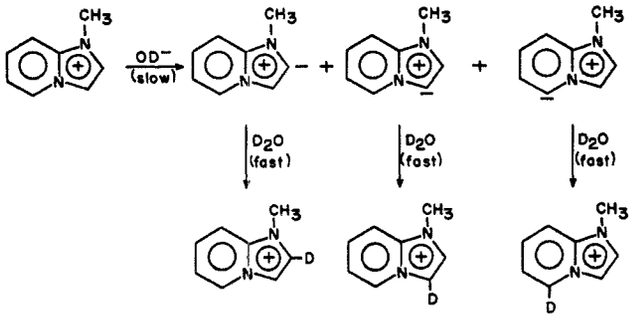
well envision the reaction sequence in Scheme I to account for these base-catalyzed exchange reactions.[7]

SCHEME I



(7) Related studies dealing with some five- and six-membered ring nitrogen heterocyclic compounds have been the subject of several recent publications cited in ref 1. Some more recent publications in this area are Y. Kawazoe and M. Ohnishi, *Chem. Pharm. Bull.* (Tokyo) **15**, 826 (1967); R. A. Abramovitch, M. Saha, E. M. Smith, and R. T. Coutts, *J. Amer. Chem. Soc.*, **89**, 1537 (1967).

Experimental Section

Nmr spectra were obtained with a Varian A-60 spectrometer. Elemental analyses were done on all new compounds by Mrs. K. Decker of this department.

General Procedure of H–D Exchange.—A weighed sample of the appropriate polyazaindene was placed in an nmr tube and dissolved in a measured quantity of standardized acid or base. The nmr spectrum was immediately run and integrated. Exchange was followed by repeated integrations at selected time intervals. Exchange at 35° was obtained by allowing the sample to remain in the nmr probe. Exchange at 65 and 100° was obtained by placing the sample in refluxing methanol or water, respectively, and by removing the sample periodically for nmr analysis. All exchanges were followed to 85% completion.

3-Deuterioimidazo[1,2-*a*]pyridine Methiodide.—Imidazo[1,2-*a*]pyridine was heated at 95° for 19 hr in 3 *M* D_2SO_4, cooled, and neutralized with anhydrous Na_2CO_3 to pH 9. The aqueous solution was extracted with $CHCl_3$, the chloroform extract evaporated to dryness, and the residue dissolved in acetone. Excess iodomethane was added and the solution was allowed to stand overnight. The solution was then filtered, yielding 3-deuterioimidazo[1,2-*a*]pyridine methiodide containing 90% deuterium at position 3 as determined by nmr analysis.

Synthesis of the 6- and 7-Hydroxy-5,8-dioxocarbostyrils[1a]

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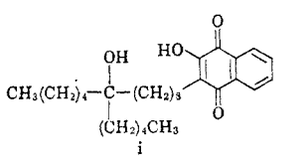
Utilizing a condensation reaction between amine I and methyl propiolate to obtain pyridone III followed by reaction with potassium *t*-butoxide and oxygen in dimethyl sulfoxide, a convenient synthesis of 6-hydroxy-5,8-dioxocarbostyril (V) was achieved. Conversion of 8-hydroxycarbostyril *via* dinitro (XII) and diamino (XIIIa) intermediates provided the isomeric 7-hydroxy-5,8-dioxocarbostyril (XV). The structures assigned to hydroxyquinones V and XV received support from mass spectral and proton magnetic resonance studies.

The potential application[2] of hydroxyquinolinequinones in certain malaria and cancer chemotherapy problems suggested extending our earlier study of carbostyrils[3] to the isomeric 6- (Scheme I) and 7-hydroxy-5,8-dioxocarbostyrils (Scheme II) (V and XV). Whereas syntheses of 6- and 7-hydroxy-5,8-quinolinequinones have been described,[4] no examples of the corresponding carbostyrils appear to have been reported. To allow quinones V and XV to serve efficiently as key intermediates for future studies in this area, initial emphasis was placed upon devising practical routes to both substances.

From a number of potential approaches to quinone V considered, one based on transforming 1,3-dioxocyclohexane to pyridone III appeared most attractive. In 1961, Zymalkowski[5] reported condensing propargyl aldehyde with an amine (I) derivative of 1,3-dioxocyclohexane and obtained the corresponding pyridyl ketone. More recently, the reaction was modified by using methyl propiolate and synthesis of pyridone III by this means was noted, albeit without detail, in a preliminary communication.[6] After brief warming, direct contact between amine I and methyl propiolate led to an exothermic reaction. At the end of 1 hr reaction temperature was raised to approximately 170° to complete cyclization (II → III). Employing lower reaction temperature allowed isolation of *trans*-olefin intermediate IV. The *trans* configuration was supported by a coupling constant of 17 cps for the olefin protons. Heating amino ester IV above 170° caused

(1) (a) This study received support from the U. S. Medical R and D Command under Contract DA-49-193-MD-3010 and National Science Foundation Grant GB-4939. The present manuscript is contribution number 279 from the Army Research Program on Malaria. (b) National Science Foundation Predoctoral Fellow.

(2) For example, from a number of napthoquinones prepared by L. F. Fieser and colleagues for antimalarial evaluation, lapinone (i) proved most promising. For an interesting and valuable review, see L. F. Fieser, J. P.



i

Schirmer, S. Archer, R. R. Lorenz, and P. I. Pfaffenbach, *J. Med. Chem.*, **10**, 513 (1967), and L. F. Fieser, "The Scientific Method," Reinhold Publishing Corp., New York, N. Y., 1964, p 190. Furthermore, the metabolic products of certain antimalarials have been shown to be quinolinequinones and carbostyrils: refer to R. R. Holmes, J. Conrady, J. Guthrie, and R. McKay, *J. Amer. Chem. Soc.*, **76**, 2400 (1954), and a review by P. B. Russell, "Medicinal Chemistry," A. Burger, Ed., Interscience Publishers, Inc., New York, N. Y., 1960, p 814. These facts augmented by an increasing number of naturally occurring quinones with cytotoxic and antibiotic properties enhanced our interest. Recent studies related to the quinolinequinone antitumor agent streptonigrin have been described by T. K. Liao, W. H. Nyberg, and C. C. Cheng, *Angew. Chem. Intern. Ed. Engl.*, **6**, 82 (1967); T. Kametani, K. Ogasawara, M. Shio, and A. Kozuka, *Yakugaku Zasshi*, **87**, 262 (1967); N. S. Nizuno, *Biochem. Pharm.*, **16**, 933 (1967); and C. W. B. Kremer and J. Laszlo, *Cancer Chemotherapy Rept.*, **51**, 19 (1967).

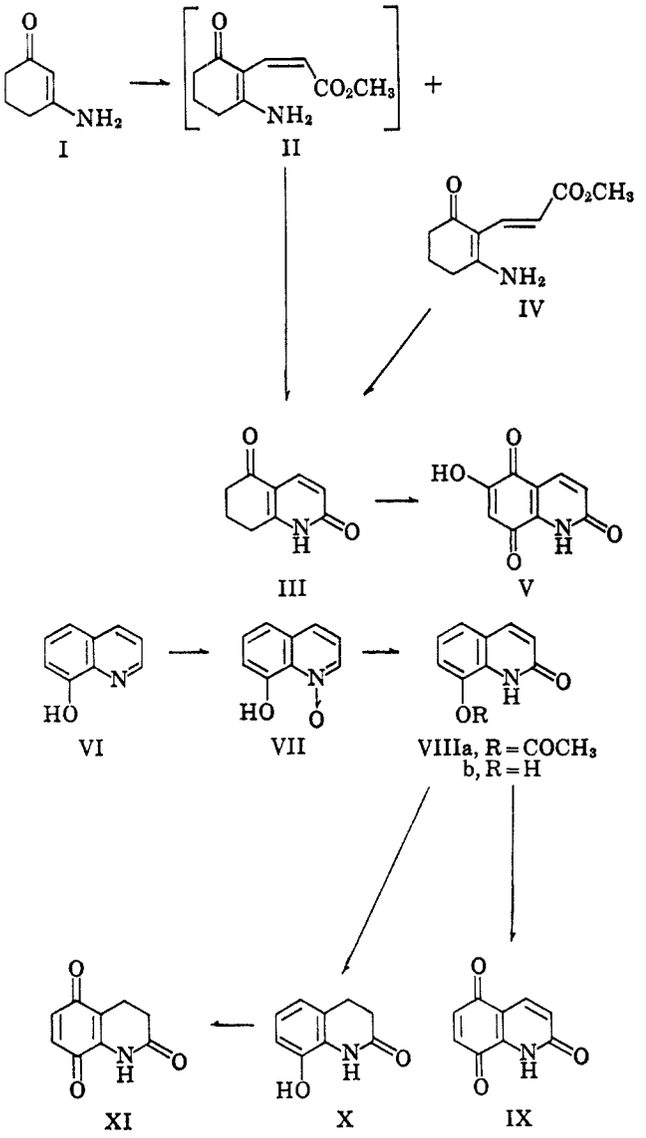
(3) G. R. Pettit and A. B. Neill, *Can. J. Chem.*, **42**, 1764 (1964); G. R. Pettit and M. Kalnins, *J. Org. Chem.*, **25**, 1365 (1960).

(4) The investigations of Drake and colleagues provide a useful summary of prior routes to hydroxyquinolinequinones; *cf.*, Y. T. Pratt and N. L. Drake, *J. Amer. Chem. Soc.*, **79**, 5024 (1957). Interestingly, certain of these quinolinequinones have displayed significant amebicidal activity against induced *E. histolitica* in the guinea pig.

(5) F. Zymalkowski and H. Rimek, *Arch. Pharm.*, **294**, 759 (1961).

(6) M. A. T. Sluyter, U. K. Pandit, W. N. Speckamp, and H. O. Huisman, *Tetrahedron Lett.*, 87 (1966).

SCHEME I



ready cyclization to the pyridone (III). Allowing ketone III to react with oxygen[7] and potassium *t*-butoxide in dimethyl sulfoxide solution afforded a brick-red potassium salt of quinone V. Acidification led to deep orange quinone V, dec pt 285–305°. The two important steps in this sequence, that is, I → III and III → V, proceeded in 39 and 70% yields (pure material), respectively.

The commercial availability of 8-hydroxyquinoline and easy transformation to 8-hydroxycarbostyril[3,8] (VIIIb from N-oxide VII) favored phenol VIIIb as precursor of hydroxy quinone XV. Initial attempts to oxidize phenol VIIIa using a Fremy's[9] salt or 80% hydrogen peroxide[10] procedure proved unrewarding.

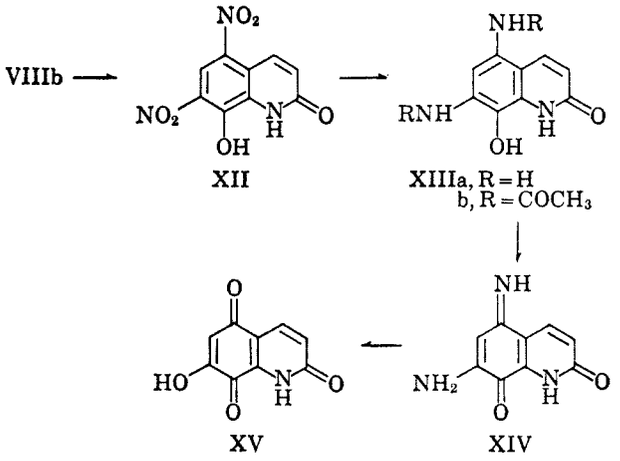
(7) The utility of this approach to hydroxyquinolinequinones was suggested by the excellent application of similar conditions for transformation of α-tetralones to hydroxy napthoquinones: T. R. Kasturi and T. Arunachalam, *Can. J. Chem.*, **44**, 1086 (1966); A. C. Baillie and R. H. Thomson, *J. Chem. Soc., Sect. C*, 2184 (1966). We wish to thank Dr. Kasturi for providing us with experimental details of the reaction prior to publication. A similar reaction has been used to oxidize ketones to diosphenols. For example, see G. R. Pettit, D. S. Alkalay, P. Hofer, and P. A. Whitehouse, *Tetrahedron*, **20**, 1755 (1964), and a reference contained therein.

(8) K. Ramaiah and V. R. Srinivasan, *Proc. Indian Acad. Sci., Sect. A*, **55**, 221 (1962); *Chem. Abstr.*, **57**, 6761*f* (1962).

(9) R. P. Singh, *Can. J. Chem.*, **44**, 1994 (1966); D. J. Cram and A. C. Day, *J. Org. Chem.*, **31**, 1227 (1966); R. Kuhn, *Ber.*, **93**, 2829 (1960).

(10) D. Bryce-Smith and A. Gilbert, *J. Chem. Soc.*, 873 (1964).

SCHEME II



However, a dichromate technique[11] was successful in oxidizing phenol VIIIb to quinone IX. The dichromate method proved even more effective for oxidation of dihydrocarbostyril X to quinone XI. The original purpose for quinone IX was a Thiele acetylation[12] step and thereby to a possible mixture of quinones V and XV. Before this route was adequately evaluated (in two initial attempts only starting material was recovered), treating phenol VIIIb with dilute nitric acid was found to yield (83%) dinitrocarbostyril XII. The structure of carbostyril XII was supported in general by elemental composition and specifically by its proton magnetic resonance spectrum. Protons at C-3 and C-4 appeared as doublets at δ 6.90 and 8.55 with J = 10 cps. A signal corresponding to the C-6 proton appeared at δ 8.50. A possible alternative arrangement involving 3,5-dinitro substituents seemed unlikely because of difficulty experienced in nitrating carbostyrils at C-3.[13]

Reducing nitro compound XII with sodium dithionite[4] in aqueous sodium hydroxide solution, followed by treatment with oxygen led to the green imine XIV. For analytical purposes a specimen of imine XIV hydrochloride was prepared by catalytic (palladium on carbon) reduction of the dinitro compound (XII) suspended in 1 *N* hydrochloric acid and then performing the oxidation step. Unfortunately, the imine proved too insoluble in a variety of solvents for further purification by recrystallization. Amine XIIIa because of its transient existence in air was characterized as acetamide XIIIb. The amide (XIIIb) was easily obtained by subjecting carbostyril XII to catalytic hydrogenation in tetrahydrofuran–acetic anhydride. Owing to the precarious stability of imine XIV and its transformation products under acid conditions, hydrolysis to hydroxyquinone XV required considerable experimentation. Heating imine XIV with 6 *N* sulfuric acid for 20 min followed by continuous extraction of quinone XV from the cool mixture using diethyl ether proved effective. Quinone XV was obtained in 40% yield from XIV (as yellow needles decomposing at 280–300°).

Structural assignments for quinones V and XV received support from results of mass and pmr measure-

(11) H. Gilman, Ed., "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 1944, p 375.

(12) V. P. Bhatia and K. B. L. Mathur, *Tetrahedron Lett.*, 4057 (1966); W. A. Remers, R. H. Roth, and M. J. Weiss, *J. Org. Chem.*, **30**, 4381 (1965).

(13) A. Kaufmann and V. P. de Petherd, *Ber.*, **50**, 336 (1917); *Chem. Abstr.*, **11**, 2799 (1917).

ments. Molecular ions (M^+ 191) were obtained from both quinones and fragments (loss of C=O) at *m/e* 163, 135, 107, and 79 were in complete agreement.[14] The three distinctive sets of pmr signals shown by each of the isomeric quinones was reassuring.[15] The C-3, C-4 vinyl proton doublets (for example, with V at δ 6.83 and 7.97, J = 9 cps) and a sharp signal (at δ 6.05 for V) assigned to the lone quinone-ring proton was readily apparent in both quinones. The mass and pmr measurements combined with thin layer chromatography proved particularly valuable in dealing with these quinones as assessment of purity by recrystallization and melting point behavior was severely limited.

Experimental Section

Dimethyl sulfoxide was distilled from calcium oxide, redistilled from calcium hydride and stored under nitrogen in the dark. Reagent grade *t*-butyl alcohol was distilled from sodium. Solvent extracts of aqueous solutions were dried over calcium chloride or magnesium sulfate. Thin layer chromatography plates were prepared using silica gel G (E. Merck, AG Darmstadt).

Melting points were observed employing a Kofler melting point apparatus. Ultraviolet (methanol solution, Cary-14 instrument), infrared (in potassium bromide using a Beckman IR-12 instrument), and proton magnetic resonance (Varian Associates, A-60 spectrometer, trifluoroacetic acid as solvent) measurements were performed by Miss K. Reimer. Chemical shifts (δ) are in parts per million relative to tetramethylsilane as external standard. Mass spectra were recorded by Dr. P. Brown and P. A. Whitehouse using an Atlas CH-4B spectrometer equipped with a molecular beam inlet system (70 eV). Elemental microanalyses were provided by Dr. A. Bernhardt, Max Planck Institute, Mülheim, Germany.

1-Amino-3-oxocyclohex-1-ene (I).—The title substance was prepared by treating 89–99-g quantities of 1,3-dioxocyclohexane (Aldrich Chemical) in dry benzene with ammonia essentially as previously described.[5] After the calculated amount of water was collected, the hot solution was cooled and the liquid phase decanted. The residue was triturated with hot dioxane (70 ml) and the hot solution was separated from a dark viscous residue. Upon cooling the yellow crystals of amine I (40–56% yield) which separated were collected and used without further purification.

2,5-Dioxo-1,2,5,6,7,8-hexahydroquinoline (III).—In a typical experiment 1-amino-3-oxocyclohex-1-ene (94.5 g) was ground to a fine powder and mixed with methyl propiolate (95 ml, *caution* potent vesicant). The mixture became homogeneous on warming and by this time the reaction become exothermic. Heating at approximately 105° was continued 1 hr. The condenser was removed and residual methyl propiolate was evaporated over a period of a few minutes by raising the temperature to approximately 170°. The latter increment in temperature promoted cyclization of intermediates II and IV. The solid residue was triturated with two portions (200 ml each) of hot methylene chloride and the pale yellow crystalline product was recrystallized from methanol to yield 53.3 g (39%) of pyridone III. An analytical sample was recrystallized from methanol as colorless plates melting at 285–288° (lit.[6] mp 290–298°): pmr, δ 1.90 (quintuplet, two protons), 2.46 (triplet, two protons), 2.78 (triplet, two protons), 6.74 (doublet, one proton, J = 10 cps) and 8.29 (doublet, one proton, J = 10 cps).

Anal. Calcd for $C_9H_9NO_2$: C, 66.40; H, 5.56; N, 8.52. Found: C, 66.48, 66.23; H, 5.64, 5.70; N, 8.44.

When reaction between amine I and methyl propiolate was conducted without the final period of heating to approximately 170°, it was possible to isolate *trans* olefin IV (in, *e.g.*, 8% yield depending on temperature) by fractional recrystallization of the crude product from methanol. A pure specimen was recrystallized from dioxane as colorless plates: mp 163–166°; pmr, δ 1.77 (quintuplet, two protons), 2.60 (multiplet, four protons), 3.61 (singlet, three protons), 6.36 (doublet, one proton, J = 17 cps), and 7.35 (doublet, one proton, J = 17 cps).

Anal. Calcd for $C_{10}H_{13}NO_3$: C, 61.53; H, 6.71; N, 7.17. Found: C, 61.56; H, 6.57; N, 7.33.

Heating ester IV at 180° for 15 min readily caused cyclization to pyridone III and elimination of methanol.

6-Hydroxy-5,8-dioxocarbostyril (V).—To a solution prepared from *t*-butyl alcohol (40 ml), potassium *t*-butoxide (freshly prepared from 11.8 g of potassium), and dimethyl sulfoxide (160 ml) was added pyridone III (12.0 g). The flask was quickly stoppered and the mixture stirred until a clear dark red solution was obtained. A slight positive pressure of oxygen was applied and the mixture was stirred and maintained at approximately 30° for 47 hr. During this period 3.3 l. of oxygen was absorbed. Next, the solution was filtered (sintered-glass funnel) and the solid washed with dimethyl sulfoxide (50 ml) and with several portions of dry diethyl ether (600 ml total). The remaining dark solid was dissolved in 500 ml of water. The deep red solution was filtered and cooled and the filtrate acidified with cold 2 *N* sulfuric acid (150 ml). The yellow solid which separated was collected and washed with 0.15 *N* sulfuric acid (30 ml) and 0.05 *N* sulfuric acid (30 ml). Following drying in a vacuum desiccator 9.8 g (70%) of hydroxyquinone V was obtained. Recrystallization from tetrahydrofuran gave an analytical specimen decomposing at 285–305°: λ_{max} 244, 308, and 427 mμ (log ϵ 4.04, 4.35, and 2.62); ν_{max} 3620–3400 (broad), 1680, 1655, 1620, 1551, 1470, 1420, 1270, 1090, and 865 cm^{-1}; pmr, δ 6.05 (one proton at C-7), 6.83 (doublet, one proton, J = 9 cps), and 7.97 (doublet, one proton, J = 9 cps).

Anal. Calcd for $C_9H_5NO_4$ (191): C, 56.55; H, 2.64; N, 7.33. Found: C, 57.03; H, 2.99; N, 7.29; mol wt (mass spec), 191.

8-Acetoxycarbostyril (VIIIb).—A mixture of 8-hydroxyquinoline N-oxide (20 g) and acetic anhydride (120 ml) was heated at steam bath temperature 5 hr.[16] The dark solution was poured into water, cooled, and basified with concentrated ammonium hydroxide. Cooling was continued 30 min and the light brown solid collected to yield 19.9 g (77%) of carbostyril VIIIa melting at 251–254°. Four recrystallizations from ethanol–water gave an analytical sample of shiny leaflets melting at 252–254° (lit.[17,18] mp 247–248° and 250°): pmr, δ 2.15 (three methyl protons), 6.65 (doublet, one proton, J = 9 cps), 7.15 (broad multiplet, three phenyl protons), and 7.85 (doublet, one proton, J = 9 cps).

Anal. Calcd for $C_{11}H_9NO_3$: C, 65.02; H, 4.46; N, 6.89. Found: C, 65.17; H, 4.12; N, 6.94.

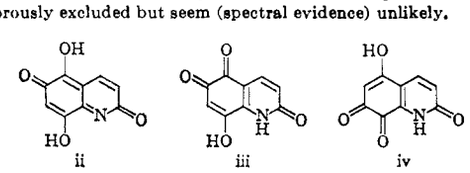
8-Hydroxycarbostyril (VIIIb).—A suspension of 8-acetoxycarbostyril (VIIIa, 20 g) in concentrated hydrochloric acid (200 ml) was heated at steam bath temperature 4 hr. Following dilution with water (200 ml) and cooling (ice bath) the dark tan solid (13.2 g, 84%) was collected. Repeated recrystallization from ethanol (Norit-A)–water and trituration with hot 6 *N* hydrochloric acid gave an analytical sample as light tan needles melting at 297–299° (lit.[17,19] melting points of 250, 287–288 and 260–290° with decomposition): pmr, δ 6.80–7.15 (multiplet, four protons) and 8.15 (doublet, one proton, J = 9 cps).

Anal. Calcd for $C_9H_7NO_2$: C, 67.08; H, 4.38; N, 8.69. Found: C, 66.85; H, 4.82; N, 8.85.

5,8-Dioxocarbostyril (IX).—A solution of sodium dichromate (2.0 g) in water (50 ml) was added dropwise to a stirred mixture composed of chloroform (50 ml), 8-hydroxycarbostyril (0.5 g) and dilute (20%) sulfuric acid (100 ml). Two minutes later the chloroform layer was separated and replaced with another 50-ml quantity of chloroform. Another portion (5 ml) of the dichromate solution was added and the preceding operation was duplicated. The process was repeated four more times using 10-ml

(14) A mass spectral study of hydroxynapthoquinones has been summarized: D. Becker, C. Djerassi, R. E. Moore, H. Singh, and P. J. Scheuer, *J. Org. Chem.*, **31**, 3650 (1966).

(15) Structures ii and iii for quinone V and iv for quinone XV have not been rigorously excluded but seem (spectral evidence) unlikely.



ii iii iv

(16) The reaction is initially exothermic and due care should be exercised in larger scale experiments.

(17) J. P. Phillips, E. M. Barrall, and R. Breese, *Trans. Kentucky Acad. Sci.*, **17**, 135 (1956); *Chem. Abstr.*, **51**, 11349*a* (1957).

(18) Y. N. Sheĭnker and I. Y. Postouskiĭ, *Zh. Fiz. Khim.*, **32**, 394 (1958); *Chem. Abstr.*, **52**, 18406*i* (1958).

(19) K. Inagami, M. Kaihara, and J. M. Price, *J. Biol. Chem.*, **240**, 3682 (1965); *Cancer Research*, **24**, 596 (1954).

quantities of the sodium dichromate solution and waiting 5 min between extractions. The combined chloroform extract was concentrated to a bright yellow powder weighing 0.14 g (26%), dec pt 212–222°. Three recrystallizations from ethyl acetate gave a pure sample of orange-yellow plates decomposing at 218–222°: λ_{max} 265, 303, and 418 mμ (log ε 4.10, 3.92, and 3.11); ν_{max} 1685, 1650, 1618, 1602, 1426, 1331, 1062, and 842 cm^{-1}; pmr, δ 6.55 (singlet, two quinone protons); 6.65 (doublet, one proton); 7.80 (doublet, one proton, J = 9 cps).

Anal. Calcd for $C_9H_5NO_3$: C, 61.72; H, 2.88; N, 8.00. Found: C, 61.92; H, 2.84; N, 8.24.

3,4-Dihydro-5,8-dioxocarbostyril (XI).—A specimen (0.5 g) of 3,4-dihydro-8-hydroxycarbostyril (prepared in 74% yield, mp 195–200° by treating 8-hydroxycarbostyril in ethanol containing 5% rhodium on aluminum oxide and 72% perchloric acid as acid catalyst with a slightly positive atmosphere of hydrogen during 24 hr)[20] was suspended in 10% sulfuric acid (100 ml) and treated over 5 min with a solution of sodium dichromate (1.0 g) in water (20 ml). The solution was stirred 30 min while the carbostyril slowly dissolved and was then extracted with five 25-ml portions of chloroform. The combined extract was concentrated to a bright yellow solid (0.29 g, 54%) melting at 181–185°. Three recrystallizations from ethyl acetate gave an analytical sample of yellow needles melting at 185–188° with decomposition: λ_{max} 249 and 415 mμ (log ε 4.18 and 3.19); ν_{max} 1701, 1650, 1600, 1470, 1364, 1323, 1218, and 851 cm^{-1}; pmr, δ 2.50 (narrow multiplet, four aliphatic protons), and 6.60 (singlet, two quinone protons). The precursor dihydrocarbostyril X displayed pmr signals at δ 1.80 (multiplet, four aliphatic protons), and 5.80–6.40 (multiplet, three aromatic protons).

Anal. Calcd for $C_9H_7NO_3$: C, 61.02; H, 3.98; N, 7.91. Found: C, 60.93; N, 4.06; N, 7.97.

5,7-Dinitro-8-hydroxycarbostyril (XII).—To a stirred solution of 8-hydroxycarbostyril (VIIIb, 5 g) and water (100 ml) was slowly added concentrated nitric acid (100 ml). A yellow solid began to separate in about 1 min and the mixture was heated (steam bath) 10 min, and diluted with water (100 ml). After cooling (overnight), the bright yellow needles (6.5 g, 83%) were collected. Three recrystallizations from ethanol–water provided a pure sample as yellow needles: dec pt 279–280°; ν_{max} 3560 (w), 3440 (w), 3090, 1685, 1670, 1612, 1593, 1532, 1405, 1335, 1183, 1022, 851, and 738 cm^{-1}; pmr, δ 6.90 (doublet, one proton, J = 10 cps), 8.50 (one proton at C-6), and 8.55 (doublet, one proton, J = 10 cps).

Anal. Calcd for $C_9H_5N_3O_6$: C, 43.04; H, 2.01; N, 16.73. Found: C, 43.24; H, 2.22; N, 16.84.

5-Imino-7-amino-8-oxocarbostyril (XIV). Method A.—The following procedure proved more convenient and reliable. To a suspension of 5,7-dinitro-8-hydroxyquinoline (XII, 5 g) in water (200 ml) was added 2 N sodium hydroxide (10 ml). Addition of sodium dithionite (40 g) was continued until the initial dark mixture was replaced by an orange solution. Following a 15-min heating (steam bath) period the solution was acidified with 6 N hydrochloric acid and heating continued 1 hr. The resulting yellow solution was cooled, filtered, and made basic with sodium bicarbonate. Oxygen was passed into the solution for 20 min and the green solid which separated was collected. The crude product (XIV) was used without further treatment for conversion into quinone XV.

(20) V. G. S. Sidhu, G. Thygarajan, and S. Ansari, *Ann.*, **627**, 218 (1959).

Method B.—A mixture composed of carbostyril XII (0.5 g) 1 N hydrochloric acid (60 ml) and 10% palladium on carbon (0.03 g) was stirred under a slightly positive pressure of hydrogen 18 hr. The yellow solution was filtered, adjusted to pH 4 with sodium bicarbonate, and cooled (ice bath). Oxygen was slowly bubbled through the solution during 10 min while green triangular crystals separated. The solid was collected to afford 0.31 g (69%) of amine XIV hydrochloride decomposing at 290–293°. The iminoquinone appeared blue in neutral to acid aqueous solutions and green in aqueous base. Owing to the pronounced insolubility of carbostyril XIV in all solvents investigated, the product could not be effectively recrystallized.

Anal. Calcd for $C_9H_8ClN_3O_2$: C, 47.91; H, 3.57; Cl, 15.71; N, 18.67. Found: C, 47.63; H, 4.16; Cl, 15.61; N, 18.53.

5,7-Acetamido-8-hydroxycarbostyril (VIIIb).—A stirred mixture composed of 5,7-dinitro-8-hydroxycarbostyril (XII, 0.5 g), tetrahydrofuran (100 ml), acetic anhydride (3 ml), and 10% palladium on carbon (0.035 g) was hydrogenated (slightly positive pressure) at room temperature during 24 hr. The grey solid which had slowly separated was collected and partially dissolved in hot methanol (200 ml)–water (50 ml). The solution was filtered and cooled and the colorless solid which separated was collected to yield 0.28 g (51%). Three recrystallizations from methanol–water gave nearly colorless needles: dec pt 324–327°; ν_{max} 3390, 3270, 1670 (broad), 1611, 1557, 1530, 1468, 1379, 1360, 1276, 838, and 730 cm^{-1}; pmr, δ 2.05 (six methyl protons), 7.00 (doublet, one proton, J = 9 cps), 7.20 (one proton at C-6), and 8.30 (doublet, one proton, J = 9 cps).

Anal. Calcd for $C_{13}H_{13}N_3O_4$: C, 56.73; H, 4.76; N, 15.27. Found: C, 56.34; H, 4.97; N, 15.44.

7-Hydroxy-5,8-dioxocarbostyril (XV).—Among a number of procedures explored, the following was found most effective. A suspension of iminocarbostyril XIV (0.5 g) in 6 N sulfuric acid (60 ml) was heated at reflux 20 min. The solution was cooled and transferred (using 60 ml of water) to a continuous extraction apparatus. While stirring the aqueous layer extraction with diethyl ether was allowed to proceed 4 hr. At this point the yellow needles (0.04 g, dec pt 280–300°) which had crystallized from the ether solution were collected. Four hours later another 0.06 g was isolated and after an additional 6 hr, a 0.10-g quantity to provide an over-all yield of 40%. Extending the extraction time led to dark solids. Attempts to further purify quinone XV by recrystallization from a variety of solvents led to less pure material which ranged in color from orange to red. Thus, the yellow needles which initially crystallized from the diethyl ether solution were eventually used for elemental analyses and such specimens displayed λ_{max} 252, 313, and 420 mμ (log ε 4.08, 4.13, and 2.66); ν_{max} 1673, 1635, 1601, 1424, 1382, 1344, 1313, 1201, 1036, 860, and 684 cm^{-1}; pmr, δ 6.00 (one proton at C-6), 6.80 (doublet, one proton, J = 9 cps), and 7.90 (doublet, one proton, J = 9 cps).

Anal. Calcd for $C_9H_5NO_4$(191): C, 56.55; H, 2.64; N, 7.33. Found: C, 56.33; H, 2.72; N, 7.32; mol wt (mass spec), 191.

Registry No.—III, 15450-69-8; IV, 15450-70-1; V, 15450-71-2; VIIIa, 15450-72-3; VIIIb, 15450-76-7; IX, 15450-73-4; XI, 15544-52-2; XII, 15450-74-5; XIIIb, 15450-75-6; XIV hydrochloride, 15444-53-3; XV, 15544-54-4.