

## Design and synthesis of the new bis-vainilline derivatives containing hydralazine and isoniazide moieties for the detection of trivalent metal cations

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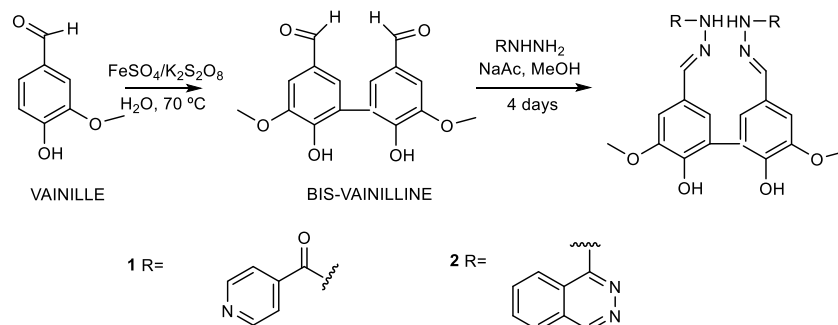
### Introduction

The design and synthesis of new chemosensors for the determination of metal cations represent an area of high interest in supramolecular chemistry. The detection and quantification is important in many fields of application such as environmental bioinorganic chemistry, developmental biology, clinical toxicology, waste management, and bioremediation of radionuclides and metal ions[1]. Besides, there is a growing concern for determining trivalent metal cations as  $\text{Fe}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Al}^{3+}$  which are highly toxic. Classic chemosensors for  $\text{Cr}^{3+}$  and  $\text{Fe}^{3+}$  interfere between them, consequently, the development of systems that allow selective and sensitive detection is desirable.

It is known that derivatives of bis-vainilline that contain semicarbazide or hydrazines can act as sensors of cations[2]. In that direction two new probes were developed from bis-vainilline condensed in positions 3- and 3'- with hydrazoline and isoniazide, using fluorescence as analytical signal for detection of analytes, because fluorimetry is rapidly performed, nondestructive and highly sensitive[3].

### Methodology

News ligands (**1** and **2**) were prepared according to the following sequence:



**Figure 1:** Preparation of the compounds **1** (derived from isoniazide) and **2** (derived from hydralazine)

The structures of the products were analyzed by theoretical calculations and characterized by spectroscopy. Quantum yields were determined using Rhodamine B in DMSO as standart.

Complexation experiments were carried out by addition of one equivalent of the corresponding cations ( $\text{Fe}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Al}^{3+}$ ) as salts to the solutions of the ligands in DMSO. Subsequently their UV-Vis and fluorescence spectra were determined at  $\lambda_{\text{exc}} = 280 \text{ nm}$ .

Through spectrophotometric titration were calculated the coupling constants and stoichiometry metal-ligand, adding different equivalents of each cation to solutions  $10^{-5}$  M of the ligand. The values of the constants K were determined by a nonlinear least squares fit using the model proposed by J. Bourson[4].

## Results

The synthesized molecules were obtained with 85% yield after precipitation.

Spectral data  $^1\text{H NMR}$  (DMSO- $d_6$  300MHz) are detailed below:

**1** 8,77 (d, 4H,  $\text{C}_{\text{py}}\text{-H}$ ); 8,31 (s, 2H,  $\text{CH=N}$ ); 7,86 (d, 4H,  $\text{C}_{\text{py}}\text{-H}$ ); 7,73 (s, 2H,  $\text{C}_{\text{Ar}}\text{-H}$ ); 7,36 (s, 2H,  $\text{C}_{\text{Ar}}\text{-H}$ ); 7,9 (s, 2H, NH); 5,66 (s, 2H, OH); 3,84 (s, 6H,  $\text{OCH}_3$ )

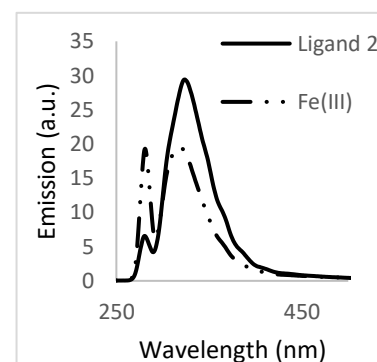
**2** 8,77 (s, 2H,  $\text{C}_{\text{hidralz.}}\text{-H}$ ); 8,23 (s, 2H,  $\text{HC=N}$ ); 7,95 (m, 4H,  $\text{C}_{\text{hidralz.}}\text{-H}$ ); 7,88 (m, 4H,  $\text{C}_{\text{hidralz.}}\text{-H}$ ); 7,47 (s, 2H,  $\text{C}_{\text{Ar}}\text{-H}$ ); 7,58 (s, 2H,  $\text{C}_{\text{Ar}}\text{-H}$ ); 4,03 (2H, NH); 3,41 (s, 6H,  $\text{OCH}_3$ ).

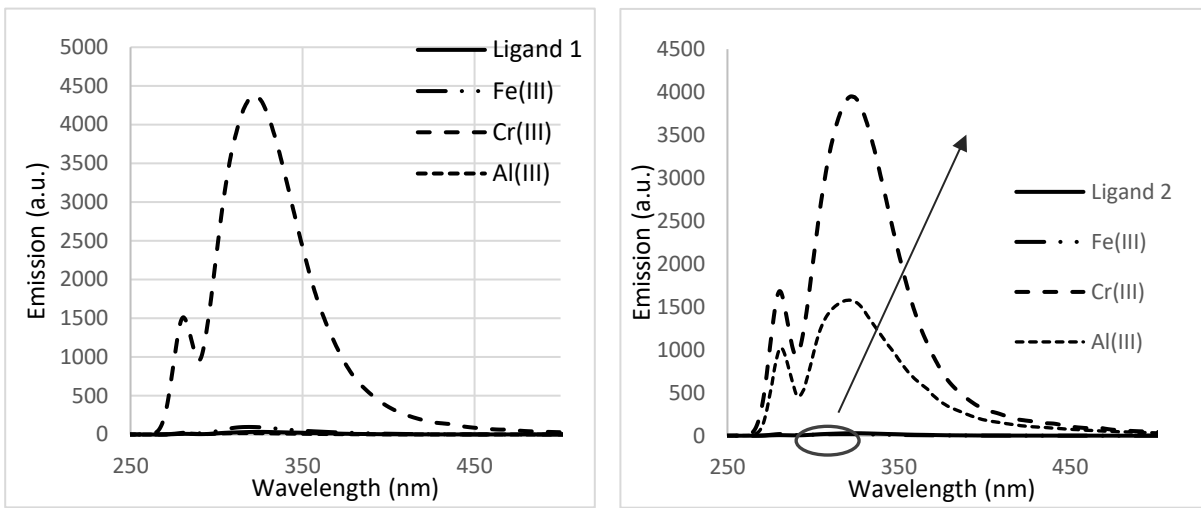
Theoretical calculations were determined for the Gaussian 09 program, using the B3LYP method with the basis set 6-311G (d,p). The geometries of the molecules studied, with and without the cation were optimized and vibrational frequencies were calculated to ensure the validity of each structure. Also, global and FMO energies values were obtained and compared. The dihedral angles and the energy variations between the sensors themselves and their complexes with metal cations were analyzed.

	Dihedral angle	$\Delta E$ (Kcal/mol)		Dihedral angle	$\Delta E$ (Kcal/mol)
<b>1</b>	59,35°	84,55	<b>Al<sup>3+</sup>-1</b>	54,51°	9,88
<b>2</b>	59,26°	75,87	<b>Al<sup>3+</sup>-2</b>	53,83°	6,75

**Table 1.** GAPs energy between FMO the sensors and complexes including  $\text{Al}^{3+}$  and dihedral angles.

Compound **1** showed bands at 230 and 340 nm, while **2** showed at 230 and 380 nm. Furthermore, **2** showed a significant quantum efficiency  $\phi = 0.39$  ( $\lambda_{\text{exc}} = 280$  nm) relative to **1** that showed less fluorescence  $\phi = 0.039$  ( $\lambda_{\text{exc}} = 280$  nm). With trivalent cations, 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  $\text{Fe}^{3+}$  and  $\text{Al}^{3+}$  whereas with  $\text{Cr}^{3+}$  a strong enhancement in fluorescence was seen. With **1** a decrease in fluorescent properties with  $\text{Al}^{3+}$  and a significant increase with  $\text{Cr}^{3+}$  were observed (Figure 2).





**Figure 2.** Fluorescence spectra of ligands **1** and **2** ( $10^{-5}$  M in DMSO) in the presence of free and 1 equiv.  $\text{Fe}^{3+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Al}^{3+}$

Therefore, **1** would allow to discriminate  $\text{Fe}^{3+}$  from  $\text{Cr}^{3+}$  and  $\text{Al}^{3+}$ . Also **2** be useful discriminating  $\text{Cr}^{3+}$  from  $\text{Al}^{3+}$  because of their opposite responses.

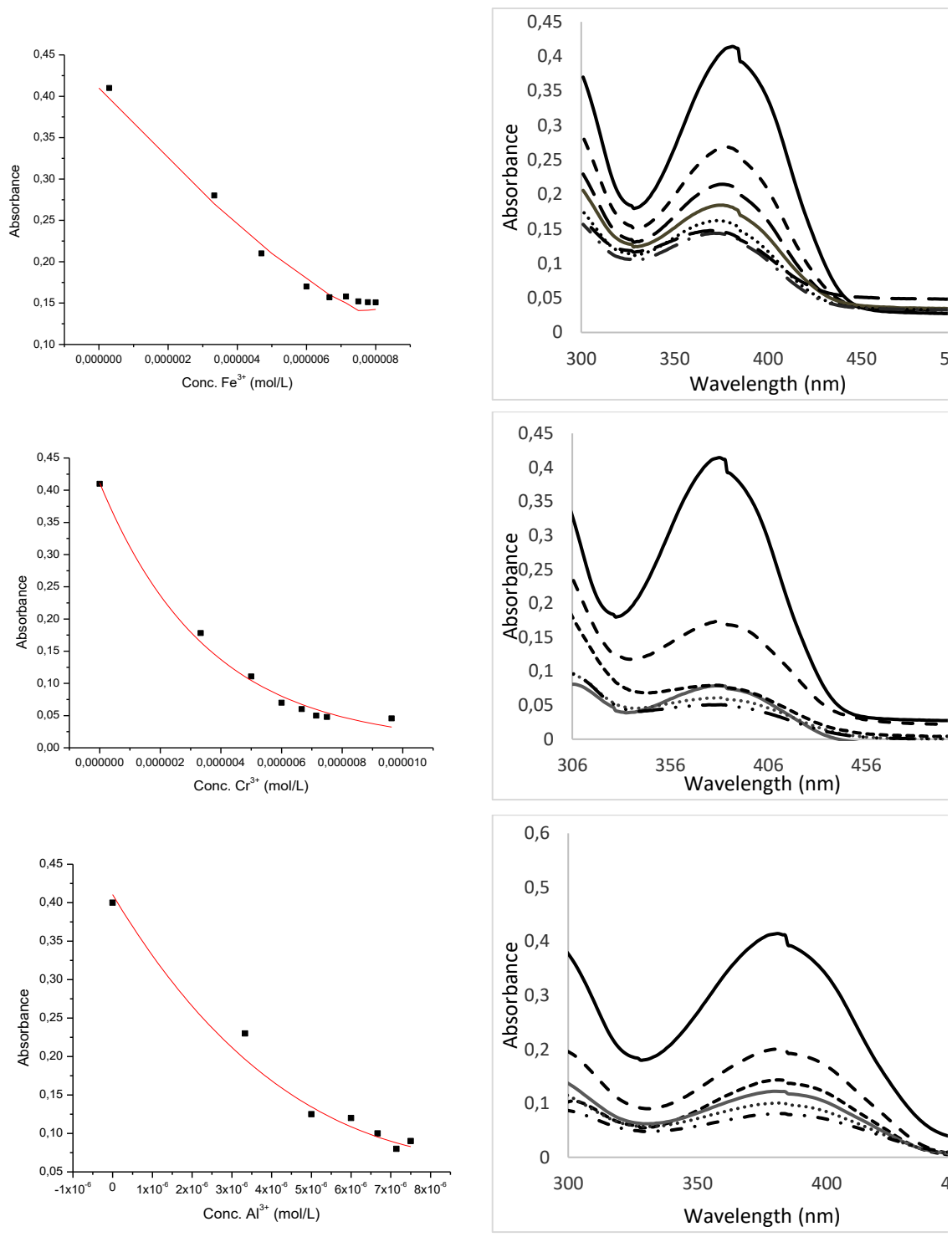
From a structural comparison between **1** and **2** it could be observed that the presence of a carbonyl group would lead to a major change in the ability to detect  $\text{Al}^{3+}$  but the difference was not observed with  $\text{Cr}^{3+}$ .

The values of the constants  $K$  were determined by a nonlinear least squares fit using the model proposed by J. Bourson[3]. In the case of the formation of complexes with 1:1 stoichiometry, the stability constant would be calculated from the following equation:

$$A = A_0 + \frac{A_{lim} - A_0}{2C_0} \left[ C_0 + C_M + \frac{1}{K} - \sqrt{\left( C_0 + C_M + \frac{1}{K} \right)^2 - 4C_0C_M} \right]$$

Where  $A$  = absorbance of the solution during the titration,  $A_{lim}$  = absorbance of the complexe,  $A_0$  = absorbance of the free ligand,  $C_0$  and  $C_M$  = ligand and metal concentration during titration, respectively,  $K$ = complexation constant.

The coupling constants  $K$  of **2** were determined in 1:1 stoichiometry being  $\log K = 4.19$ ;  $2.74$ ;  $2.74$  ( $\text{Fe}^{3+}$ ,  $\text{Cr}^{3+}$  and  $\text{Al}^{3+}$ ) (Figure 3). In all cases, the error in the nonlinear fits were less than 10%.



**Figure 3.** Curves adjust and valuation ligand  $2 \cdot 10^{-5}$  M in DMSO solution with (a) Fe<sup>3+</sup> (b) Cr<sup>3+</sup> (c) Al<sup>3+</sup>.

## Conclusions

Bis-vanillin derivatives with hydralazine and isoniazide groups in the positions 3,3' were studied as sensors of trivalent cations. DFT determined stability and geometric structures. As a result of the dihedral angle decrease, fluorescent properties change in presence of  $\text{Al}^{3+}$ . In addition, the gap values of complexation of  $\text{Al}^{3+}$  with the used ligands, indicates that the energy between HOMO and LUMO decreases, thereby increasing the stability of these systems. Furthermore, both compounds exhibit a strong enhancement intensity with  $\text{Cr}^{3+}$ . A quenching effect was observed for **1**-  $\text{Fe}^{3+}$ . Finally, it was concluded that a mixture of **1** and **2** can be used to discriminate between  $\text{Fe}^{3+}$ ,  $\text{Al}^{3+}$  and  $\text{Cr}^{3+}$ .

## References

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