[Contribution from the Chemistry Department of Temple University]

SUBSTITUTED 1,10-PHENANTHROLINES. VII. SYNTHESIS OF CERTAIN PHENANTHROLINES FOR USE IN THE DETECTION OF Cu(I)[1]

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The extreme sensitiveness of the test for Cu^+ given by 2,9- and 4,7-dimethyl- and by 4,7-diphenyl-1,10-phenanthroline (1–3) has prompted the preparation of the following compounds: 2,4,7,9-(I); 2,3,8,9-(II); 2,5,6,9-(III) tetramethyl- and 2,9-dimethyl-4,7-diphenyl-1,10-phenanthroline (IV).

The synthesis of I was accomplished by treating 8-amino-2,4-dimethylquinoline (4) with 4-hydroxy-2-pentanone [prepared by the method of Claisen (5)] under the conditions of a Skraup reaction. By the use of glycerol as the second component in the Skraup reaction, 2,4-dimethyl-1,10-phenanthroline was synthesized.

For the synthesis of II, 2,3-dimethyl-8-nitroquinoline (V) was first prepared by the action of tiglic aldehyde on *o*-nitroaniline in a Doebner-Miller reaction. However, the yield by this method was poor and an attempt was made to prepare the compound by nitration of 2,3-dimethylquinoline obtained by the method of Plant and Rosser (6). The nitration was found to yield no more than traces of the desired product, and was not further investigated. Next 7-nitroisatin was made according to Buchman's procedure (7), and treated with butanone in presence of alkali. Again the desired product could not be isolated. We therefore returned to the original method, repeating the experiment until enough material could be obtained. The preparation of 2,3,8,9-tetramethyl-1,10-phenanthroline was accomplished by using a second Doebner-Miller reaction in which the reactants were tiglic aldehyde and the amine obtained by reduction of V.

For the preparation of III, 4,5-dimethyl-2-nitroaniline (1a) was converted into 2,5,6-trimethyl-8-nitroquinoline (VI), by a Skraup reaction using crotonaldehyde diacetate. Attempts to prepare III from the amine obtained by the reduction of VI by a similar Skraup reaction, again using crotonaldehyde diacetate, were unsuccessful. The Doebner-Miller procedure, however, gave satisfactory results.

The synthesis of IV required as a starting material 2-methyl-8-nitro-4-phenylquinoline (VII). According to the literature this has been prepared (m.p. 94°) by Brahmachari and Bhattacharyvya (8) from acetophenone, paraldehyde, *o*-nitroaniline, and hydrogen chloride. We were unable to duplicate the results of these authors, but we obtained it (m.p. 136–137°) in poor yield by a Doebner-Miller reaction from *o*-nitroaniline and phenyl propenyl ketone ($C_6H_5COCH{=}CHCH_3$) (9). The final preparation of 2,9-dimethyl-4,7-diphenyl-

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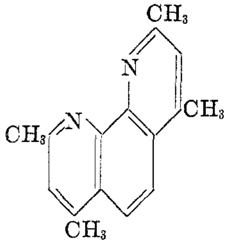
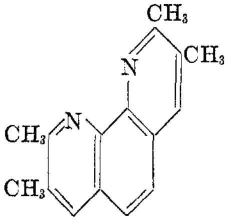
1,10-phenanthroline involved a modified Skraup reaction (10) in which 8-amino-2-methyl-4-phenylquinoline and phenyl propenyl ketone were the reactants.



I



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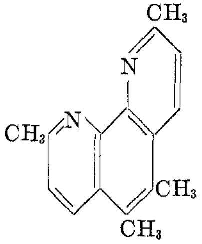

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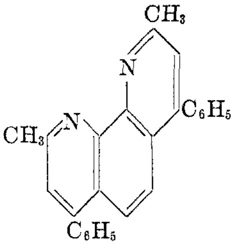

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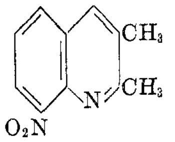
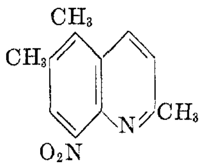
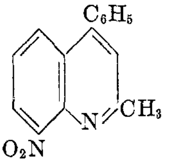


V



VI



VII

Attempts to prepare 4-methyl-8-nitro-2-phenylquinoline and 8-nitro-2,4-diphenylquinoline by the action of benzalacetone and of benzalacetophenone, respectively on *o*-nitroaniline have failed, although several different conditions have been tried. Tests by Professor G. Frederick Smith indicate the following molecular extinction coefficients for the cuprous complexes. (The numbers in parenthesis are the wave lengths of maximum absorption): I, 9440 (451.4); II, 8114 (439.7); III, 9270 (464.7); IV, 14160 (479.0).

EXPERIMENTAL PART

2,4-Dimethyl-1,10-phenanthroline. A mixture of 15 g. (0.09 mole) of 8-amino-2,4-dimethylquinoline, 6.4 ml. of water, 19.2 ml. of concentrated H_2SO_4, and 12.7 g. of arsenic acid was placed in a 250-ml. Soxhlet extraction flask and heated with stirring in an oil-bath at 100°. After the addition of 32 g. (0.35 mole) of glycerol the temperature was raised gradually to 140°, where it was maintained for two hours. The mixture was then poured into water, made alkaline, and the tarry precipitate was removed by filtration. The filtrate was extracted three times with benzene, which was then used to extract the phenanthroline from the solid material. After removal of the benzene, and crystallization from petroleum ether (b.p. 90–100°), 7.7 g. (42.5%) was obtained of pure product, melting at 123–124°.

Anal. Calc'd for $C_{14}H_{12}N_2$: C, 80.74; H, 5.81.
Found: C, 81.11; H, 5.78.

2,4,7,9-Tetramethyl-1,10-phenanthroline. This was prepared in the same way as 2,4-dimethylphenanthroline, using the same molar quantities of reagents except that 2 moles of 4-hydroxy-2-pentanone were substituted for glycerol. From 12.5 g. of 8-amino-2,4-dimethylquinoline, 3.9 g. of 2,4,7,9-tetramethyl-1,10-phenanthroline (23.5%) was obtained The pure product, crystallized from benzene, melted at 199–200°.

Anal. Calc'd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83.
Found: C, 81.32, H. 6.65.

2,3-Dimethyl-8-nitroquinoline. In a 1-liter round-bottom 3-neck flask equipped with dropping-funnel, reflux condenser, and stirrer with mercury seal, were placed 200 ml. of conc'd hydrochloric acid, 13.8 g. (0.1 mole) of *o*-nitroaniline, 11.5 g. of arsenic acid, and 10 g. of anhydrous zinc chloride. To the mixture, heated on the steam-bath to gentle reflux, was added 17 g. (0.23 mole) of tiglic aldehyde during half an hour. Refluxing was continued for two more hours. After cooling, the resulting solution was decanted from the tar, which was extracted twice with 50-ml. portions of concentrated hydrochloric acid, and made strongly alkaline. The precipitate and solution were extracted with hot benzene. The residue from the benzene was crystallized from methanol. The yield of product from five runs according to the above procedure was 11.5 g. (m.p. 143–144°), or 11.4%. The pure product melts at 144–145°.

Anal. Calc'd for $C_{11}H_{10}N_2O_2$: C, 65.33; H, 4.98.
Found: C, 65.43; H, 4.90.

2-Methyl-8-nitro-4-phenylquinoline. The procedure for this preparation was entirely similar to that above, with the substitution of an equivalent amount of phenyl propenyl ketone for tiglic aldehyde. From two runs each using 20.7 g. of *o*-nitroaniline and proportional amounts of other ingredients, there was obtained 8 g. of material crystallized from methanol, and melting at 135°. Yield, 10.1%. The pure product melts at 136–137°.

Anal. Calc'd for $C_{16}H_{12}N_2O_2$: C, 72.73; H, 4.55.
Found: C, 72.50; H, 4.68.

2,5,6-Trimethyl-8-nitroquinoline. A mixture of 21 g. of 4,5-dimethyl-2-nitroaniline, 19 g. of arsenic acid, 28 ml. of concentrated sulfuric acid, and 10 ml. of water was warmed to 100°. Crotonaldehyde diacetate (44 g.) was then added at such a rate that the temperature did not exceed 140°. Heating was continued with stirring at this temperature for two hours. The reaction mixture was then poured into ice-water and made alkaline with sodium hydroxide. The resulting precipitate was removed by filtration, dried, and extracted with hot benzene. From two batches of material run as above there was obtained, after removal of the benzene and crystallization from the same solvent, 19.5 g. of pure material, melting at 181–182°.

Anal. Calc'd for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59.
Found: C, 66.77; H, 5.71.

8-Amino-2,3-dimethylquinoline. This was prepared by the catalytic reduction of the corresponding nitro compound. After crystallization from petroleum ether, it melted at 105–106°. Yield 76.5%.

Anal. Calc'd for $C_{11}H_{12}N_2$: C, 76.71; H, 7.02.
Found: C, 76.94; H, 7.03.

8-Amino-2,5,6-trimethylquinoline. Catalytic reduction of the corresponding nitro compound gave the above amine in 74.1% yield. After crystallization from petroleum ether, it melted at 80–81°.

Anal. Calc'd for $C_{12}H_{14}N_2$: C, 77.38; H, 7.58.
Found: C, 77.33; H, 7.64.

2,3,8,9-Tetramethyl-1,10-phenanthroline. A mixture of 170 ml. of concentrated hydrochloric acid, 12.5 g. of 8-amino-2,3-dimethylquinoline, 10 g. of arsenic acid, and 8 g. of zinc chloride was treated with 24 g. of tiglic aldehyde according to the procedure for the preparation of 2,3-dimethyl-8-nitroquinoline. The yield of pure phenanthroline, crystallized from benzene, and melting at 225–226° was 1.3 g. or 7.6%.

Anal. Calc'd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83.
Found: C, 81.37; H, 6.87.

2,5,6,9-Tetramethyl-1,10-phenanthroline. The general procedure was similar to that used in the preparation of 2,3,8,9-tetramethyl-1,10-phenanthroline. From 16.5 g. of 8-amino-2,5,6-trimethylquinoline, 224 ml. of concentrated hydrochloric acid, 12.8 g. of arsenic acid, 11.2 g. of anhydrous zinc chloride, and 64 g. of crotonaldehyde diacetate, there was obtained, after evaporation of the benzene, a product which on crystallization from moist benzene, melted at 99–100°. The yield of anhydrous product (m.p. 170°), obtained by drying the above hydrate at 80°, was 3.6 g., or 17.2%. By crystallization from ethanol-water, and drying as before the pure product (m.p. 171–172°) was obtained.

Anal. (Phenanthroline dihydrate) Calc'd for $C_{16}H_{20}N_2O_2$: H_2O, 13.23.
Found: H_2O, 13.46.

Anal. (Anhydrous phenanthroline) Calc'd for $C_{16}H_{16}N_2$: C, 81.32; H, 6.83.
Found: C, 81.22; H, 6.93.

2,9-Dimethyl-4,7-diphenyl-1,10-phenanthroline. A mixture of 12 g. of 8-amino-2-methyl-4-phenylquinoline (obtained as a liquid by the catalytic reduction of the corresponding nitro compound, but not purified), 40 ml. of 85% phosphoric acid, and 9 g. of phenyl propenyl ketone was heated for half an hour at 120° with stirring. Arsenic acid (14 g.) was then added and the heating was continued for two hours. The reaction mixture was neutralized with potassium hydroxide, and both precipitate and solution were extracted with hot benzene. Removal of the solvent and crystallization from benzene yielded 3.3 g. (17.8%) of pure product, melting at 282–283°.

Anal. Calc'd for $C_{26}H_{20}N_2$: C, 86.67; H, 5.56.
Found: C, 86.57; H, 5.64.

SUMMARY

The preparation of the following compounds, of probable value as reagents for Cu(I), is described: 2,4,7,9-, 2,3,8,9-, and 2,5,6,9-tetramethyl-; 2,9-dimethyl-4,7-diphenyl-; and 2,4-dimethyl-1,10-phenanthroline.

PHILADELPHIA 22, PA.

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