recrystallized at 0 °C from benzene/petroleum ether.[3] The physical and spectral data[5,8] for 1 and 2 showed the compounds to be pure (≥99%).

Deuteriated α-Azo Hydroperoxides 1-*d* and 2-*d*. One gram of α-azo hydroperoxide 1 or 2 was dissolved in 5.0 mL of dry acetonitrile, and 1.0 mL of deuterium oxide was added. The homogeneous solution was capped and allowed to sit at −10 °C overnight. Dry diethyl ether was added, and the aqueous phase separated. The organic layer was dried over anhydrous magnesium sulfate, and the solvents were removed under reduced pressure. The deuteriated compounds were recrystallized from the standard solvents, and *small quantities* were dried under vacuum at 0 °C. (Caution!) Preparation of 2-*d* was carried out in the dark since the compound is light sensitive. Total deuterium incorporation, assessed by ^{1}H NMR spectroscopy, was determined to be ≥90% for both compounds. (Note: Shaking of solutions of the α-azo hydroperoxides with D_2O at room temperature did not result in the rapid incorporation of significant amounts of deuterium.)

Kinetic Studies. The following general procedure was employed for all kinetic runs. For 1 and 1-*d*, a small sample of vacuum-dried, pure α-azo hydroperoxide (~0.03 mmol) was weighed in a new 5-mm NMR sample tube. Aliquots of 500 μL of chloroform-d_3 (Aldrich; obtained from a sealed ampule) and 5.0 μL of *cis*-3-hexene (peroxide stabilizer) were added. After the ^{1}H NMR spectrum was recorded, the desired quantity of substrate (alkene, amine, sulfide) was added, via syringe, to the solution at 34 °C and mixed. The ^{1}H NMR signals were recorded and integrated vs. time. The rate data, determined by monitoring the appearance of product and the disappearance of hydroperoxide relative to an internal standard (anisole), were identical. The former set of data was more convenient (accurate), since the product signals were well resolved. Product yields were calculated relative to internal standard (anisole). Product isolation and characterization were performed as previously reported.[3] The kinetic data, obtained for at least 2 half-lives, were analyzed by standard procedures and yielded excellent correlations (correlation coefficients (>0.99 in all cases). For the runs with pure acyclic α-azo hydroperoxides 2 and 2-*d* the above procedure was modified as follows: sample preparation was carried out in the dark; benzene-d_6 (Merck) was used as the solvent (since this type of hydroperoxide is unstable in $CDCl_3$); *tert*-butylbenzene was used as the internal standard; and no *cis*-3-hexene was added. Excellent agreement was obtained with previously published[3] kinetic data for 1 and 2 in all cases except for the results with *N*-methylmorpholine.[6b] The present data supercede the earlier values.

Acknowledgment is made to the National Science Foundation (Grant CHE-8506665) for support of this work.

Decarboxylated Methoxatin Analogues. Synthesis of 7- and 9-Decarboxymethoxatin

J. Barry Noar and Thomas C. Bruice*

Department of Chemistry, University of California, Santa Barbara, Santa Barbara, California 93116

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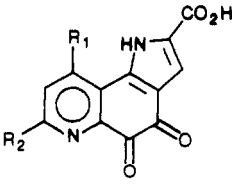
A total synthesis of two monodecarboxylated analogues of methoxatin (1) is described. The synthesis of 9-decarboxymethoxatin (4) was achieved starting with 8-hydroxyquinoline, constructing an appropriately substituted quinolylhydrazone of ethyl pyruvate with a Japp–Klingemann reaction and annulating the remaining pyrrole ring through a Fischer indole synthesis. The synthesis of 7-decarboxymethoxatin (3) first necessitated the construction of an appropriate indole from which the remaining pyridine ring could be annulated via a Doebner reaction.

Methoxatin[1-3] (1) is a novel *o*-quinone cofactor present in certain non-flavin- or nicotinamide-dependent bacterial dehydrogenases (quinoenzymes). Recently 1 was found to serve as a covalently bound coenzyme for bovine serum amine oxidase,[4] suggesting that methoxatin may be a cofactor for other mammalian enzymes, including those of humans, and that it may be a dietary requirement as a vitamin.

In order to evaluate the structural requirements of methoxatin as a reconstitutable cofactor and as an amine and alcohol oxidant,[5-8] we synthesized decarboxylated methoxatin analogues. The synthesis of 7,9-didecarboxymethoxatin (2) has been reported in a previous paper.[8] In this paper we report the total synthesis of 7-decarboxymethoxatin (3) and 9-decarboxymethoxatin (4).[9]



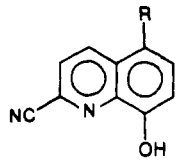
1: R_1 = COOH, R_2 = COOH
2: R_1 = H, R_2 = H
3: R_1 = COOH, R_2 = H
4: R_1 = H, R_2 = COOH

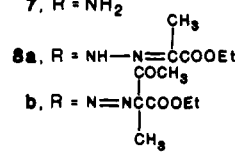
Our strategy for the synthesis of 4 was similar to the strategy employed in the synthesis of 2: i.e., the construction of an appropriately substituted quinolylhydrazone of ethyl pyruvate via a Japp–Klingemann reaction followed by a Fisher indole synthesis to create the third ring.

(1) Ohta, S.; Fujita, T.; Toabari, J. *J. Biochem.* **1981**, *90*, 105.
(2) Duine, J. A.; Frank, J. *Biochem. J.* **1980**, *187*, 213.
(3) Ameyama, M.; Matsushita, K.; Ohno, Y.; Shinagawa, E.; Adachi, O. *FEBS Lett.* **1981**, *130*, 179.
(4) Lobenstein-Verbeek, C. L.; Jongejan, J. A.; Frank, J.; Duine, J. A. *FEBS* **1984**, *170*, 305.
(5) Dekker, R. H.; Duine, J. A.; Frank, J.; Verwiel, P. E. J.; Westerling, J. *Eur. J. Biochem.* **1982**, *125*, 69.
(6) Eckert, T. S.; Bruice, T. C.; Gainor, J. A.; Weinreb, S. M. *Proc. Natl. Acad. Sci. U.S.A.* **1982**, *79*, 2533.
(7) Forrest, H. S.; Salisbury, S. A.; Kilty, C. G. *Biochem. Biophys. Res. Commun.* **1980**, *97*, 248.
(8) Sleath, P. R.; Noar, J. B.; Eberlein, G. A.; Bruice, T. C. *J. Am. Chem. Soc.* **1985**, *107*, 3328.
(9) A preliminary account of this synthesis has appeared: Noar, J. B.; Rodriguez, E. J.; Bruice, T. C. *J. Am. Chem. Soc.* **1985**, *107*, 7198.

0022-3263/87/1952-1942$01.50/0

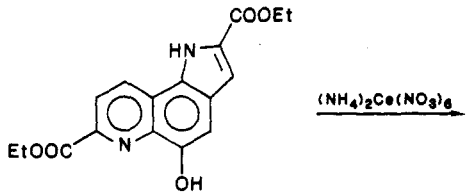
Our starting material for the synthesis was the cheap and readily available 8-hydroxyquinoline, which was converted to 2-cyano-8-hydroxyquinoline (5) in three steps by a literature route.[10] Nitration of 5 in concentrated nitric

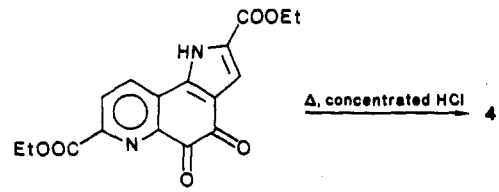




acid–acetic acid at 20 °C produced a mixture of the 5- and 7-nitro isomers from which the 5-nitro isomer 6 could be separated by recrystallization from acetone–ethanol (37%). Hydrogenation of 6 in methanol at room temperature (3 atm) over 10% Pd/C catalyst followed by addition of 1 N HCl afforded the amine hydrochloride 7 (93%). Treatment of 7 in aqueous HCl with sodium nitrite at 5 °C yielded the diazonium salt, which was added to a stirred ethanolic solution of ethyl α-methylacetoacetate and KOH at 0 °C. Ether extraction afforded the crude arylhydrazone 8a as an orange solid (18%). The intermediate acetylated azo compound 8b was also isolated (15%) from the reaction. Fischer indole cyclization and transformation of the nitrile function to an ester function (Pinner synthesis) to yield indole 9 was performed in one step by treatment of 8a with saturated ethanolic HCl (77%). 8b could also be converted to 9 in the same manner as 8a.

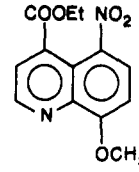
Oxidation to o-quinone 10 was accomplished by adding an aqueous solution of ceric ammonium nitrate to a suspension of 9 in acetonitrile to afford the bright orange

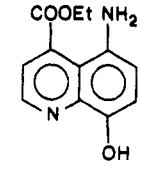




o-quinone 10 after recrystallization from acetonitrile (22%). Hydrolysis of the two carboethoxy groups was accomplished by stirring a solution of 10 in concentrated hydrochloric acid at 100 °C to produce a precipitate of 9-decarboxymethoxatin (4) (86%).

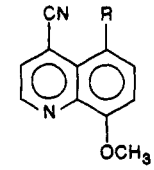
A similar synthetic strategy was attempted in the synthesis of 3. Application of the Doebner quinoline synthesis to o-anisidine[11] using pyruvic acid and formaldehyde yielded, after esterification and nitration, quinoline 11.

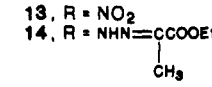




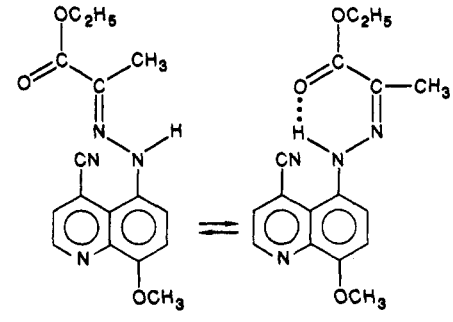
However, subsequent reduction of the nitro function did not yield a stable quinoline. A synthesis with the methoxy function replaced by the less electron-donating hydroxy function did afford the aminoquinoline 12, but the subsequent Japp–Klingemann reaction to give the quinolylhydrazone was unsuccessful due to the rapid decomposition of the intermediate diazonium salt.

We encountered more success using quinoline 13, which was again synthesized by a Doebner reaction on o-anisidine using pyruvic acid and formaldehyde followed by conversion to the acid chloride, amination, dehydration to the nitrile function, and nitration. The rationale for replacing





the carboethoxy function by a nitrile function was to lessen steric hindrance around the intermediate diazonium salt in the Japp–Klingemann reaction after reducing the nitro function and diazotizing the amino function in situ to help prevent oxidation. The greater electron-withdrawing power of the nitrile function may also assist in this respect. This strategy did indeed afford us the desired quinolylhydrazone 14. However, all attempts to perform a Fischer indole cyclization on 14 employing a variety of Lewis acid catalysts and conditions were unsuccessful. The only product isolated from the attempted cyclizations was the syn isomer 16 of the starting hydrazone, which had been isolated as the anti isomer 15 and became interconverted in the reaction solution.[12] The effect of intramolecular



hydrogen bonding in 16 could be observed by the pronounced downfield shift of the NH proton in the NMR from 8.50 to 12.59 ppm.

It became apparent that the synthetic strategy that afforded us 4 was not going to be successful in the con-

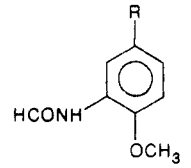
(10) Krasavin, I. A.; Dziomko, V. M.; Radin, Yu. P. *Metody Poluch. Khim. Reakt. Prep.* **1965**, *68*(13), 94.

(11) p-Anisidine has been converted via a Doebner reaction to 6-methoxyquinoline-4-carboxylic acid ethyl ester in low yield by: Pictet, A.; Misner, R. R. *Ber.* **1912**, *45*, 1800.

(12) The syn and anti isomers of 5-quinolylhydrazones have been separated and identified by: Gryaznov, A. P.; Akhvlediani, R. N.; Volodina, T. A.; Vasil'ev, A. M.; Babushkina, T. A.; Suvorov, N. N. *Chem. Heterocycl. Compd.* **1977**, *13*, 298.

struction of 3, since substitution in the 4-position on the quinoline ring was having a deleterious effect on the construction of a pyrrole ring from substituents in the 5-position. We decided to reverse the order of ring construction and first synthesize an appropriately substituted phenylhydrazone of ethyl pyruvate through a Japp–Klingemann reaction that would then undergo Fischer indole cyclization. Annulation of the pyridine ring would then be accomplished via a Doebner reaction.[13]

The starting material for this synthesis was the commercially available 2-methoxy-5-nitroaniline, which was converted in two steps to 5-amino-2-methoxyformanilide (17) by a literature route.[13] Diazotization of 17 followed

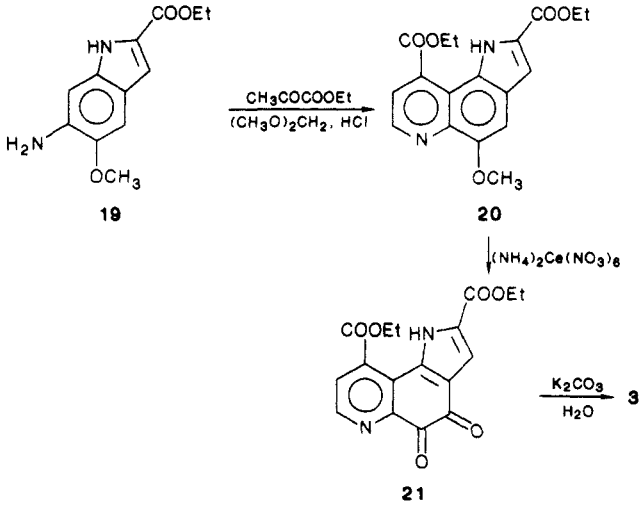


17, R = NH_2
18, R = NHN=CCOOEt
CH3

by a Japp–Klingemann reaction with ethyl α-methylacetoacetate yielded, after column chromatography, the orange arylhydrazone 18 (36%). Fischer indole cyclization with accompanying hydrolysis of the formyl function was effected by treatment of 18 with saturated ethanolic HCl to afford aminoindole 19 in 69% yield.

The key step in the synthesis was to annulate the pyridine ring onto 19 via a Doebner reaction. Although the yield of product was very low, this was accomplished by treating a mixture of ethyl pyruvate and dimethoxymethane with HCl gas until saturation. Addition of the resulting solution to 19 in ethanol followed by reflux afforded the quinoline 20 (5%).

Treatment of a solution of 20 in acetonitrile with an aqueous solution of ceric ammonium nitrate effected oxidation to the orange *o*-quinone 21 (95%). A facile hydrolysis of the two carboethoxy groups of 21 was effected by stirring in 0.1 M aqueous K_2CO_3 at 60 °C to afford 7-decarboxymethoxatin (3) (66%).



Experimental Section

General Methods. Melting points were obtained in open capillary tubes on a Mel-Temp apparatus and are uncorrected. Infrared spectra were recorded as Nujol mulls on a Perkin-Elmer 137 spectrophotometer. Ultraviolet and visible absorption spectra were recorded on a Cary Model 118C spectrophotometer. ^1H nuclear magnetic resonance spectra were recorded on a Varian T60 (60-MHz), a Varian CFT20 (90-MHz), or Nicolet NT-300 (300-MHz) spectrometer. Chemical shifts are reported in δ units downfield of tetramethylsilane. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet. Low-resolution and high-resolution mass spectra were obtained on a VG 70-250HF double-focusing magnetic sector mass spectrometer operating in either the electron impact mode, the positive chemical ion mode (methane), or the fast atom bombardment mode with glycerol as matrix. Elemental analyses were determined by Galbraith Laboratories, Inc., Knoxville, TN. Thin-layer chromatography was performed by using 0.2-mm silica gel 60 F_{254} plates (Merck) or reversed-phase KC 18 plates (Whatman). Column chromatography was carried out by using 230–400-mesh silica gel "flash" (Merck) as the stationary phase.

2-Cyano-8-hydroxy-5-nitroquinoline (6). To a stirred solution of 94 g (0.553 mol) of 2-cyano-8-hydroxyquinoline (5) in 2.5 L of glacial acetic acid was added dropwise 36 mL (0.56 mol) of concentrated HNO_3, keeping the temperature below 20 °C with ice cooling. A yellow precipitate formed that was collected by filtration and recrystallized from acetone/EtOH to afford 43.85 g (37%) of 6 as fine golden needles: mp >230 °C (sublimes); IR 2240, 3600 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 7.30 (1 H, d, H_7), 8.29 (1 H, d, H_4), 8.67 (1 H, d, H_6), 9.29 (1 H, d, H_3) 12.25 (1 H, br s, OH); mass spectrum (electron impact) *m/e* 215 (M^+).

5-Amino-2-cyano-8-hydroxyquinoline Hydrochloride (7). A suspension of 11.6 g (54 mmol) of nitroquinoline 6 in 200 mL of methanol containing 1.5 g of 10% Pd/C was shaken in a Parr apparatus at room temperature under 3 atm of H_2. After 6 h when uptake of hydrogen ceased, the mixture was treated with 100 mL of 1 N HCl and the catalyst was removed by filtration. The solution was concentrated in vacuo, and the solid residue was treated with ethanol and filtered to yield 11.1 g (93%) of the aminoquinoline hydrochloride 7 as a white solid: mp >250 °C dec; IR 2250, 3300 cm^{-1}; mass spectrum (positive chemical ionization), *m/e* 185 (M^+), 186 (M + 1).

Ethyl Pyruvate 2-Cyano-8-hydroxy-5-quinolylhydrazone (8a). To a stirred mixture of 11.08 g (50 mmol) of amine hydrochloride 7 in 500 mL of 0.1 N HCl (50 mmol) was added portionwise at 5 °C (ice/salt) 3.45 g (50 mmol) of sodium nitrite. The resulting diazonium salt solution was stirred a further 10 min at 5 °C before being added to a rapidly stirred solution of 8.65 g (60 mmol) of ethyl α-methylacetoacetate and 3.85 g (60 mmol) of KOH pellets in 250 mL of ethanol at 0 °C. The resulting mixture was stirred for 1 h at 0 °C and then stored at 4 °C for 18 h. The solvent was removed in vacuo, water added to the oily residue, and the product extracted with ether. The organic layer was washed with water, dried ($MgSO_4$), and concentrated in vacuo. Treatment of the residue with ether/hexane afforded an orange solid that was collected by filtration, yielding 2.7 g (18%) of hydrazone 8a, which was of sufficient purity to be used in the next step: mp 170–176 °C dec; IR 1700, 2250, 3250 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.24 (3 H, t, CH_3), 2.09 (3 H, s, CH_3), 4.20 (2 H, q, CH_2) 7.24 (1 H, d, H_7), 7.55 (1 H, d, H_6), 8.03 (1 H, d, H_4), 8.97 (1 H, d, H_3), 9.68 (1 H, s, OH), 10.04 (1 H, s, NH); mass spectrum (electron impact), *m/e* 298 (M^+).

5-[[1-(Ethoxycarbonyl)-1-(methylcarbonyl)ethyl]azo]-2-cyano-8-hydroxyquinoline (8b). Concentration in vacuo of the ethereal liquors from the above reaction followed by chromatography of the residue on 800 g of silica gel, eluting with ether, yielded 2.5 g (15%) of the azoquinoline 8b as a yellow solid: mp 96–100 °C; IR 1710, 1740, 2250, 3350 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 1.19 (3 H, t, CH_3), 1.66 (3 H, s, CH_3), 2.38 (3 H, s, CH_3), 4.25 (2 H, q, CH_2), 7.35 (1 H, d, H_7), 7.96 (1 H, d, H_6), 8.19 (1 H, d, H_4), 9.09 (1 H, d, H_3); mass spectrum (positive chemical ionization), *m/e* 341 (M + 1).

Diethyl 5-Hydroxy-1*H*-pyrrolo[2,3-*f*]quinoline-2,7-dicarboxylate (9). A solution of 2.0 g (6.71 mmol) of hydrazone 8a in 50 mL of a saturated solution of HCl in ethanol was stirred at room temperature for 3 days. Evaporation in vacuo and treatment of the residue with aqueous acetone afforded a yellow solid that on filtration produced 1.7 g (77%) of 9, which was of sufficient purity to be used in the next step: IR 1680, 1720, 3600

(13) A similar synthetic approach has been used in the synthesis of methoxatin by: Corey, E. J.; Tramontano, A. J. *J. Am. Chem. Soc.* **1981**, *103*, 5599.

cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 1.36 (3 H, t, CH_3), 1.40 (3 H, t, CH_3), 4.37 (2 H, q, CH_2), 4.46 (2 H, q, CH_2), 7.21 (1 H, s, H_4), 7.34 (1 H, s, H_3), 8.24 (1 H, d, H_9), 9.01 (1 H, s, OH exchangeable), 9.29 (1 H, d, H_8), 12.89 (1 H, s, NH exchangeable); mass spectrum (positive chemical ionization), m/e 328 (M^+), 329 (M + 1).

Diethyl 4,5-Dihydro-4,5-dioxo-1*H*-pyrrolo[2,3-*f*]quinoline-2,7-dicarboxylate (10). A solution of 15.38 g (28.05 mmol) of ceric ammonium nitrate in 15 mL of water was added to a suspension of 1.67 g (5.1 mmol) of **9** in 60 mL of acetonitrile at 0 °C. The resulting dark red solution was stirred for 15 min at 0 °C and concentrated in vacuo. The residue was treated with water and the mixture sonicated to yield an orange solid that was collected by filtration. Purification was accomplished by recrystallization from acetonitrile, yielding 0.386 g (22%) of the *o*-quinone diester **10** as bright orange flakes: mp 314–316 °C; TLC (silica) R_f 0.74 (CH_2Cl_2/EtOH, 9:1); IR 1650, 1715, 3100 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 1.34 (3 H, t, CH_3), 1.36 (3 H, t, CH_3), 4.33 (2 H, q, CH_2), 4.42 (2 H, q, CH_2), 7.19 (1 H, s, H_3), 8.27 (1 H, d, H_9), 8.85 (1 H, d, H_8), 13.42 (1 H, s, NH exchangeable); mass spectrum (fast atom bombardment), m/e 345; UV (CH_3CN) λ_{max} 329 nm, 318 (sh), 308 (sh), 275, 242, 220. Anal. Calcd for $C_{17}H_{14}N_2O_6$: C, 59.65; H, 4.09; N, 8.19. Found: C, 59.80; H, 4.15; N, 8.45.

4,5-Dihydro-4,5-dioxo-1*H*-pyrrolo[2,3-*f*]quinoline-2,7-dicarboxylic Acid (4). A solution of 171 mg (0.5 mmol) of *o*-quinone diester **10** in 3 mL of concentrated HCl was stirred at 100 °C for 20 h. The reaction mixture was cooled, and the orange-brown precipitate that formed was collected by filtration and dried under vacuum to yield 123 mg (86%) of diacid **4**: IR 1660, 1700 cm^{-1}; TLC (reversed phase) R_f 0.9 (H_2O/EtOH/NEt_3, 70:30:1); ^{1}H NMR (Me_2SO-d_6) δ 7.15 (1 H, s, H_3), 8.24 (1 H, d, H_9), 8.82 (1 H, d, H_8), 13.35 (1 H, s, NH exchangeable); UV (H_2O, pH 7) λ_{max} 315 nm, 275, 243. Anal. Calcd for $C_{13}H_6N_2O_6 \cdot {}^1/_2H_2O$: C, 52.88; H, 2.37; N, 9.49 Found: C, 52.95; H, 2.59; N, 9.31.

Spectral Data for the Anti Isomer of Ethyl Pyruvate 4-Cyano-8-methoxy-5-quinolylhydrazone (15): IR 1690, 2225, 3320 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (3 H, t, CH_3), 2.21 (3 H, s, CH_3), 4.19 (3 H, s, CH_3), 4.35 (2 H, q, CH_2), 7.54 (1 H, d, H_3), 7.94 (1 H, d, H_7), 8.19 (1 H, d, H_6), 8.50 (1 H, s, NH), 8.94 (1 H, d, H_2); mass spectrum (electron impact), m/e 312 (M^+).

Spectral Data for the Syn Isomer of Ethyl Pyruvate 4-Cyano-8-methoxy-5-quinolylhydrazone (16): IR 1685, 2200, 3200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.40 (3 H, t, CH_3), 2.25 (3 H, s, CH_3), 4.18 (3 H, s, CH_3), 4.35 (2 H, q, CH_2), 7.52 (1 H, d, H_3), 7.92 (1 H, d, H_7), 8.17 (1 H, d, H_6), 8.95 (1 H, d, H_2), 12.59 (1 H, s, NH); mass spectrum (electron impact), m/e 312 (M^+).

Ethyl Pyruvate 3-Formamido-4-methoxyphenylhydrazone (18). To a stirred solution of 16.6 g (0.1 mol) of 5-amino-2-methoxyformanilide (**17**) in 667 mL of 0.3 N HCl (0.2 mol) was added portionwise at 5 °C (ice/salt) 6.9 g (0.1 mol) of sodium nitrite. The resulting dark red diazonium salt solution was stirred a further 10 min at 5 °C before being added to a rapidly stirred solution of 17.3 g (0.12 mol) of ethyl α-methylacetoacetate and 7.77 g (0.12 mol) of KOH pellets in 650 mL of ethanol at 0 °C. The resulting mixture was stirred for 1 h at 0 °C and then stored at 4 °C for 15 h. The solvent was removed under reduced pressure before water was added and the crude oily product extracted with ethyl acetate. The organic layer was washed with water, dried ($MgSO_4$), and evaporated in vacuo. The resulting dark red oil was chromatographed on a column of silica gel (500 g), eluting with ether followed by ethyl acetate to afford 10.0 g (36%) of the hydrazone **18** as an orange solid: mp 136–142 °C; IR 1670, 1680, 3230, 3350 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 1.26 (3 H, t, CH_3), 2.05 (3 H, s, CH_3), 3.81 (3 H, s, CH_3), 4.19 (2 H, q, CH_2), 6.98 (1 H, d, H_5), 7.00 (1 H, s, H_2), 8.21 (1 H, d, H_6), 8.31 (1 H, s, CH) 9.57 (1 H, s, NH exchangeable), 9.75 (1 H, s, NH exchangeable); mass spectrum (positive chemical ionization), m/e 280 (M + 1).

Ethyl 6-Amino-5-methoxyindole-2-carboxylate Hydrochloride (19). A solution of 6.975 g (25 mmol) of hydrazone **18** in 50 mL of a saturated solution of HCl in ethanol was stirred for 15 h at room temperature during which time the product precipitated out of solution. The solvent was removed in vacuo and the residue treated with a little ethanol to afford 4.65 g (69%) of indole **19** as a beige solid after filtration: IR 1680 cm^{-1}; ^{1}H NMR (Me_2SO-d_6 + D_2O) δ 1.37 (3 H, t, CH_3), 3.94 (3 H, s, CH_3), 4.35 (2 H, q, CH_2), 7.20 (1 H, s, H_4), 7.43 (1 H, s, H_3), 7.70 (1 H, s, H_7); mass spectrum (electron impact), m/e 234 (M^+).

Diethyl 5-Methoxy-1*H*-pyrrolo[2,3-*f*]quinoline-2,9-dicarboxylate (20). A mixture of 3.83 g (33 mmol) of ethyl pyruvate and 2.74 g (36 mmol) of dimethoxymethane was saturated with HCl gas at a temperature below 30 °C and added to a suspension of 4.06 g (15 mmol) of indole **19** in 60 mL of ethanol. The mixture was stirred for 1 h at room temperature and refluxed for 18 h. The solvent was removed in vacuo and the residue treated with water and filtered. The filtrate was neutralized with aqueous ammonia and the resulting light brown precipitate filtered off and chromatographed on a silica column, eluting with ethyl acetate to afford 255 mg (5%) of **20** as a yellow solid: mp 123–124 °C; IR 1700, 3220 cm^{-1}; ^{1}H NMR ($COCl_3$) δ 1.45 (3 H, t, CH_3), 1.52 (3 H, t, CH_3), 4.13 (3 H, s, CH_3) 4.45 (2 H, q, CH_2), 4.61 (2 H, q, CH_2), 7.28 (1 H, d, H_3), 7.32 (1 H, s, H_4), 8.14 (1 H, d, H_8), 9.04 (1 H, d, H_7), 12.07 (1 H, br s, NH); mass spectrum (electron impact), m/e 342 (M^+).

Diethyl 4,5-Dihydro-4,5-dioxo-1*H*-pyrrolo[2,3-*f*]quinoline-2,9-dicarboxylate (21). A solution of 603 mg (1.1 mmol) of ceric ammonium nitrate in 0.58 mL of water was added to an ice-cold solution of 68.4 mg (0.2 mmol) of **20** in 2.3 mL of acetonitrile. The mixture was stirred for 20 min at 0 °C and evaporated in vacuo. The solid residue was treated with water and extracted three times with methylene chloride. The combined organic layers were dried ($MgSO_4$) and concentrated in vacuo to yield 65 mg (95%) of the *o*-quinone **21** as an orange solid, of sufficient purity to be used in the next step: mp 160–163 °C; TLC (silica) R_f 0.85 (CH_2Cl_2/EtOH, 9:1); IR 1670, 1710 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.42 (3 H, t, CH_3), 1.51 (3 H, t, CH_3), 4.42 (2 H, q, CH_2), 4.60 (2 H, q, CH_2), 7.44 (1 H, d, H_3), 8.11 (1 H, d, H_8), 8.85 (1 H, d, H_7), 12.84 (1H, br s, NH); mass spectrum (electron impact), m/e 344 (M^+ + 2).

4,5-Dihydro-4,5-dioxo-1*H*-pyrrolo[2,3-*f*]quinoline-2,9-dicarboxylic Acid (3). A solution of 34.2 mg (0.1 mmol) of dione **21** in 20 mL of 0.1 M K_2CO_2 solution was stirred at 60 °C for 16 h. The cooled solution was acidified with concentrated HCl to pH 2 and evaporated to low volume. The resulting red-brown precipitate was collected by filtration, washed with a little water and dried under vacuum to afford 19 mg (66%) of **3**: TLC (reversed phase) R_f 0.95 (MeOH/H_2O, 7:3); IR 1660, 1700 cm^{-1}; ^{1}H NMR (Me_2SO-d_6) δ 7.09 (1 H, s, H_3), 8.01 (1 H, d, H_8), 8.60 (1 H, d, H_7), 13.04 (1 H, br s, NH); mass spectrum (positive chemical ionization), m/e 287 (M + 1); UV (H_2O, pH 7) λ_{max} 315 (sh) nm (ϵ 8100 M^{-1} cm^{-1}), 271 (ϵ 21 000), 245 (ϵ 17 900); exact mass for $C_{13}H_7N_2O_6$, calcd 287.0305, found 287.0354.

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