$C_7H_7Cl_3$: C, 42.57; H, 3.57; Cl, 53.86. Found: C, 42.79; H, 3.40; Cl, 52.70; ash, 1.29. Found (corrected for ash): C, 43.27; H, 3.44; Cl, 53.29%.

Doping of Poly(1,6-heptadiyne). (a) Iodine. Samples were attached to four Pt wires with Electrodag conductive adhesive in the glovebox. The Pt wires were fused into a glass cap which fit the doping vessel. The closed assembled doping vessel containing other pieces of film was then removed from the glovebox and attached to an argon line and iodine vapor was admitted on the argon stream. Alternatively, a vacuum-sealed ampule containing degassed iodine and equipped with a break seal was placed in the doping vessel in the glovebox. The doping vessel was evacuated on the vacuum line and isolated. Then, the break seal was broken by means of a magnet to release the iodine. The low-temperature (-78 °C) doping experiment was carried out by using 8 mL of a saturated solution of iodine in toluene prepared at -78 °C to cover a 4 × 11 mm 60 μm thick film; the doping was carried out in a dry ice-acetone bath under argon.

(b) AsF_5. The sample was mounted in a doping vessel as described above. This vessel was attached to the vacuum line and to a flask containing AsF_5 at a pressure of 350 torr. The apparatus was then isolated from the vacuum line and the valve to the AsF_5 opened. At the completion of the experiment the doping vessel was evacuated again to remove excess AsF_5, prior to handling in the glovebox.

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Registry No. $Al(C_2H_5)_3$, 97-93-8; $Ti(O\text{-}n\text{-}C_4H_9)_4$, 5593-70-4; $Ti(O\text{-}i\text{-}C_3H_7)_4$, 546-68-9; $Ti(O\text{-}n\text{-}C_9H_{19})_4$, 6167-42-6; AsF_5, 7784-36-3; $Al(CH_3)_3$, 75-24-1; $Al(i\text{-}C_4H_9)_3$, 100-99-2; poly(1,6-heptadiyne), 30523-92-3.

Chemical Properties of Phenanthrolinequinones and the Mechanism of Amine Oxidation by *o*-Quinones of Medium Redox Potentials

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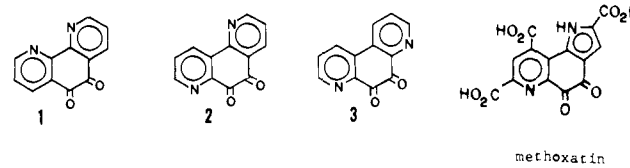
Abstract: The protonic acid-base properties, equilibria for hydroxide-mediated hydrations and ring contraction, and electrochemistry of the three isomeric phenanthroline-5,6-quinones [1,10 (**1**), 1,7 (**2**), and 4,7 (**3**)] are reported and discussed. Pyridine nitrogens peri to the *o*-quinone carbonyl groups increase the equilibrium constants for addition of H_2O and MeOH to the latter (**3** > **2** > **1**). The reductions of the phenanthroline-5,6-quinones by 1-phenylethanols, hydrazine, cyclohexylamine, glycine, morpholine, and *N*,*N*-dimethylbenzylamine have been examined. In general the order of the rate of substrate oxidation is **3** > **2** > **1**. Various mechanisms for amine oxidation by high-potential quinones (such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone) and low- or medium-potential quinones (such as **1**, **2**, and **3**) are discussed, and it is concluded that the mechanisms are different. Hydrazine and *N*,*N*-dimethylbenzylamine reduce the phenanthrolinequinones to the corresponding quinols. The oxidation of *N*,*N*-dimethylbenzylamine is catalyzed by the amine-free base and hydroxide ion. The oxidations of cyclohexylamine (to cyclohexanone) and glycine provide 5-amino-6-hydroxyphenanthrolines while the oxidation of morpholine provides the aminoquinol **5**. The nature of the quinone reduction products and the involvement of general base catalysis establish that the quinone plus amine redox reactions proceed via the covalent addition of amine to quinone followed by α-proton removal by general base catalysis.

The mechanisms by which quinones are reduced by organic substrates have been and remain of paramount importance. The possible mechanisms include consecutive one-electron transfers involving a radical pair intermediate two-electron transfer requiring the formation of a covalent intermediate of quinone and substrate, and hydride transfer. These various possibilities were considered and discussed by Hamilton in 1971.[1] High-potential quinones are of use as oxidants in organic synthesis, and attention has been given to the mechanisms of reduction of these reagents (see Discussion). Very little attention has been paid to the mechanisms of organic substrate oxidations by quinones of moderate redox potentials. Corey and Achiwa[2] realized that such quinones could be useful reagents in the oxidation of amines to ketones and studied the oxidation of cyclohexylamine by 3,5-*tert*-butylbenzo-1,2-quinone. This *o*-quinone was employed to obviate competing 1,4-additions of amine to the quinone oxidant. Jackman in 1960[3] proposed that phenanthrene-4,5-quinone should be investigated as an oxidant since it could not undergo 1,4-addition of nucleophilic substrates. To our knowledge this suggestion has never been followed.

In this study we have investigated the phenanthrolinequinones **1**, **2**, and **3**. They possess the advantage that Jackman appreciated



in the phenanthrene-*o*-quinone but possess more positive potentials than the latter (vide infra). In addition, quinones **1**, **2**, and **3** bear an obvious structural similarity to the natural product methoxatin, a bacterial coenzyme for the enzymatic oxidation of alcohols, glucose, aldehydes, and methylamine.[4] Among other findings, there is presented evidence that the oxidation of amines occurs via formation of carbinolamine and imine intermediates and that

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electron flow from an amine moiety to a derivatized quinone occurs by α-proton ionization—reminiscent of 3-hydroxypyridine-4-carboxaldehyde transamination reactions[5] and a mechanism favored but not firmly established by Corey and Achiwa[2] for *o*-quinone oxidation of cyclohexylamine.

Experimental Section

Ultraviolet and visible absorbance data were obtained on Cary Models 15, 16, and 118 spectrophotometers. Stopped-flow absorbances were measured with a Durrum Model D-131 spectrometer linked to a Biomation Model 805 waveform recorder. Values of pH were determined on a doubly standardized Radiometer 26 pH meter. Values of pH* for aqueous solutions containing 20–22% (by volume) MeCN were calculated by adding 0.11 to pH meter readings.[6] Infrared spectra were recorded on a Perkin-Elmer 137 spectrophotometer, and H^1 NMR spectra were obtained in $CDCl_3$ solutions on a Varian T60 spectrometer. Mass spectra (MS) were obtained in house on a VG Micromass ZAB-2F mass spectrometer at 70 eV. Galbraith Laboratories, Knoxville, TN, determined the elemental analyses. TLC was performed on silica gel sheets with fluorescence indicator (EM Reagents). For column chromatography silica gel 60, 0.063–0.200 mm (EM Reagents) was used. HPLC was performed on an Altex Model 100 with a Schoeffel Model SF770 monochromator detector. The quinones **1** and **2** are from a previous study, and **3** was obtained as a gift from Ciba Pharmaceutical Co.

Acid–Base Titrations. The acid-dissociation constant of diprotonated **1** was determined at 30 °C from UV spectra of 5×10^{-5} M **1** in 11 concentrations of aqueous H_2SO_4. The other acid–base dissociation constants for species **1**, **2**, and **3** were determined at 30 °C by spectrophotometric titration of the diones in a 25-mL titration cell with a 3.387-cm path length. Solutions from 1.8×10^{-5} to 2.9×10^{-5} M in dione were titrated with aqueous KOH (Baker Dilut-it). Ionic strength for the dissociation of the monoprotonated diones was 0.1, whereas KCl brought the ionic strength to 1.0 for the hydroxide association of the diones. The acid-dissociation constant of protonated $BzNMe_2$ was found by volumetric titration at 30 °C of an aqueous solution containing 0.100 M amine, 20% (by volume) MeCN, and 0.1 M HCl with an aqueous solution containing 0.817 M KOH (Baker Dilut-it) and 20% (by volume) MeCN.

Electrochemistry. Quinones in the concentration range 10^{-4} to 10^{-3} M were examined at 23–24 °C with a modified Princeton Applied Research Model 174 polarographic analyzer. A three-electrode cell with a platinum wire counter electrode was used throughout. Potentials of aqueous solutions were analyzed by cyclic voltammetry, scanning at 2 mV/s with a thin-layer platinum working electrode, designed and built by A. T. Hubbard. In Table II the potentials vs. NHE were obtained by adding 0.22 V to the experimental values referenced to aqueous Ag/AgCl/1 M NaCl. Buffer solutions were prepared from 0.5 M $HClO_4$, 0.5 M phosphate, 0.5 M acetate, and 0.5 M carbonate by addition of acid or base to the desired pH values of 0.30, 3.0, 5.6, and 9.5, respectively. In certain experiments excess Fe(III) was achieved by adding 5 mg of $FeSO_4 \cdot 6H_2O$ (subsequently oxidized) to 3 mL of solution. Experiments using the solvent MeCN from Burdick and Jackson Laboratories were performed in a dry glovebox. A 1-mm platinum sphere electrode, a Ag/0.1 M $AgNO_3$ (MeCN) reference electrode, and 0.1 M tetraethylammonium perchlorate electrolyte were combined for potential determinations in MeCN. Scans were made at a rate of 100 mV/s. By addition of 0.58 V to the experimental potentials, the values in Table III vs. NHE were obtained.[7] For both aqueous and MeCN solutions, the thin-layer electrode scanning at 2 or 4 mV/s was used in the determination of cyclic voltammetric curves, which were integrated to yield the number of electrons exchanged.

Acetone Adduct of 1,10-Phenanthroline-5,6-dione (1). From 20 mg (0.088 mmol) of **1** monohydrate a known method[8] was used to obtain 7 mg (30% yield) of white crystalline adduct: mp 192 °C dec; TLC (5% MeOH–95% CH_2Cl_2) R_f 0.1; UV (95% EtOH) λ_{max} 296 nm (ϵ 10 100 M^{-1} cm^{-1}), 228 nm (ϵ 22 900 M^{-1} cm^{-1}); IR (KBr) 3300 m (OH), 1710 s, 1690 s (C=O) cm^{-1}; MS, *m/e* 268 (M, 10%), 182 (100%). Anal. Calcd ($C_{15}H_{12}N_2O_3$): C, 67.16; H, 4.51; N, 10.44. Found: C, 67.03; H, 4.45; N, 10.36.

Acetone Adduct of 1,7-Phenanthroline-5,6-dione (2). From 20 mg (0.095 mmol) of **2**, a known method[8] was used to obtain 11 mg (43% yield) of pale greenish crystals: mp 163 °C dec; TLC (5% MeOH–95% CH_2Cl_2) R_f 0.5; UV (95% EtOH) λ_{max} 286 (ϵ 12 000 M^{-1} cm^{-1}), 229 nm (ϵ 27 200 M^{-1} cm^{-1}); IR (KBr) 3200 m (OH), 1710 s, 1690 s (C=O) cm^{-1}; MS, *m/e* 268 (M, 3%), 183 (100%). Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.10; H, 4.62; N, 10.36.

Acetone Adduct of 4,7-Phenanthroline-5,6-dione (3). By the same method[8] used to obtain acetone adducts of **1** and **2**, 50 mg (0.24 mmol) of **3** reacted to give 29 mg (45% yield) of pale, yellowish crystals: mp 188 °C dec; TLC (5% MeOH–95% CH_2Cl_2) R_f 0.2; UV (95% EtOH) λ_{max} 284 (ϵ 10 800 M^{-1} cm^{-1}), 230 nm (ϵ 25 000 M^{-1} cm^{-1}); IR (KBr) 3400 m (OH), 1710 s, 1700 s (C=O) cm^{-1}; MS, *m/e* 268 (M, 2%), 183 (100%). Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.22; H, 4.68; N, 10.34.

1,10-Phenanthroline-5,6-diol Hydrachloride. This compound was made by a published method[9] from hydrazine and 50 mg (0.22 mmol) of **1** monohydrate. Yellow-brown solid product was collected, washed with cold, aqueous 0.1 M HCl, and recrystallized from hot 0.1 M HCl under N_2 to give 34 mg (62% yield) of brown crystals: UV (0.05 M HCl) λ_{max} 294 nm (ϵ 32 000 M^{-1} cm^{-1}) [lit.[3] 295 nm (ϵ 35 300 M^{-1} cm^{-1})]; IR (KBr) 3000 m br (intramolecularly bonded OH), 1620 s cm^{-1}, no carbonyl peak. Anal. Calcd for $C_{12}H_8N_2O_2 \cdot HCl$: C, H, N. Found: C, H, N agree with calculated values within ±0.2%.

1,7-Phenanthroline-5,6-diol Hydrochloride. The above procedure for making 1,10-phenanthroline-5,6-diol hydrochloride was used to make the isomer from 30 mg (0.14 mmol) of **2**, but no heating was necessary to evolve gas. After 10 min at room temperature a yellow solid precipitated. After the mixture was cooled at 0 °C the precipitate was filtered, washed with cold 0.1 M HCl, and recrystallized from hot 0.1 M HCl under N_2 to give 14 mg (40% yield) of yellow crystals: UV (1 M HCl) λ_{max} 357 (ϵ 6000 M^{-1} cm^{-1}), 295 nm (ϵ 23 000 M^{-1} cm^{-1}); IR (KBr) 3100 m, br (intramolecularly bonded OH), 1615 s cm^{-1} no carbonyl peak; MS, *m/e* 212 (M – HCl, 57%), 182 (40%), 36 (100%); high-resolution MS, *m/e* 212.0602 (M – HCl, 100%); calcd for $C_{12}H_8N_2O_2$ 212.0586.

4,7-Phenanthroline-5,6-diol Hydrochloride. The above procedure for making 1,10-phenanthroline-5,6-diol hydrochloride was used to make the isomer from 50 mg (0.24 mmol) of **3**, but no heating was necessary to produce gas evolution. After 3 min of heating at 50 °C and cooling at 0 °C, a dark red precipitate was filtered, washed with cold 0.1 M HCl, and recrystallized from hot 0.1 M HCl under N_2 to give 33 mg (56% yield) of dark red, needle crystals: mp 150 °C dec; UV (0.1 M HCl) λ_{max} 356 (ϵ 8600 M^{-1} cm^{-1}), 278 (ϵ 14 500 M^{-1} cm^{-1}), 258 nm (ϵ 18 500 M^{-1} cm^{-1}); IR (KBr) 3350 m (OH), 1590 m cm^{-1}, no carbonyl peak; MS, *m/e* 212 (M – HCl, 80%), 183 (100%); high-resolution MS, *m/e* 212.0597 (M – HCl, 100%); calcd for $C_{12}H_8N_2O_2$ 212.0586.

Reaction of 1-(4-Methylphenyl)ethanol with 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone, 1,10-Phenanthroline-5,6-dione (1), 1,7-Phenanthroline-5,6-dione (2), or 4,7-Phenanthroline-5,6-dione (3). Four anaerobic solutions of 27.2 mg (0.20 mmol) of 1-(4-methylphenyl)ethanol (synthesized from the ketone[10]) in 10 mL of MeCN were prepared; to these was added 45.4 mg (0.20 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, 45.6 mg (0.20 mmol) of **1** monohydrate, 42.0 mg (0.20 mmol) of **2**, or 42.0 mg (0.20 mmol) of **3**. Some **2** and some **3** failed to dissolve, but all four reaction mixtures were anaerobically sealed and incubated in the dark at 60 °C. After 7 days all reaction mixtures were clear except the one with **3**, which showed a little unreacted **3**. The MeCN was removed from all the reaction mixtures by rotary evaporation. After two successive additions and evaporations of CH_2Cl_2 to purge all MeCN, the residues were analyzed by NMR and the spectra compared with those of authentic starting alcohol and authentic 1-(4-methylphenyl)ethanone.

Reaction of 1-(4-Nitrophenyl)ethanol with 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone, 1,10-Phenanthroline-5,6-dione (1), 1,7-Phenanthroline-5,6-dione (2), or 4,7-Phenanthroline-5,6-dione (3). The same reagents, amounts, procedure, and workups were used as in the above reaction with 1-(4-methylphenyl)ethanol, except that 27.2 mg (0.20 mmol) of 1-(4-nitrophenyl)ethanol was substituted for its methyl analogue. Again the product residues were analyzed by NMR and the spectra compared with those of authentic starting alcohol and authentic *p*-nitroacetophenone.

Oxidation of Cyclohexylamine by 1. A purple anaerobic solution of 34 mg (0.15 mmol) of **1** monohydrate, 1.00 mL (8.67 mmol) of cyclohexylamine, 6.0 mL of 1 M HCl, and 53 mL of water was sealed and

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allowed to stand at 30 °C for 7 days. The yellow solution was filtered under nitrogen from a white precipitate. The filtrate was acidified to pH 1.3 with 1 M HCl and extracted with 3 × 25 mL of ether. The combined ether extracts were washed with water and treated with 2,4-dinitrophenylhydrazine to produce 35 mg (84% yield) of the crude 2,4-dinitrophenylhydrazone of cyclohexanone: TLC (CH_2Cl_2) R_f 0.7 (identical with authentic material). The crude hydrazone derivative was purified by column chromatography to yield 16 mg of material with an electronic spectrum, mass spectrum, and elemental analysis (C, H, N) in agreement with those of authentic material.

Oxidation of Cyclohexylamine by 2. The same reagents, amounts, procedure, workup, and derivatization were used as in the above reaction with **1** except that 32 mg (0.15 mmol) of **2** replaced **1**. After column chromatography, 28 mg (67% yield) of the pure 2,4-dinitrophenylhydrazone of cyclohexanone was obtained. TLC (CH_2Cl_2), mass spectra, and NMR agreed with those of authentic material.

Oxidation of Cyclohexylamine by 3. The same reagents, amounts, procedure, workup, and derivatization were used as in the above reaction with **1** except that 32 mg (0.15 mmol) of **3** replaced **1**. The pure 2,4-dinitrophenylhydrazone of cyclohexanone (23 mg) was obtained after column chromatography (55% yield). TLC (CH_2Cl_2) and NMR agreed with those of authentic material.

Reduction of 4,7-Phenanthroline-5,6-dione (3) by Cyclohexylamine. In a nitrogen box an anaerobic solution of 32 mg (0.15 mmol) of **3**, 471 mg (3.48 mmol) of cyclohexylamine hydrochloride (recrystallized from EtOH–ether), and 7 mL of water was brought to pH 10 with 1 M NaOH. Upon mixing of the solution a brown solid precipitated. After 2 days at room temperature the mixture with the brown precipitate was brought to pH 7 with 1 M HCl and filtered. The precipitate was washed with H_2O, dissolved in 1 M HCl, and aerobically lyophilized to a brown solid. This solid was recrystallized under N_2 from hot 0.1 M HCl. The resulting amorphous brown solid crystallized into yellow needles upon heating above 100 °C: mp 178 °C dec; UV (0.1 M HCl) λ_{max} 255, 275, 353 nm; IR (KBr) 3300 w, 1610 m, 1580 s cm^{-1}, no carbonyl peak.

Reduction of 4,7-Phenanthroline-5,6-dione (3) by Glycine. In a nitrogen box an anaerobic solution of 32 mg (0.15 mg) of **3**, 751 mg (10 mmol) of glycine (recrystallized from EtOH–water), and 12 mL of H_2O was brought to pH 9.5 with 1 M NaOH. After 3 days at room temperature a light-brown precipitate was collected, washed with H_2O, and dissolved in 1 M HCl. The solution was aerobically lyophilized and the resulting orange solid was recrystallized under N_2 from hot 0.1 M HCl to yield 5-amino-6-hydroxy-4,7-phenanthroline hydrochloride as orange crystalline needles: mp 215 °C dec; UV (0.1 M HCl) λ_{max} 255 nm (ϵ 21 000 M^{-1} cm^{-1}), 275 nm (ϵ 16 000 M^{-1} cm^{-1}), 353 nm (ϵ 9300 M^{-1} cm^{-1}); IR (KBr) 3400 w (OH), 3300 m (NH_2), 1620 s, 1590 cm^{-1}, no carbonyl peak; MS, *m/e* 211 (M − HCl, 100%), 182 (57%); high-resolution MS, *m/e* 211.077 (M − HCl, 100%); calcd for $C_{12}H_9N_3O$ 211.075.

Reduction of 4,7-Phenanthroline-5,6-dione (3) by Morpholine. In a nitrogen box an anaerobic solution of 32 mg (0.15 mmol) of **3**, 637 mg (5.15 mmol) of morpholine hydrochloride (recrystallized from EtOH–ether), and 7 mL of water was brought to pH 8.3 with 1 M NaOH. After 3 days at room temperature a dark red-brown precipitate was collected, washed with H_2O, and dissolved in 1 M HCl. The solution was aerobically lyophilized, and the resulting dark red-brown solid was recrystallized under N_2 from hot 0.1 M HCl to yield 5-hydroxy-6-(4-(3-hydroxymorpholinyl))-4,7-phenanthroline hydrochloride as dark red-brown crystalline needles: mp 211 °C dec; UV (0.1 M HCl) λ_{max} 258 (ϵ 19 000 M^{-1} cm^{-1}), 385 nm (ϵ 3900 M^{-1} cm^{-1}); IR (KBr) 1660 s, 1570 s cm^{-1}; MS, *m/e* 297 (M − HCl, 100%), 239 (95%), 211 (45%), 183 (14%); high-resolution MS, *m/e* 297.111 (M − HCl, 100%); calcd for $C_{16}H_{15}N_3O_3$ 297.112.

Reduction of 4,7-Phenanthroline-5,6-dione (3) by *N,N*-Dimethylbenzylamine. In a nitrogen box an anaerobic solution of 21 mg (0.1 mmol) of **3**, 0.200 mL (1.33 mmol) of $BzNMe_2$, 0.50 mL of 1 M HCl, and 5 mL of water was allowed to stand at room temperature. After 3 days a white precipitate was collected by filtration, washed with water, and dissolved in 5 mL of 1 M HCl. The solution was lyophilized aerobically and the resulting yellow solid was recrystallized under N_2 from hot 0.1 M HCl. The dark red crystals showed electronic (0.1 M HCl) and IR (KBr) spectra identical with those of authentic 4,7-phenanthroline-5,6-diol hydrochloride. For various kinetic runs (see below) the yield of the diol is estimated to be greater than 90% by comparison of the final absorbance at 370 nm with the known absorbance at 370 nm of authentic diol under the same kinetic conditions.

Formation of Benzaldehyde from *N,N*-Dimethylbenzylamine and 4,7-Phenanthroline-5,6-dione (3). An anaerobic aqueous solution 4.46 × 10^{-5} M in **3**, 0.24 M in benzaldehyde-free $BzNMe_2HCl$ (recrystallized from ether–EtOH), and 20% (by volume) in MeCN was maintained at 30 °C and pH* 8.98. After 3 days, the solution was brought to pH 1 with 1 M HCl and injected into the HPLC (0.46 × 25 cm Altex Ultrasphere Octyl reverse phase column; 2750 psi; 244 nm monitor; 1 mL min^{-1} flow rate; 50% (by volume) MeOH, 1% (by volume) 1 M HCl aqueous eluent). By comparison with standard solutions of benzaldehyde (retention time = 9.6 min), a yield of 27% (average of 2 runs) benzaldehyde was determined. The presence of benzaldehyde was confirmed by the formation of a 2,4-dinitrophenylhydrazone with TLC (70% CH_2Cl_2–cyclohexane) and IR (KBr) identical with those of the authentic derivative of benzaldehyde.

Formation of Formaldehyde from *N,N*-Dimethylbenzylamine and 4,7-Phenanthroline-5,6-dione (3). An anaerobic aqueous solution 4.8 × 10^{-5} in **3**, 0.218 M in $BzNMe_2HCl$ (recrystallized from ether–EtOH), and 20% (by volume) in MeCN was maintained at 30 °C and pH* 9.6. After 3 days the solution was brought to pH 2 with 1 M HCl and assayed spectrophotometrically for formaldehyde by using the Hantzsch reaction.[11] By comparison with a standard solution of formaldehyde, a yield of 39% (average of two runs) formaldehyde was determined.

Comproportionation Equilibrium Constant for the Formation of the Semiquinone of 4,7-Phenanthroline-5,6-dione (3). Five anaerobic combinations of **3** and its quinol in 20% (by volume) MeCN–80% H_2O at μ = 0.1 and 30 °C, buffered at pH* 9.74 with 7.5 × 10^{-2} M carbonate, were monitored at 485 nm for semiquinone. Initial concentrations of **3** varied from 3.62 × 10^{-5} to 3.62 × 10^{-4} M while concentrations of quinol varied from 7.00 × 10^{-5} to 2.50 × 10^{-5} M. After allowing for the absorbance at 485 nm by quinol, a nonlinear least-squares program (see below, eq 4) computed a comproportionation equilibrium constant of 8 × 10^{-3}.

Kinetics. Kinetic experiments were run anaerobically at 30.0 ± 0.2 °C with μ = 0.1, after determining by repetitive spectrophotometric scanning that intermediates could not be observed and that a reduced species formed. Experiments with **1** were performed in glassware rinsed with 0.01 M EDTA. Values of pH were determined immediately after each experiment.

A. Reductions of 1, 2, and 3 by Hydrazine at pH 1.0. Three aqueous solutions containing 3.33 × 10^{-3} M hydrazine monohydrochloride (recrystallized from EtOH–H_2O) and 0.10 M HCl were made either 4.59 × 10^{-5} M in **1**, 5.52 × 10^{-5} M in **2**, or 5.30 × 10^{-5} M in **3**. These solutions were monitored spectrophotometrically at 291 and 255 nm, respectively, for the time dependence of production of the respective quinols.

B. Reductions of 1, 2, and 3 by Hydrazine at pH* 7.3. Three aqueous solutions containing 3.33 × 10^{-3} M hydrazine monohydrochloride (recrystallized from EtOH–H_2O), 0.1 M phosphate, and 22% (by volume) MeCN were made either 4.53 × 10^{-5} M in **1**, 5.20 × 10^{-5} M in **2** or 6.95 × 10^{-5} M in **3**. These solutions were monitored spectrophotometrically at 280, 282, and 320 nm, respectively, for the production of the respective quinols. Values of pH* for the three solutions were found to be 7.31, 7.28, and 7.29, respectively.

C. Reduction of 1 by Cyclohexylamine. Aqueous solutions at pH 10 containing from 2.5 × 10^{-5} to 1.5 × 10^{-4} M **1** and from 3.6 × 10^{-2} to 1.3 × 10^{-1} M cyclohexylamine were monitored spectrophotometrically at 290 and 360 nm for production of reduced species.

D. Reductions of 1, 2, and 3 by Glycine. Three aqueous solutions containing 8.01 × 10^{-3} M glycine (recrystallized from EtOH–H_2O), 3.2 × 10^{-3} M KOH, and 9.18 × 10^{-2} M KCl were made either 3.66 × 10^{-5} M in **1**, 3.91 × 10^{-5} M in **2**, or 3.81 × 10^{-5} M in **3**. These solutions were monitored spectrophotometrically at 291, 370, and 370 nm, respectively, for production of the respective reduced species. Values of pH were found to be 9.45, 9.46, and 9.48, respectively.

E. Reductions of 1, 2, and 3 by Morpholine. Three aqueous solutions containing 0.119 M morpholine, 0.08 M HCl, and 0.02 M KCl were made either 7.90 × 10^{-5} M in **1**, 8.26 × 10^{-5} M in **2**, or 3.81 × 10^{-5} in **3**. These solutions were monitored spectrophotometrically at 255 and 281 nm, 265 and 360 nm, and 245 and 360 nm, respectively. Values of pH were found to be 8.17, 8.21, and 8.16, respectively.

F. Reduction of 1, 2, and 3 by *N,N*-Dimethylbenzylamine. Aqueous solutions containing 20% (by volume) MeCN, 1.33 × 10^{-1} M $BzNMe_2$, 5 × 10^{-2} M HCl, and either 1.90 × 10^{-4} M **1** or 6.57 × 10^{-5} M **2** were monitored spectrophotometrically with time at 365 and 377 nm, respectively, for the production of the respective quinols. Both pH* values were found to be 8.84. Formation of quinol (375 nm) from 3 was followed by using various aqueous solutions containing 20% (by volume) MeCN, from 2.67 × 10^{-2} to 2.40 × 10^{-1} M $BzNMe_2$, and from 3.33 × 10^{-5} to 5.38 × 10^{-5} M **3**. Values of pH* from 8.30 to 9.63 were obtained by adding varying amounts of 1 M HCl. Ionic strength, μ = 0.1 was achieved by adding varying amounts of metal-free[12] 2 M KCl.

(11) Nash, T. *Biochem. J.* **1953**, *55*, 416–421.
(12) Skibo, E.; Bruice, T. C. *J. Am. Chem. Soc.*, in press.

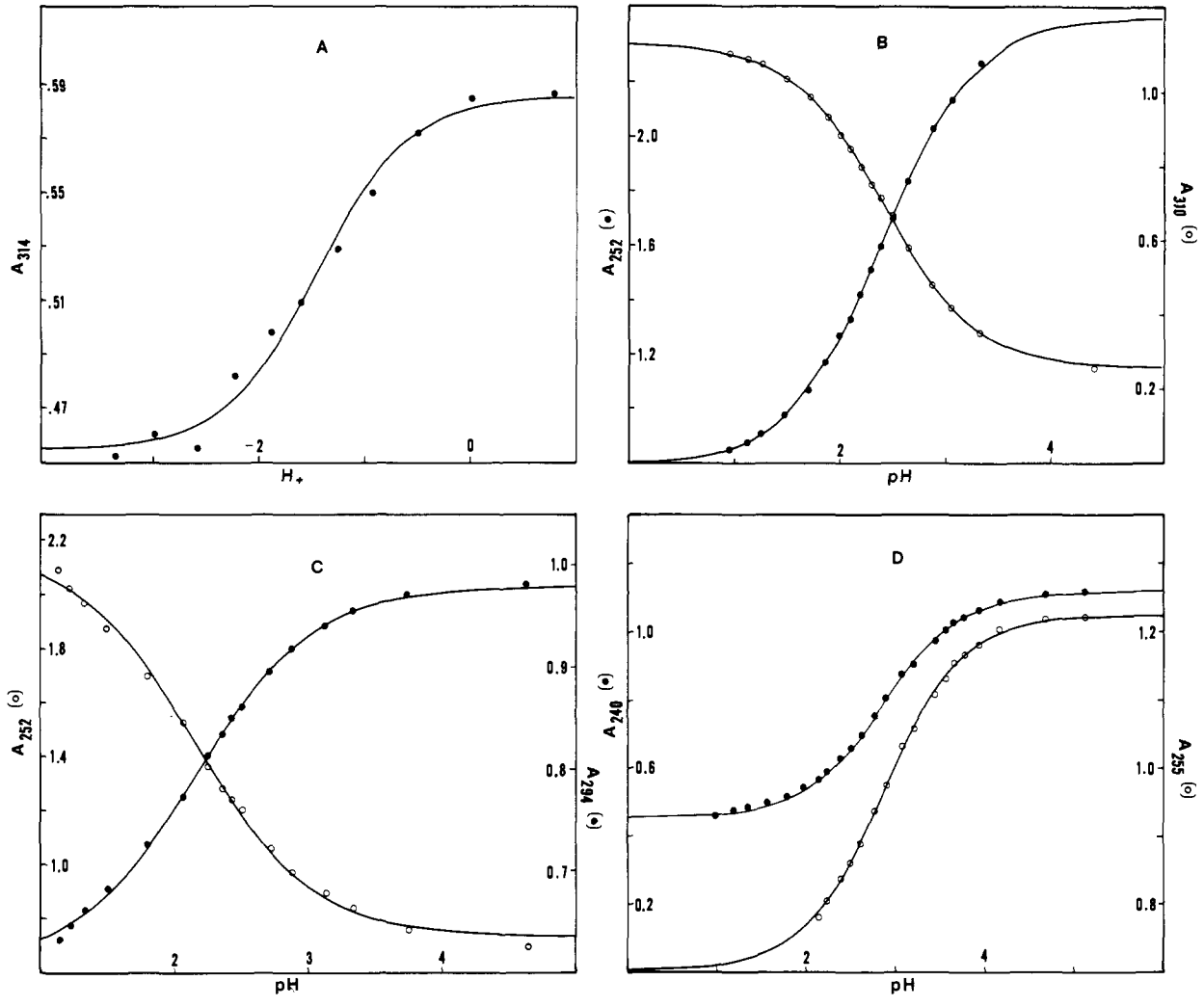
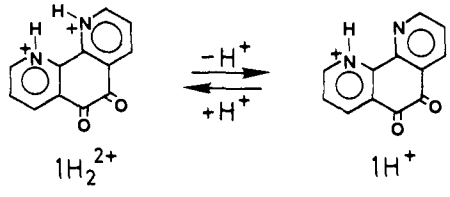


Figure 1. Spectrophotometric pK_a determinations (30 °C, N_2, μ = 0.1 with KCl) for (A) dissociation of $1H_2^{2+}$ determined at 314 nm with a 1-cm cell with total [1] at 5.0×10^{-5} M; (B) dissociation of $1H^+$ determined at 252 nm (●) and 310 nm (○) with a 3.387-cm cell with total [1] at 2.63×10^{-5} M; (C) dissociation of $2H^+$ determined at 294 (○) and 252 nm (●) with a 3.387-cm cell with total [2] at 2.74×10^{-5} M; (D) dissociation of $3H^+$ determined at 240 nm (●) and 255 nm (○) with a 3.387-cm path cell at total [3] of 2.11×10^{-5} M.

Results

Aqueous Acid–Base Chemistry. The acid-dissociation constant of diprotonated **1** ($1H_2^{2+}$) was determined spectrophotometrically by monitoring the change in absorbance at 314 nm with change in the acidity function, H_+,[13] appropriate for the protonation of a cation (eq 1). Change in H_+ from 0.79 to −3.36 was accom-

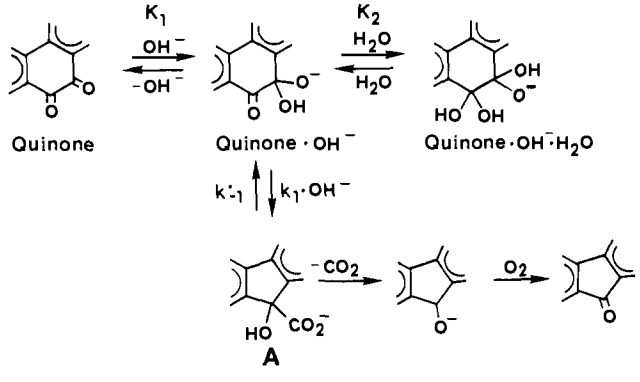


(1)

panied by an increase in A_{314} with isosbestic points at 292 and 340 nm. The increase in absorbance at 314 nm followed a least-squares titration curve with $pK_a = -1.45 \pm 0.08$ for dissociation of a single proton (Figure 1A). Spectrophotometric titrations in the pH range of acidity were used to determine the dissociation constants of the monoprotonated diones, $1H^+$, $2H^+$, and $3H^+$. In the instance of $1H^+$, increase in pH from 0.95 to 4.41 was accompanied by increasing absorbance at 252 nm and decreasing absorbance at 310 nm with an isosbestic point at 283 nm. These absorbance changes provided a best fit to a titration plot for a monobasic acid of $pK_a = 2.41$ (Figure 1B). Similarly while an isosbestic point remained at 277 nm on increase in pH from 1.14 to 4.65, increasing absorbance at 252 nm and decreasing absorbance at 294 nm allowed the calculation of a least-squares pK_a of 2.16 for $2H^+$ (Figure 1C). A pK_a of 2.86 was determined for $3H^+$ from the increasing absorbance at 240 and 255 nm in the pH range 0.98–5.12 (Figure 1D), while an isosbestic point stood at 285 nm.

Changes in the electronic absorbance of **1** with time at various pH values above pH 8 suggested that a quickly established

Scheme I



(13) Vetesnik, P.; Bielavsky, J.; Vecera, M. *Collect. Czech. Chem. Commun.* **1968**, *33*, 1687–1692. Corrections for 30 °C were made according to: Tickle, P.; Briggs, A. G.; Wilson, J. M. *J. Chem. Soc., B* **1970**, 65–70.

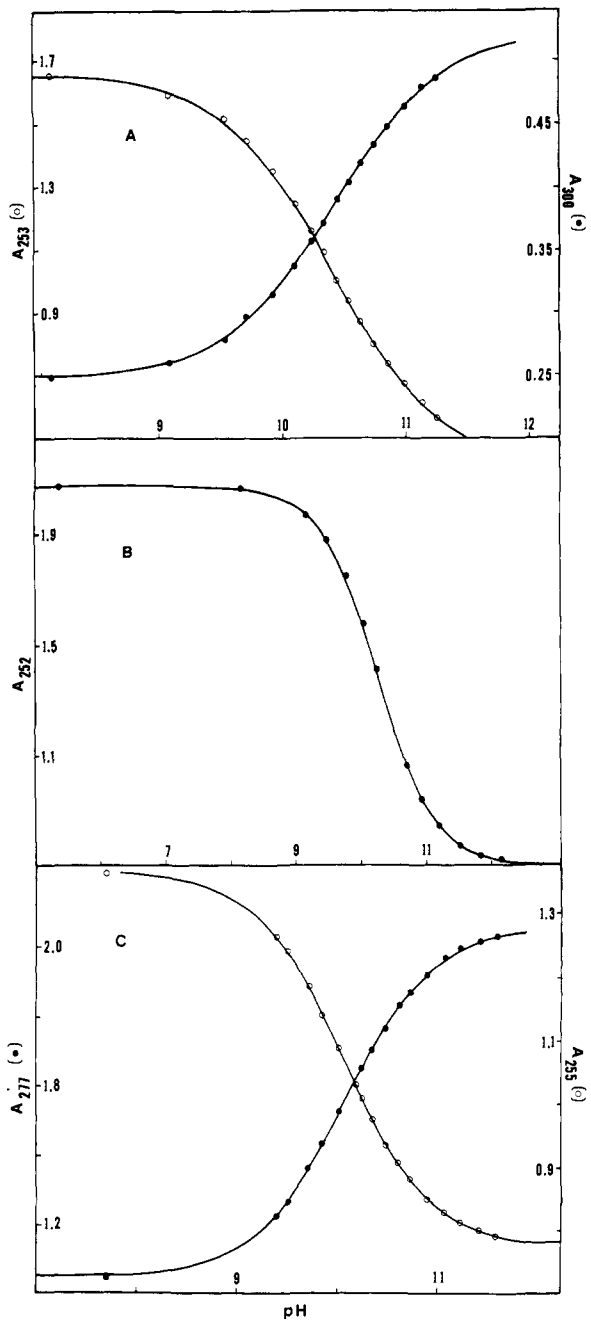


Figure 2. Spectral determination of the apparent pseudobase K_{app} (= $K_1(K_2 + 1)$) at 30 °C (H_2O, μ = 1.0) with a 3.387-cm path cell for addition of HO^- and H_2O to phenanthroline *o*-quinones (as in Scheme I; see eq 2); (A) [**1**] = 1.76 × 10^{-5} M, observed at 353 nm (○) and 300 nm (●); (B) [**2**] at 2.90 × 10^{-5} M measured at 252 nm; (C) [**3**] at 2.42 × 10^{-5} M measured at 227 nm (●) and 255 (○).

Table I. Final Absorbances at 318 nm Accompanying Anaerobic Ring Contraction of $1OH^-$ [a]

pH	final A
10.91	0.314
11.12	0.386
11.35	0.446
11.62	0.476
12.01	0.629
12.33	0.676

[a] Initial [1] = 5.03 × 10^{-5} M, μ = 1.0.

equilibrium preceded a slowly established one. Similar to a scheme previously proposed[9] for the rearrangement of **1** in aqueous base at 100 °C, Scheme I corresponds well to the chemistry of **1** at 30 °C.[14] The equilibria associated with K_1 and K_2 were studied

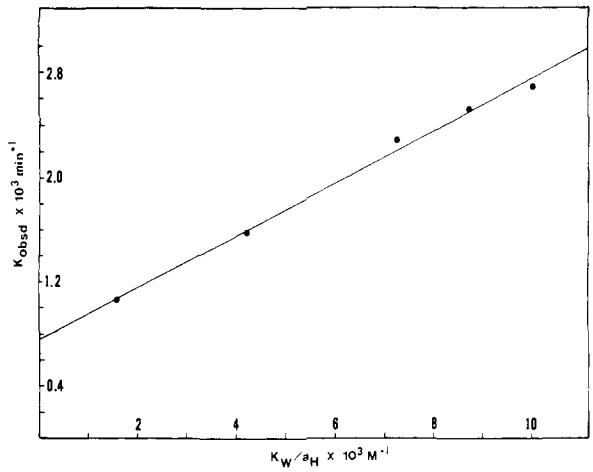


Figure 3. Plot of the pseudo-first-order rate constants (k_{obsd} min^{-1}) vs. K_w/a_H for attainment of equilibrium between $1OH^-$ and species A (Scheme I).

between pH 8.13 and 11.25. With increase in pH the absorbance decreased at 254 nm and increased at 300 nm with an isosbestic point at 277 nm. Plots of A_{254} and A_{300} vs. pH fit titration curves for the dissociation of a single proton (Figure 2A). According to eq 2 $K_1(K_2 + 1)$ can then be calculated as (2.57 ± 0.03) × 10^3 M^{-1}. Absorbance increases during the slow reaction of the monohydrate $1OH^-$ with hydroxide were monitored at 318 nm. The reaction followed the first-order rate law for about 3 half-lives at constant pH values between 11.00 and 12.87. The absorbance (318 nm) at the completion of reaction exhibited a marked increase with increase in pH (Table I). The kinetic attainment of equilibrium between $1OH^-$ and rearranged product A is a likely explanation. Thus, according to Scheme I, $k_{obsd} = (k_1K_w/a_H) + k_{-1}$. Least-squares analysis of a plot of k_{obsd} vs. K_w/a_H for five anaerobic runs (Figure 3) shows a slope of k_1 = 0.20 ± 0.01 min^{-1} M^{-1} and a Y intercept of k_{-1} = (7.6 ± 0.7) × 10^{-4} min^{-1}. The persistence of two isosbestic points at 299 and 327 nm during the monitoring of the slow reaction indicates no stable intermediate during this rearrangement. The identity of the product as the ring-contracted alcohol acid (A) is supported by the IR spectrum of the neutralized, lyophilized reaction mixture, which showed a strong, broad absorption at 1640 cm^{-1} and a broad, medium band at 3400 cm^{-1}, attributable to a carboxylate with α electron-withdrawing groups[16] and an intramolecularly hydrogen-bonded hydroxyl group,[17] respectively. Furthermore, attempts to isolate this product by neutral extraction into dichloromethane or by diazomethane esterification yielded a new compound with a TLC (EtOAc), IR spectrum, acidic and neutral UV spectra, and mass spectrum identical with those of the end product 4,5-diazafluoren-9-one (Scheme I).

$$\frac{a_H}{K_wK_1(1 + K_2) + a_H} = \frac{[\text{quinone}]}{[\text{quinone}] + [\text{quinone OH}^-] + [\text{quinone OH}^-\cdot H_2O]} = \Delta A \quad (2)$$

Compound **2** also demonstrated a quickly established equilibrium in aqueous base.[14] Titration from pH 5.36 to 12.16 was characterized by an isosbestic point at 276 nm and decreasing absorbances at 252 nm. A plot of A_{252} vs. pH provided a least-

(14) The shoulder bands at 1650 cm^{-1} in the IR spectra of **1** dissolved in D_2O at pD 12.4 and of **2** dissolved in D_2O at pD 12.1 suggest the substantial presence of carbonyl in both hydroxide adducts. The carbonyl band of 2-hydroxy-1-phenylethanone is found at 1635 cm^{-1} (spectrum 24179, ref 15).

(15) "Standard Infrared Grating Spectra", Sadtler Research Laboratories, Inc., Philadelphia, 1972.

(16) Compare the IR carboxylate absorption of sodium trichloroacetate at 1670 cm^{-1} with the carboxylate absorption of potassium acetate at 1575 cm^{-1} (spectra 23383 and 10116, respectively, ref 15).

(17) A broad IR band at 3430 cm^{-1} is found for sodium 2-hydroxypropionate (spectrum 7606, ref 15).

Table II. Redox Potentials of 1, 2, and 3 in Aqueous Solution

compd, pH	E_M, V[a]	no. of e⁻
1, 0.30	0.53	1.9
2, 0.30	0.59	1.9
3, 0.30	0.67	*b*
1, 3.01	0.38	2.0
2, 3.02	0.41	1.9
3, 2.98	0.46	2.1
1, 5.64	*c*	2.0
1, 5.64 (+excess Fe(III))	0.32	2.9
2, 5.62	0.24	2.1
3, 5.63	0.24	2.0
1, 9.51	0.01	2.1
2, 9.50	0.04	2.1
3, 9.50	0.04	2.0

[a] Midpoint potential vs. NHE. [b] The number of electrons increased with time. [c] No reoxidation; cathodic E_p = 0.23 V.

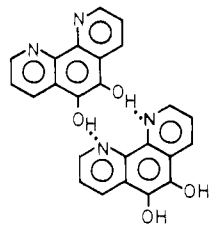
Table III. Redox Potentials of 1, 2, and 3 in MeCN

compd	E_M, V[a] (no. of e⁻)
1	−0.25 (1.1), −1.00 (0.82)
2	−0.25 (1.0), −0.97
3	−0.25 (1.2), −1.08

[a] Midpoint potential vs. NHE.

squares titration curve (eq 2) with $K_1(1 + K_2) = (3.55 \pm 0.07) \times 10^3$ M^{-1} (Figure 2B). For quinone **3** a similar combined equilibrium constant $K_1(1 + K_2)$ was determined to be $(5.50 \pm 0.06) \times 10^3$ M^{-1}, from the increase in absorbances at 227 nm and decrease at 255 nm during a titration from pH 7.70 to 11.61 (Figure 2C). Isosbestic points stood at 239 and 278 nm. The kinetics of the slow HO^--catalyzed ring contractions of **2**OH^- and **3**OH^- were not investigated.

Electrochemistry. For the most part, aqueous solutions of **1**, **2**, and **3**, like other quinones, were reduced and reoxidized in single, two-electron steps (Table II). At pH 0.30 or 3.0, quinone **3** showed the highest oxidation potential and **1** the lowest. At the less acidic pH values of 5.6 and 9.5 the three quinones exhibited approximately equal potentials. Two solutions gave unexpected results. At pH 5.64, **1** was reduced with two electrons but not reoxidized. In the presence of excess Fe(III), however, the reduction of **1** did proceed reversibly in a single three-electron step. This result has been explained in terms of intermolecular self-complexation of the quinol, which is reversed by its complexation with Fe(III).[8]



The other anomalous experiment occurred with **3** at pH 0.30. A miniscule reduction peak, measuring 0.01 e⁻, and a small, 0.80-e⁻ reoxidation peak were observed in the first cycle, but continuing cyclic voltammetry with the thin-layer electrode yielded increasing waves in both directions. By the fifth cycle the peaks were increasing more slowly, and 0.24 and 1.3 e⁻ were observed for the reduction and oxidation, respectively.

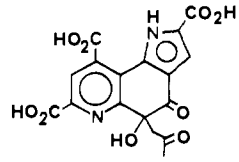
In the aprotic solvent MeCN **1**, **2**, and **3** behaved like other quinones in displaying two reduction and two oxidation waves (Table III). Quasi-reversible electrode kinetics resulted in differences of potentials for the corresponding cathodic and anodic peaks ranging from 70 to 130 mV. Although the slow scan speed of the thin-layer electrode did not allow an accurate determination of the numbers of electrons involved in the second reduction steps of **2** and **3**, the apparent one-electron nature of the first step suggests that the intermediate was the semiquinone, which was subsequently reduced to the quinol. The initial potentials for the one-electron reductions of the three quinones to semiquinones were found to be the same (E_m = −0.25), but the semiquinone of **3** was somewhat more difficult to reduce.

Table IV. Extinction Coefficients of 1, 2, and 3 and Adducts in Various Solvents

compd	solvent	λ_{max}, nm (ϵ, M^{-1} cm^{-1})
1	CH_2Cl_2	257 (31 200), 295[b] (2500)
1	*t*-BuOH	255 (32 400), 295[b] (4300)
1	MeOH	251 (21 400), 292[b] (6700)
1OH^-	H_2O	251[a] (6800), 295 (9000)
acetone adduct of 1	EtOH	251[a] (5730), 296 (10 100)
2	CH_2Cl_2	255 (32 000), 286[b] (2700), 230[a] (~11 000)
2	*t*-BuOH	252 (30 900), 285[b] (5900), 230[a] (12 600)
2	MeOH	252[b] (12 300), 283 (9300), 230 (32 000)
2OH^-	H_2O	252[a] (7100), 287 (9100), 230 (*c*)
acetone adduct of 2	EtOH	252[a] (6430), 286 (12 000), 229 (27 200)
3	CH_2Cl_2	253 (30 900), 285[b] (6100), 230[a] (10 400)
3	20% MeCN/ *t* BuOH	250 (28 700), 285[b] (10 500), 230[a] (*c*)
3	MeOH	253[a] (9300) 282[b] (9300), 230 (15 800)
3OH^-	H_2O	253[a] (9400) 282 (10 400), 227 (25 000)
acetone adduct of 3	EtOH	253[a] (8600), 282 (10 800), 229 (25 000)

[a] Wavelength does not correspond to a λ_{max}. [b] Wavelength corresponds to a shoulder peak. [c] Data not available.

Adducts. Acetone formed stable, crystalline, 1:1 adducts with all three quinones. It is assumed, based on the characterized acetone adduct **4** of the analogous quinone coenzyme, methoxatin,[18] that C-2 of acetone added to one of the carbonyl carbons to produce a hydroxy diketone.



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The UV spectrum of each of the three quinones changed very little with a change in solvent from CH_2Cl_2 to *t*-BuOH (Table IV). Each spectrum in these solvents contained a large peak absorbance ($\epsilon \sim 30\,000$) at 250–257 nm and a small shoulder band at ~290 nm. The solvent MeOH, however, altered the spectra of **2** and **3** radically into spectra approaching those of their hydroxide and acetone adducts. In contrast, MeOH modified the spectrum of **1** only slightly toward the spectra of its hydroxide and acetone adducts. The MeOH adducts of **2** and **3** were not sufficiently stable to survive evaporation of the MeOH solvent.

Oxidations. The dynamics of the reaction of the three quinones as oxidants with a number of reducing agents have been investigated. Two benzylic alcohols were tried as reductants. When equivalent amounts of 1-(4-methylphenyl)ethanol and quinone in MeCN were maintained under N_2 for 7 days at 60 °C, only the reaction mixture with **3** showed evidence of a redox reaction. This quinone yielded about 6% *p*-methylacetophenone product, according to integration of NMR peaks. Likewise under the same conditions, **3** oxidized 1-(4-nitrophenyl)ethanol to *p*-nitroacetophenone in 7% yield. In the instances of **1** and **2** the interpretations of the NMR were complicated by an adjacent hydroxyl proton resonance. No product, however, could be discerned to be formed in the latter experiments. In contrast, when 2,3-dichloro-5,6-

(18) Salisbury, S. A.; Forrest, H. S.; Cruse, W. B. T.; Kennard, O. *Nature (London)* **1979**, *280*, 843–844.

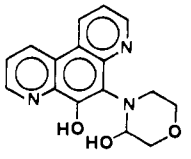
dicyano-1,4-benzoquinone (DDQ) was employed as quinone oxidant, under the same conditions as with **3**, there were formed a 90% yield of the methylated ketone and a 20% yield of the nitrated ketone.

The strongly reducing amine, hydrazine, readily reduced all three quinones to their respective quinols under anaerobic conditions. At 30 °C reactions in 0.10 M HCl of 3.33×10^{-3} M hydrazine and **1**, **2**, or **3** were associated with the pseudo-first-order rate constants (>4 half-lives) of $(6.80 \pm 0.05) \times 10^{-4}$, $(1.28 \pm 0.01) \times 10^{-2}$, and $(1.63 \pm 0.01) \times 10^{-2}$ min^{-1}, respectively. When 22% MeCN cosolvent was added and the pH* adjusted to 7.3, data over 5 half-lives indicated pseudo-first-order rate constants of 1.32 ± 0.01 and 25.2 ± 0.2 min^{-1} for **1** and **2**, respectively. The reaction of **3** with hydrazine was found to follow consecutive first-order kinetics ($k_1 = 90$ and $k_2 = 6$ min^{-1}), indicative of intermediate formation on or off the reaction path.

Less active amines also reduced the quinones. At pH 10 in aqueous solution (30 °C) cyclohexylamine reduced **1**, **2**, and **3**. After 7 days cyclohexanone could be isolated from the reaction solutions as the purified hydrazone derivative in >50% yield. Kinetic studies were carried out only with **1**. That neither simple nor consecutive first-order kinetics consistently fit the changes in absorbance at 290 and 360 nm for the reduction of **1** indicates the formation of covalent intermediate(s). From a reaction solution containing **3** and cyclohexylamine there was isolated a major phenanthroline product with an electronic spectrum in acid very much like that of authentic quinol. Unlike the quinol, which is oxidized to the quinone in neutral, aerobic, aqueous solution, the product does not decompose in neutral, aerobic aqueous solution as shown by the reappearance of the original spectrum upon reacidification. The IR spectrum of the recovered product differed from that of the quinol.

The reduction of **2** and **3** ($\sim 4 \times 10^{-5}$ M) (30 °C and pH 9.47) by glycine (8.01×10^{-3} M) followed pseudo-first-order kinetics to >6 half-lives with associated rate constants of 0.170 ± 0.002 and 0.287 ± 0.002 min^{-1}, respectively. The reaction of **1** (3.66×10^{-5} M) with glycine (8.01×10^{-3} M) at pH 9.45 followed consecutive first-order kinetics ($k_1 = 1.33 \times 10^{-2}$ and $k_2 = 2.89 \times 10^{-3}$ min^{-1}) indicative of intermediate formation. In the reaction with **3**, the major reduced product is 5-amino-6-hydroxy-4,7-phenanthroline. Although its electronic spectrum is very similar to that of the quinol, this product, unlike the quinol, could be neutralized and reacidified in the presence of O_2 to obtain its original spectrum in acid solution. The stability of the amino quinol at neutrality in water and in the presence of O_2 agrees with the higher oxidation potential for 2-aminophenol ($E_{1/2} = 0.48$ V vs. SCE at pH 7.4[19]) when compared to catechol ($E_{1/2} = 0.18$ V vs. SCE at pH 7.0[20]).

The kinetics for the reduction of **1**, **2**, and **3** by morpholine (0.119 M) were studied at pH 8.2 (30 °C). Monitoring for appearance of product from **1** at 281 nm, from **2** at 265 and 360 nm, and from **3** at 245 and 360 nm established a short lag phase, followed by the first-order appearance of products. The pseudo-first-order constants for product formation were determined to be $(6.83 \pm 0.07) \times 10^{-4}$ min^{-1} (2.7 half-lives) for **1**, $(2.27 \pm 0.07) \times 10^{-3}$ min^{-1} (5.0–6.0 half-lives) for **2**, and $(2.48 \pm 0.05) \times 10^{-3}$ min^{-1} (4.6 half-lives) for **3**. The final absorbance spectra of all these reaction mixtures, although resembling those of the respective quinols, only very slowly lost the product bands upon exposure to air. In particular, **3** yielded the amino quinol **5**, whose



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electronic spectrum at acid pH matched that of the acidified final reaction mixture. Upon neutralization of an acidic solution of **5** in the presence of O_2 and reacidification, the original acidic spectrum was obtained.

A fifth amine reductant for the quinones was the tertiary amine $BzNMe_2$. The limited solubility of $BzNMe_2$ and the reduced products, the competition of amine and HO^- for quinone (Scheme I), and buildup and disappearance of radical due to reaction of quinone with quinol product presented difficulties in the determination of reaction rates and kinetic law for the oxidation of $BzNME_2$ by the quinones. To improve solubilities 20% (by volume) MeCN was added. At pH* 8.8 and 30 °C with 0.133 M amine, **2** and **3** (less than 7×10^{-5} M) were reduced with pseudo-first-order constants of $(1.23 \pm 0.02) \times 10^{-3}$ (5.1 half-lives) and $(3.87 \pm 0.05) \times 10^{-3}$ min^{-1} (4.4 half-lives), respectively. Under the same conditions **1** only very slowly reacted in a non-first-order way to generate bands at 480 and 365 nm suggestive of the semiquinone and quinol, respectively. By the eighth day the band at 365 nm was still increasing by 20% per day. The predominant reduced product of the reaction with **1**, **2**, and **3** is the quinol. The quinol of **3** was isolated from the reaction mixture, the electronic spectra (anaerobic) of both the final reaction mixture and the authentic quinol show the same 370-nm bnd with a similar extinction coefficient (assuming 90–100% yield of reduced species in the reaction mixture). As with the quinol, air quickly extinguishes the 370-nm band of the product in neutral solution. Both benzaldehyde in 27% yield and formaldehyde in 39% yield were recovered from reaction mixtures.

Table V. Kinetic Data for the Reduction of **3** with *N,N*-Dimethylbenzylamine at 30 °C in 20% MeCN–H_2O (v/v)

$[BzNMe_2]$ free base,[a] M	pH*	no. of half-lives for calculation	$k_{obsd} \times 10^3$, min^{-1} exptl	$k_{obsd} \times 10^3$, min^{-1} calcd
0.0517	8.67	4.8	1.4	1.1
0.0545	8.71	5.1	1.2	1.2
0.0697	8.91	4.5	2.3	2.0
0.0758	8.99	5.0	2.5	2.4
0.0512	9.12	4.3	1.5	1.6
0.0853	9.12	5.9	2.8	3.1
0.120	9.12	6.5	4.8	5.0
0.152	9.11	6.7	6.9	7.1
0.0902	9.19	6.2	3.2	3.5
0.0672	9.59	6.1	3.7	3.9
0.179	9.59	6.0	13.2	13.8
0.142	9.61	5.9	10.6	10.2
0.102	9.63	6.0	7.6	6.9

[a] The concentration of free amine base was calculated by using a pK_a* of 8.87 for $BzNMe_2H^+$.

Table V shows the rate data for reaction of **3** ($3–5 \times 10^{-5}$ M) with $BzNMe_2$ at various concentrations and over a small range of acidities. At concentrations of free amine below 0.05 M the reaction did not follow the first-order rate equation due to buildup of semiquinone (vide infra). In Figure 4A there are plotted the pseudo-first-order rate constants (k_{obsd}) determined for reaction of **3** with $BzNMe_2$ vs. the calculated concentrations of amine free base at pH* 9.1, and in Figure 4B there is plotted $k_{obsd}/[BzNMe_2]$ vs. $[BzNMe_2]$. The curvature of the first plot and the linearity of the second are supportive of a third-order reaction involving general catalysis by $BzNMe_2$. Within the narrow pH range investigated, the kinetics for the reaction of $BzNMe_2$ with **3** follow the rate eq 3. The slope of the plot of Figure 4B equals k_{gb} and

$$k_{obsd} = (k_{gb}[BzNMe_2] + k_N + k_{HO}K_w/a_H)[BzNMe_2] \quad (3)$$

the intercept at $[BzNMe_2] = 0$ equals $(k_N + k_{HO}K_w/a_H)$. From a secondary plot of $(k_{obsd}/[BzNMe_2]) - k_{gb}[BzNMe_2]$ vs. $1/a_H$, k_N is obtained as the intercept at $1/a_H = 0$ and $k_{HO}K_w$ as the slope. The determined constants are $k_{gb} = 0.17$ M^{-2} min^{-1}, $k_N = 9 \times 10^{-3}$ M^{-1} min^{-1}, and $k_{HO}K_w = 1 \times 10^{-11}$ M^{-2} min^{-1}.

In Table V the experimental values of k_{obsd} are compared to those calculated by employing eq 3 and the derived constants. That semiquinone formation is responsible for the lack of pseu-

(19) Bezuglyi, V. D.; Beilis, Yu. I. *J. Anal. Chem. USSR (Engl. Transl.)* **1965**, *20*, 1060–1065.
(20) Pungor, E.; Szepesuary, E. *Anal. Chim. Acta* **1968**, *43*, 289–296.

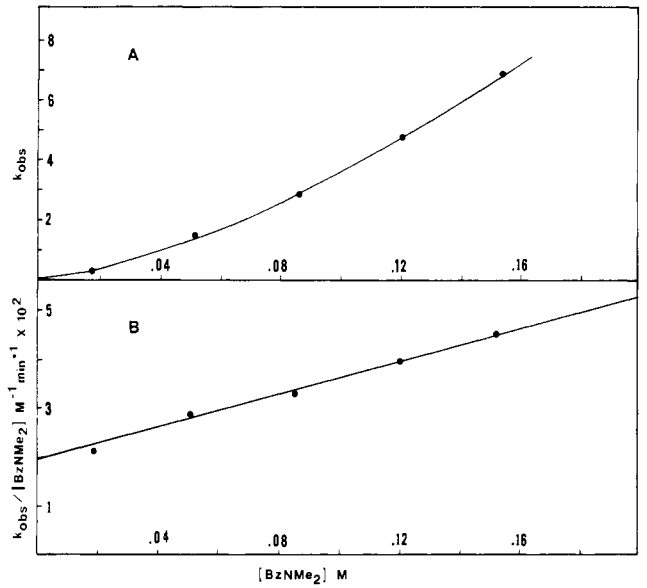
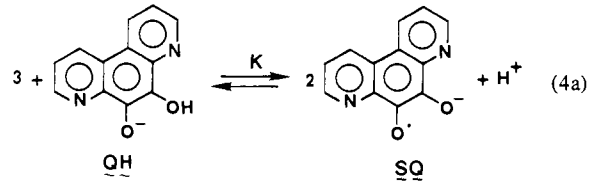


Figure 4. (A) Plot of the pseudo-first-order rate constants (k_{obsd} min^{-1}) vs. the concentration of amine free base [$BzNMe_2$] for the reaction of *N*,*N*-dimethylbenzylamine with quinone **3** at pH* 9.1 (H_2O at 30 °C). (B) Plot of $k_{obsd}/[BzNMe_2]$ vs. [$BzNMe_2$] for the reaction of *N*,*N*-dimethylbenzylamine with quinone **3**.

do-first-order kinetics when [$BzNMe_2$] < 0.05 M is shown by the following experiments. At low free-amine concentrations repetitive spectral scanning showed the buildup and slow disappearance of an absorbance with λ_{max} at 480 nm. The species absorbing at 480 nm was shown to be the semiquinone. Thus, a λ_{max} at 480 nm appeared when **3** and its quinol were mixed in 20% MeCN at pH* 9.74. In separate experiments, best fits of the absorbances at λ = 485 nm to eq 4 using various initial concentrations of quinone



(4a)

$$K = \frac{[SQ]^2}{([3]_i - 0.5[SQ])([QH]_i - 0.5[SQ])}$$

$$OD_{485} = ([QH]_i - 0.5[SQ])\epsilon_{OH} + [SQ]\epsilon_{SO} \quad (4b)$$

and quinol yielded a comproportionation equilibrium constant of 8×10^{-3} (pH 9.74, where ϵ_{QH} = 710 and ϵ_{SQ} = 18 000).

Generally, the slower the oxidation of $BzNMe_2$, the more obvious was the appearance of semiquinone and the poorer the fit of the kinetics to the first-order rate law. It can be shown by computer simulation that when oxidation of amine is slow, as it is with oxidant **1** or at low free-amine concentrations with oxidant **3**, comproportionation of QH and quinone competes with the reaction of quinone with $BzNMe_2$.

Discussion

The redox potentials of **1**, **2**, and **3** are lower than the redox potential of 1,4-benzoquinone (E_0 = 0.711 V)[21] due to a smaller resonance gain upon reduction of their carbonyl groups to "K-region" aromatic diols. By interpolation, the phenanthroline-quinones show potentials about 0.12 V higher than does 9,10-phenanthrenequinone with $E_{1/2}$ = 0.00 V at pH 7.6.[22] Also in MeCN the midpoint potential of −0.25 V for the first electron reduction of the phenanthrolinequinones is greater that the $E_{1/2}$ value of −0.42 for the comparable reduction of 9,10-phenanthrenequinone.[23] Clearly the electron-withdrawing pyridine rings destabilize the *o*-quinone function.

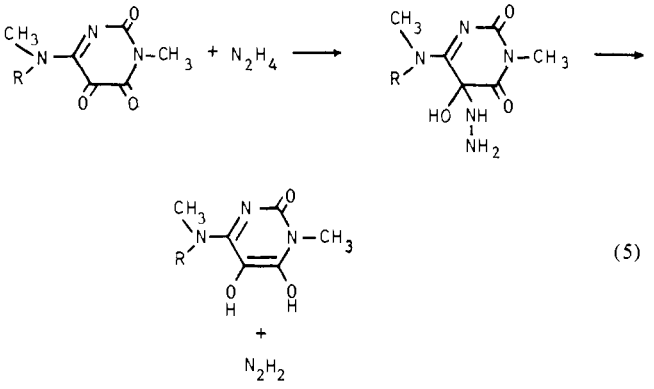
The acid-dissociation constants of the three monoprotonated quinones demonstrate different structural effects. The pK_a of 2.41 for $\mathbf{1H^+}$ is smaller than the value of 4.98 for monoprotonated 1,10-phenanthroline.[24] The lower pK_a for $\mathbf{1H^+}$ is due to electron withdrawal by the quinone carbonyls and the consequent diminished electron density in the pyridine rings. The smaller pK_a of 2.16 for $\mathbf{2H^+}$ probably results from the inability of this quinone's two pyridine nitrogens to act in concert in binding the proton. Most surprising is the relatively high pK_a of 2.86 for $\mathbf{3H^+}$. The stronger basicity of its nitrogens suggests a diminished inductive effect by the carbonyl groups. This, in turn, suggests that the *o*-quinone moiety of **3** is in equilibrium with its hydrate in aqueous acid. If so, the apparent acid-dissociation constant, K_{app}, is related to the actual acid-dissociation constant, K_a, and the constant for the hydration of $\mathbf{3H^+}$, K_h, by the equation $K_{app} = K_a/(1 + K_h)$. If the 1-nitrogen of **2** is more basic than its 7-nitrogen,[25] then pK_a for $\mathbf{3H^+}$ should be less than the pK_a = 2.16 for $\mathbf{2H^+}$. With a pK_{app} = 2.86 for $\mathbf{3H^+}$, K_h should be greater than 4. Support for this conjecture arises from the anomalous cyclic voltammetry of **3** in aqueous solution at pH 0.30. The observation of a tiny reduction peak likely results from acid-catalyzed hydration of a quinone carbonyl. The larger reoxidation peak and the gradual growth of both oxidation and reduction peaks with continued anodic and cathodic cycles testify to the reversibility of this hydration and to the majority of time spent at cathodic potentials during the voltammetry. The two peri pyridine nitrogens of **3** account for its greater hydration. Analogous to the trimethyl ester of methoxatin[8] is the apparent addition of MeOH to **2** and **3** in methanolic solutions, deduced from UV spectral changes in three solvents. The fact that **1** forms the adduct only to a small extent, if at all, suggests that the presence of a pyridine nitrogen peri to a quinone carbonyl group in **2**, **3**, and the trimethyl ester of methoxatin aids adduct formation. The $K_1(K_2 + 1)$ values of eq 2 for the combined hydroxide addition–hydration equilibria of Scheme I also indicate the propensity of the quinone carbonyls to undergo addition reactions. In the tendency for stepwise addition of both hydroxide and water, the value for **3** shows only a modest increase over those for **2** and **1**. The values of $K_1(K_2 + 1)$ are 5500, 3550, and 2570, respectively. The formation of stable acetone adducts from all three quinones confirms an analogy with methoxatin,[18] as well as with other *o*-quinones,[26] in this behavior.

Oxidations of the benzylic alcohols 1-(4-methylphenyl)ethanol and 1-(4-nitrophenyl)ethanol (in MeCN) to the respective ketones could only be shown with **3**. Whereas the oxidation of 1-(4-methylphenyl)ethanol by the very-high-potential DDQ occurs in 90% yield, the 1-(4-nitrophenyl)ethanol is oxidized in 20% yield under the same conditions. However, **3** oxidizes both benzylic alcohols about equally well. These observations possibly suggest that the mechanism for oxidation of alcohols by **3** and high-potential quinones differ (vide infra).

From the studies presented herein one can derive some meaningful comparisons of the mechanisms of oxidation of amines by *o*-quinones such as **1**, **2**, and **3** and by high-potential quinones such as DDQ. This comparison may well extend to the cofactor methoxatin. It has been proposed that the ease of amine oxidations by quinones correlates with the redox potentials of the quinones as well as with the propensities of the quinones to form charge-transfer complexes with the amine. For the oxidation of various tertiary amines by *p*-quinones, the formation of a charge-transfer complex seems to precede the oxidation step, both steps depending on a high potential for the quinone.[27]

(21) Braude, E. A.; Jackman, L. M.; Linstead, R. P. *J. Chem. Soc.* **1954**, 3548–3563.
(22) Berg, H.; Kramarczyk, K. *Ber. Bunsenges. Phys. Chem.* **1964**, *68*, 296–301.
(23) Peover, M. E. *J. Chem. Soc.* **1962**, 4540–4549.
(24) Irving, H.; Mellor, D. H. *J. Chem. Soc., Dalton Trans.* **1974**, 1217–1236.
(25) The values of pK_a (25 °C) for 2-acetylpyridine and 3-acetylpyridine are 2.64 and 3.26, respectively (Cabani, S.; Conti, G. *Gazz. Chim. Ital.* **1965**, *95*, 533–545).
(26) Magnusson, R. *Acta Chem. Scand.* **1960**, *14*, 1643–1653.

At pH 1 the first-order rate constants for the hydrazine (3.33 × 10^{-3} M) reductions of $1H^+$, $2H^+$, and $3H^+$ are in a ratio of 1:18.8:24.0, respectively, which accords with the difference in the potentials of the three quinones at pH 0.30. The unknown potential of **1** at pH 5.64 (Table II) and the non-first-order reduction of **3** do not allow a similar correlation between rate constants and potentials for the hydrazine reductions at pH* 7.3 of the unprotonated quinones. The quinone **3** reacts most rapidly with hydrazine. The formation of quinol from **3** follows sequential first-order kinetics establishing the formation of a discrete covalent compound of **3** and NH_2NH_2, which may or may not be on the reaction path from **3** to quinol. In a recent study[28] it was found that the NH_2NH_2 reduction of 6-[[2-(dimethylamino)-4,5-dimethylphenyl]methylamino]-3-methyl-5-oxouracil involves the formation of a covalent intermediate. This covalent intermediate was shown not to be the hydrazone, and the mechanism of eq 5



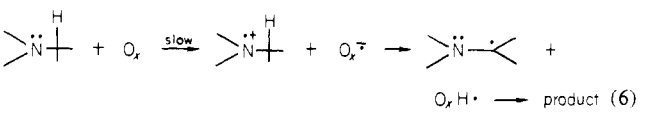
(5)

R = 2-dimethylamino-4,5-dimethylphenyl

was suggested.

The rates of reductions of the quinones by glycine, morpholine, and $BzNMe_2$ at higher pH levels provoke more interest. A 1:13:22 ratio of pseudo-first-order rates holds for the reductions of **1**, **2**, and **3**, respectively, at pH 9.5 by glycine at 8.01 × 10^{-3} M. At pH 8.2 the ratio of pseudo-first-order rates for reductions of **1**, **2**, and **3** by morpholine at 0.119 M is 1:3.3:3.6, respectively. Finally, $BzNMe_2$ (0.133 M) at pH* 8.8 shows a first-order rate ratio of 1:3.14 for the reductions of **2** and **3**, respectively, while **1** is reduced in a non-first-order fashion much slower than is **2**. In all three cases the order in rate for amine oxidation is **3** > **2** > **1**. Any difference in the ability of the three quinones to form charge-transfer complexes with amines is not apparent. Furthermore, in the 8–10 pH range, within which the organic amines have been oxidized, very little potential difference can be determined among **1**, **2**, and **3** (Table II). The two related factors suggested as necessary for oxidation of amines by quinones, high redox potential and ability to form charge-transfer complexes, should be about equally satisfied by the three quinones. Yet significant rate differences arise.

Many examples exist for which it is believed that electron transfer from the amine to the oxidant forms the rate-determining step, followed by loss of a proton (eq 6).[29-32] In support of this



(6)

mechanism, for example, it has been shown that the rates for chlorine dioxide oxidations of amines increase with decreases in the peak oxidation potentials of the amines.[32] The mechanism of eq 6 does not suit the amine oxidations by **1**, **2**, and **3**, whose rates do not reflect the quinones' potentials. If oxidations of the three amines by **3** occurred by this mechanism, the apparent second-order rate constant under a given set of conditions (k_{obsd}/[free amine]) should reflect the expectations of the mechanism. Such values are presented in Table VI.

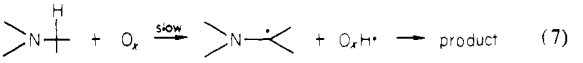
Table VI. Kinetic Data for the Oxidations of Amines by 3

amine	pH	$[N_f]$,[a] M	k_{obsd},[b] min^{-1}	$k_{obsd}/[N_f]$, min^{-1} M^{-1}
glycine	9.48	3.35×10^{-3}	2.87×10^{-1}	85.7
morpholine	8.16	4.81×10^{-2}	2.48×10^{-3}	5.16×10^{-2}
$BzNMe_2$	9.63 (pH*)	1.02×10^{-1}	7.56×10^{-3}	7.41×10^{-2}

[a] Free amine concentration calculated from pK_a values of 9.78, 8.33, and 8.87 (pK_a*) for glycine, morpholine, and *N*,*N*-dimethylbenzylamine, respectively. [b] Pseudo-first-order rate constant.

Glycine shows by far the greatest rate of oxidation by **3**. If the electron-transfer mechanism were operative, then this faster rate should be reflected in a lower oxidation potential for glycine. Primary amines, as a class, have peak oxidation potentials in MeCN from 1.2 to 2.0 V vs. Ag/0.1 M Ag^+,[33] while secondary amines exhibit potentials in MeCN in the range 0.82 to 1.08 V vs. Ag/0.1 M Ag^+.[34] The oxidation potential for $BzNMe_2$ in MeCN is known to be 0.71 V vs. Ag/0.1 M Ag^+.[34] Therefore, if the mechanism of eq 6 pertained, the primary amine glycine among the three amines examined would almost certainly show the slowest rate of reaction. It does not. Thus the potentials of the three amines, as well as the potentials of the quinones, suggest that one-electron transfer is not rate determining in the quinone oxidations under consideration herein.

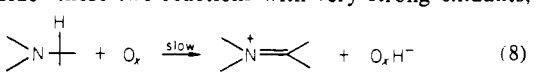
Hydrogen atom transfer from an α-carbon to the oxidant (eq 7) has also been considered in the oxidation of tertiary amines.



(7)

A good example is the oxidation of tertiary amine by photoexcited singlet *trans*-stilbene in hexane.[31] The hydrogen atom transfer mechanism avoids the formation of charged species, and for this reason one might expect it to be favored in nonpolar aprotic solvents such as hexane. In the reaction of singlet *trans*-stilbene with $BzNMe_2$ hydrogen abstraction only from the benzyl carbon, not from the methyl carbons, was observed. This result is consistent with a preference for the most stabilized α-amino radical.[35] From the present study, oxidation of $BzNMe_2$ by **3** in aqueous MeCN at pH* 9.6 leads to a 39% yield of formaldehyde and a 27% yield of benzaldehyde. According to eq 7, the formation of formaldehyde would result from the unlikely hydrogen atom abstraction from a methyl carbon. Thus, hydrogen abstraction is inconsistent with these product analyses. Similarly, this product ratio would not be anticipated for a reaction in which one-electron transfer is rate limiting (eq 6).

The aqueous permanganate oxidation of benzylamine[36] and the oxidation of *N*,*N*-dimethylaniline by arenediazonium ion[37] have been suggested to occur by the hydride-transfer mechanism of eq 8. Besides these two reactions with very strong oxidants,

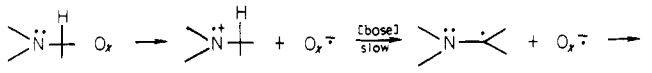


(8)

dehydrogenations of hydroaromatic compounds, allylic and benzylic alcohols, and carbonyl compounds by high-potential quinones are suspected to occur also by hydride transfer.[38] The catalysis

(27) Buckley, D.; Dunstan, S.; Henbest, H. B. *J. Chem. Soc.* **1957**, 4880–4900.
(28) Wessiak, A.; Bruice, T. C. *J. Am. Chem. Soc.*, submitted for publication.
(29) Audeh, C. A.; Lindsay Smith, J. Rl. *J. Chem. Soc. B* **1971**, 1741–1744.
(30) Linsay Smith, J. R.; Sadd, J. S. *J. Chem. Soc., Perkin Trans. 2* **1976**, 741–747.
(31) Lewis, F. D.; Ho. T.-I.; Simpson, J. T. *J. Am. Chem. Soc.* **1982**, *104*, 1924–1929.
(32) Hull, L. A.; Davis, G. T.; Rosenblatt, D. H.; Mann, C. K. *J. Phys. Chem.* **1969**, *73*, 2142–2146.
(33) Barnes, K. K.; Mann, C. K. *J. Org. Chem.* **1967**, *32*, 1474–1479.
(34) Mann, C. K.; Barnes, K. K. "Electrochemical Reactions in Nonaqueous Systems", Marcel Dekker: New York, 1970; p 279.
(35) Viehe, H. G.; Merenyi, R.; Stella, L.; Janousek, Z. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 917–932.
(36) Wei, M.; Stewart, R. *J. Am. Chem. Soc.* **1966**, *88*, 1974–1979.
(37) Suschitzky, H.; Sellers, C. F. *Tetrahedron Lett.* **1969**, 1105–1108.

of the oxidation of $BzNMe_2$ with **3** by the general bases HO^- and $BzNMe_2$ (eq 4) is inconsistent with a rate-determining hydride transfer (eq 8), which should not require general base catalysis. Another mechanism that should be considered is shown in eq 9.

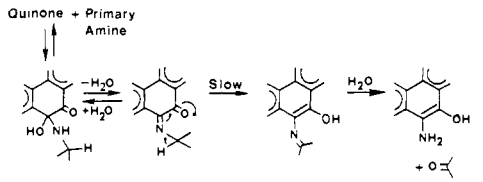


product (9)

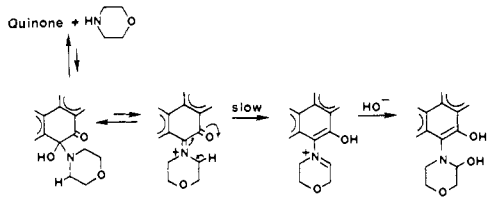
The mechanism of eq 9 is similar to that of eq 6 but with general base proton abstraction being rate determining.

Of most importance is the fact that the mechanisms considered to this point require that the sole form of reduced quinone produced with amine reductants is the quinol. In fact when $BzNMe_2$ is oxidized by **3**, the quinol is the predominant reduced species. On the other hand, cyclohexylamine, glycine, and morpholine do not generate quinol as the predominant reduced species. From the reaction with glycine, 5-amino-6-hydroxy-4,7-phenanthroline was isolated. Morpholine produced the amino quinol **5**. These results clearly suggest reaction mechanism that involve covalent intermediates.

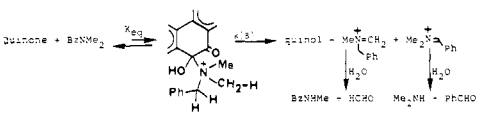
Equations 10–12 present mechanisms for the oxidation of the primary, secondary, and tertiary amines consistent not only with the product analyses but also with the kinetic results. Common



(10)



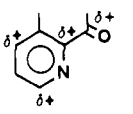
(11)



(12)

to all three mechanisms are the reversible, unfavorable addition of amine to a quinone carbonyl group and the rate-determining abstraction of a proton from a carbon α to the amine nitrogen. Thus the quinol product of the $BzNMe_2$ oxidation is seen to result from proton abstraction from the ammonium ion, whereas proton abstractions from a quinone imine, in the case of the primary amines, or from a quinone iminium ion, in the case of morpholine result in amino quinol species. The relatively fast rate of glycine oxidation can be explained by the acidity of the α-proton of the glycine moiety and the formation of a neutral quinone imine adduct. In contrast the initial equilibria involving morpholine or $BzNMe_2$ lead to less stable cationic adducts.

According to the mechanism of eq 10–12, the rate of amine oxidation should depend on those features that control the rate and/or equilibria of carbinolamine and imine formation (pK_a of amine, electrophilicity of carbonyl carbon, etc.). Structure **10** shows the orientation of electron-deficient pyridine carbons relative to the electron-deficient carbonyl carbon when the pyridine nitrogen is peri to the carbonyl. Structure **11** shows the comparable orientation in **1**. Because of adjacent electron-deficient carbons, structure **10** should be less stable than **11**. The same argument



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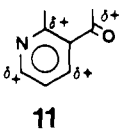

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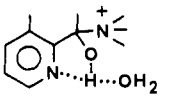
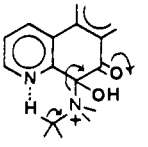


12

applies to the quinone imine adducts found in eq 10. Again a quinone imine with a peri pyridine nitrogen should be less stable than a quinone imine derived from **1**. Yet the imine carbon should be less electron deficient than a carbonyl carbon, and so the degree of destabilization should be less for the former.[39] Therefore the equilibrium of formation of imine (eq 10) should be less unfavorable with **2** or **3** than with **1**. For **2** and **3**, therefore, imine formation is favored when compared to **1** so that the 1.4 kcal mol^{-1} kinetic advantage for oxidation of glycine by **2** or **3** can be explained. The formation of the reduced covalent adduct with morpholine (eq 11), on the other hand, involves an intermediate quinone iminium ion adduct. The iminium carbon is more electron-deficient than the carbonyl or imine carbon, so that there may not be any equilibrium advantage for a peri pyridine nitrogen in quinone iminium formation. The less than 0.8 kcal mol^{-1} kinetic advantage for oxidation of morpholine by **2** or **3** is difficult to explain.

In the oxidation of $BzNMe_2$ (eq 12) the ease of formation of the intermediate carbinolamine should also be important. Structure **12** represents one conformation of the carbinol ammonium ion adduct when **2** or **3** is the oxidant. An intramolecular hydrogen bond between pyridine nitrogen and hydroxyl hydrogen has been reported for 2-pyridylmethanol.[40] A similar intramolecular hydrogen bond involving the peri pyridine nitrogen is envisioned in **12**. The actual importance of such an intramolecular hydrogen bond in 20% acetonitrile/80% water is difficult to assess. Perhaps this effect, when coupled with the destabilization of a quinone with a peri pyridine nitrogen and the possibility of the peri nitrogen acting as an intramolecular general base ctalyst for C–H bond rupture as in structure **13**, gives **2** and **3** the advantage over **1** in oxidizing $BzNMe_2$.



13

This study may present the first evidence for carbonyl covalent adducts as intermediates in amine oxidation. It is not suggested that all amine oxidations by quinones occur by adduct formation. For example, the oxidation of $BzNMe_2$ by the high-potential quinone chloranil in refluxing benzene may well proceed by the electron-transfer mechanism of eq 6. But lower potential 1,2-quinones, which will not readily undergo 1,4-nucleophilic addition, have the alternative pathways of intermediate carbinolamine and imine formation. Methoxatin forms a stable imine with urea where the imine function is peri to the pyridine nitrogen.[41] Methoxatin is proposed to oxidize amines by the same covalent mechanisms established herein for **3**. The potentials of **1**, **2**, and **3** and me-

(38) For a review see: Becker, H.-D. "The Chemistry of the Quinonoid Compounds"; Patai, S., Ed.; Wiley: New York, 1974; pp 335–423.

(39) The dipole moment of an imine double bond has been estimated to be 0.9 D, whereas the dipole moment of a carbonyl double bond has been determined to be 2.3 D (Smyth, C. P. *J. Am. Chem. Soc.* **1938**, *60*, 183–189).

(40) A similar intramolecular hydrogen bond has been found for 2-pyridylmethanol (Kuhn, L. P.; Wires, R. A.; Ruoff, W.; Kwart, H. *J. Am. Chem. Soc.* **1969**, *91*, 4790–4793).

(41) Dekker, R. H.; Duine, J. A.; Frank, J.; Verwiel, P. E. J.; Westerling, J. *Eur. J. Biochem.* **1982**, *125*, 69–73.

thoxatin do not differ significantly.

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Registry No. 1, 27318-90-7; **1** (acetone adduct), 85554-17-2; **1OH⁻**, 85554-21-8; **2**, 82701-91-5; **2** (acetone adduct), 85554-15-0; **2OH⁻**, 85554-16-1; **3**, 84-12-8; **3** (acetone adduct), 85554-18-3; **3OH⁻**, 85554-22-9; **5**, 85554-20-7; 5-amino-6-hydroxy-4,7-phenanthroline hydrochloride, 85554-19-4; 1,10-phenanthroline-5,6-diol hydrochloride, 85565-50-0; 1,7-phenanthroline-5,6-diol hydrochloride, 85565-51-1; 4,7-phenanthroline-5,6-diol hydrochloride, 85565-52-2; acetone, 67-64-1; 1-(4-methylphenyl)ethanol, 536-50-5; 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, 84-58-2; 1-(4-nitrophenyl)ethanol, 6531-13-1; cyclohexylamine, 108-91-8; glycine, 56-40-6; morpholine, 110-91-8; *N,N*-dimethylbenzylamine, 103-83-3; hydrazine, 302-01-2.

Structure of Caesalpinine A: A Novel Spermidine Alkaloid from *Caesalpinia digyna* Rottl.

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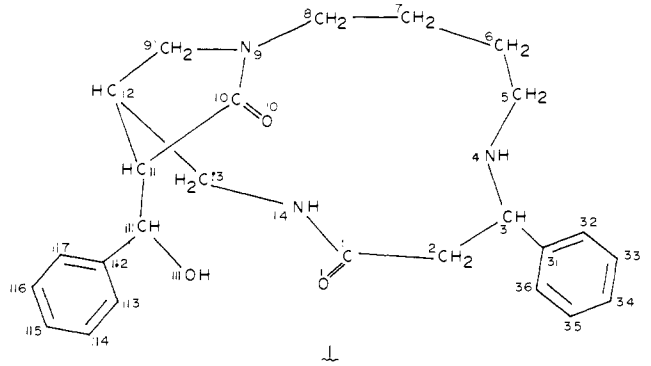
Abstract: The structure and stereochemistry of caesalpinine A (**1**), a novel macrocyclic spermidine alkaloid isolated from *Caesalpinia digyna* Rottl., have been determined by means of single-crystal X-ray analysis. The high-resolution mass and NMR spectra could satisfactorily be interpreted on the basis of the X-ray structure. The compound, $C_{25}H_{31}N_3O_3$, is orthorhombic, with space group $P2_12_12_1$ and unit-cell dimensions a = 24.017 (6) Å, b = 19.346 (2) Å, c = 9.578 (2) Å, V = 4450.3 Å^3, and Z = 8. The crystal structure was solved by direct methods and refined by least-squares methods including anisotropic (for non-hydrogen atoms) and isotropic (for hydrogen atoms) thermal parameters to a final R value of 4.5%. Caesalpinine A possesses a 13-membered lactam ring fused to a five-membered lactam ring. It also contains two monosubstituted benzene rings.

Caesalpinia digyna Rottl. (Leguminosae) is a prickly scandent shrub growing in eastern India, Burma, and Ceylon. It has the reputation for use in phthisis, scrofula, and diabetes.[2] Previous chemical investigations of the plant had disclosed the presence of bergenin[3,4] and gallic acid.[5] The present paper is concerned with the isolation and structure elucidation of caesalpinine A (**1**), a novel spermidine alkaloid having a new skeleton.

Results and Discussion

Caesalpinine A (**1**; mp 240-242 °C, $[\alpha]_D$ +16.6° ($CHCl_3$))



was isolated from the chloroform extract of the leaves of the plant by acid extraction followed by column chromatography and preparative TLC. High-resolution mass spectral and elemental analyses revealed the molecular formula $C_{25}H_{31}O_3N_3$ for **1**. Its UV spectrum showed absorptions at 222 nm (ϵ 17 762) and 258, 265, and 275 nm (ϵ 3921, 4383, and 4152 respectively). The IR spectrum showed strong bands at 3400, 3270 (OH and NH), 1650, 1550 (amide), 775, and 710 cm^{-1} (aromatic). The ^{1}H NMR spectrum contained signals for two monosubstituted benzene rings, methylene and methine groups, and a carbinyl proton. The presence of a secondary hydroxyl group and a secondary amine group was established by preparation of its diacetate (M^+ 505, accurate mass 505.2611, $C_{29}H_{35}N_3O_5$). Moreover, the hydroxyl group could be smoothly oxidized with Jones' reagent to a ketone as was evident from the CD curve. However, the mass spectrum

Table I. ^{13}C Chemical Shifts of **1** (Me_4Si = 0)[a]

δ	multiplicity	tentative assignment
22.3	t	C6[a]
28.6	t	C7[a]
31.6	d	C12
40.2	t	C2[b]
42.1	t	C5[b]
42.9	t	C8[b]
43.0	t	C13[b]
49.0	d	C11
51.0	t	C91
59.5	d	C3
71.3	d	C111
126.0	d	C32 + C36[c]
127.4	d	C34[d]
127.6	d	C113 + C117[c]
128.1	d	C115[d]
128.4	d	C114 + C116[e]
128.6	d	C33 + C35[e]
141.0	s	C31[f]
142.3	s	C112[f]
171.9	s	C1
176.2	s	C10

[a] Key: a-f may be reversed.

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