonium chloride with hot alcohol.²⁰ It would appear that an unstable red intermediate was formed and that this immediately decomposed into 4-aminoquinoline, nitrogen, and nitrobenzene. By analogy with 2-aminoquinoline, the formation of a diazoamino compound could be expected. No reason can be given for the instability of the red intermediate without more specific data.

The 2,4-diaminoquinoline was tried in coupling

reactions since Morgan and Wootton²¹ were able to couple at the position between the two amino groups in substituted meta-phenylenediamines. By analogy it was expected that the 2,4-diamine would couple in the 3-position, no matter which one of the three tautomeric forms might represent the structure. It was found that in glacial acetic acid both benzenediazonium chloride and *p*-nitrobenzenediazonium chloride gave readily yellow-orange compounds which formed yellow hydrochlorides. Without exception it was found that in this series the color of the hydrochlorides of the true azo compounds was red or a deep orange-red, whereas that of the hydrochlorides of the diazoamino compounds was yellow. On this basis it is believed that these compounds are diazoamino. Since 4-aminoquinoline did not undergo coupling reactions under the conditions tried, while 2-aminoquinoline formed a diazoamino compound, it is postulated that 2-diazoamino-4-aminoquinolines are formed.

Experimental Part^{22,23}

Bz-Aminoquinolines

6-Amino-5-phenylazoquinoline.—Method I: Benzene-diazonium chloride was coupled with 6-aminoquinoline in 0.25 molar hydrochloric acid solution over a period of twelve hours. On salting out the hydrochloride at 60°, it first formed an oil, which on stirring solidified to a light-orange flocculent precipitate. It was purified by dissolving in a minimum amount of water and adding an equal volume of alcohol, whereupon orange needles separated, m. p. 250–255°. These crystals analyzed for the monohydrochloride trihydrate. This product was converted to the monohydrochloride by drying at 120°. The free base was prepared by precipitating it from a solution of the hydrochloride with ammonium hydroxide. It was recrystallized from alcohol, forming light orange needles, m. p. 247–249°.

Method II: Coupling was accomplished in acetic acid-sodium acetate solution in approximately ten minutes. After coupling was complete, the solution was made alkaline with ammonium hydroxide. The precipitated solid was recrystallized from a solution of alcohol and water.

The free base was reduced by means of stannous chloride and concentrated hydrochloric acid. The procedure was the following: after refluxing the reaction mixture for half an hour, it was evaporated to dryness on a water-bath. The residue was dissolved in water and the tin removed by means of hydrogen sulfide. The water solution was evaporated almost to dryness and cooled. The hydrochloride crystallized. It was purified by dissolving in alcohol and

(17) Backeberg and Friedmann, *J. Chem. Soc.*, 976 (1938). These authors did not prepare 3,4-diaminoquinoline.

(18) Claus and Howitz, *J. prakt. Chem.*, [2] 50, 237 (1894).

(19) Maler-Bode, *Ber.*, 69, 1536 (1936).

(20) Cameron, *Am. Chem. J.*, 20, 251 (1898).

(21) Morgan and Wootton, *J. Chem. Soc.*, 87, 935 (1905).

(22) The experimental work on the bz-aminoquinolines was performed by F. J. Gajewski, that on py-aminoquinolines by H. L. Friedman.

(23) All melting points are corrected.

precipitating with ether. The 5,6-diaminoquinoline was obtained by making a solution of the hydrochloride strongly alkaline with potassium hydroxide. A melting point of 135° was found for this product, whereas that reported is 95²⁴ and 145°.²⁵ The phenanthroquinoline azine melted at 294–295°; reported²⁴ 287–288°.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.58, 22.48. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: N, 19.56, 19.60. Calcd. for $C_{15}H_{12}N_4 \cdot HCl \cdot 3H_2O$: N, 16.54. Found: N, 16.66, 16.57.

5-Amino-8-phenylazoquinoline was first prepared by W. A. Jacobs and M. Heidelberg.¹⁸ It was found, however, that the product after several recrystallizations melted at 191–194°, whereas the reported m. p. is 209–211°. This is to be attributed to the fact that a mixture of two coupling products was obtained as shown below. The hydrochloride, m. p. 225–227°, precipitated as a violet powder when dry hydrogen chloride was passed into a chloroform solution of the free base.

The free base was reduced with stannous chloride and concentrated hydrochloric acid. After refluxing the reaction mixture for one-half hour, the solution became decolorized. Solid potassium hydroxide was added under cooling until a 50% solution was obtained. The yellow solid was filtered and dissolved in ether. By slowly evaporating the ether solution, a crust formed on the side of the evaporating dish, which melted over the range 150–155°. There was present in this crust some 5,6-diaminoquinoline, for a phenanthrenequinone ortho condensation product was obtained. The main diaminoquinoline, obtained in long crystals on the bottom of the evaporating dish, was 5,8-diaminoquinoline, m. p. 163°.

Anal. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: N, 19.36, 19.32.

8-Amino-5-phenylazoquinoline was prepared by coupling benzenediazonium chloride with 8-aminoquinoline in acetic acid–sodium acetate solution. The product was recrystallized from alcohol, forming lustrous, deep orange plates, m. p. 133°. No trace of any other coupling product was found. The hydrochloride precipitated as a violet powder, m. p. 221–223°, from a chloroform solution of the free base. The hydrochloride was hydrolyzed readily in water.

The free base was reduced by means of stannous chloride and hydrochloric acid to form 5,8-diaminoquinoline, m. p. 163°. No phenanthrenequinone condensation was obtained even after heating for five hours.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.66, 22.56. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: N, 19.49, 19.30.

7-Amino-8-phenylazoquinoline was prepared by coupling benzenediazonium chloride with 7-aminoquinoline in acetic acid–sodium acetate solution. At first a deep orange oil formed which solidified after one week. Recrystallization from alcohol and water gave light orange needles, m. p. 170–173°. The hydrochloride, m. p. 210–211°, was precipitated by dry hydrogen chloride from a solution of the free base in chloroform. It is easily soluble in water.

Reduction of the free base with stannous chloride and

hydrochloric acid, by the same method used for 5-amino-8-phenylazoquinoline, gave a new diaminoquinoline, which crystallized from water as a monohydrate in the form of light yellow needles, m. p. 95–97°. It forms an ortho condensation product with phenanthrenequinone after four hours of heating, m. p. 314°. The structure assigned to this new diamine is the 7,8-diaminoquinoline.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.65, 22.41. Calcd. for $C_{15}H_{12}N_4 \cdot HCl$: N, 19.67. Found: 19.27, 19.30. Calcd. for $C_{15}H_{12}N_4 \cdot H_2O$: N, 23.73. Found: N, 23.65, 23.87. Calcd. for $C_{15}H_{12}N_4$: N, 12.69. Found: N, 12.57, 12.44.

Py-Aminoquinolines

General Directions for Coupling Reactions.—Different methods had to be used in effecting coupling of the py-aminoquinolines and benzenediazonium chloride. Directions are given for 1 g. of amine and an equivalent amount of benzene diazonium chloride. (1) Dilute hydrochloric acid—as for the bz-aminoquinolines. (2) Acetic acid–sodium acetate—as for the bz-aminoquinolines. (3) Excess hydrochloric acid—method according to Ostromisslenski²⁶ and K. H. Meyer.²⁷ (4) Aqueous alcohol—the aqueous diazonium solution (15 cc.) was added slowly with stirring to an equal volume of a methanol solution of the amine at a temperature below 5°. (5) Glacial acetic acid—the dry diazonium chloride²⁸ in 5 cc. of solvent was slowly added with stirring to an equal volume of amine solution keeping the temperature below 10°. (6) Absolute alcohol—the dry diazonium chloride in 15 cc. of solvent was slowly added with stirring to a 5 cc. solution of the amine at a temperature below 10°.

Benzenediazonium chloride was used in all cases except where otherwise specified. Coupling reactions which are recorded in Table II as unsuccessful are not described in detail. In all unsuccessful cases aqueous solutions remained overnight below 5° and non-aqueous solutions were allowed to stand for one week below 10°. These reactions were characterized by a lack of color change and non-appearance of precipitate (in a few cases in excess hydrochloric acid solutions, some amine hydrochloride precipitated). The bulk of the amine was always isolated unreacted from the solutions.

2-Benzenediazoaminoquinoline was formed in both aqueous and absolute alcoholic coupling. The yields were small. From 1 g. of the amine 0.375 g. of product was obtained in absolute alcohol. The product on recrystallization from 95% ethanol formed light tan needles, m. p. 165–166.5°, identical in appearance with that of 2-benzenediazoaminopyridine. It is also stable to hot dilute sodium hydroxide and hydrochloric acid.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.49, 22.70.

3-Benzenediazoaminoquinoline.—The 3-aminoquinoline was dissolved in a dilute hydrochloric acid solution and the diazonium chloride solution was added. Then a saturated solution of sodium acetate was added until turbidity appeared. After standing overnight below 5°, an orange-tan

(26) Ostromisslenski, *THIS JOURNAL*, **56**, 1714 (1934).

(27) Meyer, *Ber.*, **54**, 2272 (1921).

(28) Hantzsch and Borghaus, *Ber.*, **30**, 90 (1897); Hantzsch and Jochem, *ibid.*, **34**, 3337 (1901).

(24) Kaufmann, *Ber.*, **50**, 1630 (1917).

(25) Rudy, *ibid.*, **71B**, 847–857 (1938).

precipitate of the diazoamino compound formed. The same compound was obtained from aqueous alcoholic coupling. The compound could be recrystallized from water, m. p. 156–157° (with decomposition). Recrystallization from hot 10% sodium hydroxide gave identical crystals but melting at 177–178° (with decomposition). Undoubtedly different degrees of hydration occurred to account for these discrepancies. It was noted that the melting point of a sample would rise after heating at 80° for several hours. The new melting point was always sharp. Boiling dilute hydrochloric acid destroyed the compound readily with the appearance of the blue fluorescence of 3-aminoquinoline.

Reduction of the compound with stannous chloride and hydrochloric acid resulted in the formation of 3-aminoquinoline.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 21.95, 21.46.

4-Phenylazo-3-aminoquinoline was obtained by coupling in absolute ethanol. On mixing the diazonium and amine solutions, a bright red color developed immediately. After standing overnight small dark red crystals formed, m. p. 125–135°. Free chloride ion was present. From 0.5 g. of the amine, 0.45 g. of product was obtained. This product was purified by dissolving in 100 cc. of 0.1 *N* hydrochloric acid, then boiling to decompose any diazoamino compound, filtering to remove a small amount of tar, and precipitating the orange-red free base with ammonia, m. p. 198–201°. This purification yielded 70% of product from the crude. On extracting the basic mother liquor with ether, it was found that 0.015 g. of 3-aminoquinoline per 0.1 g. of crude could be isolated. Hence, the original precipitate was a mixture of the azo compound and the diazoamino or of the azo compound and the amine as hydrochlorides. The azo compound was further purified by recrystallization from hot alcohol and water solution. It formed small, lustrous, light red needles, m. p. 203–204°. Evaporation of a hydrochloric acid solution of the free base gave the dark red hydrochloride, m. p. 228–230°.

Anal. Calcd. for $C_{15}H_{12}N_4$: N, 22.57. Found: N, 22.65, 22.37.

3,4-Diaminoquinoline was obtained by the reduction of the azo compound with stannous chloride and hot dilute hydrochloric acid. After the reaction, excess of base was added and the product extracted with ether. The product was further purified by crystallization from toluene, after bone blacking. White crystals were obtained, m. p. 176–177°.

The same product was obtained by bromination of 4-aminoquinoline¹⁸ and conversion of the 3-bromo-4-aminoquinoline to the diamine by heating with concentrated aqueous ammonia and copper sulfate as a catalyst for twelve hours at 155–160°. The diamine was isolated

and purified as above. With hot acetic anhydride the acetyl derivative was obtained, which on crystallization from water formed long, white, cottony needles, m. p. 229–229.5°. The diamine also formed in glacial acetic acid with phenanthrenequinone after heating for one hour, an azine, m. p. 280–281°.

Anal. Calcd. for $C_9H_9N_3$: N, 26.41. Found: N, 26.52.

An attempt to couple 4-aminoquinoline with benzene-diazonium chloride failed in all cases tried. The coupling in absolute alcohol as pointed out above was of particular interest. As described above, when the solutions were mixed at –5°, a light red color occurred, but rapidly faded with the evolution of nitrogen. The red color would not develop below –10°. Usually about ten minutes were required for a total loss of color. When *p*-nitrobenzene-diazonium chloride was used, unreacted amine and *p*-nitrobenzene were isolated from the solution.

2-Benzenediazoamino-4-aminoquinoline was formed in small yields when coupling was effected in dilute hydrochloric acid solution, and in better yields in aqueous alcohol, and in glacial acetic acid. In excess hydrochloric acid and in absolute alcohol the coupling did not proceed. The product after crystallization from an alcohol–water solution is orange-brown in color, and after drying at 110° for eleven hours melted at 247.5–248.5°. The compound is stable in boiling hydrochloric acid solution.

Anal. Calcd. for $C_{15}H_{13}N_3$: N, 26.61. Found: N, 26.88.

2-*p*-Nitrobenzenediazoamino-4-aminoquinoline precipitated in about ten minutes when coupling was effected in glacial acetic acid. In absolute alcohol a dark red solution was first formed. This color disappeared in about fifteen minutes at –5° accompanied by slow evolution of nitrogen. After this time the yellow hydrochloride precipitated, m. p. 323–325°. It was identical with the product from the former coupling. It is only slightly soluble in hot water and on cooling forms gels. Neutralization of the aqueous solution gave a highly water insoluble, orange free base, m. p. 315.5–316.5°.

Anal. Calcd. for $C_{15}H_{12}N_6O_2$: N, 27.27. Found: N, 27.05, 27.78.

Summary

The orientation in the quinoline ring has been determined by a study of the coupling reactions of all the mono-aminoquinolines. Proofs for the structures of the resulting compounds are given. The results are those to be expected from the application of the Erlenmeyer structure for quinoline.

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