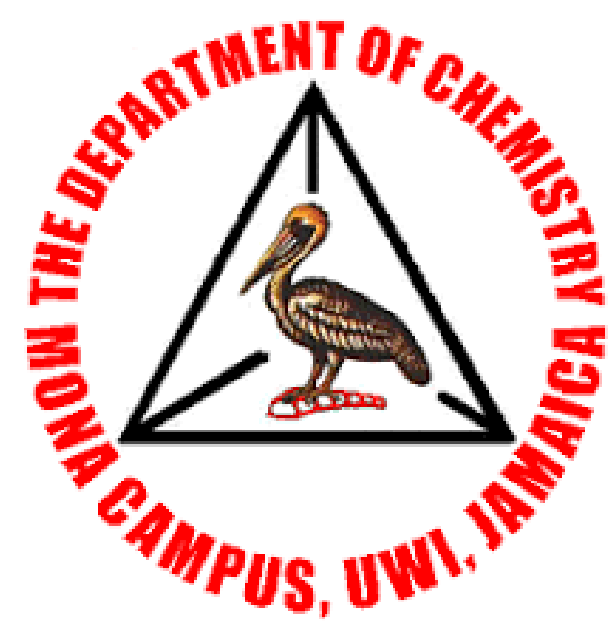




AN EXPLORATORY, EXPERIMENTAL, AND DFT STUDY OF THREE SMALL MOLECULAR COPPER(II) SENSORS

Tahjna I. Robertson, Peter N. Nelson

Department of Chemistry, The University of the West Indies, Mona
Jamaica, West Indies

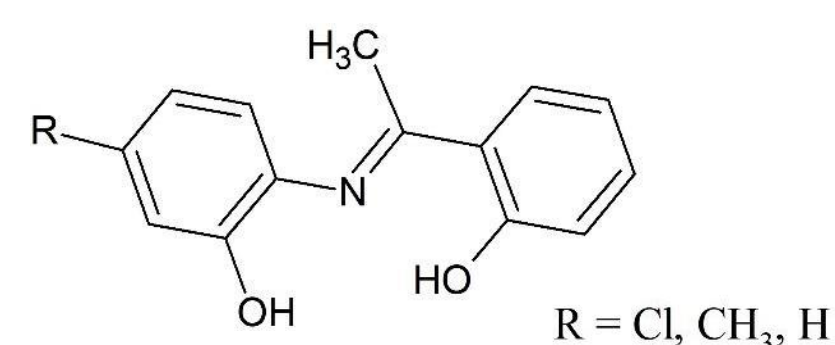


ABSTRACT

Three benzylideneaniline-based colorimetric Cu(II) sensors were successfully synthesised and their sensing behaviours characterized *via* absorption spectroscopy and rationalized with DFT and TD-DFT calculations at the B3LYP/6-31++G(d,p) level. The favourable binding process leading to a visible colour change is controlled by entropic effects in combination with the relative hardness of the binding sites. These compounds allow selective detection of copper and have limits of detection within the range 0.16 – 0.49 ppm, linear ranges with upper limits of 1 - 5 ppm, and quantification limits in the range 0.52 – 1.6 ppm. While only zinc leads to reduced accuracy for HAPAP, at equimolar levels, for the other derivatives hard-soft interactions allow significant interference from various metals. Such competition can be reduced by controlling binding site hardness through substitution effects.

INTRODUCTION

Copper is highly abundant in the environment due to its extensive industrial use, and has significant biological relevance evidenced by its presence in enzyme complexes. However, an excess of copper in the body will lead to various pathologies such as Wilson's disease. Moreover, excess copper in the environment is known to be harmful to wildlife. Therefore, it is critical that the levels of copper be assessed and monitored. Traditionally, techniques for Cu(II) determination have been based on methods which require the use of expensive equipment and trained personnel. In response, many researchers have developed optical Cu(II) sensors which enable the quick and reliable determination of the metal ion; however, many of these sensors suffer from poor sensitivity, and selectivity issues. The use of molecular modelling can enable the assessment of these sensors from a fundamental perspective, and thereby provide reasons for their poor performance, potentially proffering suitable remedies. In this study, spectrophotometry in combination with DFT methods was used to evaluate the copper-sensing performance of three benzylideneaniline-based compounds varied only at the 4' position.



RESULTS AND DISCUSSION

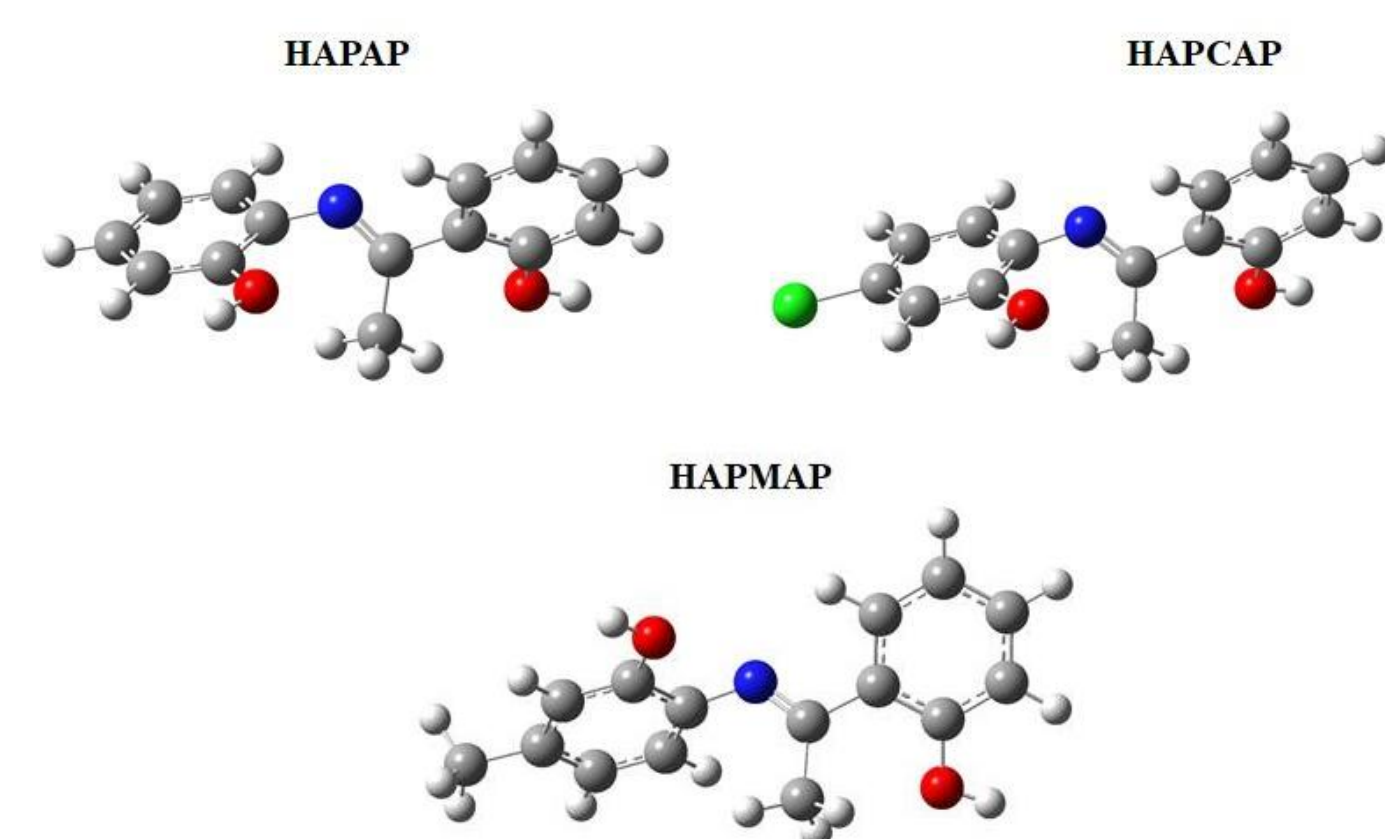


Fig. 1. Optimized gas-phase structures for all compounds

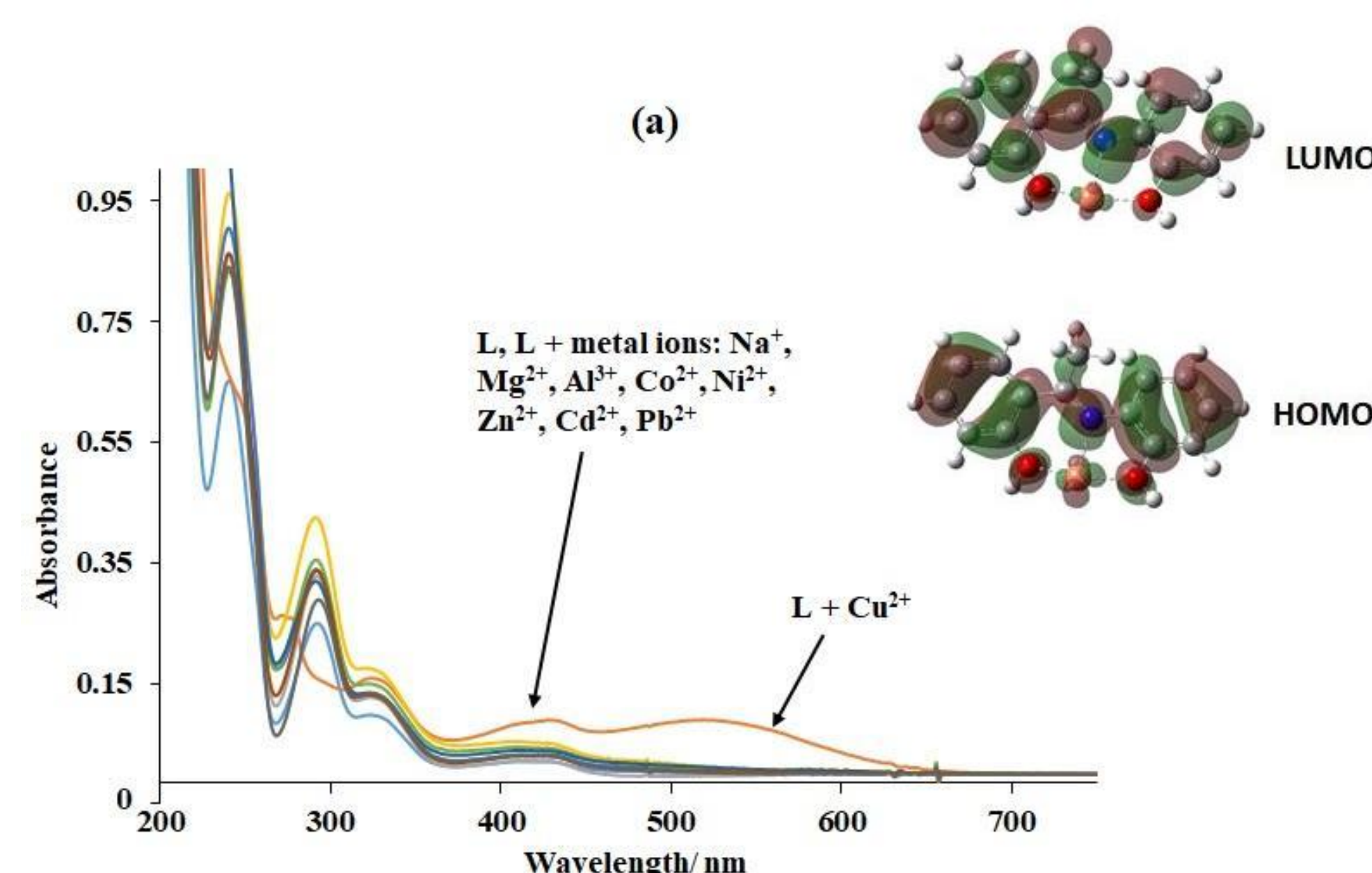


Fig. 3. Metal survey of HAPAP with various metal cations. Top right: Molecular orbital surfaces (HOMO and LUMO) responsible for producing charge transfer (CT) band

Table 1. Experimental binding thermodynamic parameters for all compounds

Compound	Log K	$\Delta G_{298.15}^{298.15}$ [kJ/ mol]	$\Delta H/R$	$\Delta S/R$ [K ⁻¹]
HAPAP	1.03	-22.3	-5377.50 $\pm$ 497.76	27.05 $\pm$ 1.63
HAPCAP	6.72	-26.5	-11377.60 $\pm$ 955.33	48.87 $\pm$ 3.14
HAPMAP	2.86	-24.4	-6652.47 $\pm$ 215.25	32.19 $\pm$ 0.70

Structure and optimization calculations (Fig. 1) reveal that **all compounds have acoplanar rings** likely due to the presence of the methyl group on the alpha carbon and its interaction with the 2-OH and 2'-OH groups

Acoplanarity of rings correlate positively with the **electron-withdrawing strength of the 4' substituent** and is significantly reduced upon metal binding

The ESP maps (Fig. 2) reveal **high electron density on the imine nitrogen** and both the **oxygen atoms** of hydroxy groups indicating that these atoms participate in metal binding

The **basicity of the imine nitrogen** increase with the **electron-donating strength of the 4' substituent**. The opposite is true for the oxygen atoms of the OH groups

In the presence of **Cu(II)**, compounds produce a distinct **CT band at 525 nm** (Fig. 3) which manifests as a change **from colourless to purple**. This is not obvious with other metal ions

Expectedly this **colour was most intense for HAPAP** for which the **metal complex** was calculated to be the **most planar**- a feature which facilitates a higher transition dipole moment

This CT band is revealed to consist of transitions from the **d orbitals on the central Cu(II) metal ion (HOMO) to ligand-centered orbitals (LUMO)** in addition to **intra-ligand $\pi \rightarrow \pi^*$ electronic rearrangement**

All compounds exhibit **1:1 binding** with Cu(II)

Binding is exergonic for all compounds [Table 1] ($\Delta G_{binding} = -20$ – -26 kJ mol⁻¹) but **endothermic**; therefore, **entropy control** is evident

Strongest binding is observed for HAPCAP which has the highest entropy of binding ($\Delta S_{binding}$) probably due to **rearrangement of the solvent population in the vicinity of the basic chlorine atom** stemming from molecular electron density rearrangement to facilitate Cu(II) ion binding

HAPAP selectively binds Cu(II) even in the presence of equimolar amounts of several other metal ions. Only **Zn(II)**, which is similar to Cu(II) in hardness, is observed to **diminish binding**, and by approximately 50% (Fig. 4)

HAPCAP and HAPMAP suffer significant interference from other metal ions (Fig. 4) likely due to the influence of the 4'-Cl and 4'-CH₃ substituents, respectively which influence the **hardness/softness of the binding atoms** and facilitate binding of other metal ions

The analytical parameters of spectroscopic methods based on the proposed sensors were favourable when compared to a method based on FAAS (Table 2)

HAPMAP and HAPAP had relatively **low LOD values** compared to HAPCAP- a likely consequence of the **higher molar absorptivities** of their metal complexes

The **LOD and LOQ values of HAPAP and HAPMAP** were significantly **lower** than that of FAAS though the **linear ranges** were significantly **more limited**

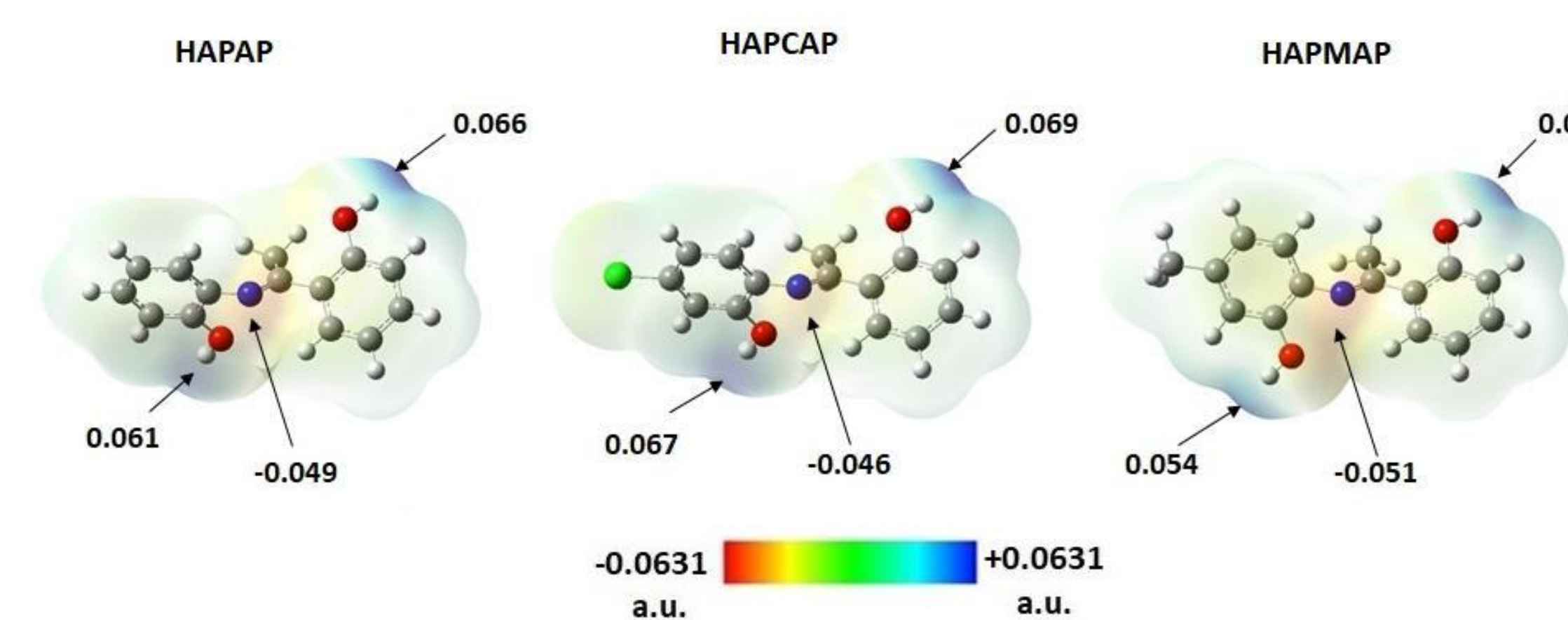


Fig. 2. Calculated electrostatic potential maps for all compounds.

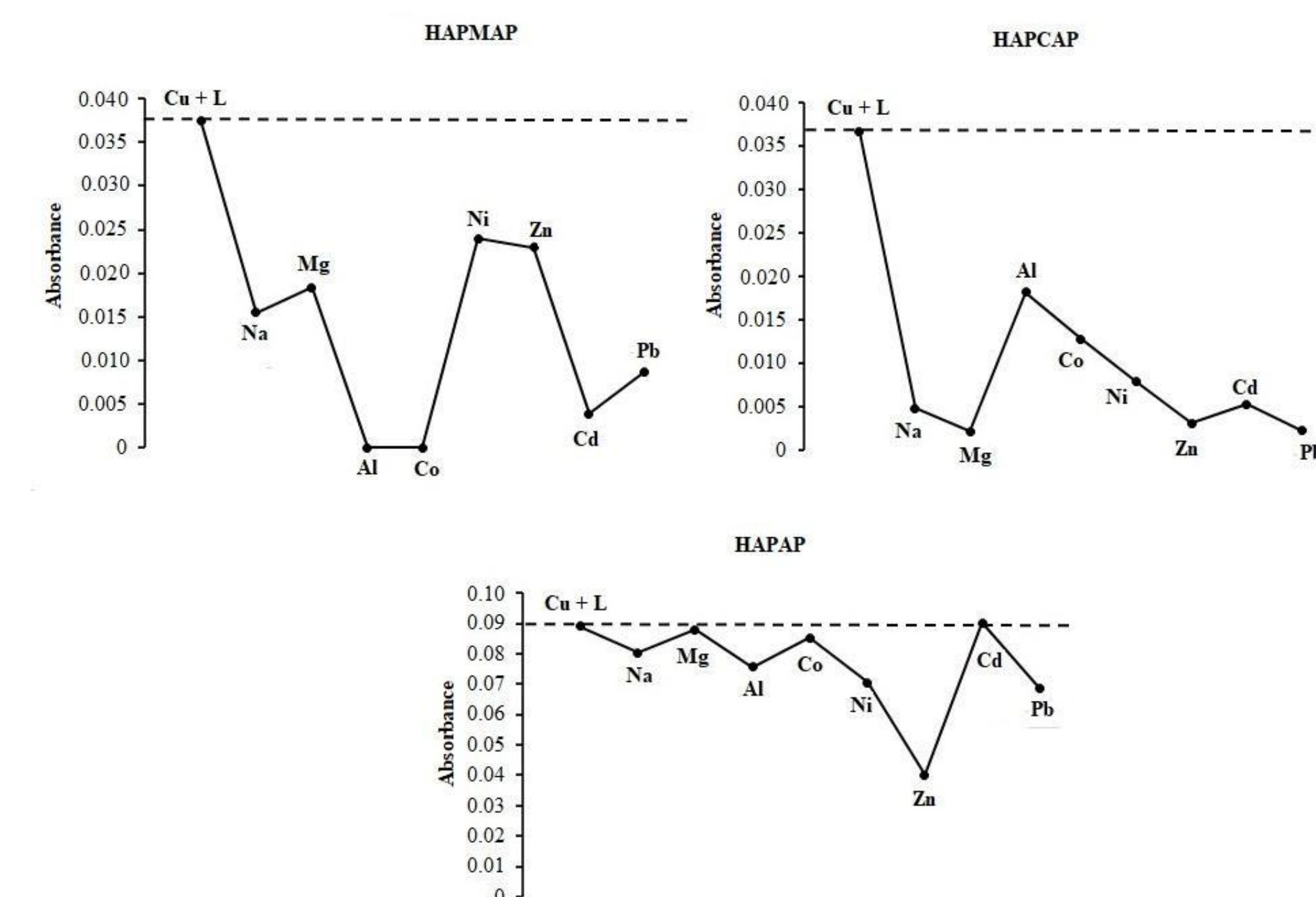


Fig. 4. Effect of other metal ions on the absorbance of Cu²⁺-Sensor complexes

Table 2. Analytical copper sensing and quantification parameters for all three compounds, compared to those for Flame Atomic Absorption Spectroscopy (FAAS)

Sensor	LOD [ppm]	LOQ [ppm]	LR [ppm]
HAPAP	0.19	0.63	0 – 5
HAPMAP	0.16	0.52	0 – 1
HAPCAP	0.49	1.6	0 – 0.3
FAAS	0.27	0.90	>40

CONCLUSION

The copper-sensing capabilities of three benzylideneaniline-based compounds were probed. These compounds were found to enable successful detection of copper in the lower ppm range with greater sensitivity than one of the most popular traditional methods, FAAS, often applied for such analysis. Though all three compounds allow quantification of copper in the lower ppm range (< 10 ppm), in the presence of equimolar quantities of other metal ions, only the unsubstituted derivative allows accurate quantification of copper, except in the presence of an equimolar quantity of zinc. Ultimately, the readiness with which Cu(II) is bound by these compounds is determined by entropic effects. Their copper selectivity in the presence of other metals may be attributed to effects on the hardness and softness of the binding sites by the 4' substituents.

