a gas whose infrared spectrum was that expected for formaldehyde methyl isopropenyl acetal; this material could be concentrated by gas chromatography but not purified for analysis, as it decomposed slowly to acetone and a polymer not further identified. The residue was purified by a short path distillation; $n^{25}D$ 1.4540. The product had the correct analysis for methoxymethyl (β-methoxymethoxy) crotonate.

Anal. Calcd. for $C_9H_{14}O_5$: C, 50.52; H, 7.42. Found: C, 51.12; H, 7.52.

A chemical structure proof for this material has been given by Simonsen[3]; no physical properties are available for comparison. β-(*p*-Methoxybenzyloxy)crotonic acid (15 mmoles) similarly yielded 10.6 mmoles of carbon dioxide, 4.0 mmoles of acetone, and a compound whose infrared spectrum was characteristic of isopropenyl ethers. Attempts to purify this material by elution chromatography on alumina resulted in its polymerization; an attempt to purify it by gas chromatography (235°, Silicone 90 column) resulted in the isolation of 4-*p*-methoxyphenyl-2-butanone, m.p. 9.5–10° (9.7–9.8°).[23]

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.11; H, 7.92. Found: C, 73.88; H, 8.09.

Semicarbazone, m.p. 167–168° (169–170°).[24]

The residue was chromatographed on an alumina column eluted by hexane–benzene mixtures. This resulted in a yellow solid, white after treatment with activated charcoal and recrystallization from 25% benzene–75% hexane, m.p. 74–76°.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.16; H, 6.48. Found: C, 70.37; H, 6.62.

Prolonged base-catalyzed hydrolysis of this ester (which turned out to be very resistant to such treatment) resulted in the formation of the parent acid (m.p. undepressed upon admixture) and *p*-methoxybenzyl alcohol, recognized by its infrared spectrum. β-*t*-Butoxycrotonic acid (4.36 mmoles) yielded 3.5 mmoles of carbon dioxide, 3.5 mmoles of acetone, 2.6 mmoles of isobutylene, recognized by its infrared spectrum,[25] and a residue that after a short path distillation yielded a compound whose infrared spectrum (two carbonyl peaks) and gas chromatographic behavior (two widely separated but unresolved peaks) are characteristic of β-keto esters; $n^{25}D$ 1.4178 (1.4178).[26]

Anal. Calcd. for $C_9H_{14}O_3$ (*t*-butyl acetoacetoacetate): C, 60.74; H, 8.92. Found: C, 61.35; H, 8.98.

Acknowledgment.—The authors gratefully acknowledge financial support by the Research Corporation (Frederick Gardner Cottrell Grant No. PN-2099).

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Substituted 1,10-Phenanthrolines. XIV. Hydroxy and Methoxy Derivatives[1]

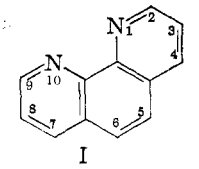
DAVID E. ZACHARIAS[2] AND FRANCIS H. CASE

Chemistry Department of Temple University, Philadelphia 22, Pennsylvania

Received March 19, 1962

With the object of preparing new chelates of iron(II) and copper(I) the following 1,10-phenanthrolines have been synthesized: 2- and 5-hydroxy-; 4-hydroxy-5-methoxy- and 4,5-dihydroxy-; 4,7-dimethoxy-, -diphenoxy-, and -diamino-; 5,6-dimethoxy- and dihydroxy-; 3-carboxy-5,6-dimethoxy-4-hydroxy- and 3-carboxy-4,5,6-trihydroxy-; 4-hydroxy-5-methoxy-2-methyl- and 4,5-dihydroxy-2-methyl-; 2,4-dihydroxy-5-methoxy- and 2,4-dihydroxy-.

Substitution of alkyl and aryl groups in the nucleus of 1,10-phenanthroline (I) has in general



I

been found to increase its chelating power for iron (II) and copper (I). These complex cations are for the most part stable when the pH of the solution is relatively low. The corresponding chelates of 4,7-dihydroxy-1,10-phenanthroline,[3] however, have been found to be stable in solutions of higher pH, and even in concentrated alkaline solution if excess ligand is provided. The present investigation seeks to furnish more of these hydroxyphenanthrolines for study, as well as certain methoxy derivatives, this type of substitution having previously been untested.

2-Hydroxy-1,10-phenanthroline was obtained by hydrolysis of 2-methoxy-1,10-phenanthroline by hydrogen iodide. The latter compound was prepared by a Skraup reaction (Yale modification[4]) on 8-amino-2-methoxyquinoline,[5] rather than from 2-chloro-1,10-phenanthroline as previously reported.[6]

5-Hydroxy-1,10-phenanthroline resulted from the hydrolysis of the corresponding methoxy derivative, obtained by us from 8-amino-6-methoxyquinoline[7] in a Skraup reaction rather than from 5-chloro-1,10-phenanthroline[8] as previously reported. The decarboxylation of 4-hydroxy-5-methoxy-1,10-phenanthroline-3-carboxylic acid[3]

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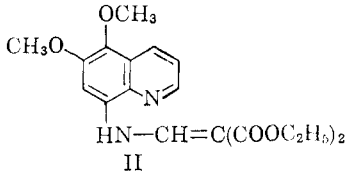
yielded 4-hydroxy-5-methoxy-1,10-phenanthroline which, on hydrolysis with hydrogen iodide, afforded 4,5-dihydroxy-1,10-phenanthroline.

From 4,7-dichloro-1,10-phenanthroline[3] were obtained 4,7-dimethoxy- and 4,7-diphenoxy-1,10-phenanthrolines by treatment with sodium methoxide and potassium phenoxide, respectively. From the latter compound 4,7-diamino-1,10-phenanthroline resulted on heating with ammonium chloride according to the method of Vompe, *et al.*[9]

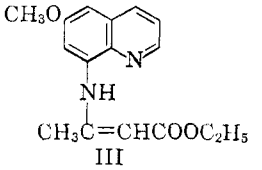
For the preparation of 5,6-dihydroxy-1,10-phenanthroline, 4,5-dimethoxy-2-nitroacetanilide[10] was subjected to a Skraup reaction (Yale modification) which gave higher yields than the method previously reported,[11] and the resulting 5,6-dimethoxy-8-nitroquinoline reduced to the amine, which after a second Skraup reaction, yielded 5,6-dimethoxy-1,10-phenanthroline. Hydrolysis with hydrogen iodide yielded the desired product.

By the action of ethyl ethoxymethylenemalonate on 8-amino-5,6-dimethoxyquinoline there was obtained 5,6 - dimethoxy - 8 - (β,β - dicarbethoxyvinylamino)quinoline (II), which on cyclization yielded ethyl 4-hydroxy-5,6-dimethoxy-1,10-phenanthroline-3-carboxylate. Alkaline hydrolysis yielded a salt of the free acid, which on treatment with hydrogen iodide afforded 4,5,6-trihydroxy-1,10-phenanthroline-3-carboxylic acid. Neither of these acids was successfully decarboxylated.



II

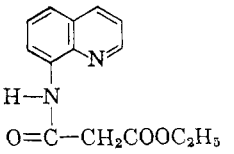
4,5-Dihydroxy-2-methyl-1,10-phenanthroline was prepared as follows: 8-Amino-6-methoxyquinoline on treatment in the cold with ethyl acetoacetate was converted into ethyl β-(6-methoxy-8-quinolyl)-aminocrotonate (III) which, on cyclization in Dowtherm, yielded 4 - hydroxy - 5 - methoxy - 2 - methyl - 1,10 - phenanthroline.[12] Hydrolysis



III

with hydrogen bromide yielded the desired product. It was hoped that, starting with 8-amino-4-hydroxy-2-methylquinoline,[12,13] and proceeding as above it would be possible to obtain 4,7-dihydroxy-2,9-dimethyl-1,10-phenanthroline. When this reaction failed the synthesis was attempted without success using the 4-methoxy derivative, prepared by methylating the acetyl derivative with dimethyl sulfate, followed by hydrolysis of the acetyl group. This method was found to be more convenient for preparing this compound than that of Halcrow and Kermack.[14]

Treatment of 8-aminoquinoline with carbethoxyacetyl chloride ($ClCOCH_2COOC_2H_5$)[15] yielded ethyl 8-quinolylmalonamate (IV), which was hydrolyzed with aqueous sodium bicarbonate[16] and the result-



IV

ing acid cyclized with polyphosphoric acid[17] to yield 2,4-dihydroxy-1,10-phenanthroline. On subjecting 8-amino-6-methoxyquinoline to the same treatment, 2,4-dihydroxy-5-methoxy-1,10-phenanthroline resulted.

Experimental

2-Methoxy-8-nitroquinoline.—The following method was found superior to that previously reported. A solution of 32.2 g. (0.15 mole) of 2-chloro-8-nitroquinoline[18] in 600 ml. of anhydrous methanol was refluxed with 11.8 g. (0.2 mole) of sodium methoxide for 1.5 hr. The warm reaction mixture was diluted with 400 ml. of water, cooled overnight, and the resulting crystalline product removed by filtration; yield, 27.3 g. (86.6%), m.p. 122–123° (lit.,[19] 124–125°).

2-Methoxy-1,10-phenanthroline.—The use of the Yale modification of the Skraup synthesis was found preferable to the method previously reported. From 17.4 g. (0.1 mole) of 8-amino-2-methoxyquinoline,[5] 28.4 g. (0.2 mole) of arsenic acid, 200 ml. of 85% phosphoric acid, and 8.4 g. (0.15 mole) of acrolein there was obtained 5.97 g. of product after purification by chromatography on alumina using benzene as eluent, m.p. 86–89° (lit.,[6] 88–89°).

2-Hydroxy-1,10-phenanthroline.—A solution of 3.0 g. (0.014 mole) of 2-methoxy-1,10-phenanthroline in 30 ml. of 57% hydriodic acid was refluxed for 6 hr. After cooling, the demethylated product was precipitated by neutralizing with 10% sodium hydroxide to pH 7. The dried, crude material weighed 2.28 g. (82.4%), m.p. 155–157°. An analytical sample, crystallized from benzene containing a little ethanol, melted at 159–160°. Infrared spectrum (λ_{max} Nujol): 2.9, 5.96, 6.12 μ.

Anal. Calcd. for $C_{12}H_8N_2O$: C, 73.46; H, 4.11. Found: C, 73.31; H, 4.13.

5-Methoxy-1,10-phenanthroline.—The following method was found to be preferable to that previously reported. In a modified Skraup reaction,[4] 34.8 g. (0.2 mole) of 8-amino-6-methoxyquinoline, 56.8 g. (0.4 mole) of arsenic acid, 400 ml. of 85% phosphoric acid, and 16.8 g. (0.3 mole) of acrolein were employed. After the solution was made alkaline with aqueous ammonia, the precipitated basic material and

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ammonium phosphate was removed by filtration and dried. The filtrate was extracted with three 100-ml. portions of chloroform. The chloroform extracts were then used to extract the dried solid in a Soxhlet extractor for 48 hr. The extracts were concentrated to 25 ml. and placed on an alumina chromatography column. By elution with 1:1 benzene–chloroform, there was obtained 3.8 g. (9.0%) of light yellow crystals, m.p. 105–106° (lit.,[8] 104–105°).

5-Hydroxy-1,10-phenanthroline.—A solution of 3.8 g. (0.018 mole) of 5-methoxy-1,10-phenanthroline in a mixture of 30 ml. of 48% hydrobromic acid, 10 ml. of glacial acetic acid, and 1 ml. of hypophosphorous acid was refluxed for 1.25 hr. The solution was cooled and neutralized with concentrated aqueous ammonia, causing the product to precipitate as a sticky red solid. The mother liquor, which was removed by decantation, was saturated with sodium chloride, causing an additional quantity of material to separate. The combined precipitates were dissolved in 200 ml. of warm 5% sodium hydroxide, the solution treated with Hyflo Super-Cel and filtered. After saturation with sodium chloride, the solution was brought to pH 6 with concentrated hydrochloric acid. The dried, precipitated product weighed 2.8 g. An analytical sample, crystallized from dimethylformamide, did not melt below 340°.

Anal. Calcd. for $C_{12}H_8N_2O$: C, 73.46; H, 4.11. Found: C, 73.43; H, 4.32.

4-Hydroxy-5-methoxy-1,10-phenanthroline.—Five grams (0.02 mole) of 4-hydroxy-5-methoxy-1,10-phenanthroline-3-carboxylic acid[3] was placed in a 100-ml. Erlenmeyer flask and heated in a Wood's metal bath at 290–300° for 10 min. with occasional manual stirring. During this time part of the product sublimed and deposited on the neck of the flask. The crude decarboxylated material weighed 3.6 g. An analytical sample was crystallized from aqueous acetone; m.p. 161–163°.

Anal. Calcd. for $C_{13}H_{10}N_2O_2$: C, 68.98; H, 4.42. Found: C, 69.30; H, 4.39.

4,5-Dihydroxy-1,10-phenanthroline.—The crude methyl ether obtained above (3.5 g. or 0.016 mole) was refluxed in 20 ml. of 57% hydriodic acid with 0.5 g. of red phosphorus for 3 hr. The cooled solution was made basic with 10% sodium hydroxide solution and filtered with suction through sintered glass. The product was precipitated by adding solid carbon dioxide; yield, 2.6 g. An analytical sample crystallized from aqueous dimethylformamide in yellow prisms, m.p. 229–230°.

Anal. Calcd. for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.77. Found: C, 67.97; H, 3.77.

4,7-Dimethoxy-1,10-phenanthroline.—Two grams (0.008 mole) of 4,7-dichloro-1,10-phenanthroline,[3] 1.5 g. (0.027 mole) of sodium methoxide, and 0.2 g. of copper powder in 50 ml. of methanol were heated in a sealed tube at 160° for 8 hr. The reaction mixture was diluted with 50 ml. of methanol, warmed, filtered, and evaporated to dryness. The residue was dissolved in 200 ml. of 2 *N* hydrochloric acid, filtered, and reprecipitated by the addition of 10% sodium hydroxide. The crude product was removed by filtration, dried, and crystallized from benzene; yield, 0.41 g. (22.8%) of light tan prisms, m.p. 209–210°.

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 70.00; H, 5.00. Found: C, 69.53; H, 4.93.

4,7-Diphenoxy-1,10-phenanthroline.—The method employed by Keneford, Schofield, and Simpson[20] in the preparation of 4-phenoxycinnoline was used. A mixture of 12.5 g. (0.05 mole) of 4,7-dichloro-1,10-phenanthroline, 30 g. of phenol, and 10 g. of powdered potassium hydroxide was heated for 9 hr. on a steam bath. The reaction mixture was digested with 100 ml. of 30% aqueous potassium hydroxide and washed five times with water by decantation. The green amorphous residue was crystallized from aqueous ethanol to give 15.0 g. (78%) of product, m.p. 175–178°. An analytical sample crystallized from benzene–hexane as white prisms, m.p. 179–180°.

Anal. Calcd. for $C_{24}H_{16}N_2O_2$: C, 79.12; H, 4.40. Found: C, 79.04; H, 4.42.

4,7-Diamino-1,10-phenanthroline Dihydrochloride.—An intimate mixture of 3.6 g. (0.01 mole) of 4,7-diphenoxy-1,10-phenanthroline and 15 g. of ammonium chloride was placed in a 125-ml. Erlenmeyer flask and heated with occasional manual stirring for 30 min. at 320–330° in a Wood's metal bath. Phenol was evolved, and the mixture acquired a deep yellow color. After cooling to room temperature, 50 ml. each of water and concentrated aqueous ammonia were added, and the precipitated yellow product was filtered and dried; weight, 2.27 g. However no suitable crystallizing solvent could be found. A dihydrochloride was prepared by dissolving the base in absolute ethanol and adding excess of ethereal hydrogen chloride. Upon crystallization from ethanol the dihydrochloride was obtained as fine yellow needles, m.p. 359–360° dec.

Anal. Calcd. for $C_{12}H_{12}Cl_2N_4$: C, 50.90; H, 4.27. Found: C, 51.09; H, 4.32.

4,5-Dimethoxyacetanilide.—This was prepared in 98% yield by the following procedure: 4,5-Dimethoxynitrobenzene[21] (18.3 g. or 0.1 mole), dissolved in 250 ml. of ethanol, was reduced over 10% palladium on carbon in a Parr shaker. After removal of the catalyst and evaporation of the solvent under reduced pressure, 12 g. (0.12 mole) of acetic anhydride and a drop of concentrated sulfuric acid were added and the mixture was warmed for 15 min. on a steam bath. The product, when crystallized from 4:1 water–ethanol, melted at 131° (lit.,[10] 130°).

5,6-Dimethoxy-8-nitroquinoline.—The Yale modification of the Skraup reaction was used. From 27 g. (0.11 mole) of 2-nitro-4,5-dimethoxyacetanilide,[10] 32.4 g. (0.023 mole) of arsenic acid, 100 ml. of 85% phosphoric acid, and 18.5 g. (0.33 mole) of acrolein there was obtained 18.8 g. (68%) of 5,6-dimethoxy-8-nitroquinoline, m.p. 126° after crystallization from aqueous ethanol (lit.,[11] 127–128°).

8-Amino-5,6-dimethoxyquinoline.—This was prepared in 97% yield by reduction of 5,6-dimethoxy-8-nitroquinoline[11] in ethanol over 10% palladium on carbon in a Parr shaker at 70°. The pure compound melted at 149° after crystallization from benzene (lit.,[11] 148–149°).

5,6-Dimethoxy-1,10-phenanthroline.—In a modified Skraup reaction involving 10.6 g. (0.052 mole) of 8-amino-5,6-dimethoxyquinoline, 13.6 g. (0.10 mole) of arsenic acid, 75 ml. of 85% phosphoric acid, and 12.5 g. (0.22 mole) of acrolein there was obtained 4.2 g. (42.5%) of light yellow needles after crystallization from petroleum ether (b.p. 75–90°), m.p. 125–126°.

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 70.00; H, 5.00. Found: C, 70.02; H, 4.96.

5,6-Dihydroxy-1,10-phenanthroline.—A solution of 2.7 g. (0.01 mole) of 5,6-dimethoxy-1,10-phenanthroline in 25 ml. of 57% hydriodic acid was refluxed for 2.5 hr. with 0.1 g. of red phosphorus. The reaction mixture was filtered through sintered glass and neutralized with 5% aqueous sodium carbonate. The precipitated material when dried weighed 1.7 g. and melted at 312–315° dec. An analytical sample crystallized from dimethylformamide in the form of yellow prisms which decomposed at 390° after sintering.

Anal. Calcd. for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.77. Found: C, 67.81; H, 3.93.

5,6-Dimethoxy-8-(β,β-dicarbethoxyvinylamino)quinoline.—A mixture of 20.4 g. (0.1 mole) of 8-amino-5,6-dimethoxyquinoline and 22 g. (0.1 mole) of ethyl ethoxymethylenemalonate was heated for 1 hr. on a steam bath. The reaction mass solidified on cooling and gave 36.6 g. (98.9%) of pure product, m.p. 113–114°, when crystallized from aqueous methanol.

Anal. Calcd. for $C_{19}H_{22}N_2O_6$: C, 60.96; H, 5.88. Found: C, 61.27; H, 5.82.

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TABLE I

SUBSTITUTED 1,10-PHENANTHROLINES—ULTRAVIOLET ABSORPTION DATA

Substituents	λ_{max} (log ϵ)—0.1 *N* HCl	λ_{max} (log ϵ)—0.1 *N* NaOH
2-Hydroxy-	218 (4.56); 284 (4.51)	222 (4.85); 286 (4.72)
5-Hydroxy-	226 (4.43); 285 (4.50)	237 (4.40); 256 (4.22); 284 (4.37); 342 (3.85)
4,7-Diphenoxy-	215 (4.66); 269 (4.68); 311 (3.96)	263 (4.50); 306 (3.94)
4,7-Diamino- (dihydrochloride)[a]	263 (4.39); 329 (4.05); 345 (4.10); 365 (3.80)	257 (4.46); 290 (4.22); 328 (4.17)
5,6-Dihydroxy-	212 (4.42); 228 (4.47); 252 (4.24); 294(4.54)	228 (4.12)
4,5,6-Trihydroxy-3-carboxy-	252 (4.47); 278 (4.43)	237 (4.38)
4-Hydroxy-5-methoxy-2-methyl-	216 (4.47); 229 (4.42); 273 (4.58)	239 (4.57); 271 (4.04); 322 (4.00)
4,5-Dihydroxy-2-methyl-	237 (4.47); 273 (4.45); 323 (3.87)	239 (4.55); 270 (4.50); 321 (3.99)
2,4-Dihydroxy-	228 (4.52); 269 (4.40)	265 (4.51)
2,4-Dihydroxy-5-methoxy-	218 (4.69); 281 (4.51)	216 (4.84); 234 (4.72); 271 (4.67)
4-Hydroxy-2-methyl-[b]	207 (4.50); 233 (4.38); 266(4.64)	241 (4.40); 272 (4.37); 319 (3.84)

[a] λ_{max} (log ϵ): 95% ethanol—207 (4.42); 241 (4.36); 253 (4.36); 301 (4.00); 336 (3.99). [b] Prepared by method given in ref. 12, m.p. 214° (lit.,[22] 196°).

5,6-Dimethoxy-4-hydroxy-1,10-phenanthroline-3-carboxylic Acid.—The previously described compound (36.6 g., or 0.10 mole) was heated in 300 ml. of refluxing Dowtherm A with stirring until ethanol evolution ceased (35 min.). The reaction mixture was cooled and diluted with 300 ml. of petroleum ether (b.p. 75–90°), which caused the ethyl ester of the above acid to separate as a red oil. The supernatant solution was decanted and the crude ester refluxed with 25 ml. of ethanol and a solution of 16.5 g. of potassium hydroxide in 200 ml. of water for 2 hr. After cooling and extraction with ether, the aqueous solution was acidified with dilute hydrochloric acid. The crude, dried acid weighed 28.8 g. An analytical sample, crystallized twice from aqueous acetic acid, and once from ethanol, melted at 273–275° dec.

Anal. Calcd. for $C_{15}H_{12}N_2O_5$: C, 60.00; H, 4.03; N, 9.33. Found: C, 60.02; H, 4.50; N, 9.38.

4,5,6-Trihydroxy-1,10-phenanthroline-3-carboxylic Acid.—A mixture of 3 g. (0.01 mole) of 5,6-dimethoxy-4-hydroxy-1,10-phenanthroline-3-carboxylic acid, 1 g. of red phosphorus, 20 ml. of 57% hydriodic acid, and 15 ml. of glacial acetic acid was refluxed for 4 hr. The cooled reaction mixture was filtered and the precipitate taken up in dimethylformamide. After removal of the red phosphorus by filtration, the solution was treated with charcoal, filtered, and concentrated to incipient crystallization. On cooling 2.6 g. of yellow needles was obtained. An analytical sample, crystallized from ethanol, melted at 330° dec.

Anal. Calcd. for $C_{13}H_8N_2O_5$: C, 57.37; H, 2.96. Found: C, 57.48; H, 3.30.

Ethyl β-(6-Methoxy-8-quinolyl)aminocrotonate.—This compound in crude form has previously been reported.[12] To a solution of 17.4 g. (0.1 mole) of 8-amino-6-methoxyquinoline in 100 ml. of absolute ethanol there was added 13 g. (0.1 mole) of ethylacetoacetate and 3 drops of concentrated hydrochloric acid. The reaction mixture was allowed to stand *in vacuo* in a desiccator over phosphorus pentoxide for 1 week. The resulting crude solid product (27.8 g.) was extracted with boiling hexane, the solution treated with carbon, filtered, and evaporated, yielding 24.7 g. of a light yellow solid which was used directly in the cyclization. An analytical sample, crystallized from hexane, melted at 83–84°.

Anal. Calcd. for $C_{16}H_{18}N_2O_3$: C, 67.13; H, 6.28. Found: C, 67.01; H, 6.33.

4-Hydroxy-5-methoxy-2-methyl-1,10-phenanthroline.—This compound was prepared essentially by the method of Misani and Bogert.[12] It melted at 242–243° after recrystallization from benzene (lit.,[12] 234–235° dec.).

Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.98; H, 5.03. Found: C, 69.86; H, 5.18.

4,5-Dihydroxy-2-methyl-1,10-phenanthroline.—A mixture of 2 g. of the 5-methoxy compound, 30 ml. of 48% hydrobromic acid, and 2 ml. of hypophosphorous acid was refluxed for 1.5 hr. Yellow prisms precipitated when the reaction flask was cooled in ice. The precipitate was removed by filtration, suspended in 30 ml. of water and 5 ml. of concentrated aqueous ammonia, allowed to stand for 15 min., filtered, and dried. It weighed 1.6 g. (88.8%), m.p. 234–238°. An analytical sample, crystallized from ethanol, melted at 237–238°.

Anal. Calcd. for $C_{13}H_{10}N_2O_2$: C, 69.02; H, 4.46; N, 12.38. Found: C, 68.71; H, 4.55; N, 12.14.

8-Acetamido-4-hydroxy-2-methylquinoline.—The procedure was essentially that of Misani and Bogert[12] except that Dowtherm was used as the cyclizing medium. From 21.3 g. of ethyl β-(*o*-acetamidophenyl)aminocrotonate there was obtained 12.5 g. (71.2%) of product melting at 287° dec. An analytical sample, crystallized from 1:1 benzene–ethanol melted at 293–294° (lit.,[12,13] 274–276°, 292–293°).

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.70; H, 5.70; N, 12.82.

8-Amino-4-hydroxy-2-methylquinoline.—This was prepared according to Misani and Bogert in 99% yield. It melted after crystallization from ethanol at 299–300° dec. (lit.,[12,13] 264–265° dec., 300° dec.).

Anal. Calcd. for $C_{10}H_{10}N_2O$: C, 69.10; H, 5.75. Found: C, 69.07; H, 5.76.

8-Acetamido-4-methoxy-2-methylquinoline.—A solution of 5.7 g. (0.026 mole) of 8-acetamido-4-hydroxy-2-methylquinoline and 2.1 g. (0.053 mole) of sodium hydroxide in 20 ml. each of methanol and water was treated dropwise with 5 ml. (0.053 mole) of dimethyl sulfate with stirring. The solution was allowed to stand for 12 hr. and made strongly basic with 40% aqueous sodium hydroxide. The product was collected by filtration, washed with water, and dried; weight, 2.9 g., m.p. 139–142°. One crystallization from aqueous alcohol raised the melting point to 143–145° (lit.,[14] 144–146°). There was recovered 1.1 g. of starting material on acidification (pH 6) of the basic filtrate. The yield of product was 60.5% based on consumed starting material.

8-Amino-4-methoxy-2-methylquinoline.—This resulted in 97.8% yield on hydrolysis (15 min.) of the acetamido compound with (1:1) hydrochloric acid on a steam bath, followed by treatment with aqueous ammonia. It melted at 113–116° (lit.,[14] 115–116°).

Ethyl 8-Quinolylmalonamate.—To a stirred solution of 14.4 g. (0.1 mole) of 8-aminoquinoline in a mixture of 20 ml. each of glacial acetic acid and dry pyridine was added 16 g. (0.10 mole) of carbethoxyacetyl chloride[15] in a thin stream.

(22) S. J. Hazlewood, G. K. Hughes, and F. Lions, *J. Proc. Roy. Soc. N.S. Wales*, **71**, 471 (1938); *Chem. Abstr.*, **33**, 6113 (1939).

The reaction mixture was stirred for an additional 5 min. and allowed to stand for 12 hr., after which time it was diluted with cold water. The resulting precipitate, after drying and crystallization from benzene–petroleum ether, weighed 13.4 g. (52%); m.p. 95°.

Anal. Calcd. for $C_{14}H_{14}N_2O_3$: C, 65.00; H, 5.43. Found: C, 65.09; H, 5.42.

Ethyl 6-Methoxy-8-quinolylmalonamate.—This compound was prepared by the same procedure used to prepare ethyl 8-quinolylmalonamate. From 20 g. (0.12 mole) of 6-methoxy-8-aminoquinoline and 17.5 g. (0.12 mole) of carbethoxyacetyl chloride there was obtained 21.2 g. of crude material. An analytical sample, crystallized from benzene–petroleum ether, melted at 113–114°.

Anal. Calcd. for $C_{15}H_{16}N_2O_4$: C, 62.50; H, 5.55. Found: C, 62.52; H, 5.60.

8-Quinolylmalonamic Acid.—A solution of 10 g. (0.039 mole) of ethyl 8-quinolylmalonamate and 20 g. of sodium bicarbonate in 270 ml. of water and 30 ml. of ethanol was heated for 4 hr. on a steam bath with vigorous stirring. The solution was cooled and acidified to pH 5 with hydrochloric acid. The precipitated product was removed by filtration and dried; yield, 7 g. An analytical sample, crystallized from water and a little alcohol, melted at 138–139° dec.

Anal. Calcd. for $C_{12}H_{10}N_2O_3$: C, 62.60; H, 4.35. Found: C, 62.64; H, 4.19.

6-Methoxy-8-quinolylmalonamic Acid.—A suspension of 5.6 g. (0.02 mole) of ethyl 6-methoxy-8-quinolylmalonamate in 60 ml. of water containing 6.3 g. of dissolved sodium bicarbonate was heated with stirring on a steam bath for 3 hr. Water was added occasionally to maintain the original volume. After treatment of the hot solution with Darco and filtration, solid sodium chloride was added to the cooled solution, which was then acidified to pH 2. The precipitated crude product was removed by filtration and crystallized from water; yield, 4.9 g. (96.8%), m.p. 145° dec.

Anal. Calcd. for $C_{13}H_{12}N_2O_4$: C, 59.99; H, 4.65. Found: C, 60.01; H, 4.85.

2,4-Dihydroxy-1,10-phenanthroline.—A mixture of 1.6 g. (0.007 mole) of 8-quinolylmalonamic acid and 50 g. of polyphosphoric acid was heated in an oil bath at 130° for 2 hr. with occasional stirring. The reaction mixture was diluted with cold water and neutralized with concentrated aqueous ammonia. The resulting product was removed by filtration and dried; yield, 1.1 g. An analytical sample, crystallized from aqueous acetic acid, melted at 315–316° with prior sintering.

Anal. Calcd. for $C_{12}H_8N_2O_2$: C, 67.92; H, 3.80; N, 13.20. Found: C, 68.17; H, 4.20; N, 13.00.

2,4-Dihydroxy-5-methoxy-1,10-phenanthroline.—From 5 g. (0.02 mole) of 6-methoxy-8-quinolylmalonamic acid and 75 g. of polyphosphoric acid, treated as above, there was obtained 4.6 g. of dry, crude product. An analytical sample melted at 250–251° after crystallization from ethanol.

Anal. Calcd. for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16. Found: C, 64.76; H, 4.36.

Angularly Arylated Decahydroquinolines, Hexahydroindolines, and Octahydropyrindine

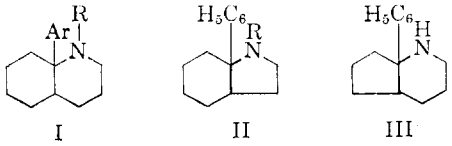
ERIK F. GODEFROI[1] AND LYDIA H. SIMANYI

Research Laboratories of Parke, Davis & Co., Ann Arbor, Michigan

Received March 23, 1962

The addition of aryllithium reagents to cyclic Schiff's bases IV, V, and VI has given decahydro-8a-arylquinolines (I), hexahydro-7a-phenylindolines (II), and octahydro-7a-phenyl-1H-1-pyrindine (III). N-Alkylated derivatives of I have also been obtained by treating N-substituted carbonitriles (VIIa and VIIb) with Grignard reagents. The products have been found to possess central nervous system depressant properties.

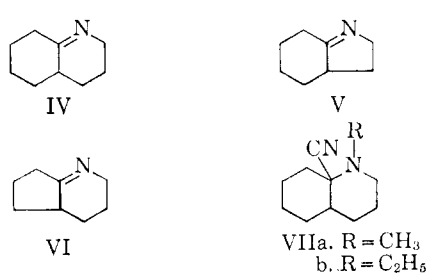
During the course of investigations on substances possessing central nervous system depressant properties, we prepared a number of decahydro-8a-arylquinolines (I), hexahydro-7a-phenylindolines (II), and octahydro-7a-phenyl-1H-1-pyrindine (III).



I II III

Examination of the literature revealed that decahydro-4a-phenylquinoline, isomeric with type I, had been previously prepared by Boekelheide[2a] and Sugimoti,[2b] but their methods were not applicable to the preparation of the desired compounds.

The addition of organolithium reagents to anils[3] suggested that the reaction of aryllithium reagents to cyclic imines IV, V, and VI would produce types I, II, and III respectively.



IV V VI

VIIa. R = CH_3
b. R = C_2H_5

2,3,4a,5,6,7,8-Octahydroquinoline (IV) was prepared according to directions of Cohen and Witkop[4] and Parcell.[5] This imine reacted with a number of aryllithium reagents to yield decahydro-

(1) Present address: Research Laboratories, Dr. C. Janssen, Beerse, Belgium.

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(3) H. Gilman and R. H. Kirby, *J. Am. Chem. Soc.*, **55**, 1265 (1933); *ibid.*, **63**, 2046 (1951).

(4) L. A. Cohen and B. Witkop, *J. Am. Chem. Soc.* **75**, 6595 (1955).

(5) R. F. Parcell, *ibid.*, **81**, 2596 (1959).