

Experimental and Theoretical Study of 5-Methoxy-2-[[4-Methoxy-3, 5-Dimethyl-2-Pyridinyl) Methyl] Sulfinyl]-1h-Benzimidazole Complexes

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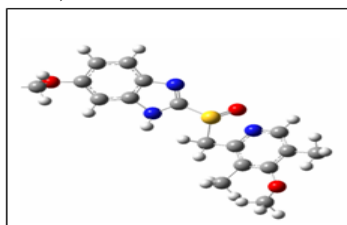
ABSTRACT

In this research work the complexes of 5-methoxy-2-[[4-methoxy-3, 5-dimethyl-2 pyridinyl) methyl] sulfinyl] -1H-benzimidazole with Co(II), Ni(II) and Cd(II) salts were prepared and characterized by conductivity, melting points and (IR and UV-Vis.) Spectroscopy studies, the ligand (omeprazole) works as bidentate O, N donor and forms co-ordinate bonds through C=N and S=O groups. Depending on the low conductivity values showed that these complexes were non – electrolytic in nature. Electronic spectra reveal octahedral geometry for all complexes. the Gaussian09 program by PM6 Semi-empirical method was used to calculate the IR and UV-Vis.) Spectroscopy and thermodynamic functions for ligand and its complexes and compared them with the experimental calculations which showed there is a simple difference between them (experimental and theoretical).

KEYWORDS: Omeprazole, complex, (IR, UV-Vis.) spectroscopy, PM6 Semi-empirical.

1. INTRODUCTION

Omeprazole 5-methoxy-2-[[4-methoxy-3, 5-dimethyl-2- pyridinyl) methyl]sulfinyl]1-H-benzimidazole is an important ulcer drug (Claramunt, 2006). It has the empirical formula of $C_{17}H_{19}N_3O_3S$, a molecular weight of (345.4), Crystal structure is given below (Al-Badr, 2010).



The crystal structure of omeprazole

It is a white crystalline powder, soluble in methanol, dichloromethane, chloroform and water (Nagarajan, 2013). It is apparent compound in the class of efficient of partial stomach cells, successful used as the antiulcer drug (Koneva, 2008). This compound is a heat-sensitive drug, per formulation studies have shown the effect of moisture, heat, solvent and acidic substances on the stability of omeprazole, other investigators have observed a degradation of omeprazole under exposure to various salts and metal ion (El-Badry, 2009). In the last years, co-ordination chemistry has become a big importance due to the synthesis and characterization of a large number of transition metal complexes in which the metal is coordinated by functional groups present in most drugs (Russo, 2014). Studies have shown that more drugs complexes with metallic salts are more effective and less toxic than the same drug. These metal complexes are found to be interesting due to their biological applications like antifungal, antibacterial and antitumor activity, a large number of drugs have been used to synthesize the complex with many metals with a view to enhance their therapeutic action (Malik, 2010). Considering the importance of drugs and their complexes, it has been desired to synthesize and study the metal complexes of omeprazole with metals. The studies presented in this thesis were carried out by computational approaches to investigate the properties of small systems, which contain one to several molecules in the studies (Gao, 2012).

Computational Details: The PM6 semi-empirical method in Gaussian09 program was used to carry out the calculations after being constructed (Bruni, 2008). PM6 semi-empirical calculations for the omeprazole molecule and its complexes was used to analyze the structural and electronic parameters, the structures are fully optimized and vibrational analysis are carried out to verify that the optimized geometries corresponded to minimum global energy (Luo, 2014). The thermodynamic functions (ΔH , ΔG and ΔS) for the ligand and its complexes were calculated using the program

2. EXPERIMENTAL

Materials and Methods: All chemicals used were analytical grade. Pure sample of omeprazole, all metal salts $Co(NO_3)_2 \cdot 6H_2O$, $CdCl_2 \cdot 2H_2O$ and $Ni(ClO_4)_2$ Were of Merck chemicals. The solvents used were distilled water and ethanol absolute. The instruments were used: FTIR spectrophotometer in the range of (4000-400) cm^{-1} , UV-Visible spectrophotometer in the range of (200-800) nm, melting point measurements was received from (stuart scientific SMP1) and conductivity measurements instruments.

Synthesis Of Complexes: The complexes were synthesized by adding the ethanolic solution of omeprazole (0.345g, 1mmol) to metal salts: $Co(NO_3)_2 \cdot 6H_2O$ (0.257g, 1mmol), $CdCl_2 \cdot 2H_2O$ (0.219g, 1mmol) and $Ni(ClO_4)_2$ (0.183g,

1mmol), respectively, and adding few drops of NH_4OH to control of pH solution refluxing the mixture for 3hours colored crystalline complexes were obtained. The complexes were filtered, washed with ethanol and dried.

3. RESULTS AND DISCUSSION

The reaction between the transition metal ions and OME was studied by the conductivity and spectroscopy studies and according to the conductivities suggestion the studied complexes of transition metals showed 1:1 (M:OME) non electrolyte behavior. The analytical data of synthesized complexes record in table.1.

Table.1. Chemical properties of ligand and its complexes

Comp.	Color	m.p. ($^{\circ}\text{C}$)	Molar conductivity $\mu\text{S}.\text{cm}^2.\text{mol}^{-1}$
Ni-OME	Yellow	300	7.5
Cd-OME	Brown	275	3
Co-OME	Brown	300	5.7

IR Spectra: The IR spectra of the complexes indicate that the ligand works as bidentate and co-ordinate the metal via C=N and S=O. the shift of C=N and S=O by $(8-25)\text{cm}^{-1}$ in the complexes groups are involved in the complexation (Malik, 2010). New bands appearing assigned to M-O and M-N in the complexes. Table.2 showed the IR spectra of the ligands and its complexes practically and theoretically. Figures.1 and 2 showed the IR spectra for the ligand and its complexes (experimentally and theoretically).

Table.2. The IR spectra of ligand and its complexes

Comp.	IR bands (cm^{-1})				
	$\nu_{\text{N-H}}$	C=N ν	$\nu_{\text{S=O}}$	$\nu_{\text{M-O}}$	$\nu_{\text{M-N}}$
OME	3389 (3401) _P	1627 (1633) _P	1070 (1061) _P	-----	-----
Ni-OME	3385 (3385) _P	1651 (1666) _P	1087 (1077) _P	628 (622) _P	454 (453) _P
Cd-OME	3443 (3443) _P	1651 (1653) _P	1020 (1021) _P	671 (672) _P	464 (466) _P
Co-OME	3471 (3429) _P	1635 (1636) _P	1045 (1041) _P	669 (668) _P	466 (463) _P



Figure.1a. Practical IR spectra of ligand (OME)

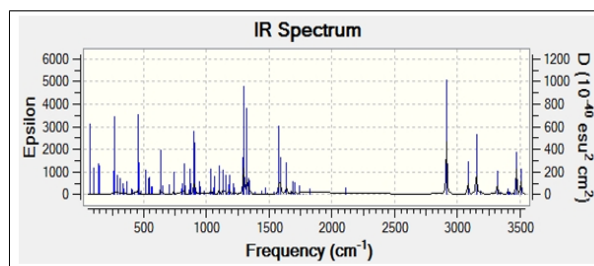


Figure.1b. Theoretical IR spectra of ligand (OME)

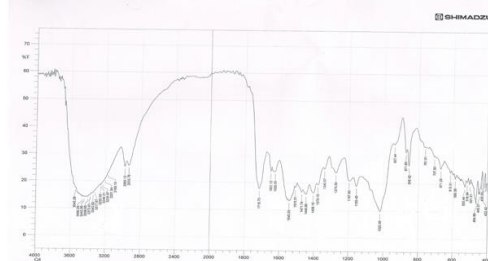


Figure.2a. Experimental IR spectra of Cd complex

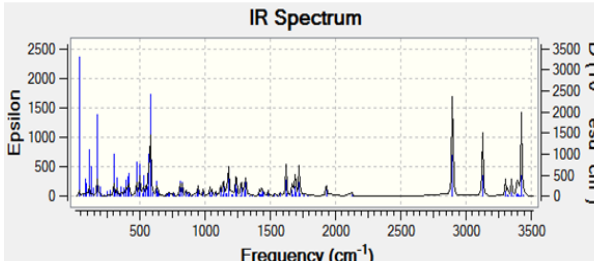


Figure.2b. Theoretical IR spectra of Cd complex

UV-VIS Spectra: The UV-Vis. Spectra of ligand (OME) in the free state using ethanol as solvent showed absorption bands at (207 and 301)nm, the first band assigned to $(\pi-\pi^*)$ transition while the second band assigned to $(n-\pi^*)$ transition, according to the complexes with Cd(II), Co(II) and Ni(II), the band of $(n-\pi^*)$ transition in the ligand was shifted to different wave lengths due to the binding of O and N electrons of ligand with metal ions (Verma, 2012), 350nm (28571cm^{-1}), 352nm (28409cm^{-1}) and 355nm (27397cm^{-1}), respectively. Table.3 showed the UV-vis. Spectra values of ligand and its complexes (practically and theoretically). The simple difference between the experimental and theoretical absorptions may be due to the change in the experiment conditions. Figures.3 and 4 showed the UV-Vis. Spectra of ligand and Cd complex (experimentally and theoretically).

Table.3. UV-Vis. Spectra of ligand and its complexes (Experimentally and Theoretically)

Proposed formula weight (M. Wt)	Band I (nm)	Band II (nm)
OME (345.42)	207 (209) _p	301 (308) _p
Cd-OME (563.81)	210 (212) _p	350 (336) _p
Co-OME (654.33)	293 (273) _p	355 (356) _p
Ni-OME (510.1)	208 (257) _p	352 (344) _p

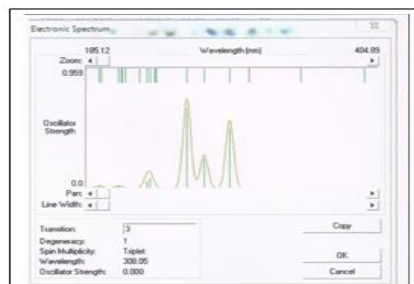
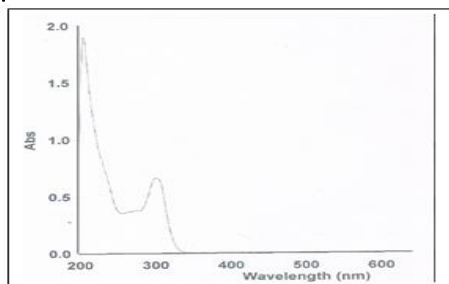


Figure.3. The UV-Vis. Spectra of ligand (OME) (Experimentally and Theoretically)

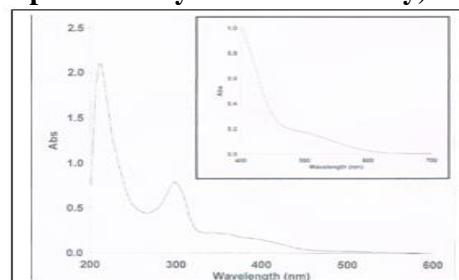
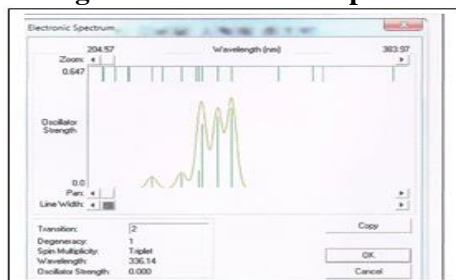
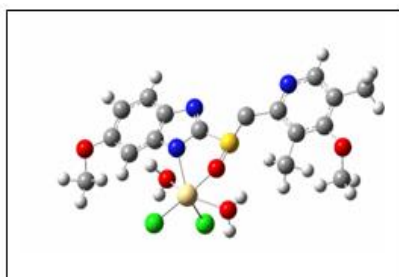


Figure.4. The UV-Vis. Spectra of Cd complex (Experimentally and Theoretically)

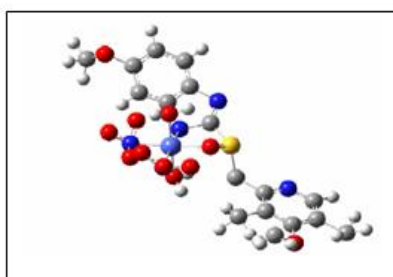
Thermodynamic Calculations: The thermodynamic functions of ligand and its complexes were calculated by Gaussian 09 using semi-empirical (PM6) method. Table.4 showed the energies values of ligand and its complexes, which means that the increasing in the distribution of electronic density due to the increasing the stability of complexes. It was noted that the enthalpy values for compounds have the same total energy values and the reason is that the program may depend on the repeated groups in the compounds and the isolation of the surrounding compounds of molecule (Verma, 2012).

Table.4. Thermodynamic functions of ligand and its complexes

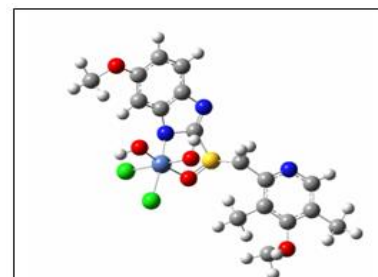
Comp.	ΔH° (Enthalpy) (Kcal.mol ⁻¹)	ΔG° (Free Energy) (Kcal.mol ⁻¹)	ΔS° (Entropy) (Kcal.mol ⁻¹ .K ⁻¹)	ΔE° (Total Energy) (Kcal.mol ⁻¹)
OME	-88767.52	-88816.4	0.164	-88767.3
Cd-OME	-141825.764	-141880	0.182	-141825
Cd-OME	-114706.162	-114775	0.231	-114706
Ni-OME	169284.122	-169347	0.211	-169284



The Crystal Structure of Cd – OME Complex



The Crystal Structure of Co – OME Complex



The Crystal Structure of Ni – OME Complex

4. CONCLUSION

We concluded in this research that the prepared complexes had octahedral geometry and non-electrolytic and compared the experimental results with theoretical results by using the Gaussian 09 program, where we noticed that there is a simple difference between the (experimental and theoretical) results that means that this type of programs can be used for a large number of organic and inorganic compounds.

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