[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF TEMPLE UNIVERSITY]

SUBSTITUTED 1,10-PHENANTHROLINES. IV. BROMO DERIVATIVES[1]

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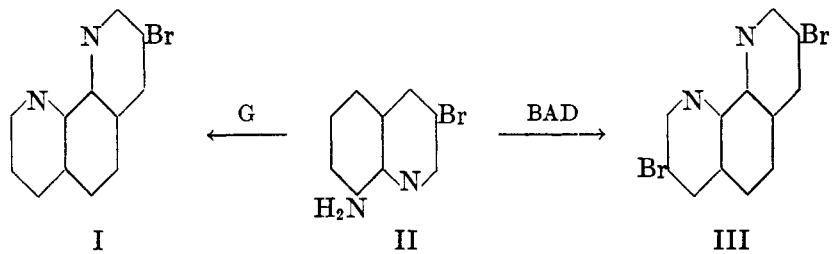
Received February 12, 1951

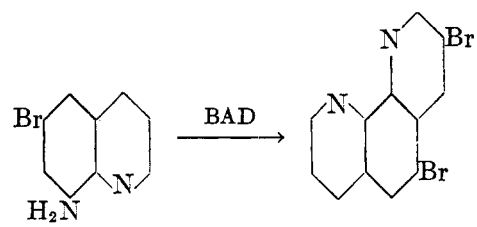
In continuation of work previously described (1) which had as its object the preparation of substituted phenanthrolines which might find use as precipitants or, in the form of their ferrous complexes, as oxidation-reduction indicators, a series of mono-, di-, tri-, and tetra-bromo-1,10-phenanthrolines has been prepared. The results of tests on most of these compounds with regard to their suitability for use in analytical chemistry have already been published (2).

In this paper many of the 3-bromoquinolines and phenanthrolines have been prepared by the action of α-bromoacrolein diacetate on a suitable amine under Skraup conditions. It was found that whereas *o*-nitroaniline and α-bromoacrolein diacetate under these conditions give a negligible yield of the corresponding quinoline derivative, with some of the bromosubstituted *o*-nitroanilines the yields are fairly satisfactory. The yields of 3-bromophenanthrolines, however, in reactions in which α-bromoacrolein diacetate is caused to react with an aminobromoquinoline are poor. The only previous mention of the use of α-bromoacrolein for the preparation of α-bromoquinolines is by Riegel and coworkers (3). In this work however the reaction medium was concentrated hydrobromic acid.

3-Bromo-1,10-phenanthroline (I) was prepared from glycerol and 8-amino-3-bromoquinoline (II) by a Skraup reaction. From II and α-bromoacrolein diace-

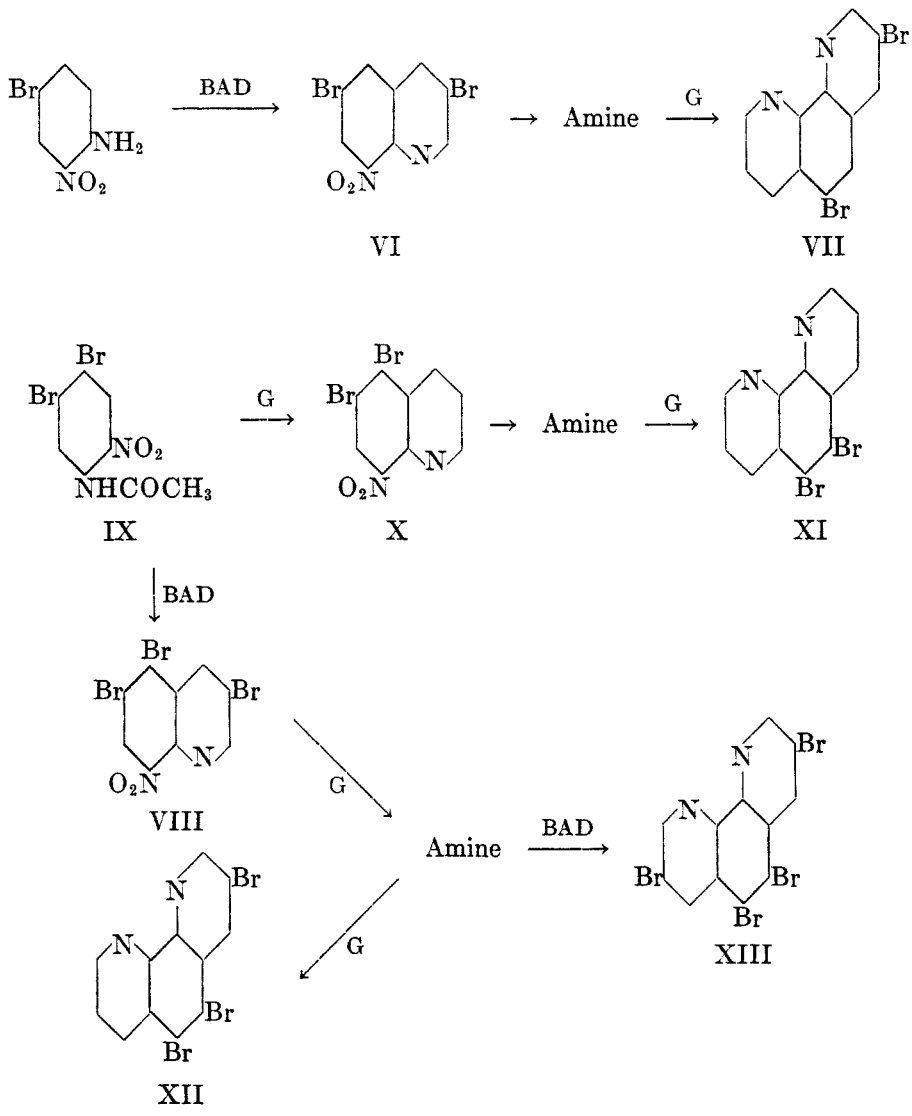


I II III



IV V

[1] This work was supported by a Grant from the Committee on Research and Publications of Temple University.



Note: G = glycerol and BAD = α-bromoacrolein diacetate.

tate using the Yale (4) modification of the Skraup reaction, 3,8-dibromo-1,10-phenanthroline (III) was synthesized. A Skraup reaction involving 8-amino-6-bromoquinoline (IV) and α-bromoacrolein diacetate provided 3,5-dibromo-1,10-phenanthroline (V) in small yield. The preparation of V by the action of glycerol on 8-amino-3,5-dibromoquinoline (from 5-bromo-2-nitroaniline and α-bromoacrolein diacetate) was not realized since the quinoline could not be synthesized.

The synthesis of 3,6-dibromo-1,10-phenanthroline (VII) was accomplished by treating 4-bromo-2-nitroaniline with α-bromoacrolein diacetate, reducing the resulting dibromonitroquinoline (VI), and treating the amine with glycerol.

A necessary intermediate in subsequent operations was 4,5-dibromo-2-nitroaniline. Its preparation by the method of Schiff (5), in which 3,4-dibromoacetanilide is treated with nitric acid (sp. gr. 1.5) was unsatisfactory, since large amounts of a dibromodinitroacetanilide were obtained. In fact the melting point recorded by Schiff for crude 4,5-dibromo-2-nitroacetanilide (225°) is much too high, due, no doubt, to contamination of the mononitro derivative with the dinitro. In this laboratory the dinitro derivative has been purified and its structure shown to be 4,5-dibromo-2,6-dinitroacetanilide by hydrolysis and deamination to 4,5-dibromo-1,3-dinitrobenzene, obtained from 6-bromo-2,4-dinitroaniline. Good yields of 4,5-dibromo-2-nitroaniline were subsequently obtained by nitration of 3,4-dibromoacetanilide with ethyl nitrate.

By a Skraup reaction involving glycerol, 4,5-dibromo-2-nitroacetanilide (IX) was converted to 5,6-dibromo-8-nitroquinoline (X). Reduction followed by a second Skraup reaction yielded 5,6-dibromo-1,10-phenanthroline (XI). The action of α-bromoacrolein diacetate on 4,5-dibromo-2-nitroacetanilide yielded 3,5,6-tribromo-8-nitroquinoline (VIII). The corresponding amino derivative yielded with glycerol, 3,5,6-tribromo-1,10-phenanthroline (XII), and with α-bromoacrolein diacetate, 3,5,6,8-tetrabromo-1,10-phenanthroline (XIII). The successful preparation of 4-bromo- and 4,7-dibromo-1,10-phenanthroline from the corresponding hydroxyphenanthrolines (6) was accomplished only after many attempts had been made to establish the proper conditions. It was found that the temperature must be kept relatively low (about 110°) to prevent formation of higher bromination products. The use of phosphoryl bromide (7) mixed with phosphorus tribromide is also essential since the latter alone is without reaction.

EXPERIMENTAL

α-Bromoacrolein diacetate (*8*). α-Bromoacrolein was prepared from α,β-dibromopropionaldehyde (9) by the method of Piloty and Stock (10). Then 59 g. of dry α-bromoacrolein in 60 ml. of acetic anhydride was treated with 4 drops of sulfuric acid and the mixture allowed to stand overnight. After the addition of 1 g. of sodium acetate the mixture was distilled *in vacuo*. The yield of α-bromoacrolein diacetate was 56 g., b.p. 140–143° (55 mm.).

Nitration of 3,4-dibromoacetanilide. A. Use of ethyl nitrate. To 6 g. of 3,4-dibromoacetanilide in 40 ml. of concentrated sulfuric acid was added 1.7 ml. of ethyl nitrate at 2°. After one hour's standing at 0°, the mixture was poured on ice and the precipitated solid was crystallized from ethanol. The yield of pure 4,5-dibromo-2-nitroacetanilide was 4.2 g., m.p. 141–142°.

Anal. Calc'd for $C_8H_6Br_2N_2O_3$. Br, 47.30. Found: Br, 47.47.

On hydrolysis the above product yielded the base described by Schiff, m.p. 200–201°. Deamination gave 3,4-dibromonitrobenzene, m.p. 56–57°.

B. Use of nitric acid (sp. gr. 1.5). 3,4-Dibromoacetanilide (100 g.) was slowly added to 800 ml. of nitric acid (sp. gr. 1.5) at 5° and allowed to stand at this temperature for one hour. The mixture was then poured on ice, and the precipitate washed, dried, and extracted with cold benzene. From the benzene-soluble portion, after evaporation of the solvent and crystallization from ethanol, 37.8 g. of 4,5-dibromo-2-nitroacetanilide was obtained. The benzene-insoluble portion yielded 21.5 g. of material, m.p. 269–270°. Pure 4,5-dibromo-2,6-dinitroacetanilide has m.p. 279–280°.

Anal. Calc'd for $C_8H_5Br_2N_3O_5$: C, 25.10; H, 1.32.
Found: C, 24.99; H, 1.10.

Hydrolysis of the above compound with dilute sulfuric acid yielded the base, which crystallizes from alcohol, m.p. 154–155°.

Anal. Calc'd for $C_6H_3Br_2N_3O_4$: Br, 46.90. Found: Br, 47.14.

On deamination with hypophosphorous acid this base gave a product, m.p. 69–70°, and unchanged when mixed with an authentic specimen of 4,5-dibromo-1,3-dinitrobenzene, prepared from 6-bromo-2,4-dinitroaniline.

5,6-Dibromo-8-nitroquinoline. To 29.3 g. of 4,5-dibromo-2-nitroacetanilide, 13 g. of arsenic acid, 36 ml. of concentrated sulfuric acid, and 12 ml. of water heated to 100° was added 28 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; when most of the benzene was removed, the product crystallized, m.p. 196°. Yield, 8.5 g. (29.4%).

Anal. Calc'd for $C_9H_4Br_2N_2O_2$: Br, 48.16. Found: Br, 47.97.

8-Nitro-3,6-dibromoquinoline. To 21.7 g. of 4-bromo-2-nitroaniline, 13.8 g. of arsenic acid, 33 ml. of concentrated sulfuric acid, and 11 ml. of water heated to 100° was added

TABLE I

BROMO-1,10-PHENANTHROLINES

1,10-PHENANTHROLINE	8-AMINOQUINOLINE USED	SECOND COMPONENT[b]	M.P., °C.	YIELD, %	ANALYSES[a] BROMINE	
					Calc'd	Found
3-Bromo	3-Bromo	G	169–170	20.4	30.86	30.80
3,5-Dibromo	6-Bromo	BAD	225–226	1.4	47.30	47.02
3,6-Dibromo	3,6-Dibromo	G	247–248	28.2	47.30	47.28
5,6-Dibromo	5,6-Dibromo	G	215–216	14.1	47.30	47.22
3,5,6-Tribromo	3,5,6-Tribromo	G	251–252	26.9	57.52	57.44
3,5,6,8-Tetrabromo	3,5,6-Tribromo	BAD	356–357	4.3	64.49	64.69

[a] Analyses were by the Clark Microanalytical Laboratory, Urbana, Illinois. [b] G = glycerol; BAD = α-bromoacrolein diacetate.

36 g. of α-bromoacrolein diacetate, the temperature being kept below 130°. Heating was then continued for an additional two hours. By the procedure used for 4,5-dibromo-8-nitroquinoline, there was obtained 8.5 g. (38.4%), m.p. 180–181°.

Anal. Calc'd for $C_9H_4Br_2N_2O_2$: C, 32.54; H, 1.21.
Found: C, 33.00; H, 1.30.

3,5,6-Tribromo-8-nitroquinoline. A mixture of 33.8 g. of 4,5-dibromo-2-nitroacetanilide, 13.8 g. of arsenic acid, 33 ml. of concentrated sulfuric acid, and 11 ml. of water was heated to 100° and treated with 36 g. of α-bromoacrolein diacetate at 130°. Then the mixture was heated for two hours at 140°. The material was worked up as before; yield 10 g. (24.3%), m.p. 208–209°.

Anal. Calc'd for $C_9H_3Br_3N_2O_2$: Br, 58.36. Found: Br, 58.26.

8-Amino-3,6-dibromoquinoline. To 63 g. of 3,6-dibromo-8-nitroquinoline in 900 ml. of 50% acetic acid was added 45 g. of iron powder, keeping the temperature at 60°. The mixture was then heated on the steam-bath for three hours. After cooling it was neutralized with sodium hydroxide solution, and the precipitate removed, dried, and extracted with benzene. After removal of the benzene the product was crystallized from methanol, yielding 37 g. of pure amine, m.p. 123–124°.

Anal. Calc'd for $C_9H_6N_2Br_2$: Br, 52.94. Found: Br, 52.88.

8-Amino-5,6-dibromoquinoline was prepared by reduction of the corresponding nitro compound (10 g.), using the method described for 8-amino-3,6-dibromoquinoline. The yield of pure product, crystallizing from methanol, m.p. 134–135°, was 5 g.

Anal. Calc'd for $C_9H_6N_2Br_2$: Br, 52.94. Found: Br, 52.98.

8-Amino-3,5,6-tribromoquinoline. Using the same procedure, 84 g. of 3,5,6-tribromo-8-nitroquinoline gave 42.5 g. of amine. Crystallized from benzene, it had m.p. 189–190°.

Anal. Calc'd for $C_9H_5N_2Br_3$: Br, 62.96. Found: Br, 63.09.

3,8-Dibromo-1,10-phenanthroline. To 22.4 g. of 8-amino-3-bromoquinoline (11), 28.4 g. of arsenic acid, and 100 ml. of H_3PO_4, heated to 100°, was added 36 g. of α-bromoacrolein diacetate at such a rate that the temperature did not rise above 130°. After two hour's heating at 140° 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 benzene gave 1.5 g., m.p. 221–222°.

Anal. Calc'd for $C_{12}H_6N_2Br_2$: Br, 47.30. Found: Br, 47.60.

General procedure for the synthesis of polybromo-1,10-phenanthrolines. A mixture of a 1-molar quantity of the appropriate mono-, di-, or tri-bromoaminoquinoline, 1.3 moles of arsenic acid, 8 moles of 97% sulfuric acid, and a volume of water equal to one-third of the volume of sulfuric acid used, was heated to 100° and treated with glycerol (4 moles) or α-bromoacrolein diacetate (1.6 moles) 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 benzene. The results for phenanthrolines synthesized in this way are shown in Table I.

4-Bromo-1,10-phenanthroline. A mixture of 4 g. of 4-hydroxy-1,10-phenanthroline (6), 3 g. of $POBr_3$, and 15 g. of PBr_3 was heated 6 hours at 105–115°. The cooled mixture was then poured on ice, made alkaline, and thoroughly stirred to dissolve unchanged material. The insoluble matter was removed, dried, and crystallized from a petroleum ether—absolute ethanol mixture. Yield, 1.6 g., m.p. 157°.

Anal. Calc'd for $C_{12}H_7N_2Br$: Br, 30.86. Found: Br, 30. 52.

4,7-Dibromo-1,10-phenanthroline. A mixture of 3.2 g. of 4,7-dihydroxy-1,10-phenanthroline (6), 4.5 g. of $POBr_3$, and 20 g. of PBr_3 was heated at 110–120° for 8 hours. The product was then treated as in the preparation of the monobromo derivative. Crystallization from benzene yielded 1.3 g., m.p. 236°.

Anal. Calc'd for $C_{12}H_6N_2Br_2$: Br, 47.30. Found: Br, 47.03.

SUMMARY

The following 1,10-phenanthrolines have been prepared: 3- and 4-bromo; 3,5-, 3,6-, 3,8-, 4,7-, and 5,6-dibromo; 3,5,6-tribromo; and 3,5,6,8-tetrabromo.

3,6- and 5,6-Dibromo- and 3,5,6-tribromo-8-nitroquinoline and the corresponding amino derivatives have been synthesized.

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