# Structure and Coordination Modes in the Interaction between Cd$^{2+}$ and 3-Mercaptopropionic Acid

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The structural, electronic, and energetic properties of cadmium ion complexes with one and two protonated and deprotonated 3-mercaptopropionic acid ligands were studied theoretically in the framework of density functional theory by using the B3LYP exchange-correlation functional coupled with 6-311++G** Gaussian orbital basis sets for C, H, O, and S atoms and LANL2DZ for the metal ion. The study was extended to the aqueous complexes introducing explicitly some water molecules in order to simulate the tetrahedral and octahedral coordination sphere of the Cd$^{2+}$ ion. Results indicate that the complexes containing only one ligand have a cyclic structure in which the metal ion binds both oxygen and sulfur atoms. The tetrahedral topology is preferred in the complexes with two ligands.

## Introduction

The role of cadmium ion as a pollutant is well-known, and a series of studies well underline the damages that this cation causes, even in low concentration, in the environmental natural equilibrium.[1−4] Cadmium contained in several industrial products (e.g., nickel−cadmium batteries, pigments, plastics, pesticides, alloys, chemical reagents, and nuclear rods) and released during rock mineralization processes is discharged into the aquatic environment.[5] Cadmium ion toxicity depends not on its concentration but on its speciation, and the possible formation of complexes with organic ligands changes its toxicity, bioavailability, mobility, and migration patterns. Animal and vegetal kingdoms have developed some strategies in order to control the presence of many heavy metals, including cadmium, synthesizing metallothionein and phytochelatin molecules able to form stable complexes due to the presence of thiol groups.[1,6] In the marine environment, thiol groups are present in several molecules that are originated by the biodegradation of sulfur-containing compounds and from organic rich sediments.[7]

One of the most important molecules present in seawater is 3-mercaptopropionic acid (MPA) because it easily coordinates the Cd$^{2+}$ ion, partitioning the resulting metal complexes into the aqueous phase. The study of these complexes is also important in view of the fact that it can give information on the interaction mechanism of heavy metals with glutathione and cysteine hydrophilic thiols contained in many biological systems. Furthermore, this kind of investigation can give insights into the binding mechanism of organic thiol ligands; the increasing amount of cadmium contained in coastal, salt-marsh sediments; and the detoxification processes of metallothioneins and phytochelatins.

Cd−MPA complexes were studied in these last years by using a variety of experimental techniques such us potentiometry, extended X-ray absorption fine structure (EXAFS), and electrospray mass spectrometry.[8] Despite these investigations, some fundamental questions are still open and a better knowledge of structural features of the complexes formed by cadmium ion

with a different number of MPA ligands can elucidate their chemistry such as stated in the recent work of Vairavamurthy et al.[8] Indeed, the authors underline in their conclusions that "chemical structure is an important factor in controlling the mobility of cadmium in biological and environmental systems containing thiol complexes".

In this paper, we have undertaken a detailed study on the coordination modes, geometrical structures, and binding energies of the complexes formed by cadmium ion with one or two MPA ligands by using the density functional theory in its B3LYP formulation. The reliability of this tool was previously demonstrated by a large amount of studies devoted to fully characterizing the structural and spectroscopic features of a wide series of transition metal containing systems.[9−17]

## Method

All the considered systems were fully optimized by using the B3LYP exchange-correlation functional[18] coupled with the extended 6-311++G** basis sets for H, C, N, O, and S atoms and the LANL2DZ[19−21] pseudopotential for cadmium, as implemented in the Gaussian 94 code.[22] Harmonic vibrational frequencies were computed in order to characterize the minimum nature of the complexes as well as to include the zero point energy corrections into the metal ion affinity (MIA) calculation. Due to the size of used basis sets, we have verified, through the counterpoise method,[22] that the basis set superposition error is negligible (less than 0.5 kcal/mol).

MIA was assumed to be the negative of the enthalpy variation at 298 K ($-\Delta H$) for the process $n$MPA + Cd$^{2+}$ → (MPA)$_n$−Cd$^{2+}$.

The nature of the metal−ligand chemical bond was established by the natural bond order (NBO) analysis.[23]

## Results and Discussion

Due to the presence in the literature of data on the formation mechanism, both in liquid and gas phase, of different complexes between cadmium ion and MPA,[8] we have considered the partial (MPAH) and total (MPA) deprotonated ligand. The possible

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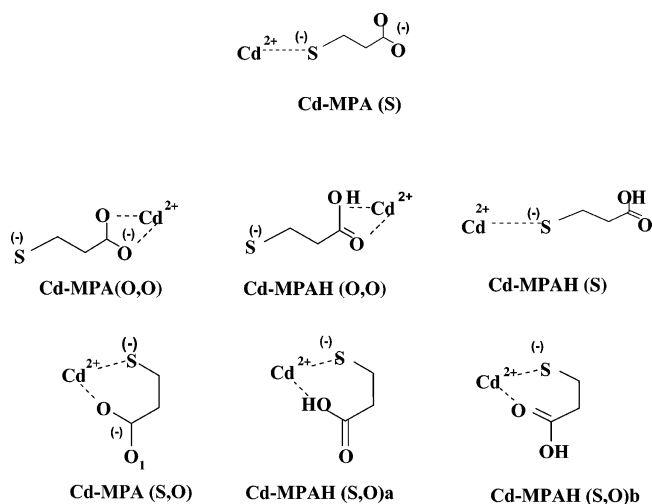\* To whom correspondence should be addressed. E-mail: nrusso@unical.it.

**Figure 1.** Possible coordination modes in the interaction of Cd²⁺ ion with one MPA or MPAH ligand.
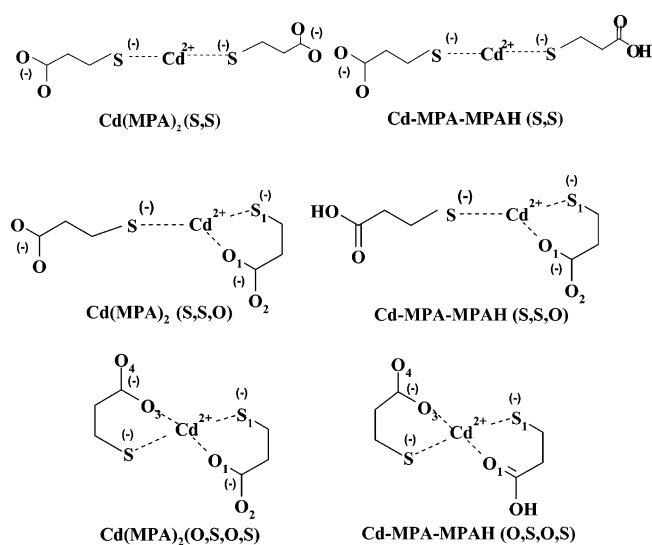


**Figure 2.** Possible coordination modes in the interaction of Cd²⁺ ion with two MPA ligands or one MPA and one MPAH ligand.

**TABLE 1:  B3LYP/6-311++G\*\* Zero Point Corrected Total (*E*) and Relative Energies (Δ*E*) and Metal Ion Affinities (MIA) at 298 K for Various Conformers of Cd−MPA and Cd−MPAH Complexes**

| compound | *E* (au) | Δ*E* (kcal/mol) | MIA (kcal/mol) |
|---|---|---|---|
| Cd−MPA (S,O) | −713.479 952 | 0.0 | 579.3 |
| Cd−MPA (O,O) | −713.425 486 | 34.2 | 545.1 |
| Cd−MPAH (S,O)a | −713.820 162 | 12.5 | 381.4 |
| Cd−MPAH (S,O)b | −713.840 006 | 0.0 | 393.9 |
| Cd−MPAH (S) | −713.803 301 | 23.0 | 370.4 |
| Cd−MPAH (O,O) | −713.746 485 | 58.7 | 334.7 |

coordination modes of Cd²⁺ ion with one or two 3-mercapto-propionic acid molecules are depicted in Figures 1 and 2, respectively. For the sake of clarity, in Figures 1 and 2 the complexes have been named omitting the total charges and indicating the coordination sites of the ligands.

As shown in Figure 1, cadmium ion can coordinate in different modes with both protonated (MPAH) and deprotonated (MPA) 3-mercaptopropionic acid. The total and relative energies of the various complexes obtained combining cadmium ion with one ligand are reported in Table 1. The bicoordinated complexes, in which cadmium ion interacts with sulfur and oxygen atoms, are the most stable for both deprotonated and protonated ligands. For the former, the S-monocoordinated species (Cd−MPA (S)

**TABLE 2:  Results of NBO Analysis of the Most Stable Cd−MPA, Cd−MPAH, Cd−(MPA)₂, and Cd−MPA−MPAH Complexes[a]**

| atoms | natural charge | atoms | natural charge |
|---|---|---|---|
| | Cd-MPA (S,O) | | |
| Cd²⁺ | 1.391 | O | −0.947 |
| S | −0.465 | O₁ | −0.598 |
| | Cd-MPAH (S,O)b | | |
| Cd²⁺ | 1.394 | O | −0.780 |
| S | −0.331 | O_H | −0.612 |
| | Cd−(MPA)₂ (O,S,O,S) | | |
| Cd²⁺ | 1.582 | S | −0.678 |
| S₁ | −0.673 | O₃ | −0.887 |
| O₁ | −0.889 | O₄ | −0.756 |
| O₂ | −0.753 | | |
| | Cd−MPA−MPAH (S,S,O) | | |
| Cd²⁺ | 1.419 | O₂ | −0.669 |
| S₁ | −0.617 | S | −0.600 |
| O₁ | −0.955 | | |
| | Cd (MPA)₂ (S,S,O) | | |
| Cd²⁺ | 1.435 | O₁ | −0.909 |
| S | −0.662 | O₂ | −0.725 |
| S₁ | −0.642 | | |

[a] Natural charges are in |e|.

of Figure 1) is not stable and collapses in the bicoordinate one (Cd−MPA (S,O) of Figure 1), while the O,O bicoordination is 34.2 kcal/mol less stable than the absolute minimum Cd−MPA (O,O) of Figure 1. In the most stable Cd−MPA (S,O) complex, the NBO analysis shows that a covalent bond exists between the S atom and the Cd²⁺ ion, together with substantial charge transfer from the ligand to the metal center. In particular, we found that the Cd−S bond (77.15% of Cd²⁺ and 22.85% of S) is mainly formed by the p orbital of the sulfur atom (96.22%) and the s orbital of the cadmium ion (96.50%) with a small participation of p (2.73%) and s (3.59%) orbitals of cadmium and sulfur centers, respectively. In addition, between Cd²⁺ and O atoms an ionic interaction is present as evidenced by the net charge values (1.391 and −0.947 |e| for Cd²⁺ and O, respectively) collected in Table 2. This behavior is reflected also on the weakening of the C−O bond with respect to the free ligand (1.327 versus 1.261 Å). A similar electronic distribution is found for the Cd−MPAH (S,O)b complex (see Table 2). From these data, it emerges that in both cases the sulfur atom transfers more charge on cadmium than on oxygen. In particular, the ionic nature of the O−Cd interaction in the Cd−MPAH (S,O)b complex is supported by a higher charge electron density on the oxygen atom equal to −0.780 |e| (more negative by 0.139 |e| than that of the free ligand). This fact causes a small lengthening of the C−O bond (1.240 Å in the complex versus 1.211 Å in the free ligand) and, also, a decrease of the C−O stretching vibrational frequency on going from the free ligand to the complex (ν = 1783.1 cm⁻¹ versus ν = 1664.9 cm⁻¹, respectively). This behavior agrees with the fact that sulfur is a soft species and prefers to interact with another soft atom such as Cd²⁺ ion. The Cd−O and Cd−S equilibrium distances are 2.097 and 2.427 Å, respectively, for Cd−MPAH (S,O)a, whereas the same distances have values of 2.265 and 2.426 Å, respectively, for Cd−MPAH (S,O)b. The coordination with the two oxygen atoms is also possible, but the resulting complex is, in both deprotonated and protonated complexes, much more unstable because of the hard nature of oxygen atoms.

The metal ion affinities of the two species are found to be 579.3 and 393.9 kcal/mol for Cd−MPA (S,O) and Cd−MPAH (S,O)b, respectively. These data, together with the preferred formation of a cyclic structure in both of the complexes,[8] support
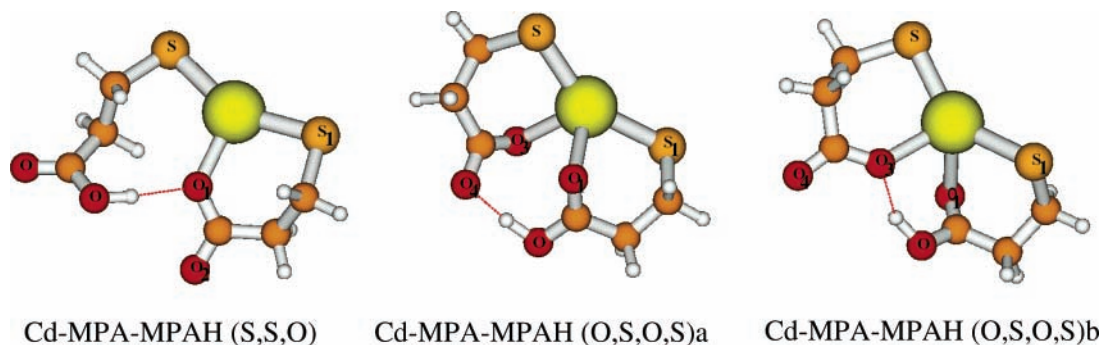
Interaction between Cd$^{2+}$ and MPA

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**Cd-MPA-MPAH (S,S,O)**     **Cd-MPA-MPAH (O,S,O,S)a**     **Cd-MPA-MPAH (O,S,O,S)b**

**Figure 3.** B3LYP-optimized structures of the most stable Cd−MPA−MPAH complexes.

**TABLE 3: B3LYP/6-311++G\*\* Zero Point Corrected Total ($E$) and Relative Energies ($\Delta E$) and Metal Ion Affinities (MIA) at 298 K for Various Conformers of Cd−(MPA)$_2$ and Cd−MPA−MPAH Complexes**

| compounds | $E$ (au) | $\Delta E$ (kcal/mol) | MIA (kcal/mol) |
|---|---|---|---|
| Cd−(MPA)$_2$ (O,S,O,S) | −1379.055 931 | 0.0 | 688.2 |
| Cd−(MPA)$_2$ (S,S,O) | −1379.046 346 | 6.0 | 681.8 |
| Cd−(MPA)$_2$ (S,S) | −1379.020 363 | 22.3 | 665.1 |
| Cd−MPA−MPAH (O,S,O,S)a | −1379.679 188 | 0.0 | 668.8 |
| Cd−MPA−MPAH (S,S,O) | −1379.672 113 | 4.4 | 664.3 |
| Cd−MPA−MPAH (O,S,O,S)b | −1379.672 013 | 4.5 | 663.9 |
| Cd−MPA−MPAH (S,S) | −1379.610 182 | 43.3 | 624.2 |

**TABLE 4: Cd$^{2+}$ Ion Affinities (MIA) for Tetrahedral ($n = 4$) and Octahedral ($n = 6$) Coordination Geometries$^a$**

| compounds | MIA, $n = 4$ | MIA, $n = 6$ |
|---|---|---|
| [Cd−(H$_2$O)$_n$]$^{2+}$ $^b$ | 244.1 | 305.0 |
| [Cd−(H$_2$S)$_n$]$^{2+}$ | 208.5 | 234.7 |
| [Cd−(H$_2$O)$_{n-1}$CH$_3$S]$^+$ $^b$ | 236.3 | 198.6 |
| [Cd−(H$_2$O)$_{n-2}$−(MPA)$_2$]$^{2-}$ | 708.4 | unstable |

$^a$ All data are in kcal/mol. $^b$ Derived from ref 24.

the hypothesis, coming from the experimental equilibrium constant measurement, that the monothio complex does not exist as a zwitterion (Cd−MPA (S) of Figure 1) but as a charge-neutralized species in a cyclic structure (Cd−MPA (S,O) of Figure 1). On the other hand, the possible zwitterionic form in the triplet state is less stable by 131.7 kcal/mol than the corresponding one in the singlet ground state.

The possible coordination modes in the interaction of Cd$^{2+}$ ion with two MPA ligands are different, and we have considered those coming from reasonable chemical arguments (Figure 2). From Table 3, it is evident that the cadmium ion coordination with two O,S sites is thermodynamically favored, giving rise to a complex with a distorted tetrahedral geometry around the metal center (Cd−(MPA)$_2$ (O,S,O,S) of Figure 2). The distortion from the ideal tetrahedral geometry is of about 15° in the valence angles and is due to the different substituents around the metal ion. In fact, we found values of 91.60° for the O−Cd−S angle of the MPA cycle and of 126.08° and 108.08° for the S−Cd−S and O−Cd−O angles, respectively. The Cd−S (2.589 Å) and Cd−O (2.273 Å) distances are closer to those found in the Cd−MPA cyclic structure. The system in which Cd$^{2+}$ is coordinated with two sulfur atoms and one oxygen (Cd−(MPA)$_2$ (S,S,O) of Figure 2) is 6.0 kcal/mol less stable than the O,S,O,S type, while the S,S bicoordination (Cd−(MPA)$_2$ (S,S) of Figure 2) is 22.3 kcal/mol higher in energy.

The NBO analysis reveals a different electronic behavior with respect to the Cd−MPA complex. In fact, the covalent bond between the Cd$^{2+}$ ion and the sulfur atom is not present in this case. The net charges on Cd$^{2+}$, S$_1$, O$_1$, S, and O$_3$ are 1.582, −0.673, −0.889, −0.678, and −0.883 |e|, respectively (see Table 2). The sulfur atoms transfer, now, on the Cd$^{2+}$ ion a smaller amount of charge (0.14 with respect to the free ligand), and all the interactions around the metal ion center are essentially ionic in nature. The MIA accounts for the high stability of the tetracoordinated complex (688.2 kcal/mol, see Table 3).

In Table 3 are also reported the results for the protonated species. Also in this case the tetracoordinated complexes are more stable than the tricoordinated and bicoordinated ones. Two complexes (Cd−MPA−MPAH (O,S,O,S)a and Cd−MPA−

MPAH (O,S,O,S)b of Figure 3) with distorted tetrahedral geometry are formed. They differ, substantially, by the direction of the H-bond formed by the O−H group with an energy difference of 4.5 kcal/mol (Table 3). In the global minimum, the S−Cd−O, S−Cd−S, and O−Cd−O valence angles are 90.00°, 151.14°, and 78.37°, respectively. The Cd−S (2.541 Å) and Cd−O (2.321 Å) distances are, again, similar to those found in the other cyclic complexes. Also the bond compositions and charge transfer (see Table 2) are close to those of the global minimum of the Cd−(MPA)$_2$ complex (Cd−(MPA)$_2$(O,S,O,S) of Figure 2).

The tricoordinated S,S,O complex (Cd−MPA−MPAH (S,S,O) of Figure 3) is also stable and lies 4.4 kcal/mol above the global minimum (Table 3). This complex is stabilized by a strong hydrogen bond (1.810 Å) between the O−H group of one ligand and the oxygen atom (O$_1$) of the other ligand that is bonded to the cadmium ion (Figure 3).

To simulate a system more close to the aqueous solution, we have added explicitly some water molecules to complete the coordination sphere of the metal ion. Previous theoretical studies on the solvation of the bare Cd$^{2+}$ ion demonstrate that this species prefers an octahedral geometry when binding water ligands.[24] The tetrahedral form is 60.9 kcal/mol less stable than the octahedral ones. If we consider the H$_2$S ligand instead of H$_2$O, the octahedral complex continues to be more stable than the corresponding tetrahedral complexes, but the energy difference is now reduced to 26.2 kcal/mol (Table 4). Increasing the dimension of one ligand, as in the case of [Cd−(H$_2$O)$_5$-CH$_3$S]$^+$, the most stable complex is now in the tetrahedral form and the octahedral geometry lies 37.7 kcal/mol higher in energy.[24] Another experimental EXAFS study[25] clearly demonstrates that a maximum of four thiol compounds (e.g., SO$_4$$^{2-}$) can bind to cadmium ion in aqueous solution. We have considered the tetracoordinated Cd−(MPA)$_2$ (O,S,O,S) complex of Figure 2 and added two water molecules to model the octahedral topology. Results show that the two water molecules are pushed out from the coordination sphere of the metal ion, giving rise to a series of hydrogen bonds with the MPA ligand as shown in Figure 4a. From this computation, it emerges that when the Cd$^{2+}$ ion coordinates two MPA ligands the tetrahedral arrangement is preferred.
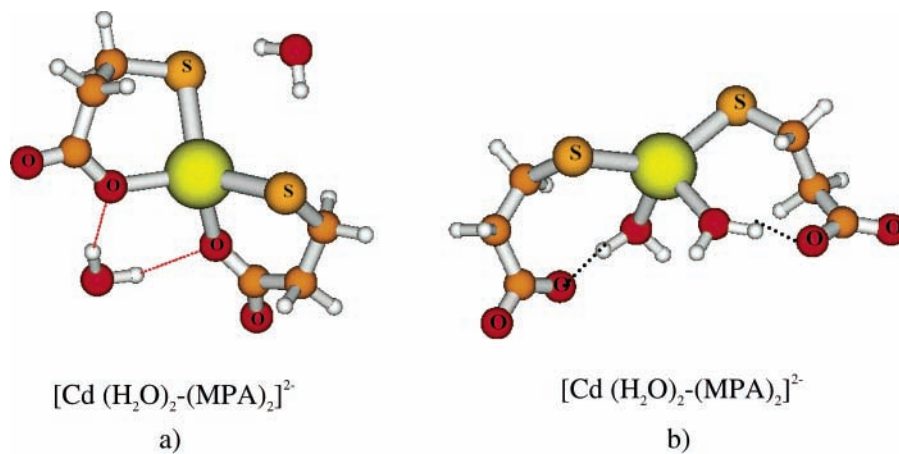
**Figure 4.** B3LYP-optimized structures of Cd—(MPA)$_2$/water complexes.

Also in the case of the bicoordinated Cd—(MPA)$_2$(S,S) relative minimum, we have explicitly added two and four water molecules to simulate the tetrahedral and octahedral coordination geometries around the cadmium ion. Results show that only in the tetrahedral form do the water molecules bind with the metal ion (Figure 4b), while the octahedral complex collapses in the tetrahedral one.

The metal ion affinity of the [Cd—(H$_2$O)$_2$—(MPA)$_2$]$^{2-}$ complex is now 708.4 kcal/mol (Table 4) versus 665.1 kcal/mol for the Cd—(MPA)$_2$ (S,S) one of Table 3. These results univocally indicate the preference of the Cd$^{2+}$ ion to give tetracoordinated complexes with both deprotonated and protonated MPA ligands. These results are in agreement with previous studies of Rulíšek et al.[24] and Frenkel et al.[25] in which there are indications that the Cd$^{2+}$ ion is likely found in tetrahedral coordinations when it is bonded to sulfur-containing ligands.

## Conclusions

In this paper, we have investigated the geometrical and electronic structures of complexes formed by a cadmium ion with one and two protonated and deprotonated 3-mercaptopropionic acid molecules in a vacuum and in an environment that simulates the first coordination sphere of the complexes in water solution. Results show the following:

The more stable complexes generated with one ligand have a cyclic structure with the metal ion that coordinates with both oxygen and sulfur atoms.

The interaction of Cd$^{2+}$ with two ligands gives linear and tetrahedral structures, the latter being much more stable.

The dominant bond in the complex with one ligand arises from the covalent interaction between sulfur and the cadmium ion in agreement with the fact that both are soft centers. The presence of another sulfur atom, belonging to the second ligand in the coordination sphere of the Cd$^{2+}$ ion, reduces the charge transfer of sulfur, and all the interactions are ionic in nature in the Cd—(MPA)$_2$ and Cd—MPA—MPAH complexes.

The explicit introduction of water ligands, with the aim to simulate the tetrahedral and octahedral environments around the metal center, favors the tetrahedral coordination.

So, from our study emerges a strong indication that Cd$^{2+}$ ion is likely to be found in tetrahedral coordinations when it is bonded to sulfur-containing ligands.

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