platinum wire in series with a 0.1 μF capacitor, was placed in parallel with the cadmium amalgam electrode.

The progress of a large-scale electrolysis was monitored periodically by cyclic voltammetry. At the conclusion of an electrolysis, the mixture was protonated in a dry helium atmosphere with an appropriate proton donor (e.g., acetic acid or diethyl malonate). The solution was then analyzed by high-performance liquid chromatography (HPLC).

Chromatography. The products of the electrolyzed solutions were separated by HPLC using a 6.35-mm diameter by 25-cm length stainless steel column packed with either LiChrosorb RP-8 or Alltech C_{18}, 10-μm mean particle size. The eluting solvent was a mixture of methanol and water; the solvent ratio was optimized for each product composition. The flow rate of the eluting solvent was 1 mL/min. The wavelengths used in the analyses were 270 nm for acetone and 254 nm for the remainder of the products. Calibration curves were constructed daily.

Chemicals. DMF (Burdick and Jackson) was purified by passage thrugh a column of alumina (80–200 mesh, Brockman activity 1, activated at 600 °C overnight) and was collected over a mixture of Davison 4-Å molecular sieves and alumina. This procedure was carried out in a dry, nitrogen-filled glovebag.

6,6-Dimethyldibenzofulvene oxide (1),[23] 2-(9-fluorenyl)propanol (2)[24] and tetraphenyloxirane (3)[25] were synthesized according to literature procedures; all other compounds were commercially available. The purities of all compounds were checked by melting point, HPLC, and/or cyclic voltammetry.

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Registry No. 1, 81277-93-2; 2, 56954-90-6; 3, 470-35-9; 4, 981-24-8.

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Electrochemical–Kinetic Study of the Oxidative Cyclization of 2,5-Dihydroxyphenylalanine, 2,5-Dihydroxyphenylethylamine, and α-Methyl-2,5-dihydroxyphenylethylamine

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The anodic oxidation reactions of 2,5-dihydroxyphenylethylamine (**1a**, DHPA), α-methyl-2,5-dihydroxyphenylethylamine (**1b**, α-MeDHPA), and 2,5-dihydroxyphenylalanine (**1c**, 2,5-dopa) were studied at the carbon-paste electrode in 1 M $HClO_4$ and in McIlvaine buffers of varying pH at 15, 20, 25, and 30 °C. Cyclic voltammetry showed that, within the pH range 6.5–7.5, each of the three compounds was oxidized via an EC mechanism involving an initial two-electron oxidation to a *p*-quinone (**2a,b,c**), which after deprotonation to the free amine **3a,b,c**, rapidly cyclized to the relatively stable 5-oxoindoline quinone imine **4a,b,c**. The indoline quinone imines **4a,b** underwent further, much slower tautomerization to the corresponding 5-hydroxyindoles **6a,b**, which could be isolated following constant potential electrolysis experiments. The indoline quinone imine **4c** from 2,5-dopa (**1c**) underwent decarboxylative rearrangement to yield 5-hydroxyindole (**6a**). Double potential step chronoamperometry of **1a**, **1b**, and **1c** afforded first-order rate constants for cyclizations of the *p*-quinonylethylamines **3** to the corresponding 5-oxoindoline quinone imines **4**. At 25 °C the transient *p*-quinonylethylamines **3a,b,c** had half-lives of 50, 5, and 7 ms, respectively. Authentic 5-hydroxyindoline (**5a**), the reduction product of **4a**, was synthesized independently by debenzylation of 5-(benzyloxy)indoline hydrochloride.

In earlier articles we reported detailed electrochemical–kinetic studies of the oxidative cyclizations of the melanin precursor 3,4-dihydroxyphenylalanine (dopa)[1] and of several related catecholamines, including dopamine,[3] α-methyldopa,[2] α-methyldopamine, and α-methylnorepinephrine.[3] The isomer of dopa, 2,5-dihydroxyphenylalanine (**1c**, 2,5-dopa) is also of some physiological significance and has shown antibiotic activity[4,5] as well as utility as a cardiac stimulant.[6] This hydroquinone amine **1c** had been suggested early[7] as a metabolic intermediate in the conversion of tyrosine to homogentisic acid in alkaptonurics but only recently has been demonstrated to play such a role in the metabolism of tyrosine by several strains of Aspergillus.[8]

As an alternative to oxidative degradation of the side chain leading to homogentisic acid, nuclear oxidation of 2,5-dopa (**1c**) should produce the corresponding *p*-quinone **2c**, a species of as yet unknown stability, which can cyclize to indolic products, paralleling the behavior of dopa quinone. For this reason it was of interest to conduct a

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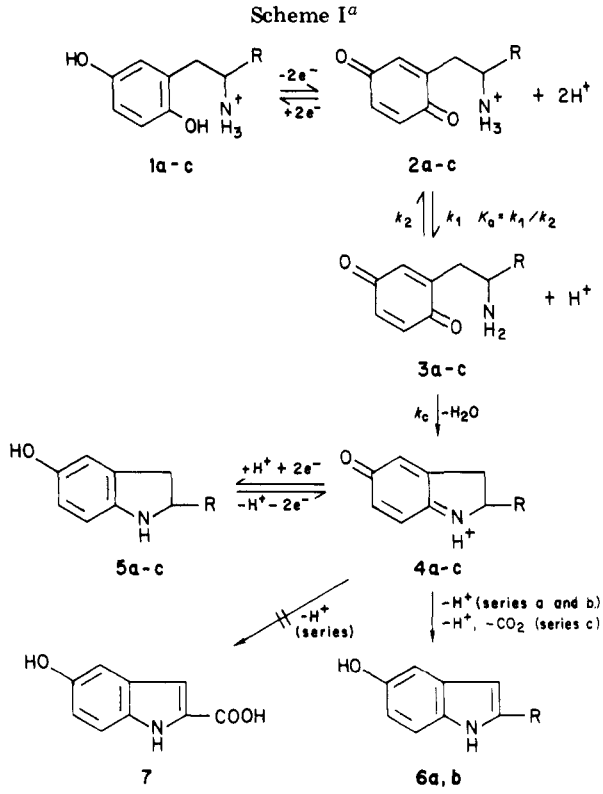
Scheme I[a]



[a] Series a: R = H. Series b: R = CH_3. Series c: R = COOH.

mechanistic–kinetic investigation of the anodic oxidation of 2,5-dopa (**1c**), along with two of its congeners, 2,5-dihydroxyphenylethylamine (**1a**, DHPA) and α-methyl-2,5-dihydroxyphenylethylamine (**1b**, α-MeDHPA).

Cyclic Voltammetry. Since a brief electrochemical survey of 2,5-dihydroxyphenylethylamine (**1a**) had already been described,[9] we chose to do a thorough study of this compound first as a reference model. A cyclic voltammogram (CV) of DHPA (**1a**, Scheme I) in 1 M perchloric acid showed an anodic peak (E_{pa} = 0.480 V) for the oxidation **1a** → **2a** and a companion cathodic peak (E_{pc} = 0.333 V) for the reduction **2a** → **1a**. The peak separation of 0.147 V was that of a quasi or irreversible charge transfer, and the anodic peak current (63.3 μA) was close to that calculated[10,11] (68.3 μA) for an irreversible two-electron transfer, assuming a value of 0.5 for the transfer coefficient (α) and using a diffusion coefficient (D = 0.59 × 10^{-5} cm^2/s) determined from chronoamperometry and the Cottrell equation.

Cyclic voltammetry of 0.57 mM DHPA (**1a**) at 25 °C and in McIlvaine buffers covering the pH range from 6.5 to 7.5 showed peak patterns consistent with an EC mechanism over steps **1a** → **2a** → **3a** → **4a** (Scheme I) leading to the formation of the 5-oxoindoline quinone imine (**4a**). A voltammogram at pH 6.70 and a fast scan rate (ν) of 0.300 V/s or higher was similar to that in perchloric acid but with greater peak separation (e.g., 221 mV at ν = 0.300 V/s). At successively decreasing scan rates the cathodic peak diminished and a new set of peaks appeared and grew in current values. Figure 1 shows a typical trace at pH 6.70 and ν = 0.100 V/s in which reduction of the new intermediate (B′) occurred at −0.091 V and its reduction

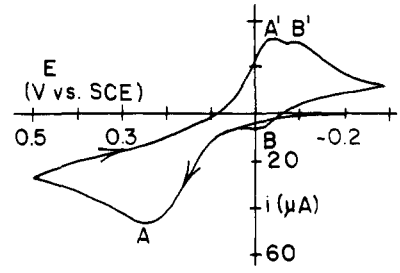


Figure 1. Cyclic voltammogram of 0.561 mM 2,5-dihdyroxyphenylethylamine (**1a**) in pH 6.70 McIlvaine buffer at a scan rate of 0.100 V/s and 25 °C. Scan was initiated at −0.2 V.

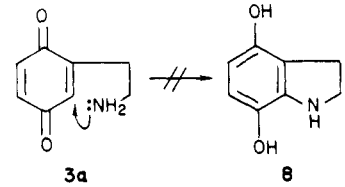
product (B) was then reoxidized at −0.006 V on the second continuous scan. Identification of the new redox couple B ⇌ B′ as 5-hydroxyindoline (**5a**) and 5-oxoindoline quinone imine (**4a**) was accomplished by synthesis of the indoline (**5a**) as described in the following paragraph.

Commercially available 5-(benzyloxy)indole was reduced to 5-(benzyloxy)indoline in 30% yield by use of Gribble's sodium cyanoborohydride procedure.[12] Catalytic hydrogenolysis of this new indoline was unsuccessful; however, conversion to its hydrochloride salt followed by hydrogenolysis over palladium–charcoal afforded a low yield of 5-hydroxyindoline hydrochloride (**5a·HCl**), which though very sensitive to autooxidation was isolated as a slightly off-white crystalline solid having the correct infrared and ^1H and ^{13}C NMR characteristics and high purity as assessed from the ^{13}C NMR spectrum.

Cyclic voltammetry of 5-hydroxyindoline hydrochloride (**5a·HCl**) at pH 7.02 showed a simple quasi-reversible scan (not illustrated) with an E_{pa} = +0.010 V and E_{pc} = −0.067 V, closely matching peaks B and B′ of Figure 1 and strongly suggesting that **4a** was responsible for the reduction peak B′. Further confirmation of identity resulted from the following electrolysis experiments.

During cyclic voltammetry of fresh DHPA (**1a**) solutions only peaks A, A′, B, and B′ were observed. However, after prolonged use of a solution or by increasing the pH to 7.8 and the temperature to 37 °C, a new oxidation peak was observed at E_{pa} = +0.336 V after a few hours. This change indicated the formation of yet another product by a relatively slow chemical transformation. Constant-potential electrolysis of both DHPA (**1a**) and of 5-hydroxyindoline (**5a**) at +0.200 V and pH 7.48 afforded solutions which after standing for a few hours showed cyclic voltammograms identical with the totally irreversible CV of authentic 5-hydroxyindole (**6a**), thus confirming the common intermediacy of the transient 5-oxoindoline quinone imine (**4a**). Furthermore, extraction of the electrolysis solution from DHPA (**1a**) gave isolable quantities of 5-hydroxyindole (**6a**) identical in all ways, including TLC and NMR, with an authentic sample.

At first glance it might have been expected that the transient 2-aminoethyl-*p*-quinone (**3a**) could also cyclize



via an alternate route involving intramolecular Michael addition of the primary amino group at carbon-3 of the

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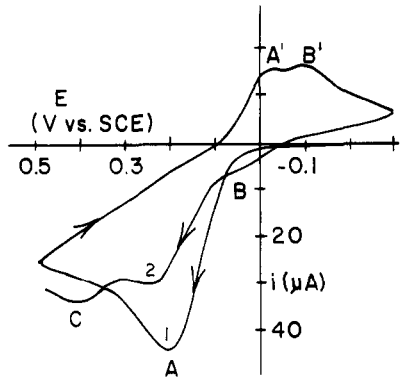

Figure 2. Cyclic voltammogram of 0.535 mM 2,5-dihydroxyphenylalanine (**1c**) in pH 6.52 McIlvaine buffer at a scan rate of 0.150 V/s and 25 °C. Scan was initiated at −0.25 V.

quinone ring leading to 4,7-dihydroxyindoline (**8**). However, such a cyclization is a 5-endo-trig reaction that is disfavored stereochemically according to Baldwin's rules of ring closure,[13] and no products other than those described above, and shown in Scheme I, are found in any of the three series (**a**, **b**, or **c**) under consideration. In contrast, the cyclization of the quinone (e.g., **3a** → **4a**) via 1,2-condensation with the carbonyl group is a 5-exo-trig process which is sterically favored and is experimentally observed.

With the foregoing as background, we next examined α-methyl-2,5-dihydroxyphenylethylamine (**1b**, α-MeDHPA), whose cyclic voltammetric behavior was entirely analogous with that of DHPA (**1a**). A typical CV of α-MeDHPA (**1b**) at pH 6.70 showed the primary oxidation **1b** → **2b** at E_{pa} = 0.164 V and rereduction **2b** → **1b** at E_{pc} = 0.009 V with the secondary redox couple **4b** ⇌ **5b** appearing at E_{pa} = −0.012 V and E_{pc} = −0.078 V.

Bulk electrolysis of α-MeDHPA (**1b**) at a carbon cloth electrode for 1 h and pH 7.23 afforded a solution containing mainly the indoline quinone **4b** as revealed by cyclic voltammetry. A CV of this electrolysis solution showed a reduction peak (**4b** → **5b**) at −0.177 V and reoxidation (**5b** → **4b**) at 0 V. As further time elapsed the solution (kept under nitrogen) developed a maroon color as the rearrangement of **4b** to 2-methyl-5-hydroxyindole (**6b**) occurred. Intermittent determination of the CV of this solution showed gradual growth of an anodic peak (0.350 V) due to oxidation of **6b**, thus permitting a crude assessment of the half-life of 2-methyl-5-oxoindoline quinone imine (**4b**) at about 3 h. Extraction of the electrolysis solution and preparative thin-layer chromatography of the products gave as the major constituent 2-methyl-5-hydroxyindole (**6b**), identified by its ^1H and ^{13}C NMR spectra, which were identical with those of an authentic sample.

2,5-Dopa (**1c**) in 1 M perchloric acid exhibited a cyclic voltammogram showing only an anodic peak at E_{pa} = 0.530 V and a subsequent cathodic peak at E_{pc} = 0.402 V, corresponding to the redox couple **1c** ⇌ **2c**. The observed anodic peak current (63.6 μA), as in the previous two series, agreed well with that calculated (61.2 μA) for an irreversible two-electron charge transfer assuming a transfer coefficient α = 0.5. Voltammograms of 2,5-dopa in the pH range 6.5–7.5 showed peaks for intermediates comparable with those of series **a** and **b** but with clear differences in timing. At pH 6.52 and a rapid scan rate of 150 mV/s (cf. Figure 2) the A, A′ peaks for the primary redox couple **1c** ⇌ **2c** and peak B′ for the secondary reduction **4c** → **5c** again appear on the first scan. However, on the second continuous scan ones sees not only reoxidation of the indoline (**5c** → **4c**) (peak B) but also a new intermediate (peak C) at +0.410 V attributable to oxidation of 5-hydroxyindole (**6a**). At a slow scan rate (50 mV/s) this peak at +0.410 V appeared even on the first scan, indicating a very rapid rearrangement of the indoline quinone **4c** to 5-hydroxyindole (**6a**). That the ultimate oxidation product was **6a** and not the carboxylic acid **7** was demonstrated by bulk electrolysis of 2,5-dopa (**1c**) which afforded a substance with the same ^1H and ^{13}C NMR spectra, infrared spectrum, melting point, and mixture melting point as authentic 5-hydroxyindole (**6a**). It seems unlikely that **7** is an intermediate on the pathway from **4c** to **6a** since several indole-2-carboxylic acids, with which we have had experience, decarboxylate only at 200 °C or above. Furthermore preparative TLC of the bulk electrolysis products showed no major component other than **6a**.

Table I. Observed First-Order Rate Constants (k_o) for Conversion of 2,5-Dihydroxyphenylethylamine (1a) to the Indoline Quinone Imine 4a at Various Temperatures[a]

	k_o, s^{-1}			
pH	15 °C	20 °C	25 °C	30 °C
6.90		0.032 ± 0.004	0.049 ± 0.004	0.094 ± 0.005
7.02	0.021 ± 0.001	0.043 ± 0.002	0.074 ± 0.003	0.138 ± 0.002
7.22	0.045 ± 0.004	0.077 ± 0.006	0.164 ± 0.009	0.256 ± 0.022
7.48	0.093 ± 0.005	0.169 ± 0.0006	0.320 ± 0.038	0.536 ± 0.051

[a] Reproducibility is shown as ± standard deviation which varied from 1.4% to 12.5% with an average of 6.6% overall.

Table II. Observed First-Order Rate Constants (k_o) for Conversion of α-Methyl-2,5-dihydroxyphenylethylamine (1b) to the Indoline Quinone Imine 4b at Various Temperatures[a]

	k_o, s^{-1}			
pH	15 °C	20 °C	25 °C	30 °C
6.70	0.049 ± 0.004	0.083 ± 0.005	0.144 ± 0.005	0.256 ± 0.016
6.91	0.072 ± 0.002	0.127 ± 0.005	0.245 ± 0.011	0.376 ± 0.015
7.02	0.107 ± 0.004	0.196 ± 0.011	0.290 ± 0.014	0.626 ± 0.068
7.23	0.165 ± 0.009	0.266 ± 0.012	0.465 ± 0.014	0.781 ± 0.027

[a] Reproducibility is shown as ± standard deviation which varied from 2.8% to 10.9% with an average of 5.0% overall.

Table III. Observed First-Order Rate Constants (k_o) for Conversion of 2,5-Dihydroxyphenylalanine (1c) to the Indole Quinone Imine 4c at Various Temperatures[a]

	k_o, s^{-1}			
pH	15 °C	20 °C	25 °C	30 °C
6.52	0.067 ± 0.004	0.128 ± 0.006	0.195 ± 0.013	0.326 ± 0.008
6.70	0.091 ± 0.006	0.161 ± 0.018	0.247 ± 0.006	0.369 ± 0.005
6.91	0.118 ± 0.005	0.182 ± 0.016	0.375 ± 0.018	0.582 ± 0.024
7.02	0.156 ± 0.011	0.260 ± 0.020	0.487 ± 0.022	0.712 ± 0.035

[a] Reproducibility is shown as ± standard deviation which varied from 1.4% to 11.0% with an average of 5.7% overall.

Cyclization Kinetics via Double-Potential Step Chronoamperometry. Double-potential step chronoamperometry was carried out on each of the compounds **1a–c**, using the method of Schwarz and Shain,[14] to determine the rates of conversion of the *p*-quinonylethylamines **2a–c** to the corresponding 5-oxoindolinyl quinone imines **4a–c** via the general EC mechanistic sequence 1 → 2 → 3 → 4

(13) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734. In the "5-endo-trig" notation the 5 denotes the number of atoms in the new ring, endo means that the double bond under attack is being broken endo to the new ring, and trig is the geometry of the carbon atom undergoing attack by the nucleophile.

(14) Schwarz, W. M.; Shain, I. *J. Phys. Chem.* **1965**, *69*, 30.

Table IV. Derived First-Order Rate Constants for the Cyclization 3a → 4a, 3b → 4b, and 3c → 4c

	k_c (s^{-1}) at			
p-quinone	15 °C	20 °C	25 °C	30 °C
3a	4.3	9.4	13.8	27.1
3b	46.0	78.6	141	244
3c	37.7	87.0	100	180

Table V. Activation Thermodynamic Parameters for the Cyclization Reactions 3a → 4a, 3b → 4b, and 3c → 4c

parameter[a]	3a	3b	3c
E_a, kcal/mol	20.5	19.5	16.8
$\Delta H^{\ddagger}$, kcal/mol	19.9	18.9	16.2
$\Delta G^{\ddagger}$, kcal/mol	15.9	14.5	14.7
$\Delta S^{\ddagger}$, eu	13.4	14.5	5.1

[a] Values of $\Delta H^{\ddagger}$, $\Delta G^{\ddagger}$, and $\Delta S^{\ddagger}$ were calculated at 25 °C.

as shown in Scheme I. Analysis of the resulting data clearly showed high reproducibility of the derived rate constants which are summarized for the three substrates **1a–c** in Tables I–III.

Application of the steady-state approximation to intermediate **3** in the sequence **2** ⇌ **3** → **4** leads to eq 1[3]

$$\frac{1}{k_0} = \frac{1}{K_a k_c}[H^+] + \frac{1}{k_1} \quad (1)$$

where k_0 is the overall observed rate constant, k_1 is the specific rate for the deprotonation **2** → **3** (Scheme I), k_c is the cyclization rate constant **3** → **4**, and K_a is the acidic dissociation constant for the ammonium group of compound **2a**, **2b**, or **2c**. The data of Tables I–III gave nicely linear plots of $1/k_0$ vs. $[H^+]$ having slopes $(1/K_a k_c)$ from whch the unimolecular rate constants (k_c) for cyclization **3** → **4** could be derived provided that the dissociation constants (K_a) were known.

Direct determination of the requisite K_a values is prohibited by the transient nature of the quinonoid amines **2**. However, reasonable estimates of microscopic pK_a values for **2a** and **2b** were obtained by potentiometric titration of 2,5-dimethoxyphenylethylamine hydrobromide (**2a**,Br^-; pK_a = 9.41) and α-methyl-2,5-dimethoxyphenylethylamine hydrobromide (**2b**,Br^-; pK_a = 9.68), following the method of Ganellin,[15] in which it is assumed that the structural perturbations are small. The pK_a of the ammonium group in 2,5-dopa (**1c**) and of its quinone **2c** was taken to be the same as that of 3,4-dihydroxyphenylalanine, reported as 9.17 by Martin.[16] Use of the estimated K_a values in the slopes of the linear regression lines defined by eq 1 afforded the first-order rate constants (k_c) for the cyclizations **3a** → **4a**, **3b** → **4b**, and **3c** → **4c**, as summarized in Table IV. Arrhenius plots of the k_c values for DHPA (**1a**), α-MeDHPA (**1b**), and 2,5-dopa (**1c**) followed the linear equations: $\ln k_c = 37.3 - (10.3 \times 10^3)(1/T)$ (correlation coefficient = 0.993), $\ln k_c = 37.8 - (9.79 \times 10^3)(1/T)$ (correlation coefficient = 0.999), and $\ln k_c = 33.1 - (8.47 \times 10^3)(1/T)$ (correlation coefficient = 0.969), respectively. Table V contains the activation thermodynamic parameters for the ring-closure reactions **3** → **4** (series **a**, **b**, and **c**).

These cyclizations, all involving attack by the side-chain amino group directly on the carbonyl carbon of the p-quinone intermediates **3**, are thermodynamically comparable with the 5-exo-trig Michael-type cyclization of the corresponding catecholamines, dopamine,[3] α-methyldopamine,[3] and 3,4-dopa,[1] and show favorably positive entropies of activation. Illuminati and co-workers[17] have also observed positive activation entropies in the S_N2 ring-closure reactions of o-(ω-bromoalkoxy)phenoxides leading to seven- and six-membered rings and showed that $\Delta S^{\ddagger}$ underwent a monotonic transition from negative to positive values as the product ring size decreased from ten to six. However, positive entropies of activation are by no means general, even for five-membered ring formation, and the absolute values are clearly influenced by indeterminate solvation effects.[18] Nevertheless, the similarities in activation thermodynamics for the series under consideration here and for the analogous catecholamines[1-3] suggest that comparable solvation effects occur around the polar functionalities undergoing cyclization in both sets of compounds.

Like the intermediate o-quinones from dopamine and its analogues[1,3] the isomeric p-quinonylethylamines **3a–c** of the present study have very short half-lives (50, 5, and 7 ms, respectively, at 25 °C) and their cyclizations are independent of pH. However, these cyclizations (**3** → **4**) lead via condensation (rather than Michael addition) to 5-oxoindoline quinoneimines **4** which are in the same oxidation state as their immediate precursors. Hence no further electrochemical reactions occur at the potentials employed; slow subsequent tautomerization of the indoline quinone imines **4** leads to 5-hydroxyindoles **6a** and **6b**, which, having higher oxidation potentials than their precursors, are easily isolated at properly selected applied potentials.

Overall the 2,5-dihydroxyphenylethylamines **1** are electrochemically well-behaved and represent one of the relatively few organic systems known[14,19] to conform to the Schwarz and Shain treatment. It is also of interest that the intermediary p-quinonylethylamines **2** undergo cyclization selectively via 1,2-addition at the carbonyl group to the exclusion of the alternative Michael type addition thereby further supporting Baldwin's[13] predictions.

Experimental Section

General Methods. Proton and carbon-13 NMR spectra were recorded on a JEOL-FX90Q multinuclear spectrometer with proton chemical shifts referenced to Me_4Si and carbon resonances referenced to the solvent. Infrared spectra were recorded on a Perkin-Elmer 283 spectrophotometer, and mass spectra were obtained on a Finnegan Model 4021 automated gas chromatograph–mass spectrometer system. Melting points (uncorrected) were determined on a Mel-Temp apparatus.

Column chromatography was performed by flash chromatographic methods in which the elution solvent was forced by nitrogen pressure through a glass column, which had been dry-packed with silica gel (Merck Silica Gel 60, 230-400 mesh), such that the solvent moved through the column at a rate of about 2 in. per min. Preparative TLC was carried out on Analtech silica gel GF plates (20 × 20 cm) of 500 or 1000 μm thickness. Whenever possible, reaction progress was followed by analytical TLC which employed Merck pre-coated TLC sheets (Silica Gel 60 F_{254}, 200 μm thickness).

Cyclic Voltammetry and Chronoamperometry. The current–potential curves were obtained by using a Princeton Applied Research (PAR) Model 173 potentiostat equipped with a PAR Model 175 programmer, a Model 176 current-follower, and a Model 178 electrometer probe. At slow scan speeds, the voltammograms wre recorded on a Houston Instrument Model 2100-4-5 X–Y recorder, and faster scans (greater than 200 mv/s) required a Tektronix Model 5103N storage oscilloscope in which case voltammograms were recorded photographically with a

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(19) Perone, S. P.; Kretlow, W. J. *Anal. Chem.* **1966**, *38*, 1760, reported studies of the EC mechanism of oxidation of ascorbic acid.

Polaroid camera. Double-potential step current–time curves were recorded digitally with a Nicolet Model 1072 instrument computer.

A PAR jacketted electrochemical cell was maintained at constant temperature (±0.1 °C) with circulated water from a Forma-Temp Jr. thermostatic bath. The electrochemical cell was arranged in a three-electrode configuration consisting of a planar carbon-paste working electrode, platinum wire counterelectrode, and a saturated calomel reference electrode. The working electrode was a Plexiglass tube possessing a 5–6-mm well, packed with carbon-paste, at the end of the tube. A platinum wire inside the tube made contact with the carbon-paste through a sealed opening in the wall dividing the carbon-paste well from the rest of the electrode. The carbon-paste was a mull of purified graphite (Matheson, Coleman and Bell) and Nujol, which were combined in a ratio of 15 g to 9 mL, respectively.[20] Two different working electrodes were used for voltammetry and chronoamperometry, and their electrochemical areas was determined by chronoamperometry of standard solutions of *o*-dianisidine at 25 °C in 1 M H_2SO_4, taking the diffusion coefficient as 0.44×10^{-5} cm^2/s[21] and applying the Cottrell equation. The electrode used in the electrochemical studies of DHPA (**1a**), α-MeDHPA (**1b**), and 2,5-dopa (**1c**) in 1 M $HClO_4$ had an electrochemical area of 0.37 cm^2. All other voltammetry and chronoamperometry were performed at a carbon-paste electrode with an area of 0.266 cm^2. All experiments were conducted under a nitrogen atmosphere.

Cyclic voltammograms of all three of the hydroquinonylethylamines (**1a, b, c**) displayed anodic peaks which showed linear variations of both peak and half peak ($E_{pa/2}$) potentials in the pH range 6.5–7.5: e.g., **1a**, $E_{pa/2}$ = 0.901–0.115 pH (corr coeff = 0.999); **1b**, $E_{pa/2}$ = 0.599–0.0755 pH (corr coeff = 0.983); **1c**, $E_{pa/2}$ = 0.700–0.0833 pH (corr coeff = 0.971).

Kinetic determinations were made at four temperatures (15, 20, 25, and 30 °C) and at four pH values within the range 6.5–7.5. Specific pH ranges varied slightly for each substrate and were selected experimentally in order that the switching time (τ) approximately matched the half-lives ($t_{1/2}$) of the *p*-quinones **3** as required for maximum accuracy.[14] Typically the τ values used were 0.8 $t_{1/2}$, $t_{1/2}$, and $t_{1/2}$ at each temperature and pH, and the observed rate constants (k_0) for the overall reaction **2** → **4** were taken as the average from three current–time curves, each of which furnished five individual values of k_0.

In application of the double-potential step method, selection of the applied anodic potential, positive of the primary oxidation peak **1** → **2**, was especially important for 2,5-dopa (**1c**) where 5-hydroxyindole (**6a**) was formed rapidly as shown by cyclic voltammetry. Possible interference was eliminated by adjusting the oxidation potential to a value about halfway between the peak potential for **1c** and **6a** (e.g., ca. 0.31 V for the conditions of Figure 2). At this potential the $it_{1/2}$ values for the anodic current were constant. For all three substrates **1a–c** the applied cathodic potential was similarly selected halfway between the peak potential for reduction of the quinones **2** and reduction of the indoline quinones **4**, e.g., between peaks A′ and B′ in Figure 2.

2,5-Dihydroxyphenylethylamine Hydrobromide (1a·HBr). This compound was prepared in 25% yield by the method of Green[22] and recrystallized from methanol–ether as white prisms: mp 167–169 °C (lit.[22] mp 160–161 °C); ^1H NMR (Me_2SO-d_6) δ 2.76 (t, *J* = 3.6 Hz, 2 H), 2.92 (t, *J* = 3.6 Hz, 2 H), 6.40–6.71 (m, 3 H), 8.06 (br s, 3 H), 8.67 (s, 2 H); ^{13}C NMR (CD_3OD) δ 30.0, 40.9, 115.8, 116.8, 118.0, 124.8, 149.3, 151.2; IR (KBr) 3425, 1620, 1500, 1453, 1203 cm^{-1}.

Anal. Calcd for $C_8H_{12}BrNO_2$: C, 41.05; H, 5.17; N, 5.98. Found: C, 41.16; H, 5.34; N, 6.09.

α-Methyl-2,5-dihydroxyphenylethylamine Hydrobromide (1b·HBr). A solution of 0.522 g (2.25 mmol) of 1-(2,5-dimethoxyphenyl)-2-aminopropane hydrochloride[23] in 5 mL of 48% HBr was heated under nitrogen at 110 °C for 2.5 h and then evaporated to dryness in vacuo to leave a glassy residue. Recrystallization from methanol–ether (under N_2) gave 0.155 g (26%) of colorless prisms of **1b**·HBr: mp 121–124 °C; ^1H NMR (CD_3OD) δ 1.27 (d, 3 H), 2.62–3.04 (dd, 2 H), 3.42–3.79 (m, 1 H), 6.52–6.75 (m, 3 H); ^{13}C NMR (CD_3OD) δ 18.6, 37.0, 49.3, 116.0, 116.9, 118.9, 124.3, 149.6, 151.3; IR (KBr) 3700–2500, 1600, 1500, 1473, 1450, 1340, 1197, 750, 690 cm^{-1}.

Anal. Calcd for $C_9H_{14}NO_2Br$: C, 43.57; H, 5.69; N, 5.65. Found: C, 43.34; H, 5.47; N, 5.65.

D,L-2,5-Dihydroxyphenylalanine (1c). This compound,[6] originally synthesized by Neuberger,[7] was a gift from Merck and Company, Inc., and was kindly provided by Dr. Lewis Mandel.

5-(Benzyloxy)indoline (9). To a solution of 5-(benzyloxy)-indole (0.399 g, 1.79 mmol) in glacial acetic acid (30 mL) which had been presaturated with nitrogen was added sodium cyanoborohydride (1.20 g, 19.1 mmol) while stirring rapidly under nitrogen. After 15 min the solution was cooled to 0 °C and made alkaline (pH >10) with 25% NaOH. The alkaline aqueous solution was extracted with ether (4 × 30 mL), the combined extracts were dried (Na_2SO_4), and the ether was removed, leaving a green oil which was purified by column chromatography ($CHCl_3$). The reaction furnished 121 mg (30%) of 5-(benzyloxy)indoline as a colorless oil which solidified to a white waxy solid at 0 °C: ^1H NMR ($CDCl_3$) δ 2.97 (t, 2 H), 3.45 (m, 3 H), 4.96 (s, 2 H), 6.57–6.81 (m, 3 H), 7.30–7.37 (m, 5 H).

Anal. Calcd for $C_{15}H_{15}NO$: C, 79.97; H, 6.71; N, 6.22. Found: C, 79.71; H, 6.94; N, 5.96.

5-(Benzyloxy)indoline Hydrochloride (9·HCl): mp 188–190 °C; ^1H NMR (CD_3OD) δ 3.37 (m, 2 H, plus solvent), 3.85 (t, 2 H), 5.11 (s, 2 H), 6.90–7.10 (m, 3 H), 7.20–7.50 (m, 5 H); ^{13}C NMR (CD_3OD) δ 30.4, 47.6, 71.5, 113.1, 116.4, 121.1, 128.6, 129.0, 129.5, 138.0, 138.6, 161.7; IR (KBr) 3410, 3000–2300, 1520, 1482, 1442, 1385, 1260, 1178, 1008, 802, 740 cm^{-1}.

5-Hydroxyindoline Hydrochloride (5a·HCl). The desired compound, 5-hydroxyindoline, was obtained by catalytic hydrogenation of 5-(benzyloxy)indoline hydrochloride (~30 mg) in 75 mL of methanol to which 10 mg of palladium/charcoal (10%) had been added. After 6 h, the catalyst was removed by filtration under nitrogen pressure through a bed a Celite and solvent removed to give 5-hydroxyindoline hydrochloride as an off-white solid which was dissolved in deaerated buffer for electrochemical studies. The reduction product had the following spectral characteristics: ^1H NMR (CD_3OD) δ 3.20 (t, *J* = 7 Hz, the low-field resonance is obscured by solvent), 3.75 (t, *J* = 7 Hz, 2 H), 6.75 (m, 2 H), 7.17 (m, 1 H); ^{13}C NMR (CD_3OD) δ 30.5, 47.7, 113.4, 115.0, 116.1, 119.6, 137.5, 159.2; IR (film) 3700–2300, 1600, 1485, 1455, 1270, 805 cm^{-1}.

Bulk Electrolysis. In general, 20–50 mg of substrate was dissolved in approximatly 100 mL of buffer and added to one compartment of a standard H-type electrolysis cell. The second, compartment, which was separated from the first by a glass frit, was filled with the same buffer until the fluid levels were the same in both halves of the cell. A saturated calomel electrode (SCE) and a platinum wire were used as the reference electrode and the auxiliary electrode, respectively, in all electrolyses. The working electrodes were constructed by weaving a platinum wire through a strip (3 × 10 cm) of carbon cloth (Union Carbide, Grade VCK). Electrolyses were performed with rapid magnetic stirring while bubbling a stream of nitrogen through the substrate solution until the current fell to a small, constant value, which was no longer enhanced by the introduction of fresh carbon cloth. The working electrodes were replaced as many times as were necessary to achieve the constant current condition. The extraction procedures varied according to substrate and are described in the following paragraphs.

Electrolysis of 2,5-Dihydroxyphenylethylamine (1a). 2,5-Dihydroxyphenylethylamine (**1a**, DHPA) was electrolyzed at +0.2 V in pH 7.48 buffer. After 1 h the oxidation was terminated and the products were extracted into ethyl acetate (4 × 50 mL). The combined extracts were dried ($MgSO_4$) and the solvent was removed, leaving a gray residue which was purified by preparative TLC. The resulting solid had TLC properties and an NMR spectrum identical with authentic 5-hydroxyindole (**6a**).

Electrolysis of α-Methyl-2,5-dihydroxyphenylethylamine (1b). Electrolysis of α-methyl-2,5-dihydroxyphenylethylamine (**1b**, MeDHPA), performed at +0.2 V and pH 7.23, afforded the oxidized form of 2-methyl-5-hydroxyindoline (**4b**) which slowly

(20) Adams, R. N. "Electrochemistry at Solid Electrodes"; Marcel Dekker: New York, 1969; Chapter 9.
(21) Reference 20, Table 8-3.
(22) Green, M. (to Polaroid Corp.), U. S. Patent 3062884, Nov 6, 1962; *Chem. Abstr.* **1963**, *58*, 5575d.
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rearranged to 2-methyl-5-hydroxyindole (**6b**). Therefore, the electrolyzed sample was allowed to stand at room temperature under nitrogen for 5 h, then the analyte was extracted with four 50-mL portions of ethyl acetate, and the combined extracts were washed with an equal volume of saturated NaCl and dried over Na_2SO_4 for 12 h. Evaporation of the solvent left a maroon residue which showed three components on TLC. The major constituent was isolated by preparative TLC ($CH_3OH/CHCl_3$, 1:9) and was identified as 2-methyl-5-hydroxyindole (**6b**) by the NMR spectra which were completely analyzed and were identical with those of an authentic sample:[24] ^1H NMR (Me_2CO-d_6) δ 2.36 (d, J = 1 Hz, 3 H), 5.96 (m, J = 1 Hz, 1 H), 6.59 (dd, J = 2.44 Hz and 8.6 Hz, 1 H), 6.85 (d, J = 2.4 Hz, 1 H), 7.11 (d, J = 8.6 Hz, 1 H), 9.98 (br s, 1 H); ^{13}C NMR (Me_2CO-d_6) δ 13.4, 99.4, 104.1, 110.4, 111.3, 130.6, 131.5, 136.5, 151.1.

Electrolysis of 2,5-Dihydroxyphenylalanine (1c). Similar electrolysis of 2,5-dopa (**1c**) was carried out at +0.2 V for 3 h at pH 7.02 to yield a crude red-brown residue which showed only one main component by TLC. Pressure filtration (N_2) of a methanol/$CHCl_3$ solution through a bed of silica gel yielded a colorless solid having IR and NMR spectra identical with those of authentic 5-hydroxyindole (**6a**). The R_f, mp, and mmp were also identical with those of **6a**.

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Registry No. **1a**, 21581-41-9; **1a**·HBr, 61429-49-0; **1b**, 30891-22-6; **1b**·HBr, 92818-35-4; **1c**, 26122-90-7; **5a**·HCl, 92818-38-7; **6b**, 13314-85-7; **9**, 92818-36-5; **9**·HCl, 92818-37-6; 1-(2,5-dimethylphenyl)-2-aminopropane hydrochloride, 24973-25-9; 5-(benzyloxy)-1*H*-indole, 1215-59-4.

Is π Delocalization Synonymous with Stabilization? A Theoretical Study of CH_2CN^+ and CH_2CN^-

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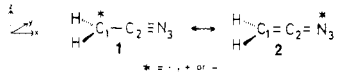
The relationship between π delocalization and stability in CH_2CN^+ and CH_2CN^- has been investigated by using SCF + CI computations. The results have been analyzed with a VB (valence-bond) technique and PMO arguments. The valence-bond analysis of the above species has shown that the π charge delocalization cannot be deduced from the geometrical parameters. The comparison of CH_2CN^+ and CH_2CN^- with CH_2CCH^+ and CH_2CCH^- has indicated that there is no obvious correlation between π charge delocalization and the electronegativity of the atoms. The σ effects have been shown to be the most important in determining the stability of such charged species.

The cyano group directly linked to a radical, a cationic or an anionic center, can lead to two main mesomeric structures.



These three species have already been studied theoretically:[1-7] for each only one minimum is found on the potential energy surface. The problem is thus to determine which mesomeric form **1** or **2** they resemble more.

One way to analyze the electronic distribution of such species is to evaluate the weight of their various valence-bond (VB) structures. This has been done for the CH_2CN· radical[3] and the same method will be employed here for the cation and the anion.

It must be noted that many experimental studies indicate that the electron-withdrawing group CN is not as destabilizing as expected for a cation.[8-9] This result is explained by an important π donation of the CN group into the vacant orbital. Therefore it would seem logical, in order to give a better description of this delocalization, to introduce a configuration interaction (CI) which has not been used in the previous calculations. Furthermore the CN group with two π systems requires often an extensive CI for a proper description.[10]

It is usually believed that there is a relationship between delocalization geometric features, π electronic structure, and stability of a given species. The purpose of this paper is to investigate these relationships in CH_2CN^+ and CH_2CN^- by performing SCF + CI calculations and analyzing the wave function in term of its VB components.

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