



International Journal of ChemTech Research
CODEN (USA): IJCRGG ISSN : 0974-4290
Vol.6, No.8, pp 3987-3992, September 2014

ICSET-2014 [6th – 7th May 2014]
International Conference on Science, Engineering and Technology

Synthesis, Characterization and DNA Binding Study of Mixed Ligand Based Metal Complexes

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Abstract: Inorganic chemistry can exploit the unique properties of metal ions for biological applications. For instance, clinical application of chemotherapeutic agents for cancer treatment such as, cisplatin. The use of cisplatin, however, is limited by severe dose limiting toxic side-effects. Transition metal ions, being an essential trace element for human body, have been focused for their versatility with respect to their tunable geometries and properties. This led to tremendous research in the development of new metal based drugs. In the current study we are reporting synthesis and characterization of mixed ligand based metal complexes of cobalt and copper. We have also assessed the DNA binding efficacy and mode of binding of both the complexes.

Keywords: Transition metal ions, mixed ligands, copper complexes, DNA binding.

Introduction:

Schiff base ligands are widely used in coordination chemistry mainly due to their tunable steric and electronic properties and good solubility in common solvents. Complexes with oxygen and nitrogen donor schiff bases are particularly focused because of their sensitivity towards molecular environment. Transition metal complexes with schiff bases are studied extensively in the past few years, as they have been found to play an important role in the biological applications¹. It binds to different metal ions forming homonuclear and heteronuclear complexes of varying geometry. In addition, these complexes act as potential antimicrobial agents, catalysts², anticancer agents, etc. The complexes have been found to show enhanced anticancer activity than that of ligands³. In the current study, we are reporting synthesis and characterization of schiff base complexes of copper and cobalt⁴. Copper being an essential trace element has been explored extensively towards their structural and electronic properties. Cobalt being an indispensable part of vitamin B¹² is also one of the essential trace element involved in metabolic process. Recently, it has been reported that ternary complexes of cobalt are more stable than binary complexes, due to steric effects and back donation⁵.

Experimental

Acetyl acetone, 2-amino phenol, acetic acid, copper nitrate trihydrate, Imidazole, cobalt acetate, yeast buffer, saline sodium citrate buffer, 0.2M NaCl, methanol, ethanol, pet-ether.

Synthesis of Hydrazone (L1) (Hapac)

Equimillimolar methanolic solutions of acetylacetone and 2-amino phenol in the presence of acetic acid were refluxed in oil bath at 70°C for about 10 h. Yellow crystalline product was filtered and recrystallized. (Fig 1)

Synthesis of copper complex (C1)

Methanolic solution of hydrazone (L1), copper nitrate trihydrate and Imidazole (L2) were stirred for 15 min. and then refluxed for 3h as shown in Fig 2. Dark brown precipitate obtained was filtered off. The solvent was evaporated and the product was washed with pet-ether and dried.

Synthesis of cobalt complex (C2)

Methanolic solution of hydrazone (L1), cobalt acetate tetrahydrate and Imidazole (L2) were stirred for 15 min and refluxed for 3h as depicted in Fig 3. Dark green compound was precipitated and filtered off.

Isolation of DNA from yeast

Yeast pellets were suspended in 30 mL of saline sodium citrate buffer (SSC) and homogenized. The solution was centrifuged at 3000 rpm for 10 min and the supernatant liquid was discarded. The cells were homogenized again using the SSC buffer and supernatant solution was discarded. The pellet obtained was suspended in 15 mL of 0.2M NaCl and centrifuged again. To the supernatant ethanol, was added and the yeast DNA strands were spooled out. Absorbance was recorded after complete isolation at 260nm and 280nm and it was found to be 0.301 and 0.197 respectively. The ratio of A_{260} and A_{280} was 1.5, indicating that DNA was sufficiently pure to proceed for binding studies.

DNA binding studies by UV spectroscopy

UV absorption titration was carried out by keeping complex concentration constant at 100 μ M for both of the complexes C1 and C2. Complex solution was prepared in the buffer:solvent ratio (8:1). Titration was carried out by monitoring ligand based transition of complex along with 2 μ l increments of isolated DNA.

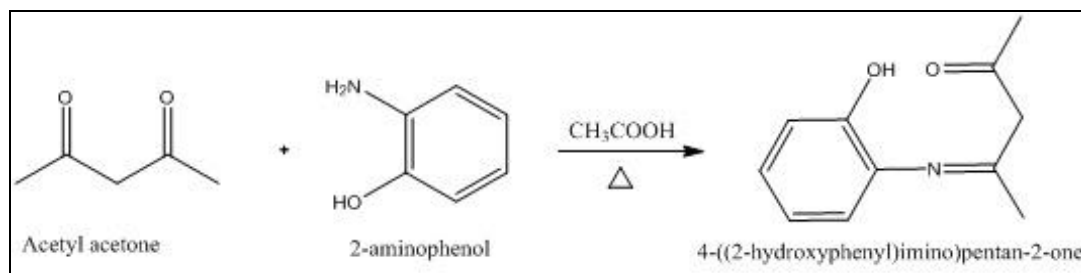


Figure 1. Synthesis of ligand 4-((2-hydroxyphenyl)imino)pentan-2one (L1)

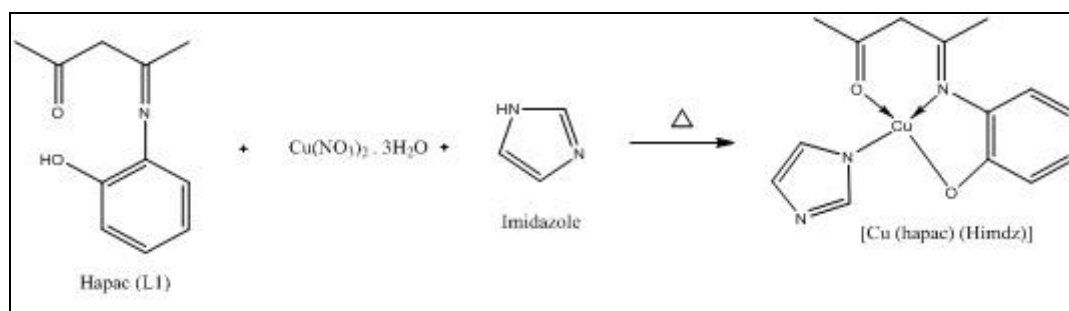


Figure 2 . Synthesis of copper complex from Hapac (L1) and Imidazole (L2)

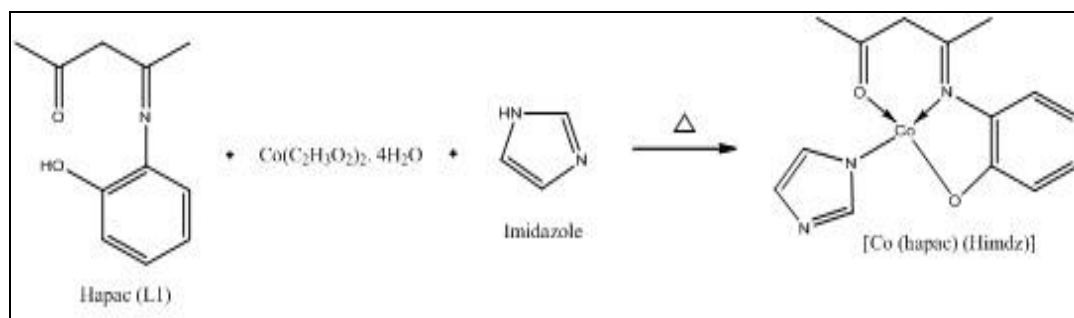


Figure 3. Synthesis of cobalt complex from Hapac (L1) and Imidazole (L2)

Results And Discussion

Characterization of complex C1 and C2

Physical Properties

Synthesized complexes were checked for their solubility, melting point and yield. The results are tabulated in Table 1.

Table 1. Physical properties of metal complexes

Parameters	L1	L2	C1	C2
mp	180 ⁰ C	90 ⁰ C	>315 ⁰ C	>310 ⁰ C
Solubility	Methanol, ethanol, DMSO, water	Methanol, ethanol, DMSO, water	Methanol, ethanol, DMSO	Methanol, ethanol, DMSO
Color	Yellow crystalline solid	White	Dark brown	Dark green
yield	~99%	Commercial	93%	90%

FTIR Studies

FTIR spectra of ligands L1 and L2 and their corresponding complexes C1 and C2 were recorded. Shifts in stretching frequencies of typical functional groups in both the ligands and complexes are compared and are mentioned below;

Table 2. FTIR stretching frequencies of L1, L2 and C1, C2

Compound name	OH group	C=N	C=O	N-H	M-O
Ligand 1	3450.56	1548.84	1606.70	-----	-----
Ligand 2	-----	1543.65	-----	3124.68	
C1	3410.15	1500.62	1571.99	3140.11	530.42
C2	3412.08	1458.18	1385.49	3140.11	653.87

Shift in free OH bond of complexes of copper and cobalt can be seen at 3410.15 and 3412.08cm⁻¹ respectively. The formation of metal and oxygen bond (M-O) can be seen at 530cm⁻¹ and 653cm⁻¹ for copper and cobalt complexes respectively. The characteristic; C=N frequency was observed in the ligand. Also, the shift in carbonyl frequency on binding to the metal centre is observed in both the complexes.

UV and Visible spectral studies

UV visible spectra of complexes and ligands were recorded.

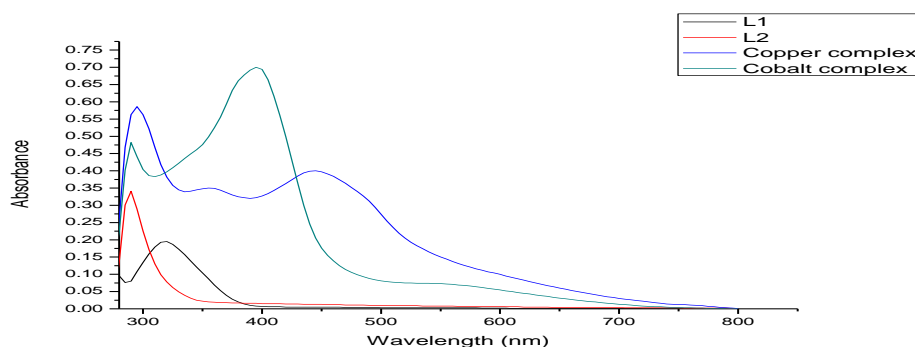


Figure 4. UV spectra of ligands and complexes

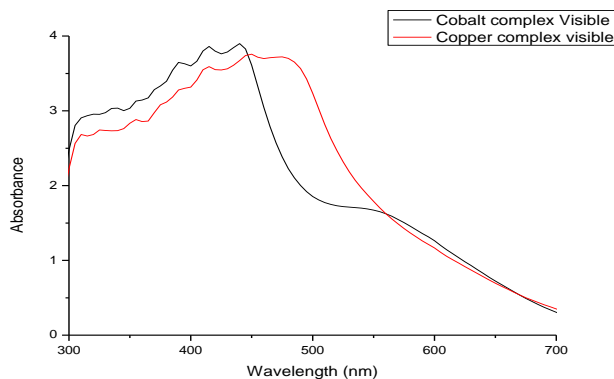


Figure 5. Visible spectra of ligands and complexes

Table 3. UV and visible transitions of L1, L2 and complexes C1, C2

Compound Parameter	Hydrazone (L1)	Imidazole (L2)	Copper complex (C1)	Cobalt complex (C2)
λ_{max} (UV region)	315nm	290 nm	295 nm	290 nm
λ_{max} (visible region)	-----	-----	475 nm	440 nm

Table 3. UV and visible transitions of L1, L2 and complexes C1, C2

Discussions

The UV spectra of ligand 1 and ligand 2 show intraligand transition at 315nm and 290nm respectively, which shows a moderate shift in the complexes at 295nm and 290nm respectively. The copper complex shows highest absorbance at 475nm whereas cobalt complex at 440nm as a broad peak due to d-d transition as reported for these type of complexes.

Characterization of ligand L1

NMR spectra of L1 (Hydrazone)—

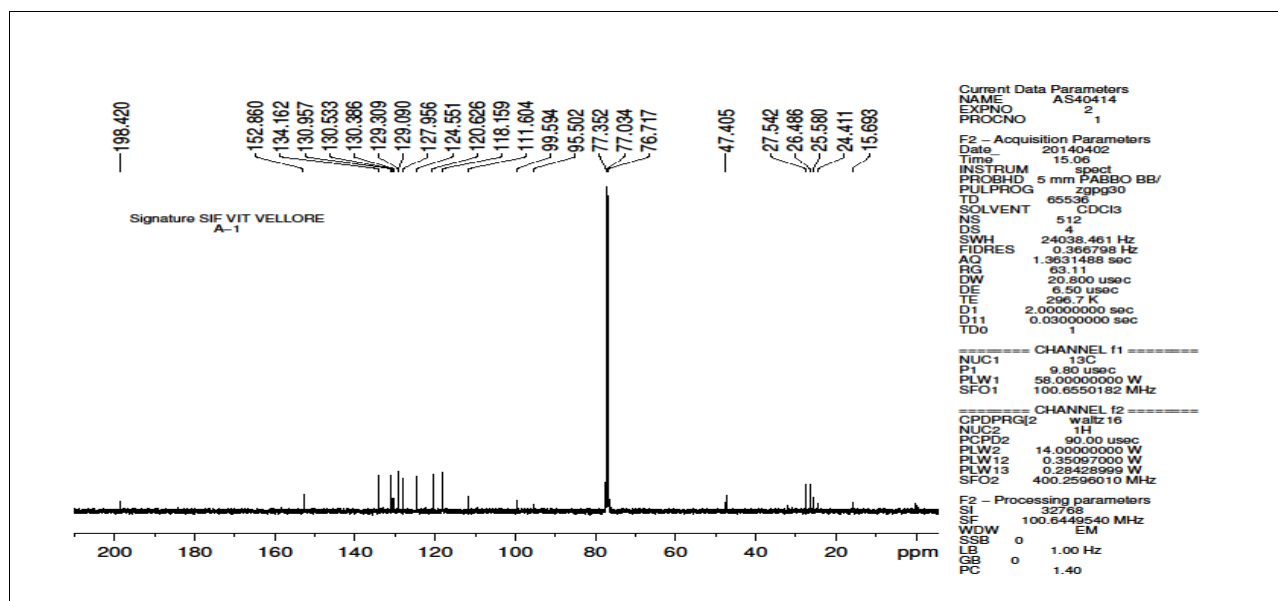


Figure 6. ¹³C NMR spectra of L1.

Discussion

C^{13} NMR spectra of L1 revealed the presence of 11 carbon atoms as observed in the structure of synthesized ligand (L1).

GC MASS analysis of hydrazone (L1)

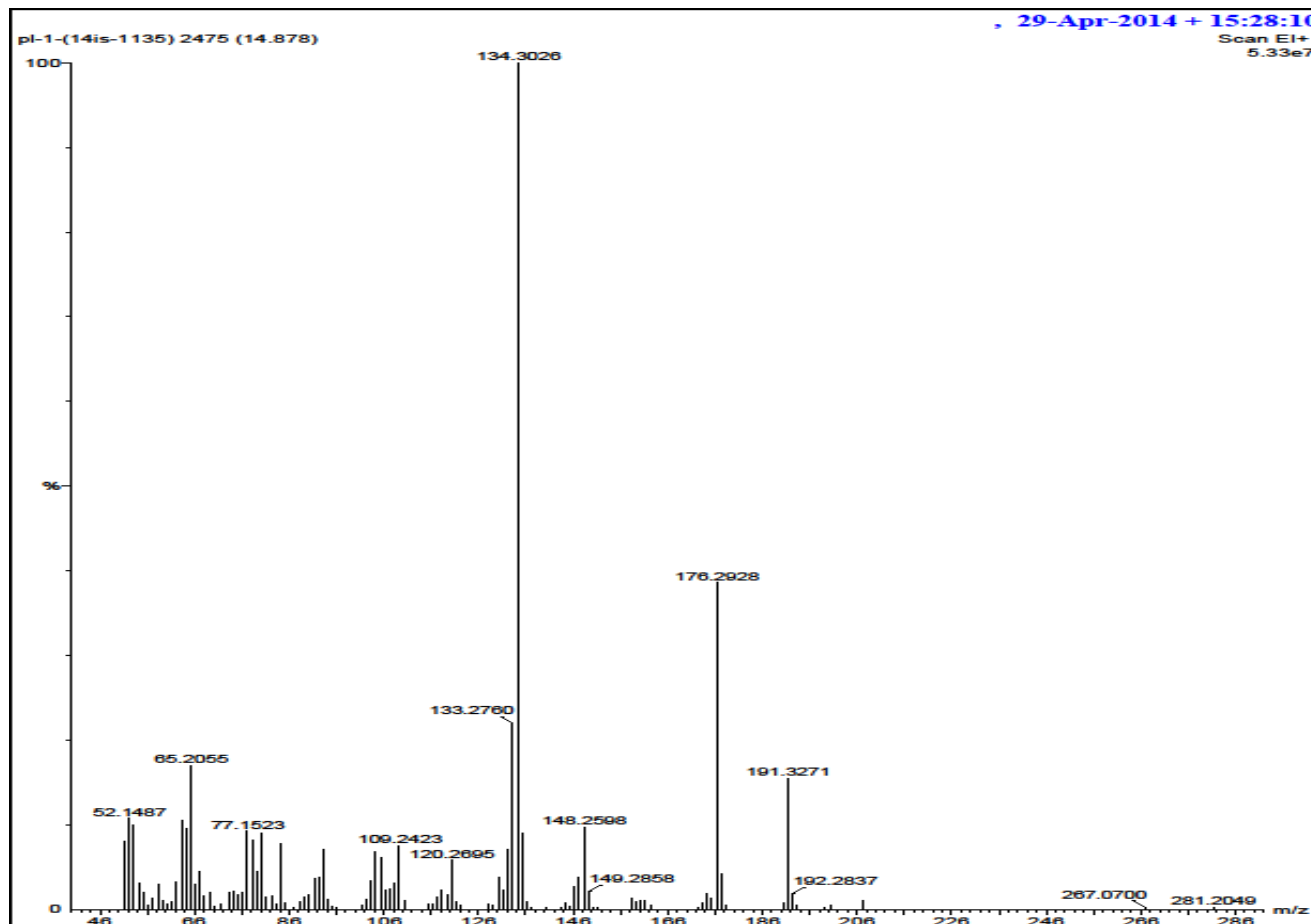


Figure 7. GC MS spectra of hydrazone L1

Discussion

Molecular ion peak (M^+) was observed at 281.2049 m/z value comparable with the expected molecular mass and the chromatogram has shown 99% purity.

DNA Binding Studies

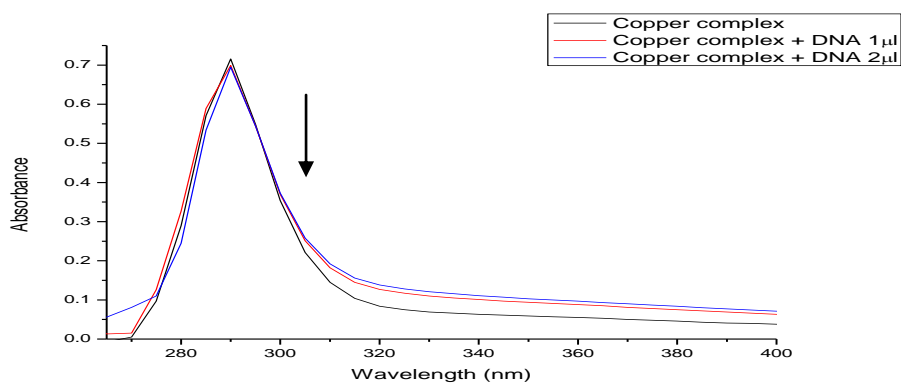


Figure 8. DNA binding of copper complex

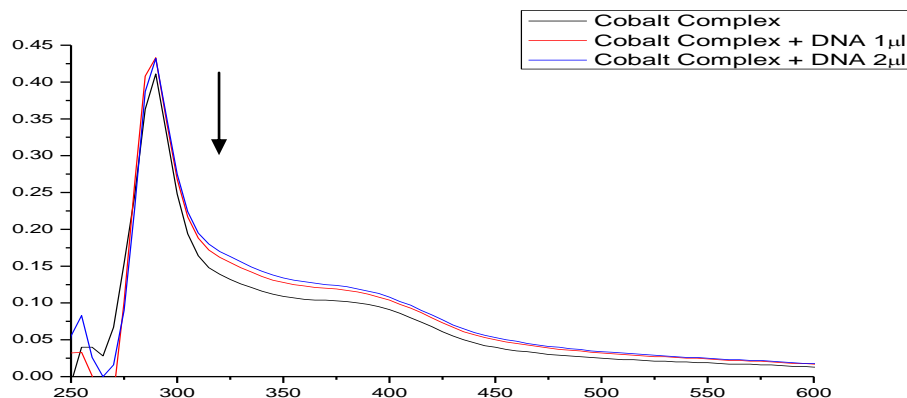


Figure 9. DNA binding of cobalt complex

Discussions

Both the complexes show hypochromic shift in the absorbance of DNA suggesting intercalative mode of binding to DNA. Further incremental addition of DNA to the metal complex, shows substantial decrease in the absorbance

Conclusion

Complexes of copper and cobalt were synthesized using a schiff base ligand synthesized from acetyl acetone and 2-aminophenol. The complexes are characterized by physicochemical and spectroscopic techniques. Further DNA was isolated from yeast cells and checked for purity, DNA binding ability of both the complexes was studied by UV absorption titration technique. From the results, it can be concluded that both the complexes show intercalative binding mode with DNA rather than groove binding.

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