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Transformations in the 1,10-Phenanthroline Series

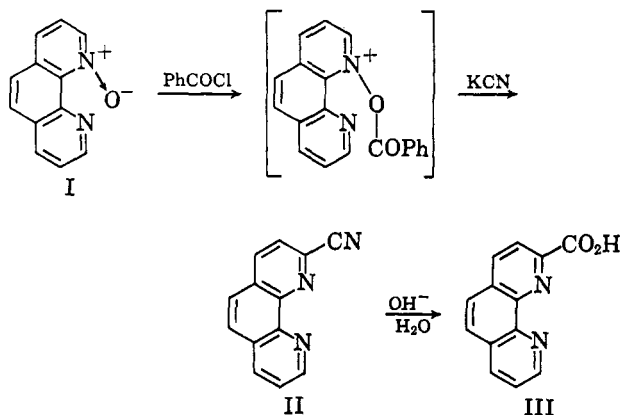
E. J. COREY, A. L. BORROR, AND THOMAS FOGLIA

Departments of Chemistry, Harvard University, Cambridge, Massachusetts, and Drexel Institute of Technology, Philadelphia, Pennsylvania

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In conjunction with a study of metal ion coordination with 1,10-phenanthroline derivatives and macrocycles derived therefrom we have investigated some of the properties and reactions of 1,10-phenanthroline 1-oxide (I). This substance, which had been prepared previously by Maerker and Case in 26.5% yield,¹ is now readily available (70–80% yields) using a modified procedure described herein. The N-oxide is a tan solid, soluble in cold water, $pK_a = 6.6$ at 22°, significantly more basic than 1,10-phenanthroline² ($pK_a = 4.8$) or pyridine 1-oxide³ ($pK_a = 0.8$).

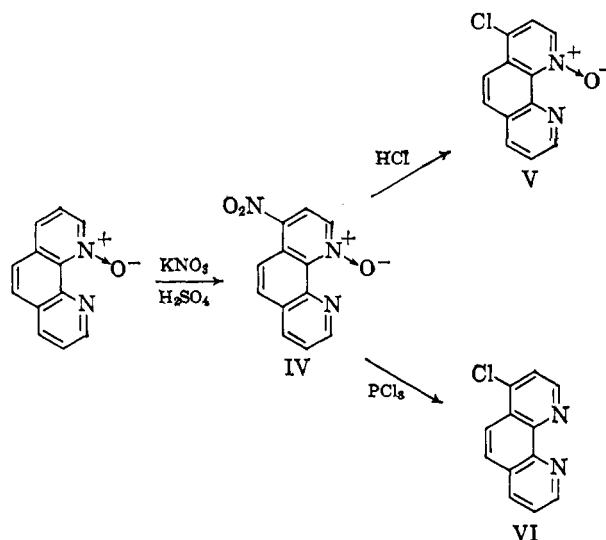
1,10-Phenanthroline 1-oxide allows the introduction of a cyano group into the 2-position of the phenanthroline ring system. Treatment of the 1-oxide with benzoyl chloride and potassium cyanide at room temperature furnished 2-cyano-1,10-phenanthroline (II) in good yield. Hydrolysis of II under basic conditions gave 1,10-phenanthroline-2-carboxylic acid (III), a hitherto unknown and very useful substance. It is interesting



to note that the observed reaction takes precedence over the Reissert reaction⁴ at C-9,N-10. The latter course would require the attachment of benzoyl to N-10 which is sterically unfavorable. In addition it should be noted that we have found 1,10-phenanthroline itself not to undergo the Reissert reaction under the conditions useful for quinolines.

Although N-oxides in general are nitrated readily,⁵ 1,10-phenanthroline 1-oxide has been reported to fail to undergo nitration.¹ On the other hand, the parent

ring system nitrates to give 5-nitro-1,10-phenanthroline in 90% yield.⁶ The apparent lack of reactivity of the N-oxide toward electrophilic substitution was reinvestigated. With potassium nitrate in sulfuric acid as a nitrating medium, the N-oxide was actually found to afford a mononitro compound in about 10% yield at 90°. The low yield was not improved by increasing the reaction temperature or time. The product of the reaction was assigned the structure 4-nitro-1,10-phenanthroline 1-oxide (IV) from the following observations. (1) The nitro group is very labile and is replaced by chloride when the compound is heated to reflux in concentrated hydrochloric acid to give 4-chloro-1,10-phenanthroline 1-oxide (V).⁷ (2) Reaction of IV with phosphorus trichloride in refluxing chloroform resulted in both deoxygenation and replacement of the nitro group by chlorine. The product, 4-chloro-1,10-phenanthroline, had been prepared previously⁸ by a different method. In agreement with the previous report⁸ we found the compound to be hygroscopic, but the melting



point which we observed was 163–165° (lit.⁸ m.p. 180–230°). Hawkins and co-workers⁹ recently repeated the original preparation, successfully purified the compound, and reported a melting point of 165–166°. The picrate of our specimen had m.p. 203–204° (reported originally for the picrate of 4-chloro-1,10-phenanthroline,⁸ m.p. 203–206°).

The conditions which effect the conversion of 1,10-phenanthroline to the 5-nitro derivative⁶ (150–160°, mixture of concentrated nitric and sulfuric acid) lead to gross degradation of 1,10-phenanthroline N-oxide. At lower temperatures the N-oxide is converted to the 4-nitro derivative in low yield and an insoluble acidic by-product is formed in considerable amount.

Our experience with N-oxide I confirms its exceptional unreactivity under the ordinary conditions of electrophilic substitution for aza-aromatic N-oxides. In all probability this effect stems from the relatively great stability of the conjugate acid of I and the consequence that the concentration of free unprotonated I, a much

(6) G. F. Smith and F. W. Cagle, *ibid.*, **12**, 781 (1947).

(7) Nitro groups *para* to an N-oxide function are known to induce facile nucleophilic displacement. See H. J. den Hertog and W. P. Combé, *Rec. trav. chim.*, **70**, 581 (1951).

(8) H. R. Snyder and H. E. Freier, *J. Am. Chem. Soc.*, **68**, 1320 (1946).

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(1) G. M. Maerker and F. H. Case, *J. Am. Chem. Soc.*, **80**, 2745 (1958).

(2) T. S. Lee, I. M. Kolthoff, and D. L. Leusing, *ibid.*, **70**, 2348 (1948).

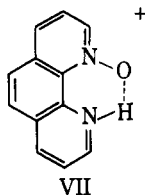
(3) H. H. Jaffe and G. O. Doak, *ibid.*, **77**, 4441 (1955).

(4) See W. E. McEwen and R. L. Cobb, *Chem. Rev.*, **55**, 511 (1955).

(5) E. Ochiai, *J. Org. Chem.*, **18**, 534 (1953).

more reactive species in electrophilic substitution, must be exceedingly small under the usual conditions of electrophilic substitution.

The relative stability of the protonated form of 1,10-phenanthroline 1-oxide, which is probably due to hydrogen bonding as shown in VII and recent papers^{10,11}



on the preparation and characterization of several complexes containing pyridine 1-oxide as a ligand, suggested that 1,10-phenanthroline 1-oxide might function as a chelate with oxygen and nitrogen serving as coordination sites. Solid complexes of 1,10-phenanthroline with copper, nickel, and cobalt chlorides were prepared by mixing ethanolic solutions of the N-oxide and the metal chloride. The ligand to metal ratio was varied from 2:1 to 6:1 but in each case the same complex precipitated from solution and analysis indicated a ligand metal ratio of 2:1 corresponding to the general formula $C_{12}H_8N_2O_2MCl_2 \cdot nH_2O$. These complexes were not unusually stable and like the pyridine N-oxide complexes they dissociated in water and regenerated the N-oxide and metal ions; the ultraviolet and visible spectra of aqueous solutions of the complexes gave absorption maxima and extinction coefficients identical in all respects with that determined for the pure N-oxide.

Experimental¹²

1,10-Phenanthroline 1-Oxide.—To a solution of 10.0 g. (0.0505 mole) of 1,10-phenanthroline monohydrate in 60 ml. of glacial acetic acid was added 6.0 ml. of 30% hydrogen peroxide. The temperature of the solution was maintained at 70–75° for 3 hr. after which an additional 6.0 ml. of hydrogen peroxide was added and the heating continued for 3 hr. The solution was concentrated to a volume of approximately 15 ml. using a rotary evaporator; 15 ml. of water was added and the concentration was continued to a volume of approximately 10 ml. The mixture was neutralized with a sodium carbonate–water paste. The solid mass was extracted repeatedly with several portions of chloroform and the extracts were evaporated. The resulting residue was dried in an oven at 50°, ground to a fine powder, and re-extracted with chloroform. The combined chloroform extracts were dried over sodium sulfate, boiled with decolorizing charcoal, and evaporated to give 7–8 g. (70–80%) of 1,10-phenanthroline 1-oxide, m.p. 176–179°. Crystallization from chlorobenzene gave fine pale yellow needles, m.p. 180–181°. The compound had been prepared previously by Maerker and Case¹ in 23.6% yield (crude product). These workers report m.p. 179–180° for the pure compound.

The picrate of 1,10-phenanthroline 1-oxide was prepared by the addition of a saturated aqueous solution of picric acid to an aqueous solution of the N-oxide. The picrate melts at 201–203° after recrystallization from ethanol.

The pK_a of 1,10-phenanthroline 1-oxide was determined by potentiometric titration using a Radiometer pH meter equipped

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(11) R. L. Carlin, *ibid.*, **83**, 3773 (1961).

(12) Melting points were determined with a capillary melting point apparatus and are uncorrected. Infrared spectra were obtained with a Perkin-Elmer Infracord by the potassium bromide pellet method. Analyses were by Pascher Microanalytical Laboratory, Bonn, Germany, by Alfred Bernhard Microanalytical Laboratory, Mülheim, Germany, and by Scandinavian Microanalytical Laboratory, Copenhagen, Denmark. 1,10-Phenanthroline was obtained from Aldrich Chemical Co., Milwaukee, Wis. Ultraviolet and visible spectra were with a Bausch and Lomb Spectronic 505.

with a type GK 2026C electrode. Duplicate titration of a 0.0185 M solution of N-oxide with 0.1 N HCl gave a pK_a value of 6.63 ± 0.02 at 22°. No correction for ionic strength was made.

Determination of the ultraviolet and visible spectra in aqueous solution gave λ_{max} 264, 309, 322 (sh), and 365 $m\mu$ ($\log \epsilon$ 4.42, 3.68, 3.59, and 3.28, respectively).

Transition Metal Complexes of 1,10-Phenanthroline 1-Oxide.
A. Bis-1,10-phenanthroline 1-Oxide Copper(II) Chloride Dihydrate.—To a solution of 80 mg. (0.408 mmole) of 1,10-phenanthroline 1-oxide in 10 ml. of 95% ethanol was added a solution of 27.5 mg. (0.205 mmole) of cupric chloride in 5 ml. of ethanol. The mixture was allowed to stand a few hours and then filtered. The collected material was dried *in vacuo* at 60° to yield 77 mg. (66.5%) of green solid.

Anal. Calcd. for $(C_{12}H_8N_2O)_2 \cdot CuCl_2 \cdot 2H_2O$: C, 51.21; H, 3.58; N, 9.95. Found: C, 51.01; H, 3.78; N, 9.94.

B. Bis-1,10-phenanthroline 1-Oxide Nickel(II) Chloride Hemihydrate.—To a solution of 500 mg. (2.55 mmoles) of 1,10-phenanthroline 1-oxide in 12 ml. of ethanol was added 294 mg. (1.23 mmoles) of $NiCl_2 \cdot 6H_2O$ dissolved in 20 ml. of ethanol. The solution was warmed slightly on the steam bath and allowed to stand a few hours. The yellowish orange solid was collected by suction filtration and dried *in vacuo* at 60° to give 585 mg. (89%) of material.

Anal. Calcd. for $(C_{12}H_8N_2O)_2 \cdot NiCl_2 \cdot 0.5H_2O$: C, 54.41; H, 3.23; N, 10.55. Found: C, 54.80; H, 3.52; N, 10.30.

C. Bis-1,10-phenanthroline 1-Oxide Cobalt(II) Chloride.—To a solution of 500 mg. (2.55 mmoles) of 1,10-phenanthroline 1-oxide in 65 ml. of ethanol was added 312 mg. (1.32 mmoles) of $CoCl_2 \cdot 6H_2O$ dissolved in 30 ml. of ethanol. The solution was warmed on the steam bath and allowed to stand for a few hours. The orange solid was collected by suction filtration and dried *in vacuo* at 60° to give 575 mg. (85%) of material.

Anal. Calcd. for $(C_{12}H_8N_2O)_2 \cdot CoCl_2$: C, 55.38; H, 3.08; N, 10.75. Found: C, 55.43; H, 3.33; N, 10.74.

These complexes were water soluble. Their ultraviolet and visible spectra in aqueous solution gave absorption maxima and extinction coefficients identical with 1,10-phenanthroline 1-oxide provided complete dissociation to the N-oxide and metal ions was assumed.

Complexes giving the same spectra and comparable analyses also were obtained when the N-oxide to metal chloride mixing ratio was 6:1.

2-Cyano-1,10-phenanthroline.—A solution consisting of 2.98 g. (0.0148 mole) of 1,10-phenanthroline 1-oxide and 3.0 g. of potassium cyanide dissolved in 50 ml. of water was stirred magnetically while 3.0 ml. of benzoyl chloride was added dropwise. The total addition required 15 min. and the reaction was stirred for an additional 15 min. The precipitated solid was collected by suction filtration, washed with water, and dried. Crystallization from ethanol afforded 2.15 g. (71%) of light tan needles, m.p. 233–234°. Further recrystallization from ethanol raised the melting point to 237–238°.

Anal. Calcd. for $C_{13}H_7N_3$: C, 76.07; H, 3.44; N, 20.48. Found: C, 75.81; H, 3.65; N, 20.34.

2-Carboxy-1,10-phenanthroline.—To a solution of 1.0 g. (0.0049 mole) of 2-cyano-1,10-phenanthroline in 10 ml. of 95% ethanol was added a solution of 0.8 g. of sodium hydroxide in 5 ml. of water and the mixture was refluxed for 2 hr. (evolution of ammonia ceased). The solution was cooled to room temperature and made slightly acidic with concentrated hydrochloric acid. The solvent was removed *in vacuo*. The residue was heated in 10 ml. of water on the steam bath and filtered. The light tan product was crystallized from ethanol to yield 0.87 g. (76%) of white solid, m.p. 209–210° dec. The compound hydrates readily and attempts to dry it completely were unsuccessful.

Anal. Calcd. for $C_{13}H_8N_2O_2 \cdot 1.25H_2O$: C, 63.28; H, 4.29; N, 11.35. Found: C, 63.24; H, 4.32; N, 11.26.

A picrate was prepared and recrystallized from aqueous methanol. Analysis indicates that the picrate is formed by combination of 2 moles of carboxylic acid and 1 mole of picric acid. The picrate melts at 230–231° dec.

Anal. Calcd. for $(C_{13}H_8N_2O_2)_2 \cdot C_6H_3N_3O_7$: C, 56.72; H, 2.83; N, 14.47. Found: C, 57.07; H, 2.92; N, 14.13.

4-Nitro-1,10-phenanthroline 1-Oxide.—To a solution of 2.0 g. (0.0102 mole) of 1,10-phenanthroline 1-oxide in 10 ml. of concentrated sulfuric acid (sp. gr. 1.84) was added 1.1 g. of potassium nitrate and the mixture was heated on the steam bath for 1 hr. An additional 1.1 g. of potassium nitrate was added and the

heating continued for 1 hr. The mixture was poured into 25 g. of ice and neutralized with solid sodium carbonate. The solution was extracted with chloroform. The chloroform extracts were dried and the chloroform was removed by evaporation. The residue weighed 1.5 g. The residue was stirred with 20 ml. of water, filtered, and dissolved in dilute sulfuric acid. Neutralization with ammonium hydroxide gave a yellow solid which was collected by suction filtration and dried. Crystallization from a chloroform-ether mixture gave 0.24 g. (10%) of material, m.p. 160° dec.

Anal. Calcd. for $C_{12}H_7N_3O_3$: C, 59.74; H, 2.93; N, 17.42. Found: C, 59.70; H, 2.99; N, 17.28.

The ammoniacal filtrate from the above reaction was evaporated to dryness. The residue was extracted with chloroform. Removal of the chloroform and examination of the infrared spectrum of the residue indicated that it was mainly unchanged 1,10-phenanthroline 1-oxide.

When the nitration was carried out at 110–115° a 10% yield of 4-nitro-1,10-phenanthroline 1-oxide was again obtained.

4-Chloro-1,10-phenanthroline 1-Oxide.—A solution of 150 mg. (0.625 mmole) of 4-nitro-1,10-phenanthroline 1-oxide in 10 ml. of 50% hydrochloric acid was refluxed for 18 hr. The mixture was cooled, neutralized with solid sodium carbonate, and repeatedly extracted with chloroform. The chloroform extracts were dried over sodium sulfate and the solvent was removed. The yield of pale yellow solid was 100 mg. (69.5%). Recrystallization from benzene furnished the analytical sample, m.p. 139–141°. The compound gave a positive test for chlorine.

Anal. Calcd. for $C_{12}H_7ClN_3O$: C, 62.42; H, 3.03; N, 12.12. Found: C, 62.30; H, 3.24; N, 12.11.

4-Chloro-1,10-phenanthroline.—To a solution of 0.5 g. (2.07 mmoles) of 4-nitro-1,10-phenanthroline 1-oxide in 15 ml. of chloroform was added dropwise a solution of freshly distilled phosphorus trichloride in 5 ml. of chloroform. A precipitate formed which dissolved upon heating. The reaction mixture was refluxed for 2 hr. The solution was cooled, poured onto crushed ice, and treated with solid sodium carbonate. The chloroform was separated and the aqueous layer was extracted with several portions of chloroform. The chloroform extracts were dried and the chloroform was evaporated. The pinkish solid that remained proved to be an acid salt. The salt was dissolved in water and neutralized with ammonium hydroxide; the resulting solution was extracted with chloroform. Drying and removal of the solvent furnished 0.283 g. (63.5%) of white solid, m.p. 159–162°. Recrystallization from benzene raised the melting point to 163–165°. Because of the hygroscopic nature of the compound it was converted to a picrate for analytical purposes. The picrate gave a positive test for chloride.

Anal. Calcd. for $C_{18}H_{10}ClN_5O_7$: C, 48.71; H, 2.27; N, 15.78. Found: C, 48.65; H, 2.42; N, 15.69.

Nitration and Degradation of 1,10-Phenanthroline in Nitric-Sulfuric Acid.—To 5 ml. of concentrated sulfuric acid (sp. gr. 1.84) was added, with cooling, 2.35 g. (0.012 mole) of 1,10-phenanthroline 1-oxide. The mixture was heated on an oil bath to 85–90° during the addition of 1.75 g. of concentrated nitric acid (Spectrograde 1.42). The addition required 40 min.; the reaction was maintained at 85–90° for an additional 3.5 hr. After 2.5 hr. an orange solid began to precipitate from solution. The mixture was cooled and poured onto 45 g. of ice. Neutralization with sodium carbonate followed by filtration gave 0.6 g. of an orange solid. The compound was extremely insoluble in most organic solvents, but could be crystallized from aqueous dimethylformamide. The crystallized material melted at 210–215° dec. and showed infrared bands at 3500 (OH?), 1710 (C=O?), 1550 (NO₂?), and 1360 cm.⁻¹ (NO₂). The compound was insoluble in mineral acids and only sparingly soluble in base.

Anal. Found: C, 54.37; H, 2.70; N, 16.87.

The aqueous filtrate from the above reaction was extracted with chloroform. Removal of the chloroform by evaporation gave 0.1 g. of 4-nitro-1,10-phenanthroline 1-oxide, identified by melting point and infrared spectrum.

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Addition Reactions of Substituted

1,4-Cyclohexadienes. I.

3,3,6,6-Tetramethyl-1,4-cyclohexadiene^{1a}

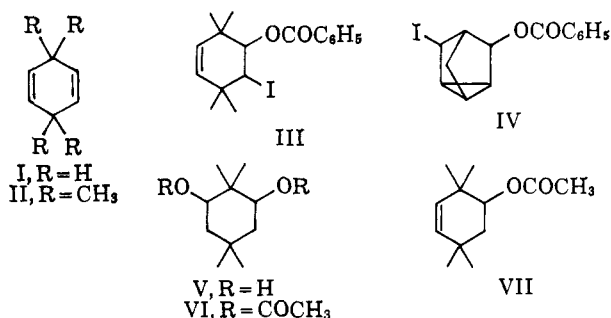
F. W. GRANT,^{1b} R. W. GLEASON, AND C. H. BUSHWELLER

Departments of Chemistry, Hamilton College, Clinton, New York, and Middlebury College, Middlebury, Vermont

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Bicyclo[2.2.1]heptadiene and bicyclo[2.2.2]octadiene are known to undergo a variety of 1,5-homoconjugate addition reactions.² Recognizing the unique disposition of the double bonds in these compounds and the spectral evidence demonstrating interaction between them,⁴ it was, nonetheless, of interest to determine whether homoconjugate addition might be induced in the related 1,4-cyclohexadiene (I) or its derivatives. Double-bond interaction in I has been inferred from its ultraviolet absorption spectrum.³ An unsuccessful attempt in this direction was reported by van Tamelen⁵ who reinvestigated the controlled Prevost addition of iodine and silver benzoate to I⁶ and confirmed that the major product was correctly described as the 1,2-addition product, cyclohexene 4,5-dibenzoate. He extended this work to include the controlled bromination of I which resulted in 4,5-dibromocyclohexene. No trace of a homoconjugate addition product was noted in either case.

Earlier reports pertinent to this problem have described the halogenation of 1-methyl,⁷ 1,2-dimethyl,⁸ 1,2-dichloro,⁹ and perfluoro-1,4-cyclohexadiene¹⁰ but in none of these cases were homoconjugate addition products isolated, although this possibility may not have been fully explored in the analysis of minor products.



Our interest has been in derivatives of I substituted at the 3- and 6-positions where bulky *cis* and equatorially oriented groups might be expected to favor

(1) (a) Taken in part from the Master's Thesis of C. H. B., Middlebury College, 1963. (b) Department of Chemistry, Hamilton College, Clinton, N. Y.

(2) A summary of pertinent publications is found in ref. 3 and should include the work of A. Gagneux and C. A. Grob, *Helv. Chim. Acta*, **42**, 1753; 2006 (1959).

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