Catalytic Reduction of O_2 by Pyrazine Derivatives

Rong Wang,[†] Takeyoshi Okajima,[†] Fusao Kitamura,[†] Susumu Kawauchi,[‡] Naoki Matsumoto,[§] Thies Thiemann,[§] Shuntaro Mataka,[§] and Takeo Ohsaka*[,†]

Department of Electronic Chemistry, Interdisciplinary Graduate School of Science and Engineering, Tokyo Institute of Technology, 4259 Nagatsuta, Midori-ku, Yokohama 226-8502, Japan, Department of Organic and Polymeric Materials, Graduate School of Science and Engineering, Tokyo Institute of Technology, O-okayama 2-12-1, Meguro-ku, Tokyo 152-8552, Japan, and Institute for Materials Chemistry and Engineering, Kyushu University, 6-1 Kasuga-koh-en, Kasuga-shi, Fukuoka 816-8580, Japan

Received: July 14, 2003; In Final Form: December 29, 2003

The catalytic reduction of molecular oxygen (O_2) by four kinds of pyrazine derivatives—2,3,5,6-tetramethylpyrazine, 2,3-dimethylquinoxaline, 2,3-diphenylquinoxaline, and phenazine—has been studied by cyclic and rotating disk voltammetry and molecular orbital calculations using the MOPAC PM5 method. In sufficiently acidic solution (pH $\approx$ 1), the pyrazine derivatives underwent two successive one-electron reductions. Therefore, it was possible to compare the reactivity of both one-electron reduced forms (the radicals) and two-electron reduced forms of the derivatives toward O_2 in this acidic solution. Theoretical calculations showed that all of the redox forms of the derivatives are protonated to be cations in this solution and that all of the reduced forms, except for that of phenazine, react with O_2. The rate constants (k_1) of the second-order reactions of the reduced forms with O_2 were estimated by rotating disk voltammetry. A linear relationship between $\log(k_1)$ and the half-wave potential ($E_{1/2}$) of the one-electron and two-electron reduced forms was observed, indicating that the catalytic reduction of O_2 proceeds by a common reaction mechanism and that its rate constant depends on its thermodynamic driving force.

Introduction

The reduction of O_2 is one of the most important reactions in electrochemical energy conversion and biological energy conversion. Many kinds of catalysts such as nanoparticles,[1,2] metal complexes,[3−5] metal oxides,[6,7] enzymes,[8−11] quinones,[12−14] and viologens[15,16] have been studied with a view toward increasing the efficiency of the electrochemical reduction of O_2.

Previous work in our group has shown that polyquinoxaline-(PQL)-modified graphite electrodes possess excellent catalytic activity for the electrochemical reduction of O_2 to hydrogen peroxide (H_2O_2) in acidic solution.[17−19] This excellent electrocatalytic activity was considered to be due to the high reactivity of reduced pyrazine rings in the polymer toward O_2. However, because the pyrazine ring can be reduced via both one-electron and two-electron processes, depending on solution pH, it remains still unclear whether either of the one-electron or two-electron reduced form of the pyrazine ring or both of them favorably react with O_2. Studying the reaction of the reduced pyrazine derivatives with O_2 can be expected to clarify the mechanism of the electrocatalytic reduction of O_2 by PQL-modified electrodes.

In the present work, the electrocatalytic reduction of O_2 by four pyrazine derivatives (i.e., 2,3,5,6-tetramethylpyrazine, 2,3-dimethylquinoxaline, 2,3-diphenylquinoxaline, and phenazine) in acidic solutions was studied by cyclic and rotating disk voltammetry as well as molecular orbital (MO) calculations using the MOPAC PM5 method. In sufficiently acidic solutions, the pyrazine derivatives were found to be electrochemically reduced by two successive one-electron processes, which enabled us to compare the reactivity of the one-electron and two-electron reduced forms with O_2 under the same conditions. According to the voltammetric results as well as MO calculations, the reaction mechanism of these pyrazine derivatives with O_2 was proposed and discussed.

Experimental Section

Materials. 2,3,5,6-Tetramethylpyrazine, 2,3-dimethylquinoxaline, 2,3-diphenylquinoxaline, and phenazine (Kanto Chemical Co. Inc., Japan) were of analytical grade and used as received. Because of the low solubility of 2,3-diphenylquinoxaline in water, a 1:4 v/v DMF−water solution (i.e., the volume percent of DMF is 20% (v/v)) was used in all of the electrochemical measurements to allow us to compare its electrochemical behavior with that of the other pyrazine derivatives. Solutions of pH 0.95, 2.62, 4.70, and 7.00 were prepared by mixing 0.1 M $HClO_4$, 25 mM citrate buffer (pH 2.35), 25 mM citrate buffer (pH 4.41), or 25 mM phosphate buffer aqueous solution with DMF in a volume ratio of 4:1. Each solution contained 0.08 M $NaClO_4$ as the supporting electrolyte.

The kinematic viscosity (ν) of the DMF−water solution containing 0.08 M $HClO_4$ and 0.08 M $NaClO_4$ was measured using an Ubbelohde viscometer at room temperature. The ν value of this solution was determined to be 0.01328 $cm^2\ s^{-1}$.

Electrochemical Measurements. Cyclic and rotating disk voltammetric measurements were performed with a CHI 604A electrochemical analyzer (CHI Instruments Inc.) using a conventional two-compartment three-electrode cell with a GC

* Corresponding author. E-mail: ohsaka@echem.titech.ac.jp. Tel: +81-45-9245404. Fax: +81-45-9245489.
† Department of Electronic Chemistry, Tokyo Institute of Technology.
‡ Department of Organic and Polymeric Materials, Tokyo Institute of Technology.
§ Kyushu University.

10.1021/jp036024k CCC: $27.50
Published on Web 02/24/2004

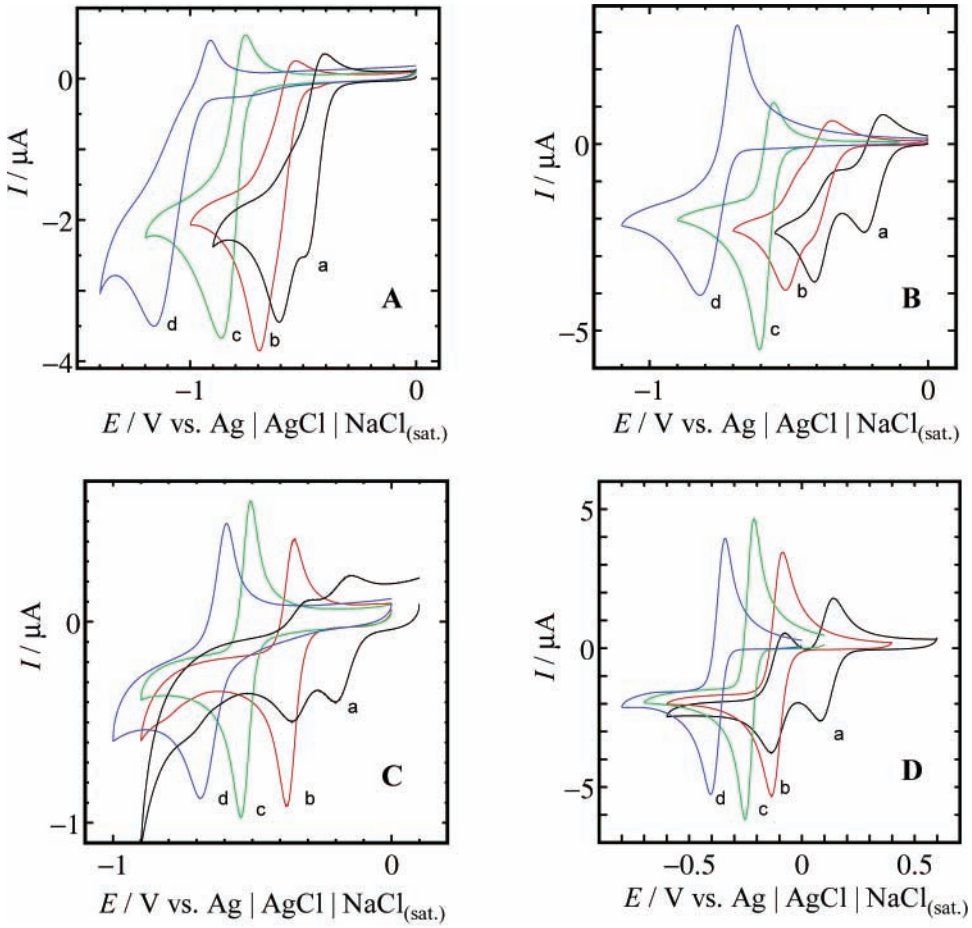


Figure 1. Cyclic voltammograms of 0.5 mM (A) 2,3,5,6-tetramethylpyrazine, (B) 2,3-dimethylquinoxaline, and (D) phenazine and 0.05 mM (C) 2,3-diphenylquinoxaline at the GC electrode in N_2-saturated DMF(20%(v/v))−water solutions. Solutions a−d were prepared by mixing (a) 0.1 M $HClO_4$ (pH 0.95), (b) 25 mM citrate buffer (pH 2.62), (c) 25 mM citrate buffer (pH 4.70), and (d) 25 mM phosphate buffer (pH 7.00) aqueous solutions with DMF in a volume ratio of 4:1. Each solution contained 0.08 M $NaClO_4$ as the supporting electrolyte. The scan rate was 10 mV s^{-1}.

working electrode, a Pt wire auxiliary electrode, and a NaCl-saturated Ag|AgCl reference electrode (Ag|AgCl|$NaCl_{(sat)}$). In the case of the measurements in the absence of O_2, N_2 gas was directly bubbled into the cell solution for 20 min to remove O_2 before the electrochemical measurements and was flushed over the cell solution throughout the measurements. All of the electrochemical measurements were performed at room temperature (25 ± 1 °C).

GC working electrodes were polished with fine emery paper and then with alumina powder (particle size: 1.0 and 0.06 μm; Marumoto Kogyo Co. Ltd.) on a polishing microcloth wetted with Milli-Q water before use. The GC electrodes were then carefully sonicated in Milli-Q water for 10 min.

Quantum Mechanical Calculations. Semiempirical molecular orbital calculations by the MOPAC PM5 method implemented in the CAChe package (version 5.02, Fujitsu) on a Fujitsu workstation were performed on the pyrazine derivatives and their reduced forms with different extents of protonation as well as the reaction coordinates of the reactions of reduced pyrazine derivatives with O_2. The restricted Hartree−Fock (RHF) or unrestricted Hartree−Fock (UHF) schemes were used, depending on whether closed-shell or open-shell systems (radicals) were considered. In the calculations of the heat of formation and frontier densities of the pyrazine derivatives, RSOLV = 1.0 and ESP = 78.4 were used for COMOS calculations to include the solvent effect.[20] Reaction coordinate calculations for the reactions of reduced pyrazine derivatives with O_2 were performed on their unsolvated reactants. The PRECISE option was used in all of the calculations to improve the accuracy of the results.

Results and Discussion

Electrochemical Generation of One-Electron and Two-Electron Reduced Pyrazine Derivatives and Their Reactions with Molecular Oxygen. To compare the electrocatalytic reactivity of the one-electron and two-electron reduced pyrazine derivatives, first it is necessary to find suitable conditions under which both one-electron and two-electron reduced pyrazine derivatives can be electrochemically generated. Figure 1 shows cyclic voltammograms of pyrazine derivatives obtained in the N_2-saturated DMF(20%(v/v))−water solutions with different solution pH values. In moderately acidic solution (e.g., at pH 4.70), the individual derivatives showed one pair of redox peaks. Under this condition, they are reduced by a single two-electron process. However, in sufficiently concentrated acidic solution (e.g., at pH 0.95), two pairs of redox peaks were observed for each of the derivatives (curve a in Figure 1), which suggest that their reductions proceed in two successive one-electron processes. Such pH-dependent one-electron and two-electron redox processes can be also supported by comparing the peak currents, for example, of curves a and c. That is, the sum of the peak currents for the first and second redox steps of curve a is almost equal to the peak current for the single redox step of curve c. The results agree with the previous reports.[21−24] The electrochemical behavior of the derivatives in the same solution (pH 0.95) as for curves a in Figure 1 was also studied by rotating

TABLE 1: Reaction Parameters of the Pyrazine Derivatives Obtained by Rotating Disk Voltammetry[a]

compounds	$D_{Py} \times 10^6$ $cm^2\ s^{-1}$	$E_{1/2}{}^{1st}$ V vs Ag/AgCl	$E_{1/2}{}^{2nd}$ V vs Ag/AgCl	$k_1{}^{1st}$ $M^{-1}\ s^{-1}$	$k_1{}^{2nd}$ $M^{-1}\ s^{-1}$
tetramethylpyrazine	4.2 ± 0.1	-0.456 ± 0.005	-0.664 ± 0.005	$(2.5 \pm 0.3) \times 10^7$	
dimethylquinoxaline	4.1 ± 0.1	-0.180 ± 0.005	-0.377 ± 0.005	$(1.1 \pm 0.2) \times 10^4$	$(1.0 \pm 0.5) \times 10^5$
diphenylquinoxaline	2.5 ± 0.1	-0.173 ± 0.005	-0.348 ± 0.005	$(3.7 \pm 0.3) \times 10^3$	$(2.9 \pm 0.5) \times 10^6$
phenazine	4.2 ± 0.1	0.116 ± 0.005	-0.105 ± 0.005	0	0

[a] Superscripts 1st and 2nd represent the first and second reduction steps of each pyrazine derivative, respectively.

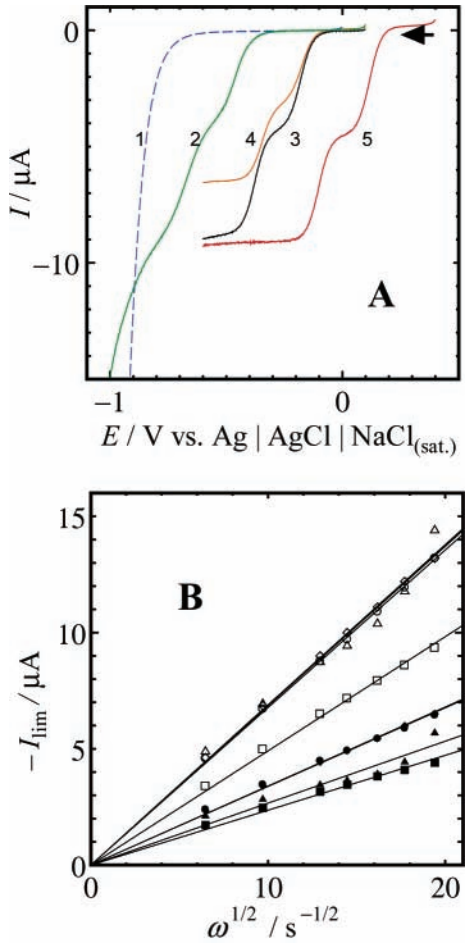


Figure 2. (A) Typical Rotating disk voltammograms obtained at the GC electrode for the reduction of 0.132 mM (2) 2,3,5,6-tetramethylpyrazine, (3) 2,3-dimethylquinoxaline, (4) 2,3-diphenylquinoxaline, and (5) phenazine in N_2-saturated DMF(20%(v/v))−water solutions. The solutions contained 0.08 M $NaClO_4$ and 0.08 M $HClO_4$ (pH 0.95). The rotation rate was 1600 rpm; the scan rate was 5 mV s^{-1}. The dashed line (1) shows the background response. (B) Levich plots of the first and second reduction steps of the pyrazine derivatives. (▲, △) 2,3,5,6-tetramethylpyrazine, (●, ○) 2,3-dimethylquinoxaline, (■, □) 2,3-diphenylquinoxaline, and (◆, ◇) phenazine. Solid symbols: first reduction step; and open symbols: second reduction step.

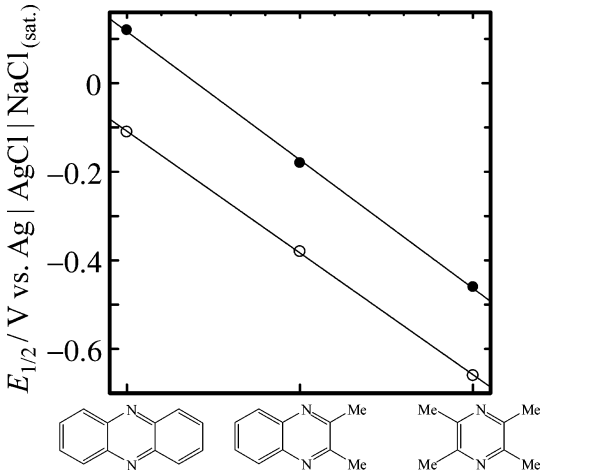


Figure 3. Relationship between half-wave potentials and relative $\Sigma\sigma$ values of phenazine, 2,3-dimethylquinoxaline, and 2,3,5,6-tetramethylpyrazine. Solid symbols: first redox step; open symbols: second redox step.

disk voltammetry. The obtained voltammograms showed two-step reduction processes with almost the same limiting current values (Figure 2A). These results again suggest that each derivative undergoes two successive one-electron reductions in this solution and that both the one-electron reduced form (the radical) and the two-electron reduced form can be generated electrochemically in this acidic solution. Therefore, we can compare the electrochemical reactivity of the one-electron and two-electron reduced forms. Figure 2B shows the Levich plots obtained for the two reduction steps of the individual derivatives. The diffusion coefficients of the derivatives were evaluated from the slopes of these linear plots using the Levich equation and are summarized in Table 1. The half-wave potentials ($E_{1/2}{}^{1st}$ and $E_{1/2}{}^{2nd}$) are also summarized in Table 1. The values of $E_{1/2}{}^{1st}$ (and $E_{1/2}{}^{2nd}$) of 2,3,5,6-tetramethylpyrazine, 2,3-dimethylquinoxaline, and phenazine were plotted against the relative values of their Hammett substituent constants ($\Sigma\sigma$) by taking the pyrazine ring as a reaction center and assuming that the difference ($\Delta\Sigma\sigma$) in $\Sigma\sigma$ values between 2,3,5,6-tetramethylpyrazine and 2,3-dimethylquinoxaline is the same as that between 2,3-dimethylquinoxaline and phenazine because the exact $\Sigma\sigma$ values of 2,3-dimethylquinoxaline and phenazine are unknown. The obtained plots are shown in Figure 3. Good linear correlations between $E_{1/2}{}^{1st}$ (and $E_{1/2}{}^{2nd}$) and $\Sigma\sigma$ were obtained, indicating that the first and second redox reactions of these derivatives obey Hammett's rule; that is, the natures of the radicals and two-electron reduced forms of the pyrazine derivatives are similar across the series.[25,26]

The reactions of reduced pyrazine derivatives with O_2 were first studied by cyclic voltammetry. Figure 4 shows the typical cyclic voltammograms of 2,3-diphenylquinoxaline in N_2- or air-saturated DMF(20%(v/v))−water acidic solutions. For comparison, the cyclic voltammogram obtained for the reduction of O_2 in the absence of 2,3-diphenylquinoxaline is also given in Figure 4. The reduction peak of O_2 was observed at ca. −0.63 V versus Ag|AgCl|$NaCl_{(sat)}$. In N_2-saturated solution, 2,3-diphenylquinoxaline gave two pairs of redox peaks with formal potentials at ca. −0.17 and −0.34 V, corresponding to the two one-electron redox steps. When the solution contained O_2, both of the reduction peak currents of 2,3-diphenylquinoxaline increased (as pointed out by arrows in Figure 5), and the corresponding oxidation peaks disappeared. This indicates that 2,3-diphenylquinoxaline can catalyze the O_2 reduction. In other words, the reduced forms of 2,3-diphenylquinoxaline can react with O_2. The cyclic voltammograms of 2,3,5,6-tetramethylpyrazine and 2,3-dimethylquinoxaline also showed similar behavior, whereas the cyclic voltammogram of phenazine was independent

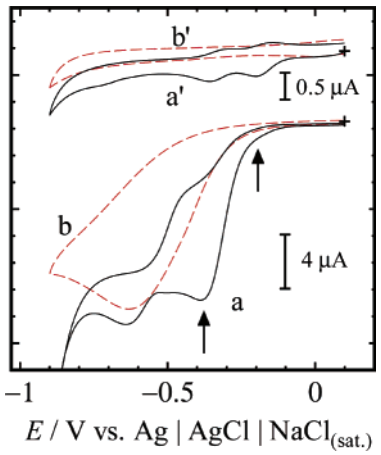


Figure 4. Cyclic voltammograms obtained at the GC electrode in (a', b') N_2- and (a, b) air-saturated DMF(20%(v/v))−water solutions (pH 0.95) containing 0.08 M $HClO_4$ and 0.08 M $NaClO_4$, (a, a') in the presence of 0.05 mM 2,3-diphenylquinoxaline, and (b, b') in the absence of 2,3-diphenylquinoxaline. The scan rate was 10 mV s^{-1}.

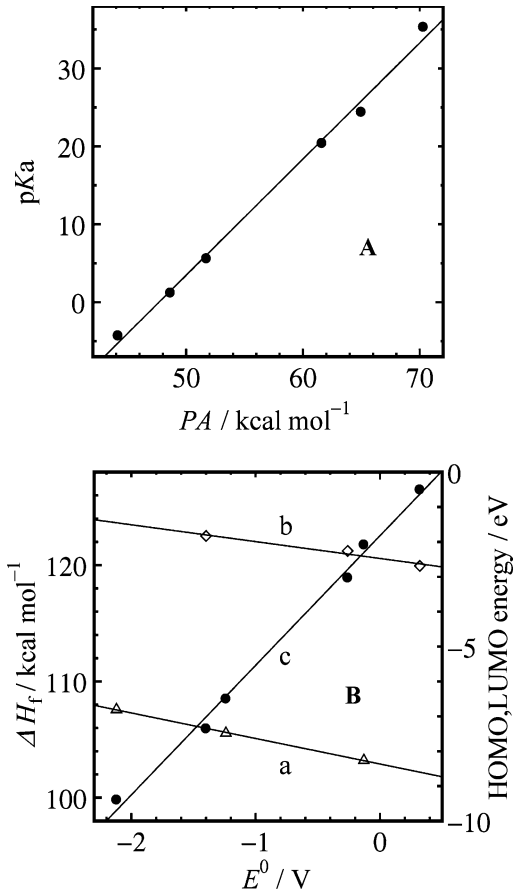
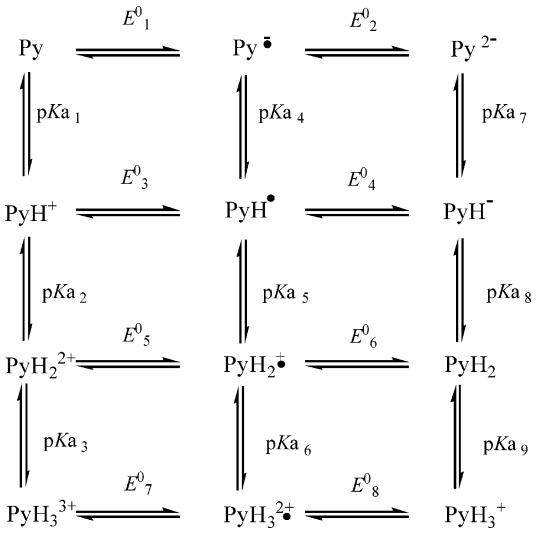


Figure 5. (A) Relationship between the pK_a values and proton affinity values of the redox forms of phenazine. (B) Relationships between the redox potentials of phenazine and its (a) HOMO, (b) LUMO, and (c) ΔH_f energies.

of the presence of O_2. This suggests that the reduced forms of phenazine cannot react with the O_2 molecule.

Protonation of the Pyrazine Derivatives. Before the discussion of the reaction mechanism of the reduced pyrazine derivatives with O_2, it is necessary to confirm which species exist in the vicinity of the electrode surface and react with O_2. The cyclic voltammograms of the derivatives at different pH values (Figure 1) show that their redox potentials shift negatively with the increase of solution pH. This indicates that protons

SCHEME 1: Two-Electron Three-Proton Reactions of Pyrazine Derivatives



are involved in their redox reactions. The influence of fast protonation on the electrochemical reaction was treated theoretically by Laviron et al.[27−33] For the case in which two electrons are involved in the reaction, a so-called nine-membered square scheme ($2e^-$, $2H^+$) was suggested. Because further protonation of the two-electron two-proton reduced forms of the derivatives under consideration is possible, a 12-membered scheme was used to describe their redox reactions (Scheme 1). On the basis of the pK_a values of the redox forms of the derivatives, we can know which species (shown in Scheme 1) exists in the vicinity of the electrode surface and reacts with O_2 at a given electrode potential. Unfortunately, to our knowledge, only the pK_a values of the redox forms of phenazine have been reported.[30,34]

The pK_a value has a good linear relationship with proton affinity (*PA*).[35,36] Using the heat of formation calculated by the semiempirical MO method, we can use eq 2 to calculate the proton affinity of a compound Py (representing each molecule of the pyrazine derivatives) according to the protonation reaction (eq 1).

$$\mathrm{Py} + \mathrm{H^+} \rightleftharpoons \mathrm{PyH^+} \tag{1}$$

$$PA = -H_f(\mathrm{PyH^+}) + H_f(\mathrm{H^+}) + H_f(\mathrm{Py}) \tag{2}$$

where $H_f(\mathrm{PyH^+})$, $H_f(\mathrm{H^+})$, and $H_f(\mathrm{Py})$ represent the heat of formation of PyH^+, H^+, and Py, respectively. $H_f(H^+)$ was evaluated as 155.35 kcal mol^{-1} by the MOPAC PM5 method. This procedure for calculating *PA* can be also applied to the other species (e.g., the *PA* value of PyH^+ can be calculated from the values of the heat of formation of PyH^+, H^+, and PyH_2^{2+}; see Schemes 1 and 2).

The plot of the pK_a values of the redox forms of phenazine against their proton affinities is shown in Figure 5A. It shows a good linear relation of $pK_a = -71.044 + 1.49 \times PA$ (kcal mol^{-1}) with the correlation coefficient of 0.99. Because of the similarity in structure between phenazine and the other derivatives (2,3,5,6-tetramethylpyrazine, 2,3-dimethylquinoxaline, and 2,3-diphenylquinoxaline),[35,36] the plot in Figure 5A was used as the working curve to calculate the pK_a values of their redox forms. The pK_a values calculated for all four pyrazine derivatives are summarized in Scheme 2.

The calculation results of pK_a values do not agree very well with the experimental results,[37,38] but they can be reasonably used to confirm the protonation states of the derivatives under

SCHEME 2 [a] Heat of Formation, pK_a, and E^0 Values of the Pyrazine Derivatives Obtained by MO Calculations

Phenazine

Py (66.3)	E^0_1 = -1.49	$Py^{-\bullet}$ (-39.6)	E^0_2 = -2.04	Py^{2-} (-139.4)
pKa_1 = 1.4		pKa_4 = 20.8		pKa_7 = 33.8
PyH^+ (173.1)	E^0_3 = -0.33	$PyH^\bullet$ (54.1)	E^0_4 = -1.26	PyH^- (-54.4)
pKa_2 = -5.3		pKa_5 = 6.0		pKa_8 = 25.9
PyH_2^{2+} (284.3)	E^0_5 = 0.35	$PyH_2^{+\bullet}$ (157.8)	E^0_6 = -0.07	PyH_2 (36.0)
pKa_3 = -73		pKa_6 = -17.7		pKa_9 = 7.0
PyH_3^{3+} (440.6)	E^0_7 = 3.66	$PyH_3^{2+\bullet}$ (277.3)	E^0_8 = 1.41	PyH_3^+ (139.0)

2,3,5,6-tetramethylpyrazine

Py (-1.0)	E^0_1 = -3.45	$Py^{-\bullet}$ (-85.1)	E^0_2 = -5.88	Py^{2-}(-142.1)
pKa_1 = 5.2		pKa_4 = 29.6		pKa_7 = 54.8
PyH^+ (103.1)	E^0_3 = -1.99	$PyH^\bullet$ (2.7)	E^0_4 = -4.38	PyH^- (-71.1)
pKa_2 = -1.9		pKa_5 = 11.1		pKa_8 = 36.1
PyH_2^{2+}	E^0_5 = -1.20	$PyH_2^{+\bullet}$ (102.9)	E^0_6 = -2.88	PyH_2 (12.4)
pKa_3 = -100.1		pKa_6 = -26.4		pKa_9 = 12.9
PyH_3^{3+}	E^0_7 = 3.21	$PyH_3^{2+\bullet}$	E^0_8 = -0.53	PyH_3^+ (111.5)

2,3-dimethylquinoxaline

Py (27.3)	E^0_1 = -2.69	$Py^{-\bullet}$ (-65.3)	E^0_2 = -4.78	Py^{2-}(-134.6)
pKa_1 = 3.30		pKa_4 = 23.0		pKa_7 = 39.1
PyH^+ (132.7)	E^0_3 = -1.51	$PyH^\bullet$ (27.0)	E^0_4 = -3.81	PyH^- (-53.0)
pKa_2 = -3.4		pKa_5 = 9.6		pKa_8 = 31.7
PyH_2^{2+} (242.6)	E^0_5 = -0.73	$PyH_2^{+\bullet}$ (128.2)	E^0_6 = -2.49	PyH_2 (33.4)
pKa_3 = -94.86		pKa_6 = -26.4		pKa_9 = 6.7
PyH_3^{3+} (413.6)	E^0_7 = 3.37	$PyH_3^{2+\bullet}$ (253.5)	E^0_8 = -0.51	PyH_3^+ (136.6)

2,3-diphenylquinoxaline

Py (107.7)	E^0_1 = -1.49	$Py^{-\bullet}$ (-1.8)	E^0_2 = -4.10	Py^{2-}(-75.1)
pKa_1 = 4.81		pKa_4 = 32.1		pKa_7 = 45.2
PyH^+ (212.1)	E^0_3 = 0.14	$PyH^\bullet$ (88.0)	E^0_4 = -3.31	PyH^- (2.4)
pKa_2 = -10.2		pKa_5 = 0.5		pKa_8 = 28.4
PyH_2^{2+} (326.6)	E^0_5 = 0.78	$PyH_2^{+\bullet}$ (195.3)	E^0_6 = -1.64	PyH_2 (91.1)
pKa_3 = -56.5		pKa_6 = -14.3		pKa_9 = 15.1
PyH_3^{3+} (472.0)	E^0_7 = 3.31	$PyH_3^{2+\bullet}$ (312.5)	E^0_8 = 0.11	PyH_3^+ (188.7)

[a] Values given in parentheses represent the heat of formation (kcal mol^{-1}) of individual species.

the present experimental conditions. Thus, we can assume from the pK_a values of the derivatives that all of them are protonated by one proton at pH 1. Similarly, the calculated pK_a values also show that the one-electron reduced forms (the radicals) and the two-electron reduced forms are protonated to become cations in this solution. And also, as the above discussion shows that the $E_{1/2}$ values of the pyrazine derivatives follow Hammett's rule (Figure 3), the redox processes of the pyrazine derivatives can be expressed similarly to that of the substituted pyrazines in aqueous acidic solution[39] by eqs 3 and 4.

$$Py + H^+ \rightleftharpoons PyH^+ \quad (1)$$

$$PyH^+ + e^- + H^+ \rightleftharpoons PyH_2^{+\bullet} \quad (3)$$

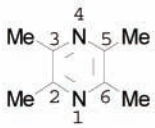
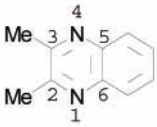
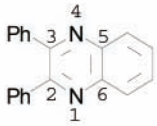
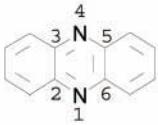
$$PyH_2^{+\bullet} + e^- + H^+ \rightleftharpoons PyH_3^+ \quad (4)$$

In accordance with Koopmans' theorem,[36] the redox potentials (E° values) of these derivatives depend linearly upon their highest occupied molecular orbital (HOMO) energy as well as the ionization potential for their oxidation; consequently, the redox potentials have a linear relationship with the lowest unoccupied molecular orbital (LUMO) energy of the derivatives and also with their electron affinity for their reduction. Though the redox potentials of the first and second redox steps of phenazine with different protonation states show linear relationships with the HOMO energies of two-electron reduced states of phenazine (Py^{2-}, PyH^-, and PyH_2) and the LUMO energies of oxidized states of phenazine (Py, PyH^+, and PyH_2^{2+}), respectively (Figure 5B, a and b), it would be better to associate all of the redox potential data of phenazine with one quantum chemical descriptor.

Pankratov et al. have found a correlation between the E° values for diphenylamine and its derivatives and the differences in formation energies (ΔH_f values) between the cation radicals (i.e., the oxidation intermediates) in acidic media and the parent molecules.[40] By applying the same approach to the phenazine system, we plotted the redox potentials for the first and second steps of phenazine with different protonation states against the formation-energy differences between the oxidized states and the one-electron reduced states (radicals) or between the radicals and the two-electron reduced states. Consequently, we obtained a good linear relation of $E^0(V) = -10.94 + 0.0892 \times \Delta H_f$ (kcal mol^{-1}) with a correlation coefficient of 0.99 (Figure 5B, c). Thus, by analogy to the plot of pK_a versus *PA* in Figure 5A, this linear relationship can also be used as the working curve to calculate the redox potentials of 2,3,5,6-tetramethylpyrazine, 2,3-dimethylquinoxaline, and 2,3-diphenylquinoxaline. Therefore, the values of H_f obtained from the MO calculation using MOPAC PM5 method were used for evaluating both the pK_a and E° values of the pyrazine derivatives, as given in Scheme 2.

Mechanism of the Reaction of Reduced Pyrazine Derivatives with Molecular Oxygen. As discussed above, the pK_a values of the pyrazine derivatives suggest that the one-electron and two-electron reduced forms exist as $PyH_2^{+\bullet}$ and PyH_3^+, respectively, in the acidic solution used in Figure 4. Thus, also in the case of 2,3-diphenylquinoxaline, 2,3-dimethylquinoxaline, and 2,3,5,6-tetramethylpyrazine, these species are the ones that react with O_2. Because the redox-active moiety of the pyrazine derivatives is similar to that of flavin, we believe that the mechanism of the reaction of the reduced forms of the pyrazine derivatives with O_2 is the same as that of the reduced flavin with O_2. It has been reported that the formation of C_{4a}-peroxyflavin from the reduced flavin and O_2 involves a rate-limiting intermolecular one-electron transfer to form a radical pair composed of a neutral flavin semiquinone ($FH^\bullet$) and a superoxide anion ($O_2^{\bullet-}$), which is followed by a radical recombination to generate the flavin peroxide.[41,42] According to the frontier orbital theory, the frontier densities of the atoms in the molecule can be treated as a quantum chemical descriptor to determine the reaction site of the molecule.[43] In the present system, the oxygen molecule works as an electron acceptor, and thus the reaction forming the peroxide intermediate may be treated as an electrophilic reaction. However, because the oxygen molecule in the ground state has two unpaired electrons, it may also be treated as a radical. Therefore, we calculated both the electrophilic frontier densities and radical frontier densities of the atoms in the reduced pyrazine derivatives, as shown in Table 2. Except for the reduced forms of phenazine, in the case of the other derivatives, both the electrophilic frontier densities and radical frontier densities show that the C_2 atoms have the highest frontier densities and are the most favorable sites to react with oxygen molecules. This site (C_2) is comparable to the C_{4a} site in the reduced flavin structure. Yamada et al. have presumed the formation of a C_2-peroxide intermediate in the reaction of O_2 with the photoreduced pyrazine derivatives.[44] Our calculations confirm their presumption and also suggest that the catalytic reduction of O_2 by the reduced forms of 2,3,5,6-tetramethylpyrazine, 2,3-dimethylquinoxaline, and

TABLE 2: Frontier Densities of the Reduced Forms of the Pyrazine Derivatives

Compounds	$PyH_2^{+\bullet}$		PyH_3^+	
	Electrophilic Frontier Density	Radical Frontier Density	Electrophilic Frontier Density	Radical Frontier Density
Tetramethyl -pyrazine				
Dimethyl -quinoxaline				
Diphenyl -quinoxaline				
Phenazine				

2,3-diphenylquinoxaline proceeds by the same mechanism as that of the catalytic reduction of O_2 by the reduced flavin. Therefore, the following reaction schemes may be proposed.

For the catalytic reduction of O_2 by the one-electron reduced form of pyrazine derivatives,

$$PyH^+ + e^- + H^+ \rightleftharpoons PyH_2^{+\bullet} \quad (3)$$

$$PyH_2^{+\bullet} + O_2 \xrightarrow{k_1} PyH_2^{+\bullet}{-}O_2 \quad (5)$$

$$PyH_2^{+\bullet}{-}O_2 \xrightarrow{k_2} PyH^+ + HO_2^{\bullet} \quad (6)$$

$$PyH_2^{+\bullet} + HO_2^{\bullet} \xrightarrow{k_3} PyH^+ + H_2O_2 \quad (7)$$

The net reaction of reactions 5 to 7 is

$$2PyH_2^{+\bullet} + O_2 \xrightarrow{k_1} 2PyH^+ + H_2O_2 \quad (8)$$

For the catalytic reduction of O_2 by the two-electron reduced form of pyrazine derivatives,

$$PyH_2^{+\bullet} + e^- + H^+ \rightleftharpoons PyH_3^+ \quad (4)$$

$$PyH_3^+ + O_2 \xrightarrow{k_1} PyH_3^+{-}O_2 \quad (9)$$

$$PyH_3^+{-}O_2 \xrightarrow{k_2} PyH_2^{+\bullet} + HO_2^{\bullet} \quad (10)$$

$$PyH_2^{+\bullet} + HO_2^{\bullet} \xrightarrow{k_3} PyH^+ + H_2O_2 \quad (11)$$

The net reaction of reactions 9 to 11 is

$$PyH_3^+ + O_2 \xrightarrow{k_1} PyH^+ + H_2O_2 \quad (12)$$

where the complexes between the one-electron and two-electron reduced pyrazine derivatives and molecular oxygen are denoted by $PyH_2^{+\bullet}{-}O_2$ and $PyH_3^+{-}O_2$, respectively. Reactions 5 and 9 were considered to be the rate-determining steps ($k_1 \ll k_2$, k_3).[41,42]

The different frontier density values of the reduced phenazines from those of the other pyrazine derivatives, as shown in Table 2, suggest that the reactivity of the reduced phenazines would be different from that of the reduced forms of the other pyrazine derivatives. In fact, as demonstrated above, the latter is significantly reactive to molecular oxygen, but the former is unreactive. Unfortunately, because the redox potential of O_2 under the present experimental conditions (i.e., DMF-(20%(v/v))−water acidic solution (pH 0.95) containing 0.08 M $HClO_4$ and 0.08 M $NaClO_4$) is unknown, we cannot determine if the reduction of O_2 by the reduced phenazines is unfavorable thermodynamically or kinetically.

Kinetics of the Reaction of the Reduced Pyrazine Derivatives with Molecular Oxygen. Rotating disk electrode voltammetry is much more convenient than cyclic voltammetry for the kinetic study of electrocatalytic reactions.[45−47] Figure 6 shows the typical steady-state voltammograms obtained at the rotating GC disk electrode in N_2- or air-saturated solutions containing each pyrazine derivative at 0.132 mM. At first glance, we can see that the difference in the voltammograms obtained under N_2 and O_2 atmospheres largely depends on the kind of pyrazine derivative. The increase in the limiting current obtained in the presence of O_2 compared with its absence reflects the reactivity of the reduced pyrazine derivatives toward O_2. In the case of phenazine, its voltammograms are independent of the presence and absence of O_2 (curves 5 and 5'), in agreement with the cyclic voltammetric results, indicating that both the one-electron and two-electron reduced forms of phenazine cannot react with O_2. However, in the case of 2,3,5,6-tetramethylpyrazine (curves 2 and 2'), the reduction current increased greatly, and the half-wave potential shifted positively in the presence of O_2. This demonstrates that the reduced forms of 2,3,5,6-tetramethylpyrazine have excellent catalytic activity toward O_2 reduction. A slight increase in the reduction currents of 2,3-dimethylquinoxaline and 2,3-diphenylquinoxaline under an O_2

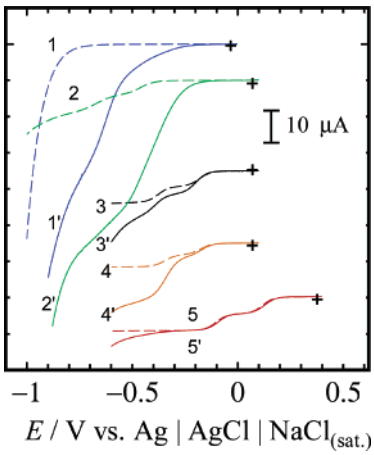


Figure 6. Rotating disk voltammograms obtained at the GC electrode in (− − −) N_2- and (—) air-saturated DMF(20%(v/v))−water solutions (pH 0.95) containing (1) 0.08 M $NaClO_4$, 0.08 M $HClO_4$ and (2) (1) + 0.132 mM 2,3,5,6-tetramethylpyrazine, (3) (1) + 0.132 mM 2,3-dimethylquinoxaline, (4) (1) + 0.132 mM 2,3-diphenyl -quinoxaline, and (5) (1) + 0.132 mM phenazine. The rotation rate was 1600 rpm; the scan rate was 5 mV s^{-1}.

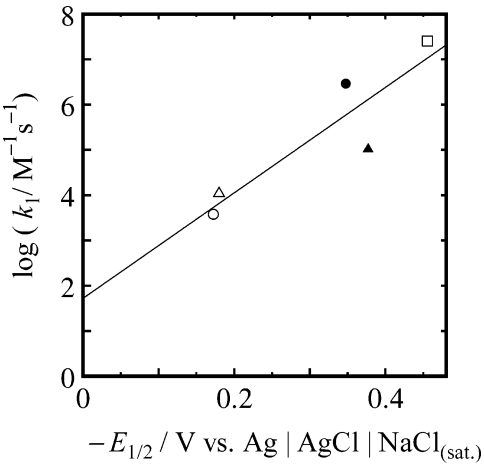


Figure 7. log plot of k_1 vs $E_{1/2}$ for the reactions of reduced pyrazine derivatives with molecular oxygen. (○) $PyH_2^{+\bullet}$ of 2,3-diphenylquinoxaline; (△) $PyH_2^{+\bullet}$ of 2,3-dimethylquinoxaline; (□) $PyH_2^{+\bullet}$ of 2,3,5,6-tetramethylpyrazine; (●) PyH_3^+ of 2,3-diphenylquinoxaline; and (▲) PyH_3^+ of 2,3-dimethylquinoxaline.

atmosphere (curves 3' and 4') indicates that the reactivity of these reduced forms toward O_2 is low compared with that of the reduced forms of 2,3,5,6-tetramethylpyrazine. A close inspection of curves 3, 3', 4, and 4' suggests that for the one-electron reduced forms the reactivity of 2,3-dimethylquinoxaline toward O_2 is higher than that of 2,3-diphenylquinoxaline, whereas for the two-electron reduced forms, 2,3-diphenylquinoxaline is more reactive to O_2 than is 2,3-dimethylquinoxaline.

Several papers have reported the determination of the rate constants of homogeneous electron-transfer reactions by rotating disk electrode voltammetry.[48−50] Nolan et al. have developed a numerical solution of rotating disk voltammograms for both pseudo-first-order and second-order homogeneous reactions and have applied it to the determination of the rate constants of the Fenton reaction and the reactions between O_2 and viologens.[15,51] In the present study, we applied this method to the determination of rate constants for reactions between O_2 and the reduced forms of 2,3-dimethylquinoxaline and 2,3-diphenylquinoxaline. To minimize the direct reduction of O_2 at the GC electrode surface, the concentration ratios of O_2 to 2,3-dimethylquinoxaline and to 2,3-diphenylquinoxaline were controlled to be exactly 4, which also meets the condition for the second-order case in the working curves presented by Nolan et al.[15] The dimensionless current ratio R was defined as $R = i_0/i_k$, where i_0 and i_k are the limiting currents obtained in the absence and presence of O_2, respectively. According to the working curve, the second-order kinetic parameter k, which is defined by eq 13, could be obtained.

$$k = (\nu/D_{Py})^{1/3} k_1 C_{Py,b} \omega^{-1} \qquad (13)$$

where D_{Py} and $C_{Py,b}$ are the diffusion coefficient and concentration of 2,3-dimethylquinoxaline and 2,3-diphenylquinoxaline, respectively. ν is the kinematic viscosity of the solution, ω is the rotating rate of the electrode, and k_1 is the second-order rate constant of the homogeneous reaction. From the slopes of the k versus ω^{-1} plots, the rate constants of reactions between O_2 and the reduced forms of 2,3-dimethylquinoxaline and 2,3-diphenylquinoxaline were evaluated and are summarized in Table 1.

Because of the fast reaction of O_2 with the reduced forms of 2,3,5,6-tetramethylpyrazine as well as the direct reduction of O_2 at the GC electrode surface, which could not be ignored experimentally, we could not determine the rate constants of the second-order reactions between O_2 and the reduced forms of 2,3,5,6-tetramethylpyrazine by the same method as mentioned above. According to Andrieux et al., the relation of the half-wave potentials of the rotating disk voltammograms obtained in the presence and absence of O_2 for the electrocatalytic reduction of O_2 by 2,3,5,6-tetramethylpyrazine can be expressed by the following equation:[47]

$$E'_{1/2} - E_{1/2} = 30 \times \log\left(\frac{2\lambda_1}{r}\right) \qquad (14)$$

with $r = C_{O2,b}/C_{Py,b}$ and $\lambda_1 = k_1 C_{Py,b} \delta^2 D_{Py}^{-1}$, where $E_{1/2}$ and $E'_{1/2}$ are the half-wave potentials obtained in the absence and presence of O_2, respectively. $C_{O2,b}$ and $C_{Py,b}$ are the concentrations of O_2 and 2,3,5,6-tetramethylpyrazine, respectively. D_{Py} is the diffusion coefficient of 2,3,5,6-tetramethylpyrazine. δ is the diffusion layer thickness, which is defined as $\delta = 1.61 D_{Py}^{1/3} \nu^{1/6} \omega^{-1/2}$.

The half-wave potentials of the rotating disk voltammograms for the first reduction step obtained in N_2- and air-saturated DMF−water acidic solutions containing 0.132 mM 2,3,5,6-tetramethylpyrazine (curves 2 and 2' in Figure 6) were estimated to be −0.456 and −0.380 V, respectively, and thus using eq 14, the rate constant of the catalytic reduction of O_2 by the cation radical of 2,3,5,6-tetramethylpyrazine was evaluated to be 2.5×10^7 M^{-1} s^{-1}. Because the half-wave potential of the second reduction step of 2,3,5,6-tetramethylpyrazine is more negative than the reduction potential of O_2 at the GC electrode, we cannot estimate the rate constant of the reaction between O_2 and the two-electron reduced form of 2,3,5,6-tetramethylpyrazine from the present data.

Figure 7 shows the relationship between the k_1 value and the half-wave potential ($E_{1/2}$) of the one-electron and two-electron reduced forms of 2,3-dimethylquinoxaline, 2,3-diphenylquinoxaline, and 2,3,5,6-tetramethylpyrazine. The linear plot of log(k_1) versus $E_{1/2}$ demonstrates the linear free-energy relation of the reactions.[52] Recent work with two flavoproteins, in which the native flavins—flavin adenine dinucleotide (FAD)[53] with *p*-hydroxybenzoate and flavin mononucleotide (FMN)[54] with L-lactate oxidase—were replaced by a series of 6- and 8-substituted flavins of different redox potentials have shown a similar

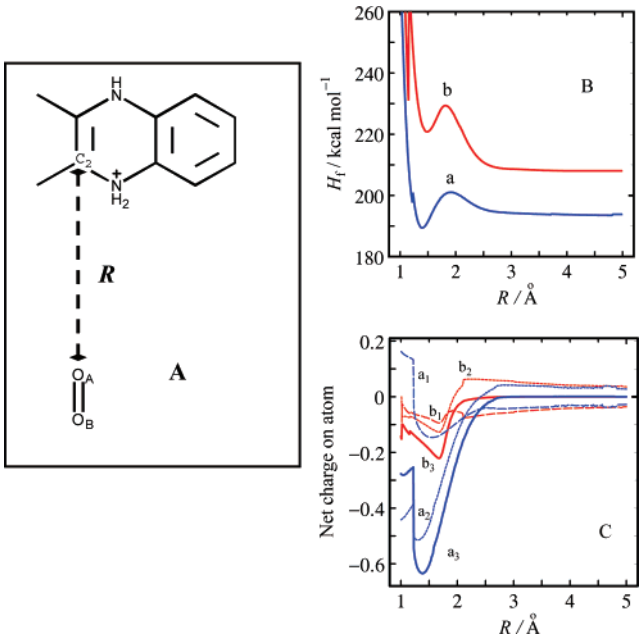


Figure 8. (A) Definition of the distance (R) for the O_2 addition reactions of the reduced forms of 2,3-dimethylquinoxaline (reactions 5 and 9). (B) Reaction coordinate of the O_2 addition reactions (i.e., the dependence of the total heat of formation (H_f) of the reaction systems on R). (a) PyH_3^+ of 2,3-dimethylquinoxaline + O_2 and (b) $PyH_2^{+\bullet}$ of 2,3-dimethylquinoxaline + O_2. (C) Dependence of the net charge of the oxygen atoms on R. The dashed (a_1, b_1), dotted (a_2, b_2), and solid (a_3, b_3) lines are the net charge values of the O_A atom, O_B atom, and O_2 molecule (sum of the net charge of O_A and O_B atoms), respectively. (a) PyH_3^+ of 2,3-dimethylquinoxaline + O_2 and (b) $PyH_2^{+\bullet}$ of 2,3-dimethylquinoxaline + O_2.

linear free-energy relationship when the redox potential of artificial flavin is more positive than that of the native flavin.

The obtained linear free-energy relationship suggests that the reactions of both the one-electron and two-electron reduced forms of the pyrazine derivatives with O_2 proceed by a common reaction mechanism and that their rate constants depend on their thermodynamical driving force, probably because the formation of the C_2-peroxide intermediate proceeds via an electron transfer from the pyrazine moiety to O_2.

To confirm this electron transfer, the reaction coordinates of the rate-determining steps of the electrocatalytic reduction of O_2 by the reduced forms of 2,3-dimethylquinoxaline (i.e., reactions 5 and 9) were calculated as shown in Figure 8B. The total heat of formation of the reaction system (i.e., the oxygen molecule and the reduced form of 2,3-dimethylquinoxaline) was minimized by varying all of the geometrical parameters except for the molecular distance R, which is defined as the distance between the C_2 atom of reduced 2,3-dimethylquinoxaline and the O_A atom of the oxygen molecule (Figure 8A). Figure 8B demonstrates that the reaction of the two-electron reduced form of 2,3-dimethylquinoxaline with O_2 has a lower activation energy and thus a higher reaction rate than that of the one-electron reduced form, which is in agreement with the results obtained by rotating disk voltammetry (Table 1). Figure 8C shows the dependence of the net charge of the oxygen atoms (O_A and O_B) on R. In both cases of the one-electron and two-electron reduced forms of 2,3-dimethylquinoxaline, when an oxygen molecule is close to the reduced forms to form the C_2-peroxide intermediates ($PyH_3^+-O_2$ or $PyH_2^{+\bullet}-O_2$), the sum of the net charge of the oxygen atoms decreases (solid lines a_3 and b_3). In addition, this decreased net charge is mainly due to the decrease in the net charge at the O_B atom of an oxygen molecule (dotted lines a_2 and b_2), which has a longer distance to the C_2 atom rather than that at the O_A atom (dashed lines a_1 and b_1). Similar dependences of the net charge of the oxygen atoms on R were also calculated for the reactions of the reduced forms of 2,3,5,6-tetramethylpyrazine and 2,3-diphenylquinoxaline with O_2. These dependences of the net charge of the oxygen atoms on R clearly demonstrate that the formation of the C_2-peroxide intermediate proceeds via electron transfer from the pyrazine moiety to an oxygen molecule and support the obtained linear free-energy relationship (Figure 8). Such distance dependencies of the net charge of the oxygen atoms have been also obtained by Wada et al. in the analysis of the reaction of reduced flavin with O_2.[41,42]

Conclusions

In sufficiently acidic solution (pH $\approx$ 1), the pyrazine derivatives examined here undergo two successive one-electron reductions. MO calculations show that all of the redox forms of the derivatives in this solution are protonated to form the corresponding cations, and all of the reduced forms, except for phenazine, can react with molecular oxygen. The rate constants of the second-order reactions of the reduced pyrazine derivatives with molecular oxygen were estimated by rotating disk voltammetry. A linear free-energy relationship between the rate constant and the half-wave potential of the pyrazine derivatives was obtained, indicating that the catalytic reductions of molecular oxygen by the one-electron and two-electron reduced forms of pyrazine derivatives proceed by a common reaction mechanism and that their rate-determining step is an electron transfer from the pyrazine moiety to an oxygen molecule. This electron-transfer process could be also confirmed by MO calculations.

Acknowledgment. This work was financially supported by Grants-in-Aid for Scientific Research on Priority Areas (no. 417), Scientific Research (A) (no. 10305064) and Scientific Research (no. 12785164) from the Ministry of Education, Culture, Sports, Science and Technology, Japan. R.W. acknowledges the government of Japan for a Monbu-Kagakusho scholarship.

References and Notes

(1) El-Deab, M. S.; Ohsaka, T. *Electrochim. Acta* **2002**, *47*, 4255.
(2) El-Deab, M. S.; Ohsaka, T. *Electrochem. Commun.* **2002**, *4*, 288.
(3) Yuasa, M. *Hyomen* **1998**, *36*, 157.
(4) Anson, F. C.; Shi, C.; Steiger, B. *Acc. Chem. Res.* **1997**, *30*, 437.
(5) Ferguson-Miller, S.; Babcock, G. T. *Chem. Rev.* **1996**, *96*, 2889.
(6) Mao, L.; Sotomura, T.; Nakatsu, K.; Koshiba, N.; Zhang, D.; Ohsaka, T. *J. Electrochem. Soc.* **2002**, *149*, A504.
(7) Mao, L.; Zhang, D.; Sotomura, T.; Nakatsu, K.; Koshiba, N.; Ohsaka, T. *Electrochim. Acta* **2003**, *48*, 1015.
(8) Collman, J. P.; Fu, L.; Herrmann, P. C.; Zhang, X. *Science* **1997**, *275*, 949.
(9) Ikeda, T.; Kano, K. *Biochim. Biophys. Acta* **2003**, *1647*, 121.
(10) Kano, K.; Ikeda, T. *Electrochemistry* **2003**, *71*, 86.
(11) Tsujimura, S.; Kano, K.; Ikeda, T. *Electrochemistry* **2002**, *70*, 940.
(12) Sarapuu, A.; Vaik, K.; Schiffrin, D. J.; Tammeveski, K. *J. Electroanal. Chem.* **2003**, *541*, 23.
(13) Tammeveski, K.; Kontturi, K.; Nichols, R. J.; Potter, R. J.; Schiffrin, D. J. *J. Electroanal. Chem.* **2001**, *515*, 101.
(14) Tatsumi, H.; Nakase, H.; Kano, K.; Ikeda, T. *J. Electroanal. Chem.* **1998**, *443*, 236.
(15) Nolan, J. E.; Plambeck, J. A. *J. Electroanal. Chem.* **1990**, *294*, 1.
(16) Andrieux, C. P.; Hapiot, P.; Saveant, J. M. *J. Electroanal. Chem.* **1985**, *189*, 121.
(17) Ohsaka, T.; Watanabe, T.; Kitamura, F.; Oyama, N.; Tokuda, K. *J. Chem. Soc., Chem. Commun.* **1991**, 487.
(18) Ohsaka, T.; Watanabe, T.; Kitamura, F.; Oyama, N.; Tokuda, K. *J. Chem. Soc., Chem. Commun.* **1991**, 1072.
(19) Watanabe, T.; Tokuda, K.; Ohsaka, T. *Denki Kagaku* (presently *Electrochemistry*) **1992**, *60*, 455.

(20) Klamt, A.; Schueuermann, G. *J. Chem. Soc., Perkin Trans. 2* **1993**, 799.
(21) Maruyama, M.; Murakami, K.; Saitho, Y. *Chuo Daigaku Rikogaku-bu Kiyo* **1974**, *17*, 147.
(22) Maruyama, M.; Murakami, K. *Nippon Kagaku Kaishi* **1975**, 1742.
(23) Murakami, K.; Maruyama, M. *Chuo Daigaku Rikogakubu Kiyo* **1977**, *20*, 271.
(24) Maruyama, M.; Murakami, K. *J. Electroanal. Chem.* **1979**, *102*, 221.
(25) Nakamura, S. *Denki Kagaku* (presently *Electrochemistry*) **1971**, *39*, 502.
(26) Nakamura, S.; Yoshida, T. *Denki Kagaku* (presently *Electrochemistry*) **1972**, *40*, 714.
(27) Laviron, E. *J. Electroanal. Chem.* **1979**, *101*, 19.
(28) Laviron, E. *J. Electroanal. Chem.* **1981**, *124*, 9.
(29) Laviron, E. *J. Electroanal. Chem.* **1982**, *134*, 205.
(30) Laviron, E.; Roullier, L. *J. Electroanal. Chem.* **1983**, *157*, 7.
(31) Laviron, E. *J. Electroanal. Chem.* **1983**, *146*, 15.
(32) Laviron, E. *J. Electroanal. Chem.* **1984**, *169*, 29.
(33) Laviron, E. *J. Electroanal. Chem.* **1984**, *169*, 23.
(34) Mugnier, Y.; Roullier, L.; Laviron, E. *Electrochim. Acta* **1991**, *36*, 803.
(35) Schmiedekamp, A. M.; Topol, I. A.; Michejda, C. J. *Theor. Chim. Acta* **1995**, *92*, 83.
(36) Pankratov, A. N.; Shchavlev, A. E. *Can. J. Chem.* **1999**, *77*, 2053.
(37) Perrin, D. D. *Dissociation Constants of Organic Bases in Aqueous Solution*; Butterworths: London, 1965.
(38) Perrin, D. D.; Dempsey, B.; Serjeant, E. P. pK_a *Prediction for Organic Acids and Bases*; Chapman and Hall: New York, 1981.
(39) Swartz, J.; Anson, F. C. *J. Electroanal. Chem.* **1980**, *114*, 117.
(40) Pankratov, A. N.; Mushtakova, S. P.; Gribov, L. A. *Zh. Anal. Khim.***1985**, *40*, 1128.
(41) Wada, N.; Sugimoto, T.; Watanabe, H.; Tu, S. C. *Photochem. Photobiol.* **1999**, *70*, 116.
(42) Sugimoto, T.; Wada, N.; Watanabe, H.; Tu, S. C. *Bioluminescence and Chemiluminescence: Perspectives for the 21st Century*; Proceedings of the International Symposium on Bioluminescence and Chemiluminescence, 10th; Sept. 4−8, 1998, Bologna, Italy; p 429.
(43) Fukui, K.; Yonezawa, T.; Nagata, C.; Shingu, H. *J. Chem. Phys.* **1954**, *22*, 1433.
(44) Yamada, K.; Katsuura, K.; Kasimura, H.; Iida, H. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2805.
(45) Andrieux, C. P.; Dumas-Bouchiat, J. M.; Saveant, J. M. *J. Electroanal. Chem.* **1978**, *87*, 39.
(46) Andrieux, C. P.; Blocman, C.; Dumas-Bouchiat, J. M.; M'Halla, F.; Saveant, J. M. *J. Electroanal. Chem.* **1980**, *113*, 19.
(47) Andrieux, C. P.; Dumas-Bouchiat, J. M.; Saveant, J. M. *J. Electroanal. Chem.* **1980**, *113*, 1.
(48) Pleskov, Y. V.; Filinovskii, V. Y. In *The Rotating Disk Electrode*; Pleskov, Yu. V., Filinovskii, V. Yu., Eds.; Studies in Soviet Science; Consultants Bureau: New York, 1976.
(49) Haberland, D.; Landsberg, R. *Ber. Bunsen-Ges. Phys. Chem.* **1966**, *70*, 724.
(50) Opekar, F.; Beran, P. *J. Electroanal. Chem.* **1971**, *32*, 49.
(51) Nolan, J. E.; Plambeck, J. A. *J. Electroanal. Chem.* **1990**, *286*, 1.
(52) Espenson, J. H. *Chemical Kinetics and Reaction Mechanisms*, 2nd ed.; McGraw-Hill: New York, 1995.
(53) Ortiz-Maldonado, M.; Ballou, D. P.; Massey, V. *Biochemistry* **1999**, *38*, 8124.
(54) Ortiz-Maldonado, M.; Gatti, D.; Ballou, D. P.; Massey, V. *Biochemistry* **1999**, *38*, 16636.