# THEORETICAL STUDY OF THE USE OF NEW LIGANDS BASED ON BIPHENYL DERIVATES CONTAINING HYDRALAZINE AND ISONIAZIDE MOIETIES AS CHEMICAL SENSORS OF METAL IONS

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**Abstract:** Metal ions are of great significance to the environment and biological system. Particularly, trivalent - iron, aluminium and chromium - and divalent - copper, mercury, cadmium, and zinc - cations are some of the more important. Recently we have report two new ligands derived from *bis*-vanillin, useful for discriminate between $Fe^{3+}$, $Al^{3+}$ and $Cr^{3+}$.

Considering these results, we present a theoretical study based on the Functional Density Theory related with structures of *bis*-vanillin derivatives contained a hydrazoline or isoniazide moiety into the complexation types of both ligands with $M^{3+}$ cations. Moreover, we realize a predictive theoretical study to explore the ligands' complexation with $M^{2+}$ cations.    The optimized structures of the ligands and their cation complexes are presented and discussed.

**Keywords:** Chemical sensors, Biphenyl, Metal ions

## 1. Introduction

There is an enormous demand for chemical sensors for many areas and disciplines. High sensitivity and ease of operation are two main issues for sensor development [1]. Fluorescence techniques can easily fulfill these requirements and therefore fluorescent-based sensors appear as one of the most promising candidates for sensing. Metal ions are of great significance to the environment and biological system. Particularly aluminum, copper and zinc are three of the most important cations in different aspects. Zinc and copper are respectively the second and third largest amount of transition elements exists in our human body and they are involved in many vital processes in the organism. However, the accumulation of excessive quantities of these elements is highly toxic, for example the accumulation of copper causes Wilson's disease in humans [2]. Aluminium, which is the most abundant metallic element and the third most abundant of all elements in the earth's crust, is widely used in our daily life and industrial fields. Although aluminium and most of its derivatives exhibit low toxicity, high doses of this metal can also cause neurotoxicity [3] and the increased amounts in the dietary may also contribute to the reduced skeletal mineralization (osteopenia), because the metal competes with calcium for absorption [4].

On the other hand, some heavy metal ions, particularly $Pb^{2+}$, $Hg^{2+}$ and $Cd^{2+}$ are the most toxic cations, causing adverse environmental and health problems. The release of these detrimental ions into the environment originates from numerous natural and man-made sources, such as fossil fuel combustion and the electronic industry and cadmium it is even found in phosphate fertilizers. $Hg^{2+}$ and $Pb^{2+}$ produce a wide variety of symptoms, including digestive, cardiac, kidney and especially

neurological diseases, suggests that they affect multiple targets in vivo [5,6,7,8]. For $Cd^{2+}$ there have been many reports on his toxicity to procreation, bones, kidneys, nerve system, and tissues, consequently resulting in renal dysfunction, calcium metabolism disorders, and an increased incidence of certain forms of cancers [9].

Therefore, selective and sensitive determination of these metal cations in biological and environmental systems is very important, resulting in the appearance of numerous sensory reports with diverse mechanisms for the selective detection of different metal ions [10,11,12,13]. Among the different chemosensors, those based on ion-induced changes in fluorescence are especially suitable as they are easy to employ and usually give an instantaneous response with high sensitivity [14]. There are many publications related to trivalent cations recognition, but in the majority of classic chemosensors for metals cations interfere between them, consequently, is important the develop of selective and sensitive systems of detection.

In this work, we realized a theoretical evaluation of the systems derivatives of 5,5'-*bis*-vanillin (shown in Figure 1) that contain semicarbazide or hydrazine groups. We have used Density Functional Theory (DFT) [15] based calculations employ Gaussian09 program suit [16] with the B3LYP method [17] and LANL2DZ basis set to analyse the structures of the ligands as well as its analogues containing attached the different cations. The calculations for $Al^{3+}$, $Cu^{2+}$, $Zn^{2+}$, $Pb^{2+}$, $Hg^{2+}$, $Cd^{2+}$, and $Mg^{2+}$ were done. Based on those data, we evaluated the change on the dihedral angle and the difference in the total energy between the L-ligand and the complex L-ligand with the cation, as well as the change in the HOMO-LUMO gap of L and L-M2+/M3+ to understand the changes of electronics and optical properties. In addition, we use the cation $Al^{3+}$ for an experimental evaluation, in which we utilize UV-Vis spectroscopy and molecular fluorescence spectroscopy for the study of the chelation between molecule and cation.

## 2. Methods

### 2.1. Experimental

The ligands (1 and 2) were prepared according to the sequence shown in the Figure 1.
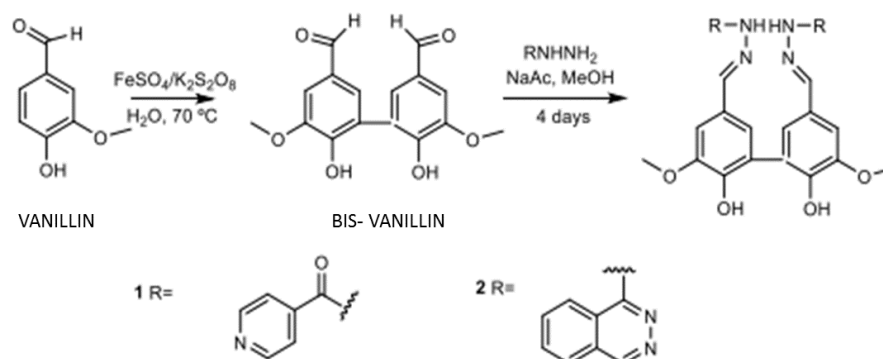


**Figure 1.** Preparation of the compounds **1** (derived from isoniazide) and 2 (derived from hydrazoline)

Ligands 1 and 2 were isolated by filtration and purified by recrystallization. Its 1H NMR, 13C NMR and MS spectroscopic data were consistent with those reported in the literature.[2]. Complexation experiments were carried out by addition of one equivalent of the corresponding cation $Al^{3+}$ as salt to the solutions of the ligands in DMSO. Subsequently his UV-Vis and fluorescence spectra was determined at $\lambda_{exc} = 280$ nm.

*2.2. Computational*

Entire theoretical calculations are done using Gaussian 09 program suit. All the molecular structures of the ligands and its metal-complexed analogues were optimized at DFT/B3LYP/LANL2DZ level of theory without imposing any constrain, and, vibrational frequencies were calculated to ensure the validity of each structure.

The global energy and the energy of HOMO and LUMO orbitals (FMO energies) of all ligands and complexes the optimized structures were also estimated using the same DFT method. In addition, the dihedrals angles of ligands and complexes were obtained.

## 3. Results

Optimized geometries of L and L-M2+/M3+ are shown in Figure 2. In the group of complexes of ligand 1, it was found that there were 2 types of complexation. $Al^{3+}$, $Zn^{2+}$, $Hg^{2+}$ and $Cd^{2+}$ were coordinated to both $=N_1$, $=N_1'$ and $=O$ sites of isoniazide, while $Cu^{2+}$, $Pb^{2+}$ and $Mg^{2+}$ were coordinated only to $=O$ sites isoniazide. The geometries show in Figure 2 (c) and (d) respectively. In the group of complexes of ligand 2, it was also found that there were 2 types of complexation. $Mg^{2+}$ was coordinated only to one N atom of each phtalazine substituent; while $Al^{3+}$, $Cu^{2+}$, $Zn^{2+}$, $Pb^{2+}$, $Hg^{2+}$ and $Cd^{2+}$ were coordinated to N=N atoms of both phtalazine substituents. The geometries show in Figure 2 (e) and (f) respectively.
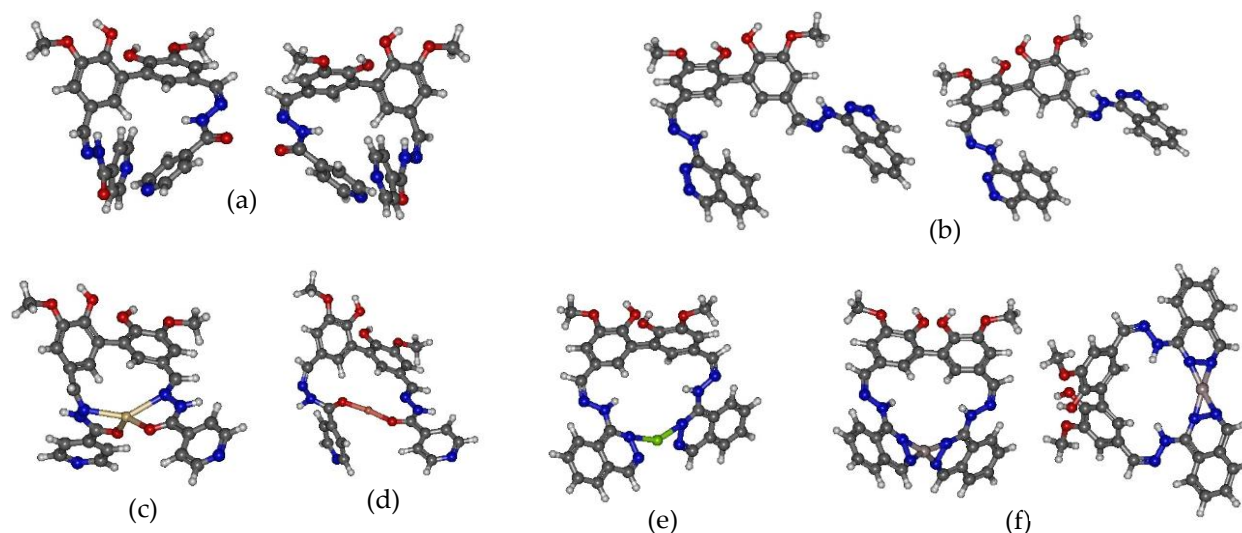


**Figure 2.** Optimized geometries of the compounds. **(a)** Ligand 1; **(b)** Ligand 2; **(c)** Complex geometry found for ligand 1 with $Al^{3+}$, $Zn^{2+}$, $Hg^{2+}$ and $Cd^{2+}$; **(d)** Complex geometry found for ligand 1 with $Cu^{2+}$, $Pb^{2+}$ and $Mg^{2+}$; **(e)** Complex geometry found for ligand 2 with $Mg^{2+}$; **(f)** Complex geometry found for ligand 2 with $Al^{3+}$, $Cu^{2+}$, $Zn^{2+}$, $Pb^{2+}$, $Hg^{2+}$ and $Cd^{2+}$.

The energies of optimized structures of ligands and complex for **1** and **2** are shows in Table 1. In both cases, the energies of the different complexes are smaller than the ligands themselves.

**Table 1.** Global energies of ligands and ligands with attached cations.

|  | Energy (Kcal/mol) |  | Energy (Kcal/mol) |
|---|---|---|---|
| **L1** | -1860,69 | **L2** | -1973,27 |
| **L1-Al³⁺** | -1861,55 | **L2-Al³⁺** | -1974,13 |
| **L1-Cu²⁺** | -2056,08 | **L2-Cu²⁺** | -2168,69 |
| **L1-Zn²⁺** | -1925,55 | **L2-Zn²⁺** | -2038,14 |
| **L1-Pb²⁺** | -1863,40 | **L2-Pb²⁺** | -1976,04 |
| **L1-Hg²⁺** | -1902,64 | **L2-Hg²⁺** | -2015,23 |
| **L1-Cd²⁺** | -1908,00 | **L2-Cd²⁺** | -2020,60 |
| **L1-Mg²⁺** | -1860,80 | **L2-Mg²⁺** | -1973,46 |

The values of dihedrals angles and values of energy GAP between FMO (HOMO – LUMO energy difference) are shows in Table 2. In both cases, the GAP for the complexes is smaller than the GAP for the ligands.

**Table 2.** Dihedral angles and GAPs energy between FMO of ligands and ligands with metal cations.

|  | Dihedral Angle | GAP (Kcal/mol) |  | Dihedral Angle | GAP (Kcal/mol) |
|---|---|---|---|---|---|
| **L1** | 55,94 | 93,86 | **L2** | 56,52 | 88,01 |
| **L1-Al³⁺** | 42,34 | 37,59 | **L2-Al³⁺** | 81,63 | 43,26 |
| **L1-Cu²⁺** | 43,76 | 13,26 | **L2-Cu²⁺** | 67,60 | 13,21 |
| **L1-Zn²⁺** | 42,12 | 66,19 | **L2-Zn²⁺** | 98,68 | 69,77 |
| **L1-Pb²⁺** | 121,83 | 59,92 | **L2-Pb²⁺** | 52,50 | 63,00 |
| **L1-Hg²⁺** | 42,20 | 52,27 | **L2-Hg²⁺** | 123,87 | 36,75 |
| **L1-Cd²⁺** | 42,27 | 65,60 | **L2-Cd²⁺** | 119,58 | 62,44 |
| **L1-Mg²⁺** | 47,86 | 44,40 | **L2-Mg²⁺** | 95,04 | 69,17 |

At last, on the experimental side, the compound **1** showed bands at 230 and 340 nm, while **2** showed at 230 and 380 nm. Furthermore, **2** showed a significant quantum efficiency $\phi = 0.39$ ($\lambda exc = 280$ nm) relative to **1** that showed less fluorescence $\phi = 0.039$ ($\lambda exc = 280$ nm). With $Al^{3+}$, showed a slight hypochromic effect and a hypsochromic shift of the band located at about 330 nm and 390 nm of **1** and **2** respectively. The emission spectrum of **2** showed a quenching effect with the addition of different equivalents of $Al^{3+}$, while **1** show a decrease in fluorescent properties with the same cation.

Figure 3 show the evolution of compound **2**'s UV-spectrum with the adittion of diferent equivalents of $Al^{3+}$ as salt to the solutions of the ligands in DMSO.
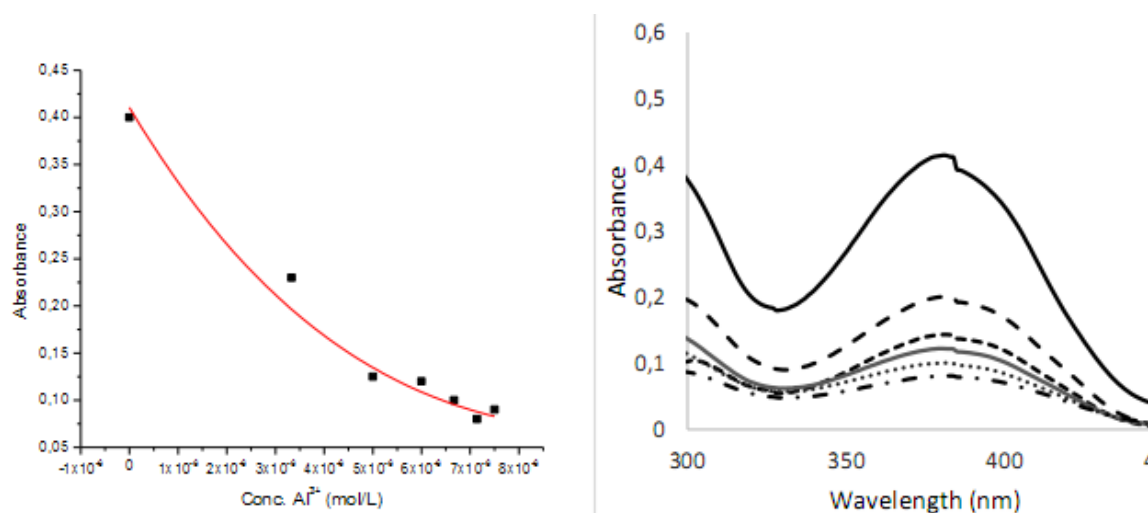


**Figure 3.** Evolution of **L2**'s UV-spectrum with the concentration of $Al^{3+}$ in DMSO $10^{-5}$ M solution.

## 4. Conclusions

*Bis*-vanillin derivatives containing hydralazine and isoniazide group, respectively, in the positions 3,3' were studied as sensors of different metal cations. DFT study determined the geometric structures of all compounds and their stability. The comparison of global energies shows that the complexes always have lower energy than the ligands, thus the formation of the complex is thermodynamically favored. Dihedral angles of both compounds change in the presence of cations. **L1** shows a decrease in dihedral angle while **L2** shows an increase with all cations except $Pb^{2+}$. The GAP values of both ligands decrease in all cases (the energy between HOMO and LUMO decreases), thereby increasing the stability of these systems. Changes in the GAP and dihedral angle could be related with the changes in the UV and fluorescence spectra which is observed in practice.

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