λ(Cu-Kα_1) = 1.5406 Å, μ = 32.27 cm^{-1}. The pattern was collected with transmission geometry, from 14 to 110° (2θ). 603 reflections (206 independent) were used with 25 structural parameters and 8 profile parameters. $R_{\text{exp}} = [(\text{N-P})/\Sigma \text{wi}(\text{yi}_{\text{obs}})^2]^{1/2} = 13.8$, $R_{\text{p}} = \Sigma\,|\,\text{yi}_{\text{obs}} - \text{yi}_{\text{calcd}}\,|\,/\Sigma \text{yi}_{\text{obs}} = 17.3$, $R_{\text{wp}} = [\Sigma \text{wi}\,|\,\text{yi}_{\text{obs}} - \text{yi}_{\text{calcd}}\,|^2/\Sigma \text{wi}(\text{yi}_{\text{obs}})^2]^{1/2} = 14.4$, $R_{\text{B}} = \Sigma\,|\,\text{Ik}_{\text{obs}} - \text{Ik}_{\text{calc}}\,|\,/\Sigma \text{Ik}_{\text{obs}} = 10.8$, $\text{GOF} = (\text{R}_{\text{wp}}/\text{R}_{\text{exp}})^2 = 1.09$. Details about the structure solution and refinement are given in the Supporting Information. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-147044. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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The Essential Role of a Zn$^{\text{II}}$ Ion in the Disproportionation of Semiquinone Radical Anion by an Imidazolate-Bridged Cu$^{\text{II}}$ – Zn$^{\text{II}}$ Model of Superoxide Dismutase[**]

Hideki Ohtsu and Shunichi Fukuzumi[*]

Copper – zinc superoxide dismutase (Cu,Zn-SOD) contains an imidazolate-bridged Cu$^{\text{II}}$ – Zn$^{\text{II}}$ heterodinuclear metal center in its active site.[1–6] This enzyme catalyzes a very rapid two-step dismutation of toxic superoxide ($O_2^{\bullet -}$) into dioxygen and hydrogen peroxide by alternating reduction and oxidation of the copper ion of the active site.[5–7] Superoxide first reduces the Cu$^{\text{II}}$ center of Cu,Zn-SOD to produce O_2, and then another molecule of superoxide oxidizes the Cu$^{\text{I}}$ center to produce H_2O_2.[6, 7]

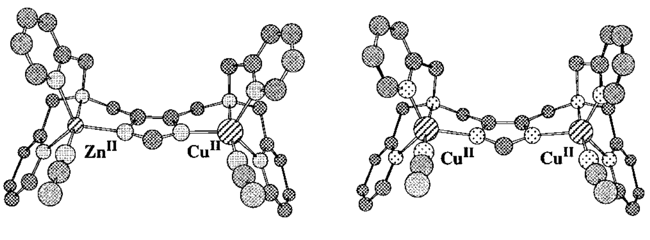
Since the oxidation potential of $O_2^{\bullet -}$ ($E^0_{\text{ox}} = -0.16$ V versus the normal hydrogen electrode (NHE) at pH 7.0)[8] is more negative than the reduction potential of Cu,Zn-SOD ($E^0_{\text{red}} = 0.36$ V versus NHE at pH 7.4),[9] the oxidation of $O_2^{\bullet -}$ may occur rapidly by electron transfer from $O_2^{\bullet -}$ to the Cu$^{\text{II}}$ center of Cu,Zn-SOD, whereas outer-sphere electron transfer from the Cu$^{\text{I}}$ center of Cu,Zn-SOD to $O_2^{\bullet -}$ is highly endergonic. Therefore, coordination of $O_2^{\bullet -}$ to the Zn$^{\text{II}}$ center of Cu,Zn-SOD was suggested to be essential to accelerate electron transfer from the Cu$^{\text{I}}$ center of Cu,Zn-SOD to $O_2^{\bullet -}$ which is bound to the Zn$^{\text{II}}$ center.[10] A central issue in bioinorganic chemistry is to clarify how the Zn$^{\text{II}}$ ion can facilitate both the oxidation and reduction of $O_2^{\bullet -}$ in Cu,Zn-SOD.[1–7] However, the instability of the reaction intermediates and the lack of appropriate model complexes which contain the substrate binding sites has so far precluded studying the essential role of the Zn$^{\text{II}}$ ion in Cu,Zn-SOD.[1–7, 9–11]

We succeeded in preparing the imidazolate-bridged Cu$^{\text{II}}$ – Zn$^{\text{II}}$ heterodinuclear and Cu$^{\text{II}}$ – Cu$^{\text{II}}$ homodinuclear complexes **1** and **2** by using the novel dinucleating ligand Hbdpi

$[\text{CuZn(bdpi)(CH}_3\text{CN)}_2](\text{ClO}_4)_3 \cdot 2\,\text{CH}_3\text{CN}$ **1**

$[\text{Cu}_2\text{(bdpi)(CH}_3\text{CN)}_2](\text{ClO}_4)_3 \cdot \text{CH}_3\text{CN} \cdot 3\,\text{H}_2\text{O}$ **2**

(Hbdpi = 4,5-bis(di(2-pyridylmethyl)aminomethyl)imidazole; Figure 1).[10] In these SOD model complexes, each metal center has a pentacoordinate environment that includes a solvent molecule which can be readily replaced by a substrate. Here we report on the dramatic difference in the stoichiometric disproportionation of semiquinone radical anion ($Q^{\bullet -}$) with the imidazolate-bridged Cu$^{\text{II}}$ – Zn$^{\text{II}}$ heterodinuclear (**1**) and Cu$^{\text{II}}$ – Cu$^{\text{II}}$ homodinuclear (**2**) complexes in propionitrile (EtCN). The presence of Zn$^{\text{II}}$ ion is shown to be essential for disproportionation of $Q^{\bullet -}$ to occur. The use of $Q^{\bullet -}$ instead of $O_2^{\bullet -}$ provides valuable mechanistic insights into the essential role of the Zn$^{\text{II}}$ ion in Cu,Zn-SOD, since the reaction intermediates are stable enough to be well characterized.



$[\text{CuZn(bdpi)(CH}_3\text{CN)}_2]^{3+}$ $[\text{Cu}_2\text{(bdpi)(CH}_3\text{CN)}_2]^{3+}$

Figure 1. Structures of **1** and **2**.

The addition of less than one equivalent of $Q^{\bullet -}$ to a deaerated solution of **1** in EtCN results in the appearance of a new absorption band at 585 nm, the absorbance of which increases linearly with increasing concentration of $Q^{\bullet -}$ (Figure 2a). The addition of more than two equivalents of $Q^{\bullet -}$ results in no further increase in the absorption band at 585 nm, but decay of the absorption band due to $Q^{\bullet -}$ ($\lambda_{\text{max}} = 422$ nm) is observed (Figure 2a). The decay rate obeys first-order kinetics (Figure 2a, inset), and the rate constant k_{obs} at 193 K is 0.4 s^{-1}. Further addition of $Q^{\bullet -}$ after the initial disappearance of $Q^{\bullet -}$ resulted in reappearance of the absorption band due to $Q^{\bullet -}$, which was stable under the present experimental conditions.

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Supporting information for this article is available on the WWW under http://www/wiley-vch.de/home/angewandte/ or from the author.

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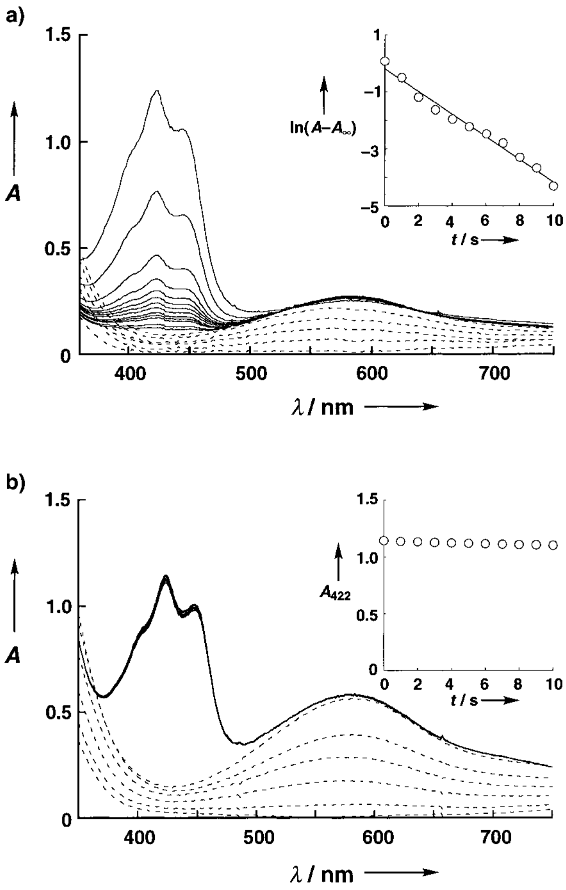


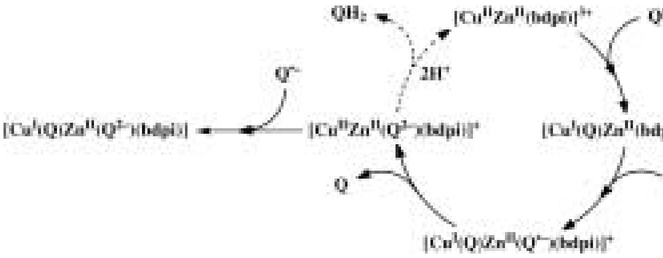
Figure 2. Changes in absorbance A observed on addition of $Q^{\bullet -}$ (0, 0.2, 0.4, 0.6, 0.8, 1.0 equiv for **1**; 0, 0.4, 0.8, 1.2, 1.6, 2.0 equiv for **2**) to an EtCN solution of a) **1** (0.1×10^{-4} M, dotted line) and b) **2** (0.1×10^{-4} M, dotted line) and spectral changes observed upon further addition of 2 equiv $Q^{\bullet -}$ to the resulting solution for a) **1** (solid line) and b) **2** (solid line) at 193 K; 1 s intervals. Inset: first-order plot of the change in absorbance for **1** and time course of the change in absorbance for **2** at 422 nm.

Appearance of the same absorption band ($\lambda_{max} = 585$ nm) is observed when **1** is replaced by **2** in the reaction with $Q^{\bullet -}$. In the case of **2**, however, the absorbance at 585 nm increases linearly with an increase in the $Q^{\bullet -}$ concentration up to two equivalents of $Q^{\bullet -}$ (Figure 2b). The addition of more than two equivalents of $Q^{\bullet -}$ results in appearance of the absorption band due to $Q^{\bullet -}$, which is stable in contrast to the case of **1** (Figure 2b).

Since the one-electron oxidation potential (E^0_{ox} versus the saturated calomel electrode (SCE)) of $Q^{\bullet -}$ (−0.51 V)[12] is more negative than the one-electron reduction potentials (E^0_{red} versus SCE) of the Cu^{II} center of **1** (−0.03 V)[10] and **2** (−0.03 V),[10] an electron transfer from $Q^{\bullet -}$ to the Cu^{II} center should occur to yield the Cu^I–Q complex **3**, which may have a metal-to-ligand charge transfer (MLCT) band at 585 nm. In the case of **2**, two equivalents of $Q^{\bullet -}$ can be reduced, since the E^0_{ox} value of $Q^{\bullet -}$ is still more negative than the second one-electron reduction potential for the other Cu^{II} center in **2** (−0.31 V).[10] This may be the reason why two equivalents of $Q^{\bullet -}$ can react with **2** to give the 2:1 complex between Q and the Cu^I center **4**, which has the same absorption band at 585 nm, and why the absorbance is twice as large as that of **3**. The Cu^I–Q complexes **3** and **4** should be diamagnetic, and it was confirmed that the reaction mixtures of one and two equivalents of $Q^{\bullet -}$ with **1** and **2**, respectively, were ESR silent at 77 K.

The resonance Raman spectra of **3** and **4** in acetonitrile (CH_3CN) at 298 K (laser excitation wavelength 632.8 nm) revealed the same strong resonance-enhanced Raman bands at 1580 cm^{-1}. The resonance Raman frequency is significantly higher than that reported for the CO stretching vibration of free $Q^{\bullet -}$ (1435 cm^{-1}), for which the CO bond order was estimated from the Raman data to be 1.5,[13] but lower than that of neutral *p*-benzoquinone (1651 cm^{-1}).[14, 15] Hence, the resonance Raman bands of **3** and **4** at 1580 cm^{-1} can be assigned with reasonable certainty to a CO stretching vibration in the Cu^I–Q complexes $[Cu^I(Q)Zn^{II}(bdpi)]^{2+}$ and $[Cu^I(Q)Cu^I(Q)(bdpi)]^+$, respectively.

The drastic difference in the reactions of $Q^{\bullet -}$ with **1** and **2** (Figure 2) may be ascribed to the presence in **1** of a Zn^{II} ion which can bind $Q^{\bullet -}$. Since the binding of $Q^{\bullet -}$ to an Mg^{II} ion is known to facilitate the electron-transfer reduction of $Q^{\bullet -}$,[16] the complexation of $Q^{\bullet -}$ with Zn^{II} ion in $[Cu^I(Q)Zn^{II}(bdpi)]^{2+}$ may also facilitate an intramolecular electron transfer from the Cu^I center, which is produced by an electron transfer from $Q^{\bullet -}$ to the Cu^{II} center, to $Q^{\bullet -}$ bound to the Zn^{II} center (Scheme 1). In **2**, however, there is no Zn^{II} center available to facilitate the reduction of $Q^{\bullet -}$. In an aprotic solvent such as EtCN, the final product of the stoichiometric disproportionation of $Q^{\bullet -}$ is $[Cu^I(Q)Zn^{II}(Q^{2-})(bdpi)]$ (Scheme 1), which was confirmed by the ESI mass spectrum (see Supporting Information; Figure S1). In the presence of H^+, **1** can act as a catalyst for the disproportionation of $Q^{\bullet -}$ to Q and QH_2 (broken arrow in Scheme 1).



Scheme 1. Mechanism for the disproportionation of $Q^{\bullet -}$ by the imidazolate-bridged Cu^{II}–Zn^{II} complex.

We successfully detected spectroscopically the Zn^{II}–$Q^{\bullet -}$ complex by using the mononuclear Zn^{II} complex $[Zn\{MeIm(Py)_2\}(CH_3CN)](ClO_4)_2$ (**5**; $MeIm(Py)_2$ = (1-methyl-4-imidazolylmethyl)bis(2-pyridylmethyl)amine).[17] The addition of a large excess of **5** to a solution of $Q^{\bullet -}$ in EtCN at 193 K resulted in the appearance of a new absorption band at 570 nm (see Supporting Information; Figure S2), which disappeared at higher temperatures.[18] We previously reported that the Mg^{II}–$Q^{\bullet -}$ complex has an characteristic absorption band at 590 nm due to a red-shifted π–π* transition of $Q^{\bullet -}$.[16, 19] Hence the absorption band at 570 nm of the Zn^{II}–$Q^{\bullet -}$ complex, which is slightly red-shifted relative to that of the Mg^{II}–$Q^{\bullet -}$ complex, can be assigned to a π–π* transition of $[Zn(Q^{\bullet -})\{MeIm(Py)_2\}]^+$. One of the decomposition products was confirmed by the ESI mass spectrum, which exhibited a

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signal at m/z 466 (see Supporting Information; Figure S3). The observed mass and isotope patterns are consistent with with the ion $[Zn(QH)\{MeIm(Py)_2\}]^+$, which is the protonated form of the reduced species of $[Zn(Q^{\bullet-})\{MeIm(Py)_2\}]^+$.

In conclusion, the Zn^{II} ion in the SOD model complex has been shown to play the essential role in facilitating the reduction of $Q^{\bullet-}$ by coordination of $Q^{\bullet-}$ to the Zn^{II} ion. The oxidation of $Q^{\bullet-}$ is also facilitated by the Zn^{II} ion, since the reduction potential of the Cu^{II} center in the imidazolate-bridged $Cu^{II}-Zn^{II}$ heterodinuclear complex **1** is shifted to a more positive value (0.21 V) relative to that without a Zn^{II} ion.[10] Thus, the Zn^{II} ion can facilitate both the oxidation and reduction of $Q^{\bullet-}$. Essentially the same mechanism may also be applied to the disproportionation of $O_2^{\bullet-}$ catalyzed by Zn,Cu-SOD.

Experimental Section

To a deaerated solution (25 mL) of *p*-benzoquinone (8.10 mg) in EtCN and hydroquinone (8.25 mg) was added two equivalents of 1 M $Bu_4NOH \cdot MeOH$ solution (72 µL) to make the stock solution of *p*-benzosemiquinone radical anion $Q^{\bullet-}$ (6.0×10^{-3} M). The reactions of imidazolate-bridged $Cu^{II}-Zn^{II}$ heterodinuclear and $Cu^{II}-Cu^{II}$ homodinuclear SOD model complexes and semiquinone radical anion were performed in a UV/Vis cell (path length 1 cm) which was held in a Unisoku temperature-controlled (±0.5 °C) cell holder designed for low-temperature experiments. After the deaerated solution of the SOD model complexes (0.1×10^{-4} M) in the cell had been kept at the desired temperature for several minutes, semiquinone radical anion was added by syringe. Formation of the Cu^I-Q complexes was followed by monitoring the absorption change at 585 nm. The rate constant k_{obs} for the stoichiometric disproportionation of $Q^{\bullet-}$ was determined by monitoring the decrease in the absorption band due to $Q^{\bullet-}$ ($\lambda_{max} = 422$ nm).

Frozen-solution ESR spectra were recorded on a JEOL JES-RE1X X-band spectrometer equipped with a standard low-temperature apparatus. All spectra were recorded at 77 K in quartz tubes with 4 mm inner diameters. The g values were calibrated with a Mn^{II} marker as a reference.

Resonance Raman spectra were excited at 632.8 nm with an He–Ne laser and detected with a JASCO NR-1800 triple polychromator equipped with a liquid-nitrogen-cooled Princeton Instruments CCD detector. Raman measurements were carried out with a spinning cell, and the laser power was adjusted to 50 mW at the sample point. Raman shifts were calibrated with acetonitrile; the accuracy of the peak positions of the Raman bands was $\pm 1 cm^{-1}$.

ESI mass spectra were obtained with an API 150 triple quadrupole mass spectrometer (PE-Sciex) in positive-ion detection mode, equipped with an ion-spray interface. The sprayer was held at a potential of 5.0 kV, and compressed N_2 was employed to assist liquid nebulization. The positive-ion ESI mass spectra were measured in the range m/z 100–1000.

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[17] $[Zn\{MeIm(Py)_2\}(CH_3CN)](ClO_4)_2$: ^1H NMR (400 MHz, CD_3CN, 25 °C, TMS): $\delta = 3.82$ (s, 3H; CH_3), 4.00 (s, 2H; NCH_2Im), 4.26 (d, $^3J(H,H) = 4.8$ Hz, 4H; NCH_2Py), 7.19 (s, 1H; Im), 7.68 (d, $^3J(H,H) = 7.6$ Hz, 2H; Py), 7.76 (m, 2H; Py), 8.09 (s, 1H; Im), 8.21 (td, $^4J(H,H) = 1.6$, $^3J(H,H) = 8.0$ Hz, 2H; Py), 8.81 (m, 2H; Py); elemental analysis calcd for $C_{19}H_{23}N_6Zn_1Cl_2O_{8.5}$ (%): C 37.55, H 3.81, N 13.83; found: C 37.43, H 3.49, N 13.95; ESI MS data: m/z: 456 $[M - ClO_4]^+$. For the details of the synthetic procedure for the ligand $MeIm(Py)_2$, see reference [10].

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New Family of Cyclopropanating Reagents: Synthesis, Reactivity, and Stability Studies of Iodomethylzinc Phenoxides**

André B. Charette,* Sébastien Francoeur, Jonathan Martel, and Nicole Wilb

The cyclopropanation of olefins is a very useful process in synthetic organic chemistry. Cyclopropane moieties are found in many natural[1] and unnatural products[2] possessing interesting biological activities.[3] These units are also very useful synthons for further synthetic transformations.[4]

Amongst the different methods of cyclopropanation, the Simmons–Smith reaction[5] has stimulated a considerable

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