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Preparation of a Hydroperoxo Zinc(II) Intermediate**

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Among biological transition-metal ions, in many cases, a Zn^{II} ion serves as a Lewis acid without participating in an electron-transfer reaction. In the late 1960s, it was discovered that copper/zinc-containing proteins (copper zinc superoxide dismutase, CuZn SOD) were capable of catalyzing the disproportionation of a superoxide ion to give molecular oxygen and hydrogen peroxide. The mechanism is considered to progress by alternating reduction/oxidation of the copper atom at the active site (first step, $O_2^{\cdot-} + Cu^{II} \rightarrow O_2 + Cu^{I}$; second step, $Cu^{I} + O_2^{\cdot-} + 2H^{+} \rightarrow Cu^{II} + H_2O_2$).[1,2] As the crystal structure of CuZn SOD indicates an imidazolate-bridged heteronuclear Cu–Zn center at the active site,[3,4] many model complexes that include copper and/or zinc ions have been synthesized and studied to understand the mechanism of disproportionation of superoxide.[5,6] However, these studies have yielded a limited amount of useful information on the formation and physicochemical properties of a metal hydroperoxide intermediate that is suggested in the second step of the SOD reaction.[7]

We have previously synthesized a mononuclear copper(II) hydroperoxide complex by using a new ligand, bis[(6-pivalamido-2-pyridyl)methyl][(2-pyridyl)methyl]amine (H_2bppa).[8] Previous investigations have suggested that copper hydroperoxide complexes tend to decompose in air to generate highly toxic hydroxyl or hydroperoxyl radicals.[9,10] Such a copper hydroperoxide species appears to be unable to release H_2O_2 efficiently with the acceptance of a proton. Thus, it would be very significant to characterize a Zn–OOH species. There is no report for the preparation of a zinc(II) hydroperoxide complex hitherto, although the preparation of a zinc(II) alkylperoxide complex was reported recently.[11] Herein, we describe the preparation and characterization of a Zn^{II}–OOH species by using a tripodal pyridylamine ligand, bis[(6-neopentylamino-2-pyridyl)methyl][(2-pyridyl)methyl]-

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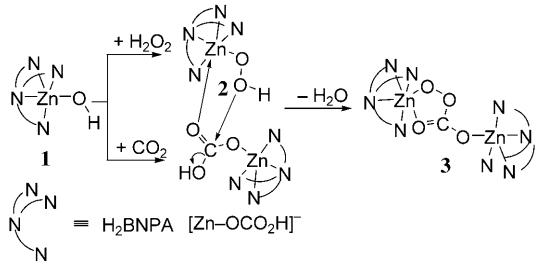
amine (H_2bnpa), and we compare the Zn complex with the corresponding Cu–OOH complex.

The initial mononuclear Zn^{II} hydroxide complex, $[Zn(H_2bnpa)(OH)]^+$ (**1**),[12] was prepared from the reaction of the ligand H_2bnpa with $[Zn^{II}–OH]^+$ in methanol/water. The crystal structure obtained from a single crystal of recrystallized **1**-ClO_4 revealed a trigonal-bipyramidally coordinated Zn^{II} with the hydroxide ion in an axial position (see Supporting Information).[12] The coordination of an hydroxide ion was also confirmed by the ^{1}H NMR spectrum of the product, which had a signal from the hydroxide hydrogen atom at 2.04 ppm (singlet) in $[D_3]$MeCN (see Supporting Information), and by the IR spectrum, which had ν(O-H) stretching vibration at $\bar{\nu} = 3626\ cm^{-1}$.

The reaction of **1** with H_2O_2 (approximately 20 equiv) in $[D_3]$MeCN solution at 20 °C gave new ^{1}H NMR signals characteristic of a trigonal-bipyramidal Zn^{II} complex, **2** (Scheme 1), which were accompanied by the disappearance



Scheme 1. Synthesis of **2** and **3** from **1**.

of the Zn–OH proton signal and appearance of a new singlet at 7.77 ppm. This signal falls within the range found for protons of HOO^- ions bound to metal centers that were reported previously.[13,14] The intensity of the singlet signal decreased with gradual addition of D_2O ($\approx 6\ \mu L$). Furthermore, upon treatment with D_2O_2, the signal at 7.77 ppm was not detected, although signals associated with the H_2bnpa ligand of **2** were obtained. Thus, these observations allow us to assign the proton signal as a resonance derived from a hydroperoxide ion coordinated to the zinc complex.

The formation of the Zn–OOH species was also monitored by ESI mass spectrometry (see Supporting Information). A solution of **1** in MeCN treated with $H_2{}^{16}O_2$ or $H_2{}^{18}O_2$ afforded prominent positive-ion peak clusters at *m*/*z* 557 or 561, respectively. These observed masses and isotope patterns correspond to the $[Zn(H_2bnpa)(^{16}O_2H)]^+$ and $[Zn(H_2bnpa)(^{18}O_2H)]^+$ ions. With D_2O_2 instead of H_2O_2, the peak at *m*/*z* 557 shifts to 560, which suggests that $[Zn(D_2bnpa)(O_2D)]^+$ is generated. These spectroscopic data provide strong evidence for the formation of a mononuclear Zn^{II} hydroperoxide complex, $[Zn(H_2bnpa)(OOH)]^+$ (**2**), in solution. The robust ligation of the hydroperoxide ion to Zn^{II} appears to be stabilized by hydrogen-bonding interactions between the amino hydrogen atoms of **2** and a hydroperoxo oxygen atom. This hydrogen-bonding interaction is confirmed by a larger down-field shift ($\delta = 4.43$ ppm) of the amine proton signals relative to that of free ligand H_2bnpa.

At this stage, it is very important to examine which of the metal hydroperoxide species has higher basicity, $Zn^{II}–OOH$ or $Cu^{II}–OOH$, because in the second step of the CuZn SOD mechanism, efficient protonation of the hydroperoxide ion is required for rapid liberation of H_2O_2.[3,4,7] To investigate the nucleophilicity/basicity of mononuclear hydroperoxo complexes of Zn^{II} and Cu^{II}, the reaction with CO_2 was carried out according to previously reported procedures.[15] Bubbling CO_2 into an acetonitrile solution of **1** treated with H_2O_2 produced an ESI mass spectrum with a new peak cluster at *m*/*z* 564, whose isotope pattern corresponds to $[\{Zn(H_2bnpa)\}_2(CO_4^{2-})]^{2+}$ (**3**). Compound **1** reacts with CO_2 to form a species containing $\{Zn–OCO_2H\}^-$;[16] the resulting change in the ESI spectra (see Supporting Information) implies that the $\{Zn^{II}–OCO_2H\}^-$ species once formed immediately reacts with the generated peroxide complex **2**, followed by release of water to afford the stable dinuclear zinc complex **3** (see Scheme 1). The formation of **3** observed under very low concentrations of CO_2 is ascribed to an extraordinary high nucleophilicity/basicity of a hydroperoxide ion bound to a Zn^{II} center.

A colorless single crystal of **3**-2 ClO_4 suitable for X-ray diffraction analysis was obtained from a THF/Et_2O solution of **2** kept at 0 °C under atmospheric CO_2. As shown in Figure 1, the crystal structure of **3** indicates that the peroxy-

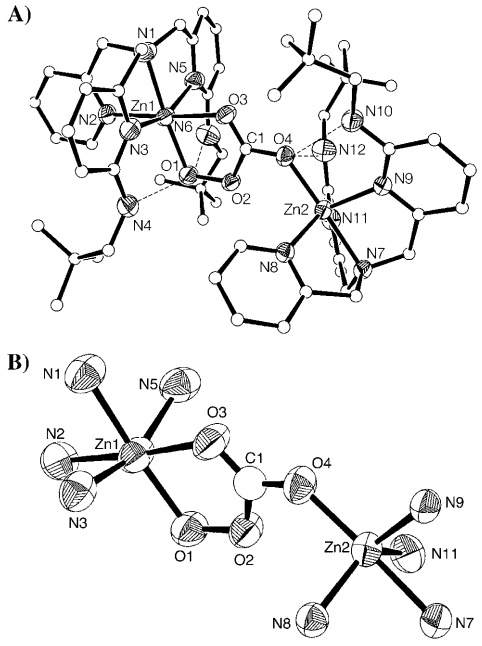


Figure 1. A) ORTEP view of the structure of **3**; thermal ellipsoids are set at the 30% level of probability. B) ORTEP view of the $[ZnOOC(O)OZn]^{2+}$ core in **3**; hydrogen atoms, counteranions, and solvent molecules are omitted for clarity; thermal ellipsoids are set at the 30% level of probability. Selected bond lengths [Å] and angles [°]: Zn1-N1 2.139(6), Zn1-N2 2.144(5), Zn1-N3 2.213(7), Zn1-N5 2.210(7), Zn1-O1 2.002(4), Zn1-O3 2.111(4), Zn2-N7 2.148(4), Zn2-N8 2.081(5), Zn2-N9 2.084(5), Zn2-N11 2.092(5), Zn2-O4 1.987(4), C1-O2 1.320(7), C1-O3 1.212(7), C1-O4 1.290(6), O1-O2 1.474(5); O1-O2-C1 114.6(4), O2-C1-O3 123.1(5), O2-C1-O4 112.7(5), O3-C1-O4 124.1(6). Hydrogen bonding interactions are observed for O1···N4 (2.928 Å), O1···N6 (2.954 Å), O4···N10 (2.884 Å), and O4···N12 (3.004 Å).

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carbonate ion bridges the Zn1 and Zn2 sites, whose coordination environments are distorted octahedral and trigonal-bipyramidal, respectively, in a μ-η^1:η^2 fashion. The two exchangeable coordination sites of the Zn1 center are occupied by the peroxide and carbonyl oxygen atoms of the peroxycarbonate ion in a bidentate fashion with Zn1–O1 and Zn1–O3 bond lengths of 2.002(4) and 2.111(4) Å, respectively, and a O2-C1-O3 angle of 123.1(5)°. The remaining carboxylate oxygen atom of the peroxycarbonate ion is coordinated to the Zn2 site with a Zn2–O4 bond length of 1.987(4) Å.

The O1–O2 bond length is 1.474(5) Å, which is within the range for known metal alkylperoxide complexes (1.36–1.52 Å) and close to that of H_2O_2 (1.49 Å).[17] This bond is slightly longer than those of the previously reported peroxycarbonate metal complexes, $KH(O_2C(O)O)\cdot H_2O_2$ (1.457(2) Å)[18] and $Ph_4P[Fe(quinaldate)_2(O_2C(O)O)]\cdot 1.5\,CH_3OH\cdot 0.5\,(CH_3)_2NCHO$ (1.455(5) Å),[19] which suggests that the peroxy oxygen atoms of the peroxycarbonate ion are derived from hydroperoxide bonded to **2**. For the shortest bond of the peroxycarbonate ligand, C1–O2 (1.320(7) Å) compared with C1–O3 (1.212(7) Å) and C1–O4 (1.290(6) Å), some double-bond character can be assumed. Moreover, as demonstrated by ^{1}H NMR spectroscopic analysis for **2**, the two amine hydrogen atoms stabilize the binding of the peroxycarbonate ion, which is also evidenced by the hydrogen-bond lengths (2.928(8), 2.954(8), 2.884(7), and 3.004(8) Å; see Figure 1). This structure determination is the first of a dinuclear zinc(II) complex with a peroxycarbonate ion in μ-η^1:η^2-coordination mode.

The behavior described above suggests that the hydroperoxo group of complex **2** is nucleophilic towards CO_2. Next, we examined the reactivity of the corresponding Cu^{II} complex with H_2bnpa to compare the nucleophilicity/basicity of the Cu–OOH and Zn–OOH species. However, both $[Cu(H_2bnpa)(OOH)]^+$ and the previously reported complex $[Cu(H_2bppa)(OOH)]^+$ did not show such a nucleophilic reactivity,[8] although the carbonate complex is also generated by the reaction of $Cu–OH(H_2bnpa/H_2BPPA)$ with CO_2. This result suggests lower nucleophilicity/basicity of a hydroperoxide ion bound to Cu^{II}, which is reasonably interpreted in terms of the decrease in electron density on the hydroperoxide oxygen atom due to its stronger binding to Cu^{II} than to Zn^{II}. Thus, only hydroperoxide bound to Zn^{II} may be sufficiently nucleophilic/basic to attract electrophilic molecules such as CO_2.

In summary, we have described the generation, spectroscopic characterization, and reactivity of a novel mononuclear Zn^{II} hydroperoxide intermediate. We have also performed the first X-ray crystallographic characterization of a dinuclear zinc peroxycarbonate complex. A comparison of the electronic and structural properties of the hydroperoxo complexes of Zn^{II} and Cu^{II} may indicate the role of Zn^{II} in the second step of the catalytic cycle of CuZn SOD.

Experimental Section

General: All reagents and solvents were obtained from commercial sources and were used as received unless otherwise noted.

Caution! The perchlorate salts used in this study are all potentially explosive and should be handled with care.

Preparation of **1**-ClO_4: A solution (pH 6.5–7, 300 mL) containing {Zn(OH)} species was prepared by mixing $Zn(ClO_4)_2\cdot 6H_2O$ (178.8 mg, 0.48 mmol) and KOH in methanol/water (1:1). A solution of H_2bnpa (184.3 mg, 0.4 mmol) in a mixture of methanol and water (1:1, 80 mL) was added dropwise to the reaction mixture at room temperature. After 30 min, the solvent was removed in vacuo to leave a white powder. Recrystallization from methanol at 25 °C afforded colorless crystals of $[Zn(H_2bnpa)(OH)]ClO_4$ (0.19 g, 74% yield) suitable for X-ray diffraction measurements (the structure of **1**-ClO_4 is the same as that reported previously, see Supporting Information).[12b]). ^{1}H NMR: see Supporting Information. Elemental analysis (%) calcd for $C_{28}H_{41}N_6O_5ZnCl$: C 52.34, H 6.43, N 13.08; found: C 52.40, H 6.43, N 13.10. MS (ESI) m/z: 541 $[Zn(H_2bnpa)(OH)]^+$.

Preparation of **3**-$(ClO_4)_2$: The treatment of **1** (12.8 mg, 20 μmol) with H_2O_2 in MeCN (0.4 mL) afforded a solution containing **2**. CO_2 dissolved in THF (0.1 mL) was added dropwise to this solution at 0 °C. Crystallization from MeCN/THF/Et_2O in air gave colorless crystals of $[\{Zn(H_2bnpa)\}_2(CO_4)](ClO_4)_2\cdot(CH_3CH_2)_2O\cdot CH_3CN$ (2.63 mg, 38% yield). Elemental analysis (%) calcd for $C_{63}H_{93}N_{13}O_{13}Zn_2Cl_2$: C 52.46, H 6.49, N 12.62; found: C 52.54, H 6.21, N 12.44. MS (ESI): m/z: 564 $[\{Zn(H_2bnpa)\}_2(CO_4)]^{2+}$, 1227 $[\{Zn(H_2bnpa)\}_2(CO_4)(ClO_4)]^+$. ^{13}C NMR (100 MHz, $[D_3]$MeCN, 25 °C, TMS): $\delta =$ 207.8 ppm (s, OC(O)OO).

Preparation of $[Cu(H_2bnpa)(OOH)]^+$: The treatment of $Cu(ClO_4)_2\cdot 6H_2O$ (148.2 mg, 0.4 mmol) with H_2bnpa (184.3 mg, 0.4 mmol) and KOH (22.4 mg, 0.4 mmol) in MeCN (0.4 mL) afforded a solution containing $[Cu(H_2bnpa)(OH)]^+$. H_2O_2 (4.0 mmol) was added dropwise to the solution of $[Cu(H_2bnpa)(OH)]^+$ at −40 °C. The mononuclear hydroperoxo copper(II) complex $[Cu(H_2bnpa)(OOH)]^+$ was characterized spectroscopically. UV/Vis (MeCN): $\lambda_{max} = 380$ nm (hydroperoxide-to-copper(II) charge transfer transition); ESR: $g_\perp = 2.22$, $g_\parallel = 2.00$, $|A_\perp| = 94$ G, $|A_\parallel| = 100$ G at 77 K; ESI MS: m/z: 556 $[Cu(H_2bnpa)(^{16}O_2H)]^+$, 560 $[Cu(H_2bnpa)(^{18}O_2H)]^+$; resonance Raman spectra: $\tilde{\nu} = 847$, 800 cm^{-1} ($\nu(^{18}O\text{-}^{18}O)$); see Supporting Information.

X-ray crystal-structure analysis of **3**-$(ClO_4)_2$: A colorless single crystal suitable for X-ray structure analysis was obtained from a THF/Et_2O solution. Crystal data: $C_{61}H_{90}N_{12}O_{13}Cl_2Zn_2$, $M_r = 1401.12$, triclinic, space group $P\bar{1}$ (no. 2), $a = 13.355(2)$, $b = 26.039(5)$, $c = 10.785(3)$ Å, $\alpha = 101.72(2)$, $\beta = 98.93(2)$, $\gamma = 75.39(1)°$, $V = 3510.5(7)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.325$ g cm^{-3}, $\mu = 8.26$ cm^{-1}, $Mo_{K\alpha}$ radiation ($\lambda = 0.71070$ Å), $T = 173$ K, $R_1 = 0.059$, $R_w = 0.084$. CCDC-267192 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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