

Quantum chemical approach (DFT) of the binary complexation of Hg(II) with L-canavanine and L-arginine.

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Abstract

The experimental study of the complexation of the two amino acids, L-canavanine, and L-arginine, with the mercuric ion Hg(II), was completed by the characterization by a quantum calculation based on the DFT method. This study covers electronic, energetic, and structural aspects in the neutral, deprotonated, and complexed states. The atomic net charges show that the active sites of the carboxyl, guanidyl, and amino groups are the oxygen and nitrogen atoms. In fact, the L-canavanine (Can) gave stable mercuric bidentate chelates via the amino and guanidyl groups. $\text{Hg}(\text{Can})(\text{H}_2\text{O})_2$, $\text{Hg}(\text{Can})_2$ and $\text{Hg}(\text{OH})(\text{H}_2\text{O})(\text{Can})$, while the L-arginine (Arg) resulted in engagement of carboxyl and amino groups to bidentate complexes: $\text{Hg}(\text{Arg})(\text{H}_2\text{O})_2$, $\text{Hg}(\text{Arg})_2$, $\text{Hg}(\text{Arg})(\text{OH})(\text{H}_2\text{O})$. The metal-ligand coordination bond is more rigid with the guanidyl and carboxyl groups than with the amino group; and the bond formed with the amino group is more rigid in the L-canavanine than L-arginine.

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1. INTRODUCTION

Each day billions of meter cube of domestic and industrial wastewater effluent are released into receiving waters throughout the world. Untreated wastewater contains organic compounds[1,2], nutrients[3], and Inorganic molecules[4], as well as free cation metals[5] and complexes compounds[6,7], this diversity of compounds has an impact on the environment that cannot be ignored and increase the need for treatment for downstream drinking water source waters[8]. The use of vegetal proteins tends to develop over the years, that comes for their abundance and profitability, in this context, we are interested in amino acid e, L-canavanine, or amino-2-(guanidinoxy)-4-butyric acid, and their structural analogue, L-arginine 2-amino-5 (carbamimid)-amido-pentanoïque [9], [10]. This two component obtainable of certain plants and legumes such as soybean, alfalfa and clover [11],[12]. It was isolated in 1929 from flour "jack bean" by Kitagawa and Tomiyama [13]. Specifically, L-canavanine is an antimetabolite of L-arginine. In addition, the L-arginine was founded in plants of the Sutherlandia type and it protects from various insect predators. The L-canavanine was generally shown as a toxic compound of vegetal proteins. This toxicity due to its structural resemblance with the L-arginine is related to two mechanisms: (i) the inhibition of enzymes in the metabolism of the L-arginine and (ii) the denaturation of the functional properties of the proteins in which it is incorporated [10]. It also induces similar lesions to that caused by the cadmium on ribonucleic proteins. This justifies the quality control interest which should permit verify its absence in vegetal protein intended for human or animal consumption. If the L-canavanine has been widely studied experimentally [14], [15] then theoretically we do not have any bibliographic data concerning the complexation of these acids with metal ions. It is in this light that we are interested in the theoretical study of the L-canavanine and L-arginine interactions with a toxic ion found in soil, mercury (II). This will provide the conclusions necessary to interpret the difference highlighted in the experimental study [12], [16], the protonic equilibria in solution of L-canavanine and L-arginine and their complexation with Hg(II) which we think is just as important [17]. To complete this work on the complexation by a theoretical study, it is necessary to characterize the different ligands in the neutral, deprotonated, and complexed states by a quantum computation using density functional theory (DFT) calculations[18]. Afterward Kohn and Sham's seminal paper in 1965[19], and innovative advancements by others in the 1980s and early1990s, DFT[20] turn into in the extreme applied computational-chemistry technique. It is not only used by specialized computational and theoretical chemists, but recognition to its availability in standard quantum chemistry software and reasonably easy technical applicability, it was used by experimentalists to theoretically support their experimental findings (our case). Phrases such as 'LanL2DZ basis set' or 'B3LYP basis set' you will find it into nearly every chemist's vocabulary. This is not strange of DFT on the discipline in general if we know the fact that one-half of the 1998 Nobel Prize in chemistry awarded to Walter Kohn.

Our study will determine:

- The active sites of the molecules via the analysis of the atomic net charges.
- The equilibrium geometries optimized of neutral and complexed molecules and their enthalpies of formation. The theoretical results will be compared with experimental data [12],[16], [17].

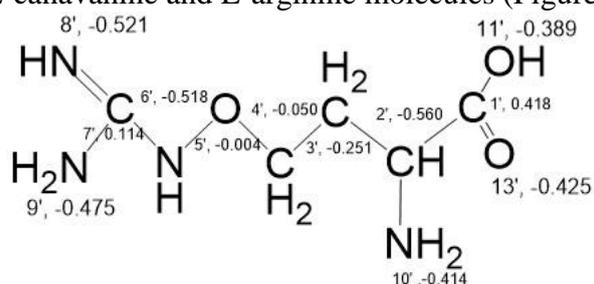
2. RESULTS AND DISCUSSION

All theoretical calculations were carried out via DFT with Becke's three-parameter Lee-Yang-Parr hybrid (B3LYP) functional [20] implemented in Gaussian 09 suite of programs [21]. GaussView 6 was used to prepare the input files generated by Gaussian 09 [22]. The 6-31++g(d,p) basis set was used, except for

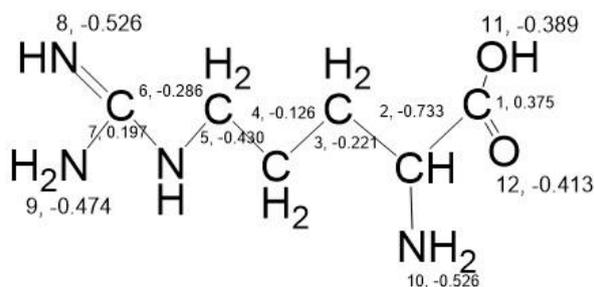
metal-ligand complexes, in which the LANL2DZ basis set (Los Alamos National Laboratory 2 double-zeta) was employed with including effective core potential functions in order to decrease the computational cost [23]. The absence of imaginary frequency confirms that the optimized geometries were stable. The conductor-like polarizable continuum model (CPCM) was used in order to take care of the solute/solvent (water) interactions [24],[25].

2.1. Atomic charges

With sum of Mulliken atomic charges equal to zero [4]. The analysis of atomic net charges was used to identify the active sites vis-a-vis the metal ion Hg (II). The different results obtained after optimization of the geometry of each molecule in the neutral and deprotonated state allows for an analysis of net charges of the characteristic party of the L-canavanine and L-arginine molecules (Figure 1).



L-canavanine



L-arginine

Fig. 1: Net atomic charges of neutral L-arginine and L-canavanine.

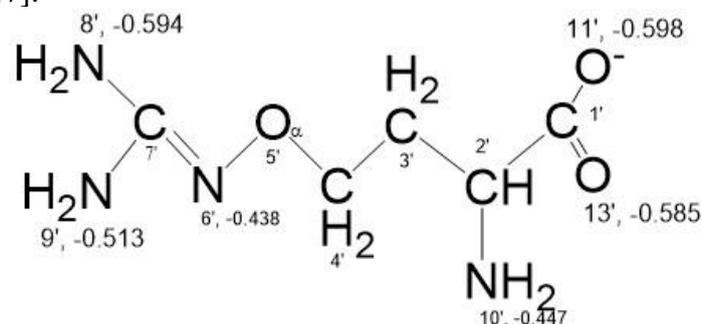
The comparison of atomic charges in the two molecules in the neutral state gives the following results:

- ✓ The negative charge of the N6 atom of the L-arginine is much larger than that of the N6' atom of the L-canavanine, which is probably due to the attractor inductive effect of oxygen O α . The N8', N9' and N10' atoms of the L-canavanine also show lower negative charge than those carried by the N8, N9 and N10 atoms of the L-arginine.
- ✓ The oxygen atoms of the acid function hold net charges that are lower than that of the guanidyl and amine groups in the L-arginine. On the contrary in the L-canavanine this order was reversed, which shows the influence of the oxygen atom O5 on the nucleophilic susceptibility of these functional groups.
- ✓ The influence of the oxygen O α is highly sensitive and particularly reaches the hydrogen atoms of the acid function of the two molecules. So, the net charges of the atoms are different and have the values 0.418 and 0.375 e in the L-canavanine and L-arginine, respectively. This means that the L-canavanine is deprotonated more easily than the L-arginine which is in good agreement with experiment; the experimental values of protonic stability constants of the L-canavanine and L-arginine at T = 298 °K are, respectively, Log K (L-canavanine) = 2.15 and Log K (L-arginine) = 2.22[16]. The DFT method involving a polyelectronic wave

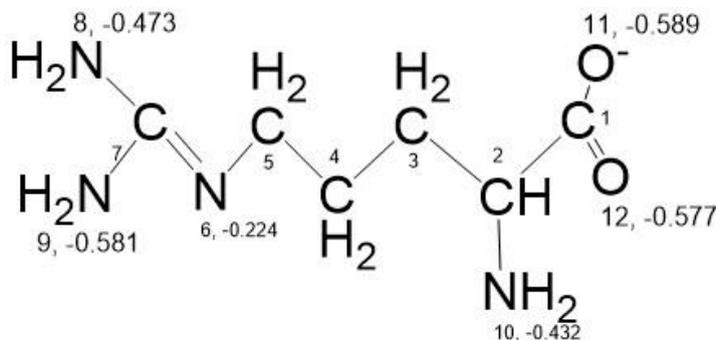
function allows assessing the influence of O α oxygen of the L-canavanine molecule on the electronic charges of atoms.

2.2. Complexation with Hg(II)

The experimental results obtained by Albourine et al. show a significant difference between the L-canavanine and L-arginine in the order of deprotonation of the amino and guanidyl functional groups [17]. In the case of L-canavanine, the guanidyl group ($\log K = 6.98$) is deprotonated before the amino group ($\log K = 9.16$), while for the L-arginine, it is well deprotonated beyond ($\log K = 11.85$). The direct consequence of this difference was reflected in the different modes of complexation vis-a-vis metallic ion Hg (II). Effectively, for the L-canavanine, the three groups (carboxyl, amine and guanidyl) will deprotonate in pH range of complexation of Hg(II), and are therefore likely to participate in the chelation. On the contrary in the case of the L-arginine, only the carboxyl and amino groups can be involved in chelating of these metals [17]. Theoretically, according to the DFT calculations results of deprotonated molecules (Figure 2), the comparison of the charges carried by the heavy atoms of each functional group shows that the oxygen atom (O11 for the L-arginine and O11' for the L-canavanine) has the highest negative charge and of the same order (Q11 = -0.588e and QO11' = -0.598e). For amino groups (QN10 = -0.432e and QN10' = -0.447e) and guanidyl (QN9 = -0.581e and QN9' = -0.513 e), the order of the charges is also similar except for N6 (-0.224 e) and N6'(-0.438 e). This means that in theory, for both molecules, the three groups are capable of participating in the complexation with the Hg(II) ions. This is in perfect agreement with the experimental results for L-canavanine [17].



L-canavanine



L-arginine

Fig. 2: Net atomic charges of deprotonated L-arginine and L-canavanine.

In our case, we realized our calculations on the resulting complexes from complexation mode of experimental results. Thus, the L-canavanine gave stable mercuric bidentate chelates formed by the contribution of the amino and guanidyl groups, Hg(Can)(H₂O)₂, Hg(Can)₂ and Hg(OH)(H₂O)(Can) (Figure

3). As for the L-arginine, it has resulted by engagement of carboxyl and amino groups to bidentate complexes: $\text{Hg}(\text{Arg})(\text{H}_2\text{O})_2$, $\text{Hg}(\text{Arg})_2$ and $\text{Hg}(\text{Arg})(\text{OH})(\text{H}_2\text{O})$ (Figure3).

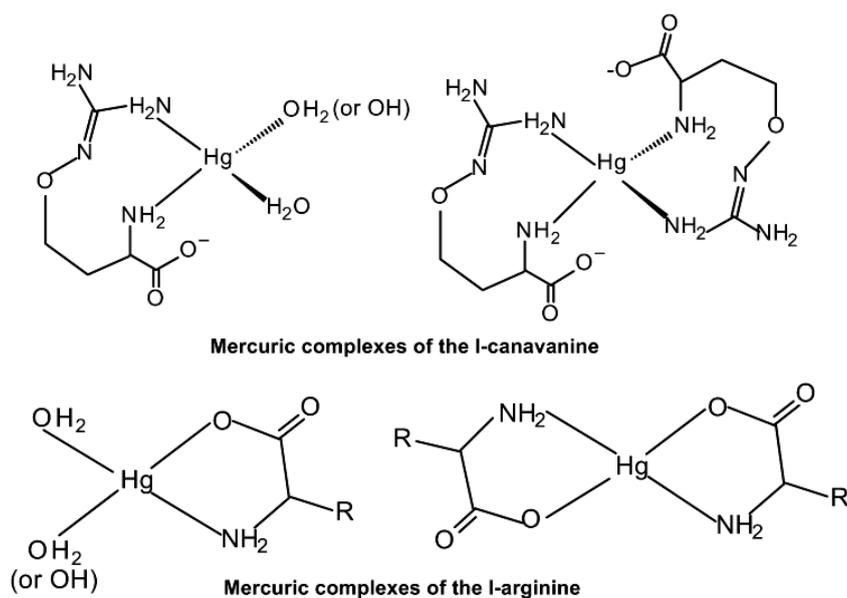


Fig. 3: Mercuric complexes of the L-canavanine and L-arginine with $\text{R} = -(\text{CH}_2)_3\text{-NHC}(\text{NH}_2)\text{NH}$.

2.2.1. Energetic aspect

We can predict the stability of these complexes by calculate their enthalpies of formation ΔH_f . Thus, we grouped in table 1 the values obtained by DFT method for L-canavanine and L-arginine. Our objective is, firstly, to compare their relative stabilities to that obtained experimentally. Secondly, to examine whether the complexation of these two molecules by a same metal ion $\text{Hg}(\text{II})$, is a way to distinguish them from their structural resemblance. And this will at the same time to examine the reliability of the DFT method regarding the metal coordination. Analysis of the Table 1 allows highlighting specific chelating behaviors for each molecule. In fact, the values of ΔH_f relative to L-arginine complexes show that these chelates exhibit thermodynamic stability significantly better than that of complexes formed with L-canavanine vis-a-vis the metal ions except for species $\text{Hg}(\text{Can})(\text{H}_2\text{O})_2$ and $\text{Hg}(\text{Arg})(\text{H}_2\text{O})_2$, which have very close ΔH_f . Consequently the L-arginine presents a better affinity for $\text{Hg}(\text{II})$ than of L-canavanine; which is in agreement with experimental results (Table 2). Thus complexation of these two acids with $\text{Hg}(\text{II})$ can be useful for distinction between the L-canavanine and L-arginine.

Table 1: ΔH_f from the sum of electronic and thermal enthalpies (in kcal/mol) of the mercuric complexes of L-canavanine and L-arginine.

L-canavanine			
Complexes	$\text{Hg}(\text{Can})(\text{H}_2\text{O})_2$	$\text{Hg}(\text{Can})_2$	$\text{Hg}(\text{OH})(\text{H}_2\text{O})(\text{Can})$
ΔH_f (Kcal/mol)	-552.83	-464.98	-551.58
L-arginine			
Complexes	$\text{Hg}(\text{Arg})(\text{H}_2\text{O})_2$	$\text{Hg}(\text{Arg})_2$	$\text{Hg}(\text{OH})(\text{H}_2\text{O})(\text{Arg})$
ΔH_f (Kcal/mol)	-498.87	-444.28	-512.67

Table 2: Stability constants β of mercuric complexes of L-canavanine and L-arginine.

Complexes	Hg(Can)	Hg(OH)(Can)	Hg(Can) ₂	Hg(Arg)	Hg(OH)(Arg)	Hg(Arg) ₂
Log β (exp)	10.75	1.49	14.13	10.24	3.83	15.20

2.2.3. Structural aspect

Structurally, it is interesting to evaluate the complexation effect on the geometric parameters of the studied molecules particularly in the immediate vicinity of the coordination site. The determination of the interatomic distance metal-ligand formed (Tables 3 and 4) in mercuric complexes (Figures 4 and 5) is equally important.

Table 3: Hg-L bond (Å) in the optimized L-canavanine complexes on DFT/B3LYP method.

M-L	Hg(Can)(H ₂ O) ₂	Hg(Can) ₂	Hg(OH)(H ₂ O)(Can)
Hg-N(I)	3.075	2.651	2.982
Hg-N(II)	3.242	2.335	3.644
O(b) - Hg	3.107	-	3.624
O(c)-Hg	3.108	-	2.383
N(IV) -Hg	-	3.873	-
N(V) -Hg	-	4.237	-

Table 4. Hg-L bond (Å) in the complexes of the optimized L-arginine by DFT/B3LYP method.

M-L	Hg(Arg)(H ₂ O) ₂	Hg(Arg) ₂	Hg(Arg)(OH)(H ₂ O)
Hg-O(I)	2.945	2.208	2.618
O(III) -Hg	2.325	2.208	2.256
Hg-N(I)	2.672	2.494	2.573
O(II) (or N(II))-Hg	2.876	2.494	2.103

i. The L-canavanine

The complexation of L-canavanine with Hg(II) resulted in tetrahedral bidentate mercuric complexes: Hg(Can)(H₂O)₂ (I), Hg(OH)(H₂O)(Can) (II) and Hg(Can)₂ (III). In these complexes, the ligand L-canavanine is bidentated and the complexation sites are the nitrogen atoms N(I) of the amino group and N(II) of the guanidyl group (Figure 4).

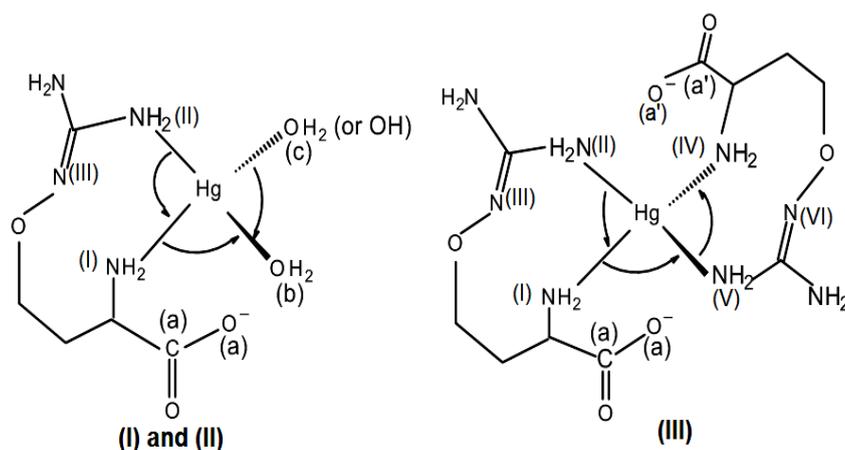


Fig. 4: Structures of the mercuric complexes with L-canavanine.

The analysis of the optimized equilibrium geometries, from the two possible tetrahedral and planar structures, revealed that, on the one hand the Hg(II) ion is tetracoordinate with a significant distortion of the tetrahedron because the bond angles (N(II)HgN(I)) (O(b)HgN(I)) (O(c)HgO(b)) and (N(V)HgN(IV)) vary between 95,35 and 103,53° instead of 109 or 90°. This deformation is most important in the chelates (I) and (II) than in (III). Probably because of the repulsion due to negative charges of the oxygen atoms, which increases the opening of these planes angles and decreases the dihedral angles (O(b)HgN(II)N(I)) and (O(c)HgN(I)N(II)), whose respective values are of the order of -134.37 and -107.94° instead of -120 and 120° (for a regular tetrahedron) or 180° (for a plan tetrahedron). On the other hand, the influence of coordination on the molecule of L-canavanine, manifested by an extension of the order of 0.01 Å for C-N(I) and C-N(II) bonds, a decrease of about 2° for (N(II)CN(III)) bond angles and an aperture which reaches 3° of the (N(I)CC(a)) angle. In fact, these bonds in the complex Hg(Can)(H₂O)₂, for example, are respectively of the order of 1.481 and 1.387 Å, in the free ligand and pass to 1.489 and 1.398Å respectively, in the complexed state. The angle (N(II)CN(III)) decreased from 125.71 to 123.98° while the angle (N(I)CC(a)) with 113.02° in the neutral state, reached 110.91° in the complexed state. On the contrary, the value of the angle (O(a)C(a)O) is practically unchanged in the three complexes remaining substantially equal to 130°.

ii. The L-arginine

The resulting species of the coordination of the L-arginine with Hg(II) ion by means of the nitrogen and oxygen atoms of acid and amine functions, respectively. Mercuric tetrahedral complexes: Hg(Arg)(H₂O)₂ (I), Hg(Arg)(OH)(H₂O) (II) and Hg(Arg)₂tran (III) are represented in the figure5.

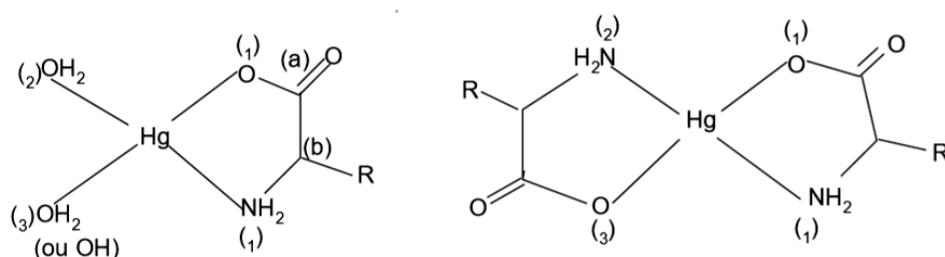


Fig. 5: Mercuric complexes of L-arginine, with R = -(CH₂)₃-NH-C(NH₂)NH.

The optimization of the geometry of these complexes, from the two possible tetrahedral and planar structures, reveals that in species (I) and (II) the L-arginine is related to the Hg(II) ion according to a deformed tetrahedron, while the complex (III) has a planar tetrahedral structure. In fact, in (I) and (II) the bond angle (N(I)HgO(I)) is only of 70.04° instead of 109° , which can be justified by the tension of the cycle of five centers formed upon binding the O and N atoms with the Hg(II) ion. As for the angles (O(II)HgO(I)) and (O(III)HgN(I)) there values are about 116.68° . This irregularity of the tetrahedron is also justified by the values of dihedral angles (O(II)HgN(I)O(I)) and (O(III)HgN(I)O(I)) which are of the order of, 106.44 and -142.96° instead of 120 and -120° , respectively. Contrary, in complex Hg(Arg)₂, the dihedral angles (N(II)HgO(I)N(I)) and (O(III)HgN(I)O(I)) tend respectively, by optimization, to 152.42 and -152.43° , indicating that the tetrahedron is partially plane. Consequently, this complex presents two isomers cis and trans for which the calculation of ΔH_f allowed us to conclude that it is the trans conformer that is more stable (-475.65 kcal/mol) than cis (-456.2 kcal/mol) and therefore we have adopted it in our study. When at the effect of coordination on the geometric structure of L-arginine ligand, we notice that he manifested especially in the immediate vicinity of complexation center. In fact, in the case of complex Hg(Arg)₂, the C-O(I) bond has shortened by 0.046 \AA (passing from 1.259 to 1.305 \AA) and C-N(I) has lengthened from 1.481 to 1.491 \AA . These opposite effects are probably due to the phenomenon of π conjugation between the two oxygen atoms for the C-O(I) bond and because of the donor inductive effect near of the nitrogen atom for the C-N(I) bond. Similar effects are sustained by the C-N(II) and C-O(III) bonds. The plane angles have not had a significant change. In fact, (O(I)C(a)C(b)) and (N(I)C(b)C(a)) angles haven't increased, respectively, only a small variation about 1 and 2° , for the first goes from 115.44 to 117.03° and the second from 112.85 to 111.74° for the Hg(Arg)(OH)(H₂O). This variation is nearly the same for Hg(Arg)₂ because (O(I)C(a)C(b)) goes from 118.13° and (N(I)C(b)C(a)) from to 111.86° .

2.2.3. Mercury-ligand bond

The complexation of a ligand (L) was reflected by the formation of a bond between the latter and the metal ion (M). The nature of this bond continues to be an interesting field of research. With this in mind we will examine in DFT/B3LYP method the order of this bond and its effects on the geometric structure of the different ligands that form coordinate covalent bonds by intervening with a free pair of electrons of the nitrogen or oxygen atom vis-a-vis Hg(II) which possesses vacant atomic orbitals in its valence-shell: $6s^0 6p^0$. As for the bond formed between the L-canavanine, L-arginine and mercuric ion, we can draw from the results shown in tables 3 and 4, several important conclusions:

In this bond, it seems that there is a considerable covalent character for both molecules.

It is partially rigid considering its length, which is about 2.1 to 4.2 \AA according to the ligands.

In the case of L-canavanine, the bonds formed with the guanidyl group (2.335 to 3.644 \AA) are more rigid than those formed with the amino group (2.651 to 3.873 \AA). This is probably due to the proximity of the carboxyl group of the amino group. Which is absent in the case of the guanidyl group.

For L-arginine, in all mercuric complexes the bond established with the oxygen of the carboxyl group, ranging from 2.208 to 2.945 \AA , is more rigid than that formed with the nitrogen of the amino group, from 2.573 to 2.672 \AA . Nevertheless, this bond is less rigid in the L-arginine than in the L-canavanine where such bonds are shorter. This means that the presence of the O α oxygen atom in L-canavanine affect the amino-metal bond. The nitrogen-metal bond of the amine function, in the complexes of arginine, which varies from 2.573 to 2.672 \AA , is more rigid than that of complexes of L-canavanine, which is 2.651 to 3.873 \AA . This can

be explained by the tension of five centers cycle formed during the complexation of the L-arginine. And it is the same, and probably for the same reason why the oxygen-metal bond of the acid function is less rigid in the L-canavanine (2.441 to 4.102 Å) than in L-arginine (2.208 to 2.945 Å).

3. CONCLUSION

From the quantum chemistry study of the complexes of L-canavanine and L-arginine with Hg(II) using DFT calculations. We found that for both molecules, the three functional groups: carboxyl, guanidyl and amino are likely to participate in the complexation of the ion Hg(II) given the high negative net charges of the active sites of each group namely oxygen atom of the acid function and the nitrogen atom for the amine and guanidyl functions. However, despite that the two molecules have similar structures that they have two different behaviors with respect to Hg(II). In fact, the L-canavanine gave stable mercuric bidentate chelates formed via the amino and guanidyl groups, $\text{Hg}(\text{Can})(\text{H}_2\text{O})_2$, $\text{Hg}(\text{Can})_2$ and $\text{Hg}(\text{Can})(\text{OH})(\text{H}_2\text{O})$, while the L-arginine resulted in engagement of carboxyl and amino groups to bidentate complexes: $\text{Hg}(\text{Arg})(\text{H}_2\text{O})_2$, $\text{Hg}(\text{Arg})_2$, $\text{Hg}(\text{Arg})(\text{OH})(\text{H}_2\text{O})$. Structurally, the optimized equilibrium geometry is a tetrahedral structure for the complexes of the two ligands molecules. Furthermore, the formed coordinate-covalent bond: ligand-metal is more rigid with guanidyl and carboxyl groups than with the amine function for the two molecules, however, the bond formed with the amino group is more rigid in the L-canavanine than in the L-arginine.

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