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# Chemical Indices of the Biomimetic Models of Oxyhemocyanin and Oxytyrosinase

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## 1. Introduction

The  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  species has attracted attention in the model studies of type III copper proteins because this structure is suggested as an important motif in biological systems (Karlin and Tyeklár, 1993; Kitajima and Moro-oka, 1994). Although oxyhemocyanin (oxyHc) and oxytyrosinase (oxyTy) have this species in the active site, they show different functions: oxygen transport and oxygen activation, respectively (Cooksey et al., 1997; Cuff et al., 1998; Holm et al., 1996; Solomon et al., 1992).

Synthetic modeling approaches have greatly developed our understanding of the chemical characters of the  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  species (Cahoy et al., 1999; Funahashi et al., 2008; Hu et al., 2001; Kitajima et al., 1992; Kitajima et al., 1989; Kodera et al., 2004; Kodera et al., 1999; Lam et al., 2000). Kitajima et al. succeeded in synthesizing  $[(\text{HB}(3,5\text{-iPr}_2\text{-Pz})_3\text{Cu})_2(\text{O}_2)]$  ( $\text{HB}(3,5\text{-iPr}_2\text{-Pz})_3$  = hydrotris{3,5-diisopropyl-pyrazolyl}borate (Trofimenko, 1999)) (**1**), which showed remarkable physicochemical similarities to oxyHc and oxyTy, and determining the crystal structures of the complex, which first characterized a  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  structure for the active site of oxyHc, before the X-ray crystallographic studies of Hc were reported (Kitajima et al., 1989). Tolman and his collaborators synthesized  $[(\text{iPr}_3\text{TACD})\text{Cu}]_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  ( $\text{iPr}_3\text{TACD}$  = 1,5,9-triisopropyl-1,5,9-triazacyclodecane (**2**) to understand how the nature of the tridentate macrocyclic supporting ligand influences the relative stability of the isomeric  $\mu\text{-}\eta^2\text{:}\eta^2$ -peroxo- and bis( $\mu\text{-oxo}$ )dicopper complexes (Lam et al., 2000). They showed that low-temperature oxygenation of  $[(\text{iPr}_3\text{TACD})\text{Cu}]_2(\text{CH}_3\text{CN})[\text{SbF}_6]$  yielded a  $\mu\text{-}\eta^2\text{:}\eta^2$  product with no trace of the bis( $\mu\text{-oxo}$ ) isomer and concluded that the size of the ligand substituents and the ligand macrocycle ring size are key factors in controlling the relative stabilities of the  $\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2$ -peroxo and bis( $\mu\text{-oxo}$ ) forms. Kodera et al. reported the reversible dioxygen binding by the room-temperature-stable complex,  $[(\text{L1})\text{Cu}]_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  ( $\text{L1}$  = 1,2-bis[2-(1,1-bis(6-methyl-2-pyridyl)ethyl)-6-pyridyl]ethane) (**3**), and showed that the long Cu–O bonds and the strong O–O bond of **3** are favorable for easy release of  $\text{O}_2$  since the O–O stretch of **3** is the strongest for  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  complexes including oxyHc from the resonance Raman spectrum (Kodera et al., 2004). Masuda and his coworkers synthesized a new  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  complex formed with  $\alpha$ -isosparteine and benzoate (**4**) and determined the novel coordination structure of a carboxylate-bridged butterfly type  $\mu\text{-}\eta^2\text{:}\eta^2$ -peroxide dicopper core (Funahashi et al., 2008). It was shown that the butterfly core is supported by

benzoate in the axial position, losing its planarity despite the Jahn–Teller effect on the Cu(II)  $d^9$ -configuration. Fig. 1 illustrates the coordinating ligands to the  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  core of the biomimetic models **1–4**, and Fig. 2 shows the X-ray crystallographic structures of **1–4**.

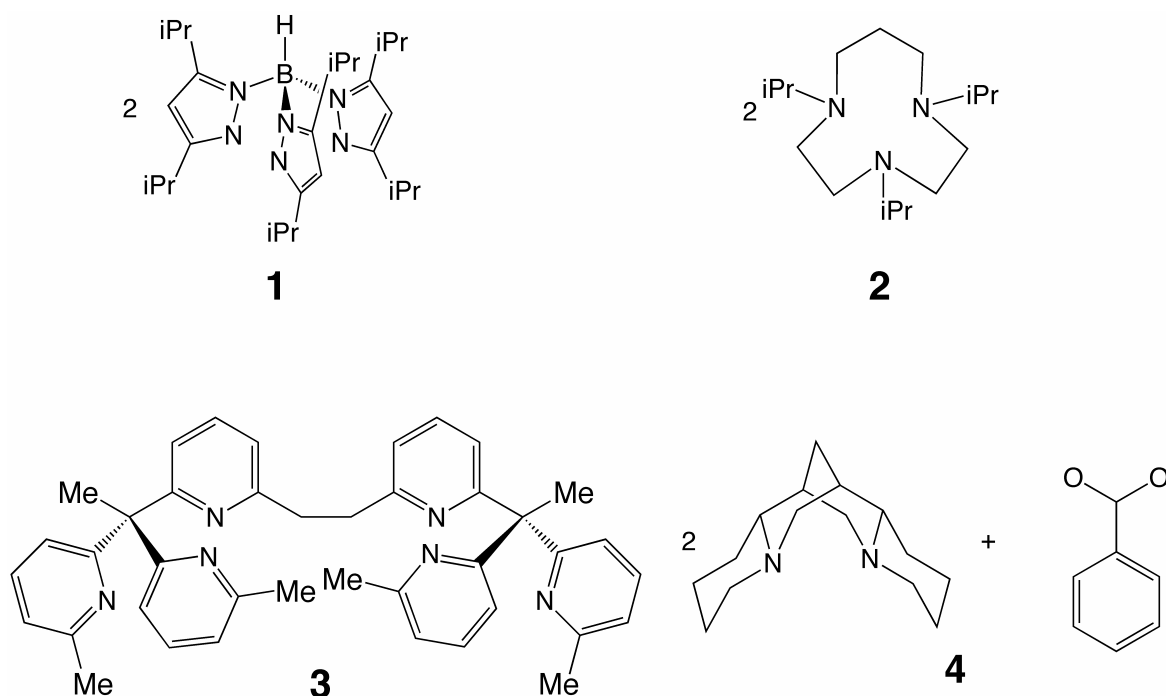


Fig. 1. Coordinating ligands utilized for the biomimetic model of Hc **1–4**.

Several theoretical investigations have also been performed on models of the dicopper active site (Aullón et al., 2006; Benson et al., 2002; Cramer et al., 2003; Cramer and Pak, 2001; Gresh et al., 2002; Siegbahn, 2006; Siegbahn and Wirstam, 2001). Siegbahn studied the catalytic mechanisms of tyrosinase and catechol oxidase using  $\text{Cu}_2\text{O}_2$  complex coordinated by six imidazole ligands at the UB3LYP level of theory (Siegbahn, 2006; Siegbahn and Wirstam, 2001). Cramer et al. investigated the mechanism of the intramolecular C–H bond cleavage in  $[\text{LCu}]_2(\mu\text{-O})_2$  ( $\text{L} = 1,4,7$ -tribenzyl-1,4,7-triazacyclononane) (Cramer et al., 2003; Cramer and Pak, 2001) using the integrated molecular orbital molecular mechanics (Maseras and Morokuma, 1995) with DFT and universal force field (Rappe et al., 1992). Aullón et al. performed UB3LYP calculations on binuclear  $[(\text{Tp})\text{Cu}]_2(\mu\text{-O})_2$  complexes ( $\text{Tp} = \text{tris}(\text{pyrazolyl})\text{borate}$ ) to examine the effect of the substituents of the Tp ligands on dioxygen activation and stabilization (Aullón et al., 2006).

Previously, we investigated the magnetic couplings and the potential energy surface for the reversible binding process of the model of Hc using unrestricted Hartree–Fock and spin-polarized density functional theory (DFT) (Becke's half and half LYP (UBHandHLYP), UB3LYP, and UBLYP) (Takano et al., 2009; Takano et al., 2001; Takano and Yamaguchi, 2007). In this model, each Cu ion is coordinated by three methylimidazole. We concluded that the superexchange interaction via the bridging dioxygen causes a strong antiferromagnetic couplings between the two copper ions of the model of oxyHc and that the structural conversion from oxy to deoxyHc controls the reversible binding of dioxygen for Hc.

To comprehend the chemical character of the  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  complexes, we have investigated the magnetic interaction and the nature of the chemical bond of the biomimetic

models of oxyHc and oxyTy, **1–4**, from the viewpoint of the shape and symmetry of the natural orbitals and chemical indices. We compared the geometries, magnetic couplings, and nature of chemical bonds of the optimized structures to those of the X-ray structures.

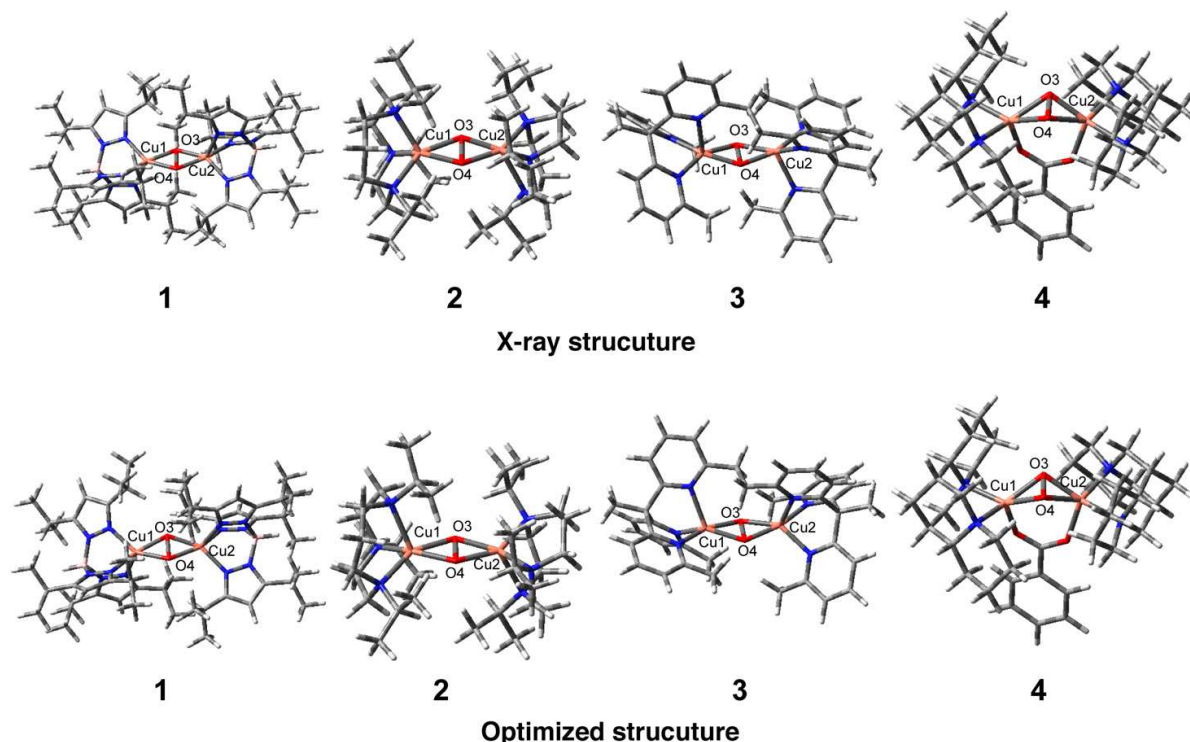


Fig. 2. X-ray crystallographic structures and optimized structures of **1–4**. Site numbers Cu1, Cu2, O3, and O4 are also illustrated.

## 2. Theoretical background

### 2.1 Magnetic coupling constant ( $J_{ab}$ )

Since a large number of transition metal complexes have unpaired d electrons, magnetic properties of transition metal complexes have been investigated in order to understand the molecular structures and the electronic structures. Magnetic coupling constants ( $J_{ab}$ ) can be experimentally determined by the measurement of magnetic susceptibility. Recent development of computational techniques of quantum chemistry has made theoretical calculations of  $J_{ab}$  values possible (Takano et al., 2001). Let us consider the superexchange interactions between  $\text{Cu(II)}\text{L}_3$  (L: ligand) fragments via peroxide. Cupric ion,  $\text{Cu(II)}$ , has the  $d^9$  configuration with half spin ( $S = 1/2$ ). If each spin is mainly localized on one site (a or b site), as illustrated in **I** of Fig. 3, we can estimate  $J_{ab}$  values between magnetic sites on the basis of the Heisenberg model (Onishi et al., 2001; Salem, 1982; Soda et al., 2000; Takano et al., 2008; Takano et al., 2002a; Takano et al., 2001; Takano et al., 2000; Takano and Yamaguchi, 2007) using the energy gap by spin-polarized DFT calculations between the highest spin (HS) and lowest spin (LS) states,

$$H = -2 \sum J_{ab} \mathbf{S}_a \cdot \mathbf{S}_b, \quad (1)$$

where  $\mathbf{S}_a$  and  $\mathbf{S}_b$  represent the spins at sites a and b, respectively. However, spin-polarized DFT solutions in the LS states usually exhibit the broken symmetry problem (Isobe et al.,

2002; Mitani et al., 2000a; Onishi et al., 2001; Salem, 1982; Takano et al., 2008; Takano et al., 2002a; Takano et al., 2001; Takano et al., 2000; Takano and Yamaguchi, 2007). Spin projection of the broken symmetry solutions should be carried out to eliminate the spin contaminations.

$$J_{ab} = \frac{{}^{\text{LS}}E_X - {}^{\text{HS}}E_X}{{}^{\text{HS}}\langle S^2 \rangle_X - {}^{\text{LS}}\langle S^2 \rangle_X}, \quad (2)$$

where  ${}^Y E_X$  and  ${}^Y \langle S^2 \rangle_X$  denote the total energy and total angular momentum of the spin state  $Y$  by spin-polarized DFT, respectively.

## 2.2 Natural orbitals

The molecular orbital picture is also feasible for elucidation of the origin of the magnetic interaction between the Cu(II) ions. In order to obtain molecular orbital-theoretical explanation of the magnetic interactions, the natural orbitals of the spin-polarized DFT solutions were determined by diagonalizing their first-order density matrices (Onishi et al., 2001; Salem, 1982; Takano et al., 2008; Takano et al., 2002a; Takano et al., 2001; Takano et al., 2000; Takano and Yamaguchi, 2007) as

$$\rho(\mathbf{r}, \mathbf{r}') = \sum n_i \phi_i^*(\mathbf{r}) \phi_i(\mathbf{r}') \quad (3)$$

where  $n_i$  denotes the occupation number of the natural orbital  $\phi_i$ . The occupation numbers of the bonding and anti-bonding natural orbitals were almost 2.0 and 0.0, respectively, except for the two singly occupied natural orbitals (SONOs), for which the occupation numbers were close to 1.0. The broken symmetry bonding orbitals are generally given by the in- and out-of phase combinations of the bonding ( $\phi$ ) and antibonding ( $\phi^*$ ) DFT natural orbital

$$\psi_i^\pm \cong (\cos \omega) \phi_i \pm (\sin \omega) \phi_i^* \quad (4)$$

where  $\omega$  is the orbital mixing coefficient (Onishi et al., 2001; Salem, 1982; Takano et al., 2008; Takano et al., 2002a; Takano et al., 2001; Takano et al., 2000; Takano and Yamaguchi, 2007).

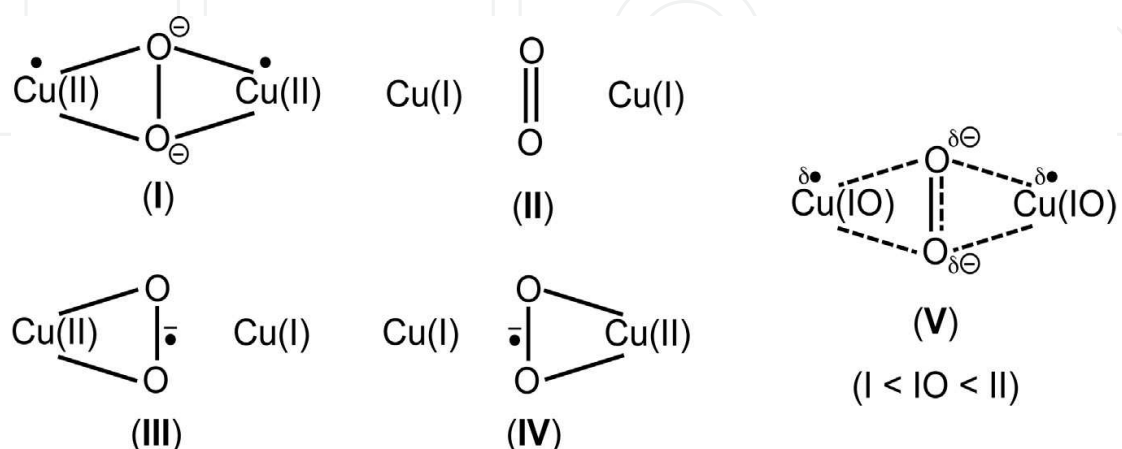


Fig. 3. Valence bond description of the Cu<sub>2</sub>O<sub>2</sub> bond.

The orbital overlap  $T_i = \langle \psi_i^+ | \psi_i^- \rangle$  between magnetic orbitals is a measure of the SE interaction, namely  $T_i = 0$  for pure metal diradical and  $T_i = 1$  for the closed-shell pair. The occupation numbers of the bonding and antibonding DNO are expressed by the  $T_i$  value;

$$n_i = 1 + T_i, \quad n_i^* = 1 - T_i \quad (5)$$

The total spin angular momentum for the BS solution is given by

$$^{LS}\langle S^2 \rangle = S_{\min}(S_{\min} + 1) + \sum (1 - T_i^2) \quad (6)$$

### 2.3 Chemical indices

In theoretical and coordination chemistries, an important issue is to understand the nature of the chemical bonds in transition metal complexes. Chemical indices are useful criteria for the nature of chemical bonds. Since the broken symmetry solutions are employed in this study, several chemical indices, which are equally defined by the symmetry-adapted CASCI and CASSCF, are expressed in terms of the occupation numbers of DFT natural orbital (Isobe et al., 2003; Mitani et al., 2000a; Yamaguchi, 1990). These indices are used as common criteria for the nature of the chemical bonds of the  $\text{Cu}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-O}_2)$  core.

The effective bond order (Isobe et al., 2003; Yamaguchi, 1990) is defined by

$$b_i = \frac{n_i - n_i^*}{2} \quad (7)$$

The effective bond order is a measure of the superexchange interaction; that is,  $b_i = 0$  for pure metal diradical and  $b_i = 1$  for the closed-shell pair.

Classical and quantum information theories and generalized entropies are now well-defined in several different fields to extract information. In chemistry, information entropy ( $I$ ) is employed to express the characteristic of chemical bonds (Ramirez et al., 1997). The Jaynes information entropy is defined by the occupation number of SONOs to express electron correlation

$$I = -n_i \ln n_i \quad (8)$$

The Jaynes information entropy for the spin-restricted DFT solution of closed-shell systems is given by

$$I_c = -2 \ln 2 \quad (9)$$

Then, the normalized Jaynes information entropy is defined as a measure of correlation correction as

$$I_n = \frac{I_c - I}{I_c} \quad (0 \leq I_n \leq 1) \quad (10)$$

The  $I_n$  value increases with the decrease of  $T_i$  in this definition, and it is parallel to the decrease of the effective bond order  $\Delta b = 1 - b = 1 - T$  (Isobe et al., 2002). The  $I_n$  and  $\Delta b$  values are, therefore, responsible for loss of bond information or covalent bonding.

The unpaired electron density  $U$  is defined as the deviation of the post HF and CI wavefunctions from the single Slater determinant (Takatsuka et al., 1978), and it is also expressed by the occupation number as

$$U = n_i(2 - n_i) \quad (11)$$

Very recently, the  $U$ -value is utilized as a measure of electron correlation by Staroverov and Davidson (Staroverov and Davidson, 2000).

The CASCI and CASSCF methods (Roos et al., 1982) are well-accepted approaches to open-shell species. Therefore, it is desirable to clarify mutual relations between the CI and BS methods. The diradical character ( $Y$ ) is defined by the weight of doubly excited configuration ( $W_D$ ) involved in the projected BS solution in comparison with CASCI and CASSCF (Isobe et al., 2002; Mitani et al., 2000b) as

$$Y = 2W_D = 1 - \frac{2T_i}{1 + T_i^2} = \frac{n_i^2 - 4n_i + 4}{n_i^2 - 2n_i + 2} \quad (12)$$

Thus, all the chemical indices introduced here are related each other through the occupation numbers of natural orbitals, which can be calculated by both symmetry-adapted solutions such as CASSCF and broken-symmetry solutions. These indices are used as common criterion for chemical bonds of biomimetic complexes **1-4**.

### 3. Computational details

#### 3.1 Computational procedure

All quantum chemical calculations were carried out on the synthetic  $\text{Cu}_2\text{O}_2$  complexes **1-4** with Gaussian03 program (Frisch et al., 2003).

In DFT calculations, exchange-correlation potentials are generally defined by

$$E_{\text{XC}} = C_1 E_{\text{X}}^{\text{HF}} + C_2 E_{\text{X}}^{\text{Slater}} + C_3 \Delta E_{\text{X}}^{\text{Becke88}} + C_4 E_{\text{C}}^{\text{VWN}} + C_5 \Delta E_{\text{C}}^{\text{LYP}} \quad (13)$$

where  $E_{\text{X}}^{\text{HF}}$  is the Hartree-Fock exchange,  $E_{\text{X}}^{\text{Slater}}$  is the Slater exchange,  $\Delta E_{\text{X}}^{\text{Becke88}}$  is the gradient part of the exchange functional of Becke (Becke, 1988),  $E_{\text{C}}^{\text{VWN}}$  is the correlation functional of Vosko, Wilk, and Nusair (Vosko et al., 1980), and  $\Delta E_{\text{C}}^{\text{LYP}}$  is the correlation functional of Lee, Yang, and Parr (Lee et al., 1988) which includes the gradient of the density. Parameters,  $C_i$  ( $i = 1-5$ ), are the mixing coefficients. The parameter sets ( $C_1$ ,  $C_2$ ,  $C_3$ ,  $C_4$ , and  $C_5$ ) are taken as (0.00, 1.00, 1.00, 1.00, and 1.00) for BLYP, (0.20, 0.80, 0.72, 1.00, and 0.81) for B3LYP (Becke, 1993), and (0.50, 0.50, 0.50, 1.00, and 1.00) for BHandHLYP (Becke, 1993). Since we showed that UBHandHLYP (referred to as UB2LYP in the previous papers (Takano et al., 2001; Takano and Yamaguchi, 2007)) can be regarded as a reliable method to examine the magnetic couplings and the dioxygen binding process of Hc and the nature of chemical bonds of the biomimetic complexes in the previous papers (Takano et al., 2009; Takano et al., 2001; Takano and Yamaguchi, 2007), we used the UBHandHLYP exchange-correlation functionals to investigate the magnetic couplings and the chemical indices: it is noteworthy that UBHandHLYP is much more reliable than conventional UB3LYP for strongly correlated electron systems such as CuO plane in oxide superconductors (Onishi et al., 2001).

Basis sets employed in all the calculations were Tatewaki-Huzinaga MIDI (533(21)/53(21)/(41)) (Tatewaki and Huzinaga, 1979) plus Hay's d diffuse function ( $\alpha = 0.1491$ ) (Hay, 1977) for Cu(II) ions, Pople's 6-31G(d) (Hariharan and Pople, 1973) for C, O, N, and B atoms, and 6-31G (Hehre et al., 1972) for H atoms.

3.2 Geometrical parameters for 1–4

The geometrical parameters of 1–4 were taken from the X-ray crystallographic data of Cambridge Structural Database (Allen, 2002) as shown in Fig. 2 (Refcode for 1: KECZEX, Refcode for 2: NAPGEQ, Refcode for 3: BEMNIR, and Refcode for 4: QOSRAS). Full geometry optimizations of 1–4 were also performed in highest- and lowest-spin states in the gas phase by using the UBHandHLYP functionals with the basis sets mentioned above. The optimized structures were characterized by using harmonic frequency calculations.

4. Comparison between X-ray structures and optimized structures

The geometrical parameters of the X-ray and optimized structures for 1–4 in the most stable state are listed in Table 1. In the geometry optimizations, models 1–3 preferred the lowest spin state to the highest spin state, while model 4 favored the highest spin state over the lowest spin state. The differences between the X-ray and optimized bond distances were within 0.1 Å except for the Cu1–Cu2, O3–O4, and Cu2–O3 parts of 2 (0.11, 0.11, and 0.15 Å, respectively) and the Cu–N part of 3 (0.12 Å). In the optimization, the changes of the dihedral angles of the Cu<sub>2</sub>O<sub>2</sub> core were less than 10° except for the d(O3–O4–Cu1–Cu2) and d(Cu1–O3–O4–Cu2) of 1 (21.3° and –17.4°) and d(Cu1–O3–O4–Cu2) of 4 (–10.3°). These differences between the optimized geometries and the X-ray structures would be due to the effects of crystal packing and the spin contamination errors during the optimization as shown below.

|                               | 1                  |                  | 2                  |                  | 3                  |                  | 4                  |                    |
|-------------------------------|--------------------|------------------|--------------------|------------------|--------------------|------------------|--------------------|--------------------|
|                               | X-ray <sup>a</sup> | Opt <sup>b</sup> | X-ray <sup>a</sup> | Opt <sup>b</sup> | X-ray <sup>a</sup> | Opt <sup>b</sup> | X-ray <sup>a</sup> | Opt <sup>b,c</sup> |
| Cu1–Cu2 <sup>d</sup>          | 3.56               | 3.58             | 3.52               | 3.63             | 3.52               | 3.61             | 3.27               | 3.24               |
| O3–O4 <sup>d</sup>            | 1.41               | 1.48             | 1.37               | 1.48             | 1.49               | 1.47             | 1.46               | 1.46               |
| Cu1–O3 <sup>d</sup>           | 1.90               | 1.95             | 1.96               | 1.96             | 1.92               | 1.93             | 1.98               | 2.08               |
| Cu1–O4 <sup>d</sup>           | 1.93               | 1.96             | 1.92               | 1.97             | 1.91               | 2.00             | 1.87               | 1.92               |
| Cu2–O3 <sup>d</sup>           | 1.93               | 1.94             | 1.81               | 1.96             | 1.96               | 1.98             | 1.91               | 1.92               |
| Cu2–O4 <sup>d</sup>           | 1.90               | 1.98             | 1.89               | 1.96             | 1.90               | 1.94             | 1.98               | 2.05               |
| Cu–N(O) <sup>d,e</sup>        | 2.08               | 2.11             | 2.11               | 2.17             | 2.05               | 2.17             | 2.03               | 2.09               |
| d(O3–O4–Cu1–Cu2) <sup>f</sup> | 0.0                | 21.3             | 10.37              | 5.30             | –15.8              | –19.6            | 48.2               | 53.7               |
| d(Cu1–O3–O4–Cu2) <sup>f</sup> | 180.0              | 162.6            | 171.9              | 176.0            | –168.2             | –164.7           | 132.3              | 122.0              |

<sup>a</sup> The parameters are taken from the X-ray structures. <sup>b</sup> The parameters were fully optimized at the UBHandHLYP level of theory. <sup>c</sup> Geometry optimization was performed in the highest spin state. <sup>d</sup> Distances are given in angstroms. <sup>e</sup> Average value for bond distances between Cu ion and N or O atom coordinating to Cu<sub>2</sub>(μ-η<sup>2</sup>:η<sup>2</sup>-O<sub>2</sub>) core. <sup>f</sup> Dihedral angles are given in degrees.

Table 1. Selected Geometrical Parameters for 1–4 in the most stable state at the UBHandHLYP level of theory.

In the biomimetic model **1**, the large changes of the dihedral angles mean that the structure of the  $\text{Cu}_2\text{O}_2$  core converts from the planar structure to the butterfly one in the geometry optimization. The geometry optimization of **2** kept the core structure planar but expanded the  $\text{Cu}_2\text{O}_2$  core, indicating that the coordinating ligand of **2** weakly suppresses the  $\text{Cu}_2\text{O}_2$  core compared to the other ligands. As opposed to **1**, though the dihedral angles of the  $\text{Cu}_2\text{O}_2$  core of **3** hardly changed in the optimization, the  $\text{Cu1-Cu2}$  distance elongated to 0.09 Å, the  $\text{O3-O4}$  length slightly shrank, the mean bond distance between the coordinating ligands and the  $\text{Cu}_2\text{O}_2$  core increased to 0.12 Å. These results imply easy release of oxygen molecule from **3**. The core structure of **4** is the most distorted of all the models **1-4**. Optimization made the  $\text{Cu}_2\text{O}_2$  core of **4** to be distorted more. It causes the strongly mixing of the character of triplet oxygen molecule, resulting in the stabilization of the highest spin state more than the lowest spin state because triplet oxygen molecule is much more stable than singlet oxygen molecule.

## 5. Magnetic couplings of the biomimetic model complexes 1-4

### 5.1 Magnetic coupling constants ( $J_{ab}$ )

Table 2 summarizes the  $J_{ab}$  values for **1-4**. All  $J_{ab}$  values calculated with the X-ray structures show strong antiferromagnetic couplings between the  $\text{Cu(II)}$  ions. The absolute values of the  $J_{ab}$  are in the order  $|J_{ab}(\mathbf{2})| \gg |J_{ab}(\mathbf{1})| > |J_{ab}(\mathbf{3})| \gg |J_{ab}(\mathbf{4})|$ . This result is mainly brought from the distortion of the  $\text{Cu}_2\text{O}_2$  core structure because the discrepancies from the planar structure ( $d(\text{O3-O4-Cu1-Cu2}) = 0^\circ$  and  $d(\text{Cu1-O3-O4-Cu2}) = 180^\circ$ ) for the  $\text{Cu}_2\text{O}_2$  core of **1-4** are in the order:  $\mathbf{1} \approx \mathbf{2} < \mathbf{3} \ll \mathbf{4}$ . The  $J_{ab}$  values are sensitive to the change of the  $\text{Cu}_2\text{O}_2$  structure because the  $\text{Cu}_2\text{O}_2$  core lies in the labile bonding region (Takano and Yamaguchi, 2007), and the core structure strongly affects the strength of the symmetry-allowed orbital interactions between the symmetric (S)  $d_{xy}-d_{xy}$  orbital of the dicopper site and the  $\sigma^*$  and  $\pi_v^*$  orbitals of  $\text{O}_2$  and between the antisymmetric (A)  $d_{xy}+d_{xy}$  orbital and the  $\pi_h^*$  orbital, as shown in Fig. 4.

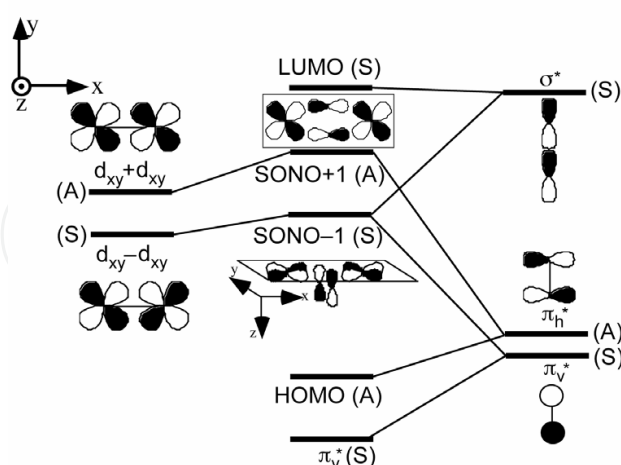


Fig. 4. Orbital diagram of the  $\text{Cu}_2\text{O}_2$  bond.

The magnetic couplings weakened after full geometry optimization, and, in particular, the  $J_{ab}$  value for **4** became positive, indicating a ferromagnetic coupling. This is because of the elongation of the  $\text{Cu-O-Cu}$  lengths ( $\text{Cu1-O3} + \text{Cu2-O3}$  and  $\text{Cu1-O4} + \text{Cu2-O4}$ ) and the change of the dihedral angles. Geometry optimization of **1** remarkably changed the  $\text{Cu}_2\text{O}_2$

structure from the planar form to the butterfly form. The structural conversion affects the orbital interactions between the Cu(II) ions via peroxide, leading to drastic reduction of the  $J_{ab}$  values in magnitude. The larger elongation of the Cu–O–Cu lengths in **2** (0.15 Å for Cu1–O3–Cu2 and 0.12 Å for Cu1–O4–Cu2) and **3** (0.13 Å for Cu1–O4–Cu2) made the magnetic coupling weak, though the shape of the Cu<sub>2</sub>O<sub>2</sub> core kept almost planar during geometry optimization. During geometry optimization of **4**, the Cu–O bond lengths elongated by about 0.1 Å, showing that the dioxygen part tends to dissociate from the dicopper core and that the spin crossover from the lowest spin state to the highest spin state occurs (Takano and Yamaguchi, 2007). However, this spin crossover during geometry optimization might be attributed to the spin contamination error (Kitagawa et al., 2007; Saito et al., 2010; Saito et al., 2008). These indicate that the ligands that can hold the Cu<sub>2</sub>O<sub>2</sub> core planar lead to the strong antiferromagnetic complexes.

| Model    | $J_{ab}^a$         |                  |
|----------|--------------------|------------------|
|          | X-ray <sup>b</sup> | Opt <sup>c</sup> |
| <b>1</b> | -1902              | -678.1           |
| <b>2</b> | -1967              | -1363            |
| <b>3</b> | -1508              | -1020            |
| <b>4</b> | -247.5             | 35.17            |

<sup>a</sup>  $J_{ab}$  is shown in cm<sup>-1</sup>. <sup>b</sup> The parameters are taken from the X-ray structures. <sup>c</sup> The parameters were fully optimized at the UBHandHLYP level of theory.

Table 2. Magnetic Coupling constants ( $J_{ab}$ )<sup>a</sup> Calculated for **1–4** at the UBHandHLYP level of theory.

5.2 Charge and spin density distributions

We have investigated the charge and spin density distributions for **1–4** to understand the characteristics of the magnetic couplings. As listed in Table 3, the charge density on the O–O group varies from the formal charge (–2.0) in **I** to 0.0 in the valence bond configuration **II** in Fig. 3, indicating the back charge transfer from peroxide to cupric ions. The back charge transfer implies that the superexchange interactions are responsible for the strong antiferromagnetic coupling of the biomimetic models.

In Table 3, the spin densities on Cu(II) ions were about 0.7 for **1–4**. The spin density populations indicate the resonance state between the one-electron transfer valence bond configurations **III** and **IV** in Fig. 3. The spin densities on the O–O group are cancelled out in this resonance state **V**; that is, intermediate valence state.

The broken symmetry orbitals in Eq. (4) are approximately expressed by the fragment orbitals responsible for these valence bond configurations in Fig. 3.

$$\psi^+ \cong (\cos\theta)\pi_h^* + (\sin\theta)d_{xy}^{Cu2}$$

(14)

$$\psi^- \cong (\cos\theta)\pi_h^* + (\sin\theta)d_{xy}^{Cu1}$$

(15)

where  $\theta$  is the orbital mixing parameter and  $d_{xy}^{Cu1}$  or  $d_{xy}^{Cu2}$  denote the localized  $d_{xy}$  orbital at Cu1 or Cu2, respectively. The broken symmetry solution is approximately given by  $|\psi^+ \bar{\psi}^- d_{xy}^{Cu1} \bar{d}_{xy}^{Cu2}|$ . The spin density at Cu1 is calculated by

| Model |                       |        | Cu1 <sup>a</sup> | Cu2 <sup>a</sup> | O3 <sup>a</sup> | O4 <sup>a</sup> |
|-------|-----------------------|--------|------------------|------------------|-----------------|-----------------|
| 1     | X-ray                 | Charge | 1.082            | 1.082            | -0.594          | -0.594          |
|       |                       | Spin   | 0.709            | -0.708           | 0.006           | -0.007          |
|       | Opt                   | Charge | 1.023            | 1.075            | -0.591          | -0.572          |
|       |                       | Spin   | 0.726            | -0.727           | 0.000           | -0.000          |
| 2     | X-ray                 | Charge | 0.985            | 1.044            | -0.641          | -0.612          |
|       |                       | Spin   | 0.661            | -0.651           | -0.009          | -0.008          |
|       | Opt                   | Charge | 0.929            | 0.937            | -0.604          | -0.601          |
|       |                       | Spin   | 0.689            | -0.676           | -0.002          | -0.005          |
| 3     | X-ray                 | Charge | 1.127            | 1.107            | -0.594          | -0.611          |
|       |                       | Spin   | 0.701            | -0.713           | 0.022           | -0.013          |
|       | Opt                   | Charge | 1.071            | 1.063            | -0.610          | -0.586          |
|       |                       | Spin   | 0.715            | -0.712           | 0.025           | -0.029          |
| 4     | X-ray                 | Charge | 0.873            | 0.887            | -0.584          | -0.601          |
|       |                       | Spin   | 0.688            | -0.687           | -0.034          | 0.030           |
|       | Opt (HS) <sup>b</sup> | Charge | 0.841            | 0.841            | -0.545          | -0.545          |
|       |                       | Spin   | 0.666            | 0.667            | 0.215           | 0.215           |

<sup>a</sup> The site numbers are shown in Fig. 2. <sup>b</sup> Geometry optimization was performed in the highest spin state.

Table 3. Charge and Spin Densities of **1–4** at the UBHandHLYP level of theory.

$$Q_{Cu1} = (1 - \sin^2 \theta) \cong 0.7$$

(16)

The  $\theta$ -parameter was determined to be 0.58 rad. The broken symmetry solution after spin projection, namely the resonance state **V**, is obtained by

$$^1\Phi \cong (spin - projected) \left| \psi^+ \bar{\psi}^- d_{xy}^{Cu1} \bar{d}_{xy}^{Cu2} \right| = N \left( \sum C_X ^1\Phi_{VB}(X) \right)$$

(17)

where  $^1\Phi_{VB}(X)$  denotes the pure singlet valence bond wavefunction responsible for the valence bond structure  $X$  ( $= \text{I–IV}$ ), and  $N$  is the normalizing factor. The configuration mixing parameters  $C_X$  are defined by the orbital mixing parameter  $\omega$ .

$$C_I = 1 + \cos 2\theta$$

(18)

$$C_{II} = 1 - \cos 2\theta$$

(19)

$$C_{III} = C_{IV} = \sin 2\theta$$

(20)

These values are determined as

$$C_I = 1.4, C_{II} = 0.6 \quad C_{III} = C_{IV} = 0.9$$

(21)

The ratios of the valence bond configurations were 5 (**I**) : 1 (**II**) : 2 (**III** = **IV**) under the drastic approximation. The antiferromagnetically coupled singlet state (**V**) in Fig. 3 is expressed by the superposition of the four valence bond structures **I–IV**. However, the broken symmetry molecular orbitals partly involve the contribution from  $\pi_v^*$  orbital as illustrated in Fig. 4. This implies that much more valence bond configurations are required to express the spin projected broken symmetry state, quantitatively. Judging from the charge and spin densities

on the  $\text{Cu}_2\text{O}_2$  core, the copper ion lies in the intermediate oxidation (IO) state ( $\text{I} < \text{IO} < \text{II}$ ), while dioxygen in turn exists in the intermediate reduction (IR) state ( $\text{O}_2^{1-} < \text{O}_2^{\text{m-}} < \text{O}_2^{2-}$ ;  $1 < m < 2$ ) as shown in **V** of Fig. 3. The intermediate valence structure **V** expresses the coupling between  $\text{Cu}(\text{IO})$  and  $\text{O}_2(\text{IR})$  anion.

In the models **1–4**, the total charge densities on the Cu sites (Cu1 and Cu2) estimated with the X-ray structures were 2.16, 2.03, 2.23, and 1.76, respectively, showing that the back charge transfer from the peroxide to the  $\text{Cu}(\text{II})$  sites in **4** is much stronger than those in **1–3**. This tendency is attributable to the conversion from peroxide to oxygen molecule due to the distorted  $\text{Cu}_2\text{O}_2$  core, which causes the strong mixing of the character of triplet oxygen molecule to the electronic structure of the  $\text{Cu}_2\text{O}_2$  core. After geometry optimizations of **1–4**, the charge densities on the Cu sites reduced, namely the oxidation number of the Cu ions become close to monovalent cation. It indicates the decrease of the magnetic couplings between the Cu ions as shown above.

## 6. Natural orbitals and chemical indices

### 6.1 Natural orbitals

The orbital correlation diagram is exhibited in Fig. 4. Fig. 5 illustrates the SONOs of **1–4** in the LS state. The bonding symmetric (S)  $d_{xy}-d_{xy}$  orbital of the dicopper site interacts with S-type orbitals ( $\sigma^*$ ,  $\pi_v^*$ , etc) of peroxide in SONO-1, while SONO+1 consists of the antisymmetric (A)  $d_{xy}+d_{xy}$  orbital and the  $\pi_h^*$  one. The  $\pi_h^*$  orbital is stabilized by the symmetry-allowed orbital interactions to afford HOMO as shown in Fig. 4. The SONOs delocalize on the whole  $\text{Cu}_2\text{O}_2$  core. The delocalized orbital on the  $xy$ -plane can be attributable to the antiferromagnetic superexchange interactions between the  $\text{Cu}(\text{II})$  ions via dioxygen. The SONO-1 of **1** was composed of the  $d_{xy}-d_{xy}$  and  $\sigma^*$  orbitals because of the planar  $\text{Cu}_2\text{O}_2$  core structures. On the other hand, that of **4** consisted of the  $d_{xy}-d_{xy}$  and  $\pi^*$  orbitals because the butterfly core structure allows the d orbitals to interact with  $\pi^*$  orbitals. In **2** and **3**, both the  $\sigma^*$  and  $\pi^*$  orbitals of peroxide was involved in the formation of the SONO-1. These results indicate that the architecture of the  $\text{Cu}_2\text{O}_2$  core strongly influences the d-p orbital interaction, attributing to the magnetic couplings and the chemical bond characters.

### 6.2 Occupation numbers and chemical indices

The natural orbital analysis clearly demonstrates that the  $\text{Cu}_2\text{O}_2$  bonds exhibit intermediate bonding. Chemical indices such as effective bond order should be a useful index for the investigation of bond character (Isobe et al., 2003; Takano et al., 2008; Takano and Yamaguchi, 2007; Yamaguchi, 1990). Using the occupation numbers of SONOs (Table 4), these indices for **1–4** can be estimated with Eqs. (7), (10), (11), and (12).

The  $b$  values for **1–4** are summarized in Table 5. The  $b_{\text{SOMO}}$  values indicate that the Cu sites intermediately interact with each other through the binding dioxygen. The  $\text{Cu}_2\text{O}_2$  bond is not a closed-shell type molecular orbital configuration ( $b_{\text{SOMO}} = 1.0$ ), but an open shell configuration, where electrons partially occupy the antibonding SONO+1. This open-shell molecular orbital configuration ensures the strong antiferromagnetic superexchange interactions. The  $b_{\text{HOMO}}$  values for **1–4** were 0.997, showing the very weak spin polarization effect. The  $b_{\text{SOMO}}$  values increases as **4** << **3** < **1** < **2**, indicating the same tendency of the  $|J_{\text{ab}}|$  values. Judging from the charge densities and the  $b_{\text{SOMO}}$  values, **4** estimates much smaller superexchange interaction between  $\text{Cu}(\text{II})$  ions via peroxide than **1–3**, showing the smaller absolute value of  $J_{\text{ab}}$ . On the other hand, the  $b_{\text{HOMO}}$  values in models **1–4** are close to each

other, indicating that the spin polarization effects are insensitive to the ligand coordination. The natural orbital analysis clearly demonstrates that the antiferromagnetic couplings of these  $\text{Cu}_2\text{O}_2$  system are dominated by the superexchange interaction and that the  $\text{Cu(II)}$  ions and the peroxide ion show an intermediate orbital interaction ( $0 < b_{\text{SOMO}} < 1.0$ ).

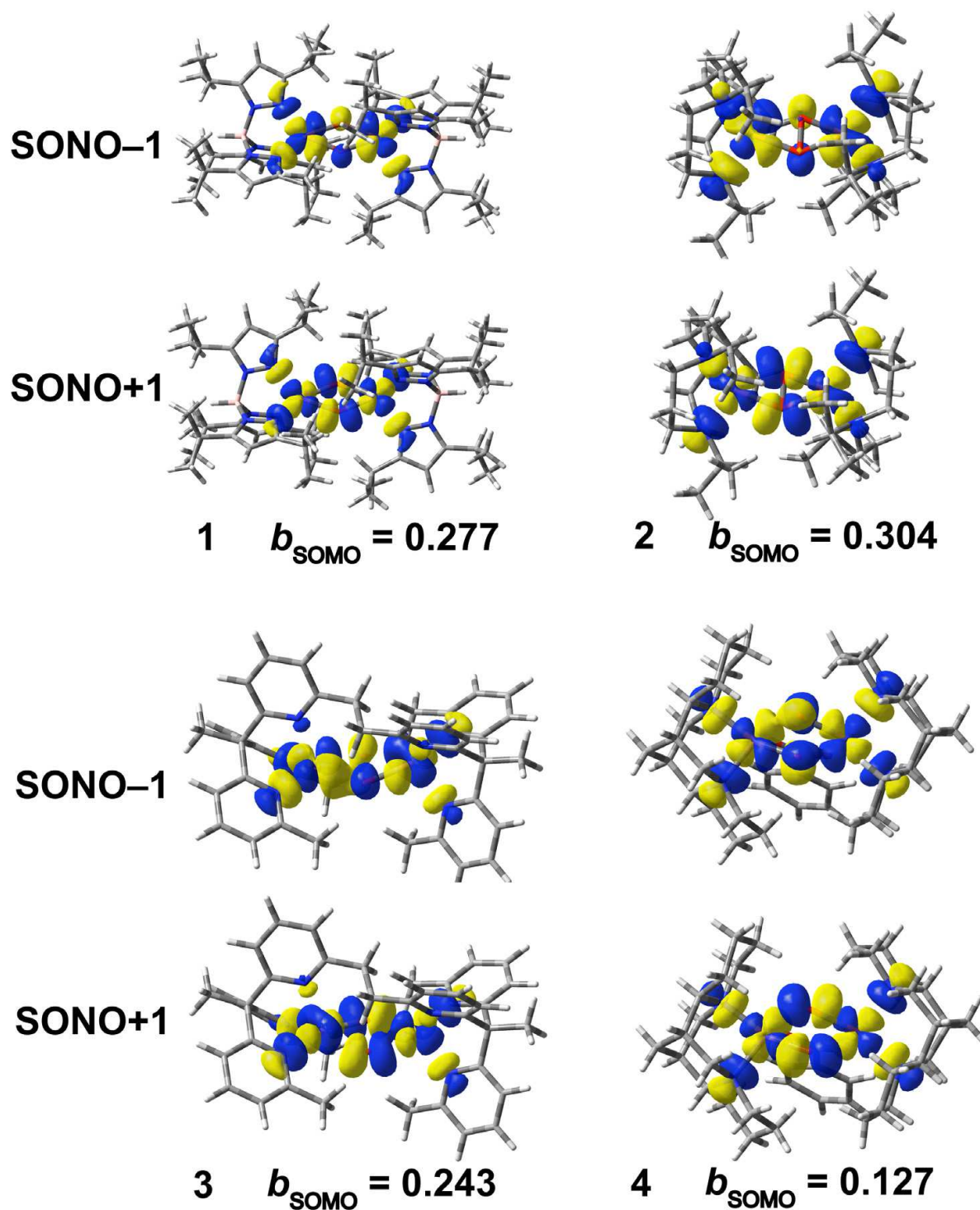


Fig. 5. Singly occupied bonding (SONO-1) and antibonding (SONO+1) natural orbitals (SONOs) obtained from UBHandHLYP calculations in the LS state with the X-ray crystallographic structures of 1-4.

| Model |                  | HOMO  | SOMO-1 | SOMO+1 | LUMO  |
|-------|------------------|-------|--------|--------|-------|
| 1     | X-ray            | 1.997 | 1.277  | 0.723  | 0.003 |
|       | Opt <sup>a</sup> | 1.997 | 1.236  | 0.764  | 0.003 |
| 2     | X-ray            | 1.997 | 1.304  | 0.696  | 0.003 |
|       | Opt <sup>a</sup> | 1.997 | 1.253  | 0.747  | 0.003 |
| 3     | X-ray            | 1.997 | 1.243  | 0.757  | 0.003 |
|       | Opt <sup>a</sup> | 1.997 | 1.222  | 0.778  | 0.003 |
| 4     | X-ray            | 1.997 | 1.127  | 0.873  | 0.003 |
|       | Opt <sup>a</sup> | 1.998 | 1.091  | 0.909  | 0.002 |

<sup>a</sup> Geometrical parameters were fully optimized.

Table 4. Occupation Numbers of HOMO and SOMOs (SONOs) of **1–4** by UBHandHLYP in the LS State.

| Model |                  | <i>b</i> <sub>HOMO</sub> | <i>b</i> <sub>SOMO</sub> |
|-------|------------------|--------------------------|--------------------------|
| 1     | X-ray            | 0.997                    | 0.277                    |
|       | Opt <sup>a</sup> | 0.997                    | 0.236                    |
| 2     | X-ray            | 0.997                    | 0.304                    |
|       | Opt <sup>a</sup> | 0.997                    | 0.253                    |
| 3     | X-ray            | 0.997                    | 0.243                    |
|       | Opt <sup>a</sup> | 0.997                    | 0.222                    |
| 4     | X-ray            | 0.997                    | 0.127                    |
|       | Opt <sup>a</sup> | 0.998                    | 0.091                    |

<sup>a</sup> Geometrical parameters were fully optimized.

Table 5. Effective bond orders of HOMOs and SOMOs (SONOs) of **1–4** by UBHandHLYP in the LS State.

The information entropy (*I*), unpaired electron density (*U*), and diradical character (*Y*) are also useful indices for the investigation of the character of the chemical bond (Soda et al., 2000). Using the occupation numbers of the SONOs, the indices were estimated with Eqs. (10)–(12). In Table 6, the *I* values express the loss of the covalency of the chemical bonds. The *U* values are equivalent to the deviation from exact singlet value <sup>LS</sup><**S**<sup>2</sup>> = 0 for the broken-symmetry solution. The *Y* values, which characterize the double excitation of electrons occupying the bonding NOs, indicate how much the unoccupied electrons can localize on the spin sites. They can be regarded as useful indices to diagnose the bond nature and measures of the strength of orbital interactions. Previously, we investigated the nature of the chemical bonds of organic systems, showing that intermolecular radical character of organic radicals, phenalenyl radical dimeric pair, were represented as 0.65 of the *I* value, 0.838 of the *U* value, and 0.30 of the *Y* value (Takano et al., 2002b, c). Comparing to the organic system, we found that the biomimetic complexes, **1–4**, show strong radical character, that is, rather weak orbital interactions; however, the weak bond character is sufficient for the cooperative intramolecular (through-bond) charge transport for the oxygen trapping, namely the dioxygen binding in the biomimetic complexes, **1–4**. The estimated effective bond orders and information entropies exhibit similar behavior responsible for the bond formation via electron delocalization. On the other hand, the evaluted unpaired electron densities are responsible for the electron correlation effects, and therefore they are about 1.0 for all the complexes, indicating an important role of the electron correlation effect. The electron

delocalization and electron correlations are competitive in the copper–oxygen systems. This is the reason why we must use UBHandHLYP instead of UB3LYP and UBLYP as discussed in detail in our previous paper (Takano et al., 2001; Takano and Yamaguchi, 2007). The optimized structure provided the larger chemical indices for **1–4** than the X-ray structure due to the relaxation of the Cu<sub>2</sub>O<sub>2</sub> core. It indicates that crystal environment strengthens the orbital interactions of the dicopper core of the biomimetic complexes, **1–4**. The evaluated information entropies, unpaired electron densities, and diradical characters show the following tendency: **4** >> **3** > **1** > **2**, qualitatively corresponds to the order of the magnetic coupling:  $J_{ab}(\mathbf{4}) \gg J_{ab}(\mathbf{3}) > J_{ab}(\mathbf{1}) > J_{ab}(\mathbf{2})$ .

| Model    |                  | $I_n$ | $U$   | $Y$   |
|----------|------------------|-------|-------|-------|
| <b>1</b> | X-ray            | 0.775 | 0.923 | 0.485 |
|          | Opt <sup>a</sup> | 0.811 | 0.944 | 0.553 |
| <b>2</b> | X-ray            | 0.75  | 0.908 | 0.443 |
|          | Opt <sup>a</sup> | 0.796 | 0.936 | 0.524 |
| <b>3</b> | X-ray            | 0.805 | 0.941 | 0.541 |
|          | Opt <sup>a</sup> | 0.823 | 0.951 | 0.577 |
| <b>4</b> | X-ray            | 0.903 | 0.984 | 0.75  |
|          | Opt <sup>a</sup> | 0.931 | 0.992 | 0.819 |

<sup>a</sup> Geometrical parameters were fully optimized.

Table 6. Information entropies ( $I$ ), unpaired electron densities ( $U$ ), and diradical characters ( $Y$ ) of SOMOs (SONOs) of **1–4** by UBHandHLYP in the LS State.

7. Concluding remarks

The magnetic couplings and the nature of the chemical bonds of the Cu<sub>2</sub>(μ-η<sup>2</sup>:η<sup>2</sup>-O<sub>2</sub>) core of the biomimetic models **1–4** were investigated by hybrid DFT calculations such as UBHandHLYP calculations. We estimated the magnetic coupling constants and examined the electronic structures for **1–4** from the viewpoint of the shape and symmetry of the natural orbitals and chemical indices. Analysis of natural orbitals and effective bond orders provide us useful insights that the antiferromagnetic couplings of the Cu<sub>2</sub>O<sub>2</sub> systems are dominated by the superexchange interaction, that Cu(II) ions and peroxide show an intermediate orbital interaction ( $0 < b < 1.0$ ), and that the distortion of the Cu<sub>2</sub>O<sub>2</sub> core from a planar structure to a butterfly structure and elongation of the Cu–O bonds cause the reduction of orbital interactions between the symmetric d<sub>xy</sub>–d<sub>xy</sub> orbital of the dicopper site and the π<sub>v</sub>\* orbital of O<sub>2</sub> and between the antisymmetric d<sub>xy</sub>+d<sub>xy</sub> orbital and the π<sub>h</sub>\* orbital, weakening the magnetic coupling between the Cu sites via μ-η<sup>2</sup>:η<sup>2</sup>-peroxide. The information entropy, unpaired electron density, and diradical character exhibited the useful information about the chemical bonds in the dicopper core of biomimetic complexes, **1–4**. Especially, the evaluted unpaired electron densities indicates the reason why we must use UBHandHLYP instead of UB3LYP and UBLYP. Thus, natural orbitals and chemical indices such as effective bond order, information entropy, unpaired electron density, and diradical character are useful for elucidation of the nature of chemical bonds based on the broken symmetry DFT calculation.

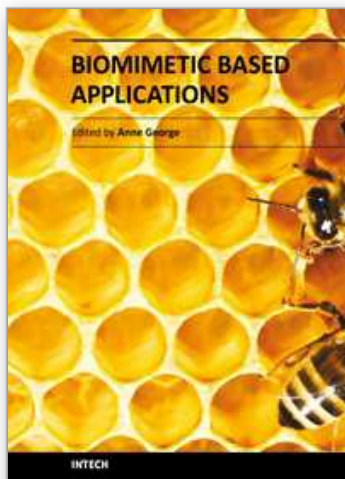
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