

**SYNTHESIS AND CHARACTERIZATION OF TRANSITION
METAL COMPLEXES OF A NEW SCHIFF BASE AND THEIR
BIOLOGICAL APPLICATIONS**

*Dissertation Project Report-2 submitted to
Lovely Professional University, India
For the partial fulfilment of the award of degree*
of
Masters of Science in Chemistry

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Under the guidance of
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**School of Physical Sciences, Department of Chemistry
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November, 2017**

DECLARATION

I hereby declare that the dissertation report entitled, “**Synthesis and Characterization of Transition Metal Complexes of a new Schiff base and their biological applications**” submitted for the M.Sc. Chemistry degree is entirely my original work and all ideas and references have been duly acknowledged. It does not contain any work for the award of any other degree or diploma at any university.

Date: 30 November, 2017

Harleen Kaur

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CERTIFICATE

This is to certify that Miss. Harleen Kaur has completed the dissertation report entitled, **“Synthesis and Characterization of Transition Metal Complexes of a new Schiff base and their biological applications”** under my guidance and supervision. To the best of my knowledge, the present work is the result of her original investigation and study.

Date: 30 November, 2017

Dr. SUMAN MAJI

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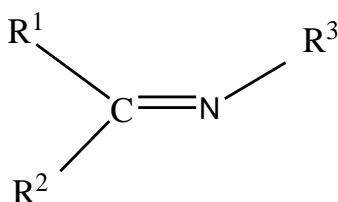
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CHAPTER 1

INTRODUCTION:

In 1864, A German chemist Hugo Schiff had discovered Schiff bases which results in the condensation of carbonyl compounds and primary amines. He was also noble prize winner. In the form of structure, Schiff base are formed by use of a ketone or an aldehyde. The carbonyl group (C=O) of the ketone or the aldehyde is replaced with an azomethine group or imine during the condensation process (Fig. 1). [1]

In the field of coordination chemistry Schiff base ligands are very much necessary, as they have the capacity to form stable complexes with metal ions.



R^1, R^2 or $\text{R}^3 =$ alkyl or aryl

Fig.1 Structure of Schiff bases

The metal complexes formed for Schiff bases are used as catalysts polymers, dyes and in different biological systems. It also proved that these compounds can perform as various enzyme preparations.

Schiff base complexes show good selectivity as well as sensitivity and very good stability. That is why many complexes with specialized metal ions like as Hg(II), Ni(II), Pb(II), Ag(II), Al(III), Co(II), Cu(II), and Zn(II), are used for the role of cation transporters in potentiometric sensors. Catalytic hydrogenation of olefins has also been performed using Schiff base complexes. They have also been studied for the potential use as effective corrosion inhibitors which work by formation of a continuous monolayer on the surface of metals for protection [2].

These are many publications appearing annually i.e 500 approx. regarding schiff bases ligands, so its interest is spontaneously increasing. These compounds are divided in biological systems and can be used in various processes such as organic and chemical catalysis, medicine, pharmacy, chemical analysis and modern technologies [3].

CHAPTER 2

LITERATURE REVIEW

2.1 Application in pharmaceutical and medicine:

Imine complexes have wide usage in the field of biological activators in the form of antitumor, antiviral, antifungal, antibacterial and antimalarials agents. In immobilization of enzymes fictionalization can lead to successful binding of the enzyme to the support material. These complexes are helpful in the treatment of blood sugar and AIDS virus. These are also helpful to understand the various biological processes occurring in living organisms and understand the structures of biomolecules. They involved in photosynthesis and oxygen transport in organisms. For the treatment of cancer drug resistance, imine complexes are involved. [4].

Biological Activity:

In this system, Schiff bases are illustrated with an imine group $-N=CH-$, that is helpful in explaining the mechanism of racemization and transamination reaction. This directs to the mechanism through which these complexes show their biological properties, like their antibacterial and antifungal effect. The metal imine complexes act as models for biologically important enzymatic systems and have been extensively used for antitumor and herbicidal activity [5].

Antibacterial Properties:

Bacteria are main causing organism which is directly caused infectious diseases and having multiple resistances to antibiotics. There are various antibacterial drugs which are having very effective mechanism of action. Schiff bases play important promising role of antibacterial agents. N-(Salicylidene)-2-hydroxyaniline is specifically active towards Mycobacterium tuberculosis which cause the diesis TB.

Antifungal properties:

In the case of contamination of surface tissues, fungal infections are not limited. Due to reports of huge increment in the incidents of systemic fungal infection, Schiff bases are presently exploited as they are known for their strong antifungal activity.

Various quinazolinones based imine derivatives exhibit strong antifungal properties against species like *Candida albicans*, *Aspergillus niger* and *Microsporum gypseum*. With several amines, there are some Metal complexes and Schiff base are taken between furan and furylglyoxal possess antifungal activity against *Helminthosporium gramineum*, which is possible to cause leaf stripe in barley, Fruit rot disease in tomato and *Colletotrichum capsici* is caused by *Syncephalostrum racemosus*, can be successfully treated by Schiff bases [6].

Antiviral Properties:

Vaccines are available for use against pathogens especially viruses like smallpox, or poliomyelitis (polio). Medications which are used against viral infections are less effective and they are only known for mutation of viruses and also give some side effects. There are some effective materials for making of new antiviral agents such as 1-amino-3-hydroxyguanidine tosylate. Schiff base ligands are having antiviral activity, it can use in the treatment of HIV virus [1].

Anticancer Properties:

There are specific Schiff bases which possess antitumor activity. In the tumor cell, Imine derivatives of N-hydroxy-N⁷-aminoguanidine blocks RNA reductase, and can be used to treat leukemia disease.

Application in synthesis and chemical Analysis:

Organic intermediates are mostly used in the synthesis as well as chemical analysis and also Schiff bases are a class of organic intermediates. These Schiff bases have important in the manufacturing of pharmaceuticals and agrochemicals. Presence of hydrogen cyanide Schiff bases can function as amino acid precursors. For the asymmetric synthesis of α -amino acids chiral Schiff bases work as initial substitutes. Condensation of arylamines and carbonyl compounds leads to the formation of imines which are very helpful in the preparation of important compounds i.e (arndiazonium, nitrates, N-arylarene carboxamides, the appropriate amines and cyanamides, β -lactams).

Schiff bases are also precursors for reaction of polycyclic derivatives of quinoline and isoquinoline receiving by oxidative ring closure in presence of UV light. For the preparation

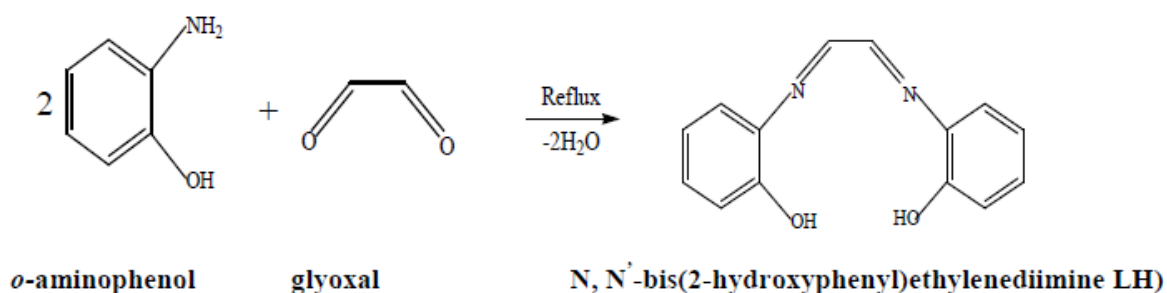
of acyclic and macrocyclic compounds these Schiff bases are considered as very useful substance. Examples of these compounds are cryptats, coronates and podates.

Ruhmann purple are very effective to assist and detect the finger prints [7].

2.2 Synthesis of Schiff base ligand and complex

Synthesis of N, N'-bis (2-hydroxyphenyl)ethyldiimine L:

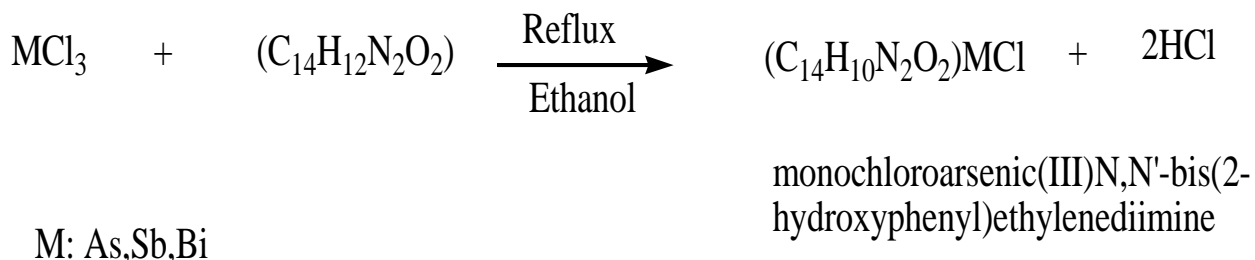
An ethanolic (50ml) solution of o-aminophenol (10.91 gm, 0.10mol) was heated and added to another hot solution of ethanolic (50 ml) solution of glyoxal (2.90 gm, 0.05 mol) in 250 ml of round bottom flask. The reaction mixture was refluxed with constant stirring for 4-5 hours at 70 ° C. The solvent was evaporated in vaccum. The reaction mixture was then filtered and washed with ethanol many times. There was recrystallization from hot ethanol. It was then dried and a yellow coloured product was obtained. TLC was checked for the purity of the ligand prepared.



Synthesis of metal-complexes:

A mixture of AsCl_3 (1.81 gm, 0.01 mol), SbCl_3 (2.28 gm, 0.01 mol) and BiCl_3 (3.15 gm, 0.01 mol) was mixed with LH (2.41 gm, 0.01 mol) in 1:1 molar ratio in a 250 ml of round bottom flask. 50 ml of ethanol was added to this mixture and then refluxed for 4 hrs at 60 °C on a water bath. There was observation of change in colour in the reaction mixture. The reaction mixture was cooled and kept for nearly 12 hours at room temperature. Fine micro crystals were collected after filtration. These crystals were given wash by ethanol until the washing became colourless.

The orange red coloured solid thus obtained was reprecipitated in acetone and dried to get the purified product [9].



2.3 Synthesis of *p*-phenyldianil of 2-thiophene glyoxal (PDATG):

Preparation of 2-thiophene glyoxal:

It was made by the oxidation of 2-acetyl thiophene having the equimolar amount of selenium dioxide in acetic acid-alcohol (3:2, v/v) with constant refluxing for 2 hrs. The mixture solution was poured in hot water and solution was boiled under reflux for 0.5 hrs. Further, this solution was cooled and after cooling dark brown viscous glyoxal settled in the bottom of the flask. The crude product was crystallised by dissolving in alcohol.

Synthesis of Schiff base:

Solutions of *p*-phenyldiamine and 2-thiophene glyoxal exhibits equimolar quantities (glyoxal in excess) chloroform, mixing properly then it shows an immediate colour changing effect. The deep colour changed from light orange to dark brown showing the formation of a new compound. The reaction mixture was then concentrated on water bath and dried in air at 45 °C. Solid formation was again washed with ether for removing unreacted glyoxal, if any. The product was purified with the help of recrystallization from acetone.

Synthesis of complexes:

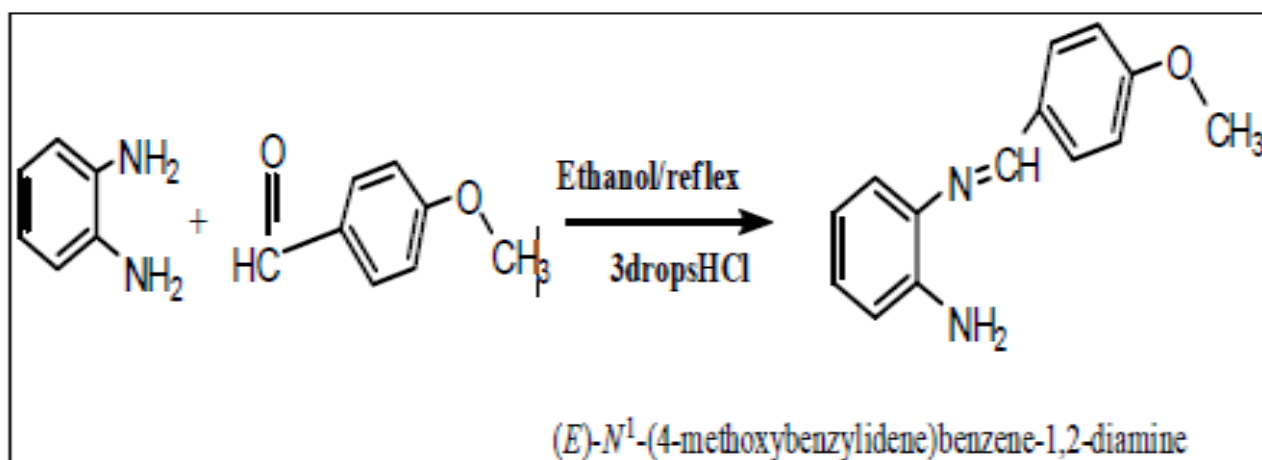
p-Phenyldianil of 2-thiophene glyoxal (PDATG) was dissolved in acetone and metal salt solutions were prepared in acetone or with mixture with alcohol or water. Then mix the

reactant solutions in appropriate proportions (PDATG in excess), complexes of Fe (III) were precipitated from the reaction mixture and the precipitates were washed with acetone and ether, respectively till free from unreacted ligand. Products after drying in hot air oven at 50 °C was collected in air tight tubes [8].

2.4 SYNTHESIS:

Synthesis of Schiff base Ligand:

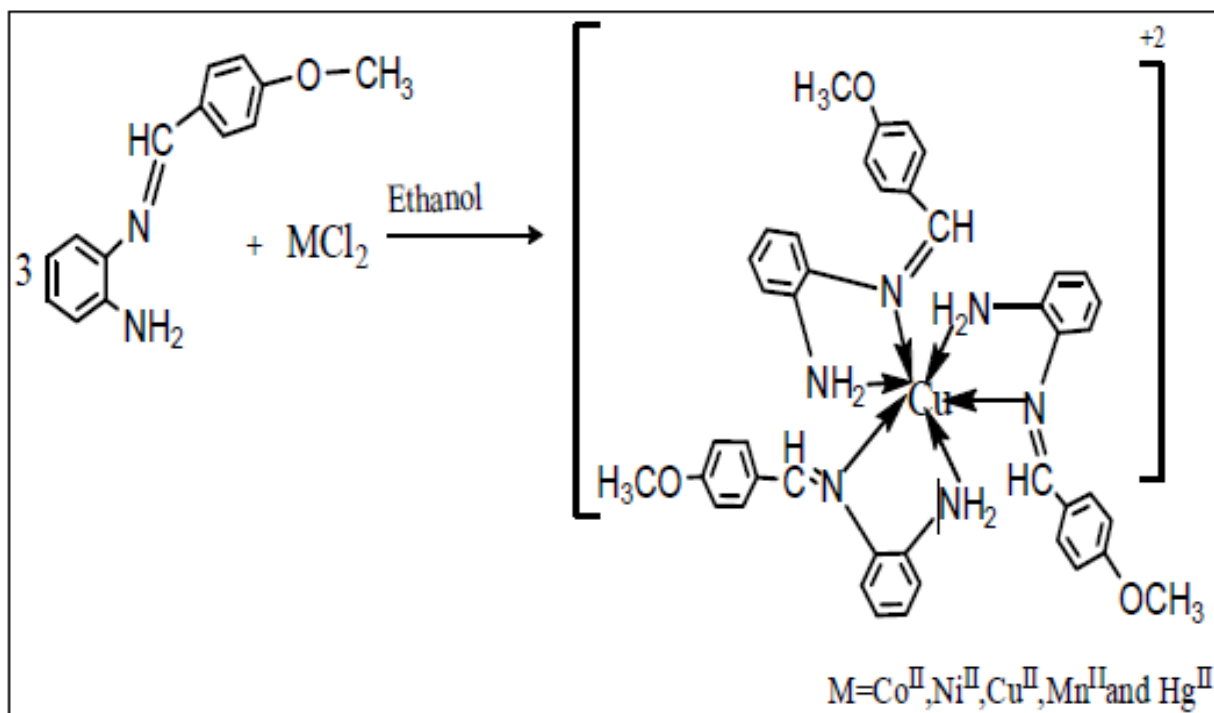
A solution of (0.108 g, 1mmole) of O- phenylene diamine in (15 mL) of ethanol was prepared. To it (0.121mL, 1mmole) of 4-methoxy benzaldehyde was added in the presence of drops of 48% HBr. The reaction mixture was stirred and refluxed for 4 hours. Pale yellow precipitate was formed. The precipitate was filtered off and then recrystallization was done using hot methanol. The compound so formed was dried at 50 °C. The preparation method of the ligand (L) is represented in scheme (1).



Synthesis of the chelates:

A mixture was prepared of respective hydrated cobalt(II), nickel(II), copper (II) Manganese(II) and Mercury (II) chlorides in ethanolic solution of ligand in molar ratio of 1:3 (M:L). (15ml) ethanol was added to the mixture and the reaction mixture was refluxed on water bath for 4-7hrs at 80°C. On cooling a coloured product was separated and washed with

dry diethyl ether. The product formed was recrystallized using hot ethanol. Using anhydrous CaCl_2 the product was dried using vacuum desiccators (yield 66-88%). All the metal complexes were soluble in water, ethanol and most of common organic solvents [10].



2.5 Synthesis of Homo-binuclear Cu(II) and Co(II) Complex:

Synthesis of Schiff base ligand:

The Schiff base was prepared by using a mixture of hot ethanolic solution of 2,6-diaminopyridine (0.22 g, 2 mmol) in ethanolic solution of glyoxal (0.18 ml, 3 mmol). The reaction mixture was stirred for 3 hours. When the mixture turned brown colour, it was filtered and given wash with ethanol several times. Then it was dried in vacuum.

Synthesis of binuclear Cu (II) and Co (II) complexes:

Cu (II) and Co(II) metal complexes of the Schiff base (HL) was obtained by template method. An equimolar solution of heated solution of metal chloride (Cu(II) and Co(II)) was

added slowly into the hot solution of the Schiff base ligand (L). The mixture so formed was dissolved in DMF and thereby refluxing for 4hrs. There was formation of coloured precipitate. Washing was given using ethanol and then dried in vacuum [11].

2.6 Synthesis of p- chloro aniline N- salicylidene Schiff base:

A solution of 1.1gm of salicyldehyde was mixed with 10 ml of ethanol. An ethanolic solution 1.28g of P-chloro aniline was added to the previous solution. Concentrated H₂SO₄ was added to the solution dropwise (2-3 drops) and then put up for stirring. Then this solution was refluxed for 2 hrs and then it left for 12hrs at room temperature. After filtration a coloured product was obtained. It was then given wash with ethanol and followed by ether consecutively. It was dried at room temperature and recrystallized with hot ethanol to obtain Schiff base.

Preparation of the Schiff base Metal Complexes:

4.62 g (0.02mol) of Schiff base was dissolved in 25 ml of ethanol. 0.01 mol metal solution was added to the former solution. Then the mixture was dissolved in 20 ml of ethanol (1:2 metal-ligands). This mixture was stirred constantly and then refluxed for 2 hrs. The coloured product was obtained and then cooled to room temperature. Then filtration was done of the coloured precipitate and given washing with ethanol many times. The product so obtained was vacuum dried [12].

CHAPTER-3:
EXPERIMENTAL WORK:

Chemical used:

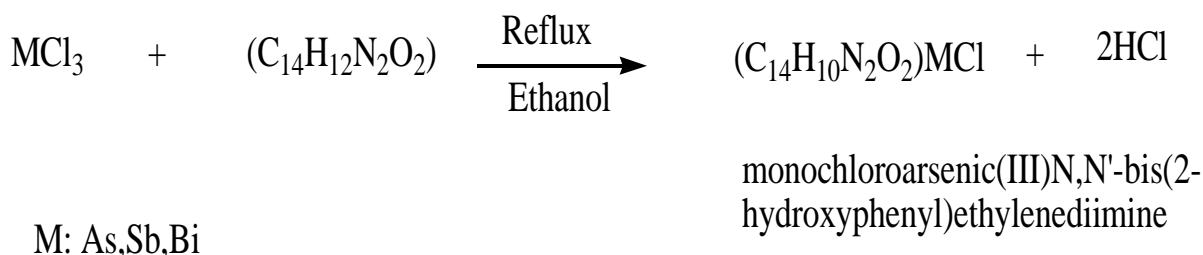
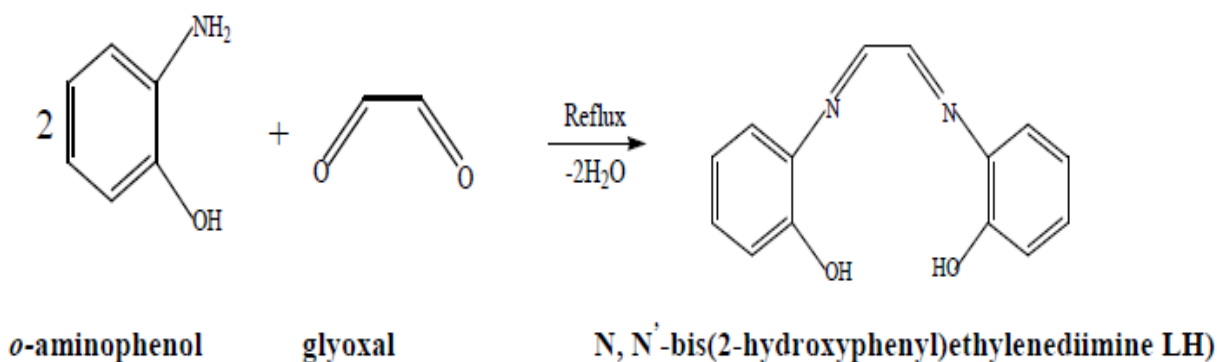
o-aminophenol, Glyoxal, Methanol, Hexane, Ethyl acetate, Chloroform.

Apparatus required:

Magnetic Stirrer, Condenser, Beaker, Watch glass, Round bottom flask.

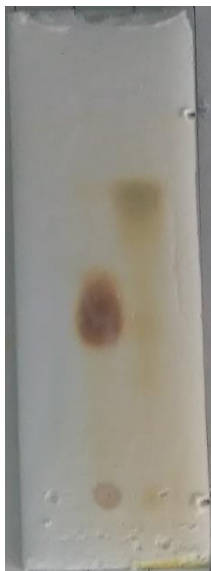
Synthesis of N, N'-bis (2-hydroxyphenyl)ethyldiimine L1:

A hot methanolic (17ml) solution of o-aminophenol (3.6 gm, 0.10 mol) was added to a hot methanolic (17ml) solution of glyoxal (1 gm, 0.05 mol) in 250 ml of round bottom flask. The reaction mixture was kept in an oil bath and refluxed with constant stirring for 4-5 hours at 70° C. The product was collected after filtration and washed many time with methanol and recrystallized from hot methanol. The colour of the product obtained was white. The purity of the prepared ligand was checked by TLC.



Percentage yield: 49.9%

TLC : solvent system 8:2 (Chloroform:Methanol)

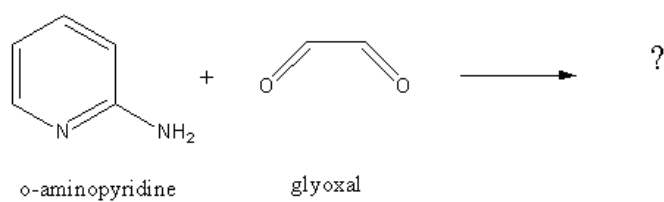


Rf Value of Reactant (Aminophenol): 0.666

Rf Value of Product: 0.928

Synthesis of Schiff base ligand (L₂):

A hot ethanolic solution of o-aminopyridine was added to a hot ethanolic solution of glyoxal in 250 ml of round bottom flask and a reaction mixture was kept in an oil bath which was then refluxed in a magnetic stirrer at 70° C. After 4 hr. the reaction mixture resulted in a sticky mass and isolation of the desired product from this is still under way



CHAPTER-4:

RESULT AND DISCUSSION

IR Analysis:

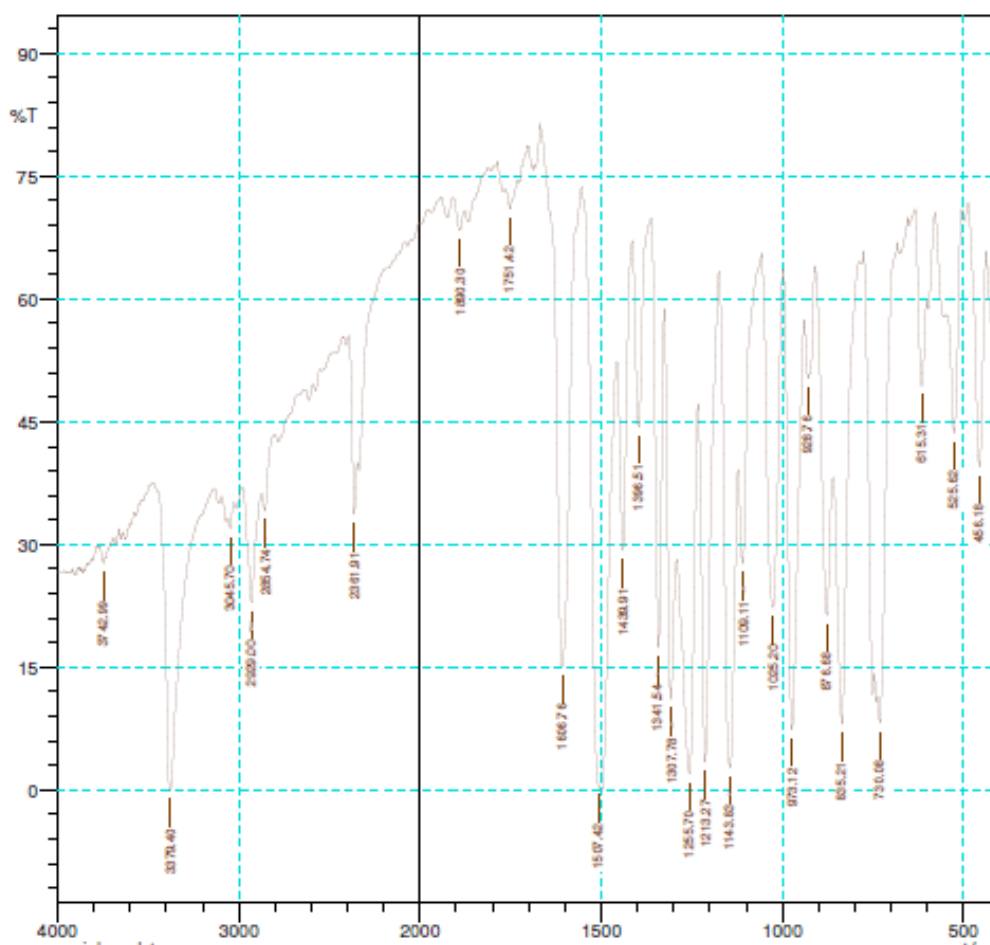


Figure 2: IR spectra of N, N'-bis (2-hydroxyphenyl)ethyldiimine L1)

Sr. No.	Type of bond	Frequency (per cm)
1.	-OH(phenolic)	3379
2.	CH Stretching	3045
3.	CH Bending	1341
4.	C=C (Aromatic)	1507
5.	C=N Stretching	1606

Z

UV Analysis:

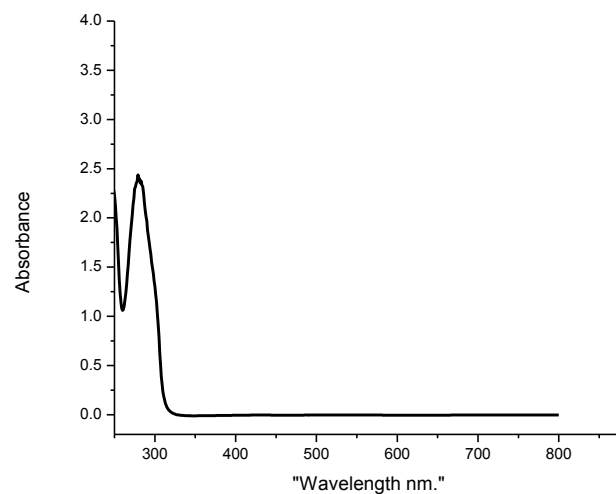


Figure 3: UV Visible Spectra of Ligand (L₁)

Sr. No.	Peak position (nm)	Extinction coefficient (L mol ⁻¹ cm ⁻¹)
1.	279.00	2400

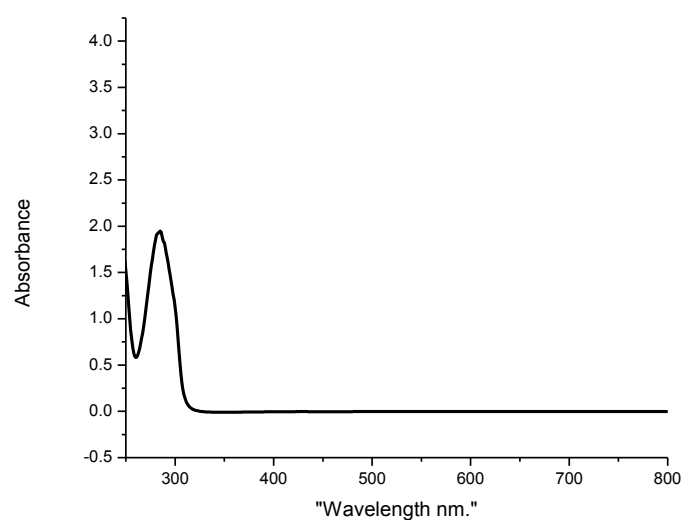


Figure 4: UV Visible spectra of Ligand (1:1)

Sr. No.	Peak position (nm)	Extinction coefficient(L mol ⁻¹ cm ⁻¹)
1.	285	970
2	271	1865

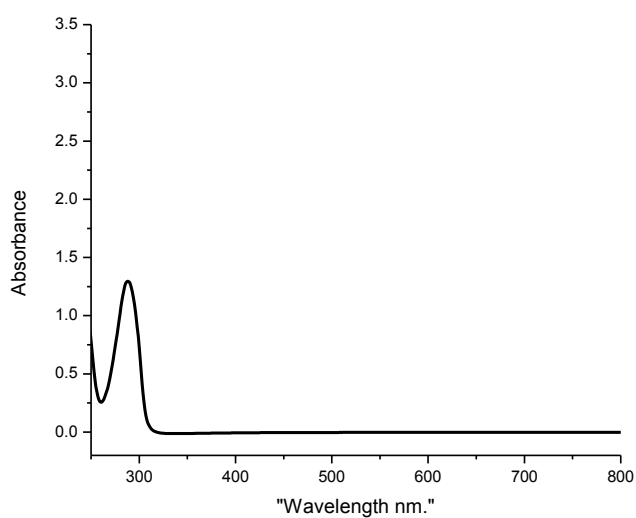


Figure 5: UV Visible spectra of Ligand (1:2)

Sr. No.	Peak position (nm)	Extinction coefficient ($L\ mol^{-1}\ cm^{-1}$)
1.	288	1612.5
2.	234	2150

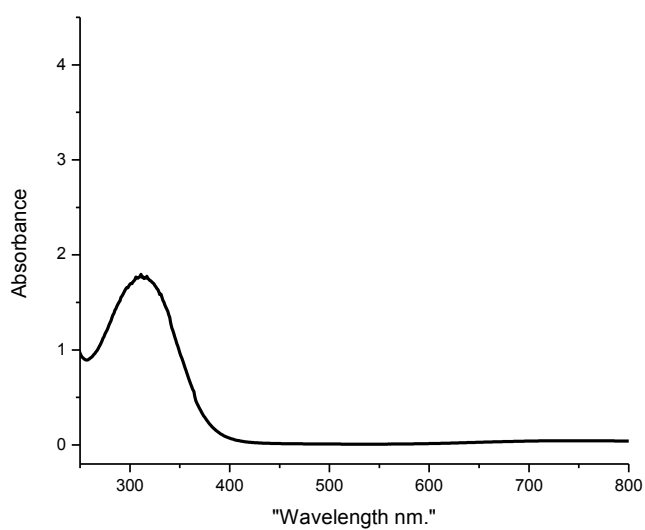


Figure 6: UV Visible spectra of $Cu(NO_3)_2$

Sr. No.	Peak position (nm)	Extinction coefficient ($L\ mol^{-1}\ cm^{-1}$)
1.	311	1790
2.	214	3800

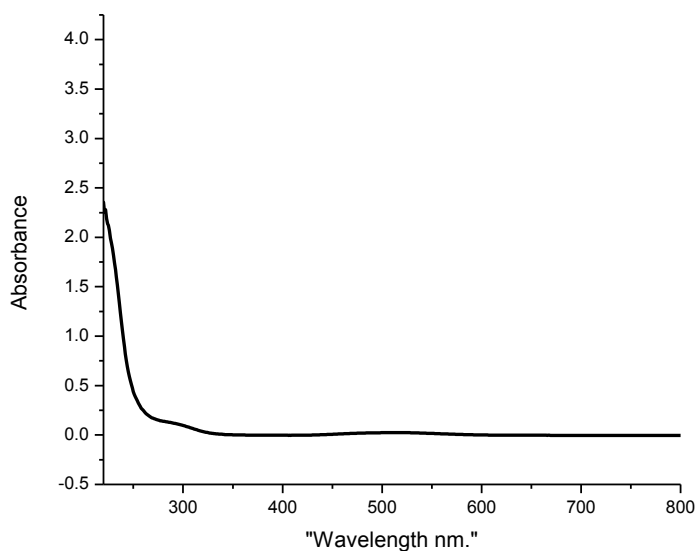


Figure 7: UV Visible spectra of $\text{Co}(\text{NO}_3)_2$

Sr. No.	Peak position (nm)	Extinction coefficient ($\text{L mol}^{-1}\text{cm}^{-1}$)
1.	511	24

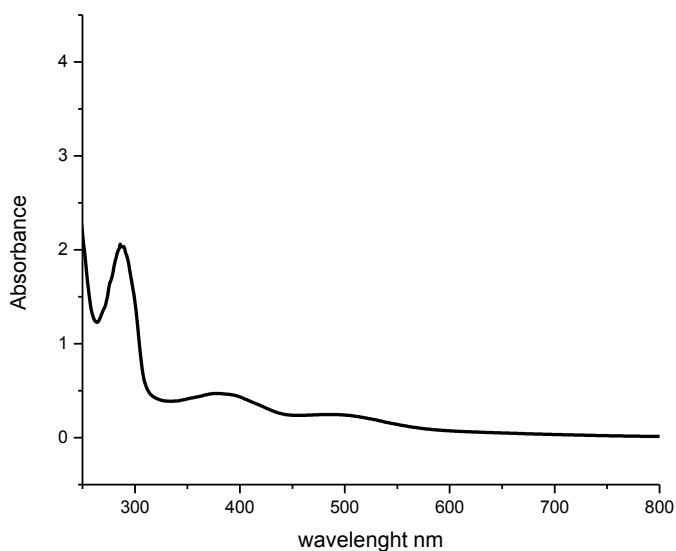


Figure 8: UV Visible spectra of $\text{Cu}(\text{NO}_3)_2$

Sr. No.	Peak position (nm)	Extinction coefficient ($\text{L mol}^{-1}\text{cm}^{-1}$)
1.	485	310
2.	375	410
3.	289	1890
4.	234	3780

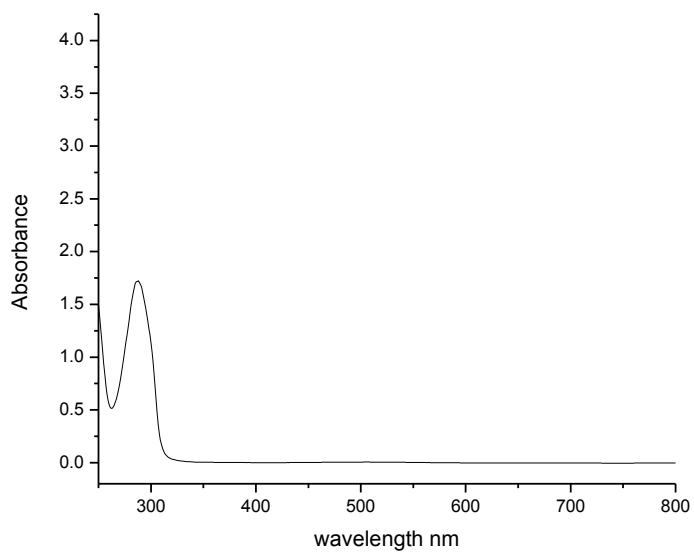


Figure 9: UV Visible spectra of $\text{Co}(\text{NO}_3)_2$ and ligand (1;1)

Sr. No.	Peak position (nm)	Extinction coefficient ($\text{L mol}^{-1}\text{cm}^{-1}$)
1.	504	5
2.	288	1720

CONCLUSION:

Most of the research has been done by using β -diketones but here in this project, we have used α diketones for the formation of Schiff base. Schiff bases and their metal complexes are known to show exemplary behaviour in medication. They have been proved to have antibacterial, anticancer, antiviral and antifungal properties. The newly synthesized bases and their metal complexes are also expected to show such biological activity.

For the synthesis of ligands o-aminopyridine, and o-aminophenol substituent are chosen as the phenolic -OH group and the pyridyl nitrogen both can act as ligating groups in addition to the imine nitrogen in these bases. With aminopyridine the ligand was isolated successfully and metal complexes have been prepared, but with o-aminopyridine, we were not able to isolate the ligand. The IR and UV Visible spectroscopy for the ligand L1 was performed. The isolation of the second ligand and the biological assay of the ligands as well as the metal complexes are under way.

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