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Hemocyanin model compounds; a quantum mechanical calculation of geometry-dependent exchange interaction*

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Abstract

Strong antiferromagnetic coupling between the two copper(II) ions of oxyhemocyanin with $-2J>600$ cm^{-1} ($\mathbf{H}=-2J_{12}S_1S_2$) was observed a long time ago. SCF–MP (self-consistent field–Møller Plesset) calculations have been performed to understand this high value. Five geometrically different model molecules were constructed to determine the contributions to J, the J values, partial charges and the involved orbitals. Information about the exchange pathway has been derived. Strong antiferromagnetic exchange interactions of $2J=-6600$ to $-17\,800$ cm^{-1} have been calculated. The exchange pathway includes the peroxo bridge via its p_x and p_y atomic orbitals, which are responsible for the high antiferromagnetic exchange. It has been shown that geometric variations have a strong effect on the J value, but the involved orbitals, d_{xy} of Cu and p_x, p_y of O, remain the same. The terminal NH_3 ligands are not involved in the exchange interaction.

Key words: Quantum mechanical calculations; Hemocyanin model compounds

Introduction

The binuclear copper protein hemocyanin functions as a molecular oxygen transporter in invertebrates. The highly aggregated molecules bind dioxygen cooperatively. There are different structure models discussed in the literature [1–5]; the structure model of Kitajima *et al.* [5] reflects most of the hemocyanin parameters very well. The active core contains the two Cu ions in a distorted tetragonal environment. Though it is very difficult to crystallize hemocyanin, Magnus *et al.* [6] succeeded in obtaining crystals of the Subunit II of *Limulus polyphemus* hemocyanin, which has a molar mass of 3.2×10^6 Da due to 48 subunits. The crystal structure has been analyzed with 2.7 Å resolution [6], but the geometry of the active core was not solved in detail. The active core is the $N_3Cu(\mu\text{-}\eta^2\text{:}\eta^2O_2^{2-})CuN_3$ chromophore with the Cu ions coordinated to two or three histidyl-imidazole ligands. The Cu ions are in the oxy form in the oxidized (2+) state. The peroxide ion seems to bridge in a μ-η^2:η^2 fashion, consistent with Kitajima *et al.* [5] who obtained a μ-η^2:η^2-peroxo-bridged binuclear Cu(II) complex, which is a good model complex for hemocyanin. The Cu–Cu separation of 3.56 Å is near the determined value [6] of 3.6 Å.

An interesting issue of oxyhemocyanin is its strong antiferromagnetic coupling between the two copper(II) ions with $-2J>600$ cm^{-1} for $\mathbf{H}=-2J_{12}S_1S_2$ [7, 8]. Due to the high molecular weight of the molecule and the low metal concentration these measurements cannot be very accurate. Even electron spectroscopic methods could not elucidate the structure and chemical reactivity with other anions, because of the d^{10} system of Cu(I) of the deoxy form.

The most important part of the hemocyanin molecule is its core, which contains the two Cu(II) atoms and the peroxo bridge between them. The terminal ligands have less influence. In 1991 Ross and Solomon [1] performed self-consistent field–Xα–scattered wave (SCF–Xα–SW) calculations on a series of Cu(II)–peroxide structure models to evaluate a model of relevance to oxyhemocyanin. Their calculations were performed to understand the differences in electronic structure and bonding of copper–peroxide complexes. They described the Cu–O and O–O bonding interactions, charge and spin distributions, and excited-state transition energies.

It is our intention to determine the contributions to the exchange interaction J, especially the charge-transfer

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ligand to copper, which is one of the most interesting contributions because it helps to determine the exchange pathway. The overlapping orbitals of Cu and O dependent on the Cu–O–Cu angle variations were discussed in order to explain the strong exchange interaction of these compounds. The peroxo bridging ligand seems to have the dominant influence. We constructed five models with different Cu–O–Cu angles α for the self-consistent field–Møller Plesset (SCF–MP) calculations. Informations about the contributions to J, the J values and the involved orbitals were obtained. Our interest is focused on the tendency of the exchange interaction and not on the absolute values.

Hemocyanin models

We used the simplified hemocyanin model $Cu_2O_2(NH_3)_4$ (Fig. 1). The molecule contains the peroxo bridge and two Cu(II) atoms as the center in a planar coordination mode. These atoms build the core of the molecule and are relevant for the exchange interaction. The remaining ligands, which determine the copper environment have only a minor influence on the exchange interaction since calculations with six NH_3 groups as terminal ligands instead of four showed no remarkable difference in the J value. Therefore we decided to perform all further calculations with four NH_3 groups as terminal ligands. Calculations with five geometrically slightly different molecules M1–M5 were performed to examine the electronic constitution of the core and the overlap densities of the Cu–O pathway. The five molecules differ only in the Cu–O–Cu angle α (Table 1). The molecules are planar and centrosymmetric. The Cu–Cu separation of the basic model M3, which corresponds to that of Ross and Solomon [1], is 3.56 Å with an angle α of 136°. For our calculations we varied this model from M1 to M5. In these models the Cu–Cu and Cu–O distances increase with α, while the peroxide O–O separation remains at 1.41 Å.

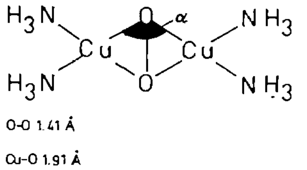

Fig. 1. The basic model compound M3 with the Cu–O–Cu angle α (°); O–O 1.41 Å, Cu–O 1.91 Å.

TABLE 1. Geometric parameters of the five model compounds

Variation of α Cu–O–Cu (°)	Cu–Cu distance (Å)	Model
131.29	3.490	M1
133.90	3.525	M2
136.00	3.560	M3
139.56	3.595	M4
142.73	3.630	M5

Computational details

The basis for these *ab initio* based calculations are the models of Anderson [9] and Hay *et al.* [10]. Further mechanisms, which stabilized the singlet state, were included by de Loth *et al.* [11]. The exchange interaction J is calculated in two steps. The first is the construction of magnetic orbitals for the definition of the total spin states. The second is the determination of the separation energy with the pertubation calculation. An open-shell SCF calculation is carried out for a given set of atomic coordinates. The open-shell SCF calculation uses the Fock operator (eqn. (1)) introduced by Nesbet, which describes single and double occupied molecular orbitals (MOs).

$$\mathbf{F}^N = \mathbf{h} + \sum(2\mathbf{J}_i - \mathbf{K}_i) + \mathbf{J}_{\sigma_g} - \mathbf{K}_{\sigma_g}/2 + \mathbf{J}_{\sigma_u} - \mathbf{K}_{\sigma_u}/2 \qquad (1)$$

with $\mathbf{h}$ as the single electron operator, $\mathbf{J}$ the Coulomb operator and $\mathbf{K}$ the exchange operator.

The sum includes all double and the two single occupied orbitals σ_g and σ_u. σ_g is the symmetric linear combination of the atomic orbitals ψ_i and σ_u the antisymmetric combination.

$$\sigma_g = \sum c_i \psi_i \sim (d_{x^2-y^2}(\mathrm{Cu1}) + d_{x^2-y^2}(\mathrm{Cu1'}))$$
$$\sigma_u = \sum c_i \psi_i \sim (d_{x^2-y^2}(\mathrm{Cu1}) - d_{x^2-y^2}(\mathrm{Cu1'})) \qquad (2)$$

For symmetric molecules the orthogonal localized magnetic orbitals a and b are derived.

$$\mathrm{a} = (\sigma_g + \sigma_u)/\sqrt{2}$$
$$\mathrm{b} = (\sigma_g - \sigma_u)/\sqrt{2} \qquad (3)$$

with $\langle \mathrm{a}|\mathrm{b}\rangle = 0$.

a is localized at Cu1 and b at Cu1′

$$\mathrm{a} \sim d_{x^2-y^2}(\mathrm{Cu1}); \qquad \mathrm{b} \sim d_{x^2-y^2}(\mathrm{Cu1'}) \qquad (4)$$

The singlet and triplet states are defined as

$${}^1\psi_0 = \mathrm{A}[(\Pi \mathrm{i}\mathit{i})(\mathrm{a}\mathit{b} + \mathrm{b}\mathit{a})/\sqrt{2}] = (\Phi_1 + \Phi_2)/\sqrt{2}$$
$${}^3\psi_0 = \mathrm{A}[(\Pi \mathrm{i}\mathit{i})(\mathrm{a}\mathit{b} - \mathrm{b}\mathit{a})/\sqrt{2}] = (\Phi_1 - \Phi_2)/\sqrt{2} \qquad (5)$$

i stands for one of the double occupied nMOs. Normal means 'spin up', italic 'spin down'. **A** is the antisymmetric operator for the $2n+2$ electrons of the system, Φ_1 and Φ_2 are the Slater determinants corresponding to

$$\Phi_1 = \mathrm{A}[(\Pi \mathrm{i}\mathit{i})\mathrm{a}\mathit{b}] \qquad (6)$$

Therefore the energy difference between the singlet and triplet state is

$$\Delta E_0 = \langle {}^1\psi_0|\mathbf{H}|{}^1\psi_0\rangle - \langle {}^3\psi_0|\mathbf{H}|{}^3\psi_0\rangle = 2K_{ab} \tag{7}$$

with

$$\mathbf{H} = \mathbf{H}_0 + \mathbf{V}; \quad \mathbf{H}_0 = \mathbf{F}^N \quad \mathbf{V} = 1/r_{12}$$

$1/r_{12}$ is the pertubation operator and K_{ab} the two electron exchange integral, which results from the interaction of the two unpaired electrons of the magnetic orbitals a and b.

$$K_{ab} = \langle a(1)b(2)|1/r_{12}|a(2)b(1)\rangle \tag{8}$$

This contribution stabilizes the triplet state because of the orthogonality $\langle a/b\rangle = 0$. Following Anderson [9] this is called 'potential exchange'.

The SCF calculation minimizes the total energy of the molecule. The energy of the singlet–triplet separation is by comparison to this very small, because it is the difference between large numbers.

The second step of the de Loth *et al.* method is the pertubation calculation. Therefore the interaction of double occupied MOs and unoccupied MOs is calculated. The singlet and triplet states are calculated for the 2nd order with an (MP) pertubation calculation, where I is the excited state.

$${}^1\epsilon_2 = \sum \langle {}^1\psi_0|\mathbf{H}|\Phi_\mathrm{I}\rangle^2/\Delta E_{0\mathrm{I}}$$
$${}^3\epsilon_2 = \sum \langle {}^3\psi_0|\mathbf{H}|\Phi_\mathrm{I}\rangle^2/\Delta E_{0\mathrm{I}}, \quad \Delta E_{0\mathrm{I}} = E_0 - E_\mathrm{I} \tag{9}$$

The contributions of 2nd order are derived if ${}^1\psi_0$ and ${}^3\psi_0$ are replaced with the Slater determinants Φ_1 and Φ_2.

$$\Delta E_2 = {}^1\epsilon_2 - {}^3\epsilon_2 = 2\sum \langle \Phi_1|\mathbf{H}|\Phi_\mathrm{I}\rangle \langle \Phi_\mathrm{I}|\mathbf{H}|\Phi_2\rangle/\Delta E_{0\mathrm{I}} \tag{10}$$

E_0 is the energy, which belongs to Φ_1 and to Φ_2, respectively, E_I is the energy of the determinant Φ_I, which describes excited states. Only the excited states Φ_I contribute to the singlet–triplet separation, if they interact also with Φ_1 and Φ_2.

The calculations were performed with a modified HONDO program [12]. This program uses contracted Gauß functions for the atomic orbitals of the valence electrons and pseudopotentials for the core electrons. The pseudopotentials were calculated with an atomic *ab initio* RHF calculation due to Barthelat and Durand [13] and Pelissier [14]. The specific parameters for copper are of the work of Pelissier [15], and the parameters for the other atoms are taken from ref. 16. The basis set for copper includes nine Gauß functions (3s, 1p, 5d), which were contracted to five groups (2s, 1p, 2d). The basis set has been optimized for the $4s^13d^9$ configuration of copper [17].

Due to the pertubation method used, the modified HONDO program also derives the contributions to J. They are the potential exchange (PE) (see eqn. (8)) and kinetic exchange (KE), introduced by Anderson [18], Kanamori [19] and Goodenough [20], the double spin polarization (DSP), charge transfer ligand → Cu (CT L → Cu), charge transfer Cu → ligand (CT Cu → L), polarization of 2nd order (P2.O) and polarization of 4th order (P4.O). The different contributions are described in detail by de Loth *et al.* [18, 21].

Results and discussion

The results of the $2J$ calculations are summarized in Table 2.

In Fig. 2 the magnitude of $2J$ is plotted versus α. The electronic constitution of the bridging oxygen and the geometry of the molecule should have an influence on the value of the singlet–triplet separation, since the oxygen orbitals are directly involved in the magnetic de-

TABLE 2. Results of the calculations

	Model				
	M1	M2	M3	M4	M5
Angle α (°)	131.29	133.9	136.0	139.56	142.73
Cu–Cu (Å)	3.49	3.53	3.56	3.60	3.63
$2J$ (cm^{-1})	−6627	−7315	−8790	−11500	−17803
$2J$ contributions (cm^{-1})					
PE	4214	5203	6641	8656	11817
KE	−6050	−6986	−8548	−11095	−16223
DSP	−330	−178	−61	24	73
CT L→Cu	−577	−680	−831	−1072	−1568
CT Cu→L	−117	−142	−175	−218	−282
P2.O	−1140	−1486	−2019	−2800	−4118
P4.O	−2627	−3046	−3797	−4995	−7502
Partial charges (|e|)					
Cu	1.292	1.237	1.172	1.129	1.075
O	−0.619	−0.602	−0.577	−0.550	−0.511
N	−0.886	−0.872	−0.855	−0.845	−0.833
H	0.374	0.369	0.364	0.360	0.354

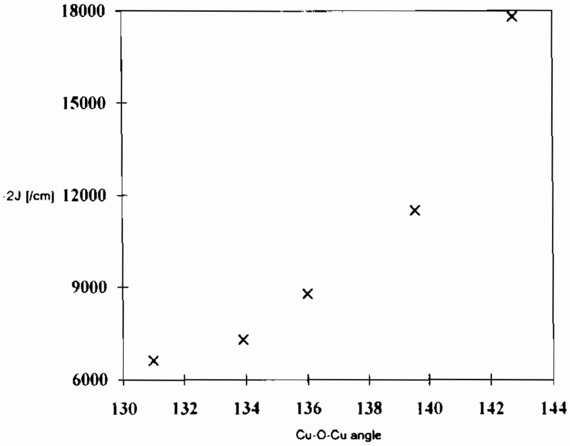

Fig. 2. The exchange interaction $2J$ (cm^{-1}) of the models M1–M5 dependent on the Cu–O–Cu angle α (°).

molecular orbitals. It can be seen that the exchange interaction becomes more antiferromagnetic with increasing α. Though the Cu–Cu and Cu–O distances increase, which should have the opposite effect on the exchange interaction J, the variation has minor influence. This was already observed for alkoxo-bridged complexes [22]. The Cu–Cu separation in our calculations increases by only *c.* 0.14 Å and should have minor effect on J.

The tendency of the $2J$–α relation agrees with a variety of experimental works [23, 24] of hydroxo-bridged copper dimers. It was found that the exchange interaction J becomes more antiferromagnetic with $\alpha > 97.6°$ and more ferromagnetic with $\alpha < 97.6°$. This behavior can be explained by the geometric arrangement of the molecular orbitals (MOs). The highest single occupied MOs are the d_{xy} orbitals of the copper atom and the p_x and p_y orbitals of the oxygen atom. The p_x and p_y orbitals of the nitrogen atoms give very small contributions.

Figure 3(a) and (b) presents the single occupied copper and oxygen orbitals [1]. Figure 3(a) shows the symmetric combination σ_g of the Cu–d_{xy} and the antisymmetric combination of the O–p_x atomic orbitals, Fig. 3(b) the antisymmetric combination σ_u of the Cu–d_{xy} and the symmetric combination of the O–p_y atomic orbitals. The d_{xy} and p_x–p_y atomic orbitals of Cu and O remain the same, independent of angle variations. The overlap density of the d_{xy} and p_x atomic orbitals increases with α (Fig. 3(a)). Therefore the MO energy of the antisymmetric p_x orbital will increase. With increasing α the overlap density of the d_{xy} and p_y atomic orbitals decreases (Fig. 3(b)), therefore the MO energy of the symmetric p_y orbital will decrease. The energy difference between the two MOs increases with α; this energy difference determines the value of $2J$.

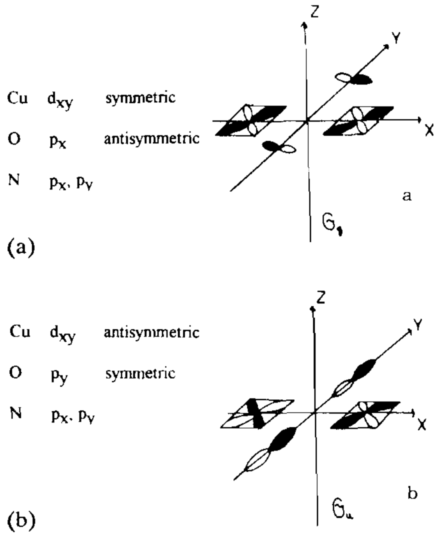

Fig. 3(a) and (b). The symmetric and antisymmetric combinations of the Cu d_{xy} and O p_x orbitals [1].

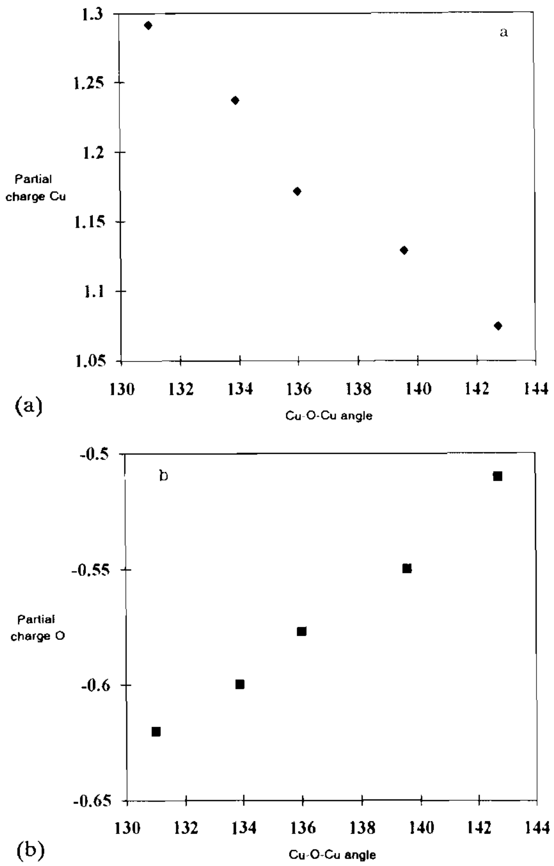

Fig. 4. Mulliken partial charges (|e|) of Cu and O dependent on the Cu–O–Cu angle α (°).

Experimental investigations of alkoxo- and hydroxo-bridged Cu(II) dimers [25, 26] resulted in a linear correlation between the exchange interaction and the angle α. In these investigations, the angle has been varied between 95 and 105°. Nevertheless the relation of our calculated values deviates from linearity, whereas the tendency larger α–higher antiferromagnetic J corresponds. Similar calculations on $Cu_2O_2(NH_3)_2(CH_3)_2Br_2$ of Astheimer [22, 27] with Cu–O–Cu angle variations of 90 to 106° also result in a small deviation from linearity.

In Table 2 the contributions of $2J$ for M1 to M5 are listed. The contributions reflect the $2J$–α tendency. The potential exchange increases with α, but the kinetic exchange becomes quite strong with increasing α. The charge transfer $L \rightarrow Cu$ increases with the angle, which manifests the antiferromagnetic $2J$ versus α tendency. A comparison of the charge transfer $L \rightarrow Cu$ with the partial charges of Cu, O and N shows that with larger charge transfer, the electron density of Cu is increasing and of O, N decreasing. Besides the polarization of 2nd order we calculated also the polarization of 4th order. The $2J$ values include the 4th order, otherwise

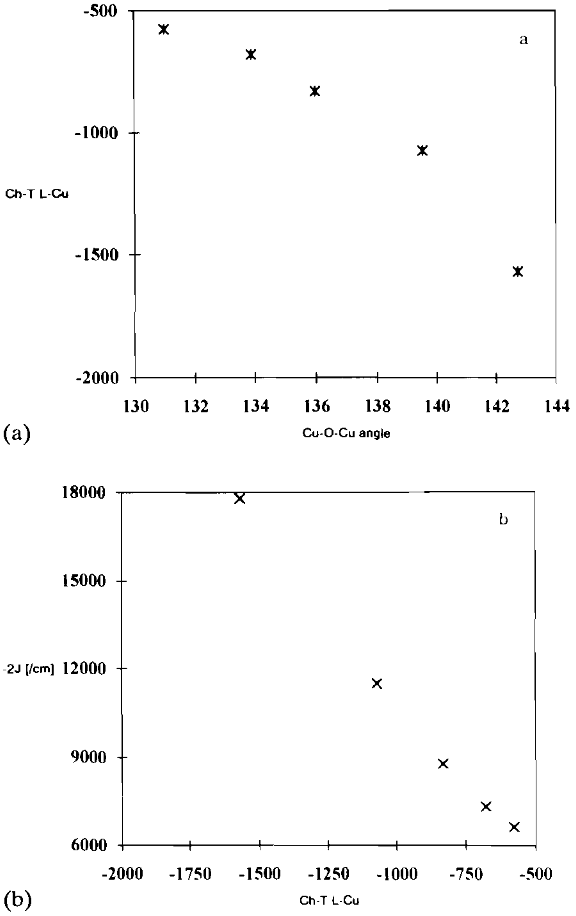

Fig. 5. (a) Charge transfer ligand–copper (cm^{-1}) dependent on the Cu–O–Cu-angle α (°). (b) The exchange interaction $2J$ (cm^{-1}) dependent on charge transfer ligand–copper (cm^{-1}).

the $2J$ values would be less antiferromagnetic, but the tendency of the $2J$ values remains the same.

In Fig. 4 the Mulliken partial charges of Cu and O of the triplet ground state, dependent on α, are shown. The partial charges can be calculated on the basis of the coefficients of the atomic orbitals of the single occupied molecular orbitals, which result from the SCF calculations. The charge distributions of the atoms elucidate the transfers of electrons and therefore give information about the exchange pathways. The positive partial charge of copper decreases with increasing α, whereas oxygen and nitrogen have negative partial charges, which become less negative with increasing α. This indicates charge transfer from oxygen and nitrogen to copper due to geometrical variations. The same charge distributions can be expected for the singlet state because the smallest charge transfer ligand–copper is dependent on small angles (Fig. 5(a)). The $2J$ values become more antiferromagnetic with increasing α, which is in good agreement with the experiments [22, 27]. High J values correspond to high charge transfer ligand–copper (Fig. 5(b)).

Conclusions

Strong antiferromagnetic coupling of peroxo-bridged Cu(II) dimers has been confirmed by theoretical calculations. The exchange pathway involves mainly the p_x and p_y orbitals of the peroxo bridge. The exchange interaction is related to the extent of overlap between the magnetic orbital wave functions and to the extent of delocalization of the magnetic orbitals over the two Cu atoms. A larger exchange interaction between the two Cu atoms is achieved by a larger overlap of the wave functions and a larger delocalization. The strength and kind of orbital superexchange pathway between the two Cu atoms depends on the bridging ligand character, which provides also a mechanism for the orbitals to delocalize between the Cu atoms. Therefore the CT L→Cu indicates electron transfer via the peroxide bridge, which determines the high $2J$ values. The NH_3 groups, as terminal ligands, are weakly involved in exchange interaction, so it has been justified to concentrate only on the core group $Cu–O_2–Cu$.

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