256 *J. Phys. Chem. A* **2008,** *112,* 256−267

Theoretical Study of Hydrated Copper(II) Interactions with Guanine: A Computational Density Functional Theory Study

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Received: June 22, 2007; In Final Form: October 1, 2007

Optimization of the hydrated Cu(II)(N7−guanine) structures revealed a number of minima on the potential energy surface. For selected structures, energy decompositions together with the determination of electronic properties (partial charges and electron spin densities) were performed. In the complexes of guanine with the bare copper cation and that with the monoaqua ligated cation, an electron transfer from guanine to Cu(II) was observed, resulting in a Cu(I)−guanine$^+$ type of complex. Conformers with two aqua ligands are borderline systems characterized by a Cu partial charge of $+0.7e$ and a similar value of the spin density ($0.6e$) localized on guanine. When tetracoordination of copper was achieved, only then the prevailing electron spin density is unambiguously localized on copper. The energetic preference of diaqua-Cu−(N7,O6−guanine) over triaqua-Cu−(N7−guanine) was found for the four-coordinate structures. However, the energy difference between these two conformations decreases with the number of water molecules present in the systems, and in complexes with five water molecules this preference is preserved only at ΔG level where thermal and entropy terms are included.

1. Introduction

Copper, despite its toxicity in its pure form, is essential for many processes in bioorganisms. Hence, study of its activity was always an aim of many experimental as well as theoretical laboratories. Thanks to the development of high-performance computers and effective quantum-chemical methods over last two decades, substantially larger systems can be addressed at present.

The role of copper in the active centers of many enzymes was studied recently. Processes dealing with oxygen transportation and insertion, electron transfer, and oxidation−reduction occur in such reaction centers. Copper proteins often exhibit unusual geometrical and electronic structures in these active centers. For instance, the redox centers became the subjects of many experimental studies employing UV−vis and electron paramagnetic resonance (EPR) spectroscopy,[1−5] EPR and electron nuclear double resonance techniques,[6] the X-ray absorption near-edge structure method,[7] pump−probe[8] and resonance Raman spectroscopies,[9] and some others.[10−14] The number of theoretical studies devoted to investigation of copper redox processes in various models of active sites is growing very fast; see, for example, refs 15−30.

The interaction of various metal cations with DNA/RNA bases represents usually the initial stage for many biochemical processes. The opening of an α-helix abolishing hydrogen bonds between Watson−Crick (WC) base pairs often proceeds in the presence of metals usually in their hydrated form. Therefore, a great deal of work has been devoted to the investigation of copper complexes with various models of the nucleotides. IR spectra have been measured and interpreted for interactions of DNA with several divalent cations in a solution.[31] The structural assignment of planar complexes based on an empirical equation has been published,[32] which allows an estimation of the ligand field strength of involved donor groups. Such a relationship can be helpful in assessing a criterion for the establishment of the axial co-ordination mode of copper(II) ion. Crystal structures of several metal complexes with cleaving activity on DNA oligomers were characterized in ref 33. The X-ray structures of $CuCl_2$/guanine compounds were examined in another work.[34] Cu(II) adducts have been considered to be a predominant reason for DNA damage by carcinogenic heterocyclic amines in a study by Murata and Kawanishi[35] who examined the oxidation of the 5′-site guanine in GG and GGG sequences in the presence of Cu(II) and NADH by an electrochemical detector coupled to a high-performance liquid chromatograph. Absorption, fluorescence, circular dichroism spectra, and viscosity experiments were used in investigations of the interactions of the two macrocyclic copper(II) complexes with DNA.[36] Meggers et al.[14] measured the melting curves of copper(II) complexes with DNA duplexes, and later they also examined some structural aspects of copper(II) coordination to WC base pairs.[37] The interactions of the polynuclear copper(I) complexes with double-strand DNA oligomers were explored by Schoentjes and Lehn.[38] Very specific oxidation of guanine at a junction between single- and double-stranded DNA by a dinuclear copper(II) complex with water molecules was reported in ref 39. Thermodynamical measurements[40] on nucleosides coordinated with Ca and Cu divalent cations suggest the following order in bonding strength, $Cu^{2+} > Ca^{2+}$ and GMP > IMP > AMP > CMP = UMP for the chosen nucleotides. The formation of macrochelates was found to be energetically favorable but entropically unfavorable. Interactions of excited copper(II)−porphyrin complexes with DNA were explored using Raman spectroscopy by Mojzes et

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10.1021/jp074891+ CCC: $40.75

al.[41] A lot of experimental work on copper interactions with nucleobases[42] and some other molecules with the first row of transition metals[43−45] were performed in the Armentrout laboratory.

A theoretical study of Cu^{2+} association with uracil and its thio derivatives has been published.[46] Another theoretical work of Martinez[47] investigates neutral, anionic, and cationic copper−guanine and −uracil complexes, but they did not consider hydration effects. Coordination and stability of Cu(II) and Zn(II) complexes with adenosine and cytidine were investigated by Gasowska and Lomozik.[48] A theoretical study on the copper(II)-catalyzed Michael reaction was published by Borowka and van Wullen[49] where the enamine was deprotonated upon coordination to Cu^{2+}, occupying three coordination sites of Cu(II) in a square-planar geometry. Binding of Cu^{+} cations to guanine and adenine[50] and in a noncomplementary DNA C−A base pair[51] were explored in our previous studies. The outer-shell and inner-shell coordination of the phosphate group to hydrated metal ions (Mg^{2+}, Cu^{2+}, Zn^{2+}, and Cd^{2+}) was explored in the work of Rulíšek and Šponer.[52] The reduction of nitric oxide in bacterial nitric oxide reductase was published by Blomberg et al.[53] Recently, also an interesting review on Cu(II) complexes with biomolecules in the gas phase appeared by Tureček.[54] Here, results of experimental methods such mass spectrometry and ionization methods are compared with ab initio and density functional theory (DFT) calculations. Some advantages of DFT techniques over “standard” ab initio methods for copper complexes are analyzed in the work of Luna et al.[55] These authors also published a comparison of experimental and computational techniques for reactions between the Cu(I) cation and guanidine[56] or urea.[57]

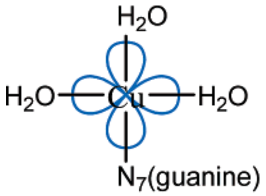
In our previous papers,[58−60] small model complexes of Cu(I)/Cu(II) cations were intensively studied. The works were devoted to the investigation of the coordination geometries and electronic properties of Cu cations interacting with molecules such as water, ammonia, and hydrogen sulfide. The present work can be regarded as a continuation of a previous study[61] devoted to the hydrated copper(I) interaction with guanine. Presented results provides a detailed investigation of interactions of copper(II) with the guanine base in the presence of several water molecules. Structural, thermodynamic, and electronic properties were determined and used to characterize copper−guanine interactions. Obtained structures are also compared with results from other theoretical and experimental works.

2. Computational Details

Interactions of the $[Cu(H_2O)_n]^{2+}$ complexes with guanine were studied where the number of water molecules varies from 0 to 5. Gradient optimizations were performed for different starting geometries. Several distinct local minima were found, but only selected lower-energy conformers for each type of coordination were considered in the further analyses.

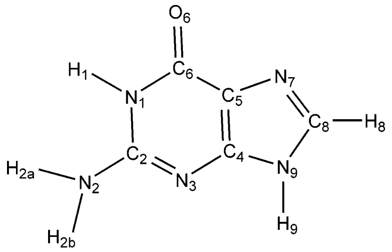
Quantum-chemical calculations were performed at the DFT level using the hybrid B3PW91 functional for structure optimization. The B3PW91 functional gives slightly better structure results and vibrational properties[56,62−64] when compared to the B3LYP functional. For the H, C, O, and N atoms, the 6-31+G(d) basis set was applied. Copper core electrons were described by Stuttgart energy-averaged effective-core pseudopotentials. A consistent basis set was adopted for copper valence electrons; i.e., the original set of pseudo-orbitals was augmented by diffuse ($\alpha_s = 0.005$, $\alpha_p = 0.01$, and $\alpha_d = 0.05$) and polarization ($\alpha_f = 0.758$) functions. The frequency analysis was performed at the same computational level, confirming the character of local minima for the obtained structures. This analysis also served for the evaluation of thermochemical potentials in the NVE microcanonical ensemble.

SCHEME 1 [a]



[a] According to the classical ligand field theory, the $3d_{x^2-y^2}$ orbital must be a single occupied molecular orbital (SOMO) because minimal Pauling repulsion with the donating electron pairs of the ligands occurs in this configuration for the square-planar complexes

SCHEME 2: Atom Numbering in Guanine



Cu(II) complexes contain the metal cation in the $3d^9$ electron configuration, resulting in doublet ground states. Some attention had to be devoted to the construction of an appropriate initial guess of the wave function in the self-consistent field procedure. First, the correct wave function (with a single occupied molecular orbital according to Scheme 1) was built at the ROHF/STO-3G level, passing subsequently to the final unrestricted B3PW91/6-31+G(d) level.

Single-point calculations for energy and charge distribution analyses were performed with the B3LYP functional with the extended 6-311++G(2df,2pd) basis set for H, C, N, and O atoms. The basis set on the copper atom was enlarged consistently by spd diffuse functions mentioned above and 2fg polarization functions with exponents $\alpha_f = 1.002$ and 0.262 and $\alpha_g = 0.662$. (The exponents were optimized for the neutral Cu atom at the CCSD level.[58])

Several different energy characteristics of the copper complexes were evaluated for every complex. First, the stabilization energies with the basis set superposition error (BSSE) corrections and corrections of the deformation energies were determined according to the equation

$$\Delta E^{\mathrm{Stab}} = -\left(E_{\mathrm{complex}} - \sum_{i}^{\mathrm{monomers}} E(i) - \sum_{i}^{\mathrm{monomers}} E(i)^{\mathrm{deform}}\right) \tag{1}$$

Here E_{complex} represents the total energy of the whole complex, and E_{monomer} represents the energy of an individual subsystem computed with basis functions on the ghost atoms from the complementary part(s) of the system. The deformation energy of the given monomer is defined as the energy difference between the optimized structure and the frozen geometry taken from the complex. Besides the ΔE^{Stab} energies, additional stabilization energies corrected by ligand repulsion (ΔE^{Stex}) were computed. In the ΔE^{Stex} energy all of the interacting ligands (guanine and waters) are treated in eq 1 as a single subsystem while another subsystem is represented by the bare central Cu cation. Then, the ΔE^{Stex} energy equals the binding energy of the cation with the fixed (preformed) ligand shell. The difference

TABLE 1: Selected Bond Lengths of $[Cu(H_2O)_n]^{2+}$ Complexes with Guanine: Cu−N(Guanine), Cu−O6(Guanine), and Cu−O(Aqua) Distances (in Å)[a]

system	CN	structure	Cu−N	Cu−O6	Cu−O(aqua)			
$[CuG]^{2+}$	1	**0**	1.952					
$[CuG(H_2O)_1]^{2+}$	2	**1**	1.892		1.894			
$[CuG(H_2O)_2]^{2+}$	3	**2a**	1.940		1.992	1.992		
	4^{chel}	**2b**	2.004	1.996	1.966	2.005		
$[CuG(H_2O)_3]^{2+}$	4	**3a**	1.971		2.012	2.047	1.893	
	4^{chel}	**3c**	2.017	2.006	1.948	1.972		
	5^{chel}	**3b**	2.032	2.024	2.026	2.000	2.258	
$[CuG(H_2O)_4]^{2+}$	4	**4a**	1.969		2.040	1.985	1.911	
	4	**4b**	1.971		2.007	1.990	1.916	
	4	**4c**	1.965		1.969	2.026	1.936	
	4	**4d**	1.987		2.028	2.060	1.850	
	4	**4e**	1.969		2.017	2.052	1.886	
	4	**4f**	1.961		2.014	2.052	1.893	
	4^{chel}	**4j**	2.013	2.022	1.951	1.932		
	4^{chel}	**4k**	2.024	2.018	1.916	1.983		
	4^{chel}	**4l**	2.010	1.995	1.953	1.977		
	4^{chel}	**4m**	2.003	2.007	1.951	1.976		
	5	**4i**	1.979		2.021	2.055	2.229	1.974
	5^{chel}	**4g**	2.035	2.039	2.001	2.277	1.985	
	5^{chel}	**4h**	2.037	2.031	1.969	2.276	2.022	
$[CuG(H_2O)_5]^{2+}$	4	**5a**	1.975		2.006	1.962	1.921	
	4	**5b**	1.960		2.004	1.977	1.933	
	4	**5c**	1.961		2.002	1.975	1.938	
	4	**5d**	1.972		1.966	1.983	1.944	
	4	**5e**	1.955		1.972	2.031	1.935	
	4	**5f**	1.955		2.003	1.976	1.941	
	4^{chel}	**5v**	1.997	1.996	1.956	1.981		
	4^{chel}	**5w**	2.021	2.033	1.919	1.941		
	4^{chel}	**5x**	2.001	2.022	1.954	1.936		
	4^{chel}	**5y**	2.007	2.009	1.955	1.937		
	5	**5m**	1.971		2.037	2.295	2.064	1.941
	5	**5n**	1.993		2.019	2.022	1.938	2.404
	5	**5o**	1.979		2.037	2.305	2.065	1.930
	5	**5p**	1.978		2.038	2.296	2.062	1.936
	5	**5q**	1.977		2.075	2.182	2.027	1.969
	5	**5r**	1.996		2.036	2.376	2.044	1.933
	5	**5s**	1.978		2.038	1.984	2.252	2.000
	5	**5t**	1.990		2.050	2.312	2.035	1.933
	5^{chel}	**5g**	2.031	2.031	2.004	1.988	2.285	
	5^{chel}	**5h**	2.027	2.026	2.005	1.989	2.291	
	5^{chel}	**5i**	1.970	2.608	2.002	1.978	1.999	
	5^{chel}	**5j**	1.966	2.666	1.988	1.957	2.012	
	5^{chel}	**5k**	1.968	2.719	2.002	1.950	1.986	
	5^{chel}	**5l**	2.018	2.042	2.007	1.987	2.288	
	5^{chel}	**5u**	2.011	2.012	2.005	2.033	2.290	

[a] The abbreviation CN is used for coordination type and structure corresponds to the identification number used in all figures.

between ΔE^{Stab} and ΔE^{Stex} represents the energy that is required for the formation of the ligand shell arrangement without the cation (in fact, its lower estimation because ligand polarization under the influence of the Cu cation is missing). Also, bonding energies (ΔE^{BE}) were evaluated using a modified form of eq 1 (without the monomer deformation corrections). Determining this energy, partition of the complex into two parts according to the cleaved Cu−L bond gives the bonding energy of the desired ligand. Note that the ΔE^{BE} value for the remote water molecule represents its association energy, and in this case deformation corrections are also added (numbers with stars in Table 2). In the determination of the copper−guanine energy, the H-bond interaction of water···O6 is included. To obtain the proper bonding energy of Cu−N7 coordination, an estimation of the H-bond energy has to be subtracted (cf. energy discussion below).

For a comparison of various conformers, relative differences of total energies ΔE_1 and ΔE_2 were evaluated at the B3PW91/6-31+G(d) and B3LYP/6-311++G(2df,2pd) levels, respectively. Relative differences of Gibbs energies ΔG (at 298 K) were calculated to enlighten the role of thermal and entropy contributions combining energies at the ΔE_2 level with vibrational corrections from the ΔE_1 level of calculations.

Partial charges of the examined systems were explored using natural population analyses (NPAs)[65] together with spin-density analyses. Maps of the spin densities were plotted on an isodensity surface ($\rho = 0.001$ e/Å^3). The Gaussian 98[66] suite of programs was used for the determination of the electronic structures of the studied complexes, and the program NBO, version 5.0, from the University of Wisconsin[67] was employed for evaluation of the natural bond orbital (NBO) characteristics. Geometries, molecular orbitals, spin densities, and vibrational modes were visualized using the freeware programs Molden 4.3[68] and Molekel 4.3.[69]

3. Results and Discussion

3.1. Structures. Optimized structures of hydrated copper $[Cu(H_2O)_n]^{2+}$ with guanine are shown in Figure 1, where *n* varies

TABLE 2: τ Coefficients for the Five-Coordinate Complexes Determining Whether a Structure is Closer to Trigonal Bipyramidal or Octahedral Arrangement[a]

system	CN	structure	τ
$[CuG(H_2O)_3]^{2+}$	5^{chel}	**3b**	0.01
$[CuG(H_2O)_4]^{2+}$	5	**4i**	0.02
	5^{chel}	**4g**	0.09
	5^{chel}	**4h**	0.12
$[CuG(H_2O)_5]^{2+}$	5	**5m**	0.19
	5	**5n**	0.16
	5	**5o**	0.20
	5	**5p**	0.20
	5	**5q**	0.16
	5	**5r**	0.24
	5	**5s**	0.00
	5	**5t**	0.19
	5^{chel}	**5g**	0.09
	5^{chel}	**5h**	0.08
	5^{chel}	**5l**	0.07
	5^{chel}	**5u**	0.03

[a] Abbreviation CN corresponds to the coordination type and structure is used for exact identification of the optimized structure.

from 0 to 3. In tetrahydrated and pentahydrated Cu(II)−guanine complexes, additional water molecules can also be localized around the guanine moiety (cf. Figures 2 and 3). In all of the studied structures, guanine is coordinated to the copper cation at the N7 position, or in the case of the chelate structures, the O6 and N7 sites are involved in the coordination. The standard numbering of guanine atoms (e.g., from ref 70) was used, and it is also displayed in Scheme 2. All of the geometries reported in present study are available in the Supporting Information

The lengths of the Cu coordination bonds are listed in Table 1 for all of the Cu(II)−guanine complexes. In the nonhydrated Cu(II)−guanine complex (actually Cu^+−guanine$^+$; structure **0** in Figure 1), the Cu−N7 bond is 1.952 Å, which is markedly shorter than the Cu−O6 distance (about 2.7 Å). These bonding characteristics are completely different in comparison with similar structures with bare alkaline earth metals or zinc group metals studied in our previous works.[50] An explanation can be seen in the reduction of the copper cation due to the electron transfer from guanine as discussed later. When one water molecule is added into the Cu(II)−guanine system, the Cu−N7 bond is slightly shortened to 1.894 Å. Moreover, this two-coordinate complex (structure **1**, Figure 1) also exhibits one of the shortest Cu−O(aqua) bonds (about 1.892 Å) among all studied complexes. Similar behavior was also discussed in the previous study[58] where the $[Cu(H_2O)_2]^{2+}$ complex exhibited shorter Cu−O distances than the $[Cu(H_2O)]^{2+}$ complex. This was a result of a different donation scheme. While in Cu(II) complexes with one ligand, the donation occurs mainly into the 3d atomic orbital (AO) of the Cu^{2+} cation, in two-coordinate complexes, the two linearly arranged ligands donate a 3d−4s hybridized orbital in accord with study of Bauschlicher et al.[71] In the present mono- and diligated complexes, the whole donation aims to 4s (due to the Cu reduction to monovalent cation). Nevertheless, substantially higher occupation of the 4s AO can be seen in the two-coordinate $[CuG(H_2O)]^{2+}$ complex.

In the three-coordinate diaqua-Cu(II)G complex (**2a**, Figure 1), both Cu−O(aq) and Cu−N7 bonds elongate in comparison to the monoaqua-Cu(II)G system. One of the water molecules is also H-bonded to the O6 position of guanine, $d(O6{-}H_w) = 1.82$ Å. However, this interaction influences the Cu−O distance only marginally, keeping both Cu−O bond distances practically equal. The global minimum of the diaqua system is represented by a four-coordinate chelate (**2b**, Figure 1). In this chelate, the Cu−O6 bond is shorter than Cu−N7, and this can be explained by the harder character of the Cu^{2+} cation in comparison with the Cu^+ cation where longer Cu−O6 distances were obtained[50] ($\eta(Cu^+) = 6.28$, $\eta(Cu^{2+}) = 8.27$[72]).

Similarly, the Cu(II)G complex with three water molecules exhibits three interesting minima (among others). The first one, a four-coordinate complex (**3a**, Figure 1), has one of the aqua ligands with a distinctively shorter Cu−O coordination, which is a consequence of the H-bonding interaction of this aqua ligand with the neighboring O6 position. The second minimum (**3b**, Figure 1) corresponds to a five-coordinate chelate where the Cu−O6 bond is (again) shorter than the Cu−N7 bond (2.024 vs 2.032 Å). The global minimum of the triaqua-Cu(II)G complex is a four-coordinate chelate (**3c**) similar to the diaqua-structure (**2b**) with the remaining water localized in the outer hydration shell, forming a bridge between both aqua ligands. The substantially larger stabilization can be partially considered as a consequence of the gas-phase optimization where the role of H-bonding interactions is overestimated. It means that such a structure would not be so distinctly preferred when a continuum polarization model is used or when a larger amount of water molecules (forming another complete hydration shell) is explicitly considered. There are many other conformers in such a system with three (and below even more) water molecules. Nevertheless, it can be expected that all of the other arrangements have higher total (and lower stabilization) energies because the dominant stabilization factor is based on H-bonding, which is the strongest in the vicinity of the aqua ligands of the Cu^{2+} cation or polar interaction sites of guanine.

Cu(II)G complexes hydrated by four water molecules exhibit many distinct local minima; 13 structures were chosen for further analyses (Figure 2). One subset contains six four-coordinate structures (**4a**−**4f**) with three aqua ligands. The remaining water molecule is “used” for the exploration of the potential energy surface (PES) of the $[CuG(H_2O)_3]^{2+}$ system. In structures **4a** and **4b**, the remote water is localized in the second solvation shell of the copper cation by bifurcated H-bonds. In structures **4c**−**4f**, the water molecule is associated with different guanine sites. Another subset is composed from three five-coordinate structures where two of them have chelate character (**4g** and **4h**) and **4i** is a monodentate (nonchelate) complex. Due to large bonding competition, this structure belongs among the least stable selected conformers. The last and most stable groups are four-coordinate chelate structures **4j**−**4m** in accord with **2b** and **3c** shown in Figure 1. One of the remaining water molecules is kept in the trans position to guanine with bifurcated H-bonds to both aqua ligands (in analogy with **4b**), and the fourth molecule scans various interaction sites of the complex in the same way as in **4a**−**4f** conformers. In these complexes the Cu−O6 bond is usually negligibly shorter than Cu−N7 (about 2.01 Å), but the influence of remote water molecules can be noticed. Structure **4j** is the global minimum of the tetrahydrated complexes.

In the case of pentahydrated Cu(II)G systems, a large number of local minima can be found. From the explored set, only selected conformers are presented in Figure 3 for further discussion. These conformers can be divided into three groups. In the first group, triaqua-Cu(II)G complexes with two remote water molecules are analyzed. This group can be further divided into four-coordinate structures (**5a**−**5f** and **5i**−**5k**) and five-coordinate chelates (**5g**, **5h**, **5l**, and **5u**). The second group contains the five-coordinate tetraaqua complexes with one remote water molecule (**5m**−**5t**). The last group of diaqua chelates has three remote water molecules, and it represents the

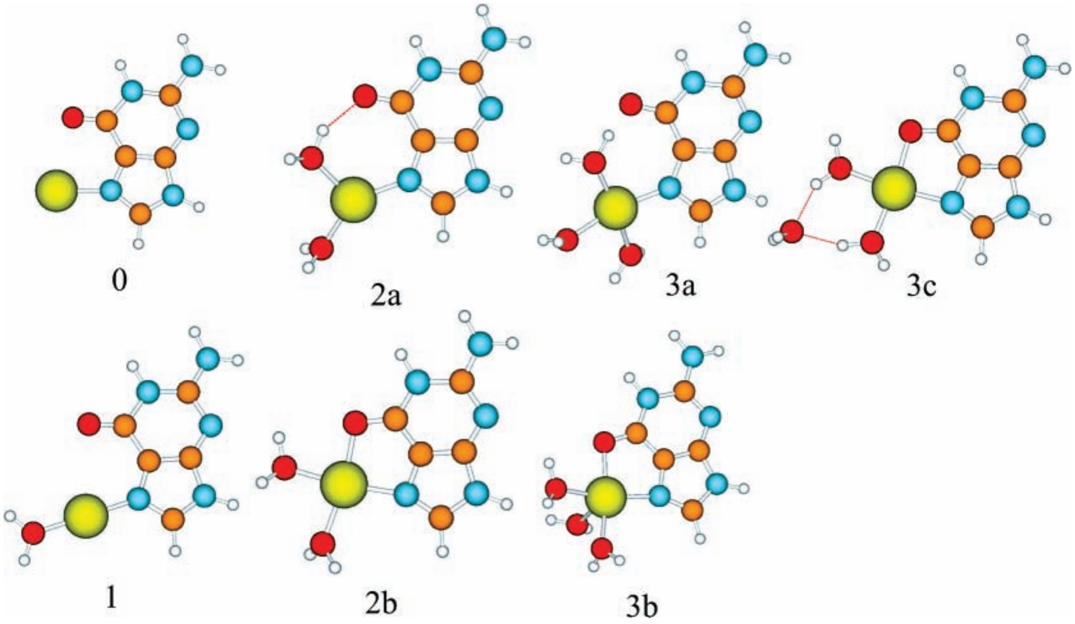


Figure 1. Aqua−copper $[Cu(H_2O)_n]^{2+}$ complexes with guanine, where $n = 0-3$.

most stable complexes in the same fashion as discussed earlier for tetrahydrated systems. Interestingly, no stable six-coordinate structure was revealed. A similar situation was also found in our previous study of copper cations in a mixed ammine−aqua ligand field.[59]

For quantification whether five-coordinate structures are closer to trigonal bipyramid or octahedral arrangement, the τ coefficients are presented in Table 2. These τ values are define by the equation

$$\tau = \frac{\theta - \varphi}{60°} \tag{2}$$

where θ is the largest ligand−metal−ligand valence angle and φ is the second largest angle. For a true octahedral structure, τ is zero, and for a bipyramidal structure, it is 1. It was found that all five-coordinate complexes (both chelated and nonchelated) belong to the distorted octahedral geometry because the τ values range from 0.0 to 0.24.

Cu−N7 bonds were found to be about 1.97 Å long in all nonchelated structures. In the case of the four-coordinate chelates (**5v**−**y**, Figure 3), the Cu−N7 distance is only slightly shorter than the Cu−O6 distance, and this result is different than that obtained in the tetrahydrated systems. Also, the five-coordinate chelates (**5g**, **5h**,**5u**, and **5l**, Figure 3) display a little bit shorter Cu−N7 bonds (averaged value 2.02 Å) than Cu−O6 bonds (2.03 Å). Interestingly in five-coordinate chelates (**4g** and **4h**) both Cu−N7 and Cu−O6 bonds are about 2.035 Å long. The fifth (axial) Cu−O(aq) bond is always perpendicular to the Cu−guanine plane, with a Cu−O distance of about 2.3 Å. It should be noted that all of the five-coordinate structures are very close to an octahedral (square-pyramidal) arrangement (Table 2).

The Cu−O(aqua) distances vary from 1.91 to 2.06 Å, depending upon the coordination number and the strength of possible H-bonds to remote water molecules. The H-bond interaction of the aqua ligand with remote water molecules shortens the Cu−O(aq) bond length. (The stronger the H-bond, the shorter the Cu−O(aq) bond.) This explains why the Cu−L (L = ligand) distances in pentahydrated Cu(II)G systems are a little shorter than those in complexes with four water molecules. Another general trend concerns the Cu−L bonds, which are shorter in the four-coordinate complexes due to smaller dative competition, as could be expected.

In our earlier work,[59] the Cu−N bonds were found to be about 2.05 Å, while Cu−O bonds varied from 1.96 up to 2.11 Å in the Cu(II) complexes with ammonia and water molecules. The Cu−N7 bonds are about 0.08 Å shorter than the Cu−N(NH_3) bonds, and this fact reflects the higher coordination ability of guanine (enhanced by a higher electrostatic contribution due to the larger dipole moment of guanine and also back-donation effect could be assumed; however, according to second-order perturbative estimates of NBO interactions no support for it was obtained). The Cu(II)−N7 bond can also be compared (with some care) with the Cu(I)−N7 bond studied previously.[61] The Cu(II)−N7 dative bond is usually by about 0.1 Å shorter than Cu(I)−N7 coordination. Considering Cu(I)G complexes, two-coordinate structures are preferred, while in the Cu(II)G complexes the four-coordinate arrangement is preferred. The obtained Cu−N7 distance of 2.03 Å in the $CuCl_2$/guanine compounds by Blazic et al.[34] using X-ray crystallographic techniques is in good agreement with our computed result.

3.2. Energy Analyses. Optimized structures were analyzed in terms of stabilization energies (ΔE^{Stab}-with and ΔE^{Stex}-without exclusion of mutual ligand interactions) and bond energies ΔE^{BE} computed according to the modified eq 1 (as mentioned in part of the Computational Details section) at the B3LYP/6-311++G-(2df,2pd) level. The obtained values are compiled in Table 3. The relative differences of the total energies of all of the conformers at both computational levels ΔE_1 (B3PW91/6-31+G(d,p)) and ΔE_2 (B3LYP/6-311++G(2df,2pd)) together with Gibbs energies ΔG are compared in Table 4 for a more detailed insight into the stability of studied complexes.

Clearly, stabilization energy increases with the number of interacting water molecules in the system. In the nonhydrated CuG complex the stabilization energy is about 293 kcal/mol due to the strong electrostatic contribution to the dative Cu−N7 bond. The inclusion of first aqua ligand raises the stabilization by about 45 kcal/mol. Including the second up to the fifth water molecules, the stabilization energy increases as follows: 24, 18, 22, and 20 kcal/mol. In the case of complexes with two water molecules, the global minimum is formed by the four-coordinate chelate (**2b**, Figure 1). The **2a** conformer lies (ΔE_2)

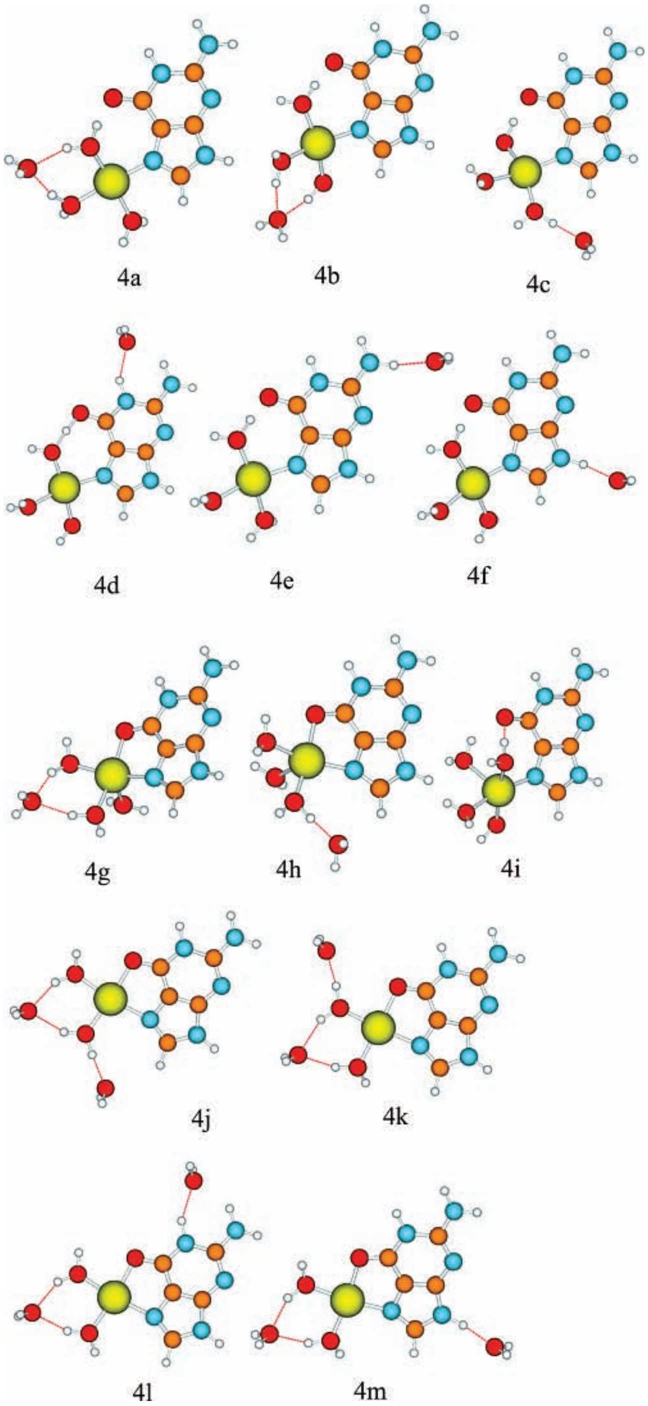


Figure 2. Tetraaqua Cu(II) complexes with guanine.

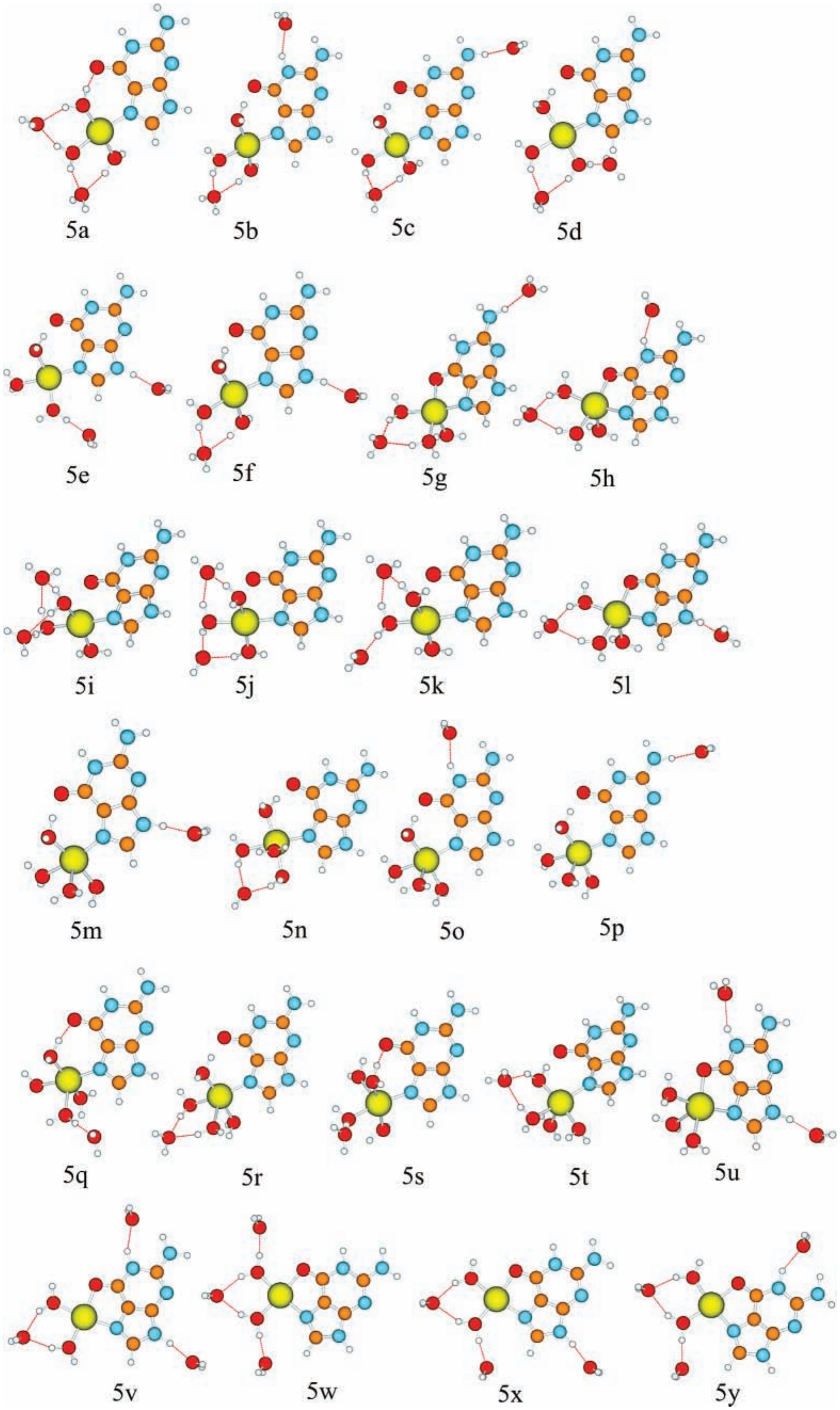
about 8 kcal/mol higher. The Cu(II)−guanine system with three water molecules prefers by 6 kcal/mol the four-coordinate chelate structure with one remote water (**3c**, Figure 2) over five-coordinate chelate **3b** and by 8 kcal/mol over five-coordinate nonchelate complex **3a**. In the system with four water molecules, it is unambiguously shown that pentacoordination is less advantageous (at least in the gas-phase calculations) than four-coordinate Cu(II) complexes with the H-bonded water molecule(s) regardless of the monodentate or chelate complexes that are considered.

The relative energies of these conformers can be seen in Table 4 for different computational schemes. From this table, it can be noticed that no substantial change in the conformer order occurs passing between individual computational levels in the $[CuG(H_2O)_4]^{2+}$ complexes. Differences of total energies ΔE_1 and ΔE_2 as well as relative stabilization energies $\Delta\Delta E^{Stab}$ revealed that the most stable structure is the four-coordinate chelate with two water molecules associated with the first coordination shell (**4j**). The **4b** conformer is the most stable nonchelate structure (about 3 kcal/mol higher in ΔE_2 energy). The five-coordinate chelated complex **4g** is slightly higher at the ΔE_2 level by about 4 kcal/mol above the global minimum. The lowest conformer of the nonchelated five-coordinate Cu(II)G complexes (**4i**) is markedly less stable by about 10 kcal/mol compared with the ΔE_2 energy of structure **4j**. Significant change does not occur when entropy contributions are taken into account. One interesting feature concerns the fact that the conformers with remote water in proximity to the N9 guanine site become more preferable by about 2−3 kcal/mol in comparison with other conformers (as noticed already in a previous study[53]). Similar ΔG preference can also be seen in the case of pentahydrated complexes for structures **5f** and **5l**. This group of complexes exhibits slightly different results than those in the case of tetrahydrated complexes. Namely, at all of the energy levels, nonchelate four-coordinate complex **5a** represents the global minimum. Only after inclusion of thermal and entropy corrections the **5w** chelate becomes thermodynamically the most stable strucure. It indicates that inclusion of the entropy term is of basic importance for prediction of correct thermodynamics. The dependence of the stabilization energy on the number of water molecules is illustrated in Figure 4. An analogous dependence is visible in the case of ΔE^{Stex} energies. The trends match well our previous results for small copper complexes with aqua and ammine ligands.[59] A more pronounced difference between tetra- and pentacoordination in guanine-containing complexes follows from stronger N7 donation.

Interaction of guanine with hydrated copper is also investigated in terms of the bonding energies ΔE^{BE}(Cu−G) and ΔE^{BE}(Cu−N7). The former (hydrated) copper−guanine interaction comprises both the dative Cu−N7 bond and either the dative Cu−O6 bond or the (aqua)H···O6 H-bond interaction (if present). The ΔE^{BE}(Cu−N7) bonding energies are corrected values for the pure Cu−N7 dative bond. In these cases the H-bond interaction is estimated from two values: 11.1 kcal/mol based on comparison of ΔE^{BE}(Cu−O) for aqua ligands in **3a** in Table 3, supposing that all three Cu−O bonds would be roughly equivalent if it were not for the H-bonding to O6 guanine (and omitting the trans influence of the N7 position). The other H-bond energy can be estimated to be about 7.5 kcal/mol from the difference of the Cu−O bond energies in the comparison of ΔE^{BE}(Cu−O) for both aqua ligands in **2a**. Because a linear dependence between H-bond energy and distance can be approximately assumed,[73] we arrive at the following correction term for the H-bond energy of the (aqua)H···O6 interaction

$$E(\text{H-bond}) = 43.67 - 13.33d(\text{O}-\text{O}) \quad (\text{in kcal/mol and Å})$$

The Cu−N7 bonding energy is 302 kcal/mol for a complex with the bare copper cation. Addition of a single water (which transfers to the aqua ligand) leads to the reduction of the Cu−N7 bonding energy by ca. 70 kcal/mol. For diaqua and triaqua complexes the energy of the dative bond further drops down to 159 and 122 kcal/mol. The limiting value of the Cu−N7 energy can be estimated to be around 90 kcal/mol for complexes with total charge of +2 as can be seen from Figure 5. Despite higher coordination energies, a similar trend can be observed also for chelate structures. Four-coordinate chelate (**2b**) has a Cu−


5a 5b 5c 5d

5e 5f 5g 5h

5i 5j 5k 5l

5m 5n 5o 5p

5q 5r 5s 5t 5u

5v 5w 5x 5y

Figure 3. Pentaaqua Cu(II) complexes with guanine.

(N7^O6) bonding energy of about 185 kcal/mol, which is reduced to 170 kcal/mol for one water present in the outer shell of the Cu cation (**3c**) and further to 156 (**4i**−**4m**) and 151 kcal/mol (**5v**−**5y**) in the systems with five water molecules. From these considerations and some additional calculations, it can be roughly estimated that the Cu−O6 bonding energy is roughly about 60 kcal/mol.

The ΔE^{BE} energy of the Cu−O(aqua) dative bond is in the range of 17−51 kcal/mol (in presence of strong H-bonding interaction(s)), giving on average ca. 29 kcal/mol. The lower

TABLE 3: ΔE^{Stab} Stabilization, ΔE^{Stex} Sterically Corrected Stabilization, and ΔE^{BE} Bonding Energies (in kcal/mol)[a]

					ΔE^{BE}						
system	CN	structure	ΔE^{Stab}	ΔE^{Stex}	guanine	Cu−N7	aqua ligands/water molecules				
$[CuG]^{2+}$	1	**0**	292.7	302.6	302.6						
$[CuG(H_2O)_1]^{2+}$	2	**1**	337.5	348.8	229.5		45.5				
$[CuG(H_2O)_2]^{2+}$	3	**2a**	353.7	363.2	166.1	158.6	32.3	24.8			
	$\mathbf{4^{chel}}$	**2b**	**360.9**	388.3	185.6		38.1	35.4			
$[CuG(H_2O)_3]^{2+}$	4	**3a**	377.0	403.6	133.6	122.5	44.2	33.1	32.9		
	$\mathbf{4^{chel}}$	**3c**	**384.8**	413.0	169.8		40.9	39.1	27.5*		
	5^{chel}	**3b**	379.0	409.2	159.0		32.4	30.1	20.8		
$[CuG(H_2O)_4]^{2+}$	4	**4a**	399.0	423.9	118.5	108.3	43.2	38.7	30.2	26.3*	
	4	**4b**	**401.2**	424.9	122.3	111.6	43.8	36.4	36.2	28.0*	
	4	**4c**	397.1	421.3	118.1	107.4	48.6	41.2	32.2	23.3*”	
	4	**4d**	393.8	433.4	114.0	102.4	47.5	31.6	31.1	18.0”	
	4	**4e**	389.2	415.6	115.5	104.1	44.7	31.5	31.5	12.8”	
	4	**4f**	392.9	417.5	112.1	100.9	43.7	31.4	31.7	16.7”	
	$\mathbf{4^{chel}}$	**4j**	**404.0**	434.1	156.5		40.2	48.2	25.0*	20.4*	
	4^{chel}	**4k**	401.8	434.1	153.6		53.1	36.8	25.2*	18.5*	
	4^{chel}	**4l**	402.3	425.6	159.2		39.5	37.6	27.1*	18.3”	
	4^{chel}	**4m**	400.8	426.4	153.8		40.0	37.7	27.1*	16.9”	
	5	**4i**	**393.9**	417.3	116.5	101.5	31.0	29.6	22.1	31.6	
	$\mathbf{5^{chel}}$	**4g**	**399.6**	430.5	145.3		35.2	32.1	18.3	25.3*	
	5^{chel}	**4h**	397.8	429.1	151.4		41.2	29.6	18.8	20.4*”	
$[CuG(H_2O)_5]^{2+}$	**4**	**5a**	**421.8**	446.2	109.7	99.8	44.6	41.4	35.0	25.7*	23.7*
	4	**5b**	417.7	436.9	108.3	97.5	43.0	35.9	35.1	27.0*	16.8”
	4	**5c**	413.4	434.7	103.6	93.1	41.7	36.2	35.0	27.1*	12.3”
	4	**5d**	419.8	444.4	108.0	97.6	48.0	43.9	35.7	25.1*	19.0*”
	4	**5e**	412.4	434.1	108.8	97.9	43.6	40.0	31.0	22.3*”	16.0”
	4	**5f**	417.0	437.8	106.4	95.9	41.8	36.4	34.8	26.9*	16.1”
	4	**5i**	410.6	430.4	113.7	106.2	39.6	32.9	29.4	23.6*	22.1*
	4	**5j**	415.9	437.3	109.5	102.6	40.7	33.4	31.9	25.4*	25.8*
	4	**5k**	413.1	435.0	109.8	103.2	51.1	32.8	29.1	24.4*	19.9*
	4^{chel}	**5v**	417.6	438.6	158.6		48.4	35.7	26.3*	17.5”	16.1”
	4^{chel}	**5w**	420.1	454.2	144.4		51.6	45.5	22.3*	19.3*	17.2*
	4^{chel}	**5x**	419.2	446.7	149.2		46.8	38.9	24.2*	19.5*	16.0”
	$\mathbf{4^{chel}}$	**5y**	**421.0**	446.3	153.8		46.8	38.5	24.2*	19.8*	17.7”
	5	**5m**	410.4	434.7	103.7	92.9	42.3	27.6	26.4	19.7	15.9”
	5	**5n**	**416.1**	441.4	110.2	99.6	44.2	32.3	31.1	18.6	24.8*
	5	**5o**	411.2	434.4	106.7	95.6	47.1	28.1	26.2	19.8	16.8”
	5	**5p**	406.8	432.0	101.6	93.2	42.6	27.9	26.6	20.0	12.2”
	5	**5q**	411.0	437.3	102.8	92.8	39.1	29.7	28.4	24.1	17.9*”
	5	**5r**	413.8	439.6	112.7	101.9	43.3	30.7	26.9	23.8	21.7*
	5	**5s**	413.5	438.2	109.3	100.8	43.5	31.0	27.5	20.5	20.1*
	5	**5t**	413.7	438.4	108.4	98.1	43.0	32.0	27.9	23.0	17.9*
	5^{chel}	**5g**	411.8	440.3	121.3		34.3	31.3	24.7	17.7*	12.8”
	$\mathbf{5^{chel}}$	**5h**	**416.5**	442.3	127.5		33.9	31.0	24.5	17.4*	17.5”
	5^{chel}	**5l**	414.7	443.0	123.9		34.4	30.7	24.5	17.4*	15.8”
	5^{chel}	**5u**	411.8	434.0	119.2		30.3	27.8	19.1	17.4”	16.0”

[a] Bold indicates the most stable conformer for a given coordination number. Structure and CN correspond to identification and coordination type, respectively. Bond energies marked by asterisks and quotation marks correspond to remote water molecules near the first coordination sphere of the copper cation and guanine sites, respectively.

values result from higher competition with other ligands. In the cases of five-coordinate conformers, the ΔE^{BE} energies can drop below 20 kcal/mol. Higher Cu−O(aqua) energies are connected with the presence of the remote (H-bonding) water molecules in proximity to the given aqua ligands. Then the electron density of the sigma O−H bond in the aqua ligand decreased because the hydrogen atom is involved in additional H-bonding with the oxygen from the remote water molecule, and therefore some part of the bonding electron density is released back to oxygen. The higher electron density on oxygen is available for better donation to the copper cation. Simultaneously, a larger partial charge of the oxygen atom leads to an enhancement of the electrostatic contribution between $Cu^{\delta+}$ and $O^{\delta-}$. The largest values of Cu−O bonding energy are connected with the presence of two H-bonds (from outer-shell water molecule(s) and the O6 guanine site) available in the vicinity of the given aqua ligand (cf., for instance, the conformers **5d** and **5k**).

In copper complexes with the variable ammine−aqua ligand field,[59] ΔE^{BE} energies of Cu−O bonds were estimated to be in the range of 33−50 kcal/mol. It is in good agreement with the $Cu-OH_2$ bonding energies presented in this work. For $Cu-NH_3$ coordination, the bond energies vary from 50 to 63 kcal/mol. The ΔE^{BE} of Cu−N7(guanine) is approximately twice as strong. This is caused by two effects. First, guanine has a larger dipole moment ($\mu(G) > 7$ D) than ammonia ($\mu(NH_3) = 1.5$ D), which electrostatically enhances the dative coordination. Second, in the case of guanine, π-back-donation can (possibly) further increase the Cu−N7 dative coordination.

The largest association energy (ΔE^{BE} values signed with asterisks or quotation marks in Table 3) was found for the remote water localized in the outer hydration shell and linked by two furcated H-bonds to Cu−aqua ligands (**4b** with $\Delta E^{\text{BE}} = 28$ kcal/mol). When the interaction of the remote water and guanine is considered, the most preferred guanine site is the

TABLE 4: Relative Differences of Total Energies at the Computational Levels ΔE_1 (B3PW91/6-31+G(d)) and ΔE_2 (B3LYP/6-311++G(2df,2pd), Gibbs Energies ΔG, and Relative Differences between Stabilization Energies $\Delta\Delta E^{Stab}$ (in kcal/mol) with Respect to Global Minima Structures (Marked by Asterisks)[a]

system	CN	structure	ΔE_1	ΔE_2	ΔG^{total}	$\Delta\Delta E^{Stab}$
$[CuG(H_2O)_4]^{2+}$	4	**4a**	4.3	4.9	4.5	6.5
	4	**4b**	**2.2**	**2.7**	**2.2**	**4.6**
	4	**4c**	6.6	6.7	5.8	7.1
	4	**4d**	9.9	10.0	7.9	8.8
	4	**4e**	15.5	14.9	12.7	12.0
	4	**4f**	11.4	11.1	9.1	8.7
	4^{chel}	**4j**	**0.0***	**0.0***	**0.0***	**0.0***
	4^{chel}	**4k**	2.4	2.2	2.0	1.0
	4^{chel}	**4l**	0.9	1.7	1.8	2.3
	4^{chel}	**4m**	3.1	3.3	2.9	2.0
	5	**4i**	**8.6**	**9.8**	**9.4**	**11.1**
	5^{chel}	**4g**	**2.7**	**4.2**	**4.3**	**4.9**
	5^{chel}	**4h**	5.2	6.2	5.9	5.5
$[CuG(H_2O)_5]^{2+}$	**4**	**5a**	**0.0***	**0.0***	**2.8**	**0.0***
	4	**5b**	3.9	4.2	6.1	4.1
	4	**5c**	9.2	8.7	8.8	8.4
	4	**5d**	2.6	2.3	3.4	2.1
	4	**5e**	10.5	9.6	8.4	9.4
	4	**5f**	5.2	5.0	5.6	4.9
	4	**5i**	8.8	10.8	14.0	11.2
	4	**5j**	4.5	5.7	9.3	5.9
	4	**5k**	7.7	8.5	9.6	8.7
	4^{chel}	**5v**	4.8	4.6	3.5	4.2
	4^{chel}	**5w**	3.5	2.0	**0.0***	1.7
	4^{chel}	**5x**	3.9	2.9	1.1	2.4
	4^{chel}	**5y**	**1.5**	**1.0**	1.1	**1.0**
	5	**5m**	11.5	11.5	10.0	11.4
	5	**5n**	**4.6**	**5.6**	**7.2**	**5.8**
	5	**5o**	10.1	10.5	10.4	10.6
	5	**5p**	15.3	15.0	13.2	15.1
	5	**5q**	10.8	10.9	10.1	10.8
	5	**5r**	7.0	7.9	9.6	8.1
	5	**5s**	7.8	8.3	8.8	8.4
	5	**5t**	7.2	8.0	9.8	8.1
	5^{chel}	**5g**	10.0	10.3	9.1	10.0
	5^{chel}	**5h**	**4.5**	**5.5**	6.4	**5.4**
	5^{chel}	**5l**	6.7	7.1	**6.1**	7.1
	5^{chel}	**5u**	10.0	10.3	8.6	10.1

[a] Bold indicates the most stable conformer for given coordination and used method. The abbreviation CN corresponds to the type of coordination, and structure is used for the exact identification of the optimized structure.

position between N1 and N2 (**4d**; ca. 18 kcal/mol). In the case of pentahydrated Cu(II)G complexes, one of the remote water molecules in the four-coordinate structures (**5b**, **5c**, and **5f**) exhibits an association energy of about 27 kcal/mol (practically equal in all three cases), which corresponds to the interaction with two aqua ligands in the first coordination shell. This is an analogous position like in the **4b** conformer. Similarly, the strongest association of water with guanine also occurs through the N1 and N2 sites of the molecule (conformers **5b**, **5h**, **5u**, and **5y**).

Comparison of association energies in Table 3 for remote water molecules revealed the following trends: (i) The largest ΔE^{BE} occurs for water linked to the first coordination sphere of the metal cation (20−28 kcal/mol). (ii) Smaller ΔE^{BE} energies (between 18 and 23 kcal/mol) connected with bifurcated H-bonds between C8 and neighboring aqua ligands (in structures **4c**, **5d**, and **5q**). (iii) A reduced ΔE^{BE} was found for water association to guanine sites (from 12 to 18 kcal/mol). The energy preference for H-bonded water to guanine sites is: N1/N2 (about 17−18 kcal/mol) then N9 (16−17 kcal/mol).

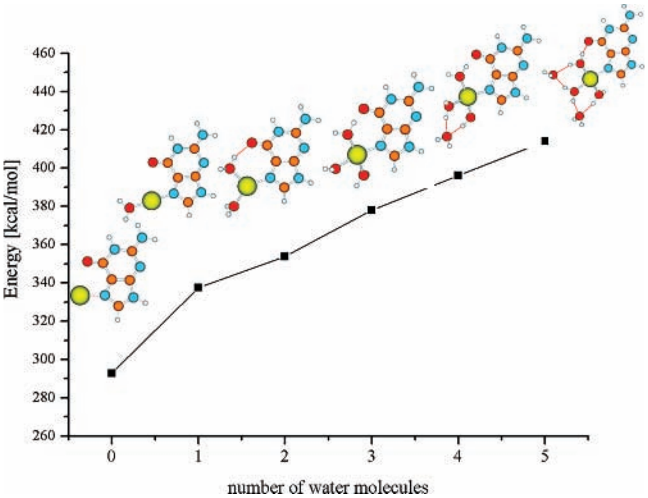


Figure 4. Stabilization energies for the $[Cu(H_2O)_n]^{2+}$ complexes with guanine, where $n = 0-5$.

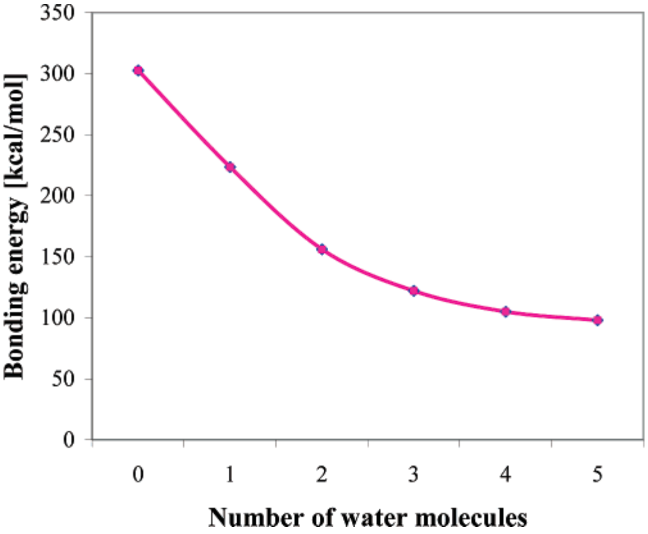


Figure 5. ΔE(Cu−N7) bonding energy of $[Cu(II)G]^{2+}$ complexes in dependence on the present water molecules.

TABLE 5: Averaged Values of Partial Charges and Spin Densities (in Electron Units) Summed for All Guanine Atoms[a]

	charge			spin density		
system	Cu	guanine	waters	Cu	guanine	waters
$[CuG]^{2+}$	0.927	1.073		0.006	0.994	
$[CuG(H_2O)_1]^{2+}$	0.822	1.081	0.097	0.023	0.975	0.001
$[CuG(H_2O)_2]^{2+}$ (*2a*)	1.128	0.734	0.138	0.332	0.620	0.048
$[CuG(H_2O)_2]^{2+}$ (*2b*)	1.432	0.357	0.211	0.696	0.204	0.132
$[CuG(H_2O)_3]^{2+}$	1.445	0.336	0.218	0.713	0.162	0.125
$[CuG(H_2O)_4]^{2+}$	1.440	0.319	0.241	0.709	0.142	0.149
$[CuG(H_2O)_5]^{2+}$	1.440	0.271	0.289	0.714	0.124	0.162

[a] The same is done for water molecules.

3.3. Partial Charge Analyses. Geometry and energy explorations can also be supported by the analysis of the distribution of electron density in terms of spin densities (collected in Table 5) and partial atomic charges (Table 6) calculated with the NPA method at the B3LYP/6-311++G(2df,2pd) level. Interesting insight into the examined complexes can be obtained from Table 5 where partial charges of copper, guanine, and water are summarized together with the spin densities. These results demonstrate the distribution of the unpaired electron among considered subsystems. When no hydration is considered, one electron from guanine is used for copper reduction, resulting

TABLE 6: Partial Atomic Charges (in Electron Units) for Copper and Selected Atoms on Guanine (N7, N9, H9, H8, H1, H2a, H2b, and O6) Obtained by the NPA Method[a]

			partial atomic charges			
system	CN	structure.	Cu	N7	N9	O6
$[CuG]^{2+}$	1	**0**	0.927	−0.627	−0.510	−0.504
$[CuG(H_2O)_1]^{2+}$	2	**1**	0.822	−0.585	−0.511	−0.473
$[CuG(H_2O)_2]^{2+}$	3	**2a**	1.128	−0.622	−0.509	−0.590
	4^{chel}	**2b**	1.432	−0.624	−0.516	−0.725
$[CuG(H_2O)_3]^{2+}$	4	**3a**	1.436	−0.625	−0.514	−0.648
	4^{chel}	**3c**	1.439	−0.619	−0.518	−0.724
	5^{chel}	**3b**	1.461	−0.615	−0.520	−0.725
$[CuG(H_2O)_4]^{2+}$	4	**4a**	1.426	−0.625	−0.516	−0.664
	4	**4b**	1.442	−0.630	−0.515	−0.652
	4	**4c**	1.440	−0.630	−0.515	−0.661
	4	**4d**	1.424	−0.617	−0.519	−0.627
	4	**4e**	1.430	−0.625	−0.517	−0.650
	4	**4f**	1.430	−0.640	−0.531	−0.653
	4^{chel}	**4j**	1.445	−0.612	−0.519	−0.725
	4^{chel}	**4k**	1.440	−0.616	−0.517	−0.707
	4^{chel}	**4l**	1.435	−0.620	−0.518	−0.734
	4^{chel}	**4m**	1.436	−0.631	−0.531	−0.730
	5	**4i**	1.466	−0.616	−0.518	−0.732
	5^{chel}	**4g**	1.452	−0.607	−0.522	−0.727
	5^{chel}	**4h**	1.455	−0.610	−0.522	−0.727
$[CuG(H_2O)_5]^{2+}$	**4**	**5a**	1.435	−0.623	−0.518	−0.664
	4	**5b**	1.422	−0.630	−0.518	−0.667
	4	**5c**	1.423	−0.631	−0.519	−0.666
	4	**5d**	1.425	−0.623	−0.518	−0.661
	4	**5e**	1.434	−0.644	−0.532	−0.667
	4	**5f**	1.422	−0.644	−0.532	−0.666
	4	**5i**	1.422	−0.616	−0.519	−0.745
	4	**5j**	1.443	−0.617	−0.519	−0.735
	4	**5k**	1.440	−0.632	−0.519	−0.724
	4^{chel}	**5v**	1.427	−0.633	−0.533	−0.739
	4^{chel}	**5w**	1.447	−0.610	−0.520	−0.708
	4^{chel}	**5x**	1.438	−0.624	−0.534	−0.731
	4^{chel}	**5y**	1.437	−0.614	−0.521	−0.736
	5	**5m**	1.449	−0.641	−0.534	−0.667
	5	**5n**	1.442	−0.628	−0.518	−0.659
	5	**5o**	1.448	−0.627	−0.519	−0.665
	5	**5p**	1.450	−0.627	−0.520	−0.666
	5	**5q**	1.462	−0.620	−0.519	−0.665
	5	**5r**	1.440	−0.627	−0.518	−0.659
	5	**5s**	1.451	−0.621	−0.520	−0.725
	5	**5t**	1.445	−0.626	−0.518	−0.666
	5^{chel}	**5g**	1.448	−0.609	−0.526	−0.735
	5^{chel}	**5h**	1.446	−0.609	−0.525	−0.738
	5^{chel}	**5l**	1.446	−0.620	−0.540	−0.733
	5^{chel}	**5u**	1.446	−0.631	−0.540	−0.744
isolated H_2O and guanine				−0.453	−0.557	−0.611

[a] Averaged partial charges for O atoms of water molecules are presented too. Bold indicates the most stable conformer. The abbreviation CN corresponds to the coordination type, and structure is used for exact identification of the optimized structure.

in a [Cu^+guanine$^+$] system. This fact was already noticed by Noguera et al. for the interaction of the Cu^{2+} cation with a GC base pair.[74] For the increasing number of interacting water molecules from 1 to 5, the spin density "moves back" to the Cu atom (from 0.02e to 0.72e) as the effect of electron transfer from guanine diminishes. For all of the four- and five-coordinate Cu(II)G complexes, the unpaired electron is basically located on the Cu atom, resulting in partial charge $\delta = 1.44e$ and spin density $\rho_s = 0.7e$. Such a behavior can be explained when the ionization potential (IP) of guanine is compared with the electron affinity (EA) of the (hydrated) Cu^{2+} cation. The IP of isolated guanine (8.8 eV) is more than twice as low as the EA of bare Cu^{2+} (20.6 eV), both estimated at the B3LYP/6-311++G(2df,2pd) level. It clearly causes the electron to move from guanine to copper. In our previous study,[60] the EA of the hydrated Cu^{2+} cation was predicted to be about 12 eV. Such a significant decrease of EA leads to stabilization of the Cu^{2+} state (because the electrostatic work for electron transfer is already not compensated for by the EA − IP difference).

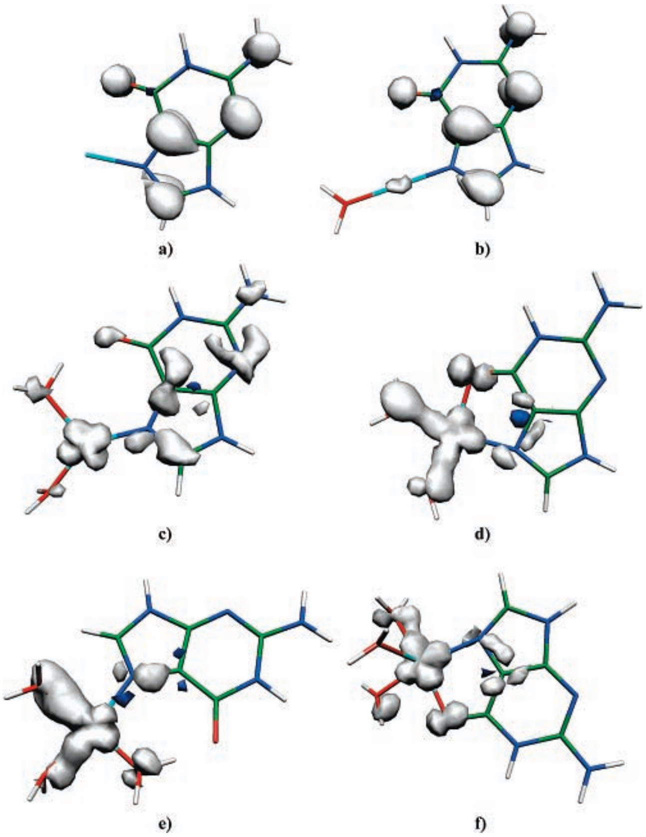


Figure 6. Plots of spin density ($\rho_s = 0.005$) of the selected aqua−Cu(II)G complexes: (**a**) and (**b**) $[CuG]^{2+}$ and $[CuG(H_2O)]^{2+}$ structures, (**c**) and (**d**) $[Cu(H_2O)_2]^{2+}$ structures **2a** and **2b**, (**e**) and (**f**) $[Cu(H_2O)_3]^{2+}$ structures **3a** and **3b**.

A theoretical study of Martinez[47] investigated neutral, anionic, and cationic copper−guanine and −uracil nonhydrated complexes. As it was just shown, such stuctures give different electronic ground state where the Cu^{2+} cation is reduced. The work of Lamsabhi et al.[46] describes the same [Cu^+uracyl$^+$] system, and we have also noticed it in our previous works.[50,75]

Electronic ground states of studied complexes were inspected by plotting the spin densities ($\rho_s = 0.005$). A complete set of these spin-density maps for systems collected in Table 5 is displayed in Figure 6.

A complete set of partial charges on key atoms of the Cu(II)G complexes is compiled in Table 6 and Table 1-SI in the Supporting information. The latter contains a more detailed data necessary to investigate the polarization of guanine, when interacting with the hydrated copper(II) cation. Strong dative coordination to the copper cation results in polarization in the N7 ← N9 direction. This trend can be clearly seen comparing partial charges of isolated and coordinated guanine. Different electron density distribution occurs in chelate structures. The O6 coordination to the Cu cation results in a decrease of the oxygen partial charge by about 0.1e. It is also possible to observe additional ("secondary") polarization of guanine when a water molecule associates (forming a H-bonded adduct) to various guanine interacting sites (N1/N2, C8, or N9).

The subject of water polarization (when coordinated to the Cu(II) cation) was already explored in our previous studies.[58−60]

4. Conclusion

In the present study, the hydrated structures of the Cu(II)-(N7−guanine) complex were explored. All of the investigated complexes were optimized at the B3PW91/6-31+G(d) level. For selected low-lying local minima on the potential energy surface, several types of energy decompositions were performed at the B3LYP/6-311++G(2df,2pd) level together with the determination of electronic properties (partial charges and electron spin densities).

It was found that for systems without water molecules or with one water electron transfer from guanine to Cu(II) occurs, resulting in a reduced Cu(I) cation and positively charged guanine. Complexes with two aqua ligands represent borderline systems with largely varying charges and spin densities localized on guanine. Only when three-coordinate copper is formed the prevailing electron spin density (more than 0.7*e*) is already localized on the copper cation.

Another result concerns the energetic ΔE^{Stab} (ΔE^{Stex}) preference of the diaqua Cu−(N7,O6−guanine) chelate over monodentate three aqua Cu−(N7−guanine) structures by about 8 kcal/mol in the cases of complexes with two and three water molecules. Nevertheless, the difference in total and stabilization energies decreases to 2 kcal/mol in tetrahydrated complexes, and for complexes with five water molecules the stabilization energies of the both groups of conformers are very close to each other.

As a consequence of a more strongly donating guanine ligand, it was found that pentacoordination is in these complexes visibly less convenient than that in the case of small inorganic ligands (in the presence of both purely aqua ligands[58] or mixed aqua−ammine ligands[59]).

Complexes with five water molecules can also be compared with structures of our previous study where pentahydrated Cu(I)−guanine systems were explored.[61] Cu(I) complexes do not create chelate structures because the linear monoaqua form with the remaining water molecules in the solvation shell is substantially more stable. Because the copper cations in these structures have very similar oxygen−nitrogen ligand fields as in aqua−ammine complexes[59] an analogous conclusion on coordination preference (two-coordination for Cu(I) and tetracoordination for Cu(II) complexes) is also observed for the Cu−water−guanine systems. In the monoaqua complexes, the strengths of the Cu−N7 bond (−81/−230 kcal/mol for Cu(I)/Cu(II)) and Cu−O(aqua) bond (−35/46) roughly follow the formal electrostatic relationship. A larger preference for N7 coordination in the Cu(II) complex is connected with electron-transfer effects discussed above. In the most stable Cu(II) structures, the Cu−N7 bonding energies suffer from the higher dative competition of other aqua ligands.

Acknowledgment. This study was supported by Grant Nos. MSM 0021620835 and GA AV IAA400550701 and MŠMT-NSF Grant No. 1P05ME784. The computational resources from the Meta-Centra Project (in Prague, Plzen, and Brno) as well as the computational cluster of the Faculty of Mathematics and Physics are acknowledged for access to their excellent computational facilities. M.K.S. and J.L. are thankful for financial support from NSF-CREST Grant No. HRD-0318519.

Supporting Information Available: Additional tables. This material is available free of charge via the Internet at http://pubs.acs.org.

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