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Chemical Exchange Reaction of Glycinatocopper(II) Complex in Water: A Theoretical Study

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The axial water exchange on glycinatocopper(II) complexes was theoretically investigated by using density functional theory (DFT) calculations. Glycinatocopper(II) complexes are well-known by the diffusion controlled exchange of axial ligands. Calculations using explicitly coordinating water molecules and solvent models showed that bis-glycinatocopper(II) complexes have a four-coordinate planar structure, in which waters are excluded from the axial positions of Cu(II) due to the Jahn−Teller effect. This may be because coordinating axial waters induce the discrepancy in the most stable ligand field splittings of inner 3d and outer 4d orbitals of the Cu(II) cation. To estimate the reactivity of the axial water exchange, we calculated the rate constant by calculating Gibbs free energies for the activation. As a result, we obtained the rate constant as $k = 3.61 \times 10^{10}$ s^{-1} in aqueous solution at $T = 298.15$ K. This rate constant is slightly larger than that of the diffusion controlled exchange of axial waters, which is experimentally observed in the order of 10^9 s^{-1}. Finally, we determined the structures of tris-glycinatocopper(II) complexes. It was consequently found that the third glycine is coordinated to Cu with the amino groups as experimentally observed.

1. Introduction

There are various proteins containing copper ions in their active sites: e.g. plastocyanin, azurin, stellacyanin, and amicyanins. Blue (type 1) copper protein is well-known for electron-transfer reactions due to the high redox potential, which gives the intense visible bands at ∼600 nm. Hence, copper-containing proteins have been widely studied both experimentally and theoretically for their complex functions and behaviors.[1,2] There have also been a lot of investigations on diseases due to abnormal foldings of copper-containing proteins. Prion is a copper(II) binding protein in which the abnormal counterpart aggregates to cause neurodegenerative diseases such as Creutzfeldt−Jakob disease.[3−5] Therefore, divalent copper complexes of amino acids constituting proteins have received significant attention for elucidating the roles in biological systems and for modeling the environments around the metal binding sites. A considerable number of studies have been conducted on copper(II) complexes with amino acids and peptides for various properties such as geometries, rate constants, and electronic structures.[6−14] Especially, copper(II)−glycine complexes have been investigated both experimentally[15−23] and theoretically[24,25] because of their simplicity and intrinsic relevance in biological reactions. Copper(II) complexes represent the so-called Jahn−Teller distortion due to the d^9 electronic configuration of the metal cation. This distortion causes the lability and plasticity of copper(II) complexes and leads to various coordination arrangements and extremely fast ligand exchange reactions. The hydrated copper(II) complex has a tetragonally distorted structure, in which the coordinate bonds of two axial water molecules are much weaker than those of four equatorial ones. Several techniques have provided information on this distorted structure, such as X-ray diffraction, neutron diffraction, NMR, X-ray absorption spectroscopy, and quantum chemical calculations.[26−30] Experiments[31−34] indicated that the exchange reactions of axial ligands are so fast that the reactions give diffusion controlled rate constants in the order of 10^9 s^{-1} or reach the detection limit of experiments used. Theoretical analyses are very useful for investigating such fast reactions, and therefore several studies have been reported.[35]

In the present study, we investigate bis-glycinatocopper(II) systems by using density functional theory (DFT) calculations. It is well-known that glycine has the high affinity for Cu(II) ions (log $\beta_1 = 8.02$, log $\beta_2 = 15.2$, and log $\beta_3 = 15.43$[19,36]). Although bis-glycinatocopper(II) complexes have possible cis and trans conformations, experiments have offered no valuable insights for the structures of the complexes because of the low solubilities. An early study[24] suggested that in aqueous solution the trans conformation is more stable than the cis one, and axial Cu−O bonds compete with hydrogen bonds of coordinated water molecules. Hence, we refine on the *trans*-bis-glycinatocopper(II) systems. Due to the Jahn−Teller effect, Cu(II) complexes are labile in axial positions. To discuss the lability of bis-glycinatocopper(II) complexes quantitatively, we determine the transition state structure of the axial water exchange reaction, in which one water molecule moves from the axial position to the second coordination sphere. The rate constant is then estimated on the basis of the conventional transition state theory. In addition, it is interesting to note that the hydration of Cu(II) and the axial hydration of square-planar complexes were investigated in molecular dynamics (MD) simulation studies with a large number of water molecules.[37,38] These studies would contribute to comprehensive understanding of the unique hydration mechanism of Cu(II).

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Besides, the structures of tris-glycinatocopper(II) complexes are also investigated to verify the lability of the axial site in the presence of the third glycine. An extended X-ray absorption fine structure (EXAFS) study[23] showed that the third glycine of Cu(II)−glycine complexes was coordinated to the metal cation with its amino group at the axial site in aqueous solution. Because the third glycine inevitably interacts with the weak axial bonds, it is natural for tris-glycinatocopper(II) complexes to have a much lower stability constant, log $K_3 = 0.23$,[36] than those of the mono- and bis-complexes, log $K_1 = 8.02$ and log $K_2 = 7.21$,[36] respectively. To confirm the EXAFS result, we determine the structures of tris-glycinatocopper(II) complexes.

2. Computational Details

Geometry optimizations of glycinatocopper(II) complexes were carried out at the DFT level using the B3LYP[39,40] functional with no symmetry constraints. Geometry optimizations were performed by explicitly attaching water molecules to the complexes. We used an energy-adjusted quasirelativistic pseudopotential with (8s7p6d1f)/[6s5p3d1f] valence basis sets[41] for copper cation in all calculations. For glycinatocopper(II) complexes, Bruin et al.[24] suggested that basis sets were saturated nearly with 6-311+G(d,p) for geometries and energies and effective core potential was appropriate for such calculations. For detemining the initial structures, we used the Stuttgart-type effective core potential[42] including one d-function of the exponent 1.0 for oxygen, and Huzinaga's basis for hydrogen,[43] and the 6-31G(d) basis for carbon and nitrogen. Final structures were then optimized with all electron 6-311+G(d) basis sets for carbon, nitrogen, and oxygen species. These two basis sets are denoted as BSI and BSII, respectively. Basis set superposition errors (BSSE) were corrected for gas-phase calculations by the counterpoise method.[44] In geometry optimizations, solvent effects were taken into account by exploiting the conductor-like polarizable continuum model (CPCM) formalism[45,46] with the dielectric constant of water, $\epsilon = 78.39$. This method was initially devised by Tomasi and co-workers,[47−49] and extended for geometry optimizations to converge efficiently. Harmonic vibrational frequencies were calculated for estimating zero-point energies and thermochemical properties. These frequencies were also used to confirm that calculated geometries are stationary points on potential energy surfaces. All calculations were performed with the Gaussian 03 program.[50]

3. Results and Discussion

3.1. The Axial Water Molecule on Bis-glycinatocopper(II) Complex. First, *trans*-bis-glycinatocopper(II) complex structures were optimized with two water molecules. As shown in Figure 1, we obtained two types of structures: one water molecule is coordinated to Cu by a hydrogen bond and another is brought out of the first coordination sphere in one structure (five-coordinate complex), and both waters are out of the first coordination sphere in another structure (four-coordinate complex). In the four-coordinate complex, two chelate glycinato rings are coplanar.

An early experiment[24] suggested that hydrogen bonds between water molecules are the main factor keeping a water molecule on the axial position. This indicates that the coordinate bonds of axial water molecules are weaker than the hydrogen bonds. Calculated results with BSII also indicated that the four-coordinate complex with no axial waters was more stable than the five-coordinate complex with one axial water by 11.9 kJ/mol in the gas phase. However, this situation is questioned by adding a solvent effect into these calculations. Calculations with CPCM showed an opposite result, in which the five-coordinate complex was 7.9 kJ/mol more stable than the four-coordinate one.

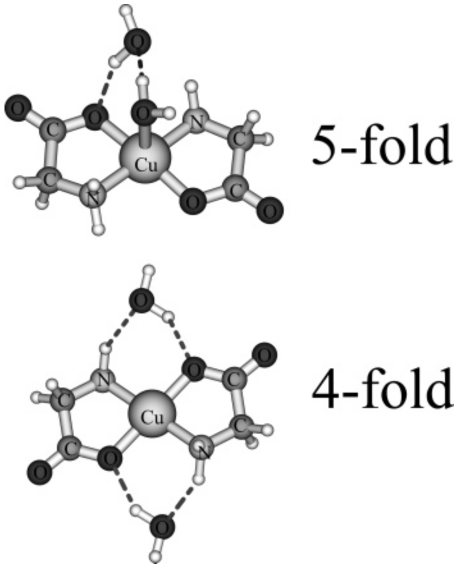

Figure 1. Optimized geometries of bis-glycinatocopper(II) complexes with two water molecules.

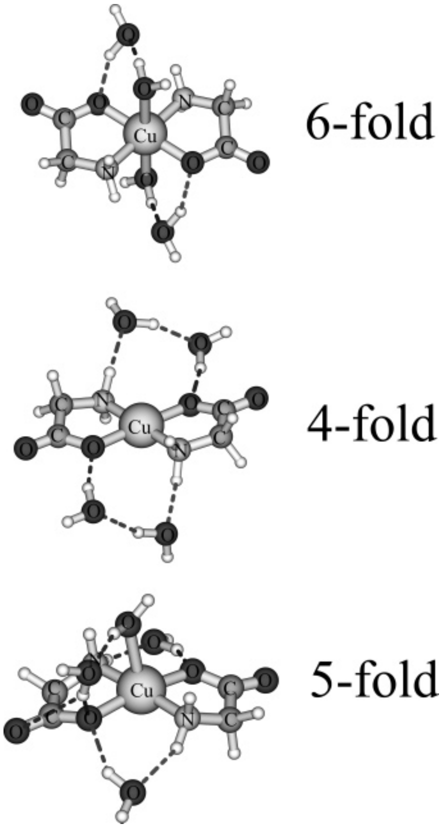

Figure 2. Optimized geometries of bis-glycinatocopper(II) complexes with four water molecules.

To evaluate the solvent effect on the stability of the axial water molecule, we therefore augmented water molecules up to six. In the geometries, water molecules were allocated keeping the symmetry of the complex. Figures2 and 3 display the optimized geometries of the complex with four and six water molecules, respectively. In both complexes, axial water molecules were coordinated due to the hydrogen bonding of water molecules.

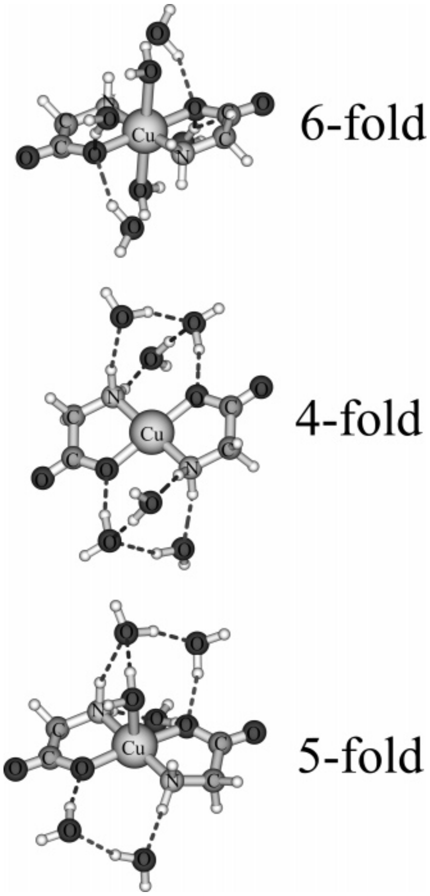

Figure 3. Optimized geometries of bis-glycinatocopper(II) complexes with six water molecules.

Table 1 summarizes calculated bond distances, dipole moments, and relative energies of the complexes containing axial water molecules. The index [*n*,*m*] denotes hereafter the complex containing *n* water molecules in the first coordination sphere and *m* molecules in the second coordination sphere. The table shows that coordinating axial water molecules destabilize the complexes both in the gas phase and in solution except when two water molecules were contained in total. Although six-coordinate complexes are unstable in comparison with others, energy differences between four- and five-coordinate complexes become relatively small. Since the solute−solvent interaction was taken into consideration by using the CPCM method, it is presumed that solvent effects might be significant for the polar complexes compensating the unstable axial coordination. Therefore, for [1,1] (5-fold) and [0,2] (4-fold) complexes, it is deduced that solvent effects are overestimated.

It is well-known that the Cu(II) cation in water forms a tetragonally distorted octahedral $[Cu(H_2O)_6]^{2+}$ complex due to the Jahn−Teller effect (see Figure 4). This octahedral Cu(II) complex is often found in crystals and solids. There, however, remains a question whether this octahedral configuration is favored even if other ligands are mixed, because the square-planar four-coordinate and tetrahedral five-coordinate complexes are also found for Cu(II) complexes. Pasquarello et al.[51] actually suggested that Cu(II) complexes preferred the five-coordinate configuration rather than the six-coordinate one due to the frequent transformation between square pyramidal and trigonal bipyramidal configurations. This indicates that in polar solvent the polarized five-coordination is more stable rather than the nonpolar six-coordination with the weakly bound axial water molecule. The solvation energy for the polar Cu(II) complex might be larger than the binding energy in the axial position. This unique configuration may result from the outermost $3d^9$ electronic configuration of the Cu(II) cation as mentioned below.

The calculated singly occupied molecular orbital (SOMO) of the glycinatocopper(II) complex with no waters is illustrated in Figure 5. It should be noted that this orbital is the SOMO even in the presence of water molecules. The figure indicates that this orbital actually contains the $3d_{x^2-y^2}$ orbital of Cu(II) as expected above. However, the electron distribution is delocalized over glycines probably to make the orbital energy higher than those of doubly occupied molecular orbitals containing 4s and 4p orbitals. It is, actually, found that the doubly occupied molecular orbitals containing 4s and 4p orbitals have lower energies than the SOMO energy.

3.2. The Relative Stability of the Four- and Five-Coordinate Complexes and the Reactivity of the Axial Site: Chemical Exchange Reaction between Bis-glycinatocopper(II) Complexes. In the previous section, we found that the bis-glycinatocopper(II) complex may have the five-coordinate structure in the gas phase. It is, however, still unclear whether this structure is also the most stable in aqueous solution. Actually, it is presumed that the four-coordinate structure may coexist in solution, because it gives only 8.8 kJ/mol higher energy than the five-coordinate one.

Now, it is interesting to elucidate the reaction pathway of the chemical exchange reaction between four- and five-coordinate complexes in aqueous solution. The exchange reaction is written as

$$[Cu(Gly)_2]\cdot 2(H_2O) \rightleftharpoons [Cu(Gly)_2(H_2O)]\cdot H_2O \qquad (1)$$

where the molecule outside the square brackets is in the second coordination sphere. Therefore, the equilibrium constant can be defined as

$$K = \frac{[[Cu(Gly)_2]\cdot 2(H_2O)]}{[[Cu(Gly)_2(H_2O)]\cdot H_2O]} \qquad (2)$$

The schematic diagram of this reaction pathway is illustrated in Figure 6. It should be noted that the reaction coordinate is set along with the $Cu-O_{ax}$ distance. On the basis of the standard transition state theory,[52,53] the rate constant of this reaction is described by

$$\vec{k} = \frac{k_B T}{h} e^{-\Delta G^{\ddagger}/RT} \qquad (3)$$

in the left-to-right process in eq 1, and

$$\overleftarrow{k} = \frac{k_B T}{h} e^{-(\Delta G^{\ddagger}+\Delta G)/RT} \qquad (4)$$

in the right-to-left process. In eqs 3 and 4, $\Delta G^{\ddagger}$ is the Gibbs free energy for the activation from four- to five-coordinate complexes. Under the equilibrium condition, the molar ratio of four- and five-coordinate complexes, *K*, is given by

$$K = \vec{k}/\overleftarrow{k} \qquad (5)$$

This can be taken as the water exchange reaction rate on the axial position of this complex.

Figure 7 displays optimized structures of the reactant (5-fold) and transition state (TS) of the complex with two water molecules which were calculated with the BSII basis set in the gas phase (top) and in solution (bottom), respectively. At the transition state, the $Cu-O_{ax}$ bond was stretched from 2.433 to

TABLE 1: Calculated Bond Distances (r_e, in Å), Dipole Moments (μ, in D), and Relative Energies (ΔE, in kJ/mol) of the Structures of Bis-glycinatocopper(II) [Cu(Gly)$_2n$(H$_2$O)]m(H$_2$O) Complexes[a]

	5-fold [1,1]	4-fold [0,2]	6-fold [2,2]	5-fold [1,3]	4-fold [0,4]	6-fold [2,4]	5-fold [1,5]	4-fold [0,6]
r_e(Cu−O$_{eq}$)	1.968	1.937	None	1.959	1.940	1.993	1.967	1.948
	(1.968)	(1.938)	(1.972)	(1.960)	(1.938)	(1.996)	(1.967)	(1.949)
	1.925	1.937	none	1.963	1.942	1.993	1.995	1.950
	(1.927)	(1.938)	(1.972)	(1.963)	(1.943)	(1.996)	(1.996)	(1.952)
r_e(Cu−N)	2.030	2.025	none	2.018	2.024	2.023	2.027	2.012
	(2.032)	(2.027)	(2.027)	(2.019)	(2.026)	(2.026)	(2.028)	(2.012)
	2.028	2.025	none	2.018	2.022	2.023	2.027	2.014
	(2.033)	(2.027)	(2.027)	(2.045)	(2.020)	(2.026)	(2.028)	(2.015)
r_e(Cu−O$_{ax}$)	2.475		none	2.456		2.510	2.412	
	(2.433)		(2.544)	(2.429)		(2.459)	(2.392)	
			none			2.510		
			(2.549)			(2.459)		
μ	2.97	0.00	0.00	2.62	1.49	0.00	3.34	1.95
ΔE_g	13.6	0	none	7.0	0	22.9	3.3	0
	(11.9)	0	(16.4)	(6.1)	0	(20.6)	(3.4)	0
$\Delta E_g^{\text{BSSE-free}}$	22.2	0	none	3.0	0	40.0	9.9	0
	(19.0)	0	(15.9)	(8.0)	0	(35.9)	(5.8)	0
ΔE_s	−7.7	0	none	6.5	0	43.5	3.5	0
	(−7.9)	0	(16.3)	(4.6)	0	(41.5)	(3.7)	0

[a] The index [*n*,*m*] indicates that the complex contains *n* water molecules in the first coordination sphere and *m* molecules in the second coordination sphere. Subscripts g and s represent the properties in gas phase and solution, and ax and eq indicate the axial and equatorial atoms attaching Cu, respectively. BSI and BSII (in parentheses) were used as the basis sets. Calculated results of [2,2] with CPCM and BSI are omitted, because no equivalent geometries was obtained for this complex.

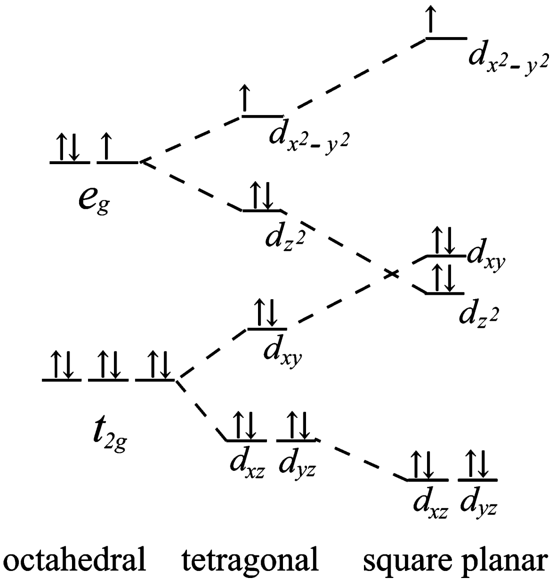

Figure 4. The correlation diagram of the energy splittings of 3d orbitals in Cu(II) for various ligand fields.

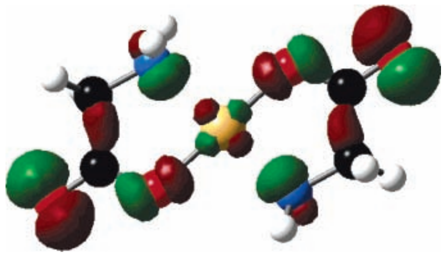

Figure 5. The calculated singly occupied molecular orbital of the glycinatocopper(II) complex. Water molecules are excluded for simplicity.

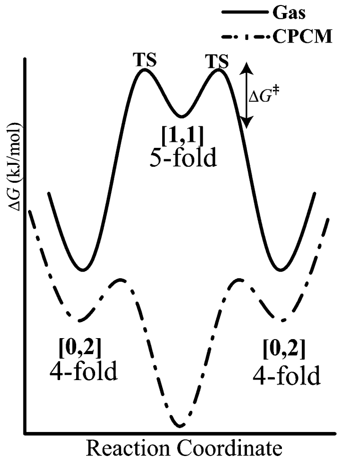

Figure 6. Schematic diagram of the chemical exchange reaction. The reaction coordinate is taken as the bond distance between the cation and the axial water molecule. The intermediate of this diagram corresponds to the reactant in Figure 7.

2.505 Å in the gas phase and 2.80 to 3.10 Å in solution, and the hydrogen bond between water molecules was alternated with the bond between the nonaxial water and glycine molecules. This bond alternation may cause the release of the axial water molecule, because the water molecule was unbound on the axial position without the hydrogen bonding with the nonaxial water molecule as mentioned in Section 3.1. It is therefore deduced that this hydrogen bond alternation may be the rate determining process.

In this rather simplified static view of the mechanism, hydration spheres around the complex that contribute to the substitution process are not considered. In the presence of the so-called cage effect by outer hydration spheres, this chemical exchange reaction could be impeded, and should result in a slightly slow reaction.

Table 2 summarizes calculated thermochemical activation and reaction energies of the axial water exchange reaction. For the solvent effect, CPCM calculations were carried out from the optimized geometries in the gas phase. Calculated CPCM results in the table indicated that the product (4-fold) of this reaction is less stable than the reactant (5-fold) in solution. This discrepancy between gas phase and solvent results may result mainly from the dipole moment of the five-coordinate complex.

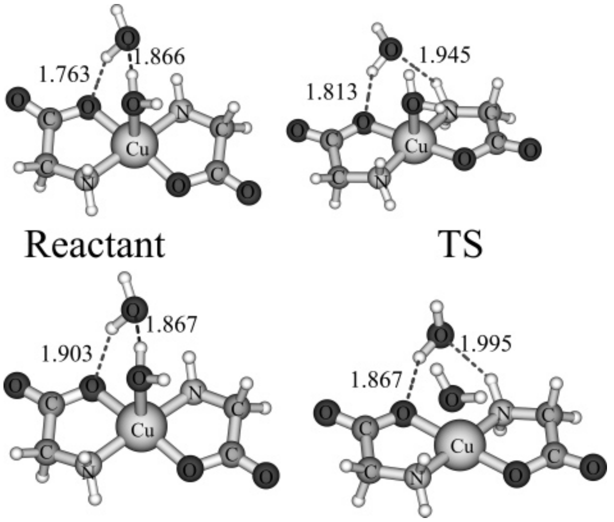

Figure 7. Optimized structures of the reactant (5-fold) and the transition state (TS) of bis-glycinatocopper(II) complex in gas phase (top) and in solution (bottom), respectively. Calculated bond distances (in Å) are attached to the significant hydrogen bonds.

Although axial water molecules tend to destabilize the complexes even in aqueous solution as mentioned above, the five-coordinate complex is stabilized in a polar solvent due to its dipole moment. It is deduced that the solvation energy of the five-coordinate complex is more significant that the destabilization energy of using the axial position. As a result, the solvent effect reduced the energy difference between four- and five-coordinate complex whereas it raised calculated activation energies.

For investigating the reactivity of the axial water exchange in more detail, we calculated the rate constant by using a conventional transition state theory. As shown in Figure 6, we now assumed that this reaction would have twin peaks along reaction coordinates between four- and five-coordinate complexes and the water exchange reaction proceeds through unstable five-coordinate intermediates. This is because this reaction is too fast to involve the interactions between water molecules. Table 2 displays calculated Gibbs free energies for the activation of the axial water exchange as $\Delta G_g^‡ = 9.5$ kJ/mol (6.3 kJ/mol after BSSE correction) in the gas phase and $\Delta G_s^‡ = 12.8$ kJ/mol in solution at $T = 298.15$ K. Taking the five-coordinate complex as the reactant, eq 3 gives the rate constants as $k_g = 1.37 \times 10^{11}$ s^{-1} (4.97×10^{11} s^{-1} with BSSE correction) in the gas phase and $k_s = 3.61 \times 10^{10}$ s^{-1} in solution. By using $\Delta G^‡_s = 9.7$ kJ/mol in Table 2, the equilibrium constant in eq 5 is estimated as $K = 50.0$. This means that the ratio of the five-coordinate complex is 50 times larger than that of the four-coodinate one. On the other hand, these four- and five-coordinate complexes coexist at almost the same rate in aqueous solution, whereas the ratio of the six-coordinate complex is approximately 10^{-4} times larger than those of these complexes. Hence, it is reasonably supposed that the axial water of this complex may be frequently exchanged in aqueous solution.

Since bis-glycinatocopper(II) complexes prefer four-coordinate geometry as mentioned in Section 3.1, it is presumed that the axial ligand exchange reactions would proceed much faster on the four-coordinate complex than on the distorted six-coordinate one. The rate constants of ligand exchange reactions on Cu(II) ion have been estimated in various experimental studies. In these experiments, it was concluded that the axial exchange reaction is so fast that the rate constants are subject to experimental errors and detection limits. By, for example, the temperature-jump relaxation method, Sokol et al.[31] estimated the rate constant of the inner-sphere solvent exchange on Cu(H$_2$O)$_6^{2+}$ complex as k(298K) = 2.0×10^9 s^{-1}. The lifetime of Jahn−Teller inversion and water exchange rate were estimated by Powell et al. with a ^{17}O NMR study:[54] the inversion process gave $\tau = (5.1 \pm 0.6) \times 10^{-12}$ s and $E = 3.5 \pm 1.5$ kJ/mol, and the water exchange process gave k(298K) = $(4.4 \pm 0.1) \times 10^9$ s^{-1}. It is found that our calculated rate constants are larger than the experimental rate constants of Cu(H$_2$O)$_6^{2+}$. We therefore conclude that coordinate glycines may accelerate the axial water exchange on Cu(II) complex as experimentally supposed.

The water exchange reactions on metal complexes have been theoretically investigated by Rotzinger et al. on quantum chemical and molecular dynamics calculations.[35,55−61] In these theoretical studies, the rate constants were estimated by using geometries and activation energies, which were calculated with no solvent effects. Rotzinger investigated the mechanism of the water exchange reaction on the first transition metal aqua ions from Sc(III) through Zn(II) by Hartree−Fock and CASSCF calculations. In this study, the Cu(II) aqua ion showed the dissociative mechanism through a square-pyramidal TS. The geometries and activation energies agreed well with the experimental values. The calculated rate constant was on the order of 10^9 s^{-1}, which is equivalent to those of water exchange reactions in various distorted octahedral complexes. It is therefore presumed that the rate constant is larger than 10^9 s^{-1} in the bis-glycinatocopper(II) complex because glycines, as stronger ligands than water molecules, coordinate to Cu(II) and the ligand field splitting of the complex becomes larger to be more labile in axial positions. This presumption was supported by our calculated results.

3.3. Tris-glycinatocopper(II) Complex. To the best of our knowledge, there has been no theoretical studies on tris-glycinatocopper(II) complexes. The stablility constants, stoichiometries, and structures of the Cu(II)−glycine system have been experimentally observed.[19,21,23,36] However, the structure of tris-glycinatocopper(II), [Cu(Gly)$_3$]$^-$, in solution is still open to question. By an X-ray diffraction study, Ozutsumi et al.[21] suggested that the tris-glycinatocopper(II) complex formed a regular octahedral geometry with the same Cu−O and Cu−N bond distances, 2.02 ± 0.01 Å. In contrast, D'Angelo et al.[23] assigned a distorted five-coordinate octahedral geometry, in which the third glycine was coordinated to Cu(II) with its amino group, by an EXAFS study. However, these structural data may not be so reliable because these data were determined by a fit to a hypothetical structure in this EXAFS study. It is therefore supposed that calculations may rather evaluate the reliability of EXAFS structures.

The present calculations proposed that this complex has the distorted five-coordinate structure, because no optimized geometries were obtained for the six-coordinate structure even when additional water molecules were taken into consideration. Figure 8 displays two types of tris-glycinatocopper(II) complex structures: the amino group of the third glycine coordinates to Cu(II) in the left structure (η-NH$_2$) and the carboxyl group coordinates to Cu(II) in the right structure (η-COO). Table 3 summarizes calculated bond distances and bond angles in comparison with the EXAFS results.[23] Coordination of the third glycine deformed the chelate rings of the first and second glycines. In Table 3, the strain of the chelate rings is displayed as N$_{eq}$−Cu−N$_{eq}$ and O$_{eq}$−Cu−O$_{eq}$ angles. In both complexes, the deviation in the O$_{eq}$−Cu−O$_{eq}$ angle is larger than that in the N$_{eq}$−Cu−N$_{eq}$ angle.

TABLE 2: Calculated Activation Energies (*E*), Enthalpies (*H*), Gibbs Free Energies (*G*, in kJ/mol), and Entropies (*S*, in J/mol·K) of Bis-glycinatocopper(II) Complex with Two Water Molecules from the Reactant Values at $T = 298.15$ K[a]

	ΔE_g	ΔH_g	ΔG_g	S_g	ΔE_s	ΔH_s	ΔG_s	S_s
reactant	0	0	0	565	0	0	0	558
TS	13.0 (10.7)	9.7 (7.4)	9.5 (6.3)	566	12.8	6.3	12.8	496
product	−11.9 (−18.2)	−11.9 (−17.8)	−15.1 (−21.8)	576	8.8	6.9	9.7	485

[a] Subscripts g and s represent the properties in gas phase and solution, respectively. The solvent effect was incorporated by the CPCM method. The BSII basis set was used in all calculations. BSSE-corrected values are also shown in parentheses.

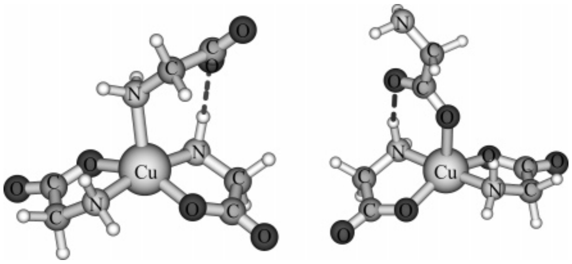

Figure 8. Two types of optimized geometries of tris-glycinatocopper(II) complexes: the third glycine was attached to Cu through its amino (left) or carboxyl (right) group.

TABLE 3: Calculated Equilibrium Bond Distances (r_e, in Å), Bond Angles (θ_e in deg), Dipole Moments (μ, in D), and Binding Energies (D_e, in kJ/mol) of the Third Glycine[a]

	η-NH$_2$	η-COO	exptl[23]
r_e(Cu−N$_{ax}$)	2.299		2.33
r_e(Cu−O$_{ax}$)		2.280	
r_e(Cu−N$_{eq}$)	2.016	2.004	2.02
	2.057	2.026	
r_e(Cu−O$_{eq}$)	1.975	1.991	1.96
	2.028	2.004	
θ_e(N$_{eq}$−Cu−N$_{eq}$)	166.9	176.4	
θ_e(O$_{eq}$−Cu−O$_{eq}$)	150.5	149.3	
μ	10.30	5.49	
D_e	2.63	2.53	

[a] Solvent effects were taken into account by using the CPCM method. The BSII basis set was used in all calculations. EXAFS results by D'Angelo et al.[23] are also shown for comparison. Subscripts ax and eq indicate the axial and equatorial atoms attaching Cu, respectively.

It is interesting to note that the energy difference between the η-NH$_2$ and η-COO complexes was reduced to approximately 0.1 kJ/mol by incorporating the solvent effect, albeit the η-COO complex was much more stable than the η-NH$_2$ one by 40.0 kJ/mol in the gas phase. This may be due to the large dipole moment of the η-NH$_2$ complex (10.30 D) in comparison with that of the η-COO complex (5.49 D). For complexation using the axial position, the dipole moment becomes the dominant factor for the stability of the complex as mentioned in the preceding sections. Table S9 in the Supporting Information displays Mulliken charges of Cu and attaching atoms, which were calculated with solvent effects. As the table shows, induced Mulliken charges by the solvent effect are similar among the η-NH$_2$ and η-COO complexes. It is therefore deduced that the strong solvent effect may be due to the permanent dipole of the η-NH$_2$ complex. Actually, the carboxyl group of the third glycine is located at the end of the η-NH$_2$ complex, whereas this group has the most negative charge in glycine.

As shown in Table 3, the binding energy of the third glycine on bis-complex was calculated as 2.63 and 2.53 kJ/mol for η-NH$_2$ and η-COO complexes in solution, respectively. Different from the water molecule, the third glycine was therefore bound on the axial position of the bis-complex, although the binding energy was much smaller than those of equatorial glycines (377 kJ/mol). This result supports the experimental observation that tris-complex is produced under rich glycines. Comparing Mulliken charges of the bis-complex in Table S8 with those of tris-complexes in Table S9 of the Supporting Information, it was found that electrons fairly moved from equatorial glycines to Cu after the coordination of the third glycine. Due to this electron delocalization, the binding energy of the third glycine consequently surpasses the energy loss that stems from the discrepancy in the ligand field splittings of 3d and 4d orbitals mentioned in Section 3.1. It is also supposed that this energy loss may be the prime reason to inhibit producing the six-coordinate tris-glycinatocopper(II) complex. This study provides theoretical grounds for the coordination structure of the species, which have already been reported in some previous experiments.

4. Conclusions

The reactivity of the axial water exchange on bis-glycinatocopper(II) complexes was theoretically investigated with use of density functional theory calculations. Several water molecules in the close vicinity of the axial position of the complex were explicitly coordinated to Cu besides the conductor-like polarizable continuum model of hydration.

First, the structures and energies of the bis-glycinatocopper(II) complex were calculated with two, four, and six water molecules. Consequently, it was found that this complex preferred the four-coordinate structure with no axial water molecules. This result may be due to the discrepancy in the energy splittings of 3d and 4d orbitals of the Cu(II) cation. That is, although Cu(II) may have the unstable singly occupied $3d_{x^2-y^2}$ orbital to stabilize the $3d^9$ configuration, the 4d orbital, which corresponds to the axial position of Cu, has to be occupied in the octahedral six-coordinate complex. Actually, it was found that the singly occupied molecular orbital of the bis-glycinatocopper(II) complex contains the $3d_{x^2-y^2}$ orbital of Cu.

Next, the rate constant of the chemical exchange reaction on this complex was estimated on the basis of the conventional transition state theory. By calculating Gibbs free energies for the activation of the reaction, the rate constant was given as $k = 3.61 \times 10^{10}$ s^{-1} in aqueous solution. Since the experimental rate constant of the water exchange on $Cu(H_2O)_6^{2+}$ is in the order of 10^9 s^{-1}, it was concluded that the axial water dissociation on the bis-glycinatocopper(II) complex is a diffusion-controlled process that is accelerated by the coordination of glycines. It was also found that the hydrogen bond alternation may be the rate determining step in this reaction.

Finally, the structures of the tris-glycinatocopper(II) complex were determined by using the hydration model. As a result, two types of five-coordinate complexes were obtained: the η-NH$_2$ and η-COO complexes, in which the third glycine was bound through the amino and carboxyl group, respectively. Comparing these complexes, we found that the η-NH$_2$ complex was favored or equivalent to the η-COO one in aqueous solution due to the large dipole moment. This result is consistent with past experimental studies.

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Supporting Information Available: Cartesian coordinates of optimized structures, bis-glycinatocopper(II) and tris-glycinatocopper(II) complexes, at the B3LYP/BSII level (Tables S1−S7) and calculated Mulliken charges of coordinated N and O atoms of glycines and O atoms of water molecules (Tables S8 and S9). This material is available free of charge via the Internet at http://pubs.acs.org.

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