[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF TEMPLE UNIVERSITY]

SUBSTITUTED 1,10-PHENANTHROLINES. V. PHENYL DERIVATIVES[1]

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The synthesis of substituted phenanthrolines suitable for use as precipitants or, in the form of their ferrous complexes, as oxidation-reduction indicators (1), has been extended to include certain mono- and di-phenyl-1,10-phenanthrolines. In certain of these syntheses, as the second component of a Skraup reaction, β-chloropropiophenone was employed. We believe this to be the first instance of its use for this purpose. It was found that although in some cases good yields may be obtained with this reagent, no reaction occurs if a phenyl group is attached to the carbon atom adjacent to the one which would be involved in ring closure.

By the action of glycerol under Skraup conditions on 3-nitro-4-acetaminobiphenyl (I) there was obtained 6-phenyl-8-nitroquinoline (II). The corresponding amino compound (III) treated with glycerol under similar conditions, yielded 5-phenyl-1,10-phenanthroline (IV), but on treatment with β-chloropropiophenone, no 4,5-diphenyl-1,10-phenanthroline resulted. It was found that I, treated with β-chloropropiophenone (2) under the conditions of the Yale modification of the Skraup reaction (3) but not under the usual Skraup conditions, gave a good yield of 4,6-diphenyl-8-nitroquinoline (V). The amine (VI) obtained by reduction of the latter yielded 4,6-diphenyl-1,10-phenanthroline (VII) on treatment with glycerol under Skraup conditions. However, attempts to prepare 4,5,7-triphenyl-1,10-phenanthroline by the action of β-chloropropiophenone on VI under either set of conditions were unsuccessful, due no doubt to steric factors.

From *o*-nitroaniline and β-chloropropiophenone under Skraup conditions was obtained 4-phenyl-8-nitroquinoline (VIII). The corresponding amino derivative (IX) yielded, with β-chloropropiophenone, 4,7-diphenyl-1,10-phenanthroline (XI). With glycerol a small yield of 4-phenylphenanthroline (X) was obtained. However, a better method of preparing X was to treat 8-aminoquinoline with β-chloropropiophenone under Skraup conditions.

Further investigations required the use of 4-nitro-3-acetaminobiphenyl (XII). The preparation of this substance according to the directions of Blakey and Scarborough (4) was found unsatisfactory due to the formation of considerable high-melting material, presumably nitrated in the unsubstituted ring. A satisfactory method of preparation was worked out, involving the use of a lower temperature, and separation of the desired substance from the higher-melting material by solution in cold benzene.

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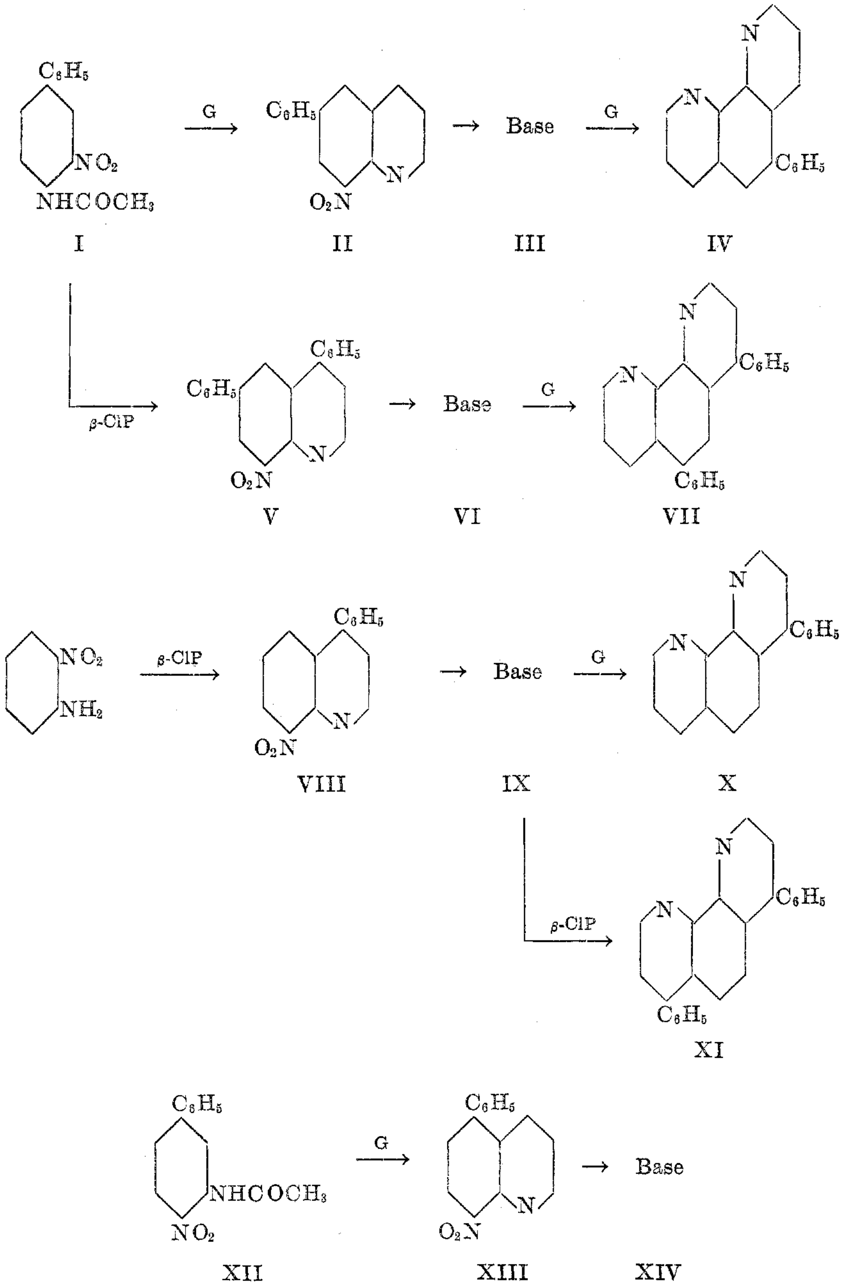
The action of XII with glycerol in a Skraup reaction yielded 5-phenyl-8-nitroquinoline (XIII) from which the base (XIV) was prepared. Deamination yielded 5-phenylquinoline, previously described by Elks and Hey (5).



In the above diagram G = glycerol and β-ClP = β-chloropropiophenone.

The action of β-chloropropiophenone on XIV was not attempted as it would lead to VII, already prepared. β-Chloropropiophenone was without action on XII although both sets of conditions were used. Steric factors are probably involved.

EXPERIMENTAL PART[2]

6-Phenyl-8-nitroquinoline. To a mixture of 67 g. of 3-nitro-4-acetaminobiphenyl, 36 g. of arsenic acid, 54 ml. of concentrated sulfuric acid, and 18 ml. of water, heated to 100°, was added 84 g. of glycerol. The temperature was raised to 140° and maintained there for two hours. The reaction mixture was then cooled and neutralized with sodium hydroxide solution. The precipitated product was dried and extracted with benzene. After removal of the solvent, it was crystallized from methanol. The yield of pure product melting at 97–98° was 27 g.

Anal. Calc'd for $C_{15}H_{10}N_2O_2$: C, 71.97; H, 4.03.
Found: C, 72.17; H, 3.91.

4-Phenyl-8-nitroquinoline. A mixture of 14 g. of *o*-nitroaniline, 14 g. of arsenic acid, 22 ml. of concentrated sulfuric acid, and 7 ml. of water, heated to 100°, was treated with 22 g. of β-chloropropiophenone [prepared by the method of Kenner and Statham (2)] using the above procedure. The residue from evaporation of the benzene, after crystallization from benzene-petroleum ether, yielded 8 g. of material, m.p. 125–126°.

Anal. Calc'd for $C_{15}H_{10}N_2O_2$: C, 71.97; H, 4.03.
Found: C, 72.20; H, 4.12.

5-Phenyl-8-nitroquinoline. A mixture of 14 g. of 4-nitro-3-acetaminobiphenyl, 7 g. of arsenic acid, 11 ml. of concentrated sulfuric acid, and 4 ml. of water was treated with 17 g. of glycerol as in the previous preparation. The yield of pure product crystallizing from benzene and melting at 140–141° was 8.5 grams.

Anal. Calc'd for $C_{15}H_{10}N_2O_2$: C, 71.97; H, 4.03.
Found: C, 71.90; H, 3.69.

4,6-Diphenyl-8-nitroquinoline. To a mixture of 16 g. of 3-nitro-4-aminobiphenyl, 21 g. of arsenic acid, and 75 ml. of 85% phosphoric acid heated to 100°, was added 16 g. of β-chloropropiophenone at such a rate that the temperature did not rise above 130°. After two hours' heating at this temperature the mixture was poured on ice and neutralized with potassium hydroxide solution. The resulting precipitate was dried and extracted with benzene. Removal of the benzene and crystallization from an ethanol-acetone mixture yielded 10.5 g. of pure product, m.p. 164–165°.

Anal. Calc'd for $C_{21}H_{14}N_2O_2$: C, 77.27; H, 4.33.
Found: C, 77.58; H, 4.43.

3-Acetamino-4-nitrobiphenyl (4). To a solution of 35 g. of *m*-acetaminobiphenyl in 210 ml. of glacial acetic acid and 70 ml. of acetic anhydride was added a mixture of 10.5 ml. of nitric acid (*sp. gr.* 1.5) and 35 ml. of glacial acetic acid at such a rate that the temperature never exceeded 40°. After the mixture had been kept at this temperature for one hour, it was poured into ice-water, and the precipitate separated. The dry product obtained by one crystallization from methanol was shaken with cold benzene. The benzene solution was evaporated and the residue crystallized from methanol. Yield, 14.5 g., m.p. 114°.

6-Phenyl-8-aminoquinoline. This was prepared by the reduction of the corresponding nitro compound by three molar proportions of $SnCl_2 \cdot 2H_2O$ in alcohol. The pure product, crystallized from methanol, melts at 110–111°. Yield, 70%.

Anal. Calc'd for $C_{15}H_{12}N_2$: C, 81.78; H, 5.49.
Found: C, 82.09; H, 5.59.

4-Phenyl-8-aminoquinoline. Prepared by a similar reduction of the corresponding nitro compound, the pure product, crystallized from methanol, melted at 90–91°. Yield, 68%.

Anal. Calc'd for $C_{15}H_{12}N_2$: C, 81.78; H, 5.49.
Found: C, 81.74; H, 5.60.

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[2] Analyses were done by the Clark Microanalytical Laboratory, Urbana, Illinois.

5-Phenyl-8-aminoquinoline. This was prepared by a similar reduction of the nitro compound; on crystallization from methanol it melted at 83–84°. Yield, 60%.

Anal. Calc'd for $C_{15}H_{12}N_2$: C, 81.78; H, 5.49.
Found: C, 81.69; H, 5.34.

On deamination with ethanol, dilute sulfuric acid, and sodium nitrite, 5-phenylquinoline was formed. This melted at 81–82° after crystallization from petroleum ether [Elks and Hey (5) report 82–83°].

4,6-Diphenyl-8-aminoquinoline. This was prepared by catalytic reduction of the nitro compound in glacial acetic acid. The pure product, on crystallization from ethanol, melted at 154–155°. Yield, 72%.

Anal. Calc'd for $C_{21}H_{16}N_2$: C, 85.09; H, 5.45.
Found: C, 84.98; H, 5.40.

4,6-Diphenylquinoline. Deamination of the above base as described under 5-phenyl-8-aminoquinoline yielded 4,6-diphenylquinoline, melting at 144–145° after crystallization from benzene-petroleum ether.

Anal. Calc'd for $C_{21}H_{15}N$: C, 89.64; H, 5.37.
Found: C, 89.26; H, 5.46.

5-Phenylphenanthroline. A mixture of 38 g. of 6-phenyl-8-aminoquinoline, 24 g. of arsenic acid, 72 ml. of concentrated sulfuric acid, and 24 ml. of water was heated to 100° and treated with 66 g. of glycerol at such a rate that the temperature did not exceed 140°. It was kept at this temperature, with stirring, for two more hours. The mixture was then poured into water, made alkaline and the precipitate removed. The filtrate was extracted three times with hot benzene, which was then used to extract the phenanthroline from the precipitate. After removal of the benzene, the phenanthroline was crystallized from the same solvent. The yield was 9 g., m.p. 202–203°.

Anal. Calc'd for $C_{18}H_{12}N_2$: C, 84.34; H, 4.73.
Found: C, 84.40; H, 4.61.

4-Phenylphenanthroline. Although a small amount of 4-phenylphenanthroline could be obtained by the action of glycerol on 4-phenyl-8-aminoquinoline in a Skraup reaction, the following procedure gave a better yield. A mixture of 16.2 g. of 8-aminoquinoline, 15 g. of arsenic acid, 24 ml. of concentrated sulfuric acid, and 8 ml. of water was heated to 100° and treated with 27 g. of β-chloropropiophenone with stirring. The temperature was allowed to rise to 130–135° and maintained there for two hours. The tarry residue, which formed after pouring the reaction mixture into water and neutralizing with alkali, was separated and repeatedly extracted with dilute hydrochloric acid. The solution, after evaporation to small volume, was made alkaline and extracted with benzene. After removal of the solvent and crystallization of the residue from benzene-petroleum ether, 3.3 g. of pure product was obtained, melting at 105–106°.

Anal. Calc'd for $C_{18}H_{12}N_2$: C, 84.34; H, 4.73.
Found: C, 84.40; H, 4.34.

4,7-Diphenylphenanthroline. A mixture of 22 g. of 4-phenyl-8-aminoquinoline, 14 g. of arsenic acid, 44 ml. of concentrated sulfuric acid, and 14 ml. of water was treated with 25 g. of β-chloropropiophenone and the product isolated under conditions similar to those for the preparation of 5-phenylphenanthroline. The yield of pure product, crystallized from benzene, and melting at 215–216° was 7 grams.

Anal. Calc'd for $C_{24}H_{16}N_2$: C, 86.71; H, 4.85.
Found: C, 86.58; H, 4.89.

4,6-Diphenylphenanthroline. A mixture of 21.6 g. of 4,6-diphenyl-8-aminoquinoline, 11 g. of arsenic acid, 48 ml. of concentrated sulfuric acid, and 15 ml. of water was treated with 29 g. of glycerol under conditions similar to those immediately preceding. There was 2.4 g. of pure product, m.p. 245° after crystallization from benzene.

Anal. Calc'd for $C_{24}H_{16}N_2$: C, 86.71; H, 4.85.
Found: C, 86.44; H, 4.86.

Reaction of β-chloropropiophenone and 6-phenyl-8-aminoquinoline. A mixture of 15 g. of the above base, 19 g. of arsenic acid, and 75 ml. of 85% phosphoric acid was treated with 15 g. of β-chloropropiophenone, the procedure throughout being similar to that used for the preparation of 4,6-diphenyl-8-nitroquinoline. The pure reaction product, (1.9 g.) crystallized from benzene, melted at 158°. Analysis and the yellow color of the product showed that it was not the desired 4,5-diphenylphenanthroline, but was probably 6-phenyl-8-(β-benzoylethyl)aminoquinoline.

Anal. Calc'd for $C_{24}H_{20}N_2O$: C, 81.88; H, 5.72.
Found: C, 82.30; H, 5.92.

SUMMARY

The following 1,10-phenanthrolines have been prepared: 4- and 5-phenyl; 4,6- and 4,7-diphenyl.

4-, 5-, and 6-phenyl- and 4,6-diphenyl-8-nitroquinolines and the corresponding amino derivatives have been prepared.

PHILADELPHIA, PA.

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