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RESEARCH ARTICLE

A New Highly Selective Chromogenic and Fluorogenic Chemosensor for Copper (II)

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Abstract: A new fluorogenic and chromogenic probe (L) for the selective, sensitive and naked-eye detection of Cu^{2+} is reported. Complexation constant, complex stoichiometry and quantum chemical (DFT) calculation for Cu^{2+} complex has been determined. Also, detection limits and the selectivity in front of other divalent and trivalent cations have been evaluated.

Keywords: Chemosensor, copper ion (II), fluorescence, chromophore, UV-Vis, DFT.

1. INTRODUCTION

The design and synthesis of chemosensors for transition and p-block metal cations is an important subject in the field of supramolecular chemistry because of their impact in the environment and in human health [1].

Divalent cations have important biological properties. Copper is the third most abundant ion in our body and is essential to the proper functioning of metabolic processes [2]. Nevertheless, its presence in abundant quantities causes poisoning in humans or plants and problems in surface waters [3].

The detection of these type of cations presents a grown interest in the field of supramolecular and coordination chemistry because their presence in biologic process, in medicine and the environmental [4, 5]. Biological sensors are usually very selective but very sensitive to changes of pH, temperature, redox potential, *etc*. Due to these facts, the design and synthesis of new more stable artificial sensors has a huge urgency.

In the last century analytical techniques to determine ions has improved, but most of these methods require expensive equipment and often the presence of other cations interferes [6]. Thus, a sensitive, more selective and simpler analytical method is an urgent need.

In this work we decided to employ 5,5'-*bis*-vanillin as a dialdehyde which is prepared from the monomeric vanillin by an oxidative coupling. It has been reported that some biphenyl sensors can suffer changes in the colorimetric or fluorescence properties as a result of the modification in the dihedral angle between both aromatic rings, which render possible the recognition of certain cations [7-9].

The carbonyl groups can be functionalized in conventional form giving a byphenyl hydrazone (L). The use of hydrazones in detecting metal cations, anions and neutral molecules has been extensively studied [10, 11].

The simple and high-yielding synthetic methods employed for the preparation of these compounds are especially attractive.

Recently we informed on several bis-vanillin derivatives containing semicarbazone moieties which have been prepared and used in discriminating trivalent cations. The prepared probes are readily obtained and they are usually highly crystalline [12].

Taking into consideration that the changes in the dihedral angle on byphenyl structures products of the interaction with metal cations can be used for the recognition of the metal, the aim of the present study is to explore sensor capacity and sensitivity of a benzothiazole hydrazone derivative from 5,5'-*bis*-vanillin to examine Cu^{2+} in front of other cations using colorimetric and fluorimetric methods. Moreover, the structure, geometry and stability of the Cu^{2+} complex can be

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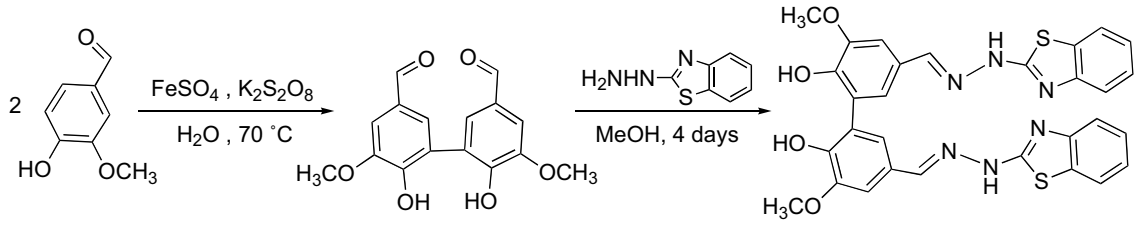

Scheme (1). Synthesis of L.

probed by density functional theory (DFT) based quantum chemical calculations.

2. RESULTS AND DISCUSSION

2.1. Synthesis and Characterization of Ligand L

The ligand L was prepared using a conventional process. 5,5'-*bis*-vanillin was obtained with excellent yield after precipitation (95 %) from the oxidative coupling of vanillin with sodium persulphate and iron sulphate by a reported procedure [13].

Ligand L was synthesized as described in Scheme **1**. Then was isolated by filtration and purified by recrystallization. Its ^{1}H NMR, ^{13}C NMR and MS spectroscopic data were consistent with those reported in the literature [12].

The UV-vis spectrum of L (10 mM) in DMSO solution exhibits two bands at 257 and 360 nm with e= 127000 and 35765 cm^{-1}M^{-1}, respectively. DMSO was the only solvent that allowed complete solubilization of L. This large value of molar extinction coefficient would indicate the absorption is due to the p→p* transition of the benzene ring. On the other hand, L shows an emission band at 327 nm under excitation at 280 nm. However, its fluorescence quantum yield is low (f_F ~ 0.015, l_{exc} = 278 nm calculated by comparing with rhodamine B as patron) [14].

2.2. Sensing Experiments

Selectivity is a fundamental parameter to determine the viability of a chemosensor [15]. To evaluate the selectivity of L for Cu^{2+}, the sensing ability of L (10 mM DMSO) toward different cations (Mn^{2+}, Sn^{2+}, Zn^{2+}, Cu^{2+}, Fe^{3+}, Cr^{3+} and Al^{3+}) as their chloride and nitrate salts were studied using UV-vis spectroscopy. The selective and instant detection of Cu^{2+} by L was also observed by the naked eye. Initially, the solution of L was colorless and after addition of 1 equiv of Cu^{2+}, the solution showed an instantaneous color change from colorless to strong red (Fig. **1**, inset). It is necessary taken into account that the cooper salt in solution shown a UV band to 460nm. Whereas, other cations did not show any notable response.

As shown in Fig. (**1**), upon addition of 1 equiv of Cu^{2+}, the absorption band of L at 360 nm gradually decreased and shifted to a new band at 490 nm. These results demonstrate that L can serve as an excellent selective chromogenic chemosensor for Cu^{2+}.

To explore L as a fluorescence sensor, fluorescence study was carried out with various cations. When a solution of Cu^{2+} in acetonitrile was added to the L solution (10 mM, DMSO), the fluorescence emission of L exhibits a notably fluorescence enhancement. This enhancement is due to the formation of the complex which adopts a molecular disposition consistent with the enhancement, instead the ligand has free rotation and for this reason the phenomenon is lower. In addition, there was a bathochromic shift from 327 nm to 340 nm under excitation at 280 nm upon the addition of different amounts of Cu^{2+} (Fig. **2**).

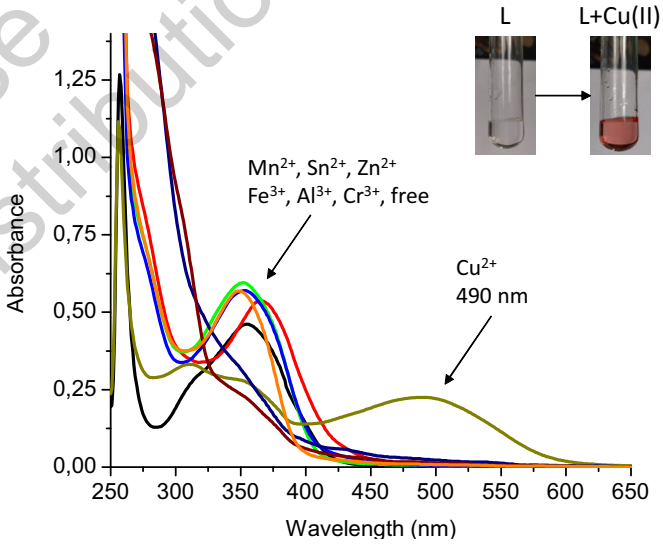

Fig. (1). UV-vis absorption spectra of L with Cu^{2+} and other metal ions (**inset:** visual colour change with Cu^{2+}).

Fluorescence quantum yields (ϕ) of L and L-Cu^{2+} were calculated by comparing the total fluorescence intensity under the whole fluorescence spectral range with that of a standard, according to the next equation:

$$\phi = \phi_R \cdot \frac{1-10^{-A_R}}{1-10^{-A}} \cdot \frac{I}{I_R} \cdot \frac{n^2}{n_R^2}$$

Where ϕ_R is the quantum yield of rhodamine B = 0.44 (DMSO, 1.10^{-5} M), I and I_R are the total fluorescence intensity under whole fluorescence spectral curve, A and A_R are the optical density of the sample and standard, and n is the refractive index of the solvent at 293 K.

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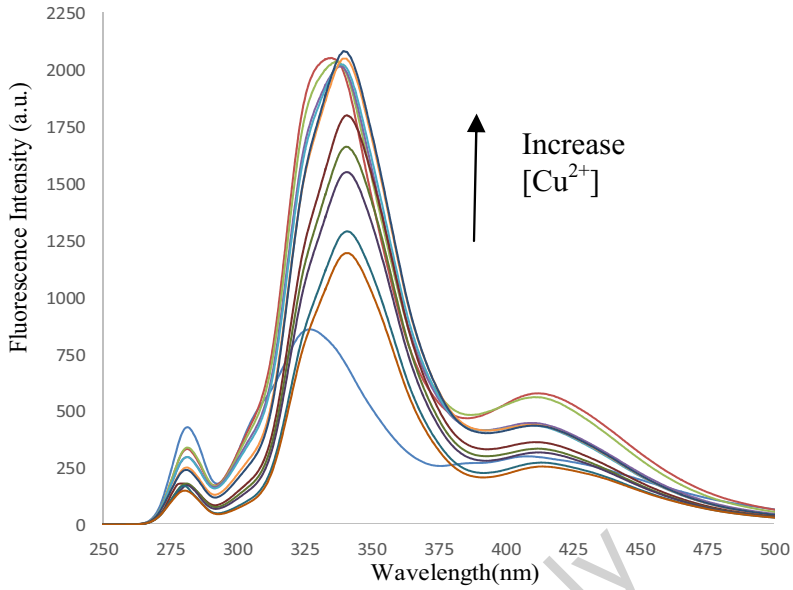

Fig. (2). Fluorescence titration spectra of L (10 mM DMSO) when different amount of Cu^{2+} were added. It shows an enhancement in emission with the increase of Cu^{2+} concentration.

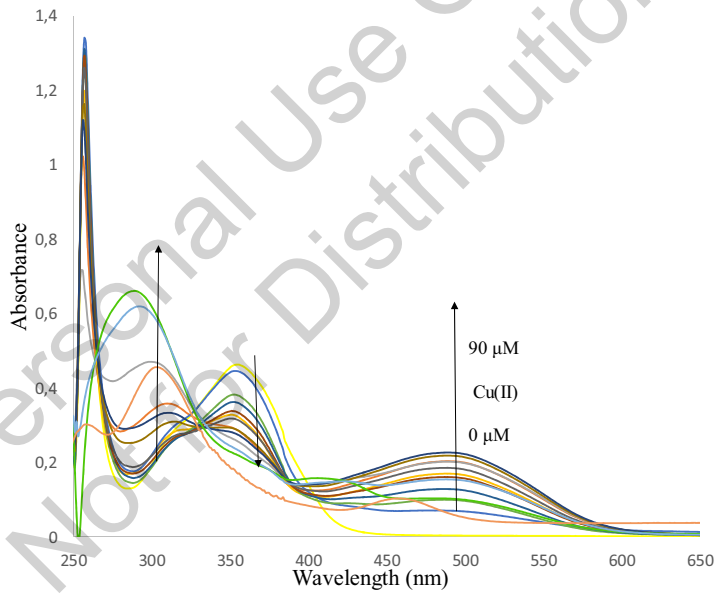

Fig. (3a). UV-vis titration spectra of **L** (10 mM DMSO) when different amount of Cu^{2+} were added.

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The calculated fluorescence quantum yield for L-Cu^{2+} with respect to rhodamine B was 0.70, an increase of 4000% respect of L. The other metal ions studied did not show fluorescence increment under the same conditions. All the above results demonstrate the utility of L to be used as a chemosensor for Cu^{2+} by the colorimetric and fluorescence dual mode.

Due to the strong effect observed with Cu^{2+}, the complexation characteristics of L were studied. Thus, Cu^{2+} titration experiments against L in DMSO were monitored using UV-vis spectroscopy. The absorption spectra of L (10 mM) in DMSO solution upon addition of Cu^{2+} aliquots is shown in Fig. (**3a**). The original band at 360 nm showed a decrease in absorption with the increase of Cu^{2+} concentration while two new bands at 290 and 490 nm increased progressively. Moreover, two isosbestic points were observed at 330 and 400 nm, which would indicate the presence of a single coordination equilibrium between L and Cu^{2+}.

In order to determinate the binding stoichiometry of the L-Cu^{2+} complex, the titration profile (Fig. **3b**) was fitted nicely a 1:1 binding model using the following equation, where A is the absorbance of the solution during the titration, A_{lim} is the absorbance of the complex, A_o is the absorbance of the free ligand, C_o and C_M ligand and metal concentration during titration, respectively and K is the complexation constant [16].

$$A = A_o + [(A_{\lim} - A_o)/2C_o]\left[C_o + C_M + K^{-1} - \sqrt{(C_o + C_M + K^{-1})^2 - 4C_oC_M}\right]$$

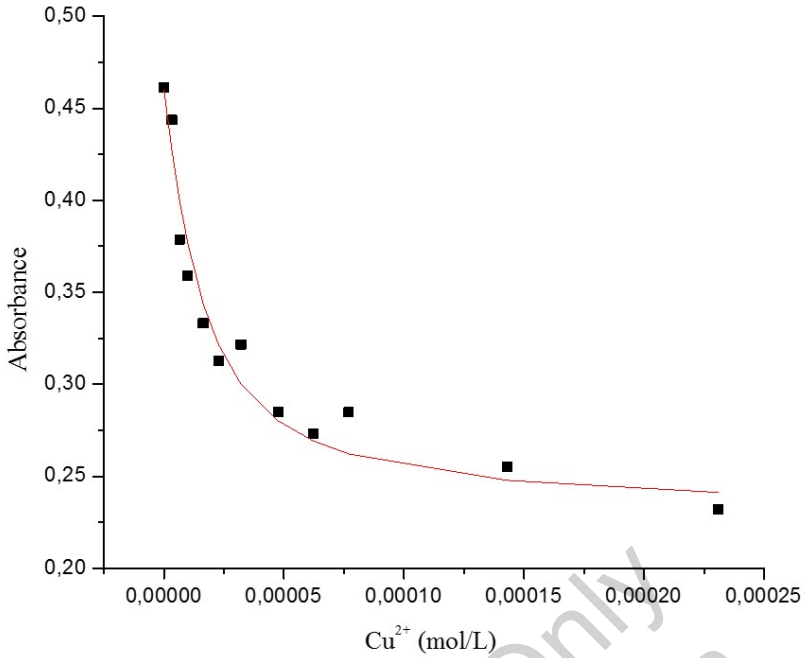

Fig. (3b). Titration profile 355 nm and fitting to 1:1 complex model.

The complexation constant was obtained to be log K = 5.17 ± 0.06 (r^2=0.96) in a DMSO-acetonitrile solution. The limit of detection (LOD) was also evaluated based on the UV-vis titration from the equation: *LOD= 3Sb/S*, where *Sb* is the standard deviation of the blank and *S* is the slope of the calibration curve [17]. Thus, the calculated detection limit was 1.47 mM (see Supplementary data).

The ^{1}H NMR spectra of L in the presence and absence of Cu^{2+} were also investigated to further elucidate the mode of interaction between Cu^{2+} and L and conformation changes (Fig. **4**). The peak at 3.37 ppm was attributable to the protons of the methoxy groups, which after the addition of 1 equiv of Cu^{2+} in a DMSO-d6:D_2O (1:1 v/v) solution, displayed an downfield shift (Dd=1.13 ppm) and broadened because of the paramagnetic nature of the cation [18]. A conformational change in the ligand as a consequence of the coordination with Cu^{2+} could explain the shifts of the methoxy signals. In addition, for further inspection of the binding mode, quantum chemical DFT calculation of the structure of L was performed[1].

Optimized geometries of L and L-Cu^{2+} are shown in Fig. (**5**). From these geometry optimizations, the values of the dihedral angle between benzene rings were obtained.

The dihedral angle for L and L-Cu^{2+} are 59, 53° and 48, 41°, respectively. These results demonstrate that the dihedral angle decreases (~11°) as a consequence of L chelation with Cu^{2+}, increasing the conformational rigidity of the ligand. This can be responsible for the bathochromic shift of L-Cu^{2+} in the UV-vis spectra and it also can be responsible of the enhanced fluorescence intensity of this complex [19].

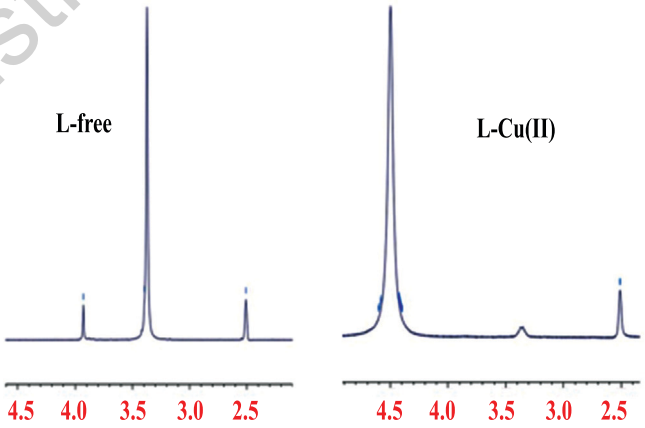

Fig. (4). ^{1}H NMR spectra of L (in DMSO-d_6) and L-Cu^{2+} (DMSO-d_6:D_2O 1:1) and fitting to 1:1 complex model.

It is found that Cu^{2+} is coordinated to both -N sites of benzothiazoles as shown in Fig. (**5b**). The Cu^{2+}-N bond length value is 1,88 Å and 1,89 Å for each -N. The total energy of optimized structures of L and L-Cu^{2+} are -2582,74 and -4222,76 Hartree, respectively. The optimization energy values suggest that the total energy of the complex was lower compared to L indicating higher stability of the L-Cu^{2+} complex.

To understand the electrical transport properties, HOMO-LUMO gap of L and L-Cu^{2+} have been also estimated using the same DFT method. The negative energy values for

[1]***Computational details.*** The calculations were performed with Gaussian 09 program using DFT level of theory. Geometry optimizations and vibrational frequencies of L5 and L5-Cu^{2+} were calculated with B3LYP (Becke's three parameter nonlocal hybrid Exchange-correlation functional) modeling method and 6-31G(d,p) set of basis functions. Frontier molecular orbitals (FMO) have been also estimated by same DFT method to show continuous charge distributions and reactive sites of the molecules.

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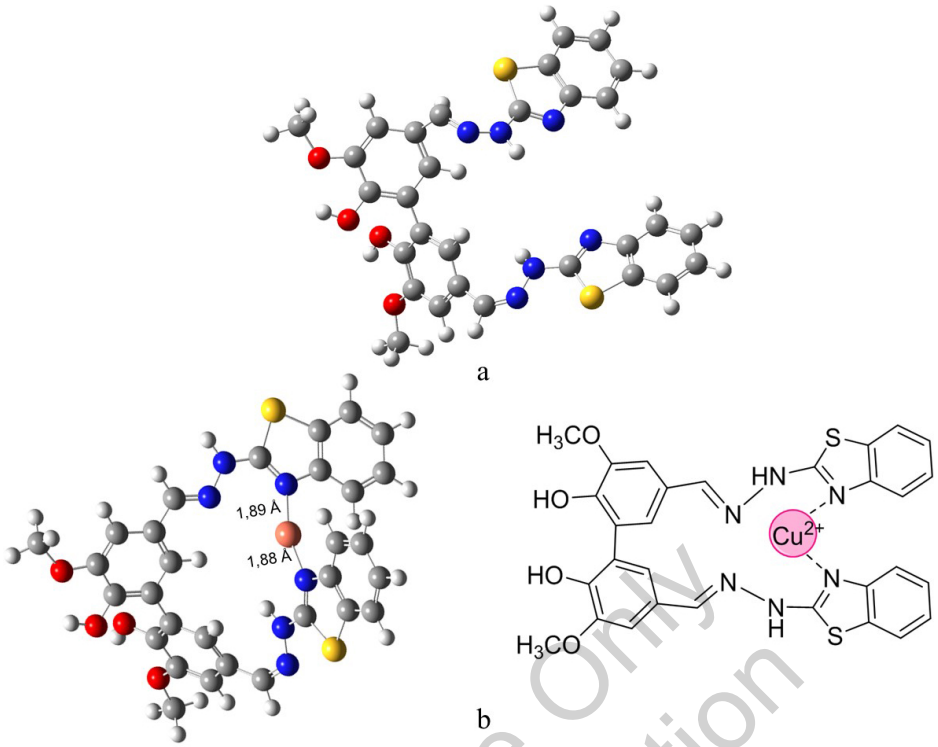

Fig. (5). Optimized structures of L (**a**) and L-Cu^{2+} complex (**b**). The dihedral angle for L and L-Cu^{2+} are 59,53° and 48,41°, respectively.

HOMO and LUMO in L and in L-Cu^{2+} signifies that both molecules are stable. The energy gaps between the HOMO and LUMO (ΔE_{H-L}) in L and L-Cu^{2+} are 89,81 Kcal/mol and 13,51 Kcal/mol respectively. It shows that the complexation decreases the HOMO-LUMO energy gap, stabilizing the system. It also suggested the process of electron transfer from electron rich L to electron deficient Cu^{2+}.

3. EXPERIMENTAL SECTION

Spectroscopic Measurements. Metal cations (Mn^{2+}, Sn^{2+}, Zn^{2+}, Cu^{2+}, Fe^{3+}, Cr^{3+}, Al^{3+}) as nitrate or chloride salts were used to obtain solutions of concentration of 10-5 M in MeOH or acetonitrile. UV-Vis spectra were recorded using a Perkin Elmer Lambda 20 spectrometer. Fluorescence spectra were recorded using a Hitachi F-7000 fluorometer. Titrations were performed by adding aliquots of different salts (in CH3CN) in a solution of L (10-5 M) in DMSO.

General procedure for limit of detection determination. Increasing amounts of Cu^{2+} solutions (in acetonitrile) were added to L in DMSO (10-5 M). The UV spectra were recorded in 1 cm path length cells at 25°C (thermostated). The representation of absorbance at 380 nm vs. concentration of Cu^{2+} allowed the limit of detection to be calculated.

CONCLUSION

In summary, a new highly selective and sensitive chemosensor has been prepared in an easy way from a *bis*-vanillin derivative. It can be utilized for the naked-eye detection of Cu^{2+}. It was also shown the probe's selectivity even in the presence of other metal cations through UV-Vis and fluorescence spectroscopies.

Additionally, through a theoretical study using DFT calculations with the B3LYP method and 6-31G(d,p) set of basis functions, we propose a model of complex between L and Cu^{2+} with 1:1 stoichiometry. It was interesting that coordination with the metal occurs through the nitrogen atoms of the heterocyclic moiety of the corresponding hydrazone.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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SUPPLEMENTARY MATERIAL

Supplementary material is available on the publisher's website along with the published article.

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