

**SYNTHESIS OF NOVEL SCHIFF BASE METAL COMPLEXES OF
AMINOPHENOLS AS POTENTIAL ANTISEPTIC AGENTS**

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**A THESIS SUBMITTED TO THE SCHOOL OF POSTGRADUATE
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JUNE 2015

DECLARATION

We hereby declare that this thesis titled **SYNTHESIS OF NOVEL SCHIFF BASE METAL COMPLEXES OF AMINOPHENOLS AS POTENTIAL ANTISEPTIC AGENTS** is an original research work carried out by **EJIAH, FELICIA NDIDI** in the Department of Chemistry, University of Lagos, Nigeria.

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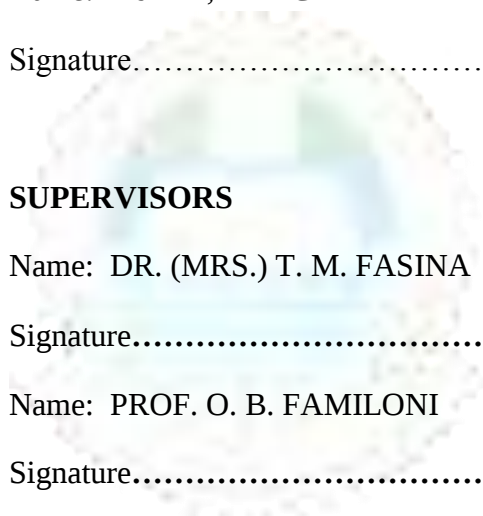
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CERTIFICATION**

This is to certify that the Thesis:
**“SYNTHESIS OF NOVEL SCHIFF BASE METAL COMPLEXES OF
AMINOPHENOLS AS POTENTIAL ANTISEPTIC AGENTS”**

Submitted to the
School of Postgraduate Studies
University of Lagos
For the award of the degree of
DOCTOR OF PHILOSOPHY (Ph.D.)
is a record of original research carried out

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DEDICATION

This research work is dedicated to ALMIGHTY GOD WHO GAVE ME GOOD HEALTH, WISDOM, KNOWLEDGE, UNDERSTANDING and to the ever loving memory of **my late husband, MR FRANCIS CHUKWUEMEKA EJIAH**, who did not live to see this program completed.



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CHAPTER ONE

1.0 INTRODUCTION

1.1 Background of Study

Advances in medicinal chemistry have been promoted by the role of organic compounds in regulating biological activities. Organic compounds such as benzimidazoles, benzothiazoles and Schiff bases have been reported to regulate biological activities (Jigna *et al.*, 2005). One of the biological agents regulated by organic compounds include antibiotics.

The discovery and development of antibacterial agents are among the most powerful and successful achievements of modern science and technology for the control of infectious diseases (Parekh *et al.*, 2005). However, there have been increasing reports of resistance to existing antibacterial agents (Pablos-Mendez, 1998, Schrag *et al.*, 2001). Resistance of microorganisms to existing antibacterial agents accounts for more than 85% of the mortality reported from infection worldwide (WHO, 2009). This has led to deaths from acute respiratory infections, diarrhoea, measles, AIDS, malaria and tuberculosis. Some of these infections are hospital acquired. Hospital-acquired infection (HAI) are infections not present and without evidence of incubation at the time of admission to a healthcare setting such as nosocomial. Hospital-onset infections have been associated with resistance of microorganisms to antiseptics and disinfectants (Coffin and Zaoutis, 2008). Common antiseptics and disinfectants used to counter HAI include chloroxylenols (*Dettol*, *Morigad*, *Tiscol*), chlorohexidines (*Savlon*, *Purit*), sodium hypochlorite (*Jik*) and hydrogen peroxide. Although chloroxylenol was launched for use in 1933, its use in hospitals has been discouraged due to reports that it is easily inactivated (Shanson, 1999), hence there is need for constant research into new compounds that are active against microorganisms and towards which resistance has not yet been developed.

The effect of various brands of chloroxylenol disinfectants on some common hospital pathogens showed that chloroxylenol and chlorhexidines had less activity against gram negative organisms, inhibiting them only in the undiluted form (Ogunsola *et al.*, 2000). Both developed and resource-poor countries are faced with the burden of healthcare-associated infections. A World Health Organization (WHO) study in 55 hospitals in 14 countries from four WHO regions showed that about 8.7% of hospitalized patients had nosocomial infections (Tikhomirov, 1987). The study on the efficacy of nosocomial infection control project (SENIC) from the 1970s showed nosocomial rates could be reduced by 32% if infection surveillance was coupled with appropriate infection control programs such as disinfection of hospital rooms (Hughes, 2008).

1.2 Statement of Problem

The increasing microbial resistance to existing antibacterial agents has necessitated the search for new compounds with potential effects against pathogenic organisms. Since microorganisms are gradually acquiring resistance, there is therefore the need to continually develop novel antibacterial agents to combat the problem of resistance.

Despite improvements in surgical and medical techniques, hospital-acquired infections still remain one of the main causes of morbidity and mortality (Ogunsola *et al.*, 2002). This has led directly or indirectly to an enormous increase in the cost of hospital care and the emergence of new pathogens that can be transmitted by a variety of routes (Simpson, 1992). Hospital-acquired infections are caused by viral, bacterial, and fungal pathogens; the most common types being bloodstream infection (BSI), pneumonia, urinary tract infection (UTI), and surgical site infection (SSI).

Disinfection of hospital rooms with hydrogen peroxide vapor in addition to standard cleaning reduces environmental contamination and the risk of infection with multidrug-resistant

organisms (MDRO). To prevent the development of bacterial resistance, rotation of disinfectants in hospitals as well as pharmaceutical and food industries has been advocated (Murtough *et al.*, 2001). There is therefore an urgent need to synthesize and investigate a variety of new antiseptics and disinfectants on a range of microorganisms.

Schiff base metal complexes have been widely used as antimicrobial agents due to their microbial resistant properties (Tansir and Saad, 2010). Studies of the *in-vitro* activity of aminophenols and aminochlorophenols also show that these compounds possess intrinsic biological properties such as inhibition of cellular function and lactate dehydrogenase (LDH) leakage (Valentovic *et al.*, 1996). Based on these reports, Schiff base metal complexes of aminophenols have been synthesized and screened for use as active compounds in the formulation of antiseptic and disinfectants.

1.3 Aim and Objectives of Study

1.3.1 Aim of Study

The aim of this work is to synthesize new antiseptic agents from copper and cobalt complexes of aminophenol Schiff bases

1.3.2 Specific Objectives are as follows:

- a) To synthesize new Schiff bases from 2-, 3- and 4-aminophenol
- b) To synthesize new Schiff base copper and cobalt complexes of aminophenols
- c) Study the structure-activity relationship of 2-, 3- and 4-aminophenol Schiff bases
- d) Evaluate the antibacterial activity of Schiff base copper and cobalt complexes of aminophenols

1.4 Significance of Study

The structure of organic compounds have been found to be related to the physio-chemical and biological activity of the compound, therefore the study of structure activity relationship (SAR) [an approach designed to establish relationship between chemical structure and biological activity] of aminophenol Schiff bases is expected to provide data for the predictive use of Schiff bases as antibacterial agents. In addition, previous studies revealed the increased potency of Schiff base metal complexes over uncoordinated Schiff base (Atmaram and Kiran, 2011). Hence, it is expected that new SBMC suitable as active ingredients in formulation of antiseptics would be identified.



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CHAPTER TWO

2.0 LITERATURE REVIEW

2.1 Schiff Bases

Schiff bases (SB) are stable compounds containing the carbon-nitrogen double bond (-HC=N-), they are also called imines. (Imines are present in various naturally derived compounds; ancistrocladinine and chitosan-derived Schiff base (Bringmann *et al.*, 2004, Guo *et al.*, 2007)). The presence of imine group in these compounds have contributed to their activities (de Souza *et al.*, 2007). Generally, Schiff bases have the formula RHC=NAr (Figure 1).



Figure 1: General representation of Schiff base

The presence of aryl group leads to conjugation in the system, hence increased stability of aryl Schiff bases. Most Schiff bases exhibit delocalized π -electron system which makes them to have large non-linear polarizabilities, this is usually enhanced by the presence of donor or acceptor groups. Schiff bases are among the most general nitrogen coordinating ligands, because the basicity of the sp^2 hybridized nitrogen lone pair of the imine nitrogen (although lower than that of amines sp^3 hybridization) is well suited to form complexes with metal ions. Schiff bases play important roles in Coordination Chemistry as they easily form stable complexes with most transition metal ions (Atmaram and Kiran, 2011). The majority of the ligand systems employed in model studies are derived from Schiff bases (Bailey *et al.*, 1986).

Schiff bases possess structural similarities with naturally occurring biological substances. This enhances their use in elucidating the mechanism of reaction processes in biological systems such as transamination and racemination reactions.

The relatively simple preparation procedures and synthetic flexibility which facilitates the introduction of tailor made structural properties allows their use as ligands for preparation of libraries (Patai, 1970).

2.2 Synthesis of Schiff Bases

Schiff bases are synthesized by condensation reactions between aldehydes and amines. The first preparation was reported in the 19th century by Hugo Schiff (Schiff, 1864).

The synthesis of Schiff bases is a reversible addition-elimination reaction, hence water elimination is crucial for product formation. The crude product can be purified by re-crystallization or column chromatography on alumina. Condensation reaction can be achieved using different reaction methods.

2.3 Methods of Synthesizing Schiff Bases

The various methods of synthesizing Schiff bases include;

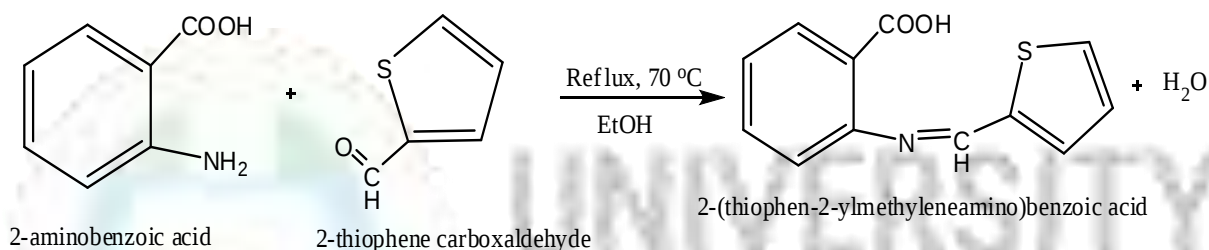
- Classical method
- Water based method
- Grindstone method
- Microwave irradiation method
- Ultrasonic method

2.3.1 Classical method

The synthetic method reported by Hugo Schiff in 1864 is termed the classical method and is still in use today. This method involves the condensation of a carbonyl compound with an amine in refluxing condition using organic solvents such as ethanol. The problem of water elimination led to the use of dehydrating agents. The presence of dehydrating agents to remove water produced normally favours the formation of SBs. An *in-situ* method for water elimination using

dehydrating solvents such as tetramethyl orthosilicate or trimethyl orthoformate was developed in the early 1990's (Love and Ren, 1993, Look *et al.*, 1995). However, this method depends on the use of highly electrophilic carbonyl compounds and strongly nucleophilic amines. Lewis acids such as ZnCl_2 , MgSO_4 , NaHCO_3 , H_2SO_4 have also been shown to activate the carbonyl group, catalyse the nucleophilic attack by amines and dehydrate the system (Chakraborti *et al.*, 2004).

The condensation of 2-thiophenecarboxaldehyde and aminobenzoic acid using ethanol as solvent in refluxing condition (Scheme 1) have been reported (Mohamed *et al.*, 2005).



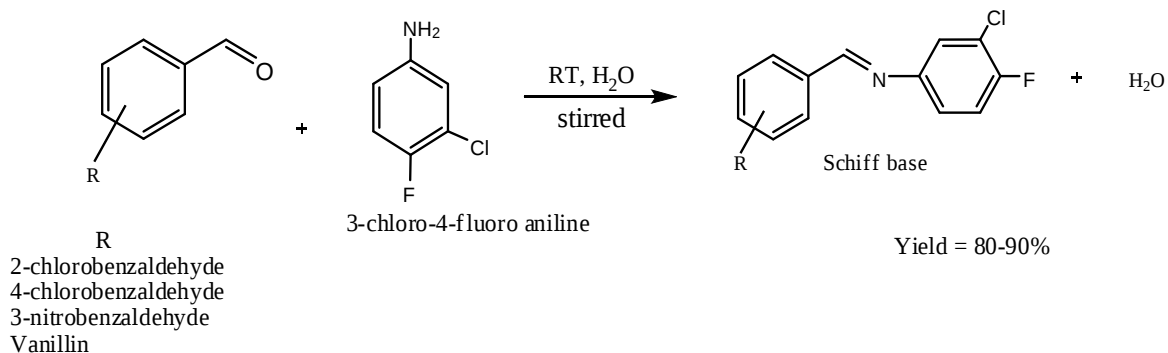
Scheme 1: Synthesis of 2-(thiophen-2-ylmethyleneamino)benzoic acid in ethanol under reflux

Several research groups have also reported the synthesis of Schiff bases in refluxing condition using ethanol as solvent (Jeeworth *et al.*, 2000, Aboaly and Khalil, 2001, Tuna *et al.*, 2006, Jadhav *et al.*, 2010, Patel *et al.*, 2011).

2.3.2 Water based method

Water based method involves the use of water as solvent. The reactants are usually water soluble and are allowed to stir at room temperature before leaving to stand for 48-72 h. The product obtained is re-crystallized from water.

Arshi *et al.* (2009) reported the synthesis of Schiff bases from 3-chloro-4-floro aniline and substituted benzaldehyde using water as solvent (Scheme 2).

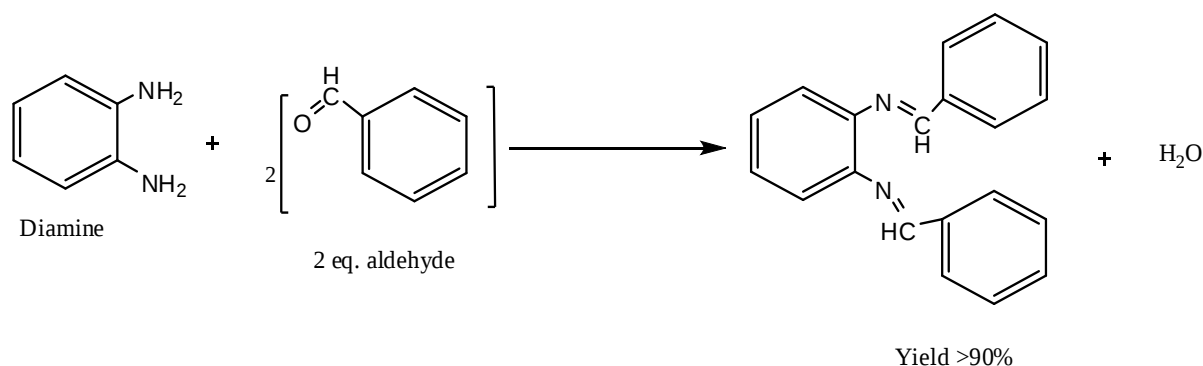


Scheme 2: Synthesis of Schiff base using water as solvent

Water being an abundantly available cheap solvent for reactions is environmentally friendly and encouraged for a green chemistry synthesis. The products are easily isolable, making reactants easier to handle. However, the method has limited application as most organic compounds are insoluble in water while the Schiff bases can also undergo hydrolysis in water. The hydrolysis of Schiff base derived from pyridoxal 5'-phosphate and n-hexylamine were determined between pH 3.5 and 7.5 in ethanol/water mixtures (Donoso *et al.*, 1986). The results indicate that the hydrolysis of imine bond started when the pH of solution was below 6.5. This was used to study the decrease in activity of phosphorylase b which is caused by the cleavage of enzyme-coenzyme binding due to protonation of the pyridine nitrogen atom of pyridoxal 5'-phosphate.

2.3.3 Grindstone method

Grindstone method of synthesis is a solvent-free reaction. Solvent free reaction used in the synthesis of imines, Aldol and Michael reactions are fast becoming the best synthetic method (Tanaka, 2003). The method involves grinding the reactants using a porcelin mortar and pestle until the mixture turns pasty. The formation of Schiff base occurs on standing over a period that ranges from several minutes to days. The crude product is re-crystallized from appropriate solvents such as ethanol. The method have been utilized for the synthesis of bis-imine Schiff base using diamine and two equivalent of aldehyde (Van den Ancker *et al.*, 2006) (Scheme 3).



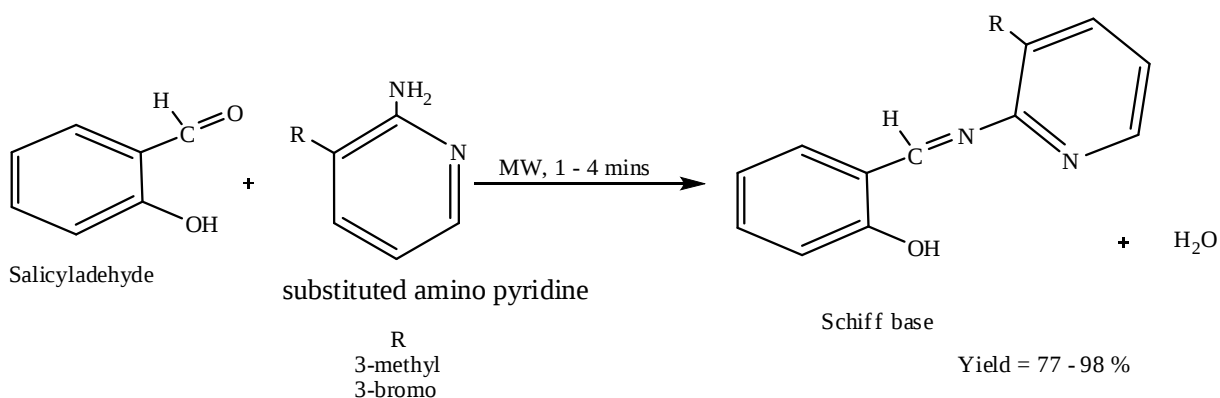
Scheme 3: Synthesis of Schiff base using Grindstone method

The use of Grindstone in synthesis has circumvented the use of heat and solvent in SB synthesis. This can be done on a larger scale by employing ultra high intensity grinding in a ball mill. The use of a cylinder reactor will lead to improved conversion without additional purification steps. This method is environmentally friendly, high yield but conversion to product reaction time can be long. However, this method cannot be used for reactants that are both liquid

2.3.4 Microwave irradiation method

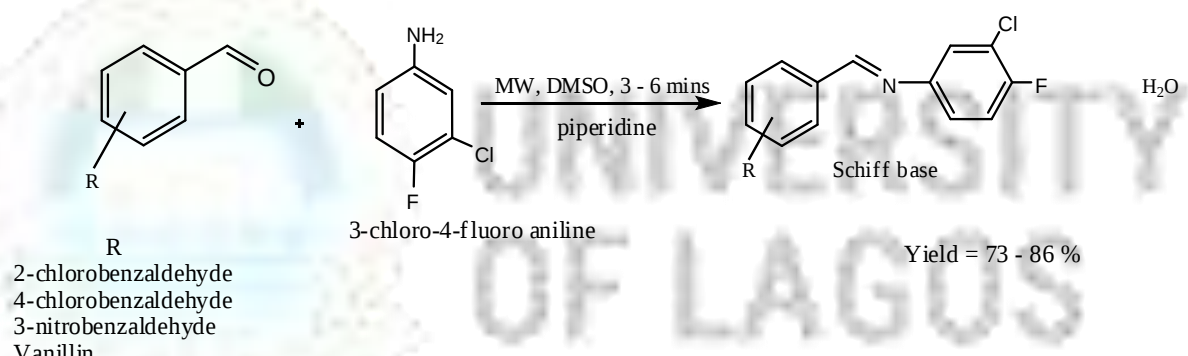
Microwave synthesis of Schiff bases have been performed using microwave irradiation. The approach uses very little solvent and can also be solvent free when using liquid reactants. The microwave-assisted condensation is usually carried out in a microwave for short reaction time usually minutes. Several research groups have reported synthesis of Schiff bases using microwave irradiation to be fast and efficient (Yang *et al.*, 2002, Yang and Sun, 2006, Gopalakrishnan *et al.*, 2006, Kamaria *et al.*, 2011).

Yang *et al.* (2002) have reported the rapid solvent-less synthesis of Schiff base under microwave irradiation using salicylaldehyde and substituted amino pyridine (Scheme 4).



Scheme 4: Microwave synthesis of salicylaldehyde and substituted amino pyridine Schiff base

Microwave irradiation was reported in the synthesis of substituted benzaldehyde and 3-chloro-4-fluoro aniline (Scheme 5) (Arshi *et al.*, 2009).

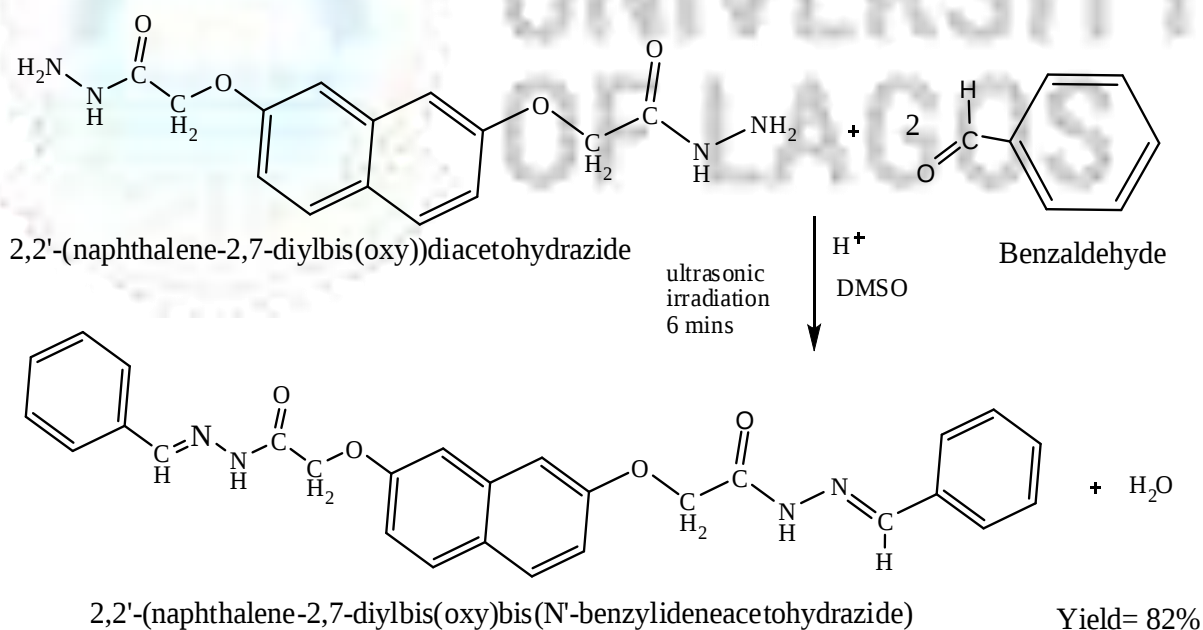


Scheme 5: Microwave synthesis of substituted benzaldehyde and 3-chloro-4-fluoro aniline Schiff base

Environmental restrictions on emissions, non-polluting and atom-efficient technologies have increased interest in such synthetic techniques. Furthermore, there are several advantages of performing synthesis using microwave irradiation, some of which include: increased safety, short reaction time, economic advantage due to absence or very little solvent. In addition, solvent free microwave processes are also clean and efficient.

2.3.5 Ultrasonic irradiation method

Ultrasound irradiation has been considered as a clean and useful method in the synthesis of organic compounds. Many homogeneous and heterogeneous reactions can be conducted smoothly by sonication to improve yield with increased selectivity. Ultrasonic irradiation involves the use of ultrasonic processor equipped with long probe, which is immersed directly in the reaction mixture. The synthesis of Schiff base derivatives containing naphthalene analogues by the reaction of 2,2'-(naphthalene-2,7-diylbis(oxy))diacetohydrazide with different substituted aryl/hetero aromatic aldehydes using ultrasonic method (Scheme 6) have been reported (Venkatesan *et al.*, 2011). Sonication was performed in a sonics, vibra cell, VC 130, ultrasonic processor equipped with a 3 mm wide and 140 mm long probe, which was immersed directly in the reaction mixture. The operating frequency was 20 kHz and the output power was 0 - 130 W.



Scheme 6: Synthesis of 2,2'-(naphthalene-2,7-diylbis(oxy))bis(N'-benzylideneacetohydrazide) using ultrasonic irradiation.

In comparison with other methods, this technique is more convenient and easily controllable. A large number of organic reactions can be carried out under milder conditions in shorter reaction time providing higher yield under ultrasound irradiation. The disadvantage is that expertise is required and the instrument is expensive.

2.4 Schiff Base Metal Complexes

Metal complexes consist of a central metal atom or ion surrounded by several atoms, ions or molecules, called ligands. The physicochemical properties of metal complexes have paved the way for their broad range of utilization in various areas of science. A number of dinuclear complexes from various ligand systems have been prepared and examined in terms of their oxygen uptake (Karlin and Zubieta, 1983) or redox processes of oxygen (Abuhijleh, 1997). Coordination compounds have been reported to act as enzyme inhibitors (Nora, 2007).

Metal complexes of penicillin with Ni(II), Zn(II), Cd(II), Fe(III) and La(III) were studied as part of efforts to understand the nature of metal drug interaction (Anaconda and Figueroa, 1999) and evaluate the antibacterial activity of *beta*-lactamic antibiotics. The penicillin binds to the metal through the amide and β -lactam groups. The weakening of the β -lactam bond increases bacteriacidal activity of the complexes compared to the free antibiotics.

Schiff base metal complexes (SBMCs) are obtained by reaction of SB ligand with transition metal ions. The high affinity for the chelation of Schiff bases towards the transition metal ions is utilized in preparation of their complexes (Cozzi, 2004). Transition metal complexes of Schiff bases are one of the most adaptable and thoroughly studied systems in bioinorganic chemistry (Mounika *et al.*, 2010). It is reported that the rapidly developing field of bioinorganic chemistry is centred on the presence of coordination compounds in living systems (Raymond and Abu-

Dari, 1977). Thus, Schiff base metal complexes may serve as models for biologically important species (Jayabalakrishnan and Natarajan, 2001).

Earlier reports (Hodnett and Dunn, 1972, Mounika *et al.*, 2010) revealed that metal chelation enhances activity of some bioactive compounds. *In-vitro* antibacterial studies of ciprofloxacin-imines and their complexes with Cu(II), Ni(II), Co(II), and Zn(II) showed that the metal complexes exhibited higher antibacterial activity than the uncomplexed ligands (Imran *et al.*, 2007).

The interactions of cephalothin (Hcephalo) with transition metal(II) ions and imidazole have also been investigated. The complexes [M(cephalo)Cl], (where M=Mn(II), Co(II), Ni(II), Pd(II)) and [M(cephalo)(Im)Cl] (where M=Ni(II), Cu(II), Zn(II), Im=Imidazole) were characterized and screened for antibacterial activity against some bacteria. The results were compared with the activity of cephalothin. The complexes were found to exhibit increased activity (Anaconda and Serranoa, 2003).

The metal complexing ability has also been exploited in their use as chromogenic reagents for determination of metal ions (Sawodny and Riederer, 1977). Schiff base having N₂O₂ donor groups which acts as a chromogenic reagent for determination of Ni in some natural food samples have been reported (Fakhari *et al.*, 2005). The determination of heavy metal ions, such as nickel, in environmental samples have become important as it poses a serious potential hazard to the human organism. United State Environmental Protection Agency has classified nickel as one of 13 priority metal pollutants for its widespread use (Patnaik, 1997). The knowledge of the nickel content in foods could be of a great interest for the dietary control of nickel-eczema patients and therefore the need to determine nickel content in biological samples such as plants and foods.

The high luminescent blue emitting nature of chelate complexes used in organic electroluminescent devices have been employed in flat-panel displays. This is based on electron transfer which plays a vital role in governing the pathway of chemical reactions. These reactions are employed in the study of electroactive species. Schiff base of calixarene have been reported for the preparation of complexes of blue luminescent zinc and beryllium (Wei *et al.*, 2003). The complexes exhibited one electron redox process.

2.5 Methods of Characterizing Schiff Bases and their Metal Complexes

Several spectroscopic methods have been used in the analysis of Schiff bases and their metal complexes. These include infrared (IR), nuclear magnetic resonance (NMR) and electronic absorption spectroscopy. The thermal analysis methods include thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). Magnetic moment measurements have also been used in assigning geometries to Schiff base metal complexes. All these elucidate different aspects of the structure.

2.5.1 Infrared spectroscopy

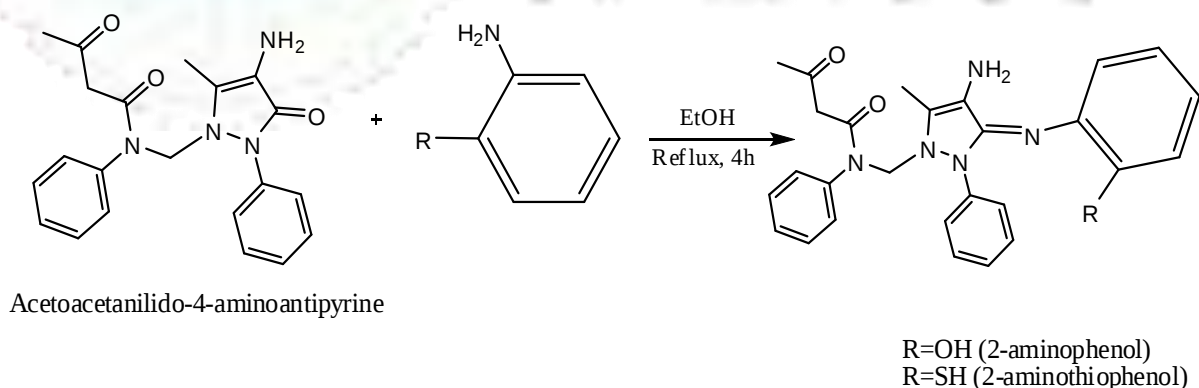
Infrared spectroscopy deals with the interaction of infrared radiation with matter. It is used to measure the vibrational frequencies of bonds in a molecule by scanning over a range of frequencies. Since each bond has a characteristic frequency, any frequency which matches the characteristic frequency of a bond will absorb infrared radiation. The IR spectrometer can therefore be used to detect functional groups and provide information about the type of bonds present. The kind of bond a compound has can be determined by the wavelength of light that are absorbed by a particular compound. The higher the frequency, the shorter the wavelength as shown in equation 1.

$$\bar{\nu} = \frac{1}{\lambda} = \frac{\nu}{C} \quad \text{----- Eqn 1}$$

$\bar{\nu}$ = wavenumber
 λ = wavelength
 ν = frequency
 C = speed of light

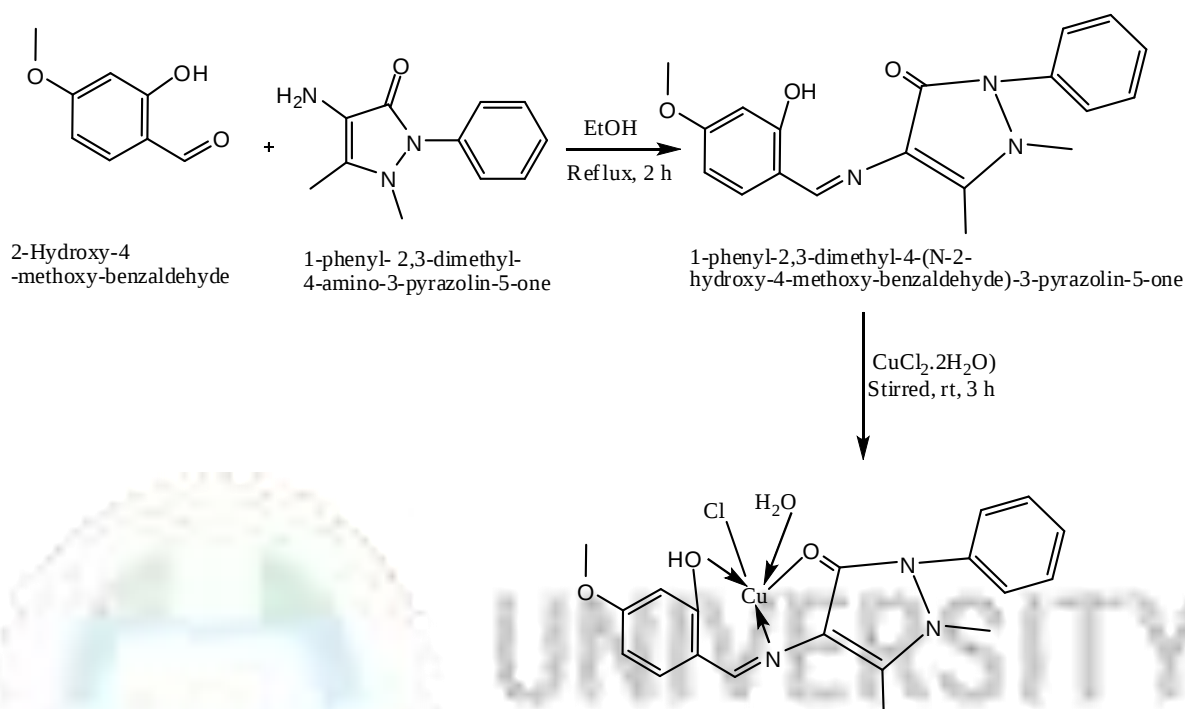
Vibrations can either involve a change in bond length (stretching) or bond angle (bending). The frequency of bond vibration is affected by the masses of the atoms in the bond and the strength of the bond. The lower the mass, the higher the vibration frequency.

A comparative study of IR spectra data of reported complexes with those of the free ligand gives meaningful information regarding bonding sites of the ligand molecule. IR spectral data of neutral tetradentate ligand derived from acetoacetanilido-4-aminoantipyrine and 2-aminophenol/2-aminothiophenol (Scheme 7) show bands around 3180 cm^{-1} for (O-H - -N=), and at 1520 cm^{-1} for (C=N), which decrease by $30\text{-}80 \text{ cm}^{-1}$ in the spectra of the complexes due to coordination (Raman *et al.*, 2003).



Scheme 7: Schiff base ligand synthesized from acetoacetanilido-4-aminoantipyrine and 2-aminophenol/2-aminothiophenol

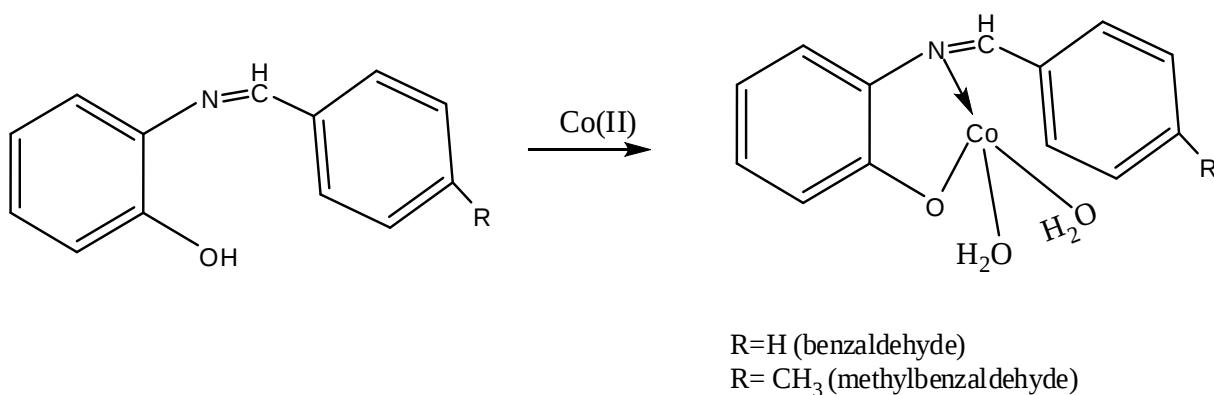
The IR spectra of Cu(II) complex containing O, N donor Schiff base have been reported (Scheme 8) (Rosu *et al.*, 2011).



Scheme 8: Synthesis of Cu(II) complex containing O, N donor Schiff base

The $\nu(\text{C}=\text{N})$ band of the ligand at 1629 cm^{-1} was found to be shifted to lower frequency ($1610\text{--}1602\text{ cm}^{-1}$) in the spectra of the complexes, indicating coordination via the azomethine nitrogen. These were confirmed by bands in the range $467\text{--}463\text{ cm}^{-1}$, which was assigned to the $\nu(\text{Cu}\text{--}\text{N})$ band. In the IR spectra of the ligand, a broad medium intensity band occurred in the $3500\text{--}3390\text{ cm}^{-1}$ range, attributed to the $\nu(\text{OH})$ vibration of the hydroxymethyl group. In the IR spectra of the complexes, peaks observed in the $3450\text{--}3434\text{ cm}^{-1}$ range supported the presence of $\nu(\text{H}_2\text{O})$ in the complexes. The phenolic $\nu(\text{C}\text{--}\text{O})$ stretching vibration in the free Schiff base was observed at 1135 cm^{-1} , which was shifted by $14\text{--}18\text{ cm}^{-1}$ towards lower wavenumbers in the complexes, indicating coordination of the phenolic oxygen to the Cu^{2+} ion.

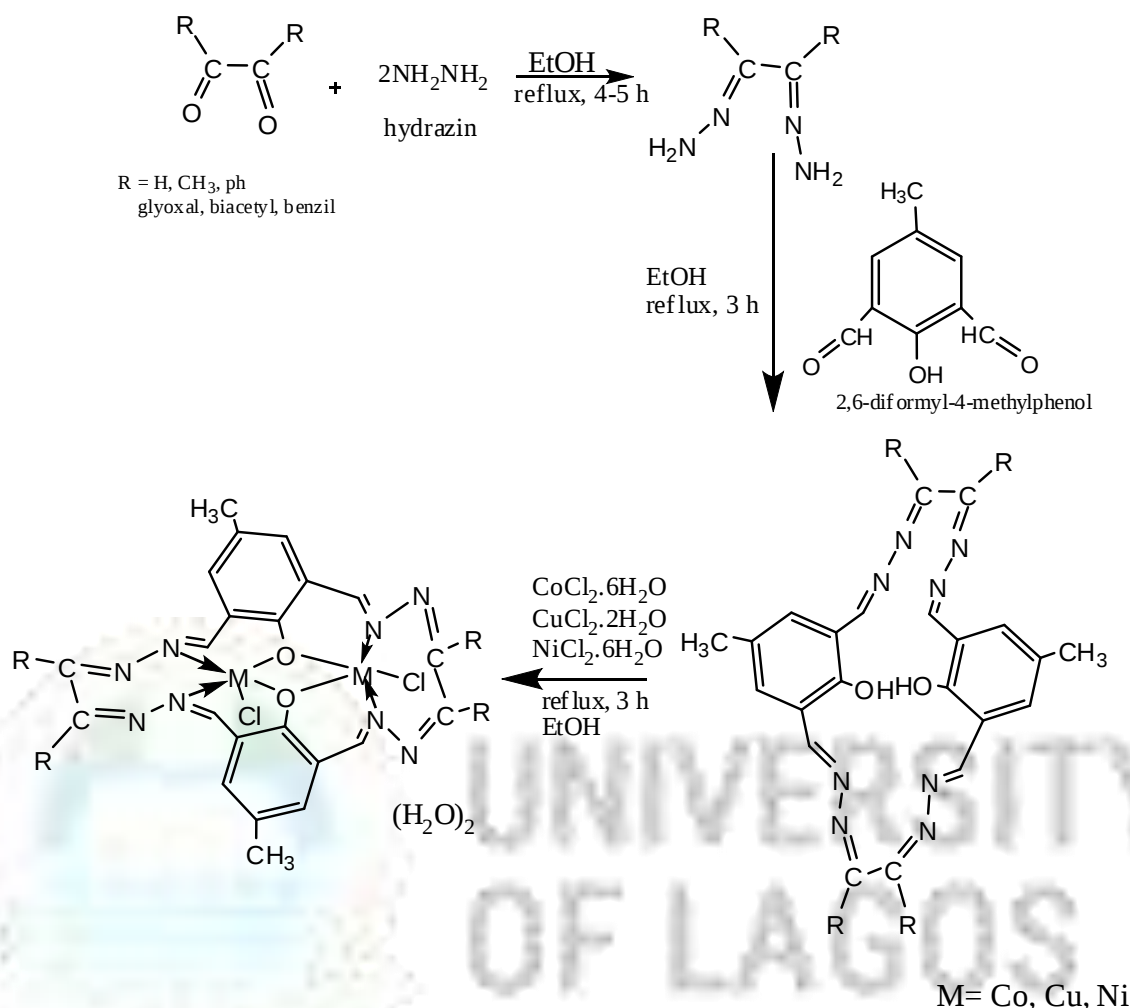
The synthesis and characterization of cobalt complexes with bidentate schiff bases have also been reported (Scheme 9) (Pandhare *et al.*, 2008).



Scheme 9: Synthesis of cobalt complexes with bidentate Schiff bases

The IR spectra of the free ligands showed an -OH absorption band in the region $3325\text{--}3419\text{ cm}^{-1}$. This sharp band disappeared in the complexes, indicating its involvement in the bond formation process. A strong band at $1618\text{--}1625\text{ cm}^{-1}$ due to C=N stretching frequency was lowered by $9\text{--}25\text{ cm}^{-1}$ in the spectra of the complexes, indicating coordination through azomethine nitrogen of the Schiff bases. The new bands appearing in the region $400\text{--}418\text{ cm}^{-1}$ and $500\text{--}599\text{ cm}^{-1}$ were reported to be due to the formation of $\nu(\text{M-N})$ and $\nu(\text{M-O})$ bonds respectively. The broad absorption band observed in all the complexes in the region $3200\text{--}3556\text{ cm}^{-1}$ were attributed to the lattice water present in the metal complexes.

Infrared spectra of novel glyoxal, biacetyl and benzil bis- hydrazide, 2,6-diformyl-4-methylphenol Schiff bases and their Co(II), Ni(II) and Cu(II) complexes (Scheme 10) exhibited a strong band at 1630 cm^{-1} , characteristic of the azomethine (C=N) stretching vibrations.



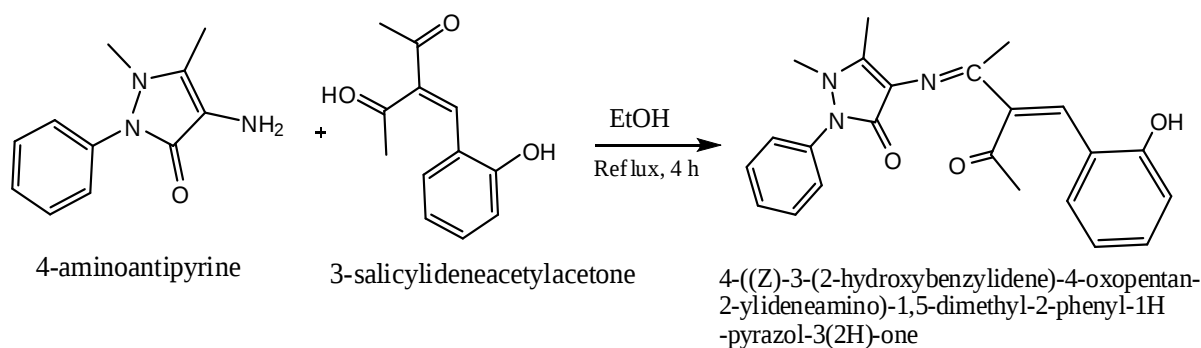
Scheme 10: Synthesis of glyoxal, biacetyl and benzil bis- hydrazide, 2,6-diformyl-4-methylphenol Schiff bases and their Co(II), Ni(II) and Cu(II) complexes

In the metal chelates, the band characteristic of the azomethine group was shifted to 1610-1590 cm^{-1} , suggesting coordination of the azomethine nitrogen atom to the metal ion. A high intensity band in the 1295-1285 cm^{-1} region, was assigned to phenolic $\nu(\text{C}-\text{O})$ vibrations. The presence of broad stretching vibrations in the 3440-3400 cm^{-1} region was attributed to coordinated or lattice water molecules in all the complexes. Bands in the regions 550-400, 474-400 and 340 cm^{-1} was assigned to $\nu(\text{M}-\text{O})$, $\nu(\text{M}-\text{N})$ and $\nu(\text{M}-\text{Cl})$ vibrations respectively (Lakshmi *et al.*, 2011).

2.5.2 ^1H -NMR spectroscopy

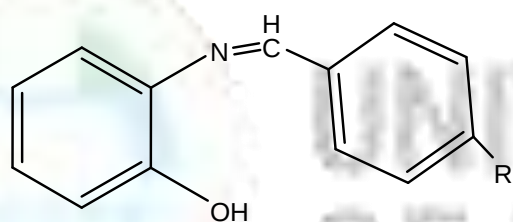
Nuclear magnetic resonance (NMR) spectroscopy is the study of molecular structure through the interaction of an oscillating radio-frequency electromagnetic field with a collection of nuclei immersed in an external magnetic field. Nuclear magnetic resonance (NMR) spectroscopy helps to identify the carbon-hydrogen framework of an organic compound. The number of signals in a ^1H NMR spectrum provides information on the kind of protons a molecule contains and the position of the signal suggests the type of protons present. These protons can be shielded or deshielded. A shielded proton requires a high applied field strength and a deshielded proton requires a lower applied field strength at which absorption occurs. Shielding shifts the absorption upfield, and deshielding shifts the absorption downfield. The presence of substituent groups affects the field strength around the protons. Electron withdrawing substituents lower the electron density in the vicinity of the proton and thus cause deshielding from the magnetic field while electron donating substituents increase the electron density in the vicinity of the proton which results in shielding from the magnetic field. The signal for these protons therefore occurs at a lower magnetic field (high δ) than the signal of the more shielded protons (low δ) which occurs at a higher magnetic field.

The proton NMR spectrum of ligand derived from 4-aminoantipyrine and 3-salicylideneacetylacetone (Scheme 11) showed the following signals: C_6H_5 as a multiplet at 6.9-7.5 δ and azomethine proton at 9.8 δ . The peak at 13.4 δ was attributed to the intramolecular bonded phenolic OH group present in salicylideneacetylacetone (Raman *et al.*, 2005).



Scheme 11: Schiff base synthesized from 4-aminoantipyrine and 3-salicylideneacetylacetone

The proton NMR spectra of a bidentate Schiff base (Figure 2) shows the following diagnostic signals: phenyl multiplets at 6.5-8.0 δ , azomethine protons at 8.65-9.10 δ . The peaks at 3.8 and 2.4 δ were attributed to OCH_3 and CH_3 group (Pandhare *et al.*, 2008).



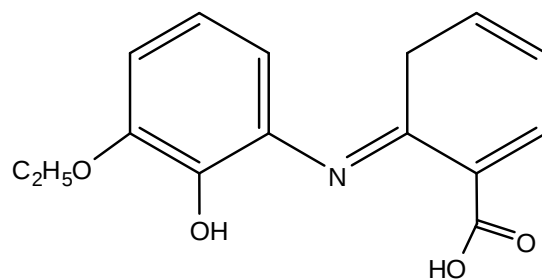
Bidentate Schiff bases

R=H (benzaldehyde)

R= CH_3 (methylbenzaldehyde)

Figure 2: Bidentate Schiff bases

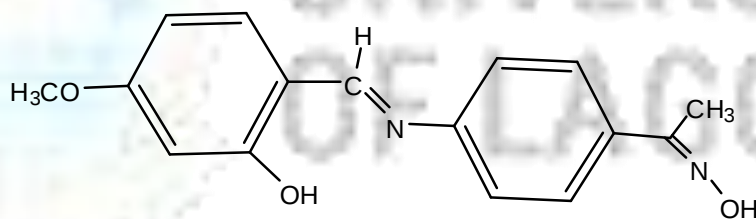
The ^1H NMR spectra of 3-ethoxy salicylidene aminobenzoic acid Schiff base (Figure 3) reported by Mounika *et al.* (2010) exhibited phenyl multiplets at 6.5-7.3 δ and the azomethine proton was seen at 7.6 δ (singlet). The peak at 10.8 δ was attributed to phenolic OH group present in the ligand. The peak at 1.5 δ , which appeared as a triplet, was assigned to $-\text{CH}_3$ group of ethoxy substituent on the benzene ring while peak at 4.1 δ , which showed as a quartet, was attributed to $-\text{CH}_2$ protons of the ethoxy substituent.



3-ethoxy salicylidene aminobenzoic

Figure 3: 3-ethoxy salicylidene aminobenzoic acid Schiff base

^1H -NMR spectra of 4-methoxysalicylidene-*p*-aminoacetophenoneoxime Schiff base ligand exhibited proton signals at 2.07 (s, 3H, $-\text{CH}_3$), 3.70 (s, 3H, $-\text{OCH}_3$), 6.34-7.34 (m, 7H, Ar-H), 8.50 (s, 1H, $\text{CH}=\text{N}_{\text{azomethine}}$), 10.87 (s, 1H, O-H oxime) and 13.46 (s, 1H, O-H phenolic) (Tuna *et al.*, 2006).



4-methoxysalicylidene-*p*-aminoacetophenoneoxime

Figure 4: 4-methoxysalicylidene-*p*-aminoacetophenoneoxime Schiff base ligand

2.5.3 Electronic absorption spectroscopy and magnetic moment measurements

The uv-vis spectroscopy measures the response of a sample to ultraviolet and visible range of electromagnetic radiation since the molecules and atoms have electronic transitions. Electronic transitions found in organic compounds include σ , π and n electrons while d and charge transfer transitions are found in complexes as shown in Figure 5 and 6.

The excitation of a molecule from its electronic ground state to an electronic excited state corresponds to absorption of light in the near-infrared, visible or ultraviolet regions of the spectrum.

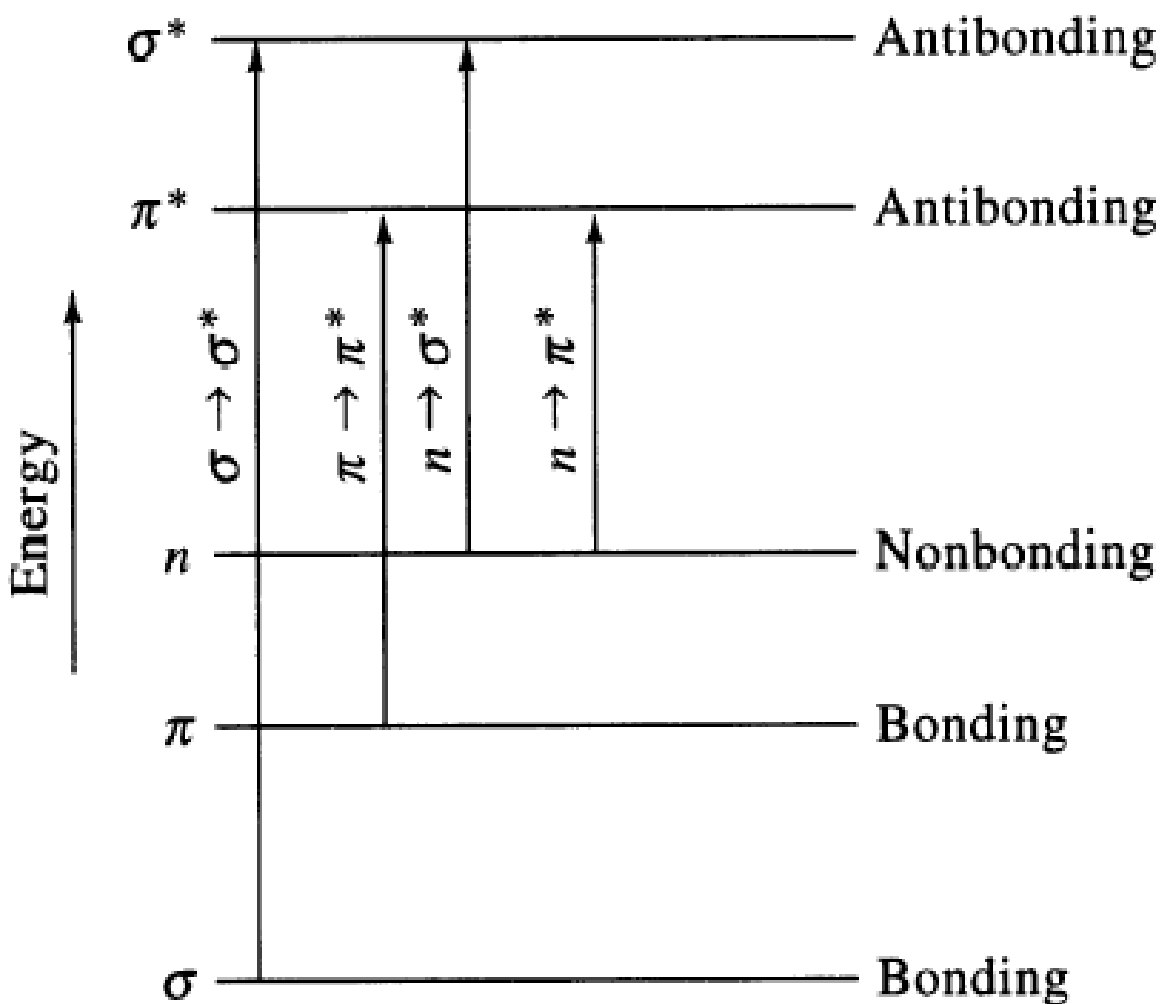


Figure 5 : Electronic transitions in organic compounds

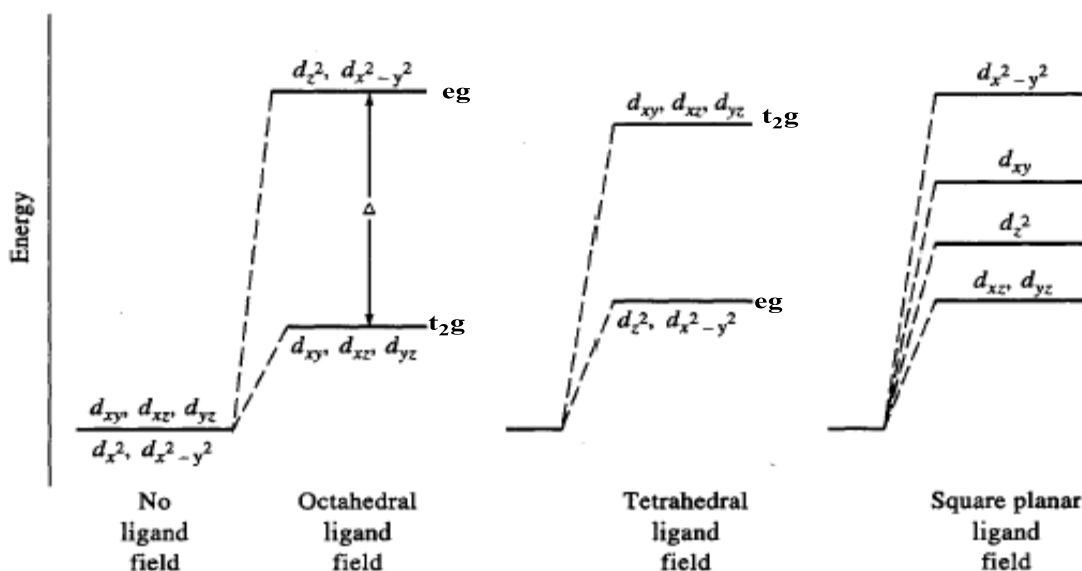
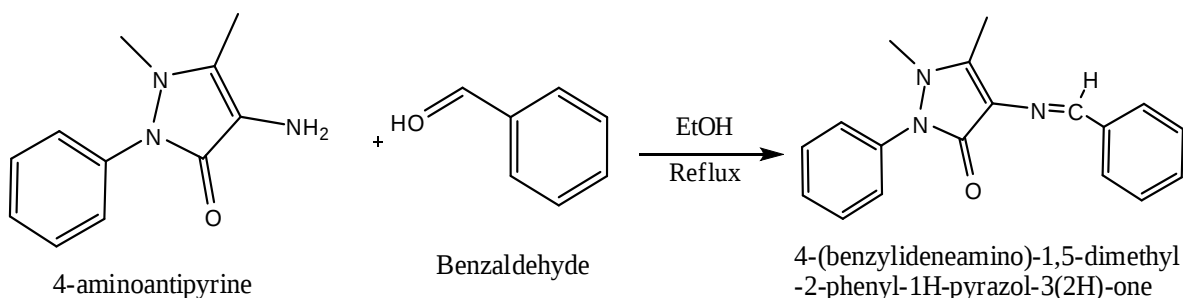


Figure 6 : Electronic transitions in metal complexes

The electronic transitions in organic compounds are usually observed in the 200-400 nm region. The first 2 bands located in the 204-270 nm is assigned to the excitation of the π -electrons of the aromatic ring ($\pi \rightarrow \pi^*$). The third band observed within the wavelength range 257-295 nm is usually due to transition between the π -orbital largely localized on the the central C=N bond. The fourth band within the wavelength range 305-360 nm is attributed to an inter-molecular charge transfer. Occasionally a fifth band could be observed due to polar solvents within the wavelength range 435-440 nm ascribed to intermolecular CT between solvent and the molecule (Soliman, 1997).

The electronic spectra of 4-aminoantipyrine and benzaldehyde (Scheme 12) in ethanol have been reported (Issa *et al.*, 2005).



Scheme 12: Schiff base derived from 4-aminoantipyrine and benzaldehyde

The ligands showed four main absorptions in ethanol between 200-400 nm. The first (210-234 nm) and second (240-281 nm) were assigned to $\pi \rightarrow \pi^*$ transitions of the aromatic ring. The band at 301-334 nm involved $\pi \rightarrow \pi^*$ transitions of the C=O and C=N groups; the longer wavelength band (325-396 nm) were assigned to an intramolecular charge transfer originating from the 4-aminoantipyrine ring to the C=O.

Electronic transitions are also observed in metal complexes. The spectra of transition metal complexes depend on the transition of unpaired electrons from the ground state to an excited state. Transitions may occur between the split d-levels of the central atom, giving rise to the *d-d* or ligand field spectra. The atomic overlap in metal—ligand bonds allows *d* electrons to penetrate from the central atom to the ligand, and *vice versa*. The transitions are affected by the effect of ligands on the energies of the *d* orbitals of the metal ions. Since octahedral, square-planar and tetrahedral fields cause splitting of d orbitals in different ways, the geometry will have a pronounced effect on the *d-d* transitions in a metal complex. Complexes with octahedral geometry has the t_{2g} (d_{xy} , d_{yz} , d_{xz}) and e_g ($d_x^2 - y^2$, d_z^2) orbital energy levels. They could be distorted octahedral complexes in which two trans metal-ligand distances are shorter or longer than the other four giving a tetragonal distortion; these complexes are said to be Jahn-Teller distorted. The Jahn-Teller theorem states that a non-linear molecule is unstable in a degenerate

state and will distort to remove the degeneracy, thus, the distorted complex is more favourable energetically than a regular octahedral complex (Housecroft and Sharpe, 2008).

The electronic absorption spectra are often very helpful in the evaluation of results furnished by other methods of structural investigation. For copper(II), two electrons will go into the $a_{1g} (d_z^2)$ and the other into $b_{1g} (d_x^2 - y^2)$ compared with three electrons in e_g for regular octahedral complex. A shoulder on the $d-d$ band of the electronic spectrum is a consequence of two closely spaced absorption bands overlapping, which arise from electronic transitions from the d_{xy} , d_{yz} , d_{xz} levels to a_{1g} and b_{1g} levels. Copper(II) (d^9) is nearly always found in a distorted ligand environment where the metal ion is surrounded by two elongated bonds opposite each other, and four shorter bonds in the xy plane. If the trans ligands are removed, a square planar geometry is obtained. Square planar complexes are particularly common at the end of the transition-metal series especially for ions with a d^8 and d^9 configuration. Palladium and platinum form many square-planar complexes. In a square-planar complex, the energy levels are; e_g which split into $a_{1g} (d_z^2)$, $b_{1g} (d_x^2 - y^2)$ and t_{2g} which split into $e_g (d_{xz}, d_{yz})$, $b_{2g} (d_{xy})$. For square planar complexes with $d_x^2 - y^2$ ground state, three spin-allowed transitions are possible, $^2B_{1g} \rightarrow ^2A_{1g} (d_x^2 - y^2 \rightarrow d_z^2 \dots v_1)$, $^2B_{1g} \rightarrow ^2B_{2g} (d_x^2 - y^2 \rightarrow d_{xy} \dots v_2)$, and $^2B_{1g} \rightarrow ^2E_g (d_x^2 - y^2 \rightarrow d_{xz}, d_{yz} \dots v_3)$ (Patel *et al.*, 2011). Square-planar complexes are usually observed with strong field ligands, weak field ligands form octahedral and tetrahedral complexes.

The orbital energy level for tetrahedral complexes consist of a lower $e (d_x^2 - y^2, d_z^2)$ and the higher $t_2 (d_{xy}, d_{yz}, d_{xz})$ levels. Virtually all tetrahedral complexes are high spin due to the smaller-crystal field splitting, thus, the bands in the spectra would be expected to be at lower wavenumber (longer wavelength) than those in the octahedral complexes. The tetrahedral complexes are also

far more intense than their octahedral counterparts at the same concentration. This is because they do not possess a center of symmetry.

A charge transfer transition involves high energy absorption greater than $d-d$ transition (Figure 7). The electron moves between orbital, i.e from metal to ligand or ligand to metal. Ligand metal charge transfer is observed in high oxidation state metal ion and lone pair ligand donor while metal ligand charge transfer is obtained in low oxidation state metal.

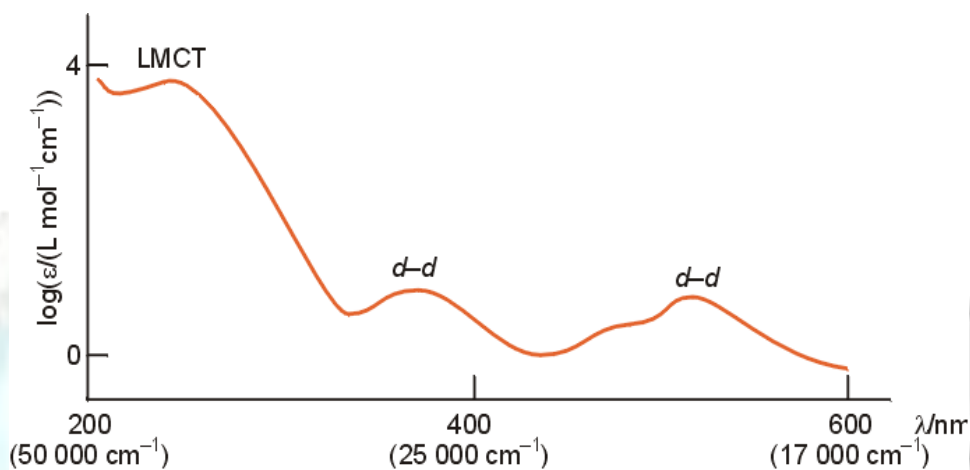
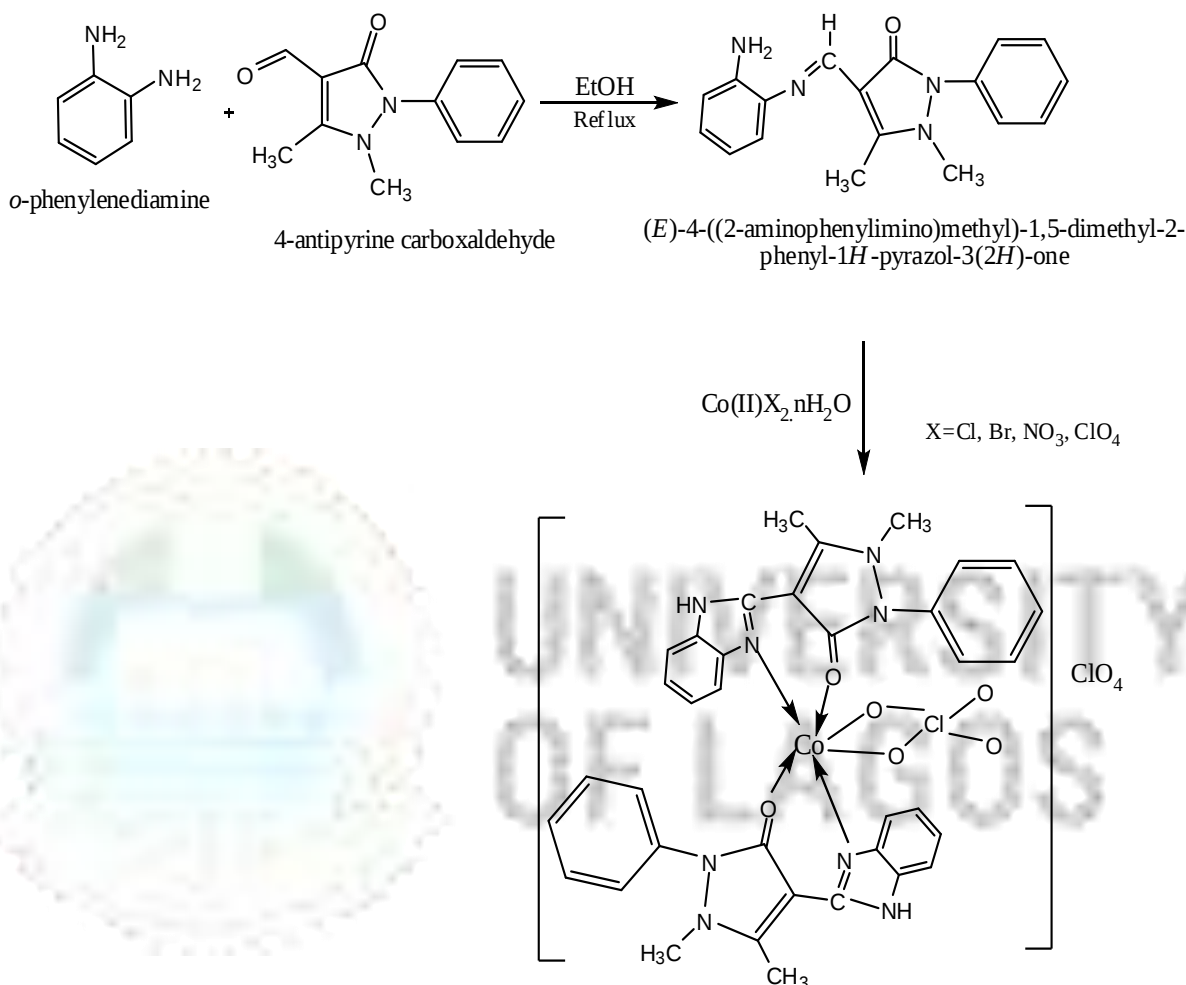


Figure 7: Spectra showing charge transfer and $d-d$ transitions in complexes

The spectral data of transition metals provide useful information about the structure of complexes. The spectra of numerous transition metal complexes containing different Schiff-base ligands have been described in literature (Kamounah *et al.*, 1998, Herzfeld and Nagy, 1999). The spectra display electronic transitions characteristic of ligands and metal ions in coordination. These spectra are sensitive to the type of ligand and have prove to be useful in identification of particular complex species. In the regular tetrahedral and near tetrahedral Co(II) complexes only one $d-d$ transition [${}^4A_2(F) - {}^4T_1(P)$] was observed in the visible region. These transitions have also been reported for tetrahedral $[Co(NCS)_4]^{2-}$ at 615 nm (Lever, 1984).

Several authors have studied changes in spectra upon the addition of metal ions. Some also interpreted the $d-d$ transitions of such metal complexes. The electronic spectra of Schiff base

obtained from condensation of *o*-phenylenediamine and 4-antipyrine carboxaldehyde and its cobalt(II) complex have been reported (Scheme 13) (Vimal-Kumar and Radhakrishnan, 2010).



Scheme 13: Schiff base synthesized from *o*-phenylenediamine and 4-antipyrine carboxaldehyde and its cobalt(II) complex

The Schiff base exhibited two main peaks at about 387 and 252 nm which were assignable to the $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions respectively. The $n \rightarrow \pi^*$ band was blue shifted to the 376-384 nm region while the $\pi \rightarrow \pi^*$ band was red shifted to the 254-258 nm region. The room temperature μ_{eff} values 4.30, 4.26, and 4.20 BM were observed for tetrahedral cobalt(II) complexes.

Rosu *et al.* (2011) reported charge transfer band for complexes in the range 26,300-25,000 cm^{-1} with a shoulder at 23,250-22,250 cm^{-1} . The values of μ_{eff} (1.76-2.06 BM) for complexes

suggested the presence of an unpaired electron. It also indicated the existence of monomeric species of copper(II). The very low magnetic moment of 1.44 BM per copper center indicates that the copper centers were antiferromagnetically coupled. The magnetic moments of cobalt complexes have been reported in the range 4.64-5.21 BM (Pandhare *et al.*, 2008). These values agree with the previously reported experimental values in range 4.70-5.20 BM for high spin octahedral cobalt complexes (Lever, 1968).

The electronic absorption spectra of Co(II), Ni(II) and Cu(II) complexes with macrocyclic Schiff bases (Figure 8) have been studied with a view to obtaining more information on the configuration of the complexes (Lakshmi *et al.*, 2011).

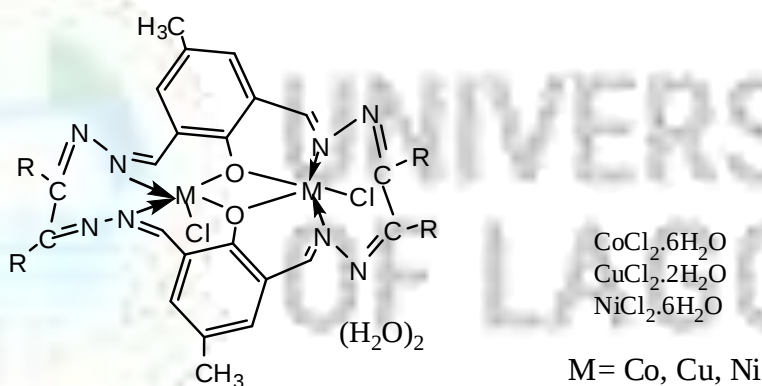


Figure 8: Macrocyclic Schiff base metal complexes

The electronic spectra of the Co(II) complexes exhibited absorption bands in the regions 10,965, 17,134 and 19,972 cm^{-1} which were assigned to the transitions $^4\text{A}_2 + ^4\text{E} \rightarrow ^4\text{B}_1$, $^4\text{A}_2 + ^4\text{E} \rightarrow ^4\text{E}$ (P) and $^4\text{A}_2 + ^4\text{E} \rightarrow ^4\text{A}_2$ (P) respectively and were characteristic of a square pyramidal geometry. The Cu(II) complexes exhibited high intensity band at 27,468 cm^{-1} attributed to $\text{L} \rightarrow \text{M}$ charge transfer transition.

The electronic spectra of Cu(II) complexes have showed three bands at 10,972, 14,828 and 23 156 cm^{-1} , and these bands have been assigned to the transition $^2\text{B}_1 \rightarrow ^2\text{A}_1$ (ν_1), $^2\text{B}_1 \rightarrow ^2\text{B}_2$ (ν_2) and $^2\text{B}_1 \rightarrow ^2\text{E}$ (ν_3) respectively. These transitions were characteristic of a square pyramidal

geometry . The magnetic moments of the Co(II) complexes exhibited values around 4.23-4.84 BM which were lower than the spin only values and indicated weak antiferromagnetic coupling interactions between the metal ions, confirming dinuclear nature of the complexes. The Cu(II) complexes showed a magnetic moment value around 1.45 BM considerably lower than the spin only value. The low value of the magnetic moment was attributed to an antiferromagnetic coupling interaction between two metal ions. These fact suggests dinuclear nature of Cu(II) complexes.

The electronic spectra of Cu(II) complexes reported by Mounika *et al.* (2010) (Figure 9) consist of a low intensity band at $16,583\text{ cm}^{-1}$ assignable to ${}^2T_{2g} \leftarrow {}^2E_g$ transition. A high intensity band in the region $24,096\text{--}32,258\text{ cm}^{-1}$ was due to symmetry forbidden ligand $\rightarrow$ metal charge transfer and sharp bands observed at $38,461\text{ cm}^{-1}$ were due to ligand bands. The magnetic moment of Cu(II) complex was seen at 1.61 BM corresponding to one unpaired electron with a slight orbital contribution to the spin-only-value and the absence of spin-spin interactions. On the basis of electronic spectra and magnetic susceptibility measurements, a distorted octahedral geometry around Cu(II) was suggested. The electronic spectra of Co(II) complex showed bands at $16,286\text{ cm}^{-1}$, $27,027\text{ cm}^{-1}$ and $32,051\text{ cm}^{-1}$ which corresponds to the transitions ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ (ν_1) , ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ (ν_2) and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ (ν_3). The magnetic moment of Co(II) complex was seen at 5.01 BM within the expected range of 4.7-5.2 BM for octahedral geometry. The electronic spectra of Ni(II) complex showed three bands around $16,077\text{ cm}^{-1}$, $26,178\text{ cm}^{-1}$ and $32,467\text{--}37,735\text{ cm}^{-1}$ corresponding to the transitions ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}$ (ν_1), ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ (ν_2) and ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ (ν_3). The magnetic moment of Ni-complex was seen at 3.32 BM within the range of 2.5-3.5 BM for octahedral Ni(II) complexes.

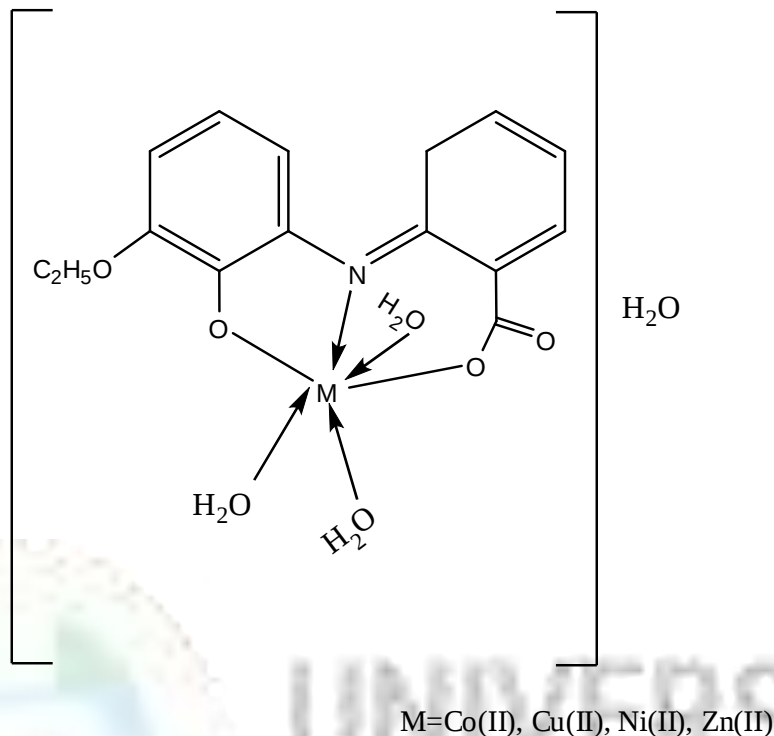


Figure 9: Octahedral structure of metal (II) complexes

The electronic spectra and magnetic properties of polymer metal complexes using DMSO- d_6 as solvent have been reported (Nishat *et al.*, 2010). Electronic spectra of the copper(II) complex showed broad bands centered at 25,000 and 16,556 cm^{-1} , which were due to square planar configuration; the magnetic moment value of Cu(II) complex at 1.70 BM was in accord with square planar geometry. The magnetic moment value of polymer Schiff base complex, PSB-Co(II) was 3.95 BM and the electronic absorption spectra showed three bands at 16,584, 23,310, and 29,412 cm^{-1} due to ${}^4T_{2g}(F) \leftarrow {}^4T_{1g}(F)$, ${}^4A_{2g}(F) \leftarrow {}^4T_{1g}(F)$ and ${}^4T_{1g}(P) \leftarrow {}^4T_{1g}(F)$ transitions. These observations suggested an octahedral environment for Co(II). PSB-Ni(II) showed three bands at 16,583, 25,510 and 29,762 cm^{-1} due to ${}^3T_{2g}(F) \leftarrow {}^3A_{2g}(F)$, ${}^3T_{1g}(F) \leftarrow {}^3A_{2g}(F)$, and ${}^3T_{1g}(P) \leftarrow {}^3A_{2g}(F)$, respectively. The μ_{eff} value 2.79 BM was observed in the range expected for the spin only value for two unpaired electrons in an octahedral or distorted octahedral geometry.

Tuna *et al.* (2006) have reported the electronic absorption spectra of 4-methoxysalicylidene-*p*-aminoacetophenoneoxime ligand and its metal complexes (Figure 10).

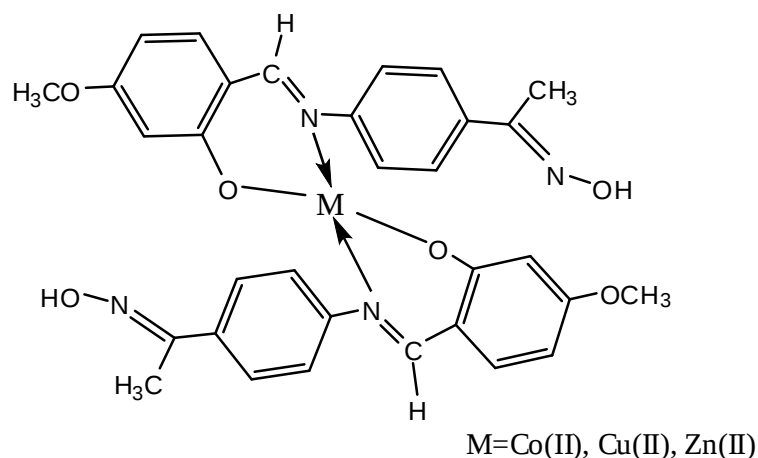


Figure 10: 4-methoxysalicylidene-*p*-aminoacetophenoneoxime Schiff base and its metal complexes

The aromatic band of 4-methoxysalicylidene-*p*-aminoacetophenoneoxime ligand at 270 nm was attributed to benzene $\pi \rightarrow \pi^*$ transition. The band around 390 nm was due to the $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the nitrogen of the azomethine group in the Schiff base. The complexes of the cobalt(II) and copper(II) showed less intense shoulders at *ca* 565–660 nm ($\epsilon = 155\text{--}190 \text{ L mol}^{-1} \text{ cm}^{-1}$), which were assigned to *d-d* transition of the metal ions. The bands were probably due to the $^4A_2 \rightarrow ^4T_1$ (P) for Co(II) and $^2T_2 \rightarrow ^2E$ (G) for Cu(II) transition of tetrahedral geometry. The complexes showed an intense band at *ca* 375–390 nm which was assigned to $n \rightarrow \pi^*$ transition associated with azomethine linkage. The spectra of the complexes showed intense band at *ca* 420–435 nm ($\epsilon = 1.60\text{--}4.05 \times 10^3 \text{ L mol}^{-1} \text{ cm}^{-1}$), which was assigned to charge transfer transition in tetrahedral geometry. Cobalt(II) and copper(II) complexes were paramagnetic while the zinc(II) complex was diamagnetic. The observed magnetic moment values of the cobalt(II) and copper(II) complexes were 4.23 and 1.76 BM respectively which were characteristic for mononuclear tetrahedral complexes.

2.5.4 Thermal analysis of Schiff base metal complexes

Thermal analysis (TA) involves a group of techniques in which changes in physical or chemical properties of the sample are monitored against time or temperature, while the temperature of the sample is programmed. The temperature program may involve heating or cooling at a fixed rate. Thermal analyses comprises a wide variety of techniques such as; thermogravimetric analysis (TGA), differential thermal analysis (DTA), differential scanning calorimetry (DSC), thermal mechanical analysis (TMA), temperature resolved X-ray diffraction, thermomagnetometry, thermoconductometry and dilatometry. The most common thermal analysis used are TGA and DSC. Thermal stability of materials, estimated lifetime of a product, decomposition kinetics of materials, moisture and volatile content of materials are obtained from the TGA study while the DSC graph gives the glass transition temperature (T_g), crystallization temperature (T_c), melting temperature (T_m) and sample purity of the materials.

As thermal energy is supplied to the sample, its enthalpy increases and its temperature rises by an amount determined, for a given energy input, by the specific heat of the sample. The specific heat of a material changes slowly with temperature in a particular physical state, but alters discontinuously at a change of state. The supply of thermal energy may induce physical or chemical processes in the sample, e.g. melting or decomposition, accompanied by a change in enthalpy, the latent heat of fusion, heat of reaction and phase transformation.

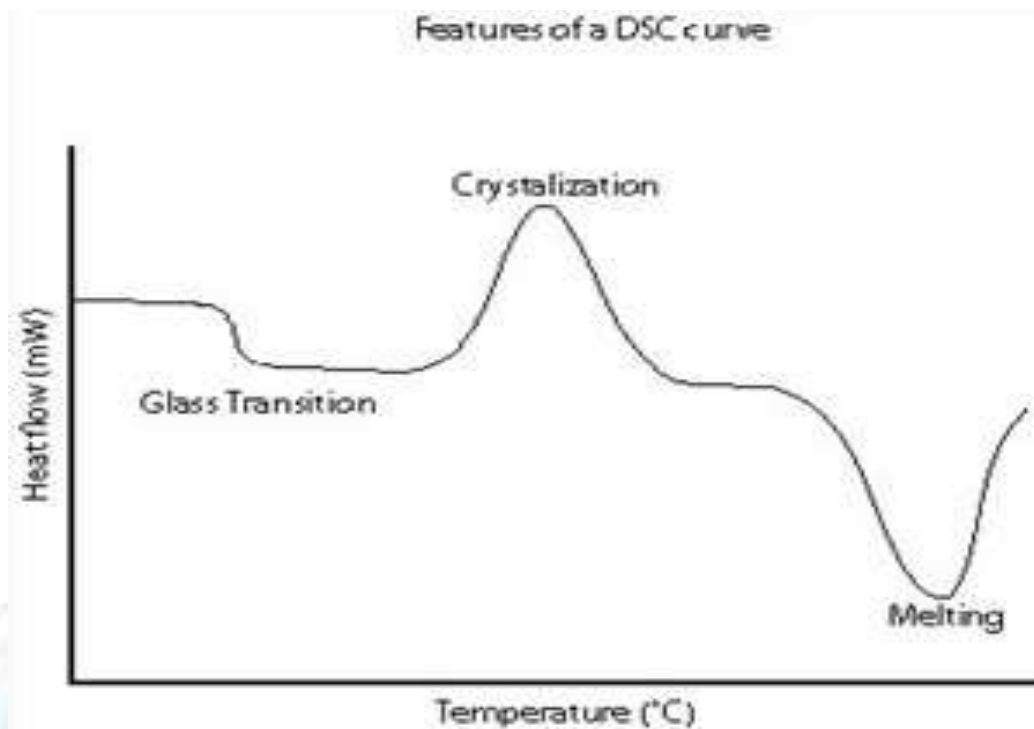


Figure 11: Features of a DSC curve

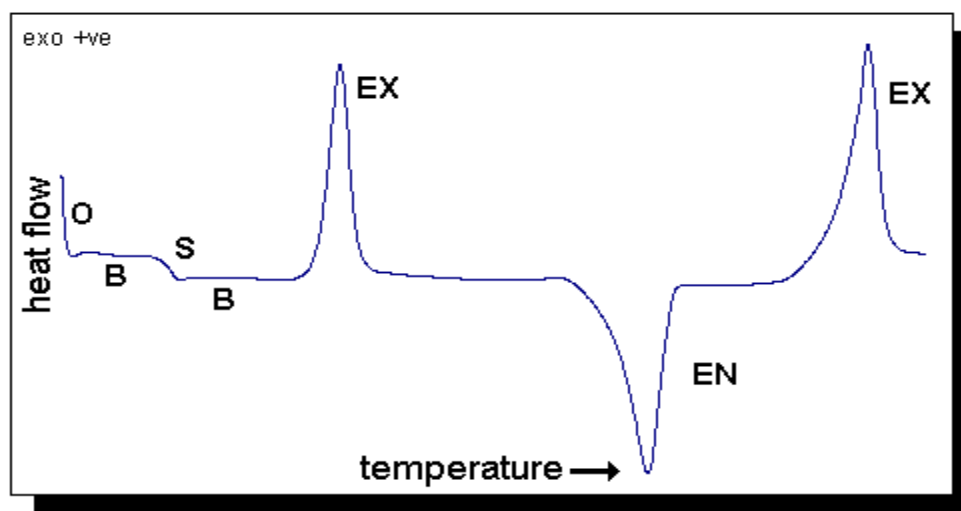


Figure 12: A DSC curve showing exothermic peak and endothermic peak

Where O= offset, B=baseline signal, S=step change EX = Exothermic peak, EN = Endothermic peak

The Figures 11 and 12 show the exothermic peak which results due to phase transitions such as crystallization, glass transition and endothermic peak which is observed during melting of a compound. The percentage mass loss with temperature ranges are typified in Figures 13 and 14 while the relationship is shown in equation 2.

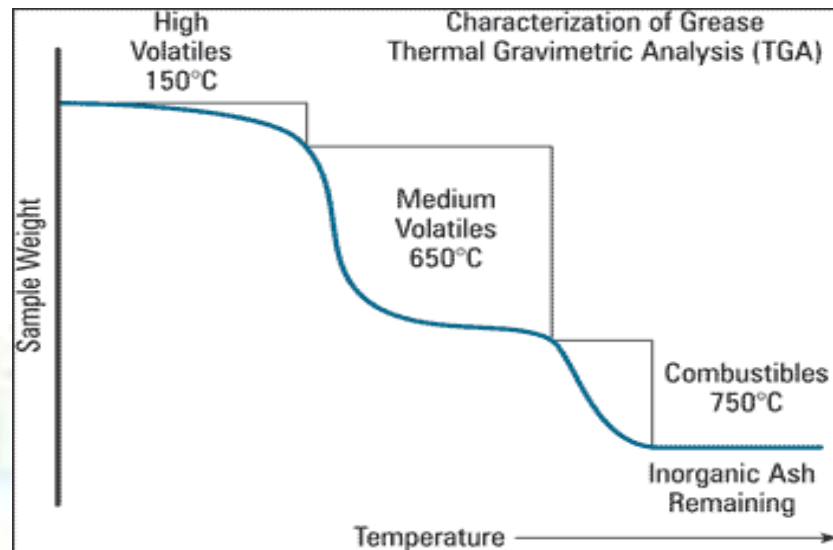


Figure 13: A TGA curve showing temperature ranges of combustible fragments

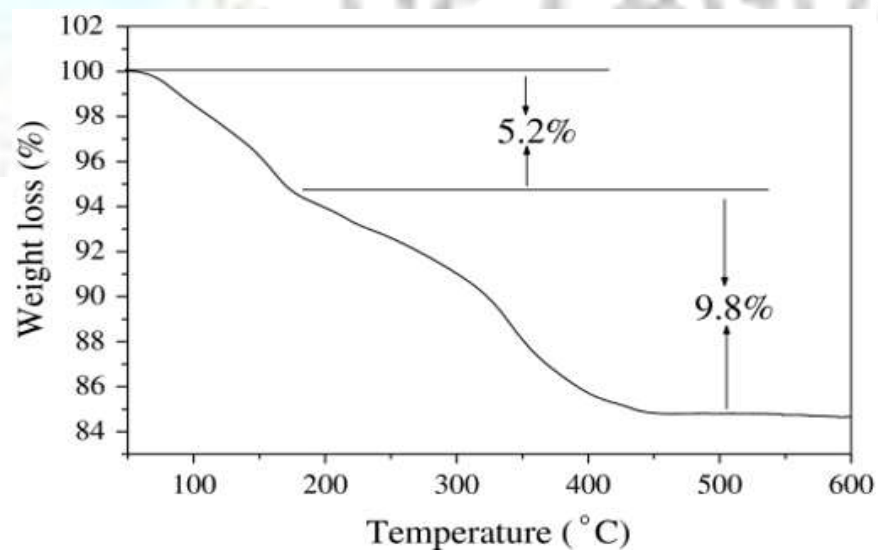


Figure: A TGA curve showing % weight loss

Calculation of percentage mass loss

$$\% \text{ Mass loss} = \frac{\text{mass of molecule lost}}{\text{molecular mass of compound}} \times \frac{100}{1} \text{ ----- Eqn 2}$$

Equation 2 shows the calculation of percentage mass loss of a compound. Thermal studies for Co(II), Ni(II) and Cu(II) complexes of macrocyclic Schiff bases showing gradual decomposition of complexes with the formation of the respective metal oxide above 400 °C have been reported (Lakshmi *et al.*, 2011). These studies were used in confirming the proposed chemical structures using the percentage loss of compounds. The thermal decomposition of Co(II), Ni(II) and Cu(II) complexes occurred in three steps, indicated by DTG peaks corresponding to the mass loss of coordinated water molecules, aldehyde moieties and bis-hydrazone moieties.

The thermal behavior of 4-methoxysalicylidene-*p* aminoacetophenoneoxime and its complexes with Co(II), Cu(II) and Zn(II) from ambient to 500 °C at a heating rate of 10 °C/min have been reported (Tuna *et al.*, 2006). The decomposition temperature and the weight losses of the ligand showed that the ligand was stable up to 207 °C and its decomposition started at 207 °C. Thermogravimetric studies of the complexes showed no weight loss up to 223 °C, indicating absence of coordinated water molecule in the complexes. It was reported that the different groups (OCH₃, OH) in the ligand led to a decrease in the stability of the complexes. The complexes were heated to higher temperatures and they decomposed to give oxides as final products.

Nishat *et al.* (2010) studied the thermal decomposition of a polymeric Schiff base and its metal(II) complexes. The thermograms showed two step decomposition with the first, faster than the second step. It was attributed to the non-coordinated part of the ligand decomposing first, while the coordinated part decomposed later. In the Mn(II), Co(II), and Ni(II) polymer metal complexes, the curve showed 8-15 % weight loss corresponding to two water molecules up to

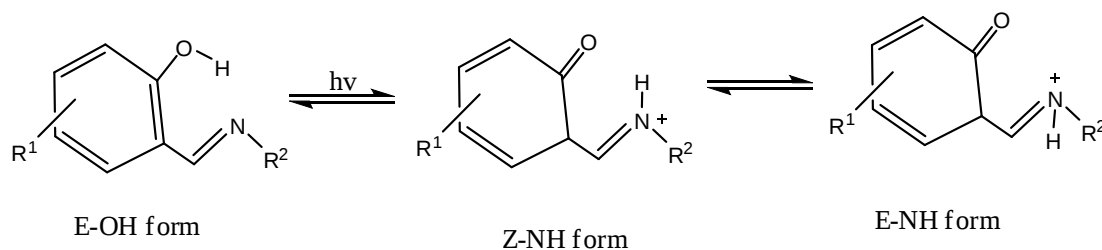
150 °C. The presence of water in these polymer metal complexes were also supported by IR studies. In the case of Cu(II) and Zn(II) polymers, the weight lost corresponded to lost solvent or absorbed water up to 150 °C. For the PSB, a steady and regular loss of weight was observed, and at 300 °C the weight lost was about 35 %. The temperature of maximum rate of decomposition for the ligand was 700 °C and the entire ligand was lost by 800 °C, whereas the polymer metal complexes lost only 75-90 %. These suggests that all the polymer metal complexes had higher thermal stability than the PSB due to chelation. The factor responsible for increased thermal stability of the polymer metal complexes were attributed to increase in molecular weight due to joining of two different polymer chains. The thermal stability of the polymeric compounds were in the order Cu(II) > Zn(II) > Ni(II) > Co(II) > Mn(II) > PSB. The greater stability of Cu(II) polymer metal complex compared with other polymer metal complexes were reported to be in agreement with the spectrochemical series, according to which Cu(II) polymer metal complex was always more stable than other polymer metal complexes.

2.6 Properties and Applications of Schiff Bases and Schiff Base Metal Complexes

Schiff bases and their metal complexes have been studied for their interesting properties and variety of applications. These include;

2.6.1 Photochromic properties

Photochromism is an optical phenomenon in which reversible transformation of a chemical species between two forms having different absorption spectra by absorption of electromagnetic radiation is observed (Bouas-Laurent and Durr, 2001, Hidetaka and Kiyoshi, 2010).



Scheme 14: Photochromism in Schiff bases

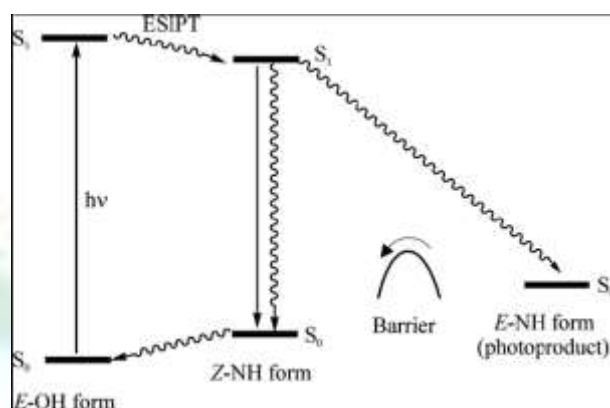


Figure 15: Energy diagram of photochromism in Schiff bases

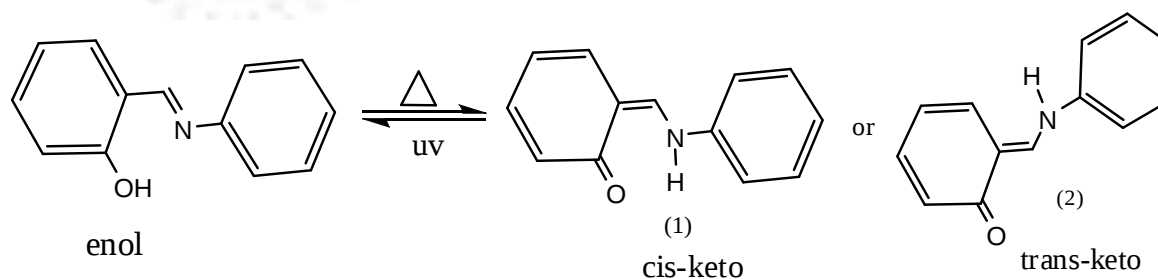
The mechanism of photochromism in Schiff bases is associated with the excitement of a proton to a $\pi \rightarrow \pi^*$ state from where the hydroxylic proton is quickly transferred to the imine atom (excited state intramolecular proton transfer (ESIPT)) with the formation of fluorescent Z-keto tautomer ($\pi \rightarrow \pi^*$ state) which may undergo relaxation to a ground state E-keto isomer (photochromic form) or return back to the ground state either by a thermal process or by fluorescence (Figure 15) (Ohshima *et al.*, 2004).

The chemical species can exist in two forms with different absorption spectra (Scheme 14). Absorption of radiation results in transformation of one form into another and such is associated by a color change. The more thermodynamically stable form is transformed by irradiation into the less stable form. Reversal to the more stable form can occur either thermally or photochemically. Photochromic compounds have the ability to optically transform between two

spectroscopically distinct states hence they have been utilized in the construction of novel photo-switching devices, supramolecular architectures, variable transmission lenses, and molecular scale optical data storage (Crano and Guglielmetti, 1999, Al-Kaysi and Bardeen, 2007, Yamada *et al.*, 2008).

Various organic compounds show photochromism based on established processes such as cis/trans isomerization, pericyclic reactions, intramolecular hydrogen transfer reactions, and dissociation processes (Brown, 1971, Irie, 2000, Bouas-Laurent and Durr, 2003).

Schiff bases have been reported to undergo photochromism in the solid state, crystalline state, rigid glasses and in solution by intramolecular hydrogen transfer reactions (Schmidt, 1967, Hadjoudis *et al.*, 1987). The hydrogen transfer reaction occurs *via* a six-membered cyclic ring transition state and produces enol-keto tautomeric species with the spectra of keto form bathochromically shifted. Screening of polycrystalline powders of N-salicylidene Schiff bases derived from mono-substituted aniline and mono, di- and tri-substituted salicylaldehyde for photochromism and thermochromism revealed that *o*-substitution in the aniline favours appearance of photochromism (Hadjoudis *et al.*, 1987)



Scheme 15: Photochromism in N-salicyldeaniline

In the photochromic compound, the colorless ground-state enol form, upon illumination with UV light, changes to any colour of the keto form through the hydrogen bridge with a rotation around the central C=N double bond, thus having a *trans*-keto configuration (Scheme 15). The spectra of

these compounds were recorded after UV-irradiation. The *cis*-keto form absorbed at longer wavelength; raising the temperature increases the population of this form and thus a deepening of color is observed. In contrast, a higher energy was required for hydrogen transfer in the ground-electronic state of molecules in photochromic crystals; as a result no absorption attributed to the *cis*-keto form was observed. Hydrogen transfer however occurred in the excited-electronic state, and the crystal structure was sufficiently open to permit a subsequent geometric isomerization which lead to the *trans*-keto photoproduct.

Harada and co-workers (1999) have also studied the photoform of salicylideneanilines by X-ray diffraction analysis. The photoreaction was performed by two-photon irradiation of N-3,5-di-*tert*-butylsalicylidene-3-nitroaniline at 730 nm which yielded dark-red photoproduct. Light easily penetrated into the crystals and gave molecules with the same energy as one-photon excitation. The result revealed that the structure of the colored species is the E-NH form. After irradiation with light at $\lambda > 530$ nm the dark-red crystal returned to the original pale yellow color.

2.6.2 Fluorescence properties

Fluorescence is the visible or invisible radiation produced from compounds as a result of incident radiation of a shorter wavelength such as X-rays or ultraviolet light. It involves a compound absorbing light of short wavelength and emitting light of longer wavelength. Nitrogen-containing ligands such as anthracene, stilbene and Schiff bases have attracted much attention due to their ability to absorb light of short wavelength and emit light of longer wavelength, hence their good performance in sensor technologies and electroluminescent devices (Das *et al.*, 2007, Shao *et al.*, 2009). Schiff bases and their metal complexes have attracted great interest due to intermolecular hydrogen bonding or aromatic $\pi \rightarrow \pi^*$ interactions in these compounds (Ruiz *et al.*, 1984, Bhattacharjee *et al.*, 2010, Fan *et al.*, 2010). These interactions has afforded the construction of luminescent compounds for various applications as chemical sensors, in photochemistry, and

electroluminescent display (McGarrah *et al.*, 2001). Application of many new analytical devices requires the presence of organic reagents as essential compounds of the measuring system. These organic reagents are used in optical and electrochemical sensors, as well as in various chromatographic methods, to enable detection of enhanced selectivity and sensitivity (Valcarcel and Laque de Castro, 1994, Spichiger-Keller, 1998). Fluorescent lighting have been found to be energy-efficient than incandescent lighting elements.

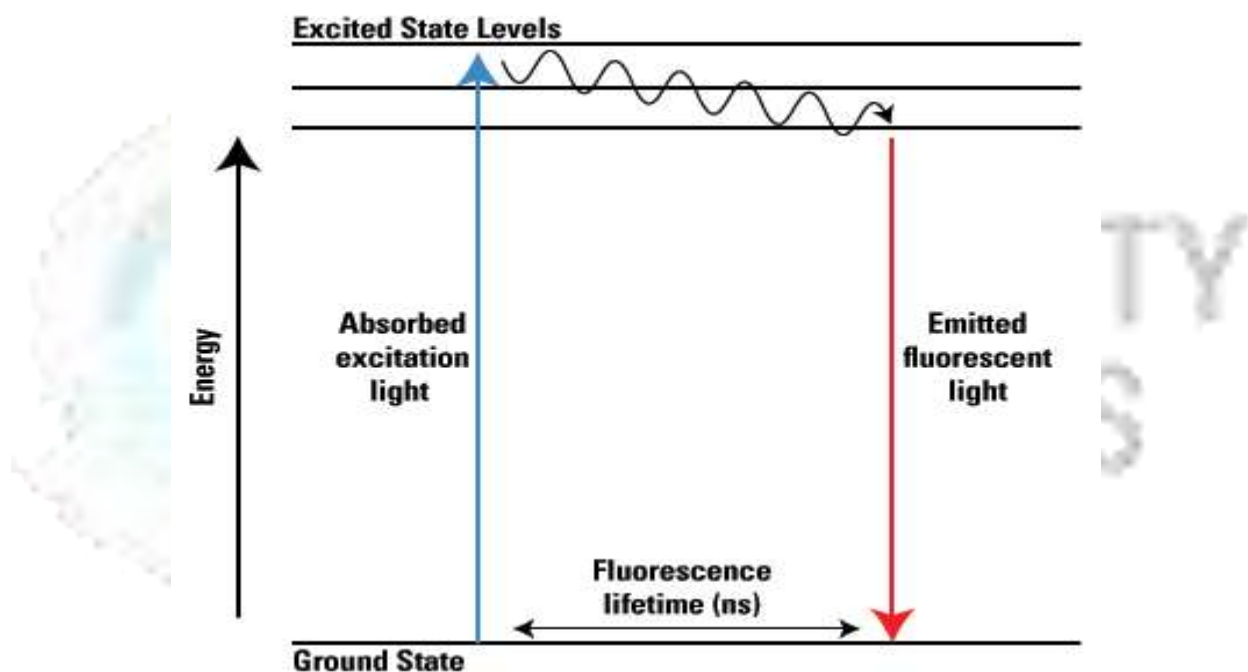


Figure 16: Energy diagram of Fluorescence

Electrons of fluorescent molecule absorb a photon of light, which raises the energy level of the electron to an excited state. During this short excitation period, some of the energy is dissipated by molecular collisions or transferred to a proximal molecule, and then the remaining energy is emitted as a photon to relax the electron back to the ground state (Figure 16). It is observed that the emitted photon usually carries less energy and therefore has a longer wavelength than the

excitation photon, the emitted fluorescence can be distinguished from the excitation light. The excitation and photon emission from a fluorophore is cyclical, and until the fluorophore is irreversibly damaged, it can be repeatedly excited. Fluorophores can emit numerous photons through this cycle of excitation and emission, hence, fluorescent molecules are used for a broad range of research applications. Schiff bases are widely applicable in analytical determination as fluorescent indicators, using reactions of condensation of primary amines and carbonyl compounds in which the azomethine bond is formed (Ibrahim and Sharif, 2007), using complex formation reactions (Cimerman *et al.*, 2000) or utilizing the variation in their spectroscopic characteristics following changes in pH and solvent (Mohamed and Salah, 2007). Fluorescent indicators have many applications and are generally employed in cases where colorimetric indicators are difficult to observe or lack sensitivity. Such cases are found in dark, turbid or coloured solutions or titrations in which a precipitate is formed (White and Aragauer, 1970). A flash of light from a fluorescent indicator is much easier to see or measure than the appearance of a weak colour. Fluorescent colours under UV light are often easier to observe than a weak change in colour in an ordinary colour indicator.

Mohamed and co-workers (2007) studied the spectroscopic characteristics and fluorescent applications of Schiff bases derived from aromatic aldehyde with aromatic mono- and diamines derivatives. The fluorescence properties of these Schiff bases were examined in acidic and basic media (Table 1).

Table 1: Fluorescence properties of some Schiff bases in acidic and basic medium

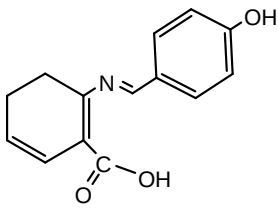
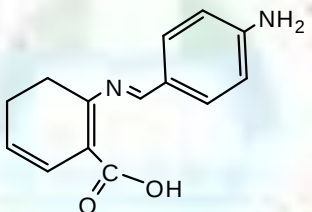
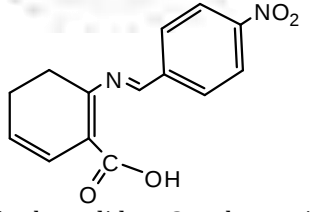
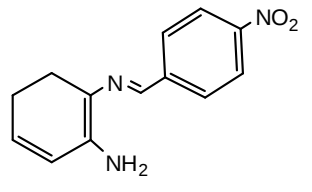
Schiff Base	Color	pH Range	Flourescent Color Change	Indicator Solution
1  <i>p</i>-Hydroxybenzylidene-2-carboxyaniline	Pale orange	1.5-2.7 2.7-6.5 6.5-12.5 12.5-14	Non-fluorescent bright Blue Dark blue Pale blue to blue-green	0.1 % solution in 50 % ethanol
2  <i>p</i>-(N,N-dimethyl)aminobenzylidene-2-carboxyaniline	Yellow white	0.9-1.4 1.5-2.0 2.0-6.0 6.0-12.5 12.5-14	Non-fluorescent Pale blue Bright blue Dark blue Pale blue to blue-green	0.1 % solution in 50 % ethanol
3  <i>p</i>-Nitrobenzylidene-2-carboxyaniline	Pale green	0.8-1.4 1.5-2.7 2.7-6.0 6.0-12.6 12.6-14	Non-fluorescent Pale blue Blue Dark blue Pale blue to blue-green	0.1 % solution in 50 % ethanol
4  <i>p</i>-(Nitrobenzylidende)-benzene-1,-2-diamine	Pale brown	1-14	Non-fluorescent	0.1 % solution in 50 % ethanol

Table 1 highlights the use of Schiff bases as fluorescent indicators. The fluorescent property was dependent on the type of substituents and pH of the medium. Compounds **1** and **2** with electron donating groups exhibited fluorescent property in acidic medium (pH 2.0-6.5) with a bright blue colour while in basic medium the compounds showed weak fluorescence. This shows that these compounds **1** and **2** can be employed as indicators due to the bright colour change. Compounds **3** and **4** with electron withdrawing groups showed weak or no fluorescence. Electron donating groups have been reported to enhance compounds to fluorescence (Yam *et al.*, 1999).

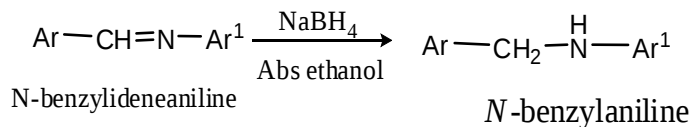
Schiff base metal complexes have also been reported to exhibit fluorescence properties. Choice of metal ion, nature and position of the substituent on the aromatic ring as well as spacers are known to greatly influence fluorescent behavior (Date and Bruce, 2004). It has been found that, for a given complex, the size of π -conjugated system of the ligand and the electronic effect of substituents on the ligand are important factors for modulating its luminescent properties (Sazanovich *et al.*, 2004). Luminescent chelating Cu(II) complexes have been reported for detection of Cu(II) (Yilmaz, 2008), as large amount of copper and its derivatives are toxic contaminants for environment.

Fan *et al.* (2010) studied luminescent properties of copper(II) complexes based on 2,6-bis(imino)pyridyl ligands and showed that the lowest absorption energy was attributable to lower steric hindrance. Emission energies were found to depend on the electron-donating ability of the substituents on the aryl rings of the bis(imino)pyridyl ligand. Zinc complexes based on salen type framework with high thermal and redox stability have found attractive use as low cost building blocks for newer light-emitting materials (Pucci *et al.*, 2009). Emission performance of such systems were dependent on the nature of central bridging diaminecore.

Novel photoluminescent hemi-disc like liquid crystalline Zn(II) complexes of N₂O₂ donor 4-alkoxy substituted salicyldimine Schiff base for applications in OLEDs, used for information storage, sensors, and enhanced contrast displays have been reported (Bhattacharjee *et al.*, 2010). Aromatic Schiff's bases of 2-hydroxyaniline-N-salicylidene was reacted with manganese, aluminium, gallium and beryllium salts. These reactions afforded metal complexes which gave fluorescent emission that could be utilized in the determination of these ions (Vazquez-Ruiz *et al.*, 1984). Aromatic Schiff base derivatives with alkyl groups, *m*- or *p*- to the -CH=N- group of salicylidene-*o*-aminophenol have also been synthesized and the effects of the substituent groups on the fluorescence properties of their metal complexes reported (Morishig, 1980). Fluorescent chemodosimeter synthesized from 1-aminopyrene Schiff base have been reported for the selective detection of Nb⁵⁺ ions in solution. Among the metal ions tested, the chemodosimeter showed a selective fluorogenic 'turn-on' response toward Nb⁵⁺ ions in mixed aqueous media (Gupta *et al.*, 2013).

2.6.3 Schiff bases as organic reagents

Schiff bases have been used in organic synthesis as precursor reagents (Qin *et al.*, 2013). They can be reduced to secondary amines in the presence of sodium borohydride (Scheme 16) (Billman and Diesing, 1957).

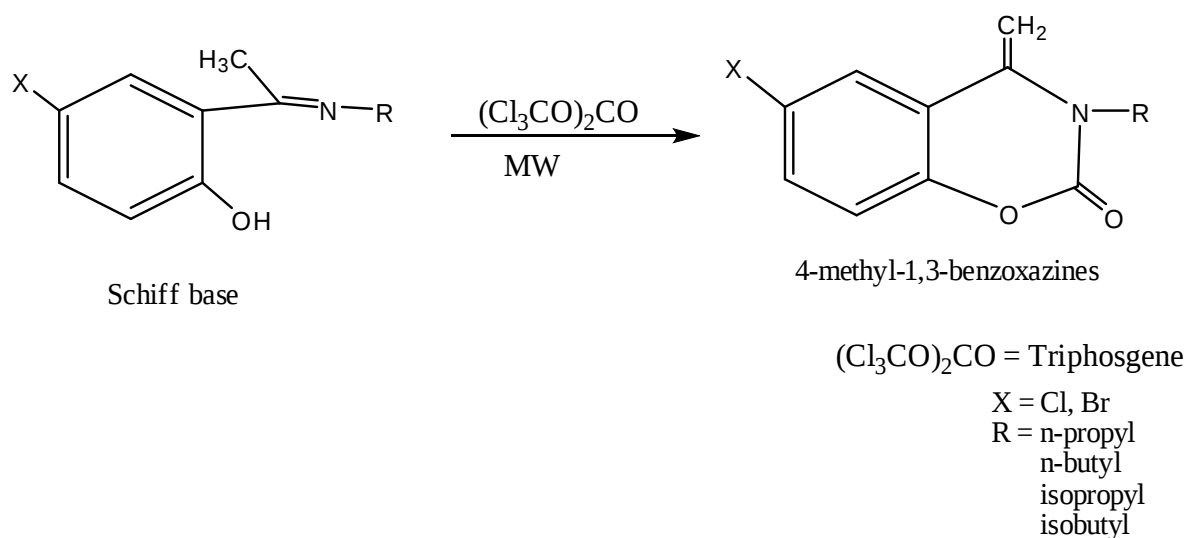


Ar and Ar¹ = phenyl group with nitro-, chloro- or methoxy- substituents

Yield: 91-99 %

Scheme 16: Synthesis of secondary amine from Schiff base of N-benzylideneaniline

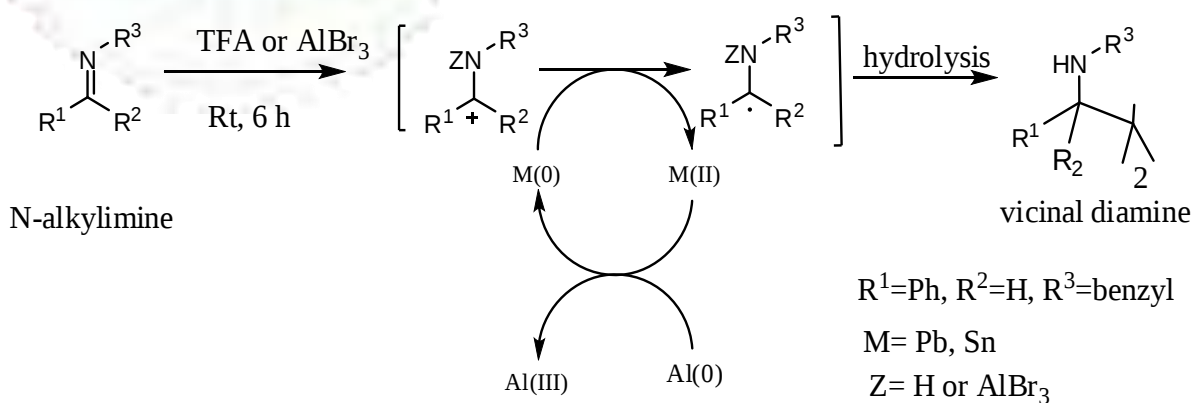
Schiff bases have also been used as starting materials in synthesis of benzoxazines (Scheme 17) (Alkhathlan, 2004).



Scheme 17: Synthesis of benzoxazines using Schiff bases as starting material

Benzoxazines have found applications in aerospace composite, electronic packaging, polymer electrolyte membrane, coatings and wear resistant composites.

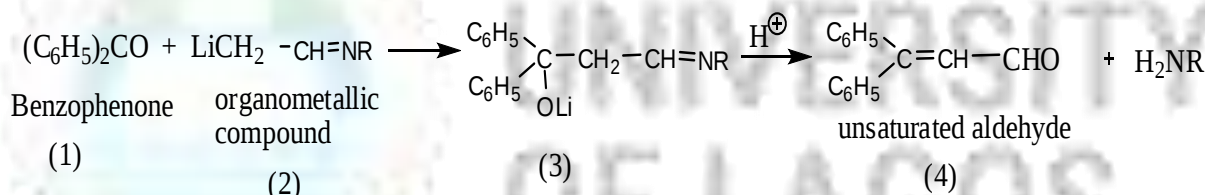
N-alkylimine undergo reductive dimerization in the presence of aluminum(III) bromide or trifluoroacetic acid (TFA) using tetrahydrofuran (THF) as solvents to form vicinal diamines (Scheme 18) (Tanaka *et al.*, 1988).



Scheme 18: Synthesis of vicinal diamines from N-alkylimines

Vicinal diamines are of interest as ligands for developing stereoselective catalysts and as intermediates in the synthesis of drugs. Vicinal diamine-based catalysts have been used for all types of reactions including oxidation, reduction, hydrolysis, and carbon-carbon bond-forming

reactions. Most bioactive compounds are based on vicinal diamines; these include anticancer, antidepressant, and antihypertensive agents. There has been a challenge to develop a facile, efficient, and general route to a wide range of vicinal diamines in enantiomerically pure form, hence the use of Schiff bases as starting material has been reported as a straightforward route. Directed Aldol condensation of an aldehyde with a ketone to effect specific combination of the CH_2 -group of the aldehyde with the ketonic carbonyl group in order that subsequent dehydration of the resulting aldol to the α,β -unsaturated aldehyde might be achieved was previously not possible (Buyer, 1954). However, Wittig *et al.* (1963) reported that it was possible if instead of the aldehyde, the corresponding Schiff base was used as starting material (Scheme 19). This can be metallated with lithium diethylamide in ether.



Scheme 19: Directed Aldol condensation using Schiff base as starting material

The organometallic compound (2) adds to benzophenone (1) to give (3), which on acidic hydrolysis afforded the unsaturated aldehyde (4) (Scheme 19). This method have been proved to be convenient for directed Aldol condensation reactions, which eliminates self condensation of aldehyde (Wittig *et al.*, 1963).

2.6.4 Schiff bases as coordinating ligands

Schiff bases can function as coordinating ligands by coordinating to metals through imine nitrogen and any other hetero atom present on the aldehyde or amine (Figure 17). The

coordinating ability of these compounds has afforded their use as corrosion inhibitors on mild steel in acid medium (Singh and Quraishi, 2012).

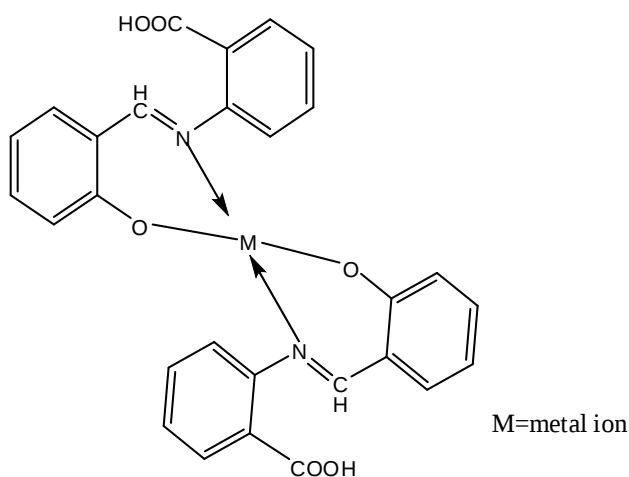


Figure 17: Coordination of Schiff base to metal ion

Schiff bases have also been applied to the direct determination of trace amounts of thallium in waste water (Asuero, 1981).

A tetradentate Schiff base, *N,N'*-bis(3-methylsalicylidene)-*ortho*-phenylene diamine (Figure 18) has been used for the spectrophotometric determination of nickel. This reagent reacted with nickel at room temperature to form a colored stable complex. The ligand and its complex were analyzed using atomic absorption spectrometry. The absorbance was determined at 450 nm. The results showed that extraction step was not required compared to chromogenic reference reagents which require extraction step making it time consuming, also the complex had a longer dynamic range ($0\text{--}1.0 \times 10^{-5} \text{ mol l}^{-1}$) than most of the reported chromogenic reagents, dimethyl glyoxime ($0\text{--}3.4 \times 10^{-6} \text{ mol l}^{-1}$), benzothiazolyldiazaoaminoazobenzene ($0\text{--}4.8 \times 10^{-6} \text{ mol l}^{-1}$), 2-(2-benzothiazolylazo)-5-dimethylaminobenzoic acid ($0\text{--}7 \times 10^{-6} \text{ mol l}^{-1}$). Its molar absorptivity was $9.5 \times 10^4 \text{ l mol}^{-1} \text{ cm}^{-1}$ better than known chromogenic reference materials such as; dimethyl

glyoxime ($1.5 \times 10^4 \text{ l mol}^{-1} \text{ cm}^{-1}$), benzothiazolyldiazoaminoazobenzene ($1.96 \times 10^5 \text{ l mol}^{-1} \text{ cm}^{-1}$), 2-(2-Benzothiazolylazo)-5-dimethylaminobenzoic acid ($1.32 \times 10^5 \text{ l mol}^{-1} \text{ cm}^{-1}$) (Fakari *et al.*, 2005).

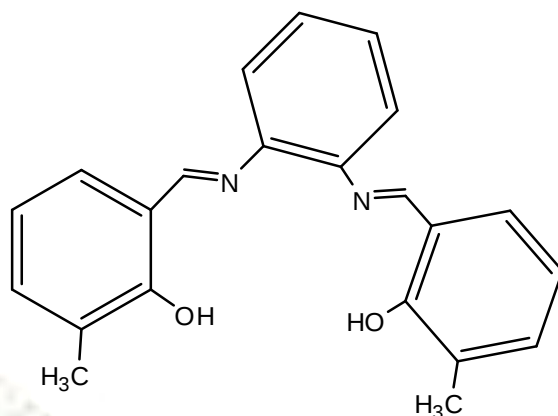
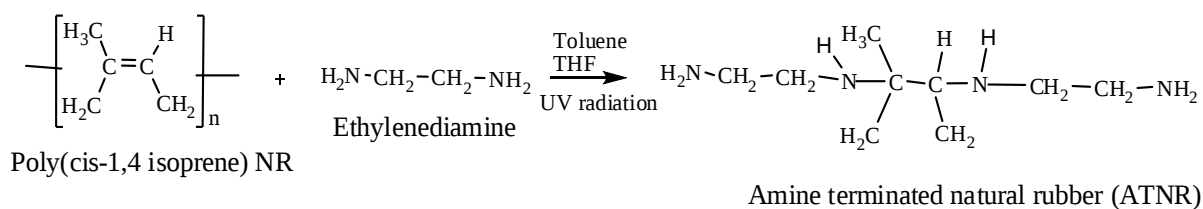


Figure 18: Tetradentate Schiff base, *N,N'*-bis(3-methylsalicylidene)-*ortho*-phenylene diamine

2.6.5 Industrial application

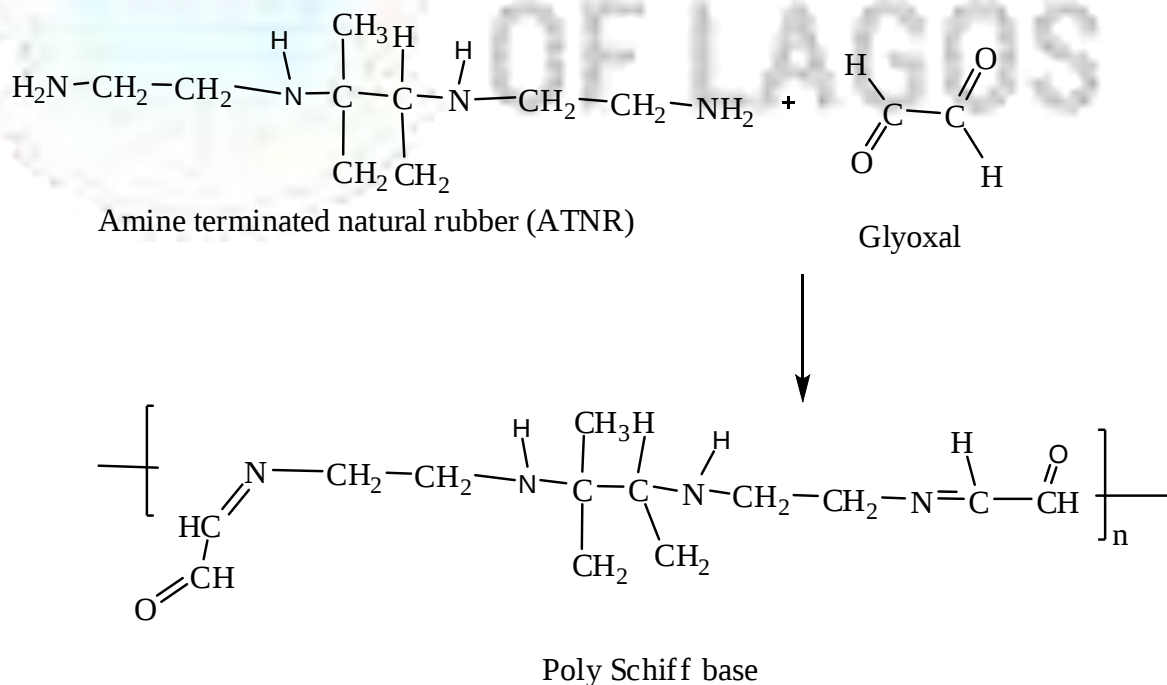
Schiff bases and their metal complexes play an essential role in the industries. In the polymer industries, poly Schiff bases synthesized from amine terminated natural rubber (ATNR) and glyoxal have been shown to improve aging resistance of natural rubber (George *et al.*, 1993).

Amine terminated liquid natural rubber (ATNR) is obtained from photodegradation of natural rubber when carried out in solution in the presence of ethylenediamine (Scheme 20).



Scheme 20: Photodegradation of natural rubber in the presence of ethylenediamine

ATNR on reaction with glyoxal yield poly Schiff bases (Scheme 21). Poly SB have been reported to improve the quality of natural rubber (George *et al.*, 1993). The introduction of desired functional groups in the natural rubber using poly SB helps to modify the functionality. This has been demonstrated by Srilathakutty *et al.* (1996) in which introduction of amino group accelerated vulcanization of NR and NBR. The scorch time and cure time of filled natural rubber (NR) and nitrile rubber (NBR) compounds were found to be reduced when oil/dioctyl phthalate (DOP) was replaced by poly SB. Tensile strength of natural rubber is associated with vulcanized oil, which can be aromatic oil or naphthenic oil. Tensile strength and tear strength of the filled vulcanized NR and NBR were found to be improved when oil/DOP was replaced by poly SB in NR and NBR respectively. Filled NR and NBR vulcanized showed better aging resistance when poly SB was used as a plasticizer.

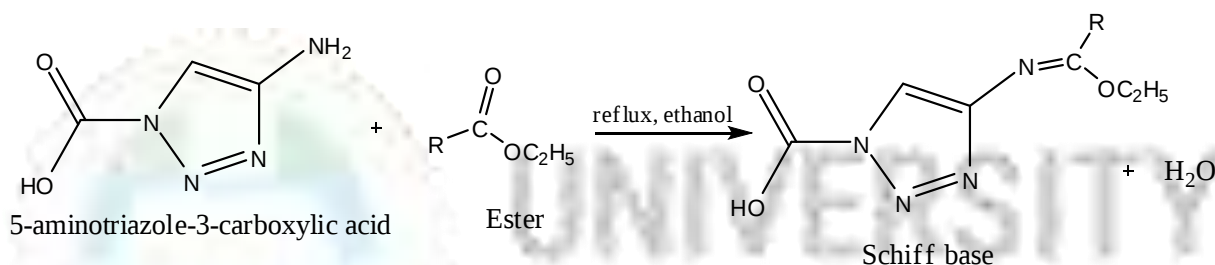


Scheme 21: Reaction of ATNR with glyoxal to give poly Schiff base

Other industrial applications of SBMCs include the use of chromium azomethine complexes which gives fast colours to leathers, food packages, wools (Befta, 1985). Cobalt complex of salicylaldehyde with diamine has excellent light resistance and storage ability and does not degrade even in acidic gases (CO₂) (Kokai, 1985). Azo groups containing metal complexes are used for dyeing cellulose polyester textiles (Dehnert and Juchemann, 1985, Bergmann, 1985).

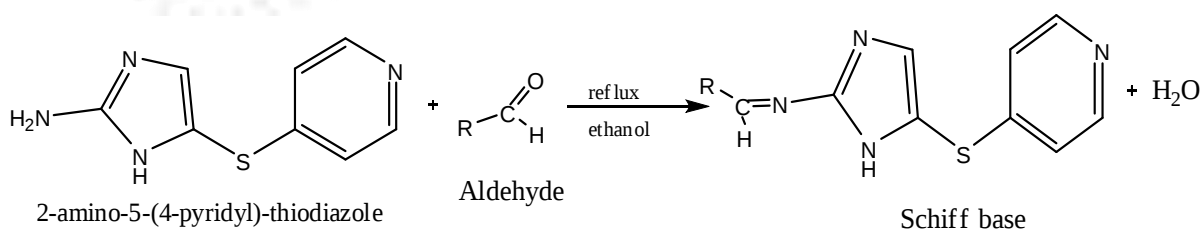
2.6.6 Plant growth regulator

Schiff base of ester and 5-aminotriazole-3-carboxylic acid have shown remarkable activity as plant growth hormone (Scheme 22) (Wang *et al.*, 2002).



Scheme 22: Reaction of 5-aminotriazole-3-carboxylic acid and ester to give Schiff base

SB of thiodiazole have been shown to have good plant growth regulatory activity towards auxin and cytokine (Scheme 23) (Song *et al.*, 2005).



Scheme 23: Reaction of thiodiazole and aldehyde to give Schiff base

2.6.7 Biological applications of Schiff bases and metal complexes of aminophenols

Antibacterial activity is a property of both inorganic and organic substances and the exploitation of such activity is of considerable practical importance in the development of antibacterial agents (Maurer *et al.*, 1977). The presence of imine bond in Schiff bases confers biological activity, this coupled with other functional groups affords these compounds antibacterial, antifungal, anti-tumor and anti-viral activity, hence they are used to design therapeutical agents (Khan *et al.*, 2002, Toliwal *et al.*, 2009, Lokhandwala and Patel, 2013). Schiff bases synthesized from 4-aminobenzoic acid exhibited antibacterial activity against *E. faecalis* while no activity against *E. coli* and *P. aeruginosa* (Jigna *et al.*, 2005). The antimicrobial activity of SBs synthesized from 5-chloro-salicylaldehyde against *B. subtilis*, *E. coli*, *P. fluorescence*, *S. aureus*, *A. niger*, *C. albicans* and *T. rubrum* revealed moderate activity against the bacterial and no activity against the fungal strains (Shi *et al.*, 2007). The *in-vitro* antibacterial, antifungal and anti-HIV activity of SBs and Mannich bases of isatin derivatives have been reported by Pandeya *et al.* (1999). It was observed that all the compounds showed mild to moderate activity against the tested bacteria, significant antifungal activity but none of the compounds showed marked anti-HIV activity.

The investigation of antibacterial screening of Schiff bases and Mannich bases bearing 2,4-dichloro-5-fluorophenyl moiety revealed that all the tested compounds showed moderate to good bacterial inhibition (Karthikeyan *et al.*, 2006).

Baluja *et al.* (2009) synthesized Schiff base from 4-aminophenol and salicylaldehyde. The Schiff base showed antibacterial activity against *B. cereus*, *P. aeruginosa*, *E. coli*, *K. pneumonia* and *S. aureus*.

Metal complexes synthesized from Schiff bases have also shown promising antibacterial properties. Metal complexes of Fe(II), Co(II), Ni(II) and Cu(II) with ligands 2,6-

pyridinedicarboxaldehydebis(*p*-hydroxyphenylimine) and 2,6-pyridinedicarboxaldehydebis(*o*-hydroxyphenylimine) showed antibacterial activity against *E. coli*, *P. aeruginosa*, *S. aureus* and *B. subtilis* (Mohamed, 2006).

Neutral tetradentate complexes of transition metals with Schiff bases derived from 2-aminophenol or 2-aminothiophenol and 1-phenyl-2,3-dimethyl-4-(4-iminopentan-2-one)-pyrazol-5-one showed antibacterial activity against *S. aureus*, *B. subtilis*, *K. pneumonia*, *S. typhi*, *P. aeruginosa*. Most of the complexes showed higher activity than the free ligand (Prakash and Adhikari, 2011).

Complexes of Co(II), Cu(II), Ni(II), Mn(II) and Cr(III) with Schiff bases derived from 2,6-diacetylpyridine and 2-pyridinecarboxaldehyde with 4-amino-2,3-dimethyl-1-phenyl-3-pyrazol-5-one showed antibacterial activities against *E. coli*, *S. aureus*, *K. pneumonia*, *P. aeruginosa*, *E. cloacae*, *B. megaterium* and *M. luteus* (Ispir et al., 2008).

Schiff bases derived from acetylferrocene with 2-aminophenol, 2-amino-5-methylphenol or 2-amino-5-chlorophenol and its cobalt(II), copper(II), nickel(II), and zinc(II) showed antibacterial activity against *E. coli* and *B. subtilis* (Abd-Elzaher, 2004).

Complexes of Co(II), Ni(II) and Cu(II) with the Schiff bases of salicylidene-2-aminophenol, furfurylidene-N-phenylthiourea and salicylidene-N-phenylthiourea were screened for their antibacterial properties. The metal complexes exhibited higher activity than the free ligand (Aboaly and Khalil, 2001).

The Schiff base of 2-hydroxybenzilidene-3-aminophenol was synthesized and used for the preparation of coordination complexes with some transition and inner transition metals (Co(II), Ni(II), Cu(II), Ce(III) and Er(III)). The antimicrobial activities were checked against four different bacterial species *E. coli*, *B. subtilis*, *S. aureus* and *P. aeruginosa* and also screened for

activity against the fungus *Rhizopus*, the common bread mould. All the complexes were found to be more active compared to the parent Schiff base. Antifungal studies against the fungus, *Rhizopus* on soaked bread showed that both the ligand and all the complexes exhibited almost hundred percent inhibition (Varghese and Nair, 2010).

Generally, Schiff base metal complexes exhibit higher antibacterial activity than the free ligands.

2.7 Biological Importance of Transition Metals of Copper and Cobalt Ions

Transition metals are essential for the normal functioning of living organisms. The major role of transition metal (T.M) ions is in oxidation-reduction reactions. The ability of T.M ions to easily accept and donate electrons explains their important role in mediating oxidation-reduction (redox) reactions. Transition metal ions have such physical properties as to make them excellent probes of their environments (Williams, 2008). The presence of transition metals in human blood plasma indicates their importance in the mechanism for storage and transport of T.M in living organisms (Joshi *et al.*, 2002). Transition metals play a key role in biological systems such as cell division, respiration, nitrogen fixation and photosynthesis (Joshi *et al.*, 2002, Tuna *et al.*, 2006).

Transition metal ions available in biological system are those of scandium, titanium, vanadium, chromium, manganese, iron, cobalt, nickel, copper, yttrium, zirconium, niobium and molybdenum (Williams, 2008). The important T.M ions are copper, cobalt, iron, manganese and molybdenum, while vanadium, chromium and niobium are of much less interest.

In development of metal based antibacterial agents, there is need to take into consideration metals of biological importance. Copper and cobalt ions have been found to be more active than other T.M because they are stable in more than one valence state (Williams, 2008). In the body,

copper moves between the cuprous (Cu^{1+}) and cupric (Cu^{2+}) forms. The ability of copper to easily accept and donate electrons explains its important role in oxidation-reduction (redox) reactions (Linder and Hazegh-Azam, 1996). Copper is a critical functional component of a number of essential enzymes known as cuproenzymes. Copper-dependent enzyme, cytochrome *c* oxidase, plays a critical role in cellular energy production. By catalyzing the reduction of molecular oxygen (O_2) to water (H_2O), cytochrome *c* oxidase generates an electrical gradient used by the mitochondria to create the vital energy-storing molecule, ATP (Uauy *et al.*, 1998).

Cobalt-containing enzymes has been associated with vitamin B_{12} (Williams, 2008). In the co-enzyme, the cobalt-carbon bond is weakened so that Co(III) may readily change from a five coordinate structure which is an unrecognised geometry to a square geometry, thus, cobalt enzyme induces a condition which would facilitate rapid redox changes (Williams, 1968). Some cobalt(II) Schiff base complexes are able to bind reversibly to oxygen and they have been used as simplified models in the study of reversibly binding of oxygen by its natural transporters (Casella and Gullotti, 1986).

The rapid redox changes in cobalt and copper metal ions contributes to the ability of these metal ions to overcome the menace of resistance by microorganisms.

2.8 Structure-Activity Relationship

Structure-activity relationship (SAR) is an approach designed to establish relationship between chemical structure and biological activity of studied compounds. A study of relationship between structure and biological activity will afford predictive use and understanding of the compound. Structure of a molecule contains the features responsible for its physical, chemical and biological properties. The basic principle of SAR is based on the hypothesis that similar molecules have

similar activities. This concept was developed by Langmuir (Langmuir, 1919). Applying SAR involves two steps; characterization of the compound and application of chemometric approach to establish the relationship between structure and activity exhibited. Analysis of SAR enables the determination of the chemical groups on the compound responsible for evoking a target biological effect in the organism. This allows modification of the effect or the potency of a bioactive compound by changing its chemical structure. Medicinal chemists use the technique of chemical synthesis to insert new chemical groups into a compound and test the modification for their biological effect. The biological activity of a particular substance depends upon a complex sum of individual properties including compound structure, affinity for the target site, and survival in the medium of application, survival within the biological system, transport properties, state of the target organism and electronic charge density distribution (Kosower and Miyadera, 1972).

Ligand–protein interaction plays a key role in the distribution and transport of small molecules in biological systems. The electronic property of the compounds has close relations with biological activity. If the distribution of charge density of drug is just suited with the specific receptor, the interaction between drug and receptor would increase, and then drug and receptor have the tendency to form complexes and increase the activity. The antibacterial structure-activity relationship of Schiff base derivatives show that the degree of delocalization of the unshared electron pairs of sulphur atom is larger than that of oxygen atom, so the electronic charge density distribution of compounds are different from each other (Bolos *et al.*, 1998). The weak antibacterial activity of thienyl compounds compared to furyl compound may be explained by their different electronic charge density distribution.

Many facts suggest that drug absorption is influenced by the hydrophilic/ lipophilic properties (Li *et al.*, 2008). The positive-gram bacteria and negative-gram bacteria of an extracellular membrane are different. The peptidoglycan content in a positive-gram bacterium is higher than that in a negative-gram bacterium, this accounts for the thickness of the positive gram bacterial cell wall. The main component of negative-gram bacteria cell wall is lipopolysacchride, which is composed of lipoid A, core polysaccharide and specific polysaccharide. The higher content of lipoprotein in *E. coli* leads to the fact that the drug needs to possess high lipophilicity when entering intracellular membrane. The enzyme inside of the cell undoubtedly is the target for many antibacterial agents. If drugs are difficult to cross the lipid bilayer, they may fail in therapy. To cross the lipid bilayer, the small molecular drugs must diffuse up to the membrane interface, absorb, cross the membrane core, desorb and diffuse away on the other sides. Drugs are usually absorbed by passive diffusion; the motive force of passive diffusion is the concentration gradient of drugs between both sides of lipid bilayers, hence, drugs require a certain degree of solubility in a solvent. Generally, the activity of antibacterial agent is increased with the increase of its lipophilicity. But increasing the lipophilicity does not enhance the anti-microbial activity for homologous family (Seydel and Wiese, 2002).

Steric hindrance effect is another reason for different antibacterial activity. The methoxy is larger than hydroxyl group, and when they are attached to the *ortho* and *meta* positions of the phenyl ring, different steric hindrance effects will be produced (Li *et al.*, 2008).

The presence or substitution of a bulky group have been reported to diminish the rate of degradation and decrease the rate of elimination, thus increasing biological activity (Sarkozy, 2001).

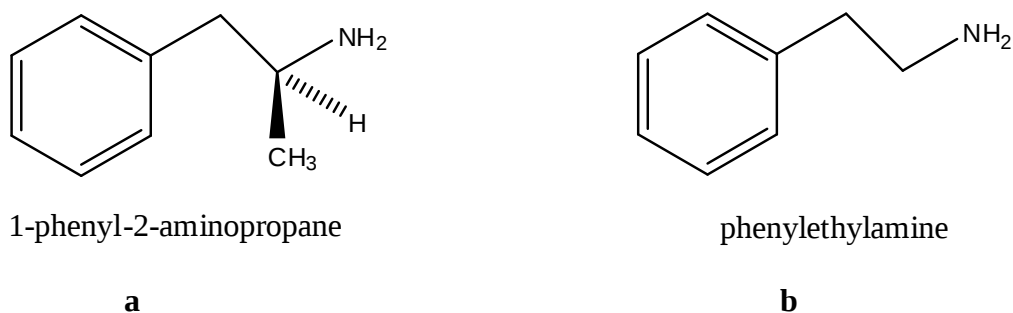


Figure 18: (a) 1-phenyl-2-aminopropane and (b) phenylethylamine

1-phenyl-2-aminopropane exhibited higher biological activity than phenylethylamine. The presence of methyl group in addition to an amino group in the compound (Figure 18a) was reported to account for the increase in biological activity due to the bulky group attached (Glennon and Higg 1992).

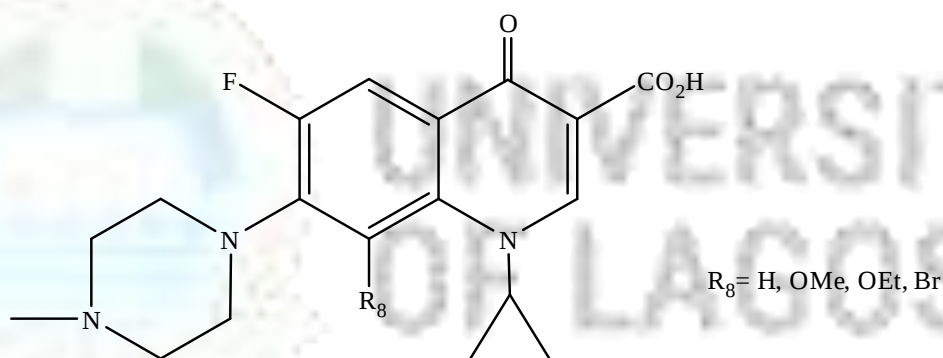
In this research, SAR has been studied based on the nature and position of substituents on the aromatic ring of the ligand.

2.8.1 Effect of substituent groups on biological activity

Substituent groups are group of atoms substituted in place of hydrogen atoms on the aromatic ring or parent chain. This could be an electron donating group (OMe, OH, NH₂) or electron withdrawing group (Cl, NO₂, CF₃). Presence of these groups have been found to lead to polar effect of the compound in many cases. Electron donating groups have been associated with high activity while electron withdrawing groups results in weak activity, although this may not be for all compounds. High antibacterial activity with electron withdrawing substituents was reported in thiazolidine-4-ones Schiff bases (Devprakash and Udaykumar, 2011). The methoxyl group is generally hydrophilic in character, while the hydroxyl group is hydrophobic, so the lipophilicity of methoxy SB compound was higher than that of hydroxyl SB compound (Zhang *et al.*, 2006). Biological activity have been found to be low in compounds in which the oxygen atom of the

methoxy group has been replaced with a sulfur group (Jacob and Shulgin, 1983). The replacement with a methylthio group reduced *in-vivo* activity by more than one order of magnitude.

Zhao *et al.* (1998) have reported killing of *Staphylococcus aureus* by C-8-methoxy fluoroquinolones (Figure 19). The report compares C-8 substituents for enhancement of fluoroquinolone lethality with *S. aureus* in which C-8-methoxy fluoroquinolones were more lethal than C-8-bromine, C-8-ethoxy, and C-8-H derivatives for *S. aureus*. The methoxy group also increased lethality against wild-type cells when protein synthesis was inhibited. These properties encourage refinement of C-8-methoxy fluoroquinolones to kill *Staphylococci*.



Fluoroquinolone

Figure 19: Substituted fluoroquinolone

Investigation of SAR of Schiff bases and Mannich bases derived from Isatin (Indole 2,3-dione) having 5-chloro and 5-bromo derivatives with 3-amino-2-methylmercapto quinazolin-4(3*H*)-one showed antibacterial activity in the order $\text{Cl} > \text{Br} > \text{H}$ (Pandeya *et al.*, 1999).

Chlorine have been found to inhibit bacterial protein synthesis (Benarde *et al.*, 1967). The comparative mode of action of chlorine, bromine, and iodine on f2 capsid bacterial virus showed

that chlorine inactivated naked f2 RNA at the same rate as RNA in intact phage, whereas f2 capsid proteins could still adsorb to the host (Olivieri *et al.*, 1975). Taylor and Butler (1982) found that the RNA of poliovirus type 1 was degraded into fragments by chlorine but the poliovirus inactivation preceded severe morphological changes.

The biological activity on a series of 5,5'-X-substituted salophen ligands, X= OCH₃, Br, and NO₂, and the corresponding Zn(II) complexes have been reported. The biological activity of these compounds were related to the different Lewis acid character of the complexes. *In-vitro* studies showed that the electron-withdrawing nitro substituents increased the electrophilic character of the metal center, thus, generate the strongest interaction with plasmid DNA (Giannicchi *et al.*, 2013).

The SAR of a series of novel pyridine amide Schiff base derivatives of furyl, thienyl, pyridyl, methoxy and hydroxyl on *E. coli* have been studied (Li *et al.*, 2008). The results revealed that the hydrophilicity of these Schiff bases had a great influence on their antibacterial activity, which resulted from the bacterial cell wall structure. Based on the substituents groups, the hydroxyl derivative was found to be most active against *E. coli* while the furyl derivative exhibited the lowest antibacterial activity. The thienyl, pyridyl and methoxy substituents exhibited moderate antibacterial activity. However, the result is different from the inhibition of *S. aureus* (Zhang *et al.*, 2006). The result showed that the thienyl derivative was more active against *S. aureus*, this was followed by the furan, pyridyl, methoxy and hydroxyl derivatives which exhibited moderate antibacterial activity. The structure-activity relationship of the Schiff base derivatives indicated that the furan ring was essential for the antibacterial activity.

Wang *et al.* (1975) studied the antibacterial activities of nitropyrroles, nitrothiophenes, and aminothiophenes. It was observed that replacement of the nitro group with an amino group enhanced the activity of the thiophene compounds.

2.8.2 Effect of position on substituent groups

The position of substituents on organic ligand can have a profound effect on the biological activity. This has been found to play an important role in modifying the DNA adducts (Figure 20).

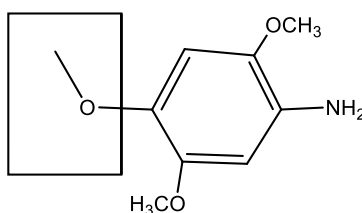


Figure 20: Substiuent at *p*-position which modify DNA

Xiao *et al.* (2007) revealed that having a chloro substituent at *p*-position significantly increased activity. Kuz'min *et al.* (2000) studied SAR in a set of Schiff bases derived from pyridines and observed that the *ortho*-substituted Schiff base exhibited the highest activity.

Singh *et al.* (2010) studied the antimicrobial activities of some 4-thiazolidinone fused pyrimidines benzodiazepines and their oxygen substituted hydroxylamine derivatives. It was observed that antibacterial activity was increased when chloro group was introduced at *p*-position in phenylimino moiety but decreased with nitro group at same position .

The synthesis and antibacterial studies of pyrazoline derivatives with different substituents groups have been reported (Baluja and Chanda, 2012). The derivatives showed different activity against different bacterial strains depending on their structural formula. Derivatives which had nitro group at *p*-position showed best antibacterial activity while the nitro group at *m*-position decreased the activity.

2.9 Antibacterial Agents

Antibacterial agents are synthetic or natural components which kill or inhibit the activity of bacteria. Antibacterial agents include antibiotics and chemotherapeutics. Antibiotics are natural substances produced by some group of microorganisms (eg penicillin) while chemotherapeutic agents are chemically synthesized compounds (eg sulfanilamides). The modern era of antibacterial chemotherapy began in 1929, with Fleming's discovery of bactericidal substance penicillin which belong to the beta-lactams class. Some other antibacterial agents include semisynthetic *beta*-lactams eg ampicillin, amoxicillin (inhibits steps in cell wall synthesis), aminoglycosides eg streptomycin, gentamycin (inhibits protein synthesis), glycopeptides eg vancomycin (inhibits peptidoglycan biosynthesis), rifamycin eg rifampicin (inhibits transcription), quinolones eg nalidixic acid (inhibits DNA replication). Some of the commonly used antibacterial agents and mechanism of action are presented in (Figure 21).

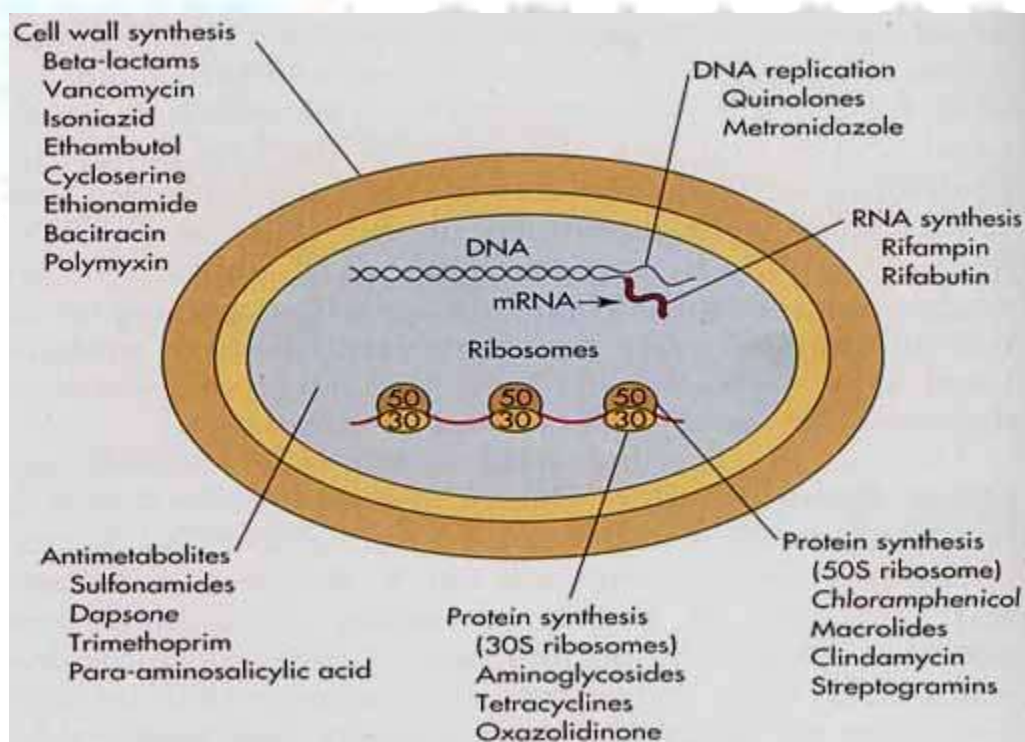
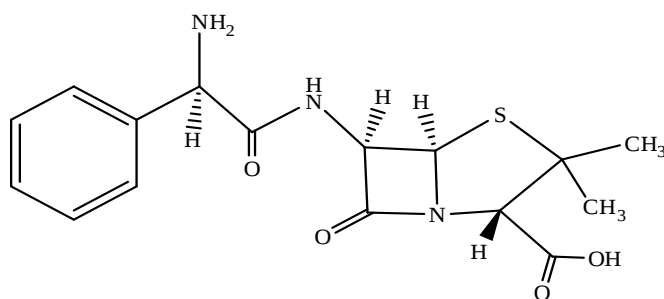


Figure 21: Targets for antibacterial agents

The structure of antibacterial agent is related to its mode of action. The mode of action of ampicillin (Figure 22) is based on the beta-lactam ring which interferes with cell wall synthesis.



Structure of ampicillin

(2S, 5R, 6R) - 6 - ((2R)-2-amino-2-phenylacetyl)amino)-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo(3.2.0)heptane-2-carboxylic acid)

Figure 22: Structure of ampicillin.

The amino group (NH_2) helps the drug to penetrate the outer membrane of the bacteria which is similar to the basic nature of Schiff bases. Ampicillin is among the first antibiotic to exhibit broad spectrum antibacterial activity. The minimum inhibitory concentration (MIC) of ampicillin against *S. aureus*, *B. subtilis* and *E. coli* was found in the range 1.56-12.5 $\mu\text{g/ml}$ as reported (Ölgena *et al.*, 2008).

Khan *et al.* 2013, reported the MIC of ampicillin against *S. aureus* in the range 0.008-2.048 mg/L.

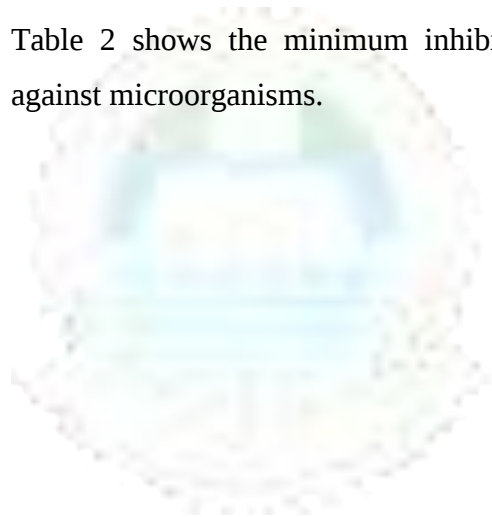
Staphylococcus aureus was resistant at ampicillin concentration of 30 $\mu\text{g/ml}$ and 60 $\mu\text{g/ml}$ and susceptible at ampicillin concentration of 90 $\mu\text{g/ml}$ and 120 $\mu\text{g/ml}$ (Udeze *et al.*, 2012).

Studies have shown that some antiseptics/disinfectants known as 'biocide' and antibiotics have similar effects on bacteria (Russell, 2002).

TABLE 2: MIC of some antiseptics and disinfectants against gram-positive and gram-negative bacteria

Chemical agent	MIC (mg/ml)		
	<i>S. aureus</i>	<i>E. coli</i>	<i>P. aeruginosa</i>
Benzalkonium chloride	0.5	50	250
Benzethonium chloride	0.5	32	250
Cetrimide	4	16	64–128
Chlorhexidine	0.5–1	1	5–60
Hexachlorophene	0.5	12.5	250
Phenol	2,000	2,000	2,000
Propamine isethionate	2	64	256
Dibromopropamide isethionate	1	4	32
Triclosan	0.1	5	>300

Table 2 shows the minimum inhibitory concentration of some antiseptics and disinfectants against microorganisms.



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CHAPTER THREE

3.0 METHODOLOGY

3.1 Materials and Methods

All reagents and chemicals namely 2-aminophenol, 3-aminophenol, 4-aminophenol, 2-methoxybenzaldehyde, 2-chlorobenzaldehyde, 2-nitrobenzaldehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde, 4-nitrobenzaldehyde, copper(II) chloride and cobalt(II) chloride were purchased from Aldrich-Sigma and used without further purification. Solvents used include ethanol, triethylamine, chloroform, dimethylsulphoxide, toluene, and dimethylformamide were of analytical grade and used without further purification.

3.2 Physical Measurements

Infrared (IR) spectra were recorded on a Bruker FT-IR attenuated total reflectance (ATR) tensor 27 spectrometer directly on small samples of the compounds from 4000 to 400 cm^{-1} . ^1H NMR spectra were recorded on a Bruker Avance III 400 MHz in DMSO- d_6 or deuterated chloroform (CDCl_3) solutions. Chemical shifts were reported in ppm relative to TMS as internal standard. Electronic absorption spectra of Schiff bases and metal complexes were recorded from 200 to 1100 nm using freshly prepared chloroform (CHCl_3) and dimethylformamide (DMF) solutions were measured on a Cary Model 50 spectrophotometer. Thermogravimetric analysis (TGA) was carried out at 15 $^\circ\text{C min}^{-1}$ heating rate using a Perkin Elmer Pyris 6 TGA from 50 $^\circ\text{C}$ to 900 $^\circ\text{C}$ in a closed perforated aluminium pan. The differential scanning calorimetric (DSC) analysis was carried out at 20 $^\circ\text{C min}^{-1}$ heating rate from room temperature to 450 $^\circ\text{C}$ using a Perkin Elmer DSC 4000 series, calibrated with indium metal. Both TGA and DSC were run under an inert atmosphere. Metal analysis was determined using Analyst 200 atomic absorption spectrophotometer (AAS) Perkin Elmer. Melting points were determined on a Reichert Thermovar melting-point apparatus and are uncorrected but calibrated. Magnetic susceptibility

measurements were performed using a Sherwood Scientific magnetic susceptibility balance on powdered samples. $\text{Hg}[\text{Co}(\text{SCN})_4]$ was used as the calibrant and corrections for diamagnetism calculated from Pascal's constants. Microanalytical data were obtained on a Perkin Elmer model 2400 series II CHNS/O elemental analyzer.

3.3 Synthesis of 2-aminophenol Schiff Bases

Schiff bases of 2-aminophenol were synthesized by reacting 2-aminophenol with substituted benzaldehydes namely 2-methoxybenzaldehyde, 2-chlorobenzaldehyde, 2-nitrobenzaldehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde and 4-nitrobenzaldehyde.

3.3.1 Synthesis of 2-(2-methoxybenzylideneamino)phenol, (L1)

2-Methoxybenzaldehyde (1.36 g, 10 mmol.) and 2-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.62 g (72 %). m.p.: 70-71 °C. IR (cm^{-1}): 3438, 1625, 1583, 1353, 1284, 1152, 1018, 894, 754. $^1\text{H-NMR}$ (δ / ppm): 9.17 (1H, s, O-H), 8.17 (1H, s, -N=CH), 6.88-7.45 (8H, m, aromatic), 3.93 (3H, s, -OCH₃). UV-Vis (CHCl_3) (ϵ / $\text{cm}^{-1}(\text{log } \epsilon / \text{L mol}^{-1} \text{ cm}^{-1})$): 35,842(4.00) (Aromatic transition, $\pi \rightarrow \pi^*$), 27,777(4.40) (Imine transition, $n \rightarrow \pi^*$). Anal. Calcd. for $\text{C}_{14}\text{H}_{13}\text{NO}_2$: C, 73.77; H, 5.77; N, 6.16. Found: C, 73.30; H, 5.77; N, 6.05.

3.3.2 Synthesis of 2-(2-chlorobenzylideneamino)phenol, (L2)

2-Chlorobenzaldehyde (1.12 ml, 10 mmol.) and 2-aminophenol (1.09 g 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.88 g (58 %). m.p.: 58-59 °C. IR (cm⁻¹): 3414, 1616, 1581, 1480, 1270, 1025, 750, 568. ¹H-NMR (δ/ ppm): 9.21 (1H, s, O-H), 8.26 (1H, s, -N=CH), 6.97-7.50 (8H, m, aromatic). UV-Vis (CHCl₃) (ν / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 36,101(4.78) (Aromatic transition, π→π*), 28,169(4.75) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀NOCl; C, 67.39; H, 4.35; N, 6.05. Found: C, 67.38; H, 4.24; N, 6.03.

3.3.3 Synthesis of 2-(2-nitrobenzylideneamino)phenol, (L3)

2-Nitrobenzaldehyde (1.51 g, 10 mmol.) and 2-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.98 g (65 %). m.p.: 64-65 °C. IR (cm⁻¹): 3360, 1626, 1456, 1269, 870, 547. ¹H-NMR (δ/ ppm): 9.15 (1H, s, O-H), 8.25 (1H, s, -N=CH), 6.93-8.05 (8H, m, aromatic). UV-Vis (CHCl₃) (ν / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 36,630(4.90) (Aromatic transition, π→π*), 28,100(4.80) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀N₂O₃: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.62; H, 4.07; N, 11.60.

3.3.4 Synthesis of 2-(4-methoxybenzylideneamino)phenol, (L4)

4-Methoxybenzaldehyde (1.21 ml, 10 mmol.) and 2-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.60 g (69 %). m.p.: 56-57 °C. IR (cm⁻¹): 3333, 1618, 1583, 1485, 1245, 841, 783, 505. ¹H-NMR (δ/ ppm): 8.63 (1H, s, O-H), 7.89 (1H, s, -N=CH), 6.90-7.29 (8H, m, aromatic), 3.91 (3H, s, -OCH₃). UV-Vis (CHCl₃) (ν / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 38,482(4.17) (Aromatic transition,

$\pi \rightarrow \pi^*$), 28,571(4.20) (Imine transition, $n \rightarrow \pi^*$). Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.08; H, 5.67; N, 6.13.

3.3.5 Synthesis of 2-(4-chlorobenzylideneamino)phenol, (L5)

4-Chlorobenzaldehyde (1.40 g, 10 mmol.) and 2-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.51 g (63 %). m.p.: 78-79 °C. IR (cm^{-1}): 3291, 1601, 1477, 1378, 1237, 1078, 820, 503. 1H -NMR (δ / ppm): 8.65 (1H, s, O-H), 7.98 (1H, s, -N=CH), 6.88-7.81 (8H, m, aromatic). UV-Vis ($CHCl_3$) (λ / cm^{-1} ($\log \epsilon$ / $L \text{ mol}^{-1} \text{ cm}^{-1}$): 36,496(4.15) (Aromatic transition, $\pi \rightarrow \pi^*$), 28,169(4.05) (Imine transition, $n \rightarrow \pi^*$). Anal. Calcd. for $C_{13}H_{10}NOCl$: C, 67.39; H, 4.35; N, 6.05. Found: C, 67.26; H, 4.30; N, 6.05.

3.3.6 Synthesis of 2-(4-nitrobenzylideneamino)phenol, (L6)

4-Nitrobenzaldehyde (1.51 g, 10 mmol.) and 2-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.86 g (77 %). m.p.: 112-113 °C. IR (cm^{-1}): 3304, 1623, 1583, 1475, 1299, 852, 754, 495. 1H -NMR (δ / ppm): 8.77 (1H, s, O-H), 8.37 (1H, s, -N=CH), 6.91-8.07 (8H, m, aromatic), 3.91 (3H, s, -OCH₃). UV-Vis ($CHCl_3$) (λ / cm^{-1} ($\log \epsilon$ / $L \text{ mol}^{-1} \text{ cm}^{-1}$): 36,496(4.16) (Aromatic transition, $\pi \rightarrow \pi^*$), 27,839(4.18) (Imine transition, $n \rightarrow \pi^*$). Anal. Calcd. for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.82; H, 4.07; N, 11.64.

3.4 Synthesis of 3-aminophenol Schiff Bases

Schiff bases of 3-aminophenol were synthesized by reacting 3-aminophenol with substituted benzaldehydes namely 2-methoxybenzaldehyde, 2-chlorobenzaldehyde, 2-nitrobenzaldehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde and 4-nitrobenzaldehyde.

3.4.1 Synthesis of 3-(2-methoxybenzylideneamino)phenol, (L7)

2-Methoxybenzaldehyde (1.36 g, 10 mmol.) and 3-aminophenol (1.09 g, 10 mmol.) were dissolved in toluene (100 ml) and stirred under reflux at 110 °C for 2 h. The yellow crude product was collected by filtration of hot reaction mixture, re-crystallized from toluene, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.99 g (48 %). m.p.: 170-172 °C. IR (cm⁻¹): 3365, 1586, 1457, 1284, 1238, 1020, 748, 683, 485. ¹H-NMR (δ/ ppm): 8.91 (1H, s, O-H), 8.11 (1H, s, -N=CH), 6.12-7.83 (8H, m, aromatic), 3.91 (3H, s, -OCH₃). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 38,461(3.93) (Aromatic transition, π→π*), 29,498(3.63) (Imine transition, n→π*). Anal. Calcd. for C₁₄H₁₃NO₂: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.77; H, 6.07; N, 5.48.

3.4.2 Synthesis of 3-(2-chlorobenzylideneamino)phenol, (L8)

2-Chlorobenzaldehyde (1.12 ml, 10 mmol.) and 3-aminophenol (1.09 g, 10 mmol.) were dissolved in toluene (100 ml) and stirred under reflux at 110 °C for 2 h. The red crude product was collected by filtration of hot reaction mixture, re-crystallized from toluene, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.32 g (57 %). m.p.: 120 °C. IR (cm⁻¹): 3325, 1617, 1500, 1428, 1217, 1032, 832, 747, 544. ¹H-NMR (δ/ ppm): 9.11 (1H, s, O-H), 8.23 (1H, s, -N=CH), 6.53-7.37 (8H, m, aromatic). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 36,496(3.97) (Aromatic transition, π→π*),

28,328(3.94) (Imine transition, $n \rightarrow \pi^*$). Anal. Calcd. for $C_{13}H_{10}NOCl$: C, 67.39; H, 4.35; N, 6.05. Found: C, 66.67; H, 4.46; N, 5.61.

3.4.3 Synthesis of 3-(2-nitrobenzylideneamino)phenol, (L9)

2-Nitrobenzaldehyde (1.51 g, 10 mmol.) and 3-aminophenol (1.09 g, 10 mmol.) were dissolved in toluene (100 ml) and stirred under reflux at 110 °C for 2 h. The brown crude product was collected by filtration of hot reaction mixture, re-crystallized from toluene, dried with vacuum pump and stored in a desiccator over silica gel.

Yield: 0.52 g (47 %). m.p.: 102-103 °C. IR (cm^{-1}): 3360, 1606, 1515, 1341, 1211, 729. 1H -NMR (δ /ppm): 8.91 (1H, s, O-H), 8.17 (1H, s, -N=CH), 6.24-7.79 (8H, m, aromatic). UV-Vis ($CHCl_3$) (ν / cm^{-1} ($\log \epsilon / L mol^{-1} cm^{-1}$): 34,843(3.09) (Aromatic transition, $\pi \rightarrow \pi^*$), 28,595(2.55) (Imine transition, $n \rightarrow \pi^*$). Anal. Calcd. for $C_{13}H_{10}N_2O_3$: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.57; H, 4.40; N, 11.54.

3.4.4 Synthesis of 3-(4-methoxybenzylideneamino)phenol, (L10)

4-Methoxybenzaldehyde (1.21 ml, 10 mmol.) and 3-aminophenol (1.09 g, 10 mmol.) were dissolved in toluene (100 ml) and stirred under reflux at 110 °C for 2 h. The orange crude product was collected by filtration of hot reaction mixture, re-crystallized from toluene, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.19 g (52 %) m.p.: 148-149 °C. IR (cm^{-1}): 3330, 1612, 1456, 1280, 835, 564.

1H -NMR (δ /ppm): 8.47 (1H, s, O-H), 7.87 (1H, s, -N=CH), 6.24-7.24 (8H, m, aromatic), 3.33 (3H, s, -OCH₃). UV-Vis ($CHCl_3$) (ν / cm^{-1} ($\log \epsilon / L mol^{-1} cm^{-1}$): 34,722(3.96) (Aromatic transition, $\pi \rightarrow \pi^*$), 29,585(3.92) (Imine transition, $n \rightarrow \pi^*$). Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.32; H, 6.01; N, 5.40.

3.4.5 Synthesis of 3-(4-chlorobenzylideneamino)phenol,(L11)

4-Chlorobenzaldehyde (1.40 g, 10 mmol.) and 3-aminophenol (1.09 g, 10 mmol.) were dissolved in toluene (100 ml) and stirred under reflux at 110 °C for 2 h. The brown crude product was collected by filtration of hot reaction mixture, re-crystallized from toluene, dried with vacuum pump and stored in a desiccator over silica gel.

Yield: 1.10 g (47 %) m.p.: decomp. IR (cm⁻¹): 3351, 1616, 1484, 1084, 811, 538. ¹H-NMR (δ/ ppm): 8.57 (1H, s, O-H), 7.95 (1H, s, -N=CH), 6.24-7.63 (8H, m, aromatic). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 34,129(3.61) (Aromatic transition, π→π*), 28,248(2.89) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀NOCl: C, 67.39; H, 4.35; N, 6.05. Found: C, 66.65; H, 4.52; N, 5.69.

3.4.6 Synthesis of 3-(4-nitrobenzylideneamino)phenol, (L12)

4-Nitrobenzaldehyde (1.51 g, 10 mmol.) and 3-aminophenol (1.09 g, 10 mmol.) were dissolved in toluene (100 ml) and stirred under reflux at 110 °C for 2 h. The red crude product was collected by filtration of hot reaction mixture, re-crystallized from toluene, dried with vacuum pump and stored in a desiccator over silica gel.

Yield: 1.37 g (52 %). m.p.: decomp. IR (cm⁻¹): 1603, 1504, 1429, 1337, 1195, 1104, 832, 535. ¹H-NMR (δ/ ppm): 8.71 (1H, s, O-H), 8.39 (1H, s, -N=CH), 6.20-8.11 (8H, m, aromatic). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 33,783(3.29) (Aromatic transition, π→π*), 28,932(2.96) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀N₂O₃: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.86; H, 4.42; N, 11.53.

3.5 Synthesis of 4-aminophenol Schiff Bases

Schiff bases of 4-aminophenol were synthesized by reacting 4-aminophenol with substituted benzaldehydes 2-methoxybenzaldehyde, 2-chlorobenzaldehyde, 2-nitrobenzaldehyde, 4-methoxybenzaldehyde, 4-chlorobenzaldehyde and 4-nitrobenzaldehyde.

3.5.1 Synthesis of 4-(2-methoxybenzylideneamino)phenol, (L13)

2-Methoxybenzaldehyde (1.36 g, 10 mmol.) and 4-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 2.10 g (93 %). m.p.: 130-131 °C. IR (cm⁻¹): 1614, 1535, 1366, 1262, 1020, 860, 752, 486. ¹H-NMR (δ/ ppm): 8.89(1H, s, O-H), 8.00 (1H, s, -N=CH), 6.86-7.53 (8H, m, aromatic), 3.96 (3H, s, -OCH₃). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 37,313(4.05) (Aromatic transition, π→π*), 29,154(4.31) (Imine transition, n→π*). Anal. Calcd. for C₁₄H₁₃NO₂: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.85; H, 5.74; N, 6.05.

3.5.2 Synthesis of 4-(2-chlorobenzylideneamino)phenol, (L14)

2-Chlorobenzaldehyde (1.40 g, 10 mmol.) and 4-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.41 g (54 %). m.p.: 120-121 °C. IR (cm⁻¹): 1625, 1522, 1372, 1273, 1043, 821, 743, 541, 494. ¹H-NMR (δ/ ppm): 8.93 (1H, s, O-H), 8.21 (1H, s, -N=CH), 6.84-7.39 (8H, m, aromatic). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 29,761(4.09) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀NOCl: C, 67.39; H, 4.35; N, 6.05. Found: C, 67.27; H, 4.15; N, 6.06

3.5.3 Synthesis of 4-(2-nitrobenzylideneamino)phenol, (L15)

2-Nitrobenzaldehyde (1.51 g, 10 mmol.) and 4-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.40 g (58 %). m.p.: 119-120 °C. IR (cm⁻¹): 1620, 1530, 1334, 1269, 735, 539, 495. ¹H-NMR (δ/ ppm): 8.98 (1H, s, O-H), 8.29 (1H, s, -N=CH), 6.87-8.03 (8H, m, aromatic). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 36,630(4.24) (Aromatic transition, π→π*), 28,169(3.86) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀N₂O₂: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.27; H, 4.02; N, 11.50.

3.5.4 Synthesis of 4-(4-methoxybenzylideneamino)phenol, (L16)

4-Methoxybenzaldehyde (1.21 ml, 10 mmol.) and 4-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.59 g (70 %). m.p.: 150-151 °C. IR (cm⁻¹): 1618, 1513, 1443, 1165, 1260, 977, 817, 752, 542. ¹H-NMR (δ/ ppm): 9.43 (1H, s, O-H), 8.35 (1H, s, -N=CH), 6.78-7.85 (8H, m, aromatic), 3.83 (3H, s, -OCH₃). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 34,482 (3.99) (Aromatic transition, π→π*), 29,395 (3.22) (Imine transition, n→π*). Anal. Calcd. for C₁₄H₁₃NO₂: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.51; H, 5.71; N, 6.12.

3.5.5 Synthesis of 4-(4-chlorobenzylideneamino)phenol, (L17)

4-Chlorobenzaldehyde (1.40 g, 10 mmol.) and 4-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The yellow precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.49 g (62 %). m.p.: 136-137 °C. IR (cm⁻¹): 1604, 1453, 1271, 865, 543. ¹H-NMR (δ/ ppm): 9.57 (1H, s, O-H), 8.61 (1H, s, -N=CH), 6.84-7.94 (8H, m, aromatic). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 37,174 (3.29) (Aromatic transition, π→π*), 29,030 (2.96) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀NOCl: C, 67.39; H, 4.35; N, 6.05. Found: C, 67.52; H, 4.22; N, 6.07.

3.5.6 Synthesis of 4-(4-nitrobenzylideneamino)phenol, (L18)

4-Nitrobenzaldehyde (1.51 g, 10 mmol.) and 4-aminophenol (1.09 g, 10 mmol.) were dissolved in ethanol (50 ml) and stirred under reflux at 70 °C for 6 h. The orange precipitate formed was separated by filtration, re-crystallized from ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 1.18 g (49 %). m.p.: 118-119 °C. IR (cm⁻¹): 3426, 1623, 1567, 1247, 754, 453. ¹H-NMR (δ/ ppm): 8.61 (1H, s, O-H), 8.53 (1H, s, -N=CH), 6.92-8.09 (8H, m, aromatic). UV-Vis (CHCl₃) (λ / cm⁻¹ (log ε / L mol⁻¹ cm⁻¹): 38,759(4.11) (Aromatic transition, π→π*), 27,666 (4.13) (Imine transition, n→π*). Anal. Calcd. for C₁₃H₁₀N₂O₃: C, 64.46; H, 4.16; N, 11.56. Found: C, 64.02; H, 3.84; N, 11.36.

3.6 Synthesis of Copper and Cobalt Complexes from 2-aminophenol Schiff Bases

The 2-aminophenol Schiff bases were each used as ligand in synthesis of Schiff base metal complexes with copper and cobalt metal ions.

3.6.1 Synthesis of bis(2-(2-methoxybenzylideneamino)phenol)copper(II) (CuL1)

An ethanolic solution (40 ml) of 2-(2-methoxybenzylideneamino)phenol (0.9090 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.71 g (52 %). m.p.: > 250. IR (cm^{-1}): 3441, 3312, 1618, 1353, 1271, 1018, 894, 745, 581, 441. UV-Vis (CHCl_3) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,041 (3.81), 30,120 (3.56); UV-Vis (DMF) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 22,988 (4.20), 30,581 (4.43). Magnetic moment (μ_{eff}): 1.52 BM. Anal. Calcd. for $\text{C}_{28}\text{H}_{24}\text{Cl}_2\text{Cu}_2\text{N}_2\text{O}_4$: C, 49.03; H, 3.53; N, 6.08; Cu, 20.96. Found: C, 48.84; H, 2.78; N, 7.74; Cu, 21.20.

3.6.2 Synthesis of bis(2-(2-methoxybenzylideneamino)phenol)cobalt(II) (CoL1)

An ethanolic solution (40 ml) of 2-(2-methoxybenzylideneamino)phenol (0.9090 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.4758 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.51 g (47 %). m.p.: > 250. IR (cm^{-1}): 1596, 1479, 1360, 1278, 1147, 1023, 868, 739, 579, 438. UV-Vis (DMF) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,255 (4.17), 30,030 (4.20). Magnetic

moment (μ_{eff}): 5.46 BM. Anal. Calcd. for $\text{C}_{28}\text{H}_{28}\text{Cl}_2\text{CoN}_2\text{O}_6$: C, 60.43; H, 5.16; N, 5.12; Co, 11.96. Found: C, 59.60; H, 4.32; N, 5.28; Co, 12.52.

3.6.3 Synthesis of bis(2-(2-chlorobenzylideneamino)phenol)copper(II) (CuL2)

An ethanolic solution (40 ml) of 2-(2-chlorobenzylideneamino)phenol (0.9242 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.48 g (44 %). m.p.: > 250. IR (cm^{-1}): 3431, 3312, 1570, 1481, 1277, 865, 739, 578, 447.

UV-Vis (CHCl_3) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,255 (4.22), 31,847 (3.93); UV-Vis (DMF) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 15,698 (3.42), 22,799 (4.39). Magnetic moment (μ_{eff}): 1.60 BM.

Anal. Calcd. for $\text{C}_{26}\text{H}_{18}\text{Cl}_4\text{Cu}_2\text{N}_2\text{O}_2$: C, 47.36; H, 2.75; N, 7.25; Cu, 17.17. Found: C, 49.91; H, 2.68; N, 7.98; Cu, 18.17.

3.6.4 Synthesis of bis(2-(2-chlorobenzylideneamino)phenol)cobalt(II) (CoL2)

An ethanolic solution (40 ml) of 2-(2-chlorobenzylideneamino)phenol (0.9267 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.4758 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.65 g (58 %). m.p.: > 250. IR (cm^{-1}): 3416, 1580, 1481, 1250, 865, 739, 542, 439.

UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,094 (4.57), 31,446 (4.66); Magnetic moment (μ_{eff}): 5.29 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{Cl}_2\text{CoN}_2\text{O}_4$: C, 55.13; H, 3.99; N, 5.04; Co, 11.54. Found: C, 54.55; H, 3.10; N, 5.04; Co, 12.64.

3.6.5 Synthesis of bis(2-(2-nitrobenzylideneamino)phenol)copper(II) (CuL3)

An ethanolic solution (40 ml) of 2-(2-nitrobenzylideneamino)phenol (0.9688 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.46 g (40 %). m.p.: > 250. IR (cm^{-1}): 3307, 1556, 1517, 1256, 837, 738, 581, 418. UV-Vis (CHCl_3) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,255 (3.95), 32,154 (3.81); UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 22,727 (4.35), 31,250 (3.89). Magnetic moment (μ_{eff}): 1.72 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{CuN}_4\text{O}_8$: C, 52.65; H, 3.81; N, 9.63; Cu, 10.03. Found: C, 52.80; H, 2.90; N, 9.82; Cu, 10.13.

3.6.6 Synthesis of bis(2-(2-nitrobenzylideneamino)phenol)cobalt(II) (CoL3)

An ethanolic solution (40 ml) of 2-(2-nitrobenzylideneamino)phenol (0.9689 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.4758 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.68 g (61 %). m.p.: > 250. IR (cm^{-1}): 1571, 1515, 1250, 849, 732, 529, 485.

UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 22,471 (3.95), 31,250 (4.13). Magnetic moment (μ_{eff}): 5.32 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{CoN}_2\text{O}_8$: C, 54.08; H, 3.84; N, 9.70; Co, 13.82. Found: C, 54.84; H, 3.04; N, 9.15; Co: 12.82.

3.6.7 Synthesis of bis(2-(4-methoxybenzylideneamino)phenol)copper(II) (CuL4)

An ethanolic solution (40 ml) of 2-(4-methoxybenzylideneamino)phenol (0.9080 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.84 g (69 %). m.p.: > 250. IR (cm^{-1}): 3440, 3320, 1596, 1572, 1477, 1375, 1178, 836, 756, 584, 448. UV-Vis (CHCl_3) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,255 (3.33), 31,152 (3.04); UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 15,698 (3.41) 22,988 (3.80). Magnetic moment (μ_{eff}): 1.56 BM. Anal. Calcd. for $\text{C}_{28}\text{H}_{24}\text{Cl}_2\text{Cu}_2\text{N}_2\text{O}_4$: C, 51.70; H, 3.72; N, 7.61; Cu, 20.87. Found: C, 51.78; H, 2.85; N, 8.01; Cu, 20.98.

3.6.8 Synthesis of bis(2-(4-methoxybenzylideneamino)phenol)cobalt(II) (CoL4)

An ethanolic solution (40 ml) of 2-(4-methoxybenzylideneamino)phenol (0.9090 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.4758 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.70 g (57 %). m.p.: > 250. IR (cm^{-1}): 3277, 1593, 1481, 1250, 1190, 1162, 1020, 826, 748, 587, 443. UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,419 (4.06), 31,152 (4.33).

Magnetic moment (μ_{eff}): 5.27 BM. Anal. Calcd. for $\text{C}_{28}\text{H}_{28}\text{Cl}_2\text{CoN}_2\text{O}_6$: C, 54.38; H, 4.56; N, 4.53; Co, 12.93. Found: C, 54.03; H, 4.30; N, 5.95; % Co: 13.13.

3.6.9 Synthesis of bis(2-(4-chlorobenzylideneamino)phenol)copper(II) (CuL5)

An ethanolic solution (40 ml) of 2-(4-chlorobenzylideneamino)phenol (0.9240 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.68 g (52 %). m.p.: > 250. IR (cm^{-1}): 3438, 3317, 1585, 1456, 1212, 1180, 845, 753, 594, 456. UV-Vis (CHCl_3) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 19,762 (3.67), 22,573 (3.70); UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 15,841 (3.24), 22,883 (4.10), 30,959 (4.08). Magnetic moment (μ_{eff}): 1.52 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{18}\text{Cl}_4\text{Cu}_2\text{N}_2\text{O}_2$: C, 47.36; H, 2.75; N, 7.25; Cu, 20.95. Found: C, 47.58; H, 2.41; N, 7.32; Cu, 19.53.

3.6.1.0 Synthesis of bis(2-(4-chlorobenzylideneamino)phenol)cobalt(II) (CoL5)

An ethanolic solution (40 ml) of 2-(4-chlorobenzylideneamino)phenol (0.9267 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.4758 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.67 g (60 %). m.p.: > 250. IR (cm^{-1}): 1577, 1473, 1277, 1250, 746, 593, 525, 496, 433. UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 22,935 (4.04), 31,152 (4.20). Magnetic moment (μ_{eff}): 5.19 BM; Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{Cl}_2\text{CoN}_2\text{O}_4$: C, 55.13; H, 3.99; N, 5.04; Co, 11.76. Found: C, 55.08; H, 3.27; N, 5.60; Co, 12.84.

3.6.1.1 Synthesis of bis(2-(4-nitrobenzylideneamino)phenol)copper(II) (CuL6)

An ethanolic solution (40 ml) of 2-(4-nitrobenzylideneamino)phenol (0.9689 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.67 g (62 %). m.p.: > 250. IR (cm^{-1}): 3441, 3317, 1595, 1517, 1449, 1343, 1291, 1054, 851, 750, 577, 453. UV-Vis (DMF) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 15,698 (3.44), 22,988 (3.80), 30,088 (4.56). Magnetic moment (μ_{eff}): 1.87 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{18}\text{CuN}_4\text{O}_6$: C, 59.19; H, 3.32; N, 10.26; Cu, 9.37. Found: C, 59.13; H, 3.09; N, 10.82; Cu, 10.36.

3.6.1.2 Synthesis of bis(2-(4-nitrobenzylideneamino)phenol)cobalt(II) (CoL6)

An ethanolic solution (40 ml) of 2-(4-nitrobenzylideneamino)phenol (0.9689 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ (0.4758 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The orange solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.95 g (87 %). m.p.: > 250. IR (cm^{-1}): 1596, 1456, 1274, 847, 750, 683, 582, 487. UV-Vis (DMF) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 20,449 (4.01), 30,674 (4.18). Magnetic moment (μ_{eff}): 4.28 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{18}\text{CoN}_4\text{O}_6$: C, 57.68; H, 3.35; N, 10.35; Co, 9.84. Found: C, 57.01; H, 3.16; N, 10.21; Co, 11.52.

3.7 Synthesis of Copper Complexes from 3-aminophenol Schiff Bases

The Schiff bases of 3-aminophenol were each used as ligand in synthesis of Schiff base metal complexes with copper metal ion.

3.7.1 Synthesis of bis(3-(2-methoxybenzylideneamino)phenol)copper(II) (CuL7)

An ethanolic solution (40 ml) of 3-(2-methoxybenzylideneamino)phenol (0.9080 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.60 g (54 %). m.p.: decomp. IR (cm^{-1}): 3337, 1581, 1484, 1244, 1235, 1019, 749, 504, 452. UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 27,932 (3.68). Magnetic moment (μ_{eff}): 1.74 BM. Anal. Calcd. for $\text{C}_{28}\text{H}_{28}\text{CuN}_2\text{O}_6$: C, 60.92; H, 5.11; N, 5.07; Cu, 8.75. Found: C, 60.48; H, 4.70; N, 5.05; Cu, 7.28.

3.7.2 Synthesis of bis(3-(2-chlorobenzylideneamino)phenol)copper(II) (CuL8)

An ethanolic solution (40 ml) of 3-(2-chlorobenzylideneamino)phenol (0.9267 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.77 g (69 %). m.p.: decomp. IR (cm^{-1}): 3342, 1586, 1503, 1226, 1221, 1032, 827, 757, 541, 437. UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 26,954 (3.85). Magnetic moment (μ_{eff}): 1.76 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{Cl}_2\text{CuN}_2\text{O}_4$: C, 55.50; H, 3.95; N, 4.99; Cu, 9.33. Found: C, 55.67; H, 3.61; N, 4.51; Cu, 8.18.

3.7.3 Synthesis of bis(3-(2-nitrobenzylideneamino)phenol)copper(II) (CuL9)

An ethanolic solution (40 ml) of 3-(2-nitrobenzylideneamino)phenol (0.9688 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.51 g (44 %). m.p.: decomp. IR (cm^{-1}): 3327, 1593, 1515, 1341, 1218, 729, 531, 452. UV-Vis (DMF) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 26,881 (3.93). Magnetic moment (μ_{eff}): 1.78 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{CuN}_4\text{O}_8$: C, 53.92; H, 3.81; N, 9.63; Cu, 9.63. Found: C, 53.65; H, 3.90; N, 8.25; Cu, 9.30.

3.7.4 Synthesis of bis(3-(4-methoxybenzylideneamino)phenol)copper(II) (CuL10)

An ethanolic solution (40 ml) of 3-(4-methoxybenzylideneamino)phenol (0.9080 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.65 g (60 %). m.p.: decomp. IR (cm^{-1}): 3336, 1592, 1170, 856, 734, 533, 442. UV-Vis (DMF) (ν / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 26,525 (3.58). Magnetic moment (μ_{eff}): 1.70 BM. Anal. Calcd. for $\text{C}_{28}\text{H}_{28}\text{CuN}_2\text{O}_6$: C, 60.92; H, 5.11; N, 5.07; Cu, 9.51. Found: C, 59.51; H, 4.57; N, 5.17; Cu, 8.48.

3.7.5 Synthesis of bis(3-(4-chlorobenzylideneamino)phenol)copper(II) (CuL11)

An ethanolic solution (40 ml) of 3-(4-chlorobenzylideneamino)phenol (0.9267 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.57 g (51 %). m.p.: decomp. IR (cm^{-1}): 1572, 1578, 1481, 1160, 1084, 821, 527, 458.

UV-Vis (DMF) (λ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 27,624 (3.68). Magnetic moment (μ_{eff}): 1.72

BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{Cl}_2\text{CuN}_2\text{O}_4$: C, 55.67; H, 3.95; N, 4.99; Cu, 7.33. Found: C, 55.31; H, 3.70; N, 4.54; Cu, 6.66.

3.7.6 Synthesis of bis(3-(4-nitrobenzylideneamino)phenol)copper(II) (CuL12)

An ethanolic solution (40 ml) of 3-(4-nitrobenzylideneamino)phenol (0.9688 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.49 g (43 %). m.p.: decomp. IR (cm^{-1}): 3368, 1590, 1507, 1338, 1214, 832, 527, 447.

UV-Vis (DMF) (λ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 27,575 (3.97). Magnetic moment (μ_{eff}): 1.70

BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{22}\text{CuN}_4\text{O}_8$: C, 53.65; H, 3.81; N, 9.63; Cu, 6.92. Found: C, 54.27; H, 4.08; N, 9.27; Cu, 5.14.

3.8 Synthesis of Copper Complexes from 4-aminophenol Schiff Bases

The Schiff bases of 4-aminophenol were each used as ligand in synthesis of Schiff base metal complexes with copper metal ion.

3.8.1 Synthesis of bis(4-(2-methoxybenzylideneamino)phenol)copper(II) (CuL13)

An ethanolic solution (40 ml) of 4-(2-methoxybenzylideneamino)phenol (0.9090 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.63 g (47 %). m.p.: > 250. IR (cm^{-1}): 3430, 3345, 1593, 1474, 1257, 1254, 805, 565, 517, 409. UV-Vis (CHCl_3) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 20,080 (3.91, 30,959 (3.18)). UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 20,833 (4.10), 30,864 (3.14). Magnetic moment (μ_{eff}): 1.80 BM. Anal. Calcd. for $\text{C}_{28}\text{H}_{26}\text{ClCuN}_2\text{O}_5$: C, 49.76; H, 3.88; N, 7.14; Cu, 13.73. Found: C, 49.94; H, 3.91; N, 8.80; Cu, 12.73.

3.8.2 Synthesis of bis(4-(2-chlorobenzylideneamino)phenol)copper(II) (CuL14)

An ethanolic solution (40 ml) of 4-(2-chlorobenzylideneamino)phenol (0.9240 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.51 g (43 %). m.p.: > 250. IR (cm^{-1}): 3352, 1662, 1609, 1485, 1255, 749, 527, 504, 429, 404. UV-Vis (CHCl_3) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 25,316 (3.69). UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 23,109 (2.56). Magnetic moment (μ_{eff}): 1.84 BM. Anal. Calcd. for

$C_{26}H_{18}Cl_3CuN_2O_2$: C, 52.41; H, 3.05; N, 6.70; Cu, 11.38. Found: C, 52.46; H, 3.95; N, 7.35; Cu, 10.67.

3.8.3 Synthesis of bis(4-(2-nitrobenzylideneamino)phenol)copper(II) (CuL15)

An ethanolic solution (40 ml) of 4-(2-nitrobenzylideneamino)phenol (0.9688 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $CuCl_2 \cdot 2H_2O$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.48 g (41 %). m.p.: > 250. IR (cm^{-1}): 3320, 1661, 1604, 1521, 1483, 1252, 834, 540, 508, 435. UV-Vis ($CHCl_3$) (ν / cm^{-1} (log $\epsilon / L mol^{-1} cm^{-1}$)): 31,847 (3.85). UV-Vis (DMF) (ν / cm^{-1} (log $\epsilon / L mol^{-1} cm^{-1}$)): 22,666 (4.08), 30,088 (4.56). Magnetic moment (μ_{eff}): 1.88 BM. Anal. Calcd. for $C_{26}H_{20}ClCuN_4O_7$: C, 52.09; H, 3.36; N, 9.35; Cu, 10.60. Found: C, 52.05; H, 3.79; N, 8.68; Cu, 10.12.

3.8.4 Synthesis of bis(4-(4-methoxybenzylideneamino)phenol)copper(II) (CuL16)

An ethanolic solution (40 ml) of 4-(4-methoxybenzylideneamino)phenol (0.9080 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $CuCl_2 \cdot 2H_2O$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.52 g (40 %). m.p.: > 250. IR (cm^{-1}): 3346, 1584, 1472, 1385, 1253, 1241, 801, 563, 525, 515, 407. UV-Vis (DMF) (ν / cm^{-1} (log $\epsilon / L mol^{-1} cm^{-1}$)): 20,080 (4.38), 30,959 (2.86). Magnetic moment (μ_{eff}): 1.82 BM. Anal. Calcd. for $C_{28}H_{26}Cl_2CuN_2O_5$: C, 49.76; H, 3.88; N, 8.14; Cu, 11.92. Found: C, 50.34; H, 3.94; N, 8.77; Cu, 12.19.

3.8.5 Synthesis of bis(4-(4-chlorobenzylideneamino)phenol)copper(II) (CuL17)

An ethanolic solution (40 ml) of 4-(4-chlorobenzylideneamino)phenol (0.9267 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.56 g (47 %). m.p.: > 250. IR (cm^{-1}): 3346, 1589, 1252, 854, 768, 565, 516.

UV-Vis (CHCl_3) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 31,948 (3.69); UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 15,698 (2.58), 23,315 (2.79), 30,959 (2.68). Magnetic moment (μ_{eff}): 1.81 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{18}\text{Cl}_4\text{CuN}_2\text{O}_2$: C, 51.41; H, 3.05; N, 6.70; Cu, 12.81. Found: C, 51.84; H, 3.66; N, 7.43; Cu, 11.98.

3.8.6 Synthesis of bis(4-(4-nitrobenzylideneamino)phenol)copper(II) (CuL18)

An ethanolic solution (40 ml) of 4-(4-nitrobenzylideneamino)phenol (0.9688 g, 4 mmol.) was mixed with an ethanolic solution (20 ml) of $\text{CuCl}_2 \cdot 2\text{H}_2\text{O}$ (0.3409 g, 2 mmol.). The solution was made alkaline with triethylamine and heated to reflux for 4 h. The brown solid product was collected by filtration, washed in ethanol, dried with a vacuum pump and stored in a desiccator over silica gel.

Yield: 0.45 g (36 %). m.p.: > 250. IR (cm^{-1}): 3345, 1591, 1256, 854, 556, 514. UV-Vis (DMF) (∇ / cm^{-1} ($\log \epsilon / \text{L mol}^{-1} \text{cm}^{-1}$)): 25,839 (4.26). Magnetic moment (μ_{eff}): 1.83 BM. Anal. Calcd. for $\text{C}_{26}\text{H}_{18}\text{Cl}_2\text{CuN}_4\text{O}_6$: C, 51.62; H, 2.94; N, 9.05; Cu, 11.96. Found: C, 51.39; H, 3.61; N, 8.51; Cu, 12.22.

3.9 Antibacterial Studies

3.9.1 Bacterial strains

The Schiff bases and metal complexes were individually tested against a panel of standard microorganisms namely *Escherichia coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538), *Pseudomonas aeruginosa* (ATCC 19582), *Bacillus cereus* (10702), *Enterococcus faecalis* (ATCC 29212) and *Klebsiella pneumoniae* (ATCC 10031). The organisms were obtained from the Department of Microbiology and Biochemistry, University of Zululand, South Africa.

3.9.2 Disc diffusion assay

Antibacterial activity of Schiff bases and metal complexes were carried out in triplicate using the disc diffusion method (Bauer *et al.*, 1996). Molten Mueller-Hinton agar was inoculated with the bacteria suspension which had been adjusted to the 0.5 McFarland standard and poured into sterile 90 mm Petri dishes. SBs and Metal complexes were dissolved in DMSO to obtain a final concentration of 10 mg/ml. Sterile Whatman No. 1 (6 mm) discs were separately impregnated with each sample to be tested and placed on the inoculated agar. The plates were incubated at 37 °C for 24 h and the zones of inhibition measured at the end of the incubation period. Ampicillin and Jik[®] (sodium hypochlorite) were used as reference compound.

3.9.3 Minimum inhibitory concentration

The minimum inhibitory concentration (MIC) of the SBs and metal complexes were determined using the 96-well micro-plate dilution method (Eloff, 1998). Serial plate concentrations of 5.0, 2.5, 1.25, 0.625, 0.312, and 0.157, 0.078 and 0.039 mgmL⁻¹ were prepared for each compound. Each was inoculated with 1.5x10⁸ CFU/mL of 0.5 McFarland standard bacteria suspension and incubated for 24 h at 37 °C. As an indicator of bacterial growth, 20 µL of 0.2 mgmL⁻¹ *p*-iodonitrotetrazolium solution (a colourless tetrazolium) was added to each well and incubated at 37 °C for 30 min. Growing bacteria metabolise this salt to give a red product (formazan).

Inhibition prevents this conversion resulting in a clear well. MIC values were recorded as the lowest concentration of compound preventing bacterial growth.

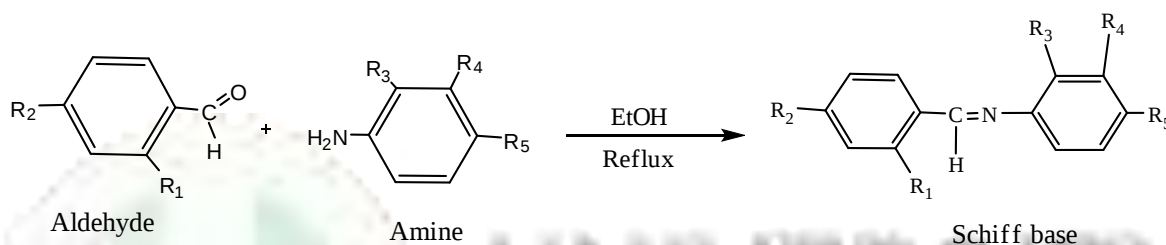


CHAPTER FOUR

4.0 RESULTS

4.1 Syntheses of Schiff Bases and Metal Complexes

Three series of Schiff bases derived from condensation of 2-aminophenol, 3-aminophenol or 4-aminophenol and substituted benzaldehydes (Scheme 23) were synthesized under reflux. The Schiff bases were used as ligands with copper and cobalt metal salts to synthesize the metal complexes.



Scheme 23: Schiff base with substituents represented by R

$R_3 = 2\text{OH}$
 $R_4 = 3\text{OH}$
 $R_5 = 4\text{OH}$

$R_1 = \text{Cl}$
 OMe
 NO_2

$R_2 = \text{Cl}$
 OMe
 NO_2

Table 3: Schiff bases and metal complexes with substituents at *o*-position

Compounds	R ₁	R ₂	R ₃	R ₄	R ₅
L1, CuL1, CoL1	OMe	H	OH	H	H
L2, CuL2, CoL2	Cl	H	OH	H	H
L3, CuL3, CoL3	NO ₂	H	OH	H	H
L7, CuL7	OMe	H	H	OH	H
L8, CuL8	Cl	H	H	OH	H
L9, CuL9	NO ₂	H	H	OH	H
L13, CuL13	OMe	H	H	H	OH
L14, CuL14	Cl	H	H	H	OH
L15, CuL15	NO ₂	H	H	H	OH

Table 4: Schiff bases and metal complexes with substituents at *p*-position

Compounds	R ₁	R ₂	R ₃	R ₄	R ₅
L4, CuL4, CoL4	H	OMe	OH	H	H
L5, CuL5, CoL5	H	Cl	OH	H	H
L6, CuL6, CoL6	H	NO ₂	OH	H	H
L10, CuL10	H	OMe	H	OH	H
L11, CuL11	H	Cl	H	OH	H
L12, CuL12	H	NO ₂	H	OH	H
L16, CuL16	H	OMe	H	H	OH
L17, CuL17	H	Cl	H	H	OH
L18, CuL18	H	NO ₂	H	H	OH

4.1.1 Synthesis of 2-aminophenol Schiff Bases and Metal Complexes

Six Schiff base ligands namely; 2-methoxybenzylidene-2-aminophenol (L1), 2-chlorobenzylidene-2-aminophenol (L2), 2-nitrobenzylidene-2-aminophenol (L3), 4-methoxybenzylidene-2-aminophenol (L4), 4-chlorobenzylidene-2-aminophenol (L5), 4-nitrobenzylidene-2-aminophenol (L6) were obtained from reaction of 2-aminophenol with 2- and 4-substituted benzaldehydes (Scheme 24) Table 24. Three of the compounds had substituents in *o*-position and the other in *p*-position. The SBs were reacted with copper and cobalt chlorides to yield copper and cobalt Schiff base metal complexes; bis(2-(2-methoxybenzylideneamino)phenol)copper(II) CuL1, bis(2-(2-methoxybenzylideneamino)phenol)cobalt(II) CoL1, bis(2-(2-chlorobenzylideneamino)phenol)copper(II) CuL2, bis(2-(2-chlorobenzylideneamino)phenol)cobalt(II) CoL2, bis(2-(2-nitrobenzylideneamino)phenol)copper(II) CuL3, bis(2-(2-nitrobenzylideneamino)phenol)cobalt(II) CoL3, bis(2-(4-methoxybenzylideneamino)phenol)copper(II) CuL4, bis(2-(4-methoxybenzylideneamino)phenol)cobalt(II) CoL4, bis(2-(4-chlorobenzylideneamino)phenol)copper(II) CuL5, bis(2-(4-chlorobenzylideneamino)phenol)cobalt(II) CoL5, bis(2-(4-nitrobenzylideneamino)phenol)copper(II) CuL6 and bis(2-(4-nitrobenzylideneamino)phenol)cobalt(II) CoL6 respectively.

4.1.2 Physical and analytical data of 2-aminophenol Schiff Bases and Metal Complexes

The physical and analytical data of Schiff bases and Schiff base metal complexes derived from 2-aminophenol are presented in Tables 5a and 5b.

Table 5a: Physical and analytical data of *o*-substituted 2-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	Empirical Formula (M.wt)	Yield (%)	Color	M.pt (°C)	% Found (calcd)			Metal (%)
							C	H	N	
L1	OMe	H	C ₁₄ H ₁₃ NO ₂ (227)	71.74	Yellow	70-71	73.30 (73.77)	5.77(5.77)	6.05(6.16)	-
CuL1	OMe	H	C ₂₈ H ₂₄ Cl ₂ Cu ₂ N ₂ O ₄ (685)	51.83	Brown	>250	48.84 (49.03)	2.78(3.53)	7.74(6.08)	21.20
CoL1	OMe	H	C ₂₈ H ₂₆ CoN ₂ O ₆ (547)	47.00	Brown	>250	59.60 (60.43)	4.32(5.16)	5.28(5.12)	12.52
L2	Cl	H	C ₁₃ H ₁₀ NOCl (231)	58.16	Yellow	58-59	67.38(67.39)	4.24(4.35)	6.03(6.05)	-
CuL2	Cl	H	C ₂₆ H ₁₆ Cl ₄ Cu ₂ N ₂ O ₂ (659)	43.76	Brown	>250	47.91(47.36)	2.68(2.75)	7.98(7.25)	18.17
CoL2	Cl	H	C ₂₆ H ₂₂ Cl ₂ CoN ₂ O ₄ (556)	58.37	Brown	>250	55.55(55.13)	3.10(3.99)	5.04(5.04)	12.64
L3	NO ₂	H	C ₁₃ H ₁₀ N ₂ O ₃ (242)	65.48	Yellow	64-65	64.62 (64.46)	4.07(4.16)	11.60(11.56)	-
CuL3	NO ₂	H	C ₂₆ H ₂₂ CuN ₄ O ₈ (582)	40.00	Brown	>250	52.80(52.65)	2.90(3.81)	9.82(9.63)	10.13
CoL3	NO ₂	H	C ₂₆ H ₂₂ CoN ₄ O ₈ (577)	61.16	Brown	>250	54.84(54.08)	3.04 (3.84)	9.15(9.70)	12.82

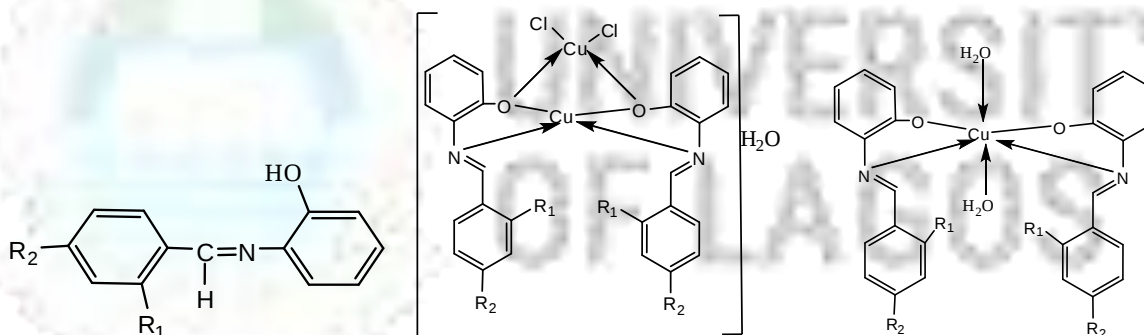


Figure 23: Schiff bases and metal complexes synthesized from 2-aminophenol

Microanalysis were obtained for each of the synthesized compounds. The percentage metal were determined for the metal complexes, methoxy and chloro substituted complexes exhibited 2 moles of metal ion per mole of complex while other complexes exhibited one mole of metal ion per mole of complex. The melting points of the Schiff bases were in the range 70-71 °C for OMe substituted SB L1, 58-59 °C for Cl substituted SB L2 and 64-65 °C for NO₂ substituted SB L3 while the metal complexes decomposed above 250 °C. The yields obtained ranges between 58-72 % for Schiff base ligands L1-L3 and 40-61 % for Schiff base metal complexes CuL1, CoL1-CuL3, CoL3.

Table 5b: Physical and analytical data of *p*-substituted 2-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	Empirical Formula (M.wt)	Yield (%)	Color	M.pt (°C)	% Found (calcd)			Metal (%)
							C	H	N	
L4	H	OMe	C ₁₄ H ₁₃ NO ₂ (227)	69.10	Yellow	56-57	74.08(73.99)	5.67(5.77)	6.13(6.16)	-
CuL4	H	OMe	C ₂₈ H ₂₄ Cl ₂ Cu ₂ N ₂ O ₄ (650)	67.68	Brown	>250	51.78(51.70)	2.85(3.72)	8.01(7.61)	20.98
CoL4	H	OMe	C ₂₈ H ₂₆ Cl ₂ CoN ₂ O ₆ (618)	56.57	Brown	>250	54.03(54.38)	4.30 (4.56)	5.95 (4.53)	13.13
L5	H	Cl	C ₁₃ H ₁₀ NOCl (231)	62.83	Yellow	78-79	67.26(67.39)	4.30(4.35)	6.05 (6.05)	-
CuL5	H	Cl	C ₂₆ H ₁₈ Cl ₄ Cu ₂ N ₂ O ₂ (659)	51.77	Brown	>250	47.58(47.36)	2.41 (2.75)	7.32 (7.25)	19.53
CoL5	H	Cl	C ₂₆ H ₂₂ Cl ₂ CoN ₂ O ₄ (556)	60.00	Brown	>250	55.08(55.13)	3.27(3.99)	5.60 (5.04)	12.84
L6	H	NO ₂	C ₁₃ H ₁₀ N ₂ O ₃ (242)	76.79	Yellow	112	64.82(64.46)	4.07(4.16)	11.64(11.56)	-
CuL6	H	NO ₂	C ₂₆ H ₁₈ CuN ₄ O ₆ (545)	61.57	Brown	>250	59.13(59.19)	3.09(3.32)	10.82(10.26)	10.36
CoL6	H	NO ₂	C ₂₆ H ₁₈ CoN ₄ O ₆ (541)	87.34	Orange	>250	57.01(57.68)	3.16(3.35)	10.21(10.35)	11.52

Microanalysis were obtained for each of the synthesized compounds. The percentage metal were determined for the metal complexes, methoxy and chloro substituted complexes exhibited 2 moles of metal ion per mole of complex while other complexes exhibited one mole of metal ion per mole of complex. The melting points of the Schiff bases were in the range 56-57 °C for OMe substituted SB L4, 78-79 °C for Cl substituted SB L5 and 112 °C for NO₂ substituted SB L6 while the metal complexes decomposed above 250 °C. The yields obtained ranges between 63-77 % for Schiff base ligands L4-L6 and 52-87 % for Schiff base metal complexes CuL4, CoL4-CuL6, CoL6.

4.1.3 Spectroscopic data of 2-aminophenol Schiff bases and Schiff base metal complexes

The Schiff bases were characterized using IR and NMR analysis and the results are presented in Tables 6a, 6b, 7a and 7b

Table 6a: IR data of *o*-substituted 2-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	$\nu(\text{O-H})$	$\nu(\text{C=N})$	$\nu(\text{C-O})$	$\nu\text{OH} (\text{H}_2\text{O})$	$\nu(\text{C-Cl})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
			cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}
L1	OMe	H	3438	1625	1284	-	-	-	-
CuL1	OMe	H	3441, 3312	1618	1271	865	-	581	441
CoL1	OMe	H	-	1596	1278	868	-	579	438
L2	Cl	H	3414	1616	1270	-	349	-	-
CuL2	Cl	H	3431, 3312	1570	1277	840	349	578	447
CoL2	Cl	H	3416	1580	1250	865	349	542	439
L3	NO ₂	H	3360	1626	1269	-	-	-	-
CuL3	NO ₂	H	3307	1556	1256	836	-	581	418
CoL3	NO ₂	H	-	1571	1250	848	-	529	485

The imine band (C=N) in the Schiff bases appears in the region 1625 cm^{-1} for OMe-substituted SB L1 (Figure 24), 1616 cm^{-1} for Cl-substituted SB L2 (Figure 25) and 1626 cm^{-1} for NO₂-substituted SB L3 (Figure 26). On coordination, the bands shifted to lower frequencies of 1618, 1596 cm^{-1} , 1570, 1580 cm^{-1} and 1556, 1571 cm^{-1} respectively. The phenolic -OH stretch in Schiff bases appears around 3414 cm^{-1} L2 and 3360 cm^{-1} L3. The IR spectra also exhibited characteristic band (C-O) in the Schiff bases in the region 1284 cm^{-1} L1, 1270 cm^{-1} L2 and 1269 cm^{-1} L3. In the metal complexes, the band appears in the region $1271, 1278 \text{ cm}^{-1}, 1277, 1250 \text{ cm}^{-1}$ and $1256, 1250 \text{ cm}^{-1}$ respectively. Coordinated water indicates a broad band in the region $3441, 3312 \text{ cm}^{-1}$ CuL1, $3431, 3312 \text{ cm}^{-1}$ CuL2, and 3307 cm^{-1} CuL3. New bands were observed at $418\text{-}485 \text{ cm}^{-1}$ and $529\text{-}581 \text{ cm}^{-1}$ in the spectra of metal complexes.

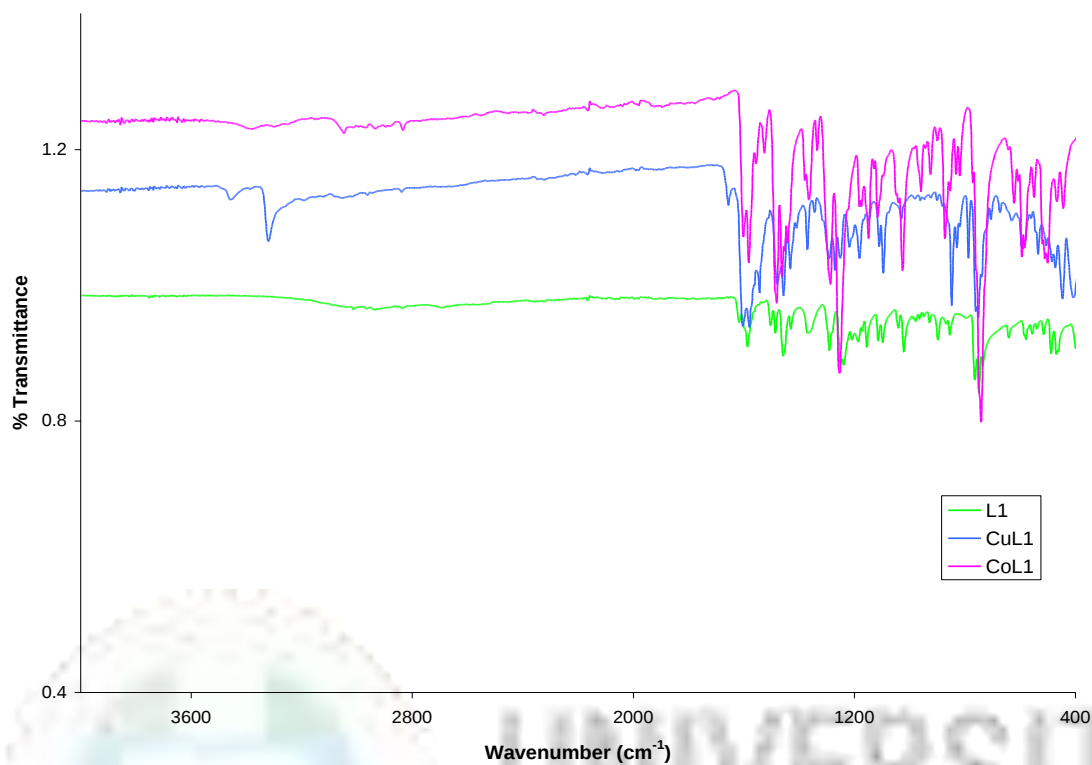


Figure 24: IR spectra of 2-(2-methoxybenzylideneamino)phenol (L1) and Cu and Co metal complexes

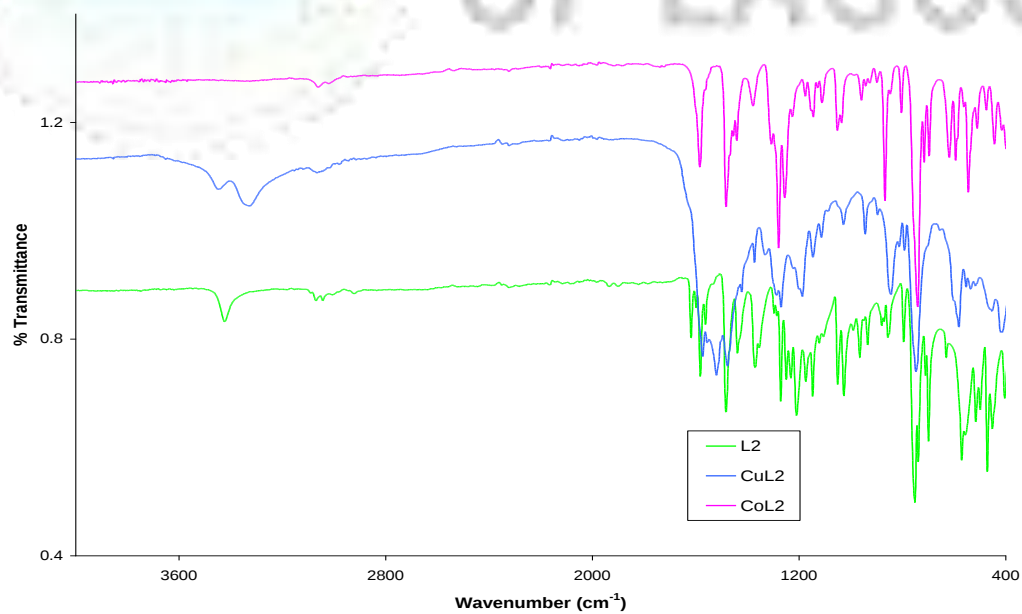


Figure 25: IR spectra of 2-(2-chlorobenzylideneamino)phenol (L2) and Cu and Co metal complexes

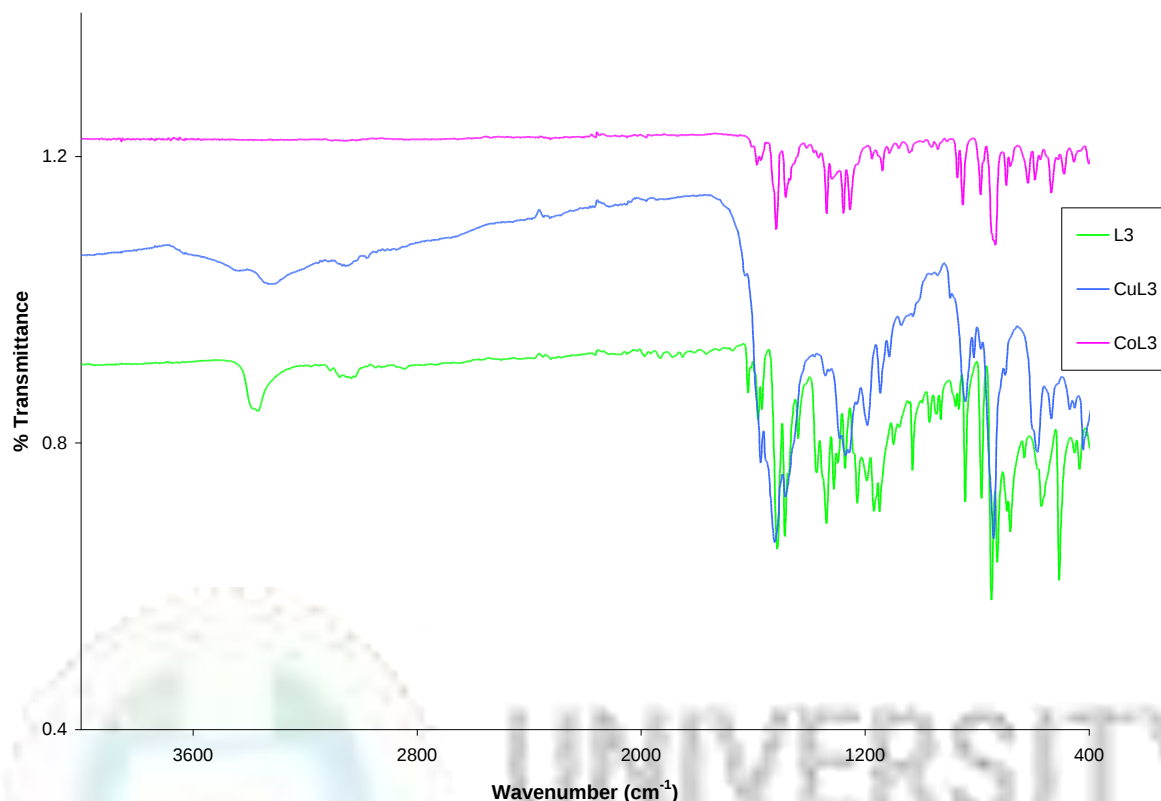


Figure 26: IR spectra of 2-(2-nitrobenzylideneamino)phenol (L3) and Cu and Co metal complexes

Table 6b: IR data of *p*-substituted 2-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	v(O-H)	v(C=N)	v(C-O)	vOH (H ₂ O)	v(C-Cl)	v(M-O)	v(M-N)
			cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹
L4	H	OMe	3333	1618	1245	-	-	-	-
CuL4	H	OMe	3440, 3320	1596	1178	835	-	584	448
CoL4	H	OMe	3277	1593	1190	827	-	587	443
L5	H	Cl	3291	1601	1238	-	350	-	-
CuL5	H	Cl	3438, 3317	1585	1212	846	350	594	456
CoL5	H	Cl	-	1577	1277	860	350	593	433
L6	H	NO ₂	3304	1623	1299	-	-	-	-
CuL6	H	NO ₂	3431, 3317	1595	1291	851	-	577	453
CoL6	H	NO ₂	-	1596	1274	846	-	582	487

The imine band (C=N) in SBs appears in the region 1618 cm⁻¹ for OMe-substituted SB L4 (Figure 27), 1601 cm⁻¹ for Cl-substituted SB L5 (Figure 28) and 1623 cm⁻¹ NO₂-substituted SB L6 (Figure 29). On coordination, the bands shifted to lower frequencies of 1596, 1593 cm⁻¹, 1585, 1577 cm⁻¹ and 1595, 1596 cm⁻¹ respectively. The phenolic -OH stretch in Schiff bases

appears around 3333 cm^{-1} L4, 3291 cm^{-1} L5 and 3304 cm^{-1} L6. The IR spectra also exhibit characteristic band (C-O) in the Schiff bases in the region 1245 cm^{-1} L4, 1238 cm^{-1} L5 and 1299 cm^{-1} L6. In the metal complexes, the band appears in the region $1178, 1190\text{ cm}^{-1}$, $1212, 1277\text{ cm}^{-1}$ and $1291, 1274\text{ cm}^{-1}$. Coordinated water indicates a broad band in the region $3440, 3320, 3277\text{ cm}^{-1}$ CuL4, CoL4, $3438, 3317\text{ cm}^{-1}$ CuL5, and $3431, 3317\text{ cm}^{-1}$ CuL6. New bands were observed at $433\text{--}487\text{ cm}^{-1}$ and $577\text{--}594\text{ cm}^{-1}$ in the spectra of metal complexes.

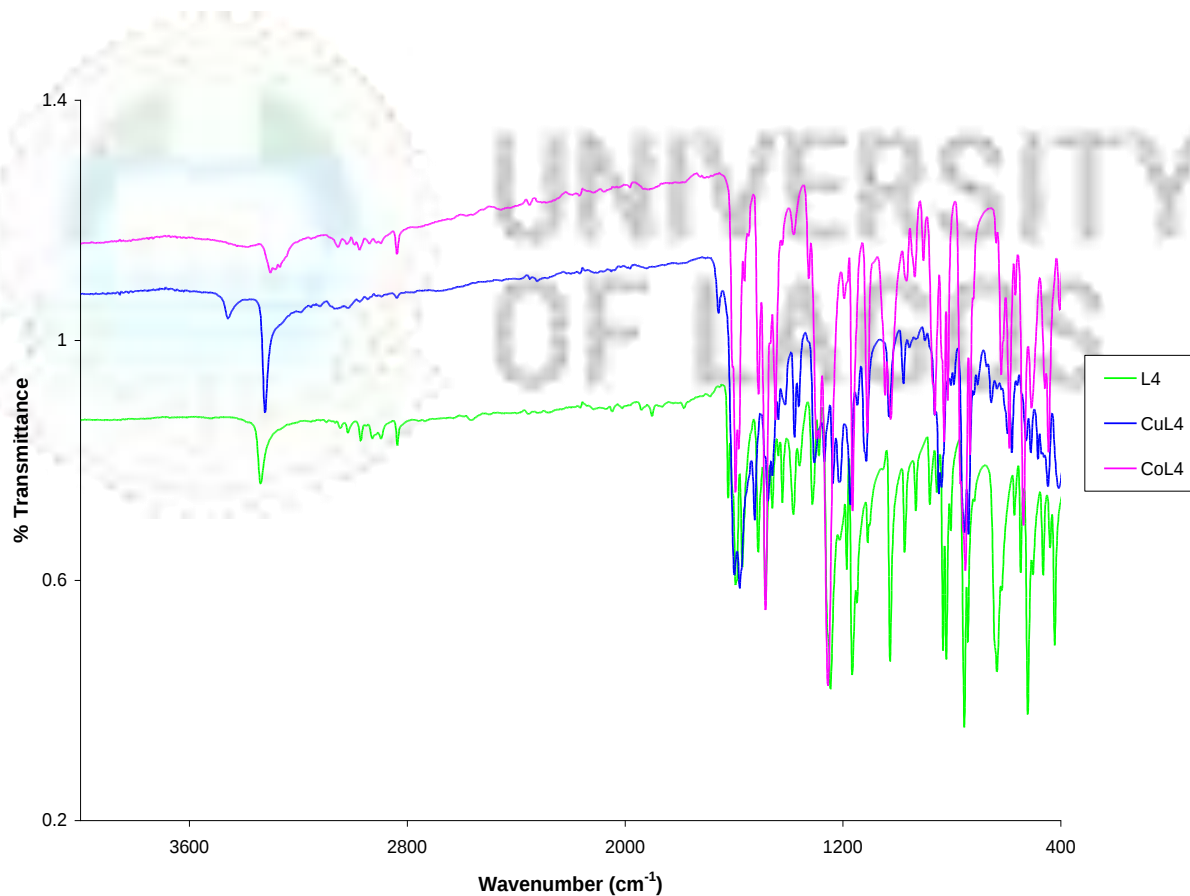


Figure 27: IR spectra of 2-(4-methoxybenzylideneamino)phenol (L4) and Cu and Co metal complexes

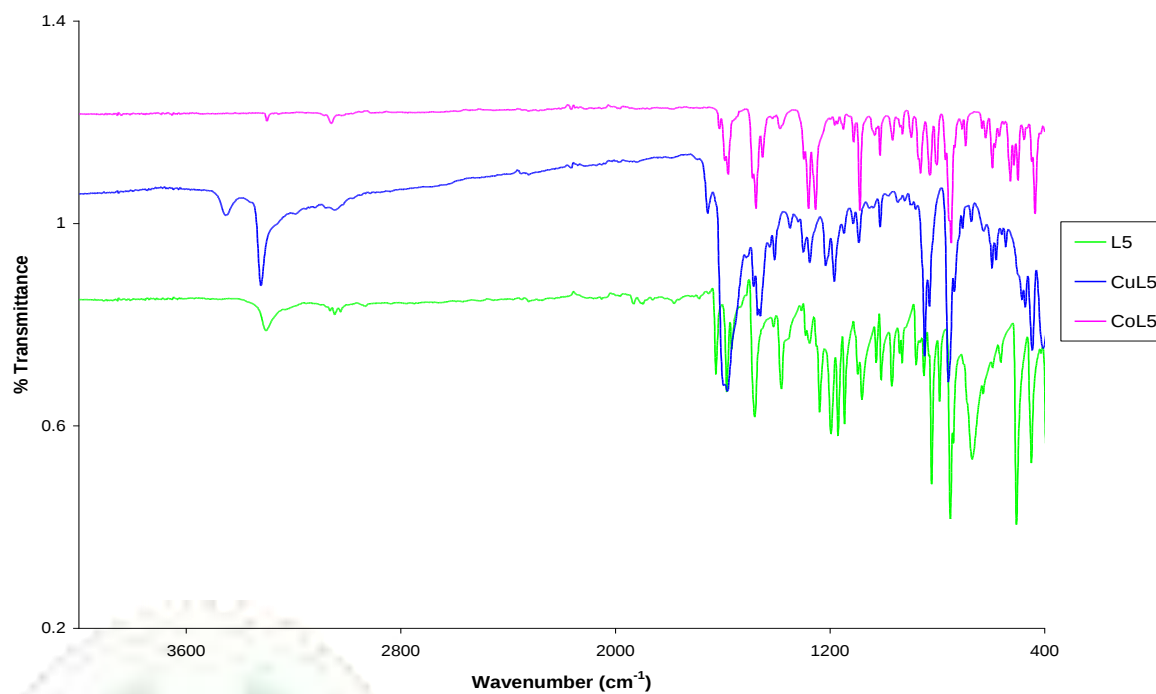


Figure 28: IR spectra of 2-(4-chlorobenzylideneamino)phenol (L5) and Cu and Co metal complexes

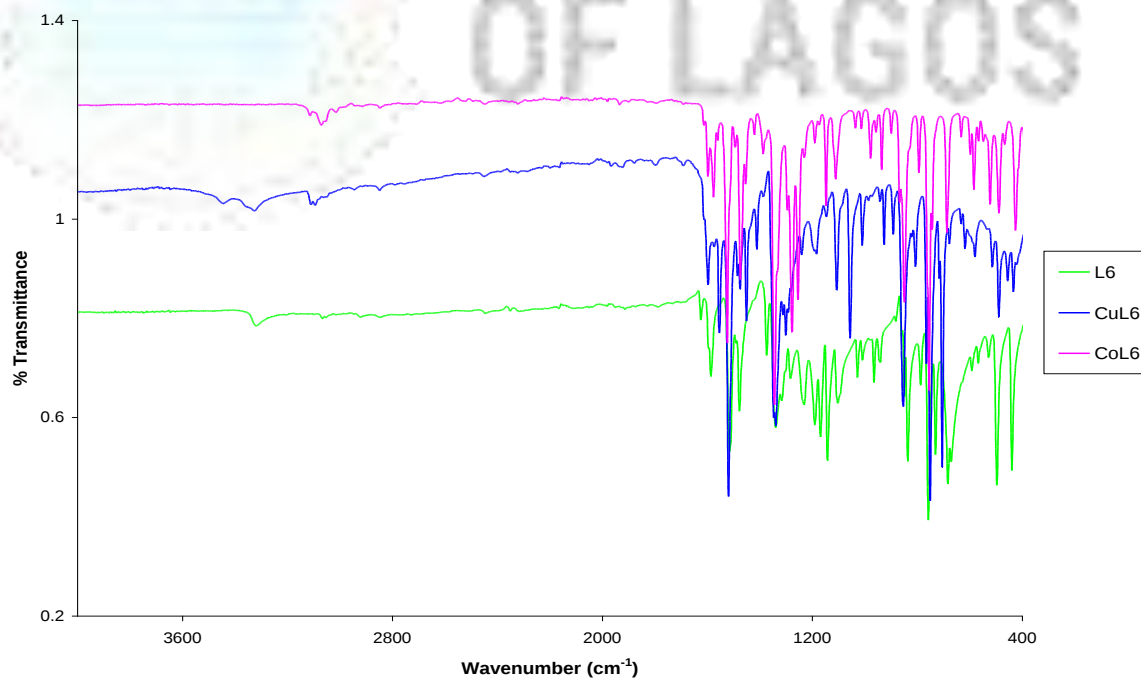


Figure 29: IR spectra of 2-(4-nitrobenzylideneamino)phenol (L6) and Cu and Co metal complexes

4.1.4. ¹H NMR Data of 2-aminophenol Schiff Bases

The ¹H NMR data of 2-aminophenol Schiff bases are presented in Tables 7a and 7b.

Table 7a: ¹H NMR data of *o*-substituted 2-aminophenol Schiff bases

Compound	R ₁	R ₂	HC=N (s, 1H) (δ, ppm)	OH (s, 1H) (δ, ppm)	OCH ₃ (s, 3H) (δ, ppm)	Aromatic, protons m, 8H (δ, ppm)
L1	OMe	H	8.17	9.17	3.93	6.88-7.45
L2	Cl	H	8.26	9.21	-	6.97-7.50
L3	NO ₂	H	8.25	9.15	-	6.93-8.05

The imine (C=N) protons show signals at 8.17 ppm for OMe-substituted SB L1 (Figure 30), 8.26 ppm, for Cl-substituted SB L2 (Figure 31), and 8.25 ppm for NO₂-substituted SB L3 (Figure 32). Methoxy protons (-OCH₃) appears as singlets at 3.93 ppm for OMe-substituted SB L1, the signal for the phenolic -OH appears at 9.17 ppm OMe-substituted SB L1 (Figure 30), 9.21 ppm for Cl-substituted SB L2 (Figure 31) and 9.15 ppm for NO₂-substituted SB L3 (Figure 32). Aromatic protons show multiple resonance signals between 6.88-8.05 ppm.

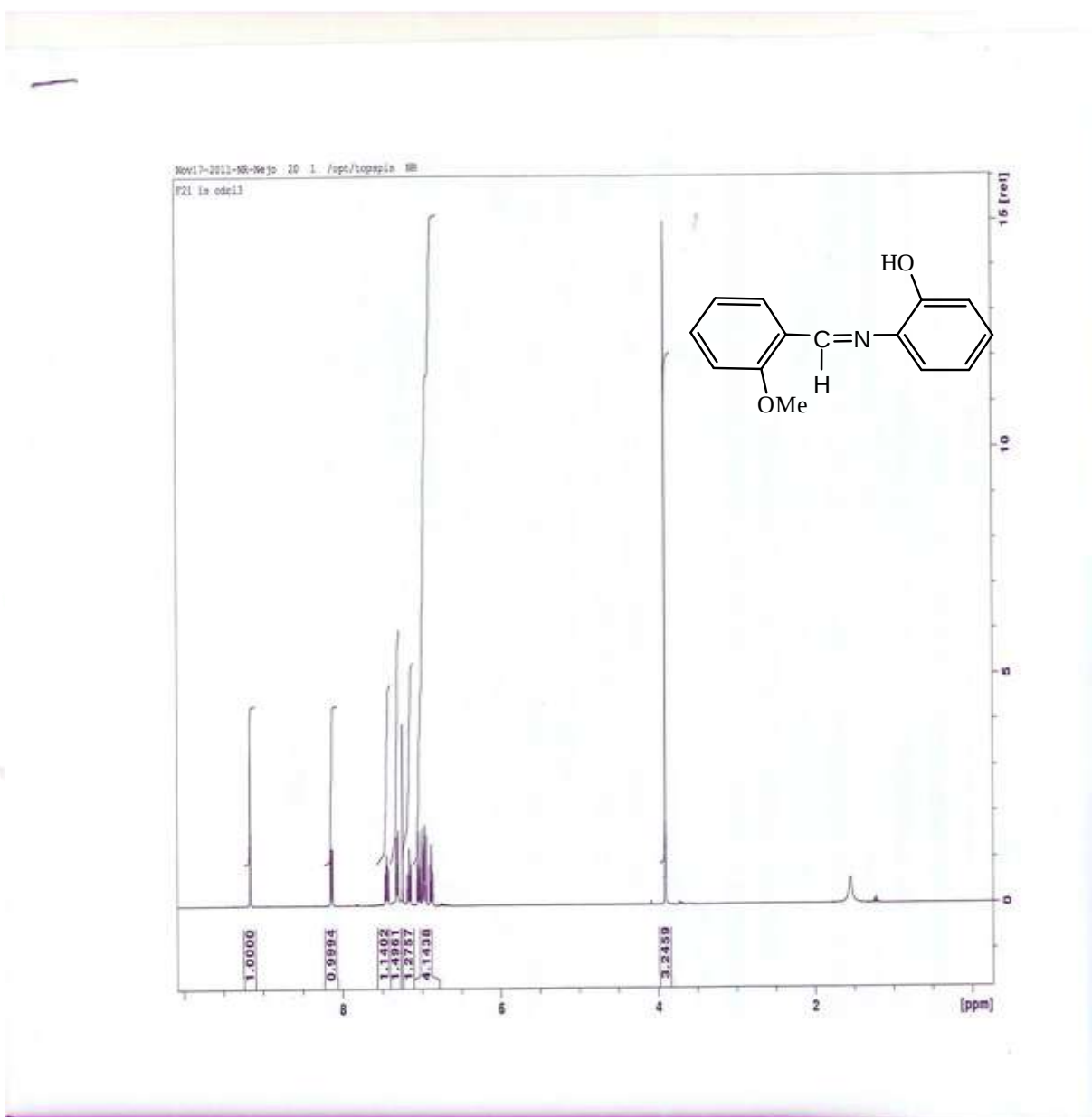


Figure 30: ^1H NMR spectrum of 2-(2-methoxybenzylideneamino)phenol Schiff base (L1)

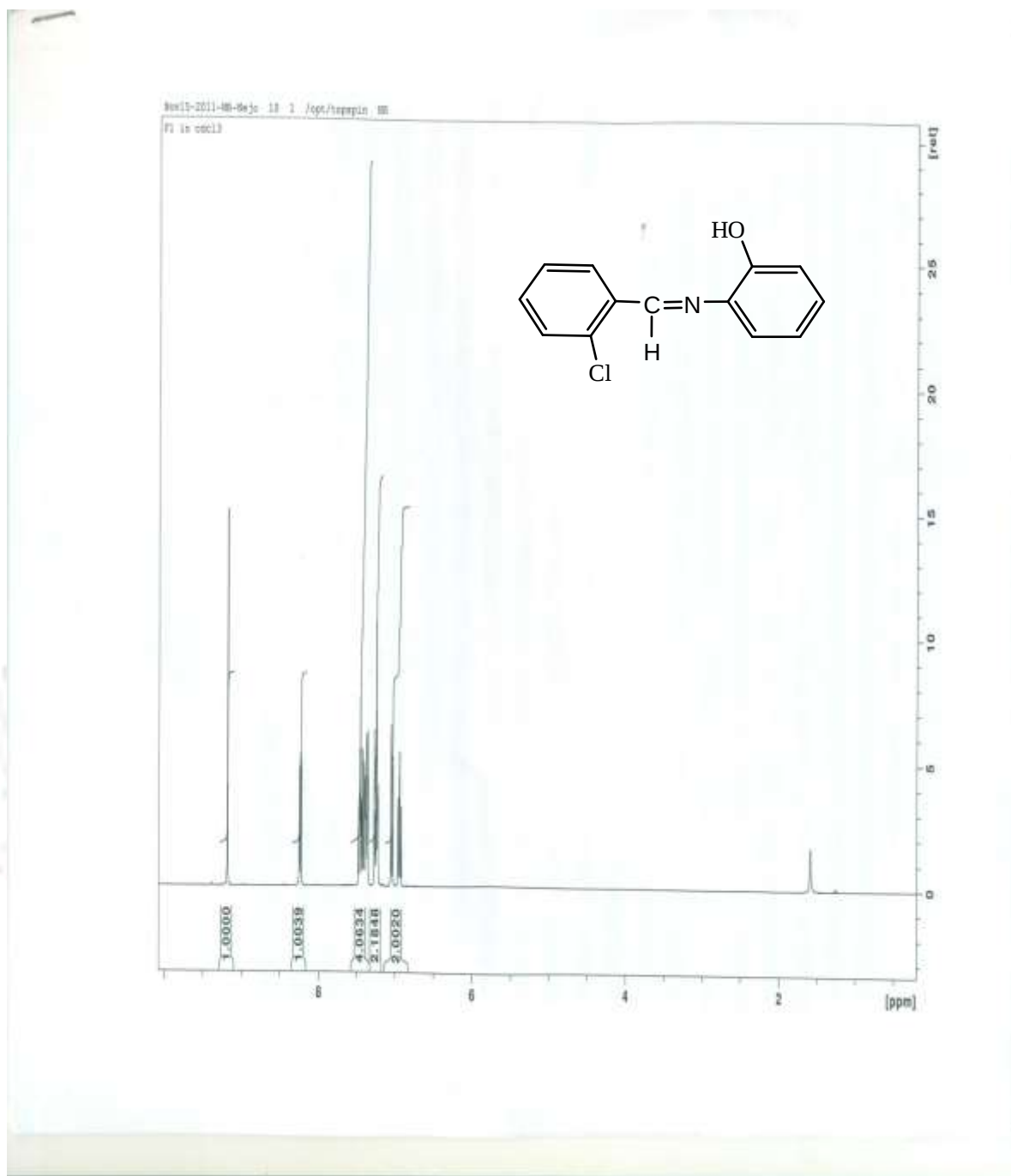


Figure 31: ^1H NMR spectrum of 2-(2-chlorobenzylideneamino)phenol Schiff base (L2)

Table 7b: ^1H NMR data of *p*-substituted 2-aminophenol Schiff bases

Compound	R ₁	R ₂	HC=N (s, 1H) (δ , ppm)	OH (s, 1H) (δ , ppm)	OCH ₃ (s, 3H) (δ , ppm)	Aromatic, protons m, 8H (δ , ppm)
L4	H	OMe	7.89	8.63	3.91	6.90-7.29
L5	H	Cl	7.98	8.65	-	6.88-7.81
L6	H	NO ₂	8.37	8.77	-	6.91-8.07

The imine (C=N) protons show signals at 7.89 ppm for OMe-substituted SB L4 (Figure 33), 7.98 ppm for Cl-substituted SB L5 (Figure 34), and 8.37 ppm for NO₂-substituted SB L6 (Figure 35). Methoxy protons (-OCH₃) appears as singlets at 3.91 ppm for OMe-substituted SB L4, the signal for the phenolic -OH appears 8.63 ppm for OMe-substituted SB L4 (Figure 33), 8.65 ppm for Cl-substituted SB L5 (Figure 34) and 8.77 ppm for NO₂-substituted SB L6 (Figure 35). Aromatic protons show multiple resonance signals between 6.88-8.07 ppm.

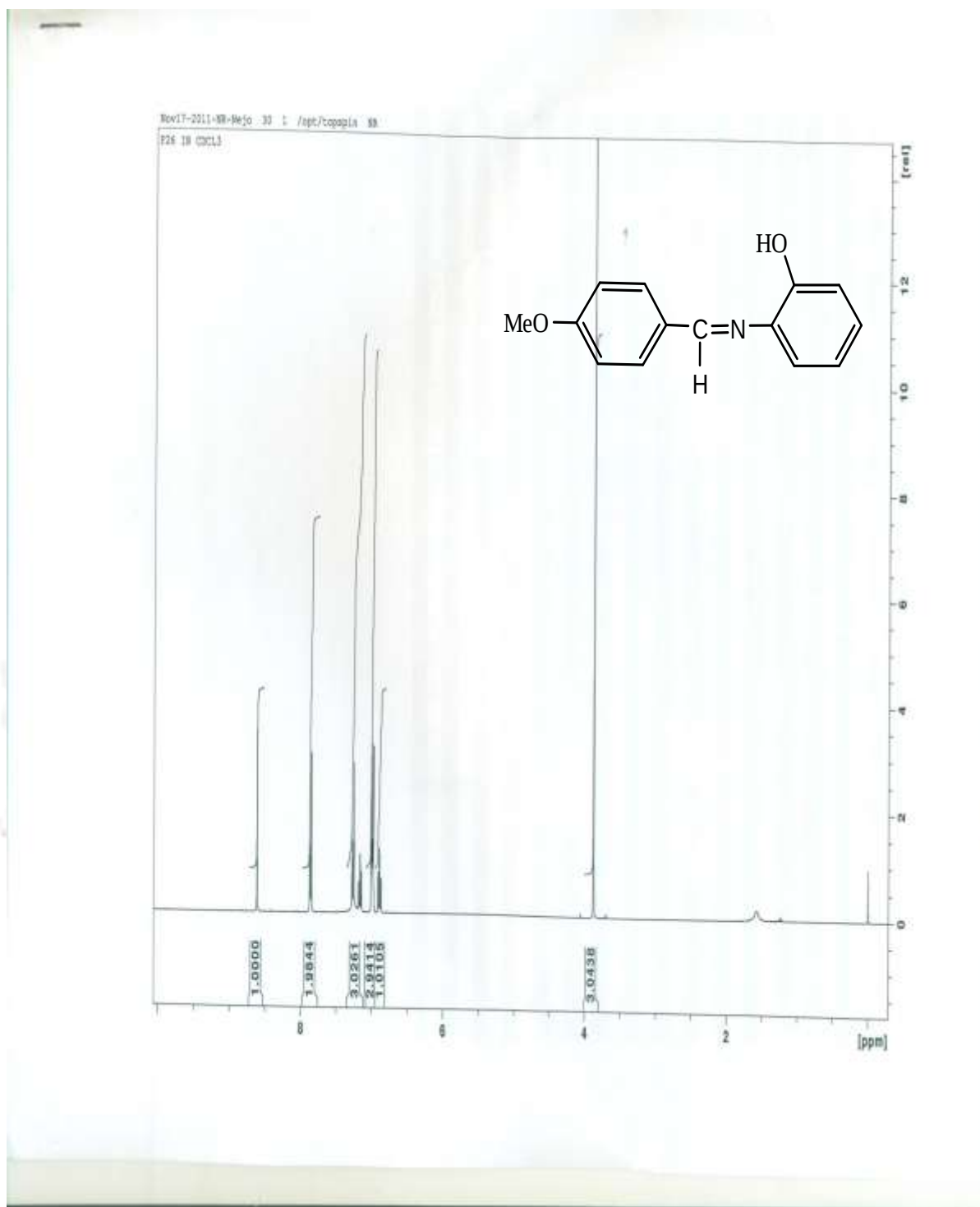


Figure 33: ¹H NMR spectrum of 2-(4-methoxybenzylideneamino)phenol Schiff base (L4)

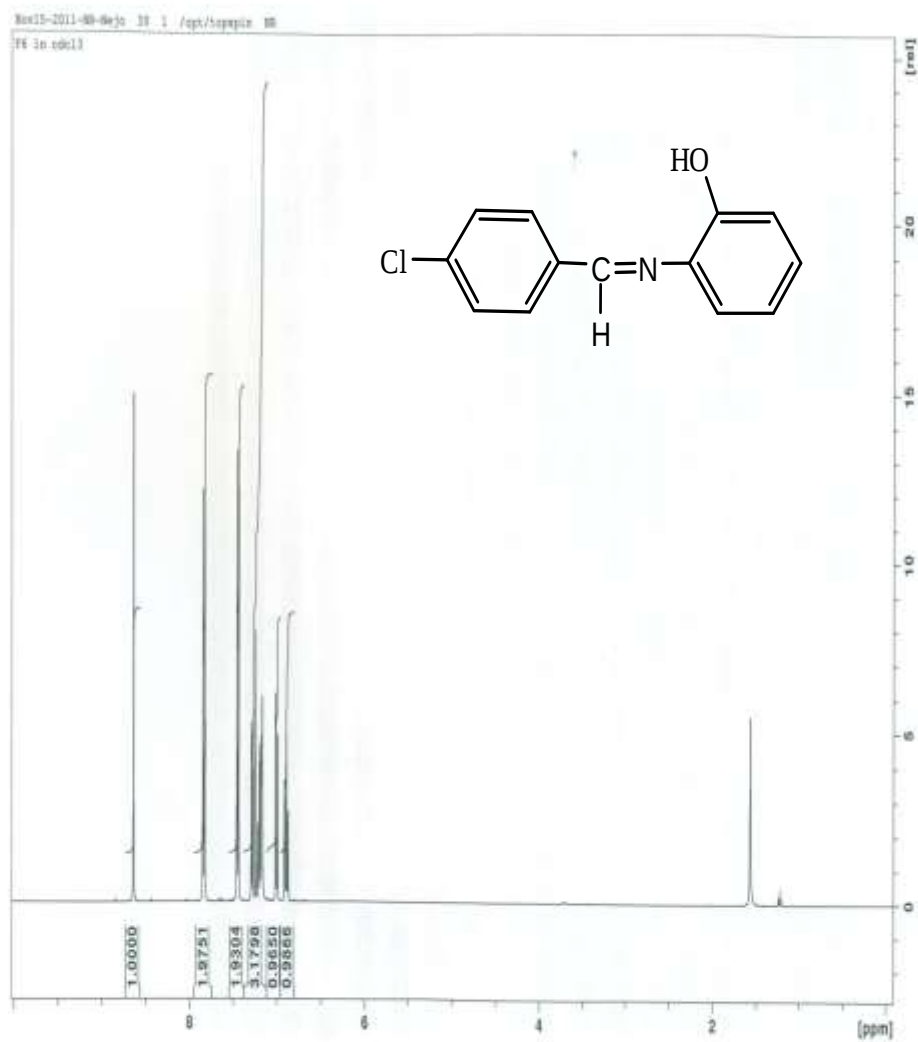


Figure 34: ^1H NMR spectrum of 2-(4-chlorobenzylideneamino)phenol Schiff base (L5)

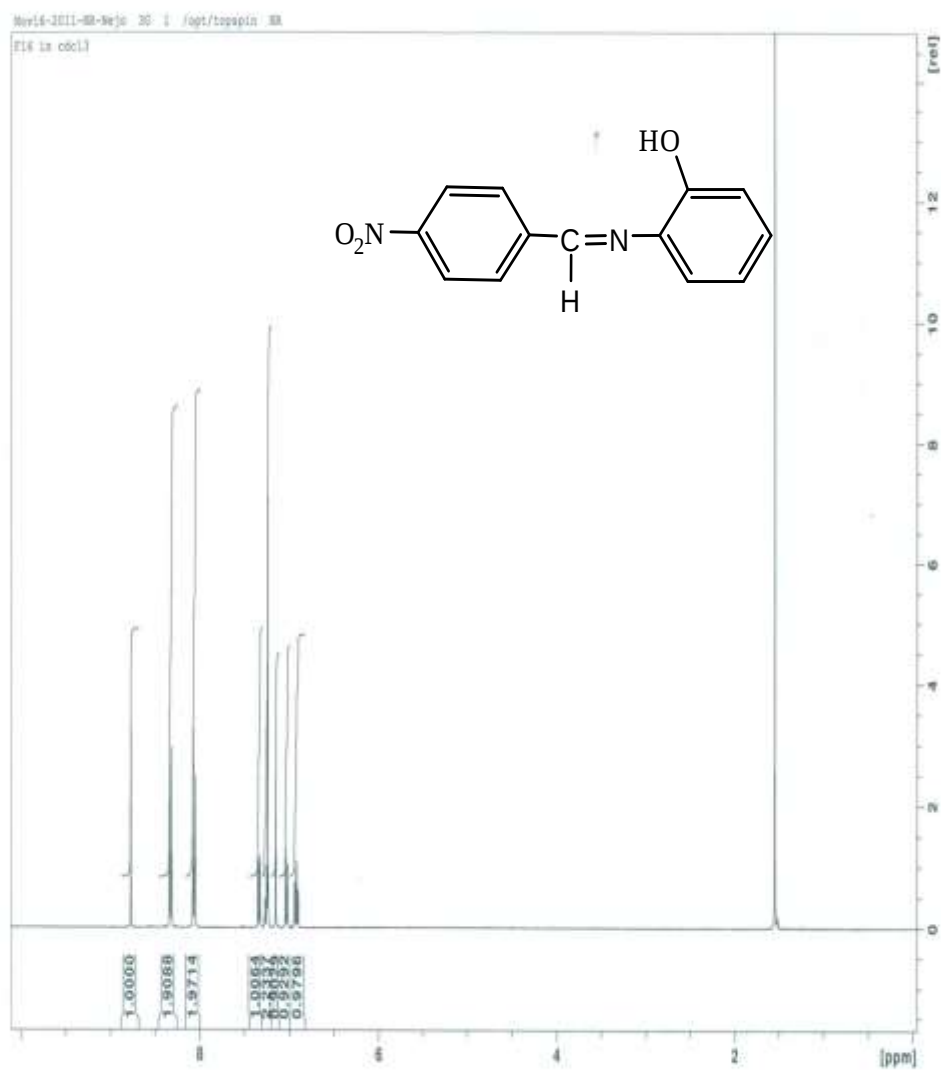


Figure 35: ^1H NMR spectrum of 2-(4-nitrobenzylideneamino)phenol Schiff base (L6)

4.1.5 Electronic Absorption Data and Magnetic Moment Measurements of 2

aminophenol Schiff Bases and Metal Complexes

The electronic spectra of the Schiff bases were recorded in CHCl_3 while those of the complexes were recorded in CHCl_3 and DMF at room temperature as presented in Tables 8a and 8b.

Table 8a: Electronic absorption data and magnetic moment measurements of *o*-substituted 2-aminophenol Schiff bases and metal complexes in CHCl_3 and DMF ($10^{-5} \text{ mol L}^{-1}$)

Compound	R ₁	R ₂	CHCl_3 (ν / cm^{-1})(log ϵ)	Assignm ent	DMF (ν / cm^{-1})(log ϵ)	Assign ment	Magnetic Moments μ_{eff} (BM)	Proposed Geometry
L1	OMe	H	35,842(4.00) 27,777(4.40)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL1	OMe	H	30,120(3.56) 23,041(3.81)	CT d-d	30,581(4.43) 22,988(4.20)	CT d-d	1.52	Square- planar
CoL1	OMe	H	- -	- -	30,030(4.20) 23,255(4.17)	CT d-d	5.46	Octahedral
L2	Cl	H	36,101(4.78) 28,571(4.75)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL2	Cl	H	31,847(3.93) 23,255(4.22)	CT d-d	22,799(4.39)	d-d	1.60	Square- planar
CoL2	Cl	H	- -	- -	31,446(4.66) 23,094(4.57)	CT d-d	5.29	Octahedral
L3	NO_2	H	36,630(4.90) 28,100(4.80)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL3	NO_2	H	32,154(3.81) 23,255(3.95)	CT d-d	31,250(3.89) 22,727(4.35)	CT d-d	1.72	Tetrahedral
CoL3	NO_2	H	- -	- -	31,250(4.13) 22,471(3.95)	CT d-d	5.32	Octahedral

Two bands were observed in the spectra of the SBs, the aromatic and azomethine bands were observed at $35,842 \text{ cm}^{-1}$ and $27,777 \text{ cm}^{-1}$ for OMe-substituted SB L1 (Figure 36) $36,101 \text{ cm}^{-1}$ and $28,571 \text{ cm}^{-1}$ for Cl-substituted SB L2 (Figure 37) $36,630 \text{ cm}^{-1}$ and $28,100 \text{ cm}^{-1}$ for NO_2 -substituted SB L3 (Figure 38).

The complexes of copper(II) and cobalt(II) show bands around $22,988\text{--}23,255 \text{ cm}^{-1}$, and $30,030\text{--}30,581 \text{ cm}^{-1}$ for OMe-substituted SBMC CuL1, CoL1 (Figure 36) $22,799\text{--}23,255 \text{ cm}^{-1}$ and $31,446\text{--}31,847 \text{ cm}^{-1}$ for Cl-substituted SBMC CuL2, CoL2 (Figure 37) $22,471\text{--}23,255 \text{ cm}^{-1}$ and $31,250\text{--}32,154 \text{ cm}^{-1}$ for NO_2 -substituted SBMC CuL3, CoL3 (Figure 38).

The observed magnetic moment values of the copper(II) complexes were in the range 1.52-1.72 BM. The magnetic moment of cobalt(II) complexes were observed in the range 5.29-5.46 BM.

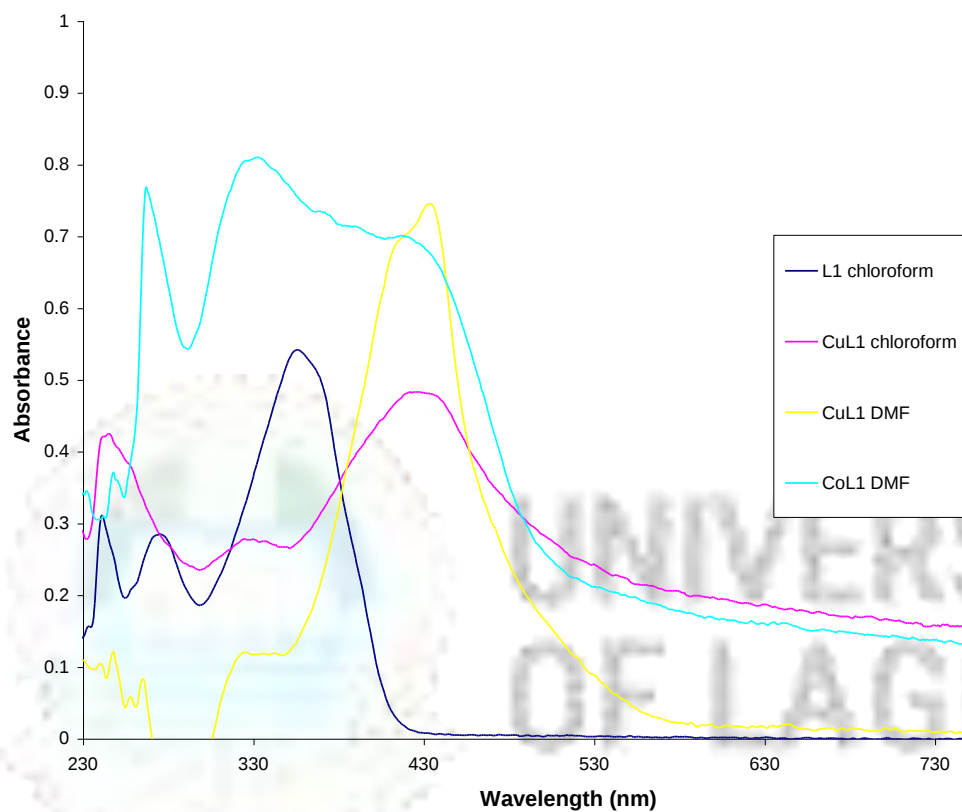


Figure 36: Electronic absorption spectra of L1 with copper and cobalt metal ions in chloroform and DMF

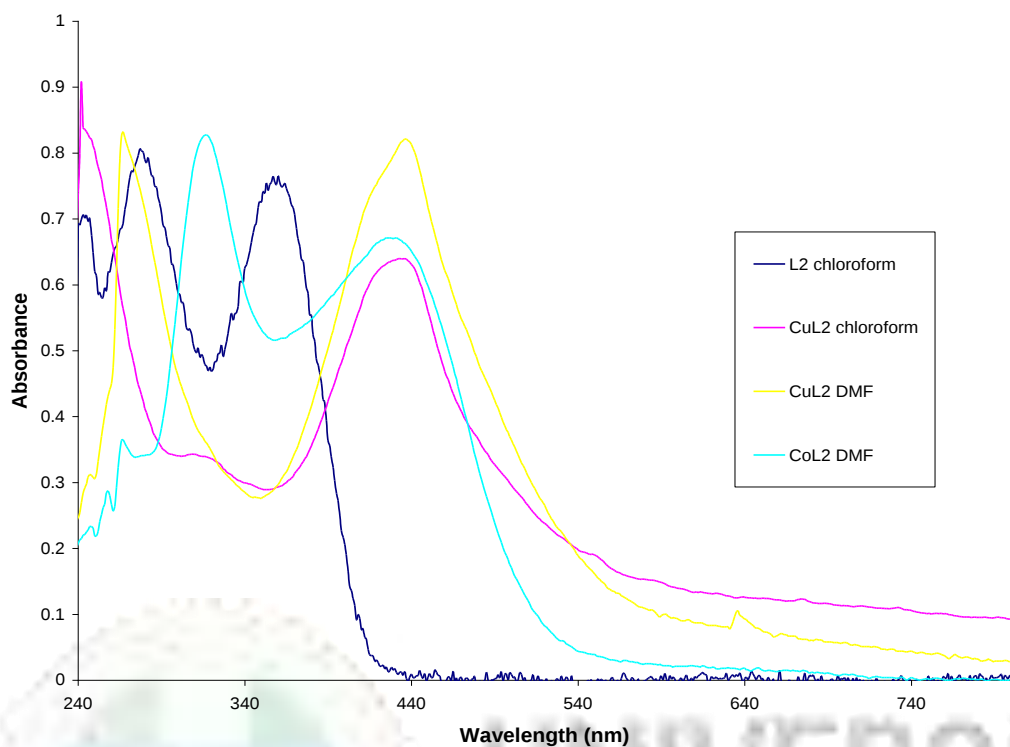


Figure 37: Electronic absorption spectra of L2 with copper and cobalt metal ions in chloroform and DMF

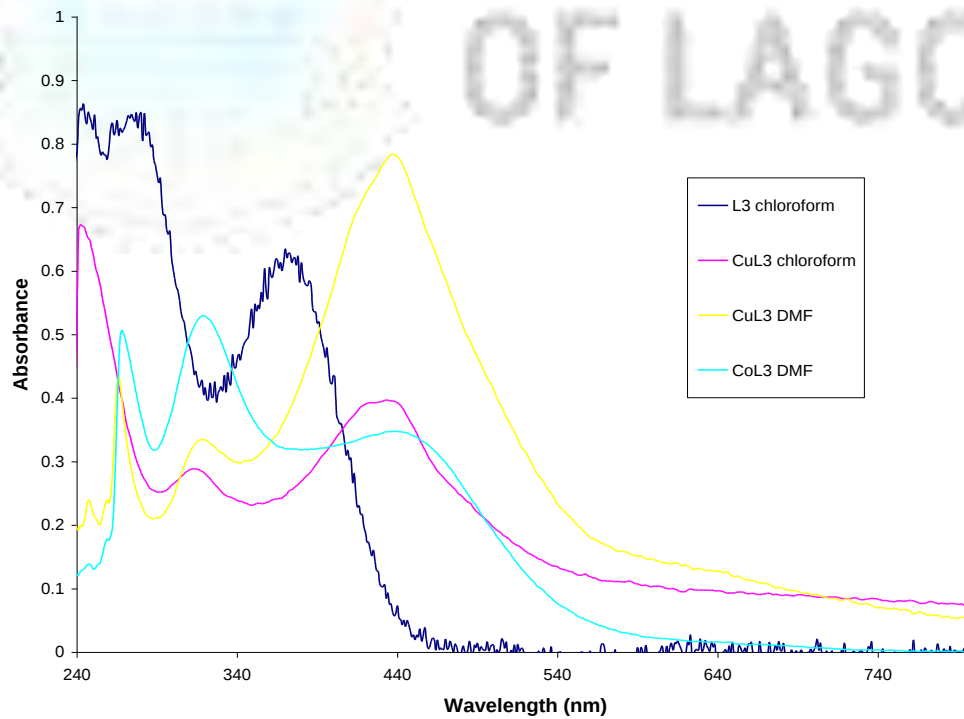


Figure 38: Electronic absorption spectra of L3 with copper and cobalt metal ions in chloroform and DMF

Table 8b: Electronic absorption data and magnetic moments measurements of *p*-substituted 2-aminophenol Schiff bases and metal complexes in CHCl₃ and DMF (10⁻⁵ molL⁻¹)

Compound	R ₁	R ₂	CHCl ₃ (ν / cm ⁻¹)(logε)	Assign ment	DMF (ν / cm ⁻¹)(logε)	Assign ment	Magnetic Moments μ _{eff} (BM)	Proposed Geometry
L4	H	OMe	34,482(4.17) 27,567(4.20)	π→π* n→π*	- -	- -	-	-
CuL4	H	OMe	31,152(3.04) 23,255(3.33)	CT d-d	22,988(3.80)	d-d	1.56	Square- planar
CoL4	H	OMe	- -	- -	31,152(4.33) 23,419(4.06)	CT d-d	5.27	Octahedral
L5	H	Cl	36,496(4.15) 28,169(4.05)	π→π* n→π*	- -	- -	-	-
CuL5	H	Cl	22,573(3.70) 19,762(3.67)	d-d d-d	30,959(4.08) 22,883(4.10)	CT d-d	1.52	Square- planar
CoL5	H	Cl	- -	- -	31,152(4.20) 22,935(4.04)	CT d-d	5.19	Octahedral
L6	H	NO ₂	36,496(4.16) 27,839(4.18)	π→π* n→π*	- -	- -	-	-
CuL6	H	NO ₂	- -	- -	30,088(4.56) 22,988(3.80)	CT d-d	1.87	Tetrahedral
CoL6	H	NO ₂	- -	- -	30,674(4.18) 20,499(4.01)	CT d-d	4.28	Tetrahedral

Two bands were observed in the spectra of the SBs, the aromatic and azomethine bands were observed at 34,482 cm⁻¹ and 27,567 cm⁻¹ for OMe-substituted SB L4 (Figure 39) 36,496 cm⁻¹ and 28,169 cm⁻¹ for Cl-substituted SB L5 (Figure 40) 36,496 cm⁻¹ and 27,839 cm⁻¹ for NO₂-substituted SB L6 (Figure 41).

The complexes of copper(II) and cobalt(II) show bands around 22,988-23,419 cm⁻¹, and 31,152 cm⁻¹ for OMe-substituted SBMC CuL4, CoL4 (Figure 39) 19,762 cm⁻¹, 22,573-22,935 cm⁻¹ and 30,959-31,152 cm⁻¹ for Cl-substituted SBMC CuL5, CoL5 (Figure 40) 20,499-22,988 cm⁻¹ and 30,088-30,674 cm⁻¹ for NO₂-substituted SBMC CuL6, CoL6 (Figure 41).

The observed magnetic moment values of the copper(II) complexes were in the range 1.52-1.88 BM. The magnetic moment of cobalt(II) complexes were observed at 4.28 BM and 5.19-5.27 BM.

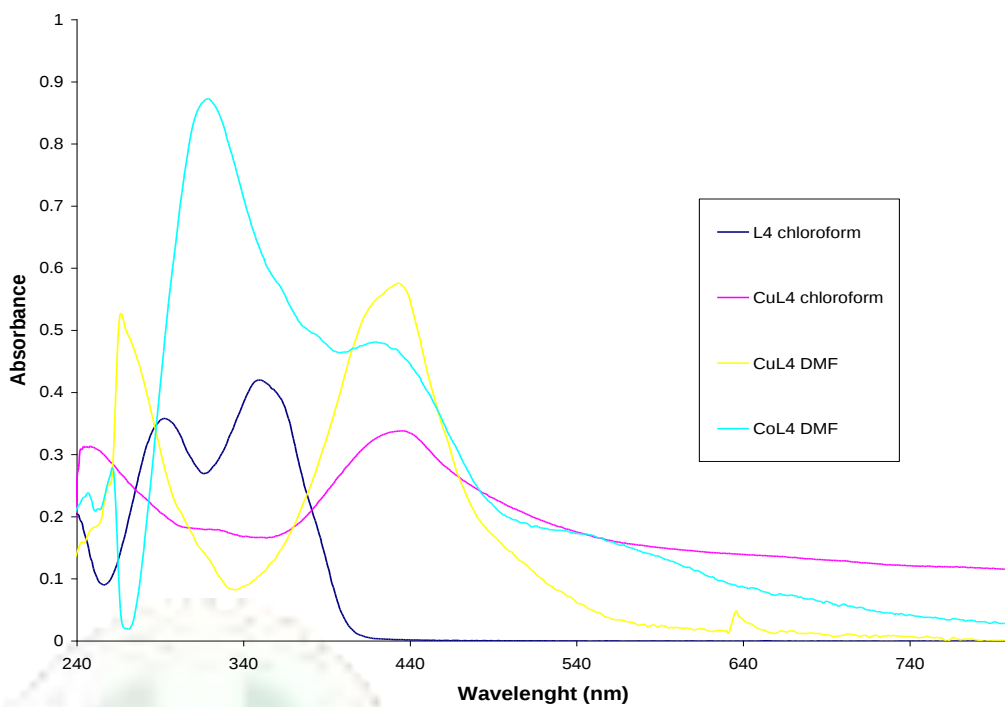


Figure 39: Electronic absorption spectra of L4 with copper and cobalt metal ions in chloroform and DMF

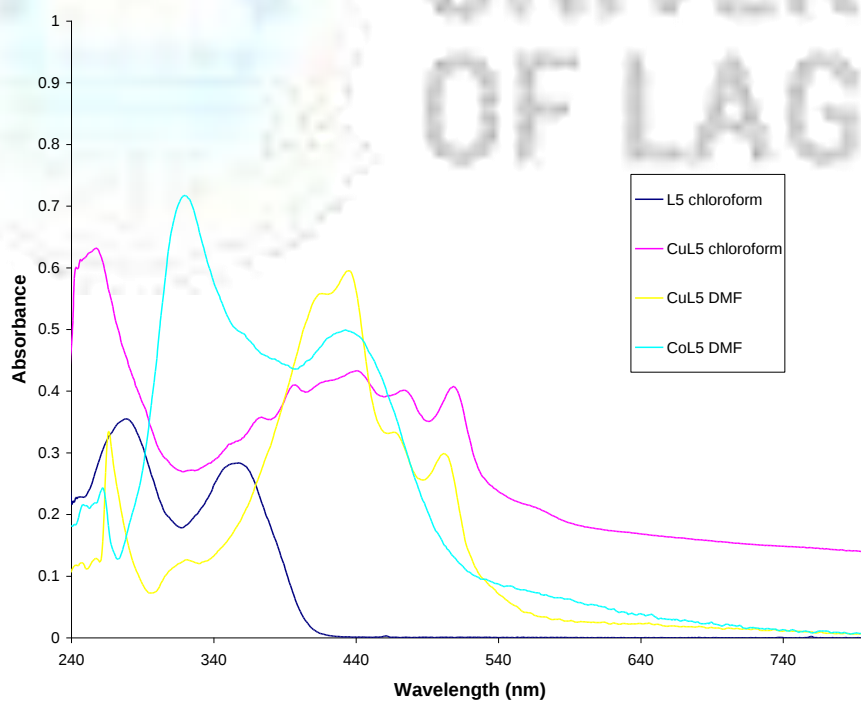


Figure 40: Electronic absorption spectra of L5 with copper and cobalt metal ions in chloroform and DMF

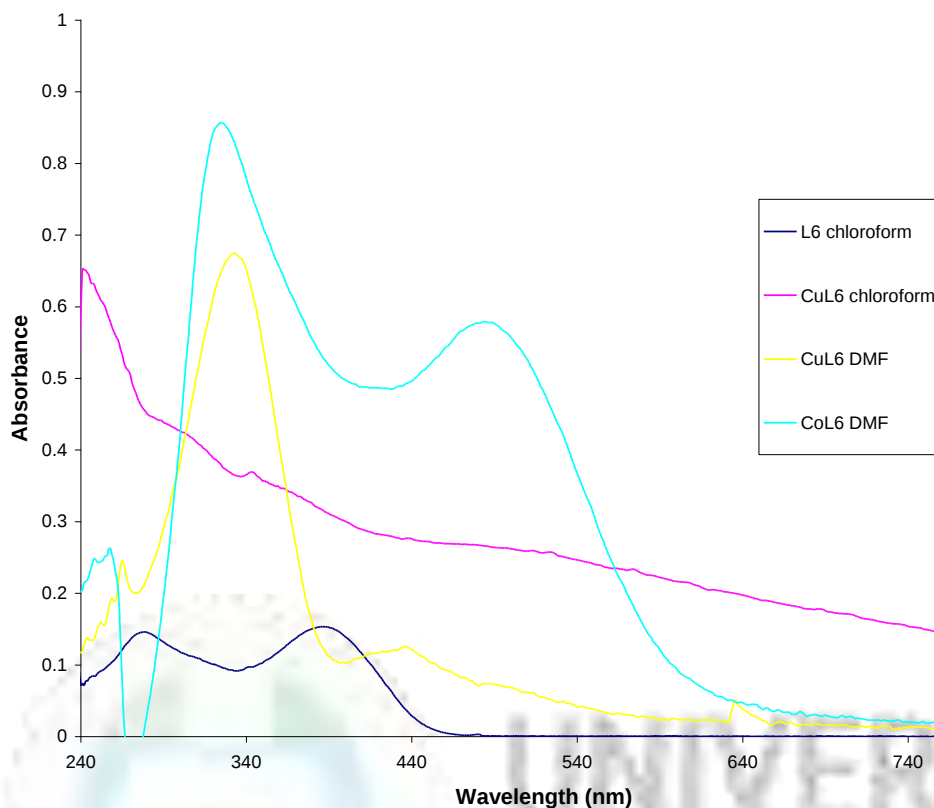


Figure 41: Electronic absorption spectra of L6 with copper and cobalt metal ions in chloroform and DMF

4.1.6 Thermogravimetric Analysis

The thermal decomposition of 2-aminophenol Schiff base metal complexes were studied using thermal analytical techniques (TGA and DSC) under nitrogen. The thermal behaviors of the complexes are summarized in Tables 9a and 9b. Their thermal behaviors are typified by Figures 42 and 43, 44 and 45 for *o*-substituted complexes and Figures 46 and 47, 48a and 48b for *p*-substituted complexes.

Table 9a: Thermoanalytical data (TGA and DSC) of *o*-substituted 2-aminophenol Schiff base metal complexes

Compound (M.Wt)	R ₁	R ₂	Endothermic ^b t _{min} (°C)	Exothermic ^b t _{max} (°C)	Temp range in TGA ^a	Weight loss ^a %Found(calcd)	Decomposition assignment
CuL1 C ₂₈ H ₂₄ Cl ₂ Cu ₂ NO ₄ (685)	OMe	H	320	340	71-227 295-343 361-504 538-786	2.83(3.12) 34.68(34.98) 25.64(26.06) 12.20(11.67)	H ₂ O C ₁₃ H ₉ NCl C ₁₅ H ₁₃ NCl CuO
CoL1 C ₂₈ H ₂₈ CoN ₂ O ₆ (547)	OMe	H	240	245	85-236 270-313 340-480 510-560 590-789 820-900	2.90(3.29) 8.11(7.67) 13.90(13.89) 5.07(5.30) 49.44(49.36) 13.71(12.98)	H ₂ O C ₂ H ₄ N C ₆ H ₄ C ₂ H ₅ C ₁₃ H ₉ N CoO
CuL2 C ₂₆ H ₁₈ Cl ₄ Cu ₂ N ₂ O ₂ (659)	Cl	H	354	370	70-220 280-338 370-740 760-870	2.73(3.12) 9.38(10.01) 56.64(56.06) 12.65(12.13)	H ₂ O Cl ₂ C ₂₆ H ₁₆ N ₂ Cl ₂ CuO
CoL2 C ₂₆ H ₂₂ Cl ₂ CoN ₂ O ₄ (556)	Cl	H	249	254	76-218 238-429 455-631 680-897	2.05(3.23) 37.45(38.48) 14.89(14.20) 13.42(13.66)	H ₂ O C ₁₃ H ₉ NCl C ₆ H ₇ C ₆ H ₅
CuL3 C ₂₆ H ₂₂ CuN ₄ O ₈ (582)	NO ₂	H	254	270	72-167 205-316 409-798 825-900	2.91(3.09) 12.79(13.05) 31.11(30.75) 13.70(13.01)	H ₂ O C ₆ H ₄ N ₂ C ₁₉ H ₁₈ N ₂ CuO
CoL3 C ₂₆ H ₂₂ CoN ₄ O ₈ (577)	NO ₂	H	239	245	70-221 238-356 385-627 637-797 820-898	2.73(3.11) 28.63(28.94) 16.04(15.77) 23.74(24.09) 13.78(13.21)	H ₂ O C ₁₂ H ₉ N C ₆ H ₅ N C ₅ H ₄ CoO

TGA ^a: data obtained from thermal gravimetry analysis
DSC^b:data obtained from differential scanning calorimetry

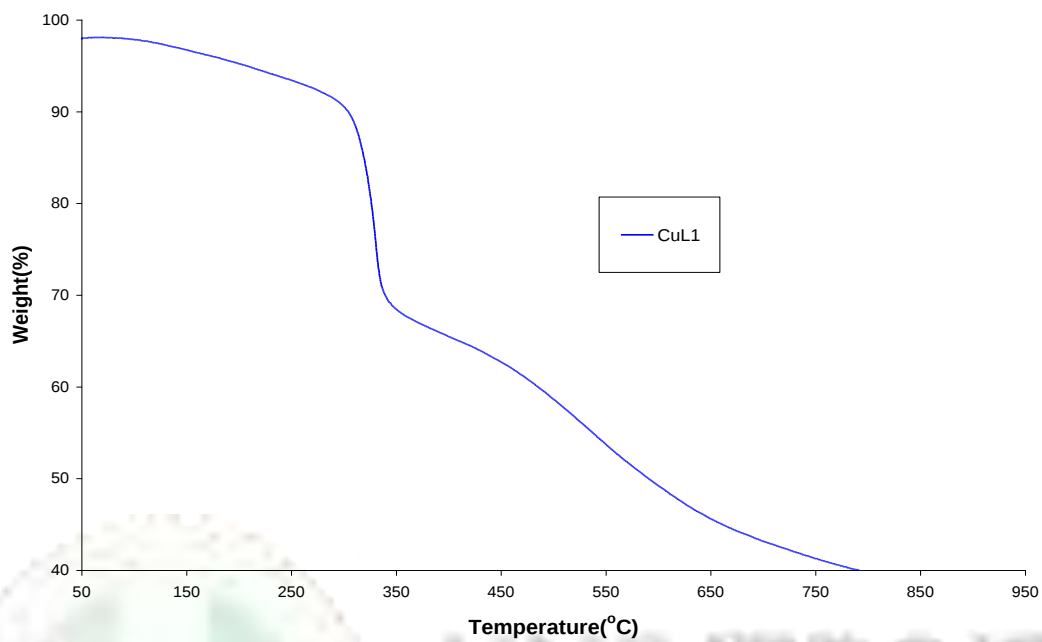


Figure 42: TGA curve of CuL1

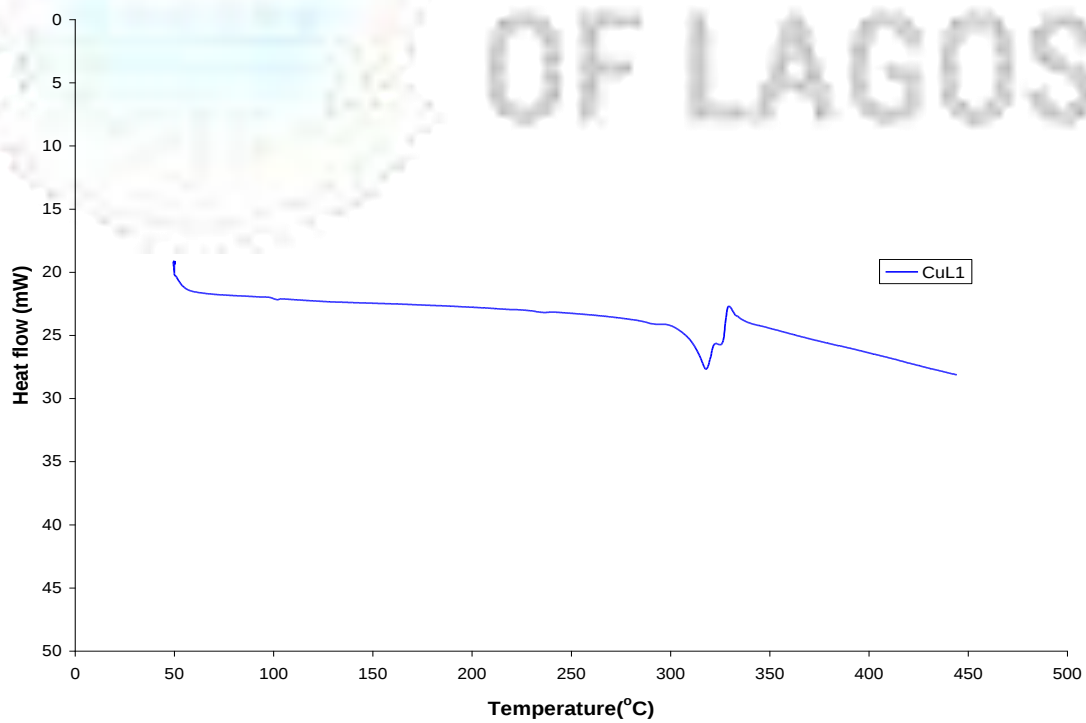


Figure 43: DSC curve of CuL1

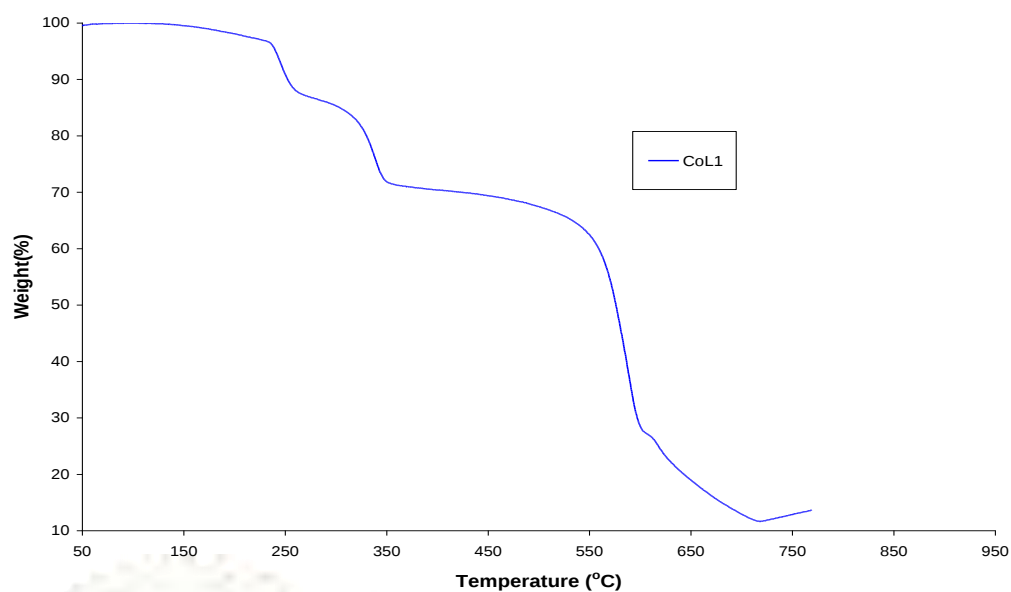


Figure 44: TGA curve of CoL1

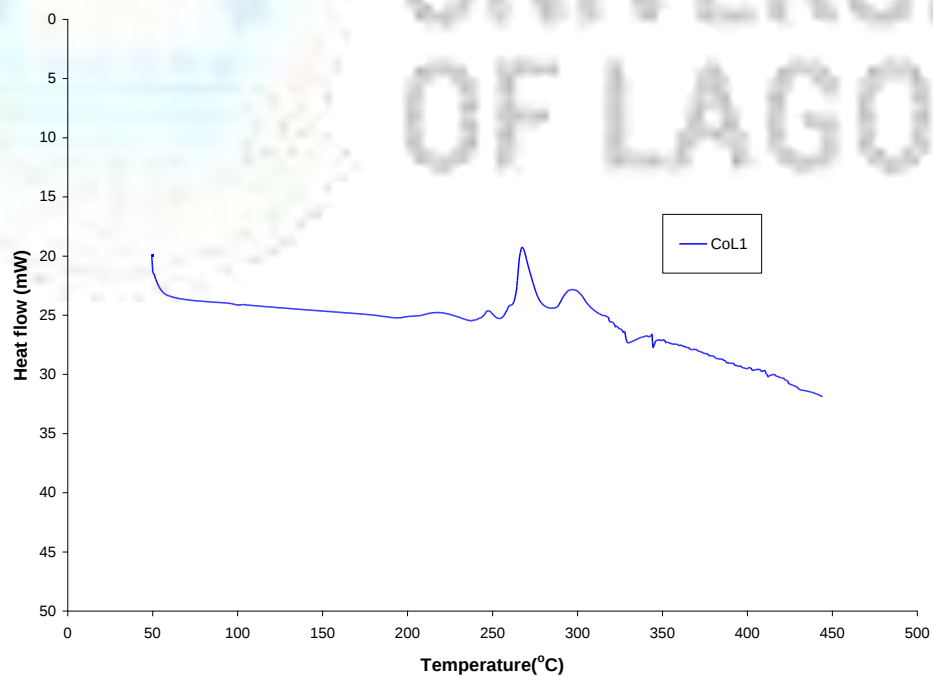


Figure 45: DSC curve of CoL1

Table 9b: Thermoanalytical data (TGA and DSC) of *p*-substituted 2-aminophenol Schiff base metal complexes

Compound (M.Wt)	R ₁	R ₂	Endothermic ^b t _{min} (°C)	Exothermic ^b t _{max} (°C)	Temp range in TGA ^a	Weight loss %Found(calcd)	Decomposition assignment
CuL4 C ₂₈ H ₂₄ Cl ₂ Cu ₂ N ₂ O ₄ (650)	H	OMe	324	337	68-198 270-337 354-481 620-820	2.53(3.21) 32.68(31.98) 23.64(24.06) 12.56(13.20)	H ₂ O C ₁₅ H ₁₂ NCl C ₁₃ H ₁₀ NCl CuO
CoL4 C ₂₈ H ₂₈ Cl ₂ CoN ₂ O ₆ (618)	H	OMe	317	330	77-231 312-470 552-810 830-900	4.69(5.66) 54.85(55.82) 25.40(24.84) 13.70(12.42)	Cl C ₁₉ H ₁₄ N ₂ C ₉ H ₁₄ Cl CoO
CuL5 C ₂₆ H ₁₈ Cl ₄ Cu ₂ N ₂ O ₂ (659)	H	Cl	332	337	68-212 278-328 357-711 756-860	2.63(3.12) 9.38(10.01) 56.64(56.06) 12.50(12.13)	H ₂ O Cl ₂ C ₂₆ H ₁₆ N ₂ Cl ₂ CuO
CoL5 C ₂₆ H ₂₂ Cl ₂ CoN ₂ O ₄ (556)	H	Cl	281	287	80-254 286-427 462-738 790-898	2.43(3.23) 43.56(43.34) 36.15(35.85) 13.28(12.99)	H ₂ O C ₁₄ H ₁₀ N ₂ Cl C ₁₃ H ₁₀ Cl CoO
CuL6 C ₂₆ H ₁₈ CuN ₄ O ₆ (545)	H	NO ₂	265	297	68-198 207-293 345-505	3.65(3.30) 69.65(70.45) 12.20(12.84)	H ₂ O C ₂₆ H ₁₆ N CuO
CoL6 C ₂₆ H ₁₈ CoN ₄ O ₆ (541)	H	NO ₂	285	296	74-308 328-501 613-763 820-900	42.81(43.43) 11.78(12.82) 14.80(14.60) 13.86(13.80)	C ₁₆ H ₉ N ₂ C ₅ H ₄ C ₁₃ H ₁₀ CoO

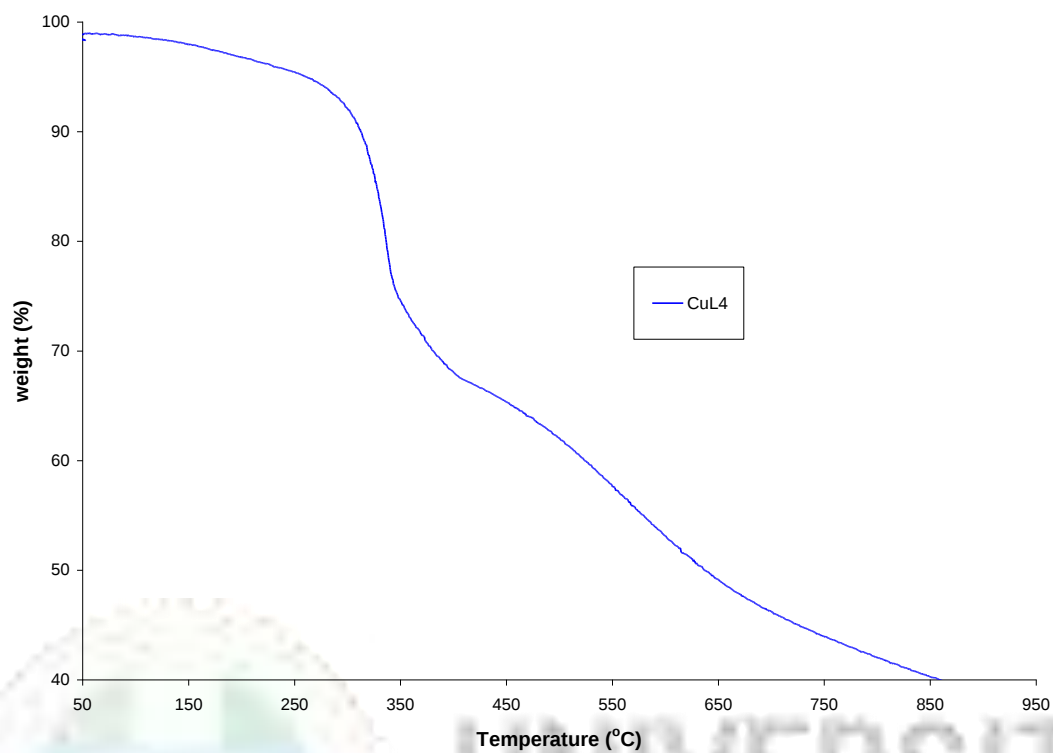


Figure 46: TGA curve of CuL4

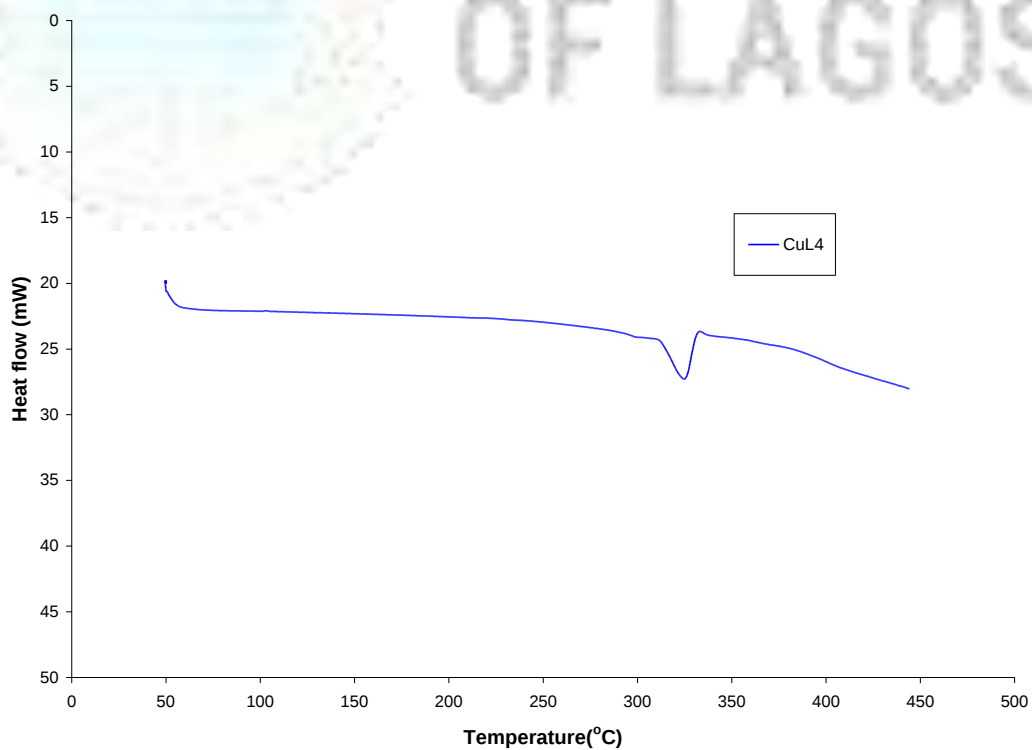


Figure 47: DSC curve of CuL4

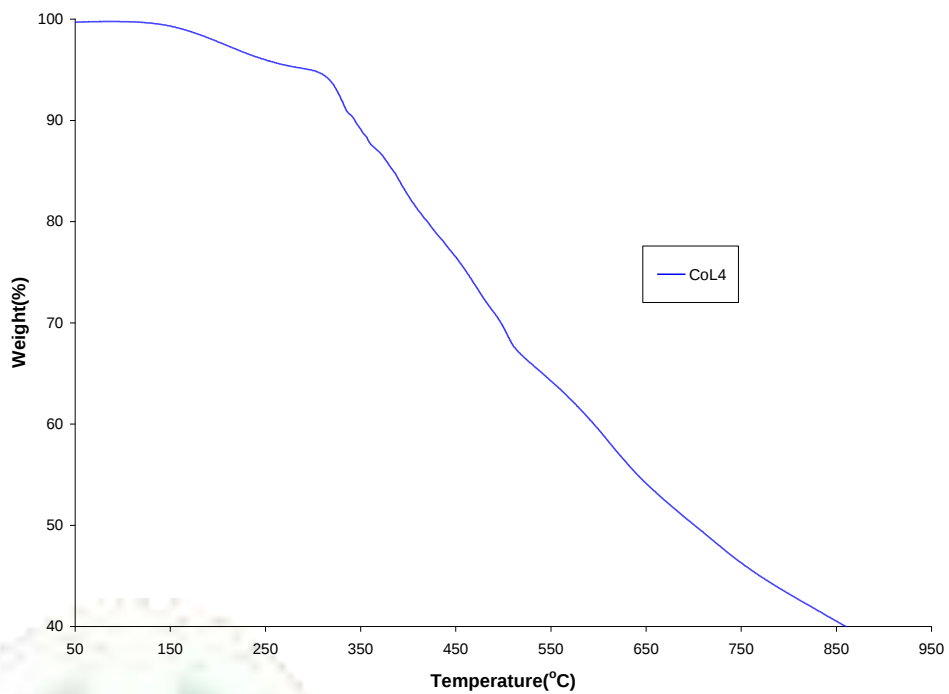


Figure 48a: TGA curve of CoL4

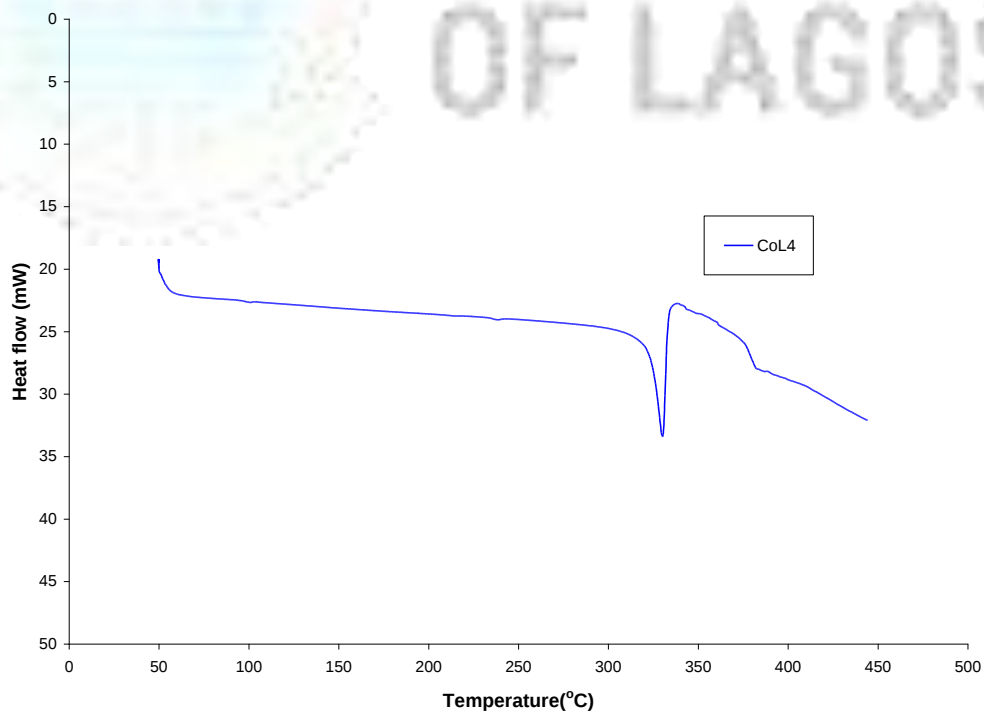


Figure 48b: DSC curve of CoL4

4.2.1 Synthesis of 3-aminophenol Schiff Bases and Metal Complexes

Six Schiff base ligands namely; 2-methoxybenzylidene-3-aminophenol (L7), 2-chlorobenzylidene-3-aminophenol (L8), 2-nitrobenzylidene-3-aminophenol (L9), 4-methoxybenzylidene-3-aminophenol (L10), 4-chlorobenzylidene-3-aminophenol (L11), 4-nitrobenzylidene-3-aminophenol (L12) were obtained from reaction of 3-aminophenol with 2- and 4-substituted benzaldehydes (Scheme 31) Table 27. Three of the compounds had substituents in *o*-position and the other in *p*-position. The Schiff bases were reacted with copper and cobalt chlorides to yield copper and cobalt Schiff base metal complexes; bis(3-(2-methoxybenzylideneamino)phenol)copper(II) CuL7, bis(3-(2-chlorobenzylideneamino)phenol)copper(II) CuL8, bis(3-(2-nitrobenzylideneamino)phenol)copper(II) CuL9, bis(3-(4-methoxybenzylideneamino)phenol)copper(II) CuL10, bis(3-(4-chlorobenzylideneamino)phenol)copper(II) CuL11 and bis(3-(4-nitrobenzylideneamino)phenol)copper(II) CuL12 respectively.

4.2.2 Physical and analytical data of *o*-substituted 3-aminophenol Schiff bases and metal complexes

The physical and analytical data of Schiff bases and Schiff base metal complexes derived from 3-aminophenol are presented in Tables 10a and 10b.

Table 10a: Physical and analytical data of *o*-substituted 3-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	Empirical Formula (M.wt)	Yield (%)	Color	M.pt (°C)	% Found (calcd)			Metal (%)
							C	H	N	
L7	OMe	H	C ₁₄ H ₁₃ NO ₂ (227)	58.15	Yellow	171-172	74.77(73.90)	6.07(5.77)	5.48 (6.16)	-
CuL7	OMe	H	C ₂₈ H ₂₈ CuN ₂ O ₆ (552)	54.31	Brown	decomp	60.48(60.92)	4.70(5.11)	5.05(5.07)	7.28
L8	Cl	H	C ₁₃ H ₁₀ NOCl (231)	56.96	Red	decomp	66.67(67.39)	4.46(4.35)	5.61(6.05)	-
CuL8	Cl	H	C ₂₆ H ₂₂ Cl ₂ CuN ₂ O ₄ (560)	68.85	Brown	decomp	55.67(55.50)	3.61 (3.95)	4.51 (4.99)	8.18
L9	NO ₂	H	C ₁₃ H ₁₀ N ₂ O ₃ (242)	47.37	Brown	102-103	64.57(64.46)	4.40(4.16)	11.54(11.56)	-
CuL9	NO ₂	H	C ₂₆ H ₂₂ CuN ₄ O ₈ (581)	44.00	Brown	decomp	53.65(53.92)	3.90(3.81)	8.25(9.63)	9.30

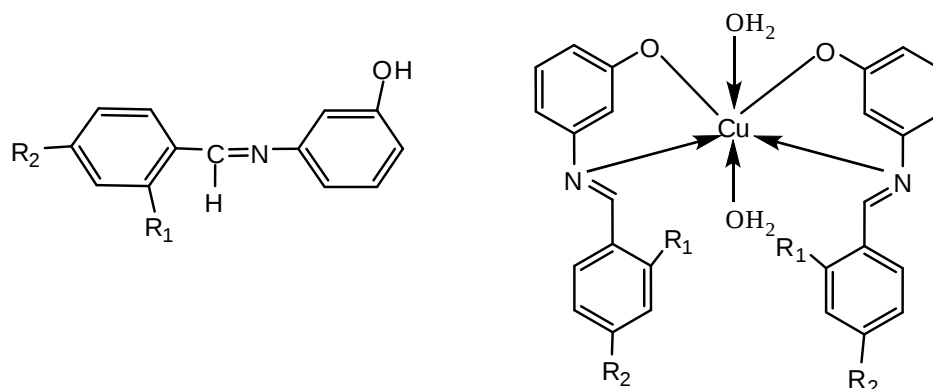


Figure 49: Schiff bases and metal complexes synthesized from 3-aminophenol

Microanalysis were obtained for each of the synthesized compounds. The percentage metal were determined for the metal complexes. The complexes exhibited one mole of metal ion per mole of complex. The melting points of the Schiff bases were in the range 171-172 °C for OMe substituted SB L7 and 102-103 °C for NO₂ substituted SB L9 while the Cl substituted SB L7 and all the metal complexes decomposed above 250 °C. The yields obtained ranges between 47-58 % for Schiff base ligands L7-L9 and 44-68 % for Schiff base metal complexes CuL7-CuL9.

Table 10b: Physical and analytical data of *p*-substituted 3-aminophenol Schiff bases and complexes

Compound	R ₁	R ₂	Empirical Formula (M.wt)	Yield (%)	Color	M.pt (°C)	% Found (calcd)			Metal (%)
							C	H	N	
L10	H	OMe	C ₁₄ H ₁₃ NO ₂ (227)	51.92	Orange	148-149	74.32(73.99)	6.01(5.77)	5.40(6.16)	-
CuL10	H	OMe	C ₂₈ H ₂₈ CuN ₂ O ₆ (551)	59.60	Brown	decomp	59.51(60.92)	4.57 (5.11)	5.17(5.07)	8.48
L11	H	Cl	C ₁₃ H ₁₀ NOCl (231)	47.38	Brown	decomp	67.65(67.39)	4.52(4.35)	5.69(6.05)	-
CuL11	H	Cl	C ₂₆ H ₂₂ Cl ₂ CuN ₂ O ₄ (559)	51.09	Brown	decomp	55.31(55.67)	3.70(3.95)	4.54(4.99)	6.66
L12	H	NO ₂	C ₁₃ H ₁₀ N ₂ O ₃ (242)	51.97	Red	decomp	64.86(64.46)	4.42(4.16)	11.53(11.5)	-
CuL12	H	NO ₂	C ₂₆ H ₂₂ CuN ₄ O ₈ (581)	42.77	Brown	decomp	54.27(53.65)	4.08(3.81)	9.27(9.63)	5.14

Microanalysis were obtained for each of the synthesized compounds. The percentage metal were determined for the metal complexes. The complexes exhibited one mole of metal ion per mole of complex. The Schiff bases and metal complexes all decomposed except the OMe substituted Schiff base L10 which melted in the range 148-149 °C. The yields obtained ranges between 47-52 % for Schiff base ligands L10-L12 and 42-60 % for Schiff base metal complexes CuL10-CuL12.

4.2.3 Spectroscopic Data of 3-aminophenol Schiff Bases and Metal Complexes

The Schiff bases were characterized using IR and NMR analysis and the results are presented in Tables 11a, 11b, 12a and 12b.

Table 11a: Spectroscopic data of *o*-substituted 3-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	v(O-H)	v(C=N)	v(C-O)	vOH(H ₂ O)	v(C-Cl)	v(M-O)	v(M-N)
			cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹
L7	OMe	H	3365	1586	1238	-	-	-	-
CuL7	OMe	H	3337	1581	1235	822	-	504	452
L8	Cl	H	3325	1617	1217	-	346	-	-
CuL8	Cl	H	3342	1586	1221	827	346	541	437
L9	NO ₂	H	3360	1606	1211	-	-	-	-
CuL9	NO ₂	H	3327	1593	1218	832	-	531	452

The imine band (C=N) in the SB appears in the region 1586 cm⁻¹ for OMe-substituted SB L7 (Figure 50), 1617 cm⁻¹ for Cl-substituted SB L8 (Figure 52) and 1606 cm⁻¹ for NO₂-substituted SB L9 (Figure 52). On coordination, the bands shifted to lower frequencies of 1581, 1586 cm⁻¹ and 1593 cm⁻¹ respectively. The phenolic -OH stretch in Schiff bases appears around 3365 cm⁻¹ L7, 3325 cm⁻¹ L8 and 3360 cm⁻¹ L9. The IR spectra also exhibited characteristic band (C-O) in the Schiff bases in the region 1238 cm⁻¹ L7, 1217 cm⁻¹ L8 and 1211 cm⁻¹ L9. In the metal complexes, the band appear in the region 1235, 1221 cm⁻¹, and 1218 cm⁻¹ respectively. Coordinated water indicates a broad band in the region 3337 cm⁻¹ CuL7, 3342 cm⁻¹ CuL8 and

3327 cm^{-1} CuL9. New bands were observed at 437-452 cm^{-1} and 504-541 cm^{-1} in the spectra of metal complexes.

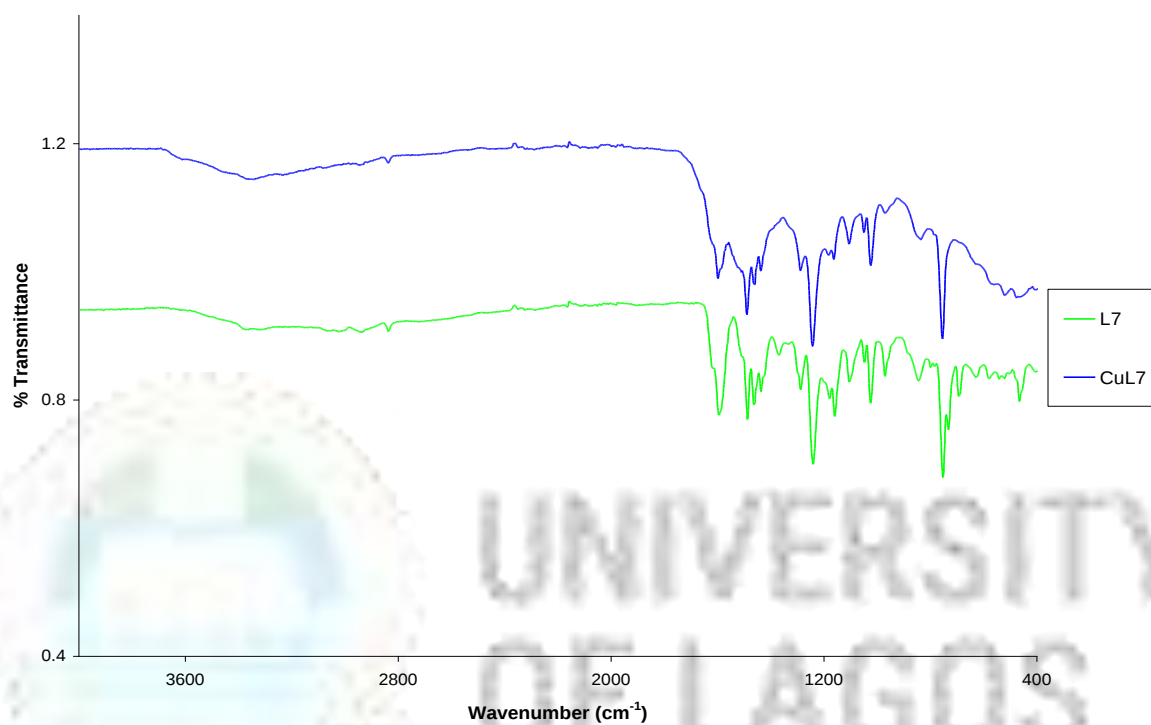


Figure 50: IR spectra of 3-(2-methoxybenzylideneamino)phenol (L7) and Cu metal complex

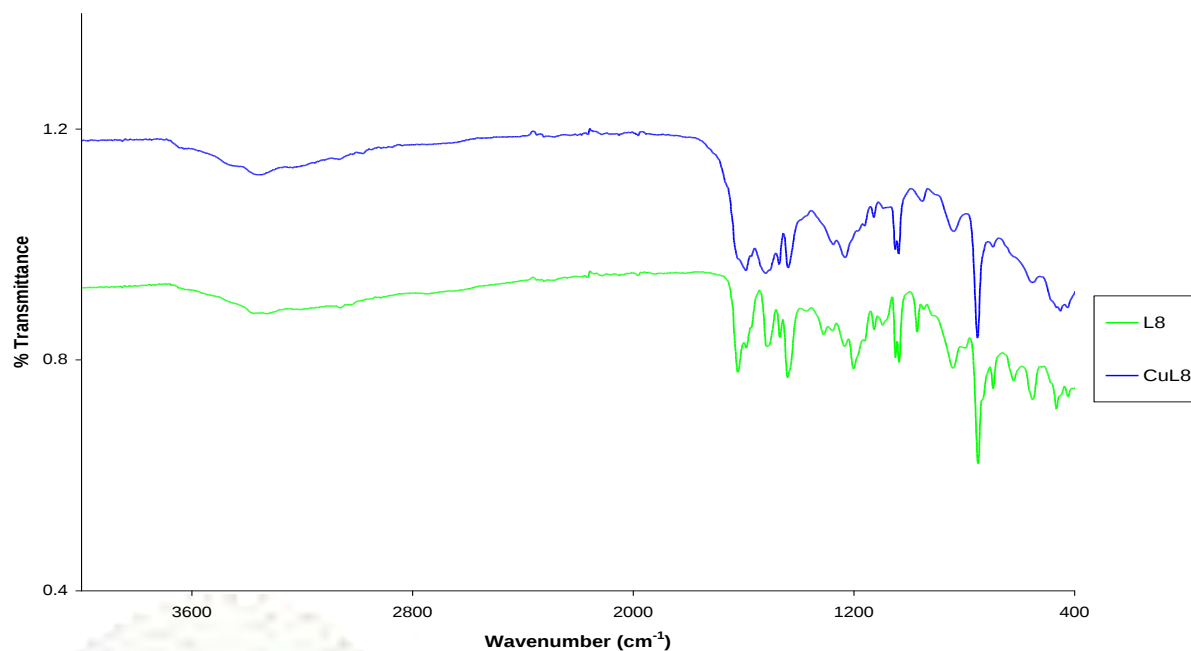


Figure 51: IR spectra of 3-(2-chlorobenzylideneamino)phenol (L8) and Cu metal complex

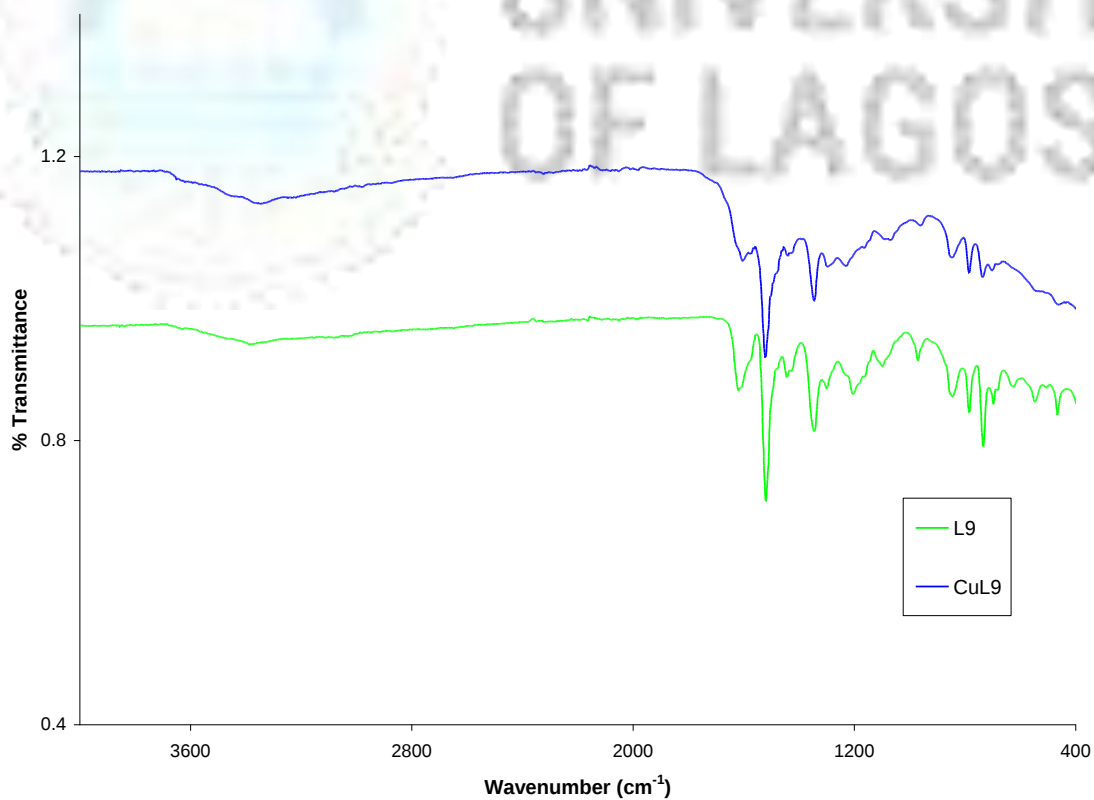


Figure 52: IR spectra of 3-(2-nitrobenzylideneamino)phenol (L9) and Cu metal complex

Table 11b: Spectroscopic data of *p*-substituted 3-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	$\nu(\text{O-H})$	$\nu(\text{C=N})$	$\nu(\text{C-O})$	$\nu\text{OH}(\text{H}_2\text{O})$	$\nu(\text{C-Cl})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
			cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}
L10	H	OMe	3330	1612	1280	-	-	-	-
CuL10	H	OMe	3336	1592	1170	826	-	533	442
L11	H	Cl	3351	1616	1219	-	326	-	-
CuL11	H	Cl	-	1572	1160	826	326	527	458
L12	H	NO ₂	-	1603	1214	-	-	-	-
CuL12	H	NO ₂	3368	1590	1195	837	-	527	447

The imine band (C=N) in the SB appears in the region 1612 cm^{-1} for OMe-substituted SB L10 (Figure 53), 1616 cm^{-1} for Cl-substituted SB L11 (Figure 54) and 1603 cm^{-1} for NO₂-substituted SB L12 (Figure 55). On coordination, the bands shifted to lower frequencies of 1592 , 1572 cm^{-1} and 1590 cm^{-1} respectively. The phenolic -OH stretch in Schiff bases appear around 3330 cm^{-1} L11 and 3351 cm^{-1} L12 for OMe-substituted SB and Cl-substituted SB respectively. The IR spectra also exhibited characteristic bands (C-O) in the Schiff bases in the region 1280 cm^{-1} L10, 1219 cm^{-1} L11 and 1195 cm^{-1} L12. In the metal complexes, the band appear in the region 1170 , 1160 cm^{-1} and 1214 cm^{-1} respectively. Presence of water indicates a broad band in the region 3336 cm^{-1} CuL10 and 3368 cm^{-1} L12. New bands were observed at 442 - 458 cm^{-1} and 527 - 533 cm^{-1} in the spectra of metal complexes.

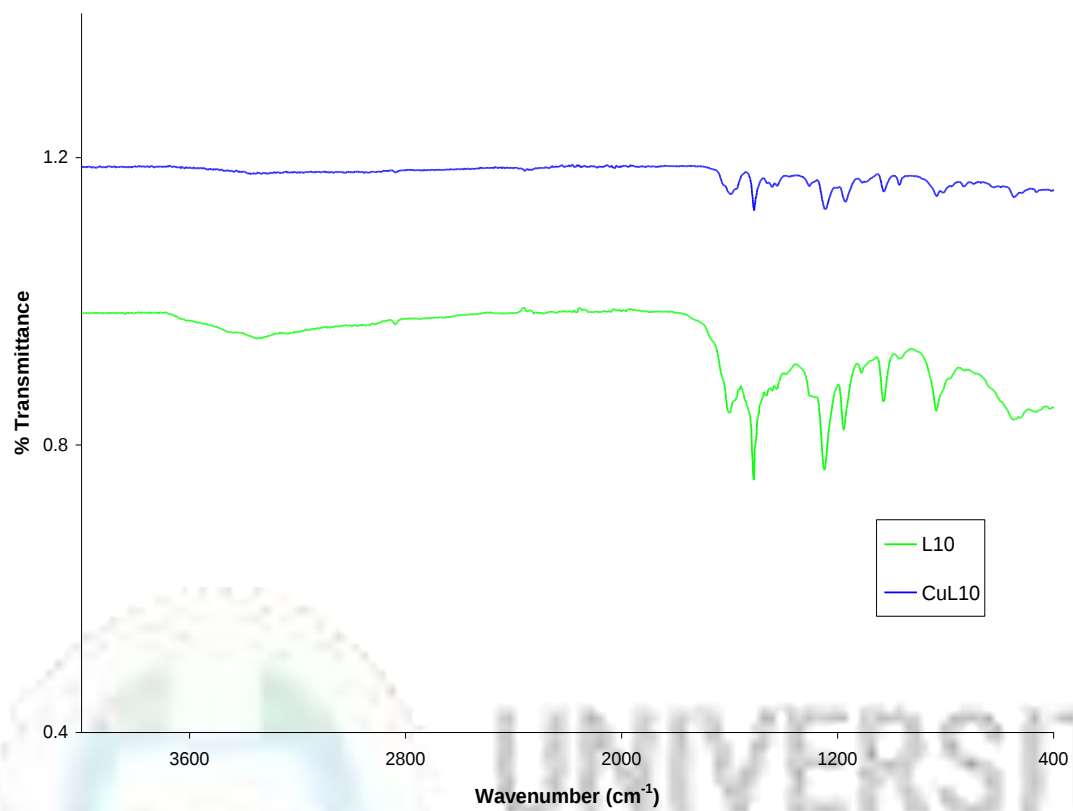


Figure 53: IR spectra of 3-(4-methoxybenzylideneamino)phenol (L10) and Cu metal complex

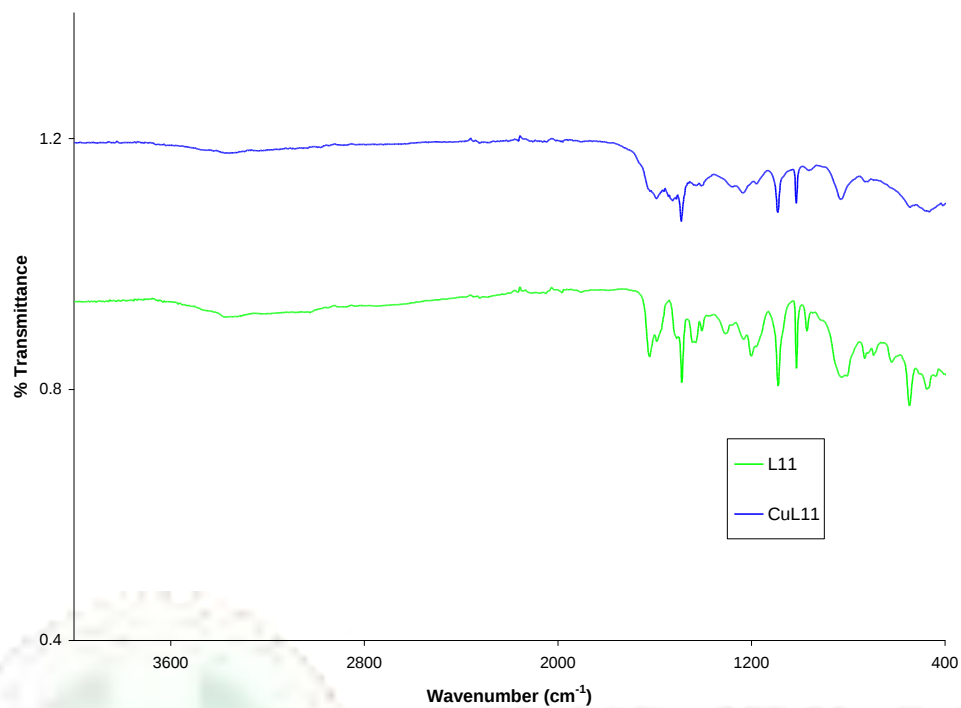


Figure 54: IR spectra of 3-(4-chlorobenzylideneamino)phenol (L11) and Cu metal complex

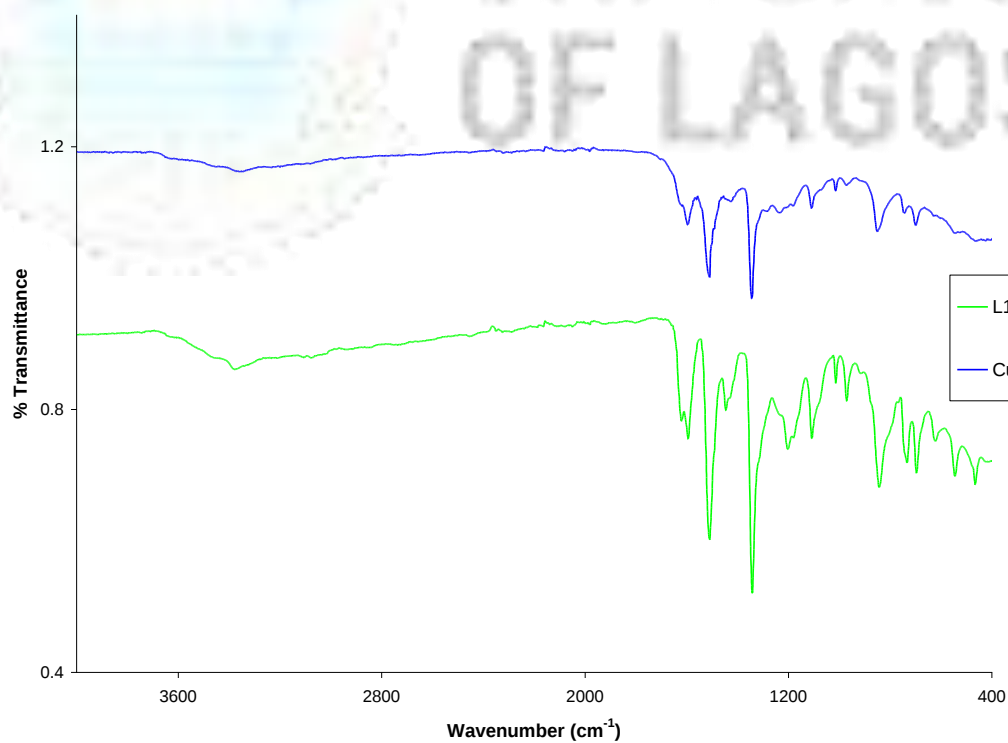


Figure 55: IR spectra of 3-(4-nitrobenzylideneamino)phenol (L12) and Cu metal complex

4.2.4 ^1H NMR Data of 3-aminophenol Schiff Bases

The ^1H NMR data of 3-aminophenol Schiff bases are presented in Tables 12a and 12b.

Table 12a: ^1H NMR data of *o*-substituted 3-aminophenol Schiff bases

Compound	R ₁	R ₂	HC=N (s, 1H) (δ , ppm)	OH (s, 1H) (δ , ppm)	OCH ₃ (s, 3H) (δ , ppm)	Aromatic, protons m, 8H (δ , ppm)
L7	OMe	H	8.11	8.89	3.91	6.12-7.83
L8	Cl	H	8.23	9.11	-	6.53-7.37
L9	NO ₂	H	8.17	8.91	-	6.24-7.79

The imine (C=N) protons show signals at 8.11 ppm for OMe-substituted SB L7 (Figure 56), 8.23 ppm for Cl-substituted SB L8 (Figure 57) and 8.17 ppm for NO₂-substituted SB L9 (Figure 58). Methoxy protons (-OCH₃) appears as singlets at 3.91 ppm for OMe-substituted SB L7, the signal for the phenolic -OH appears at 8.89 ppm for OMe-substituted SB L7 (Figure 56), 9.11 ppm for Cl-substituted SB L8 (Figure 57) and 8.91 ppm for NO₂-substituted SB L9 (Figure 58). Aromatic protons show multiple resonance signals between 6.12-7.83 ppm.

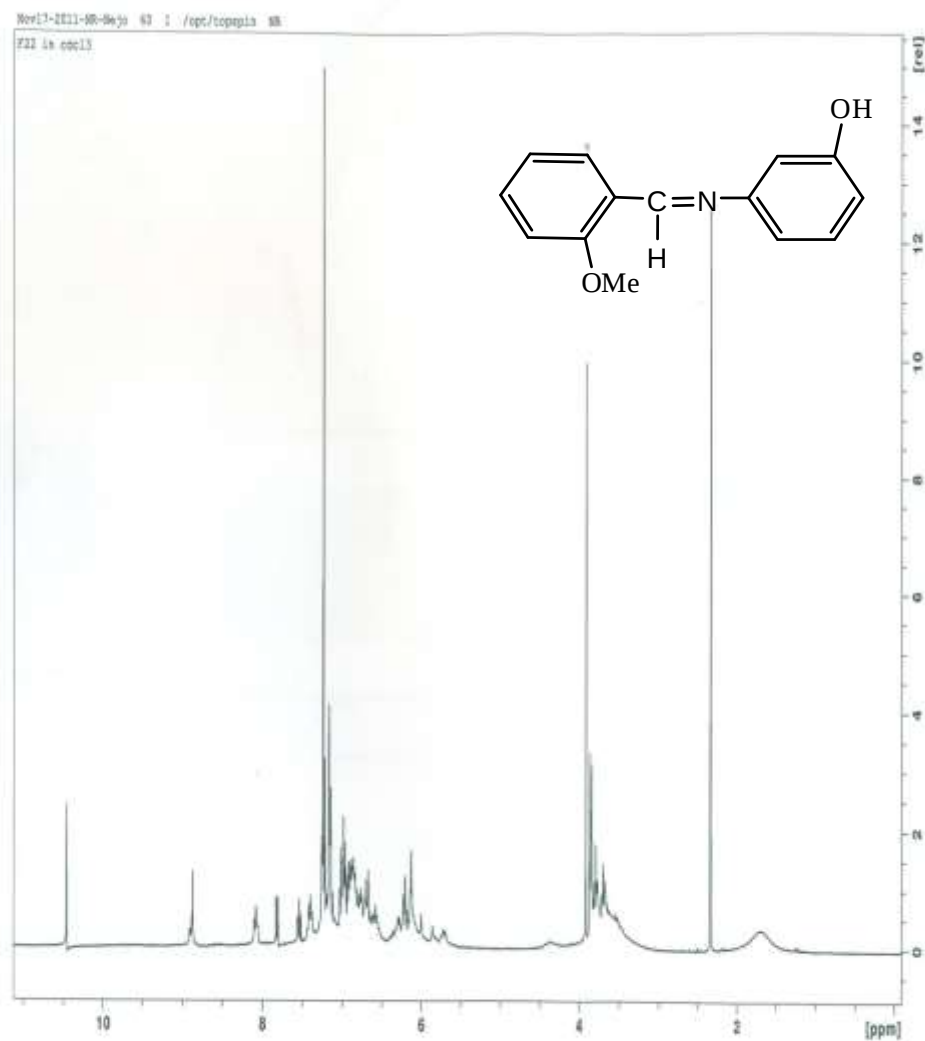


Figure 56: ^1H NMR spectrum of 3-(2-methoxybenzylideneamino)phenol Schiff base (L7)

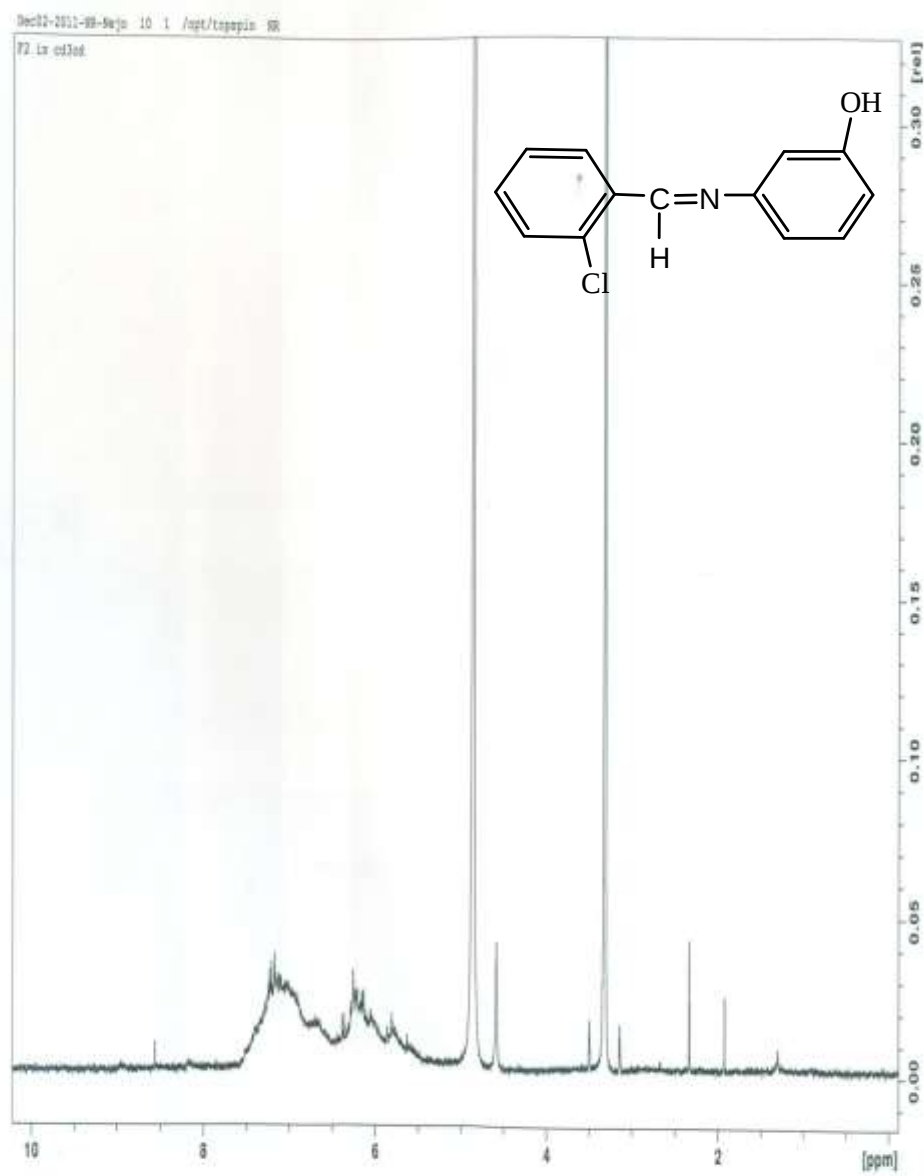


Figure 57: ^1H NMR spectrum of 3-(2-chlorobenzylideneamino)phenol Schiff base (L8)

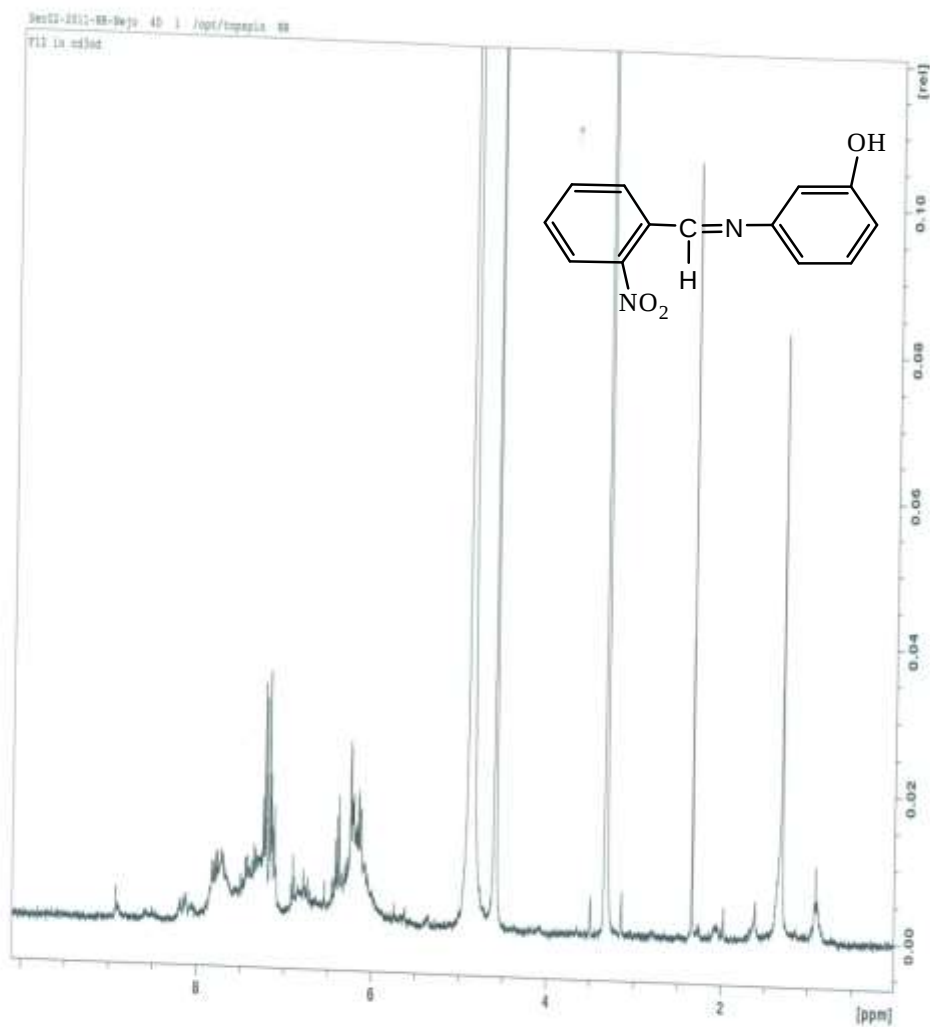
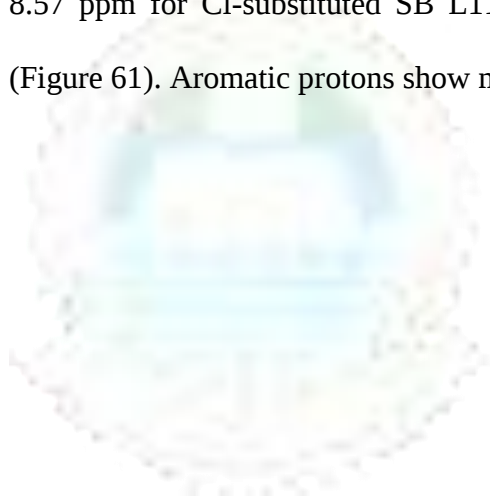


Figure 58: ^1H NMR spectrum of 3-(2-nitrobenzylideneamino)phenol Schiff base (L9)

Table 12b: ^1H NMR data of *p*-substituted 3-aminophenol Schiff bases

Compound	R ₁	R ₂	HC=N (s, 1H) (δ , ppm)	OH (s, 1H) (δ , ppm)	OCH ₃ (s, 3H) (δ , ppm)	Aromatic, protons m, 8H (δ , ppm)
L10	H	OMe	7.87	8.47	3.33	6.24-7.24
L11	H	Cl	7.95	8.57	-	6.24-7.63
L12	H	NO ₂	8.39	8.71	-	6.20-8.11

The imine (C=N) protons show signals at 7.87 ppm for OMe-substituted SB L10 (Figure 59), 7.95 ppm for Cl-substituted SB L11 (Figure 60) and 8.39 ppm for NO₂-substituted SB L12 (Figure 61). Methoxy protons (-OCH₃) appears as singlets at 3.33 ppm for OMe-substituted SB 10, the signal for the phenolic -OH appears at 8.47 ppm for OMe-substituted SB L10 Figure 59), 8.57 ppm for Cl-substituted SB L11 (Figure 60) and 8.71 ppm for NO₂-substituted SB L12 (Figure 61). Aromatic protons show multiple resonance signals between 6.20-8.11 ppm.



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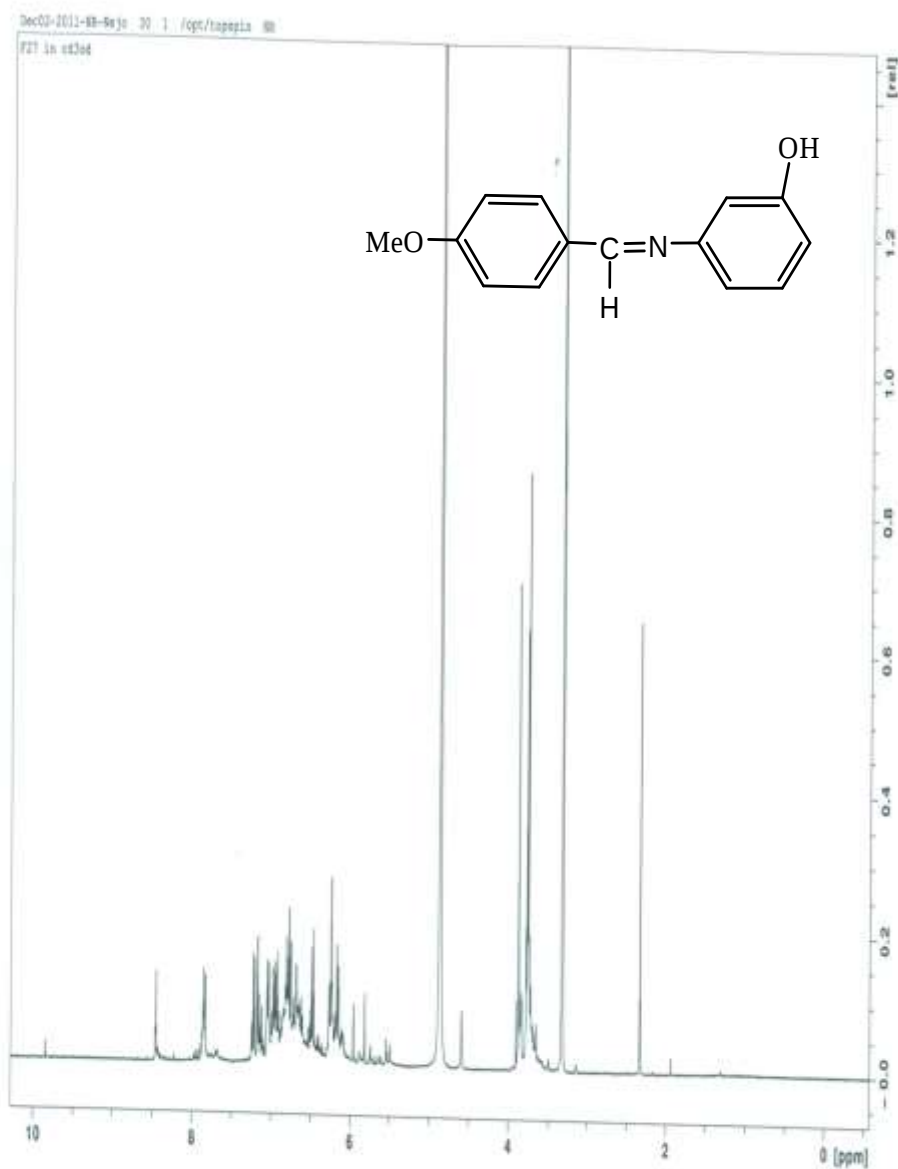


Figure 59: ^1H NMR spectrum of 3-(4-methoxybenzylideneamino)phenol Schiff base (L10)

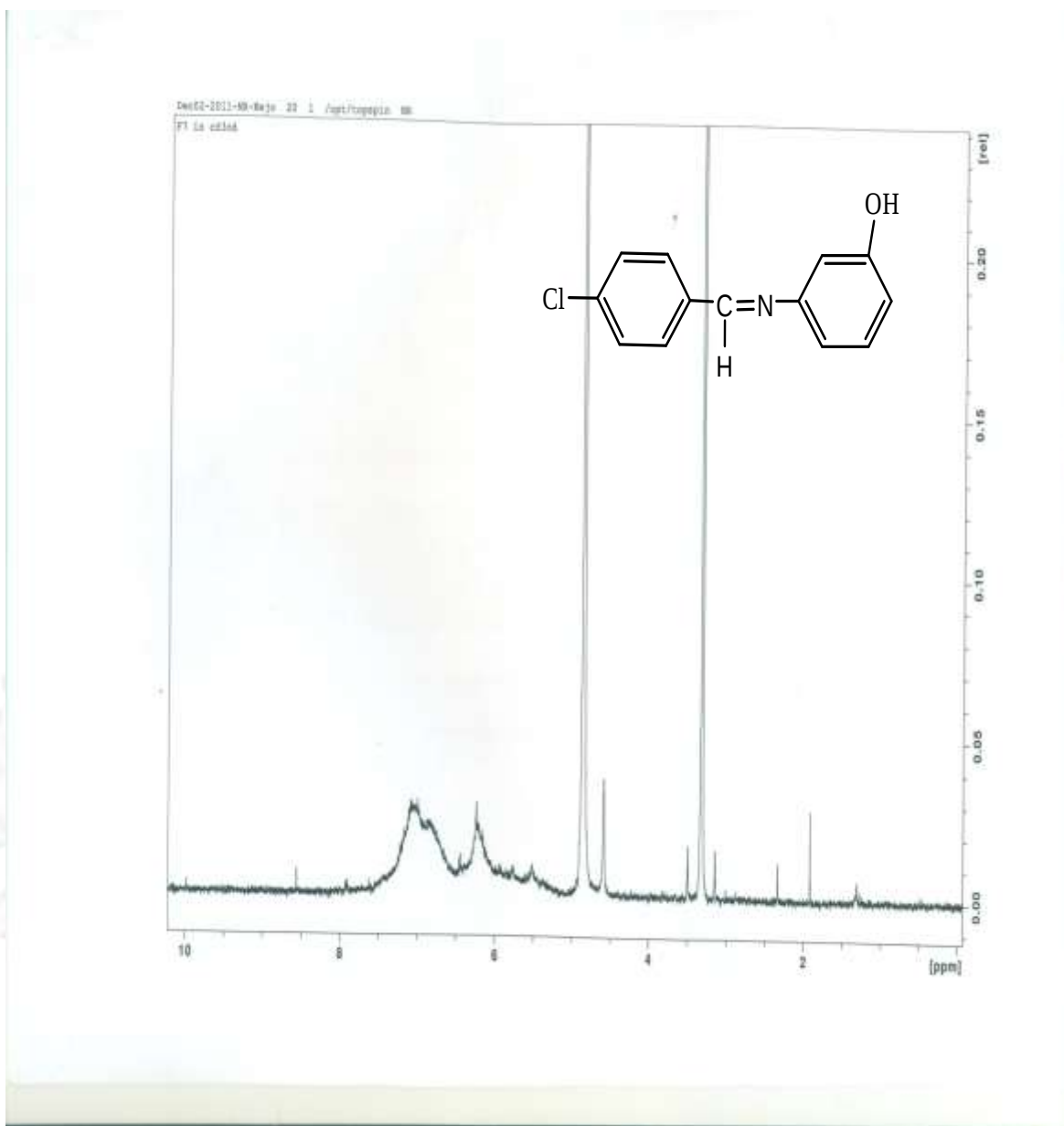


Figure 60: ^1H NMR spectrum of 3-(4-chlorobenzylideneamino)phenol Schiff base (L11)

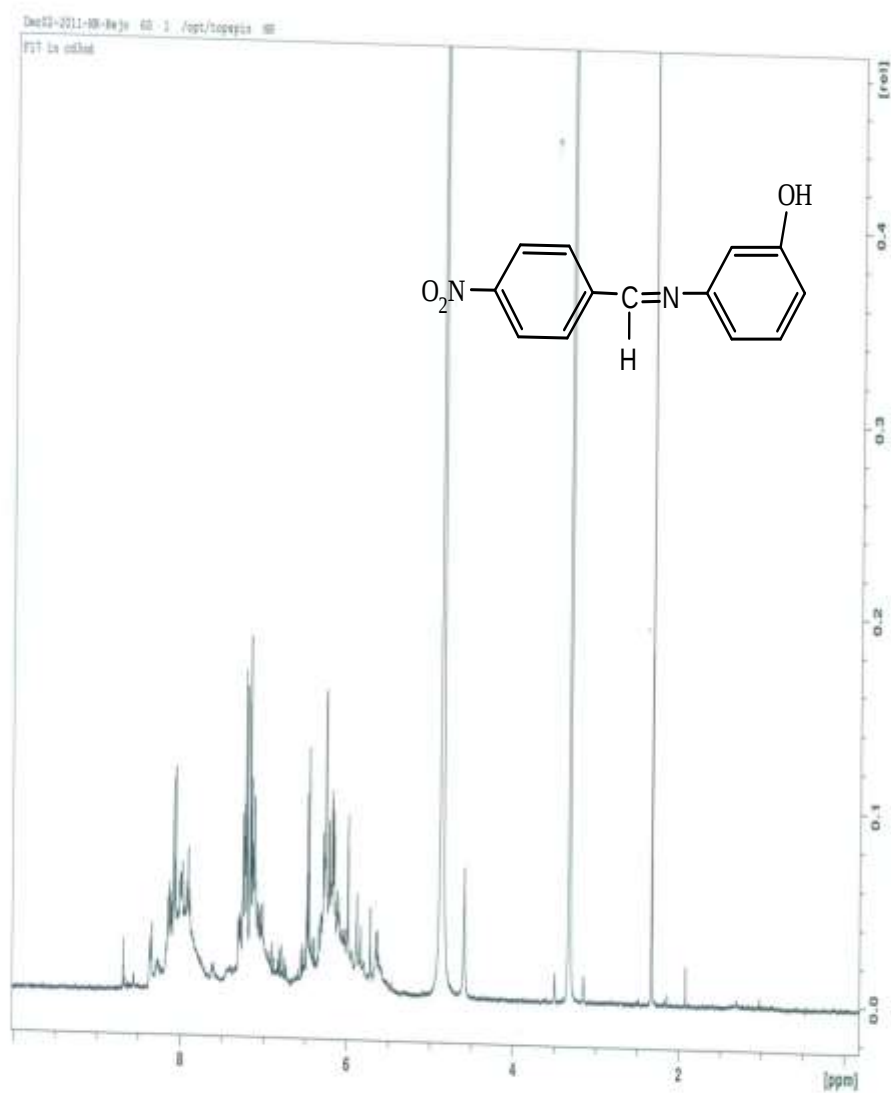


Figure 61: ¹H NMR spectrum of 3-(4-nitrobenzylideneamino)phenol Schiff base (L12)

4.2.5 Electronic Absorption Data and Magnetic Moment Measurements of 3-aminophenol Schiff Bases and Metal Complexes

The electronic absorption spectra of the Schiff bases were recorded in CHCl_3 while those of the complexes were recorded in CHCl_3 and DMF at room temperature as presented in Tables 13a and 13b.

Table 13a: Electronic Absorption Data and Magnetic Moment Measurements of *o*-substituted 3-aminophenol Schiff Bases and Metal Complexes

Compound	R ₁	R ₂	CHCl_3 (ν / cm^{-1})(log ϵ)	Assignment	DMF (ν / cm^{-1})(log ϵ)	Assignment	Magnetic Moments μ_{eff} (BM)	Proposed Geometry
L7	OMe	H	38,461(3.93) 29,498(3.63)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL7	OMe	H	-	-	27,932(3.68)	CT	1.74	Octahedral
L8	Cl	H	36,496(3.97) 28,328(3.94)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL8	Cl	H	-	-	26,954(3.85)	CT	1.76	Octahedral
L9	NO ₂	H	34,843(3.09) 28,595(2.55)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL9	NO ₂	H	-	-	26,881(3.93)	CT	1.78	Octahedral

Two bands were observed in the spectra of Schiff bases, the aromatic and azomethine bands were observed at $38,461 \text{ cm}^{-1}$ and $29,498 \text{ cm}^{-1}$ for OMe-substituted SB L7 (Figure 62), $36,496 \text{ cm}^{-1}$ and $28,328 \text{ cm}^{-1}$ for Cl-substituted SB L8 (Figure 63), $34,843 \text{ cm}^{-1}$ and $28,595 \text{ cm}^{-1}$ for NO₂-substituted SB L9 (Figure 64).

The complexes of copper(II) show bands around $27,932 \text{ cm}^{-1}$ for OMe-substituted SBMC CuL7 (Figure 62), $26,954 \text{ cm}^{-1}$ for Cl-substituted SBMC CuL8 (Figure 63) and $26,881 \text{ cm}^{-1}$ for NO₂-substituted SBMC CuL9 (Figure 64).

The observed magnetic moment values of the copper(II) complexes were in the range 1.74-1.78 BM.

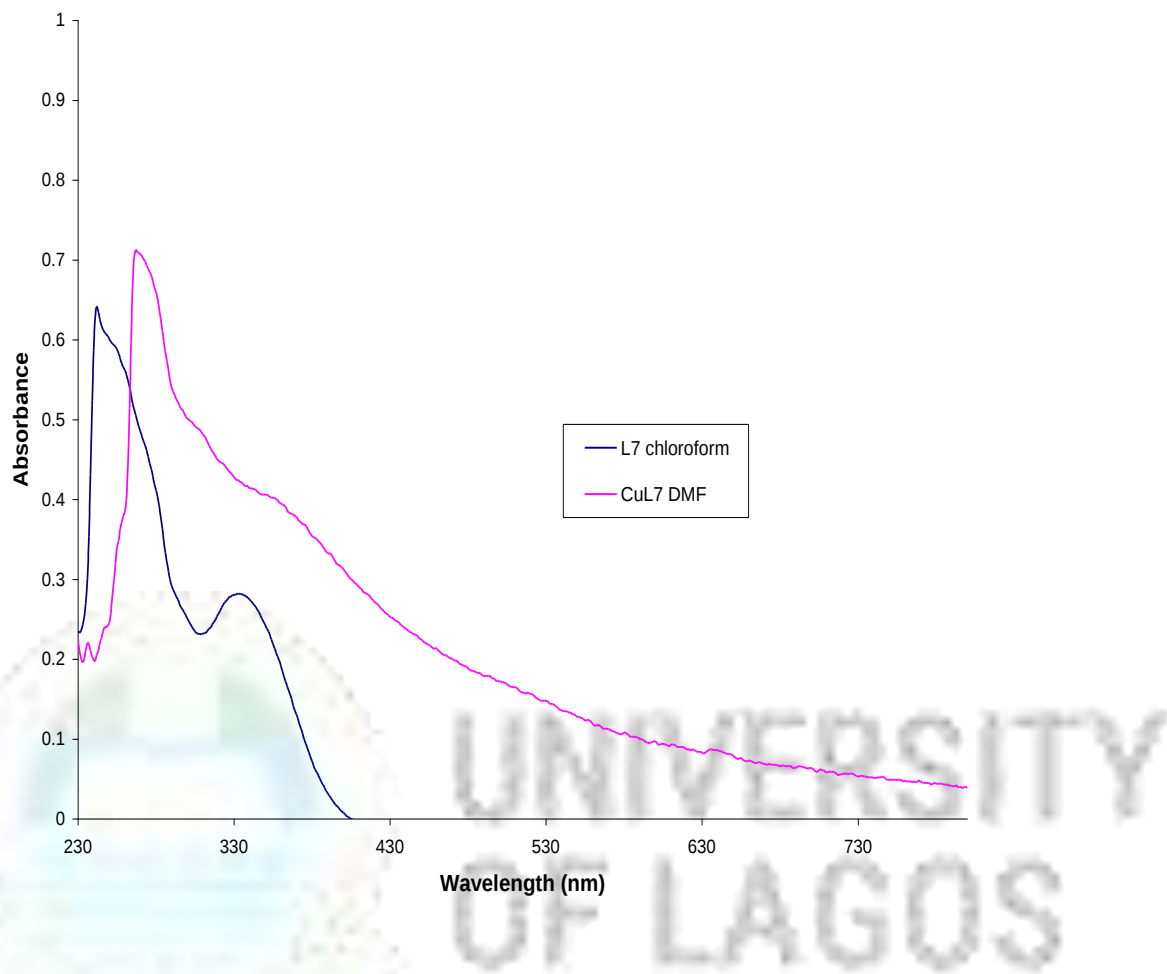


Figure 62: Electronic absorption spectra of L7 with copper metal ions in chloroform and DMF

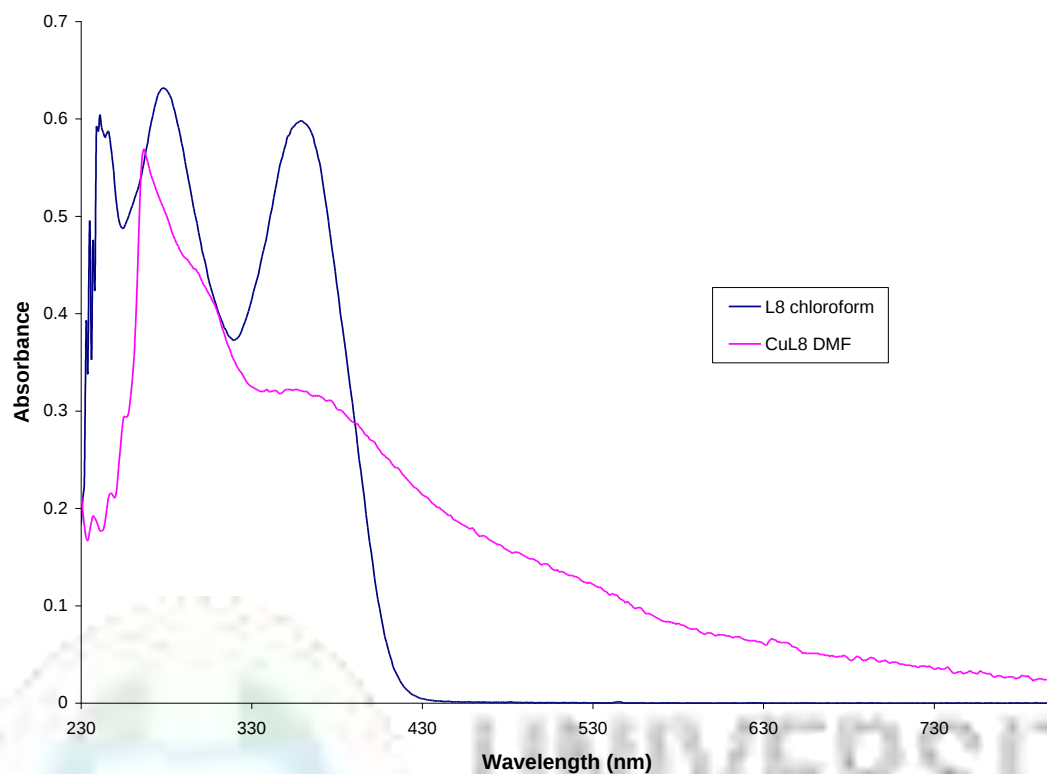


Figure 63: Electronic absorption spectra of L8 with copper metal ions in chloroform and DMF

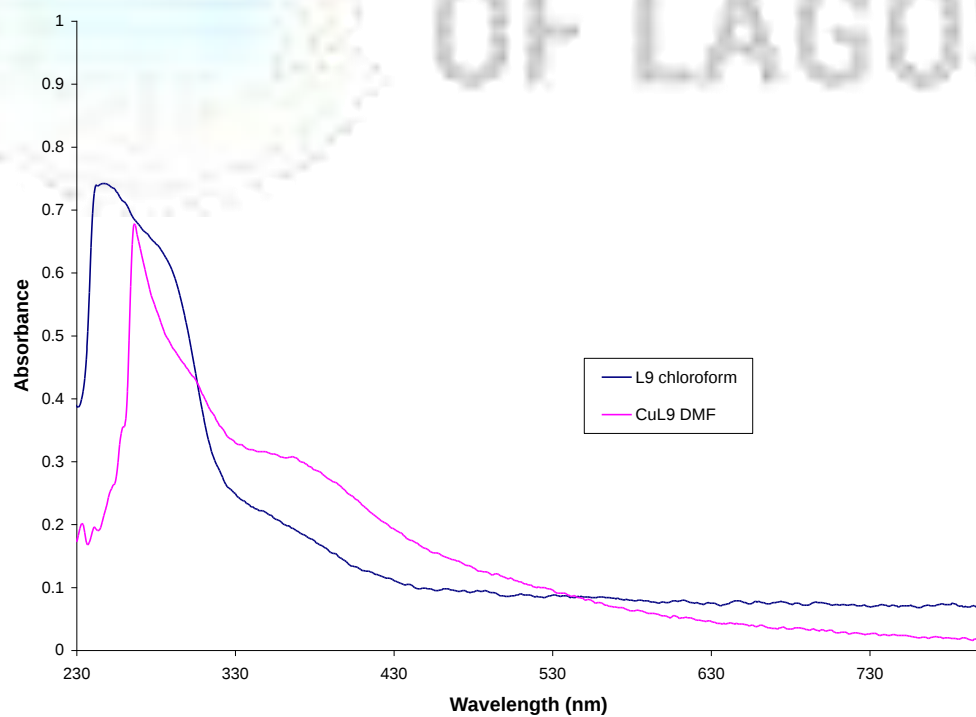


Figure 64: Electronic absorption spectra of L9 with copper metal ions in chloroform and DMF

Table 13b: Electronic Absorption Data and Magnetic Moment Measurements of *p*-substituted 3-aminophenol Schiff Bases and Metal Complexes

Compound	R ₁	R ₂	CHCl ₃ (ν / cm ⁻¹)(log ϵ)	Assignment	DMF (ν / cm ⁻¹)(log ϵ)	Assignment	Magnetic Moments μ_{eff} (BM)	Proposed Geometry
L10	H	OMe	34,722(3.96) 29,585(3.92)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL10	H	OMe	-	-	26,525(3.58)	CT	1.70	Octahedral
L11	H	Cl	34,129(3.61) 28,248(2.89)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL11	H	Cl	-	-	27,624(3.68)	CT	1.72	Octahedral
L12	H	NO ₂	33,783(3.29) 28,932(2.96)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL12	H	NO ₂	-	-	27,575(3.97)	CT	1.70	Octahedral

Two bands were observed in the spectra of Schiff bases, the aromatic and azomethine bands were observed at 34,722 cm⁻¹ and 29,585 cm⁻¹ for OMe-substituted SB L10 (Figure 65), 34,129 cm⁻¹ and 28,248 cm⁻¹ for Cl-substituted SB L11 (Figure 66), 33,783 cm⁻¹ and 28,932 cm⁻¹ for NO₂-substituted SB L12 (Figure 67).

The complexes of copper(II) show bands around 26,525 cm⁻¹ for OMe-substituted SBMC CuL10 (Figure 65), 27,624 cm⁻¹ for Cl-substituted SBMC CuL11 (Figure 66) and 27,575 cm⁻¹ for NO₂-substituted SBMC CuL12 (Figure 67).

The observed magnetic moment values of the copper(II) complexes were in the range 1.70-1.72 BM.

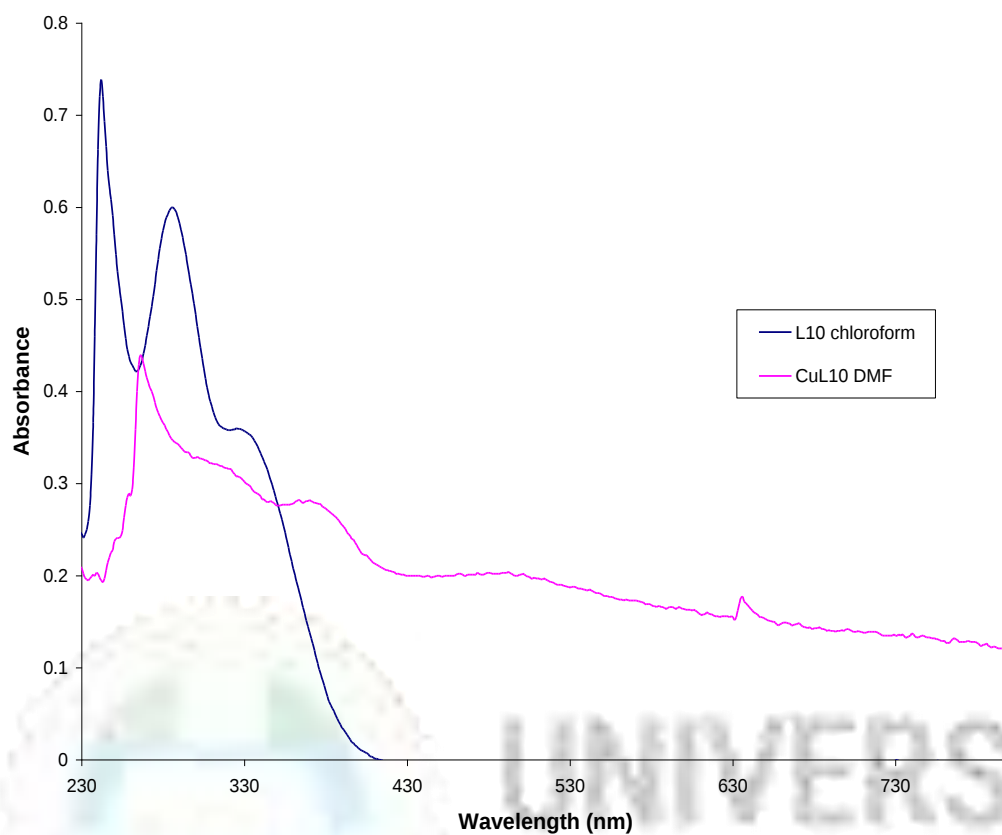


Figure 65: Electronic absorption spectra of L10 with copper metal ions in chloroform and DMF

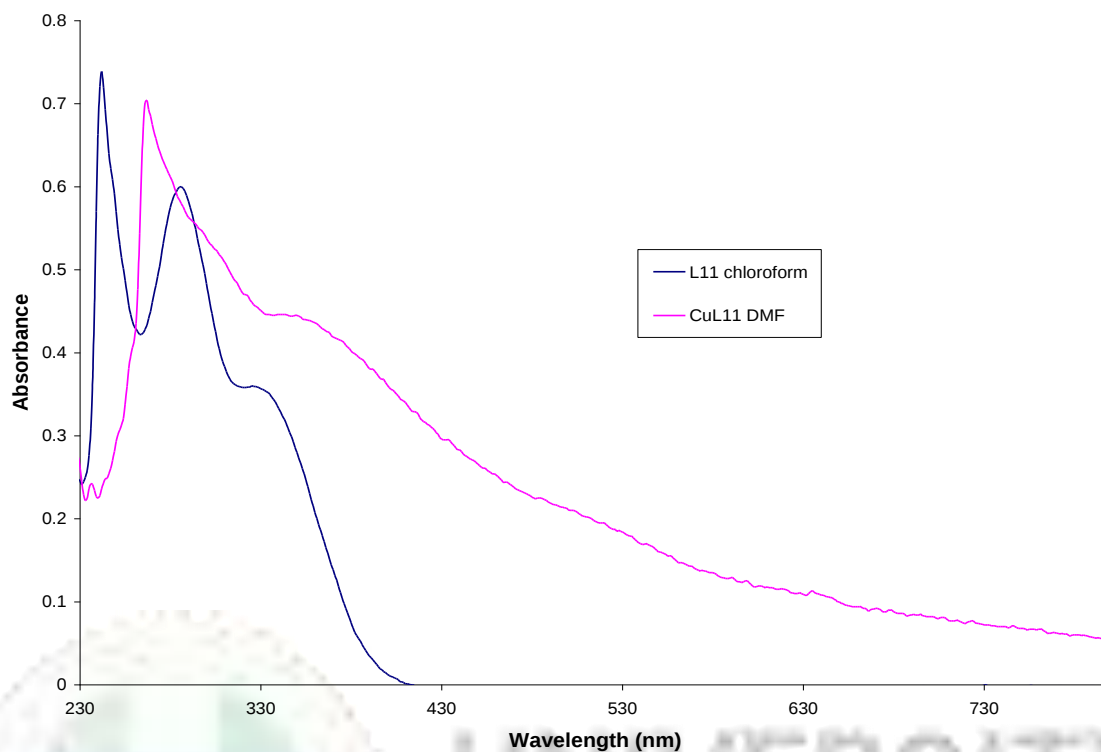


Figure 66: Electronic absorption spectra of L11 with copper metal ions in chloroform and DMF

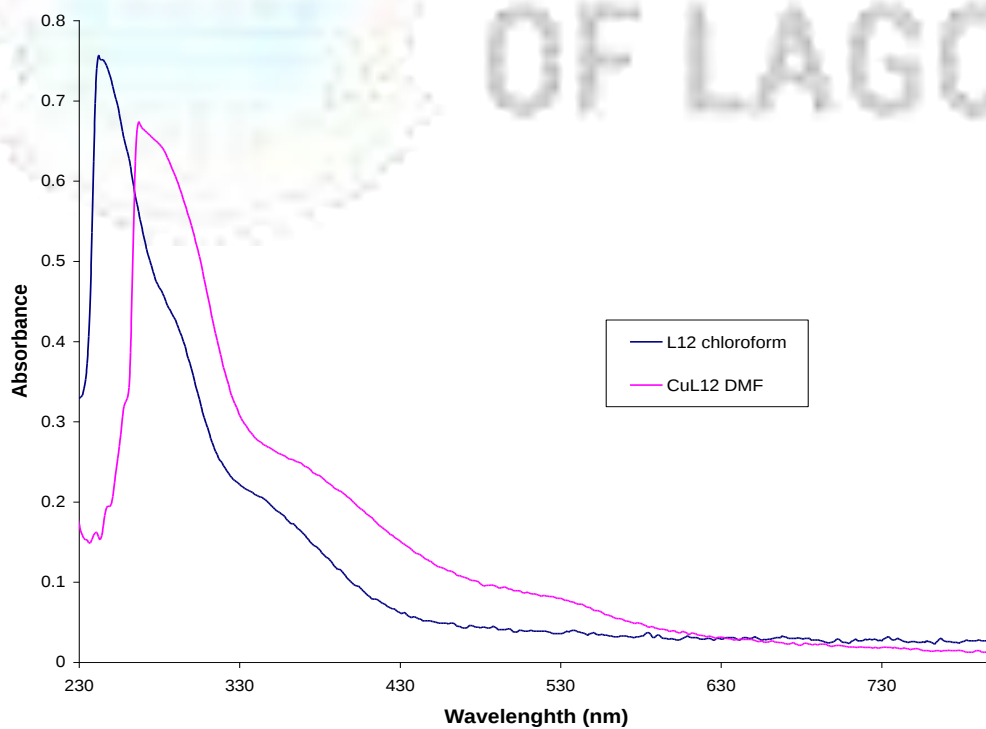


Figure 67: Electronic absorption spectra of L12 with copper metal ions in chloroform and DMF

4.3.1 Synthesis of 4-aminophenol Schiff Bases and Metal Complexes

Six Schiff base ligands namely; 2-methoxybenzylidene-4-aminophenol (L13), 2-chlorobenzylidene-4-aminophenol (L14), 2-nitrobenzylidene-4-aminophenol (L15), 4-methoxybenzylidene-4-aminophenol (L16), 4-chlorobenzylidene-4-aminophenol (L17), 4-nitrobenzylidene-4-aminophenol (L18) were obtained from reaction of 4-aminophenol with 2- and 4-substituted benzaldehydes (Scheme 33) Table 30. Three of the compounds had substituents in *o*-position and the other in *p*-position. The Schiff bases were reacted with copper and cobalt chlorides to give copper and cobalt Schiff base metal complexes; bis(4-(2-methoxybenzylideneamino)phenol)copper(II) CuL13, bis(4-(2-chlorobenzylideneamino)phenol)copper(II), bis(4-(2-nitrobenzylideneamino)phenol)copper(II) CuL15, bis(4-(4-methoxybenzylideneamino)phenol)copper(II)CuL16, bis(4-(4-chlorobenzylideneamino)phenol)copper(II) CuL17 and bis(4-(4-nitrobenzylideneamino)phenol)copper(II) CuL18 respectively.

4.3.2 Physical and analytical data of *o*-substituted 4-aminophenol Schiff bases and metal complexes

The physical and analytical data of Schiff bases and Schiff base metal complexes derived from 4-aminophenol are presented in Tables 14a and 14b.

Table 14a: Physical and analytical data of *o*-substituted 4-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	Empirical Formula (M.wt)	Yield (%)	Color	M.pt (°C)	% Found (calcd)			Metal (%)
							C	H	N	
L13	OMe	H	C ₁₄ H ₁₃ NO ₂ (227)	92.54	Yellow	130-131	73.85(73.99)	5.74(5.77)	6.05(6.16)	-
CuL13	OMe	H	C ₂₈ H ₂₈ ClCuN ₂ O ₆ (552)	47.00	Brown	>250	49.94 (49.76)	3.91(3.88)	8.80(7.14)	12.73
L14	Cl	H	C ₁₃ H ₁₀ NOCl (231)	53.62	Yellow	120-121	67.27(67.39)	4.15(4.35)	6.06(6.05)	-
CuL14	Cl	H	C ₂₆ H ₂₂ Cl ₃ CuN ₂ O ₄ (560)	43.00	Brown	>250	52.46(52.41)	3.95(3.05)	7.35(6.70)	10.67
L15	NO ₂	H	C ₁₃ H ₁₀ N ₂ O ₃ (242)	57.59	Yellow	119-120	64.27(64.46)	4.02(4.16)	11.5(11.56)	-
CuL15	NO ₂	H	C ₂₆ H ₂₂ ClCuN ₄ O ₈ (581)	41.00	Brown	>250	52.05(52.09)	3.79(3.36)	8.68(9.35)	10.12

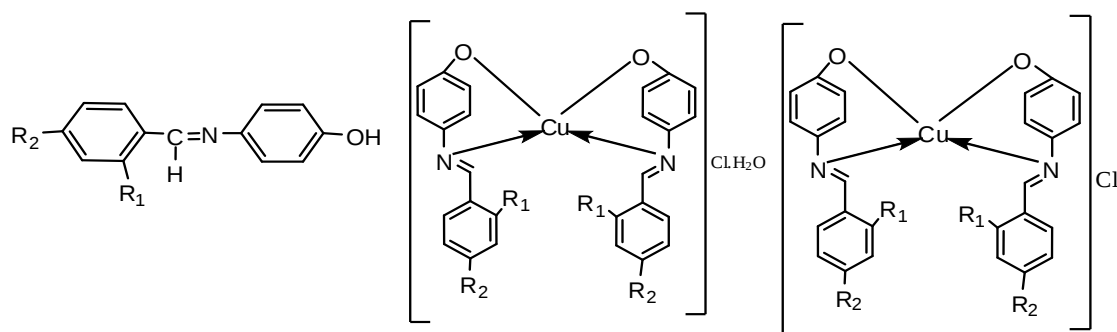


Figure 68: Schiff bases and metal complexes synthesized from 4-aminophenol

Microanalysis were obtained for each of the synthesized compounds. The percentage metal were determined for the metal complexes. The complexes exhibited one mole of metal ion per mole of complex. The melting points of the Schiff bases were in the range 130-131 °C for OMe substituted SB L13, 120-121 °C for Cl substituted SB L14 and 119-120 °C for NO₂ substituted SB L15 while the metal complexes decomposed above 250 °C. The yields obtained ranges between 54-93 % for Schiff base ligands L13-L15 and 41-47 % for Schiff base metal complexes CuL13-CuL15.

Table 14b: Physical and analytical data of *p*-substituted 4-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	Empirical Formula (M.wt)	Yield (%)	Color	M.pt (°C)	% Found (calcd)			Metal (%)
							C	H	N	
L16	H	OMe	C ₁₄ H ₁₃ NO ₂ (227)	70.12	Yellow	150-151	78.85(73.99)	5.74(5.77)	6.05(6.16)	-
CuL16	H	OMe	C ₂₈ H ₂₈ Cl ₂ CuN ₂ O ₆ (551)	46.00	Brown	>250	50.34(49.76)	3.94 (3.88)	8.77(8.14)	12.19
L17	H	Cl	C ₁₃ H ₁₀ NOCl (231)	62.30	Yellow	136-137	67.52(67.39)	4.22 (4.35)	6.07(6.05)	-
CuL17	H	Cl	C ₂₆ H ₂₂ Cl ₄ CuN ₂ O ₄ (559)	47.20	Brown	>250	51.84(51.41)	3.66(3.05)	7.43(6.70)	11.98
L18	H	NO ₂	C ₁₃ H ₁₀ N ₂ O ₃ (242)	48.80	Orange	118-119	64.02(64.46)	3.84(4.16)	11.36(11.56)	-
CuL18	H	NO ₂	C ₂₆ H ₂₂ Cl ₂ CuN ₄ O ₈ (581)	40.10	Brown	>250	51.39(51.62)	3.61(2.94)	8.51(9.05)	12.22

Microanalysis were obtained for each of the synthesized compounds. The percentage metal were determined for the metal complexes. The complexes exhibited one mole of metal ion per mole of complex. The melting points of the Schiff bases were in the range 150-151 °C for OMe substituted SB L16, 136-137 °C for Cl substituted SB L17 and 118-119 °C for NO₂ substituted SB L18 while the metal complexes decomposed above 250 °C. The yields obtained ranges between 49-70 % for Schiff base ligands L16-L18 and 40-47 % for Schiff base metal complexes CuL16-CuL18.

4.3.3 Spectroscopic Data of 4-aminophenol Schiff Bases and Metal Complexes

The Schiff bases were characterized using IR and NMR analysis and the results are presented in Tables 15a, 15b, 16a and 16b.

Table 15a: Spectroscopic data of *o*-substituted 4-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	$\nu(\text{O-H})$	$\nu(\text{C=N})$	$\nu(\text{C-O})$	$\nu\text{OH}(\text{H}_2\text{O})$	$\nu(\text{C-Cl})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
			cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹	cm ⁻¹
L13	OMe	H	-	1614	1262	-	-	-	-
CuL13	OMe	H	3430 3345	1593	1257	856	-	565	517
L14	Cl	H	-	1625	1273	-	345	-	-
CuL14	Cl	H	3352	1609	1255	-	345	504	429
L15	NO ₂	H	-	1620	1269	-	-	-	-
CuL15	NO ₂	H	3320	1604	1252	-	-	540	508

The imine band (C=N) in the SB appears in the region 1614 cm⁻¹ for OMe-substituted SB L13 (Figure 69), 1625 cm⁻¹ for Cl-substituted SB L14 (Figure 70) and 1620 cm⁻¹ for NO₂-substituted SB L15 (Figure 71). On coordination, the bands shifted to lower frequencies of 1593, 1609 cm⁻¹ and 1604 cm⁻¹ respectively. The phenolic -OH in Schiff bases were not observed. The IR spectra also exhibited characteristic band (C-O) in the Schiff bases in the region 1262 cm⁻¹ L13, 1273 cm⁻¹ L14 and 1269 cm⁻¹ L15. In the metal complexes, the band appear in the region 1257, 1255

cm^{-1} , and 1252 cm^{-1} respectively. Coordinated water indicates a broad band in the region 3430 , 3345 cm^{-1} CuL13, 3352 cm^{-1} CuL14 and 3320 cm^{-1} CuL15. New bands were observed at 429 - 517 cm^{-1} and 504 - 565 cm^{-1} in the spectra of metal complexes.

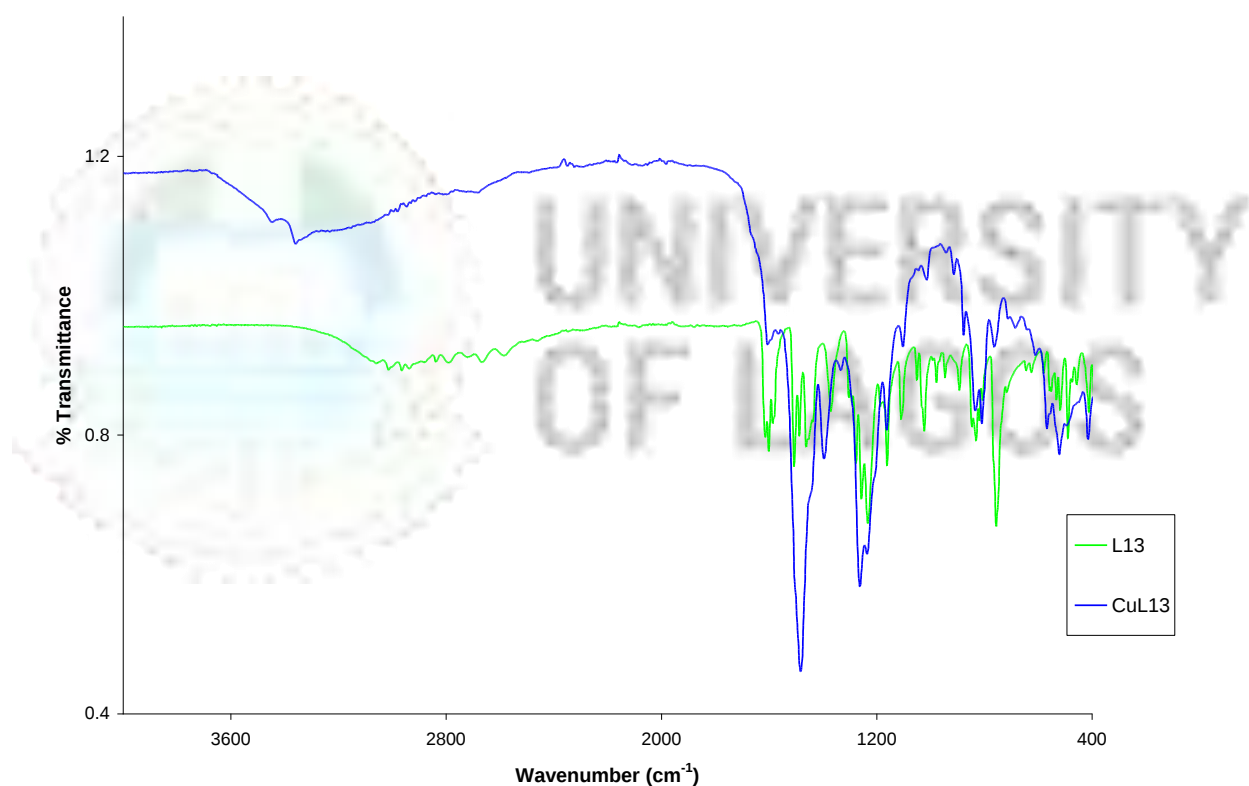


Figure 69: IR spectra of 4-(2-methoxybenzylideneamino)phenol (L13) and Cu metal complex

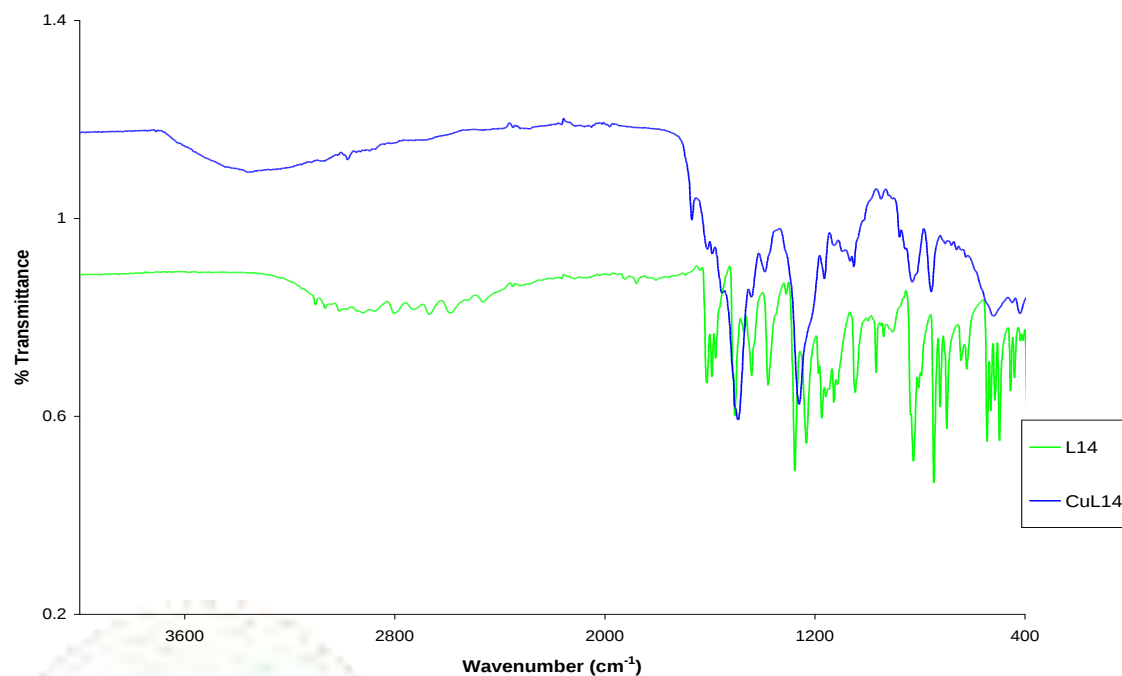


Figure 70: IR spectra of 4-(2-chlorobenzylideneamino)phenol (L14) and Cu metal complex

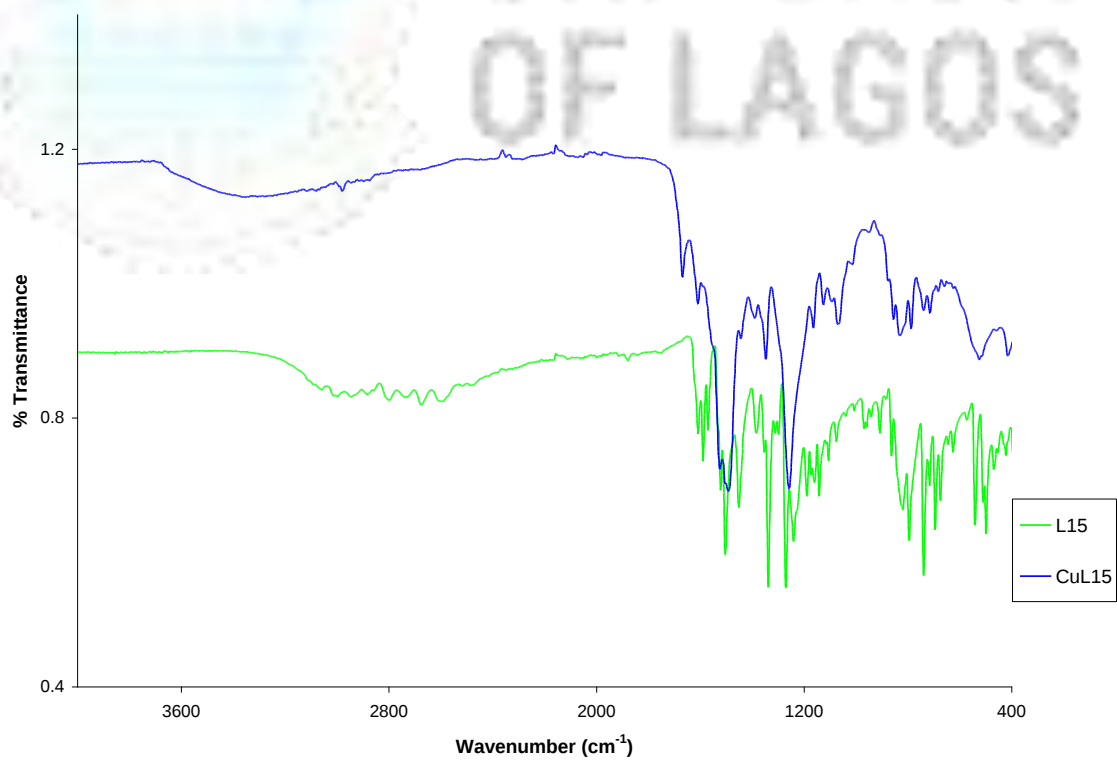


Figure 71: IR spectra of 4-(2-nitrobenzylideneamino)phenol (L15) and Cu metal complex

Table 15b: Spectroscopic data of *p*-substituted 4-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	$\nu(\text{O-H})$	$\nu(\text{C=N})$	$\nu(\text{C-O})$	$\nu\text{OH}(\text{H}_2\text{O})$	$\nu(\text{C-Cl})$	$\nu(\text{M-O})$	$\nu(\text{M-N})$
			cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}	cm^{-1}
L16	H	OMe	-	1618	1260	-	-	-	-
CuL16	H	OMe	3346	1584	1253	857	-	563	515
L17	H	Cl	-	1604	1271	-	321	-	-
CuL17	H	Cl	3346	1589	1252	-	321	565	516
L18	H	NO ₂	3426	1623	1247	-	-	-	-
CuL18	H	NO ₂	3345	1591	1256	-	-	556	514

The imine band (C=N) in the SB appears in the region 1618 cm^{-1} for OMe-substituted SB L16 (Figure 72), 1604 cm^{-1} for Cl-substituted SB L17 (Figure 73) and 1623 cm^{-1} for NO₂-substituted SB L18 (Figure 74). On coordination, the bands shifted to lower frequencies of 1584 cm^{-1} , 1589 cm^{-1} and 1591 cm^{-1} respectively. The phenolic -OH in Schiff bases was observed only in NO₂ substituted SB L18 at 3426 cm^{-1} . The IR spectra also exhibited characteristic band (C-O) in the Schiff bases in the region 1260 cm^{-1} L16, 1271 cm^{-1} L17 and 1247 cm^{-1} L18. In the metal complexes, the band appear in the region 1253 cm^{-1} , 1252 cm^{-1} , and 1256 cm^{-1} respectively. The presence of water indicates a broad band in the region 3346 cm^{-1} CuL16, 3346 cm^{-1} CuL17 and 3345 cm^{-1} CuL18. New bands were observed at $514\text{--}516\text{ cm}^{-1}$ and $556\text{--}565\text{ cm}^{-1}$ in the spectra of metal complexes.

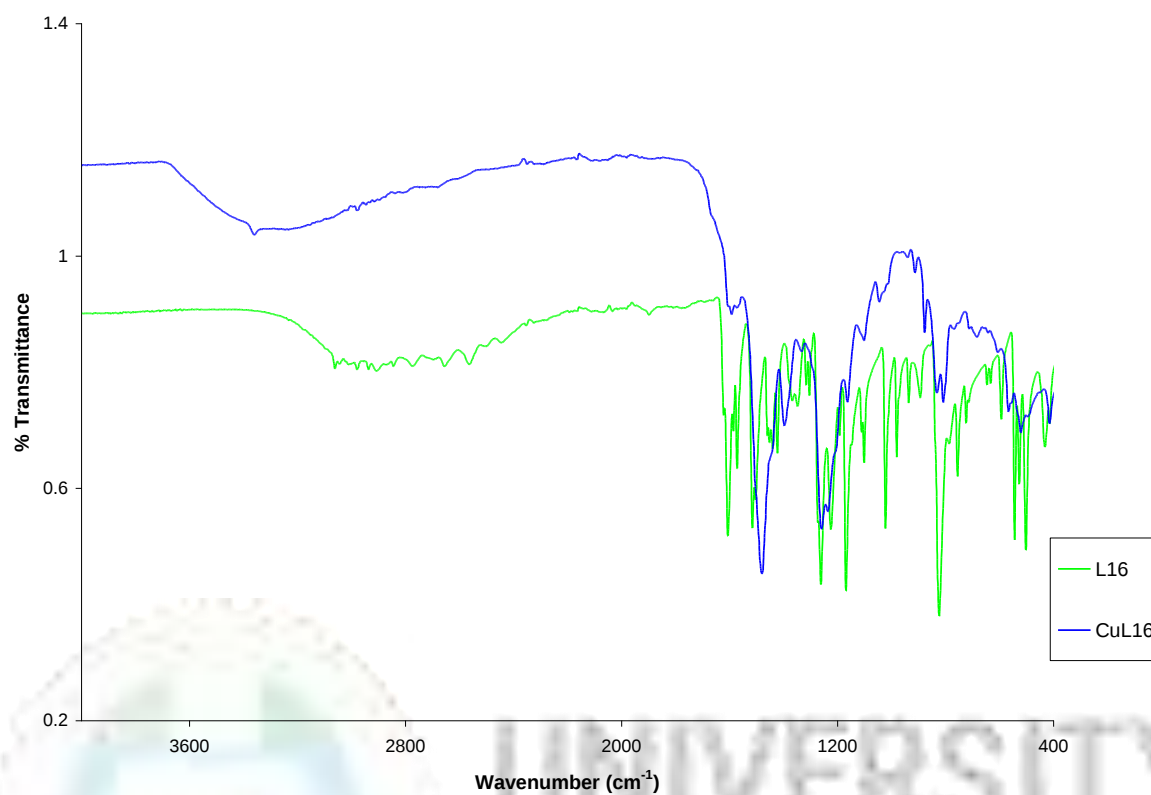


Figure 72: IR spectra of 4-(4-methoxybenzylideneamino)phenol (L16) and Cu metal complex

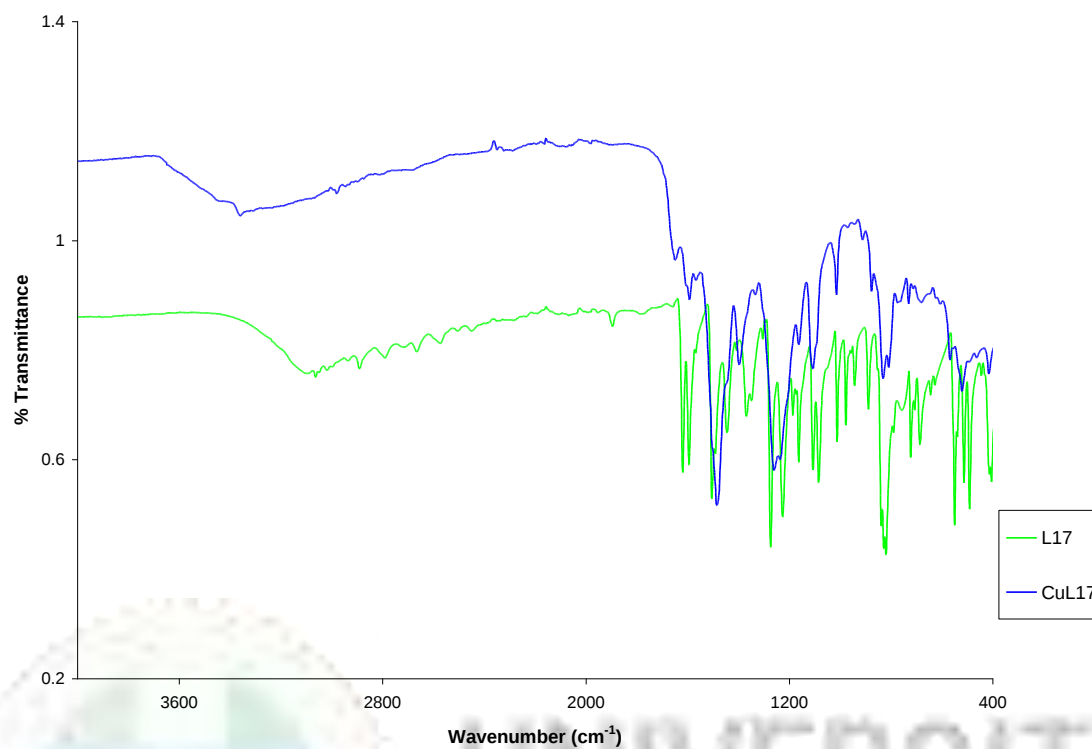


Figure 73: IR spectra of 4-(4-chlorobenzylideneamino)phenol (L17) and Cu metal complex

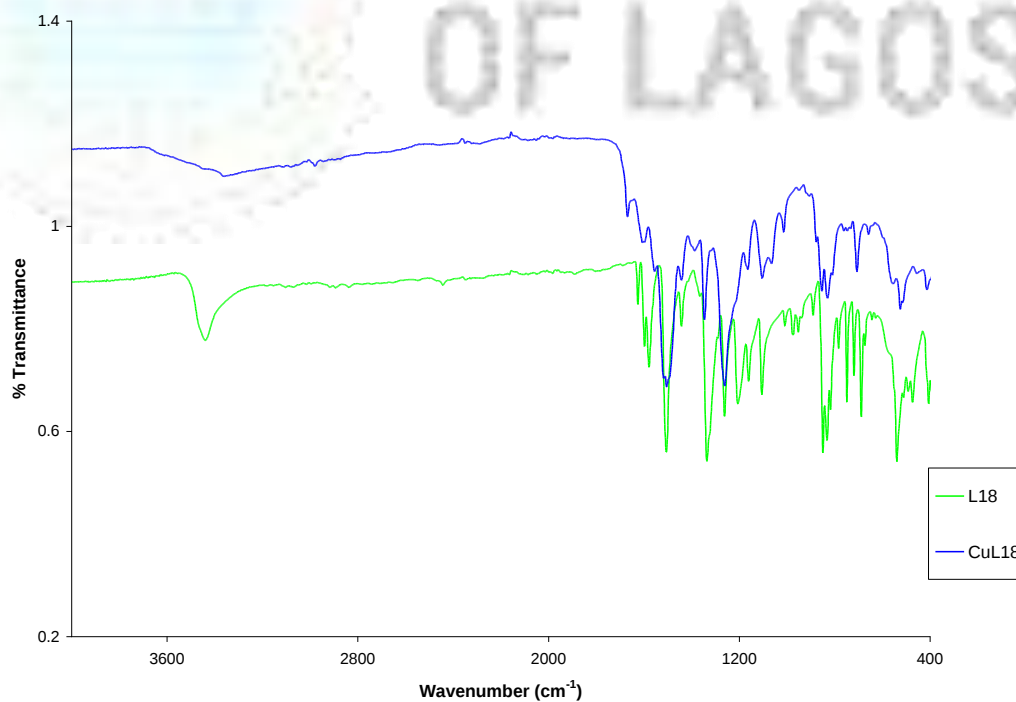


Figure 74: IR spectra of 4-(4-nitrobenzylideneamino)phenol (L18) and Cu metal complex

4.3.4 ^1H NMR Data of 4-aminophenol Schiff Bases

The ^1H NMR data of 4-aminophenol Schiff bases are presented in Tables 16a and 16b.

Table 16a. ^1H NMR data of *o*-substituted 4-aminophenol Schiff bases

Compound	R ₁	R ₂	HC=N (s,1H) (δ ,ppm)	OH (s, 1H) (δ , ppm)	OCH ₃ (s, 3H) (δ , ppm)	Aromatic, protons m, 8H (δ , ppm)
L13	OMe	H	8.00	8.89	3.96	6.86-7.53
L14	Cl	H	8.21	8.93	-	6.84-7.39
L15	NO ₂	H	8.29	8.98	-	6.87-8.03

The imine (C=N) protons show signals at 8.00 ppm for OMe-substituted SB L13 (Figure 75) 8.21 ppm for Cl-substituted SB L14 (Figure 76) and 8.29 ppm for NO₂-substituted SB L15 (Figure 77). Methoxy protons (-OCH₃) appear as singlets at 3.96 ppm for OMe-substituted SB L13, the signal for the phenolic -OH appears at 8.89 ppm for OMe-substituted SB L13 (Figure 75) 8.93 ppm for Cl-substituted SB L14 (Figure 76) and 8.98 ppm for NO₂-substituted SB L15 (Figure 77). . Aromatic protons show multiple resonance signals between 6.84-8.03 ppm.

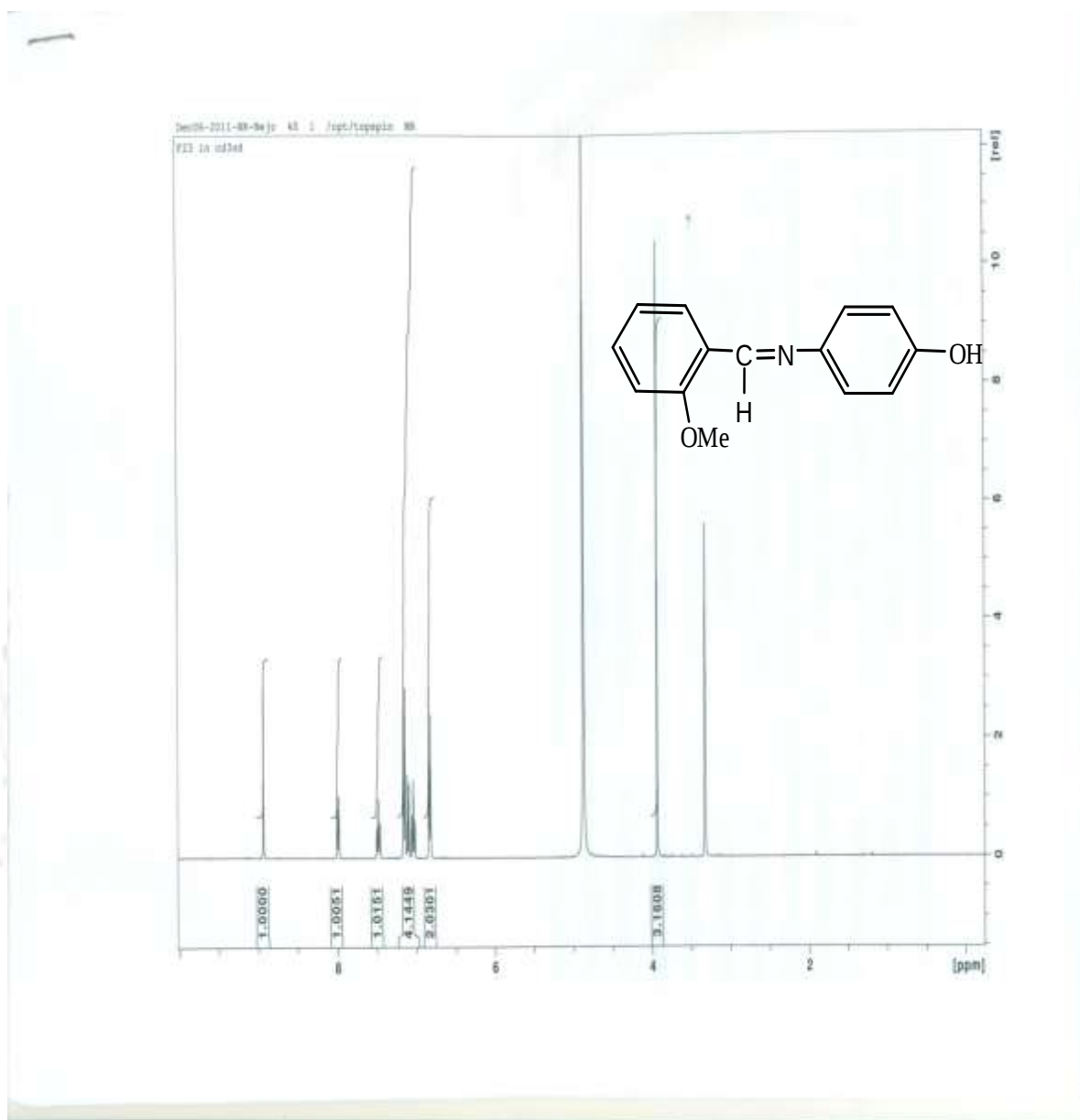


Figure 75: ^1H NMR spectrum of 4-(2-methoxybenzylideneamino)phenol Schiff base (L13)

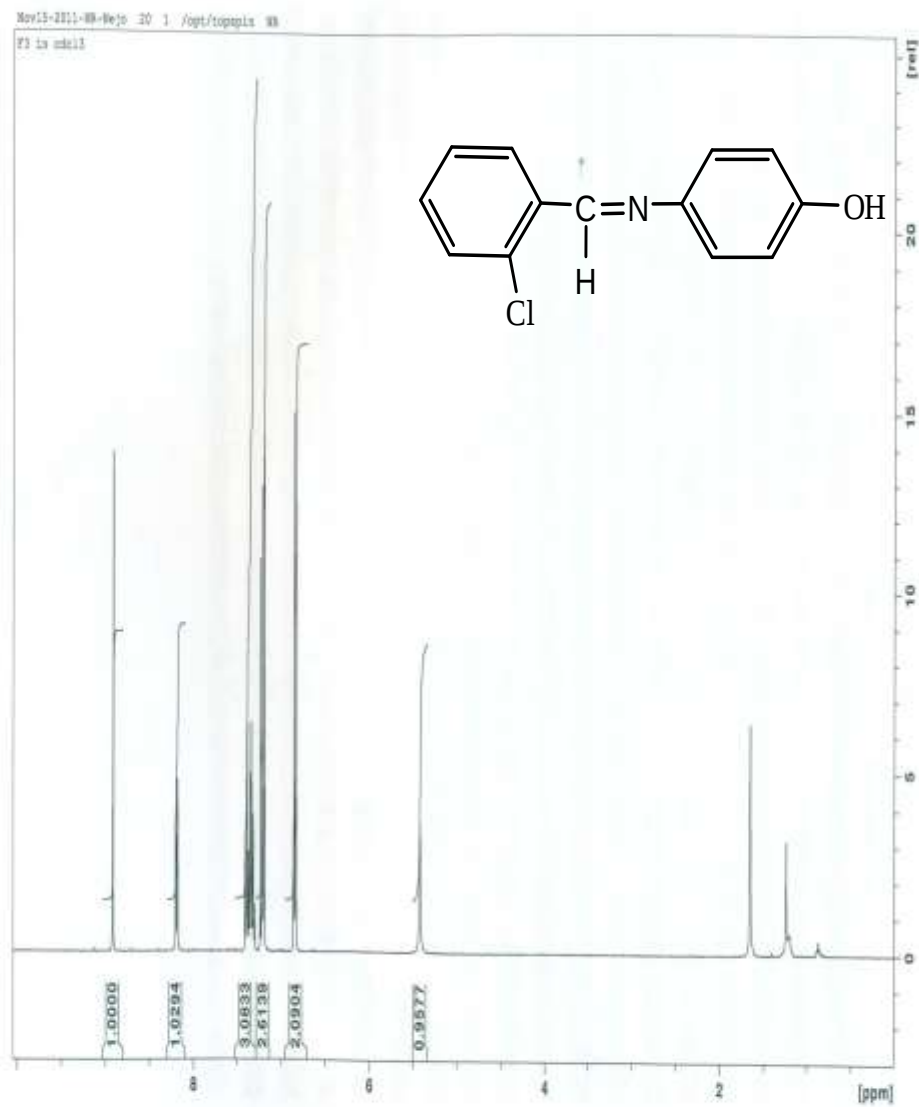


Figure 76: ^1H NMR spectrum of 4-(2-chlorobenzylideneamino)phenol Schiff base (L14)

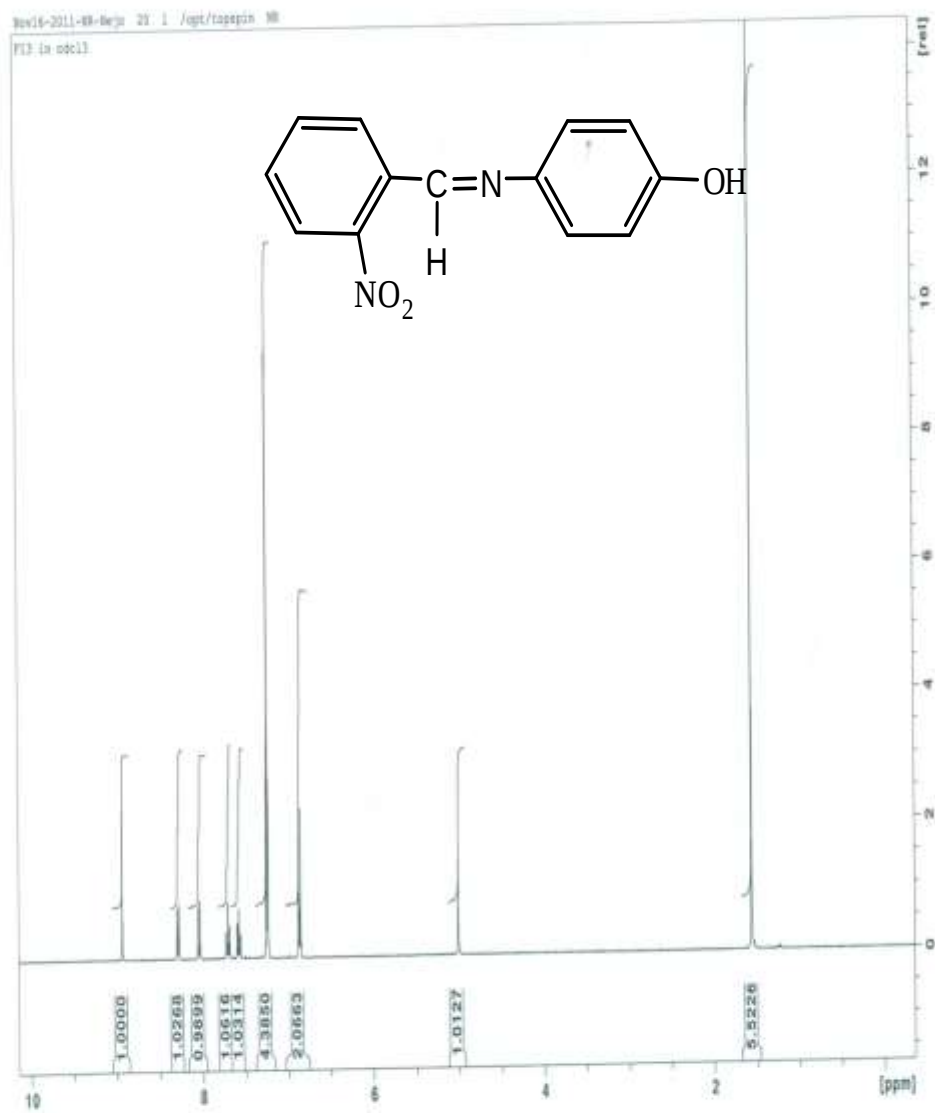


Figure 77: ¹H NMR spectrum of 4-(2-nitrobenzylideneamino)phenol Schiff base (L15)

Table 16b: ^1H NMR data of *p*-substituted 4-aminophenol Schiff bases

Compound	R ₁	R ₂	HC=N (s, 1H) (δ , ppm)	OH (s, 1H) (δ , ppm)	OCH ₃ (s, 3H) (δ , ppm)	Aromatic, protons m, 8H (δ , ppm)
L16	H	OMe	8.35	9.43	3.83	6.78-7.85
L17	H	Cl	8.61	9.57	-	6.84-7.94
L18	H	NO ₂	8.53	8.61	-	6.92-8.09

The imine (C=N) protons show signals at 8.35 ppm for OMe-substituted SB L16 (Figure 78), 8.61 ppm for Cl-substituted SB L17 (Figure 79), and 8.53 ppm for NO₂-substituted SB L18 (Figure 80). Methoxy protons (-OCH₃) appear as singlets at 3.83 ppm for OMe-substituted SB L16, the signal for the phenolic -OH appears at 9.43 ppm for OMe-substituted SB L16 (Figure 78), 9.57 ppm for Cl-substituted SB L17 (Figure 79) and 8.61 ppm for NO₂-substituted SB L18 (Figure 80). Aromatic protons show multiple resonance signals between 6.78-8.09 ppm.

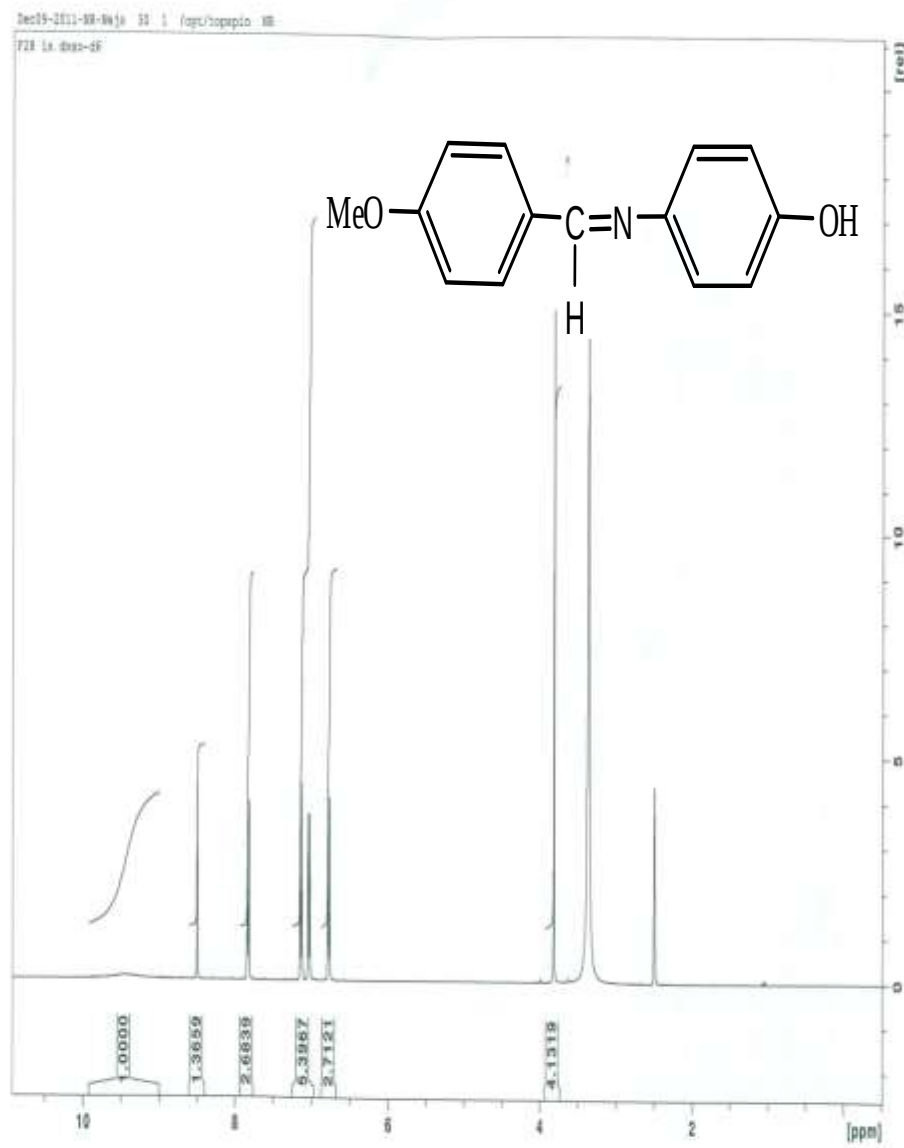


Figure 78: ^1H NMR spectrum of 4-(4-methoxybenzylideneamino)phenol Schiff base (L16)

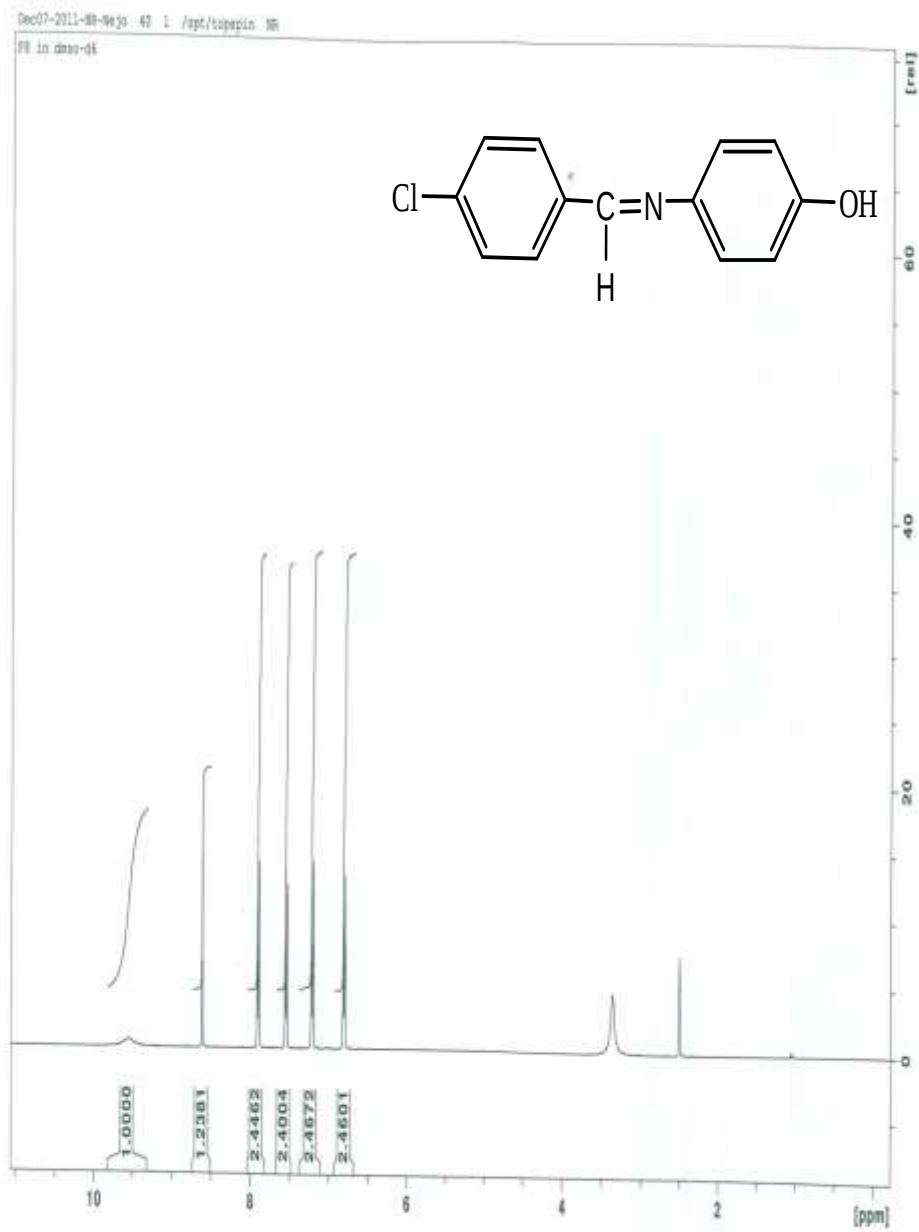


Figure 79: ^1H NMR spectrum of 4-(4-chlorobenzylideneamino)phenol Schiff base (L17)

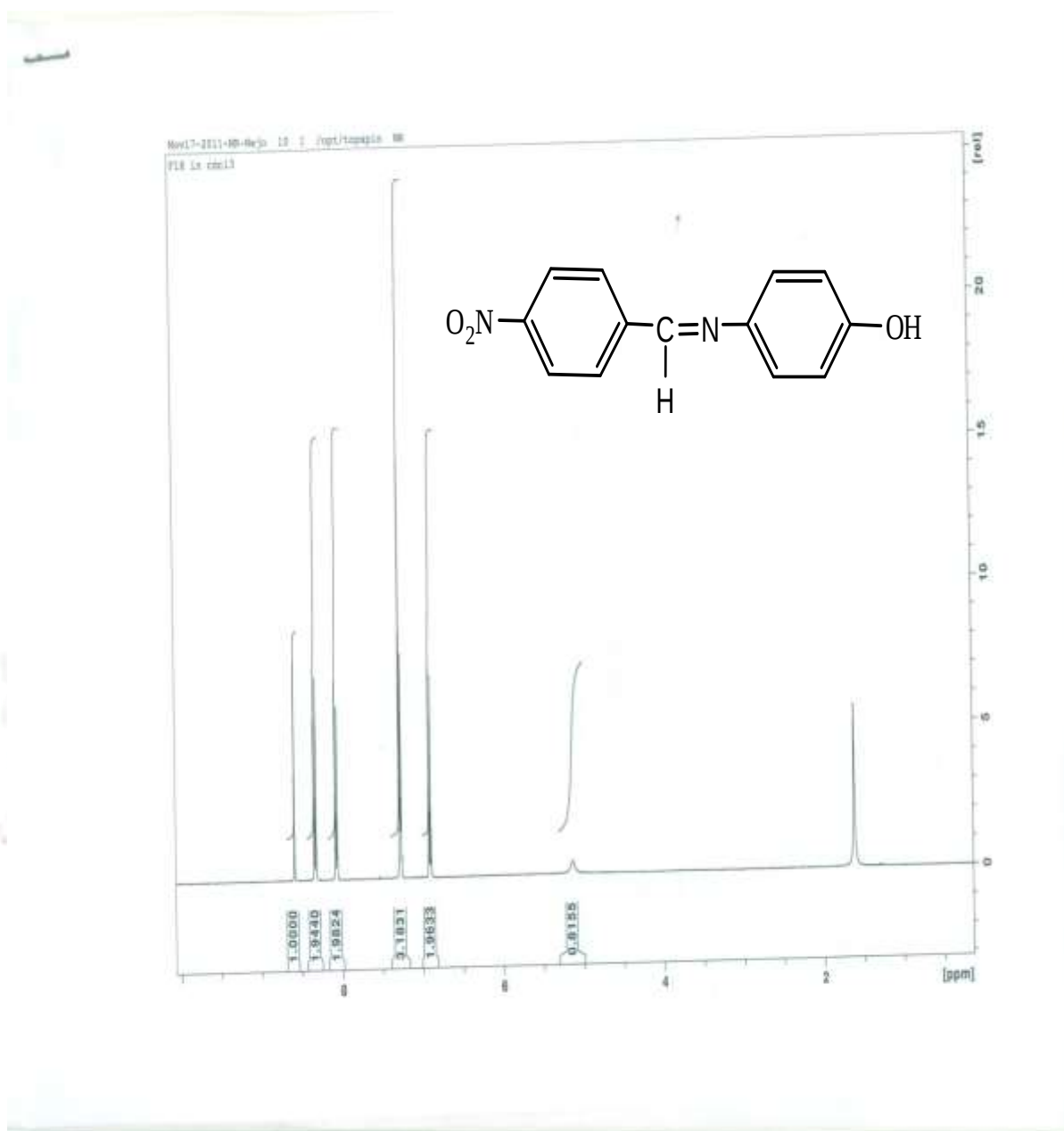


Figure 80: ¹H NMR spectrum of 4-(4-nitrobenzylideneamino)phenol Schiff base (L18)

4.3.5 Electronic Absorption Data and Magnetic Moment Measurements of 4-aminophenol Schiff Bases and Metal Complexes

The electronic spectra of the Schiff bases were recorded in CHCl_3 while those of the complexes were recorded in CHCl_3 and DMF at room temperature as presented in Tables 17a and 17b.

Table 17a: Electronic absorption data and magnetic moments measurements of *o*-substituted 4-aminophenol SB and metal complexes in CHCl_3 and DMF ($10^{-5} \text{ mol L}^{-1}$)

Compound	R ₁	R ₂	CHCl_3 (ν / cm^{-1})(log ϵ)	Assignment	DMF (ν / cm^{-1})(log ϵ)	Assignment	Magnetic Moments μ_{eff} (BM)	Proposed Geometry
L13	OMe	H	37,313(4.05) 29,154(4.31)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL13	OMe	H	30,959(3.18) 20,080(3.19)	CT d-d	30,864(3.14) 20,833(4.01)	CT d-d	1.80	Tetrahedral
L14	Cl	H	29,761(4.09)	$n \rightarrow \pi^*$	-	-	-	-
CuL14	Cl	H	25,316(3.69)	d-d	23,109(2.56)	d-d	1.84	Tetrahedral
L15	NO_2	H	36,630(4.24) 28,169(3.86)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL15	NO_2	H	31,847(3.85)	CT	22,666(4.08)	d-d	1.88	Tetrahedral

Two bands were observed in the spectra of Schiff bases, the aromatic and azomethine bands were observed at $37,313 \text{ cm}^{-1}$ and $29,154 \text{ cm}^{-1}$ for OMe-substituted SB L13 (Figure 81), $29,761 \text{ cm}^{-1}$ for Cl-substituted SB L14 (Figure 82), $36,630 \text{ cm}^{-1}$ and $28,169 \text{ cm}^{-1}$ for NO_2 -substituted SB L15 (Figure 83).

The complexes of copper(II) show bands around $20,080\text{-}20,833 \text{ cm}^{-1}$ and $30,864\text{-}30,959 \text{ cm}^{-1}$ for OMe-substituted SBMC CuL13 (Figure 81), $23,109\text{-}25,316 \text{ cm}^{-1}$ for Cl-substituted SBMC CuL14 (Figure 82) and $22,666 \text{ cm}^{-1}$, $31,847 \text{ cm}^{-1}$ for NO_2 -substituted SBMC L15 (Figure 83).

The observed magnetic moment values of the copper(II) complexes were in the range 1.80-1.88 BM.

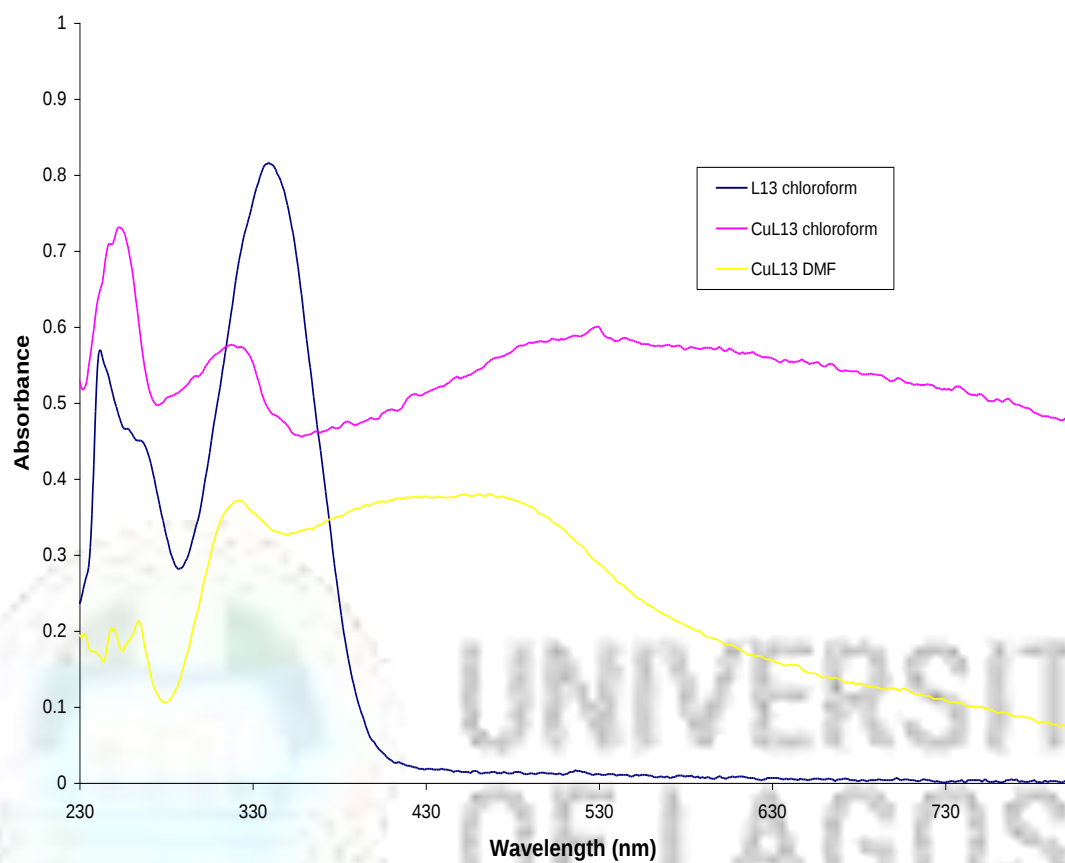


Figure 81: Electronic absorption spectra of L13 with copper metal ions in chloroform and DMF

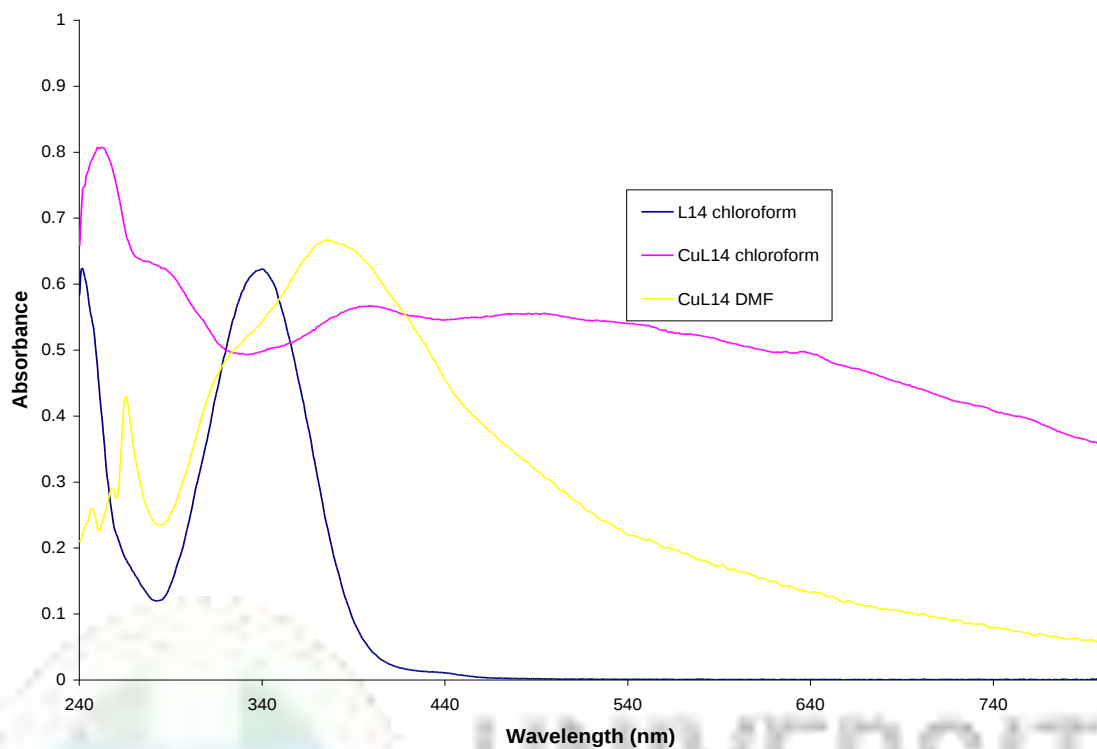


Figure 82: Electronic absorption spectra of L14 with copper metal ions in chloroform and DMF

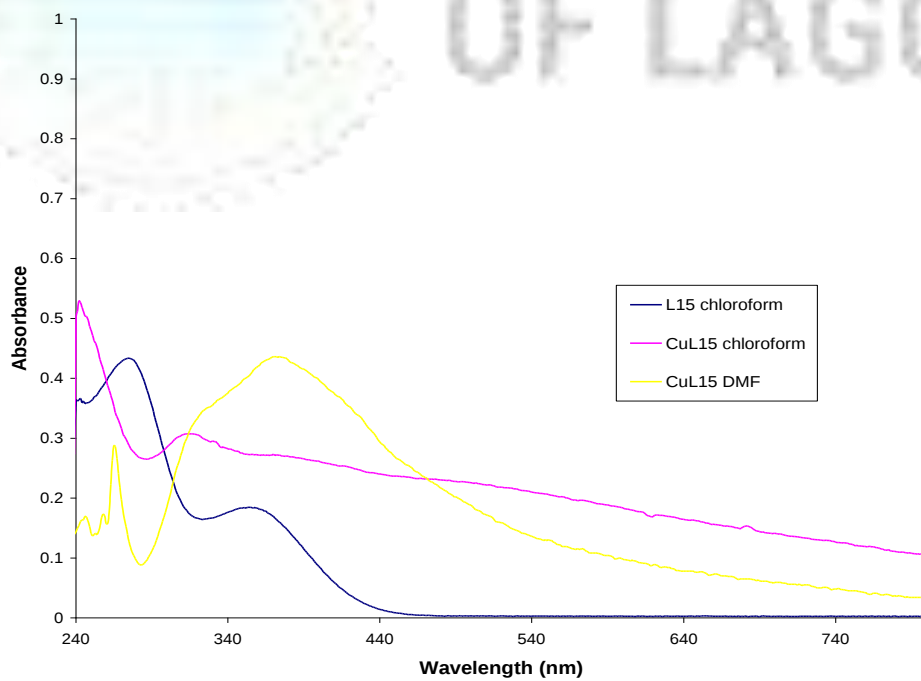


Figure 83: Electronic absorption spectra of L15 with copper metal ions in chloroform and DMF

Table 17b: Electronic absorption data and magnetic moments measurements of *p*-substituted 4-aminophenol SB and metal complexes in CHCl₃ and DMF (10⁻⁵ molL⁻¹)

Compound	R ₁	R ₂	CHCl ₃ (ν / cm ⁻¹)(log ϵ)	Assignment	DMF (ν / cm ⁻¹)(log ϵ)	Assignment	Magnetic Moments μ_{eff} (BM)	Proposed Geometry
L16	H	OMe	34,482(3.99) 29,030(3.22)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL16	H	OMe	- -	- -	30,959(2.86) 20,080(4.38)	CT d-d	1.82	Tetrahedral
L17	H	Cl	37,174(4.66) 29,395(4.55)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL17	H	Cl	31,948(3.69) - -	CT - -	30,959(2.68) 23,315(2.79) 15,698(2.58)	CT d-d d-d	1.81	Tetrahedral
L18	H	NO ₂	38,759(4.11) 27,666(4.13)	$\pi \rightarrow \pi^*$ $n \rightarrow \pi^*$	- -	- -	-	-
CuL18	H	NO ₂	-	-	25,839(4.26)	d-d	1.83	Tetrahedral

Two bands were observed in the spectra of Schiff bases, the aromatic and azomethine bands were observed at 34,482 cm⁻¹ and 29,030 cm⁻¹ for OMe-substituted SB L16 (Figure 84), 37,174 cm⁻¹ and 29,395 cm⁻¹ for Cl-substituted SB L17 (Figure 85), 38,759 cm⁻¹ and 27,666 cm⁻¹ for NO₂-substituted SB L18 (Figure 86).

The complexes of copper(II) show bands around 20,080 cm⁻¹ and 30,959 cm⁻¹ for OMe-substituted SBMC CuL16 (Figure 84), 15,698 cm⁻¹, 23,315 cm⁻¹ and 30,959 cm⁻¹ for Cl-substituted SBMC CuL17 (Figure 85) and 25,839 cm⁻¹ for NO₂-substituted SB CuL18 (Figure 86).

The observed magnetic moment values of the copper(II) complexes were in the range 1.81-1.83 BM.

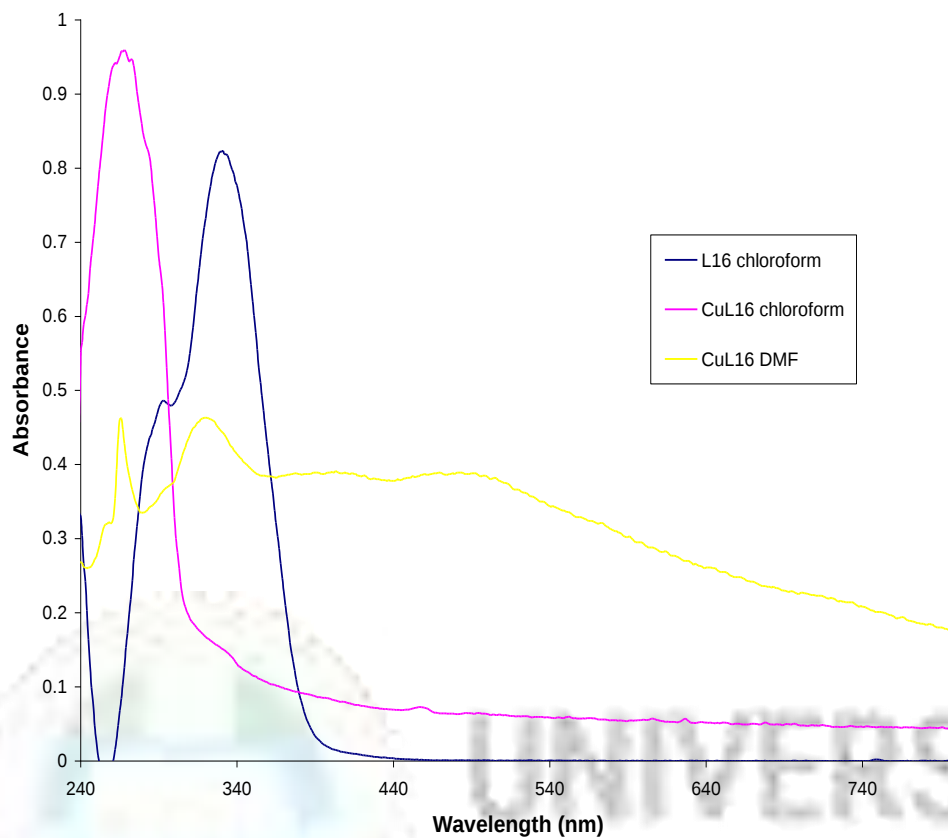


Figure 84: Electronic absorption spectra of L16 with copper metal ions in chloroform and DMF

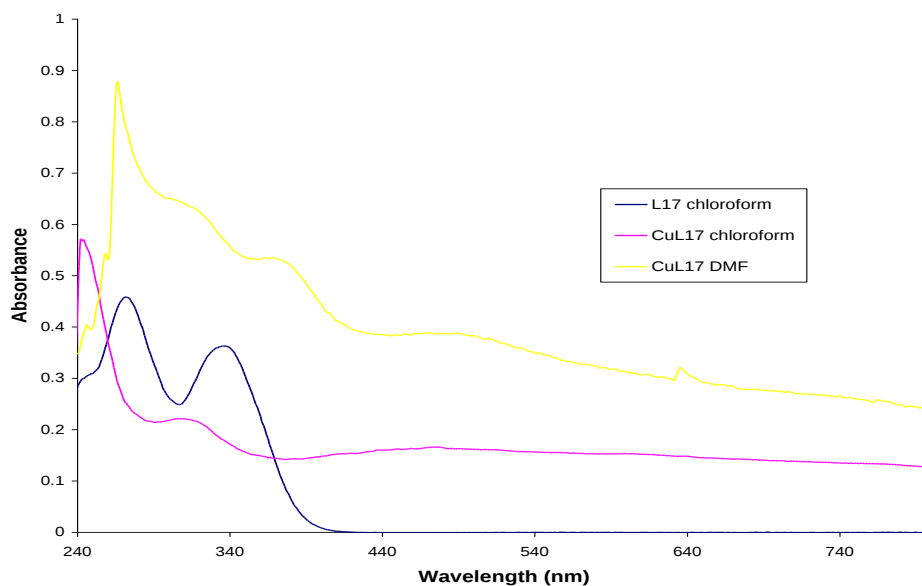


Figure 85: Electronic absorption spectra of L17 with copper metal ions in chloroform and DMF

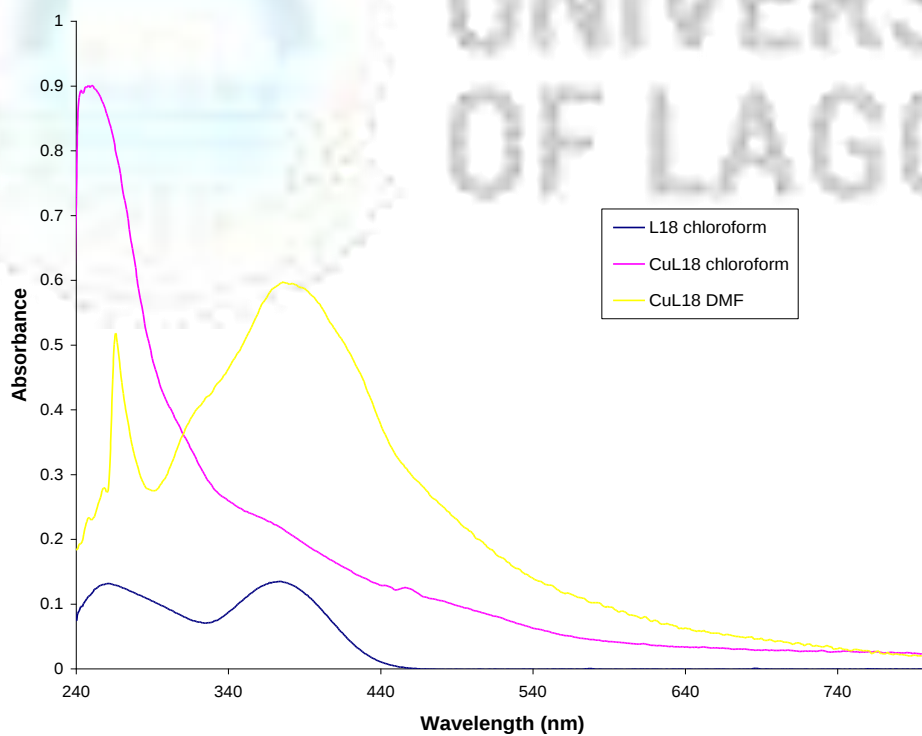


Figure 86: Electronic absorption spectra of L18 with copper metal ions in chloroform and DMF

4.4.1 Antibacterial Study

The *in-vitro* antibacterial activity of Schiff bases and metal complexes were tested against gram+ve and gram-ve bacteria. The Schiff bases and their metal complexes were tested at a concentration of 10mg/ml using the paper disc diffusion method. The growth inhibitory zones were measured in diameter (mm) and the results are summarized in Tables 18a,18b, Figure 87a, 87b (2-APH SBs and SBMCs), 19a, 19b, Figure 88a, 88b (3-APH SBs and SBMCs) and 20a, 20b, Figure 89a, 89b (4-APH SBs and SBMCs). The results of minimum inhibitory concentrations are reported in Tables 21a and 21b (2-APH SBs and SBMCs), 22a and 22b (3-APH SBs and SBMCs) and 23a and 23b (4-APH SBs and SBMCs).



Plate 1: Diameter of zones of inhibition



Plate 2: 96-micro dilution plate showing MIC

4.4.2 Diameter of Zones of Inhibition (mm) 10mg/ml in DMSO

Table 18a: Diameter of zones of inhibition (mm) of 2-aminophenol Schiff bases and metal complexes for *o*-substituents (10mg/ml). Values are mean $\pm$ SD.

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L1	OMe	H	10.0 $\pm$ 0.0	9.0 $\pm$ 0.0	7.0 $\pm$ 0.0	17.0 $\pm$ 0.0	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0
CuL1	OMe	H	14.5 $\pm$ 0.7	17.0 $\pm$ 1.4	14.0 $\pm$ 0.0	21.0 $\pm$ 1.4	19.0 $\pm$ 1.4	15.0 $\pm$ 0.0
CoL1	OMe	H	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0	8.5 $\pm$ 0.7	10.0 $\pm$ 0.0	8.0 $\pm$ 0.0	8.0 $\pm$ 0.0
L2	Cl	H	7.0 $\pm$ 0.0	7.0 $\pm$ 0.0	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	8.5 $\pm$ 0.7	8.0 $\pm$ 0.0
CuL2	Cl	H	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0	8.0 $\pm$ 0.0	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0	8.0 $\pm$ 0.0
CoL2	Cl	H	12.5 $\pm$ 0.7	13.5 $\pm$ 0.7	14.0 $\pm$ 0.0	12.5 $\pm$ 0.7	11.5 $\pm$ 0.7	12.0 $\pm$ 0.0
L3	NO ₂	H	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
CuL3	NO ₂	H	7.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	10.0 $\pm$ 1.4	0.0 $\pm$ 0.0	7.5 $\pm$ 0.7
CoL3	NO ₂	H	7.0 $\pm$ 0.0	10.5 $\pm$ 0.7	9.5 $\pm$ 0.7	8.0 $\pm$ 0.0	11.0 $\pm$ 1.4	10.0 $\pm$ 0.0
Ampicillin			13.0 $\pm$ 0.0	11.0 $\pm$ 0.2	14.0 $\pm$ 0.2	10.0 $\pm$ 0.0	9.0 $\pm$ 0.1	11.0 $\pm$ 0.1
Jik (NaOCl))			10.5 $\pm$ 0.7	8.0 $\pm$ 0.0	10.5 $\pm$ 0.7	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	11.0 $\pm$ 0.0

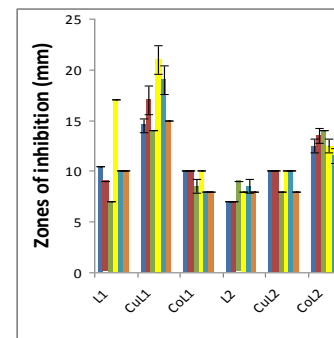


Figure 87a: Bar chart of zones of

inhibition for 2-aminophenol Schiff bases and metal complexes for *o*-substituents. Values are mean $\pm$ SD.

Table 18b: Diameter of zones of inhibition (mm) of 2-aminophenol Schiff bases and metal complexes for *p*-substituents (10mg/ml). Values are mean $\pm$ SD.

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L4	H	OMe	10.0 $\pm$ 0.0	7.0 $\pm$ 0.0	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	10.0 $\pm$ 0.0	8.0 $\pm$ 0.0
CuL4	H	OMe	12.0 $\pm$ 0.0	12.0 $\pm$ 0.0	11.0 $\pm$ 0.0	13.0 $\pm$ 0.0	15.0 $\pm$ 0.0	12.0 $\pm$ 0.0
CoL4	H	OMe	11.0 $\pm$ 0.0	12.0 $\pm$ 0.0	12.0 $\pm$ 0.0	13.0 $\pm$ 0.0	12.0 $\pm$ 0.0	10.0 $\pm$ 0.0
L5	H	Cl	10.5 $\pm$ 0.7	9.5 $\pm$ 0.7	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0	0.0 $\pm$ 0.0	11.0 $\pm$ 0.0
CuL5	H	Cl	15.5 $\pm$ 0.7	15.0 $\pm$ 0.0	17.5 $\pm$ 0.7	13.0 $\pm$ 0.0	17.0 $\pm$ 1.4	10.5 $\pm$ 0.7
CoL5	H	Cl	11.0 $\pm$ 0.0	13.0 $\pm$ 0.0	17.0 $\pm$ 0.0	11.5 $\pm$ 0.7	12.0 $\pm$ 0.0	11.0 $\pm$ 0.0
L6	H	NO ₂	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	16.0 $\pm$ 0.0	13.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
CuL6	H	NO ₂	11.0 $\pm$ 0.0	12.0 $\pm$ 0.0	0.0 $\pm$ 0.0	12.0 $\pm$ 0.0	9.5 $\pm$ 0.7	0.0 $\pm$ 0.0
CoL6	H	NO ₂	11.0 $\pm$ 0.0	11.0 $\pm$ 0.0	12.0 $\pm$ 1.4	9.5 $\pm$ 1.4	10.5 $\pm$ 0.7	11.0 $\pm$ 0.0
Ampicillin			13.0 $\pm$ 0.0	11.0 $\pm$ 0.2	14.0 $\pm$ 0.2	10.0 $\pm$ 0.0	9.0 $\pm$ 0.1	11.0 $\pm$ 0.1
Jik (NaOCl))			10.5 $\pm$ 0.7	8.0 $\pm$ 0.0	10.5 $\pm$ 0.7	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	11.0 $\pm$ 0.0

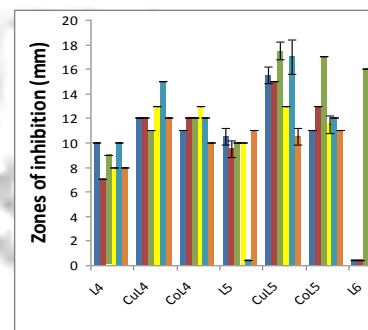


Figure 87b: Bar chart of zones of inhibition for

2-aminophenol Schiff bases and metal complexes for *p*-substituents. Values are mean $\pm$ SD.

Table 19a: Diameter of zones of inhibition (mm) of 3-aminophenol Schiff bases and metal complexes for *o*-substituents (10mg/ml). Values are mean $\pm$ SD.

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L7	OMe	H	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
CuL7	OMe	H	8.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
L8	Cl	H	10.5 $\pm$ 0.7	8.5 $\pm$ 0.7	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0	11.0 $\pm$ 0.0	10.0 $\pm$ 0.0
CuL8	Cl	H	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	8.0 $\pm$ 0.0	10.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
L9	NO ₂	H	0.0 $\pm$ 0.0	8.0 $\pm$ 0.0	8.0 $\pm$ 0.0	8.5 $\pm$ 0.7	7.5 $\pm$ 0.7	10.0 $\pm$ 0.0
CuL9	NO ₂	H	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Ampicillin			13.0 $\pm$ 0.0	11.0 $\pm$ 0.2	14.0 $\pm$ 0.2	10.0 $\pm$ 0.0	9.0 $\pm$ 0.1	11.0 $\pm$ 0.1
Jik(NaOCl))			10.5 $\pm$ 0.7	8.0 $\pm$ 0.0	10.5 $\pm$ 0.7	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	11.0 $\pm$ 0.0

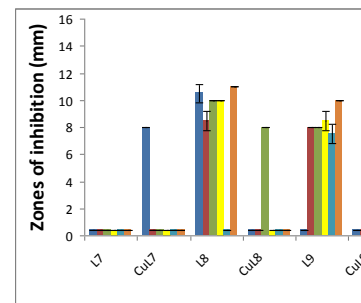


Figure 88a: Bar chart of zones of inhibition for 3-

aminophenol Schiff bases and metal complexes

o-substituents. Values are mean $\pm$ SD.

for

Table 19b: Diameter of zones of inhibition (mm) of 3-aminophenol Schiff bases and metal complexes for *p*-substituents (10mg/ml). Values are mean $\pm$ SD.

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L10	H	OMe	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	15.0 $\pm$ 0.0	10.0 $\pm$ 0.0	15.0 $\pm$ 0.0
CuL10	H	OMe	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
L11	H	Cl	11.0 $\pm$ 1.4	12.5 $\pm$ 0.7	12.0 $\pm$ 0.0	12.0 $\pm$ 0.0	0.0 $\pm$ 0.0	8.5 $\pm$ 0.7
CuL11	H	Cl	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
L12	H	NO ₂	0.0 $\pm$ 0.0	7.5 $\pm$ 0.7	10.0 $\pm$ 0.0	11.5 $\pm$ 0.7	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0
CuL12	H	NO ₂	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Ampicillin			13.0 $\pm$ 0.0	11.0 $\pm$ 0.2	14.0 $\pm$ 0.2	10.0 $\pm$ 0.0	9.0 $\pm$ 0.1	11.0 $\pm$ 0.1
Jik (NaOCl)			10.5 $\pm$ 0.7	8.0 $\pm$ 0.0	10.5 $\pm$ 0.7	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	11.0 $\pm$ 0.0

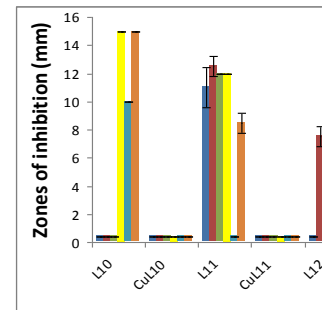


Figure 88b: Bar chart of zones of inhibition for 3-

aminophenol Schiff bases and metal complexes

for *p*-substituents. Values are mean $\pm$ SD.

Table 20a: Diameter of zones of inhibition (mm) of 4-aminophenol Schiff bases and metal complexes for *o*-substituents (10mg/ml). Values are mean $\pm$ SD.

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L13	OMe	H	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
CuL13	OMe	H	13.0 $\pm$ 0.0	9.5 $\pm$ 0.7	12.0 $\pm$ 0.0	0.0 $\pm$ 0.0	12.0 $\pm$ 0.0	0.0 $\pm$ 0.0
L14	Cl	H	10.5 $\pm$ 0.7	10.0 $\pm$ 0.0	12.0 $\pm$ 0.0	12.0 $\pm$ 0.0	0.0 $\pm$ 0.0	8.5 $\pm$ 0.7
CuL14	Cl	H	13.0 $\pm$ 0.0	10.0 $\pm$ 0.0	0.0 $\pm$ 0.0	15.0 $\pm$ 0.0	11.0 $\pm$ 0.0	0.0 $\pm$ 0.0
L15	NO ₂	H	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	15.0 $\pm$ 0.0	15.0 $\pm$ 0.0
CuL15	NO ₂	H	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0	10.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Ampicillin			13.0 $\pm$ 0.0	11.0 $\pm$ 0.2	14.0 $\pm$ 0.2	10.0 $\pm$ 0.0	9.0 $\pm$ 0.1	11.0 $\pm$ 0.1
Jik(NaOCl)			10.5 $\pm$ 0.7	8.0 $\pm$ 0.0	10.5 $\pm$ 0.7	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	11.0 $\pm$ 0.0

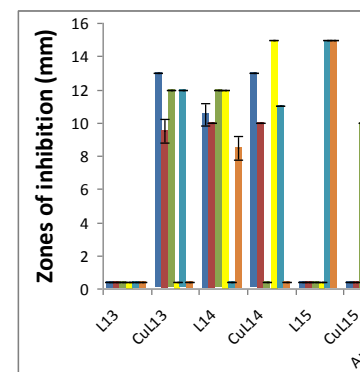


Figure 89a:

aminophenol

for o-

Bar chart of zones of inhibition for 4-

Schiff bases and metal complexes

substituents. Values are mean $\pm$ SD.

Table 20b: Diameter of zones of inhibition (mm) of 4-aminophenol Schiff bases and metal

complexes for *p*-substituents (10mg/ml). Values are mean $\pm$ SD.

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumon</i> <i>ia</i> (ATCC 10031)
L16	H	OMe	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
CuL16	H	OMe	13.0 $\pm$ 0.0	0.0 $\pm$ 0.0	7.0 $\pm$ 0.0	10.0 $\pm$ 0.0	10.5 $\pm$ 0.7	0.0 $\pm$ 0.0
L17	H	Cl	0.0 $\pm$ 0.0	8.0 $\pm$ 0.0	0.0 $\pm$ 0.0	9.0 $\pm$ 0.0	10.0 $\pm$ 0.7	10.0 $\pm$ 0.0
CuL17	H	Cl	10.0 $\pm$ 0.0	11.0 $\pm$ 0.0	0.0 $\pm$ 0.0	11.0 $\pm$ 0.0	10.0 $\pm$ 0.0	0.0 $\pm$ 0.0
L18	H	NO ₂	8.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0
CuL18	H	NO ₂	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	0.0 $\pm$ 0.0	11.0 $\pm$ 0.0	10.0 $\pm$ 0.0	0.0 $\pm$ 0.0
Ampicillin			13.0 $\pm$ 0.0	11.0 $\pm$ 0.2	14.0 $\pm$ 0.2	10.0 $\pm$ 0.0	9.0 $\pm$ 0.1	11.0 $\pm$ 0.1
Jik (NaOCl)			10.5 $\pm$ 0.7	8.0 $\pm$ 0.0	10.5 $\pm$ 0.7	9.0 $\pm$ 0.0	8.0 $\pm$ 0.0	11.0 $\pm$ 0.0

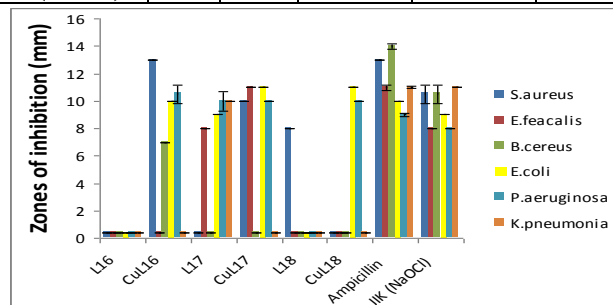


Figure 89b: Bar chart of zones of inhibition for 4-complexes for *p*- substituents. Values are mean $\pm$ SD.

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)
CuL7	OMe	H	5.00	5.00	5.00
CuL7	OMe	H	2.50	2.50	2.50
CuL8	Cl	H	2.50	2.50	2.50
L9	NO ₂	H	2.50	2.50	2.50
CuL9	NO ₂	H	2.50	2.50	2.50
Ampicillin			2.50	5.00	5.00

aminophenol Schiff bases and metal

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L1	OMe	H	2.50	2.50	2.50	1.25	1.25	1.25
CuL1	OMe	H	0.62	1.25	0.62	1.25	1.25	0.62
CoL1	OMe	H	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
L2	Cl	H	2.50	2.50	5.00	2.50	2.50	2.50
CuL2	Cl	H	0.62	0.62	2.50	1.25	0.62	0.62
CoL2	Cl	H	0.62	1.25	0.62	1.25	1.25	0.62
L3	NO ₂	H	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
CuL3	NO ₂	H	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
CoL3	NO ₂	H	1.25	1.25	0.62	2.50	1.25	1.25
Ampicillin			2.50	5.00	5.00	1.25	5.00	2.50

o-substituents
Schiff

bases and metal complexes for *o*-substituents

4.4.3 Minimum Inhibitory Concentration (mg/ml)

Table 21a: Minimum inhibitory concentration (MIC) for 2-aminophenol Schiff bases and metal complexes for

Table 22a: Minimum inhibitory concentration for 3-aminophenol

Table 21b: Minimum inhibitory concentration (MIC) for 2-aminophenol Schiff bases and metal complexes for *p*-substituents

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
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L4	H	OMe	5.00	2.50	2.50	1.25	2.50	1.25
CuL4	H	OMe	0.62	0.62	0.62	0.62	0.62	0.62
CoL4	H	OMe	0.31	0.62	0.31	0.62	0.62	0.31
L5	H	Cl	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
CuL5	H	Cl	0.15	0.31	1.25	1.25	0.31	0.15
CoL5	H	Cl	0.62	1.25	0.62	1.25	1.25	0.62
L6	H	NO ₂	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
CuL6	H	NO ₂	2.50	2.50	2.50	2.50	2.50	2.50
CoL6	H	NO ₂	0.62	2.50	1.25	1.25	1.25	0.62
Ampicillin			2.50	5.00	5.00	1.25	5.00	2.50

Table 22b: Minimum inhibitory concentration (MIC) for 3-aminophenol Schiff bases and metal complexes for *p*-substituents

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.(A</i> 8'
L10	H	OMe	>5.00	>5.00	>5.00	>
CuL10	H	OMe	2.50	2.50	2.50	.
L11	H	Cl	1.25	1.25	1.25	.
CuL11	H	Cl	2.50	2.50	2.50	.
L12	H	NO ₂	1.25	1.25	2.50	.
CuL12	H	NO ₂	2.50	2.50	2.50	.
Ampicillin			2.50	5.00	5.00	.



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Table 23a: Minimum inhibitory concentration (MIC) (mg/ml) of *o*-substituted 4-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L13	OMe	H	>5.00	2.50	>5.00	2.50	>5.00	>5.00
CuL13	OMe	H	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
L14	Cl	H	>5.00	>5.00	5.00	5.00	>5.00	>5.00
CuL14	Cl	H	1.25	1.25	2.50	5.00	1.25	1.25
L15	NO ₂	H	1.25	1.25	0.62	5.00	1.25	1.25
CuL15	NO ₂	H	2.50	2.50	2.50	2.50	2.50	2.50
Ampicillin			2.50	5.00	5.00	1.25	5.00	2.50

Table 23b: Minimum inhibitory concentration (MIC) (mg/ml) of *p*-substituted 4-aminophenol Schiff bases and metal complexes

Compound	R ₁	R ₂	<i>S.aureus</i> (ATCC 6538)	<i>E.feacalis</i> (ATCC 29212)	<i>B.cereus</i> (ATCC 10702)	<i>E.coli</i> (ATCC 8739)	<i>P.aeruginosa</i> (ATCC 19582)	<i>K.pneumonia</i> (ATCC 10031)
L16	H	OMe	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
CuL16	H	OMe	2.50	2.50	2.50	5.00	2.50	2.50
L17	H	Cl	2.50	2.50	2.50	2.50	2.50	0.62
CuL17	H	Cl	1.25	1.25	1.25	1.25	1.25	1.25
L18	H	NO ₂	>5.00	>5.00	>5.00	>5.00	>5.00	>5.00
CuL18	H	NO ₂	1.25	2.50	1.25	2.50	1.25	1.25
Ampicillin			2.50	5.00	5.00	1.25	5.00	2.50

CHAPTER FIVE

5.0 DISCUSSION OF RESULTS

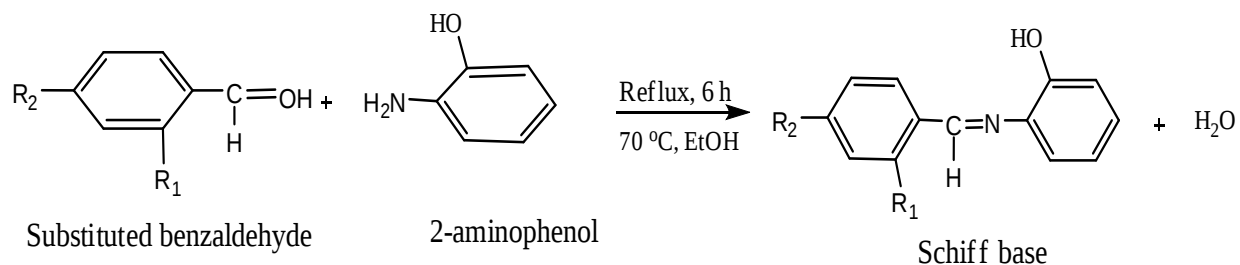
The discussion will focus on the synthesis of 2-, 3- and 4-aminophenol Schiff bases and metal complexes, their characterization using micro analysis, infrared spectroscopy, ^1H NMR spectroscopy, electronic absorption spectroscopy, atomic absorption spectroscopy, magnetic moments measurements, thermal gravimetry analysis and differential scanning calorimetry. Antibacterial studies of the synthesized compounds would also be discussed in relationship to effect and position of substituents groups attached to the compounds.

5.1 Synthesis of 2-aminophenol Schiff Bases and Metal Complexes

Schiff bases (**L1-L6**) were synthesized by condensation of equimolar quantities of 2-aminophenol with methoxy, chloro and nitro substituted benzaldehydes in ethanol (Scheme 24). Three of the compounds (**L1-L3**) had the substituents in *o*-position and the other three in *p*-position (**L4-L6**). The synthesized Schiff bases were recrystallized from ethanol. The reaction afforded stable products.

Table 24: Schiff bases (L1-L6) with different substituents at *o*- and *p*-position

Ligand	R ₁	R ₂
L1	OMe	H
L2	Cl	H
L3	NO ₂	H
L4	H	OMe
L5	H	Cl
L6	H	NO ₂

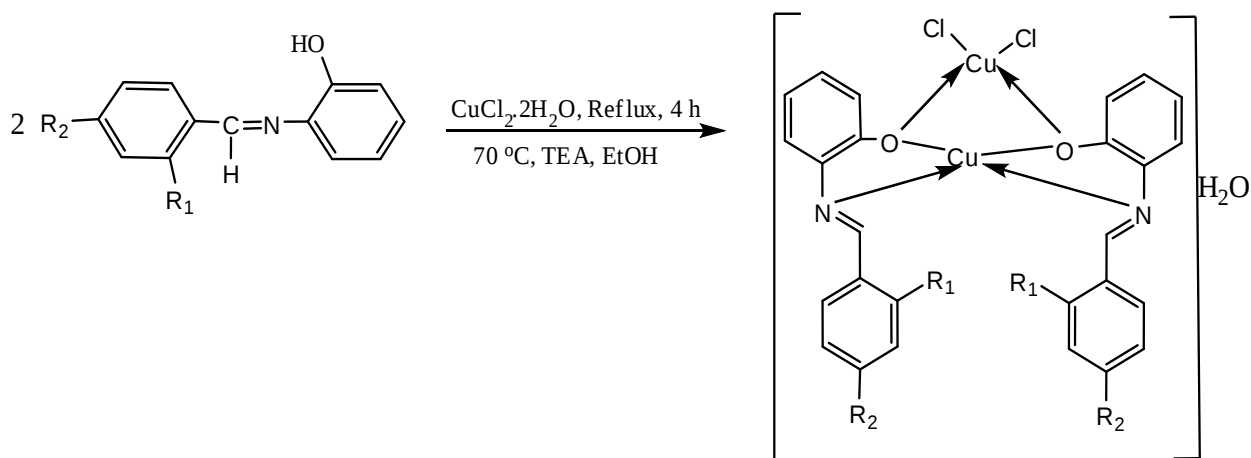


Scheme 24: Synthesis of 2-aminophenol Schiff bases (L1-L6)

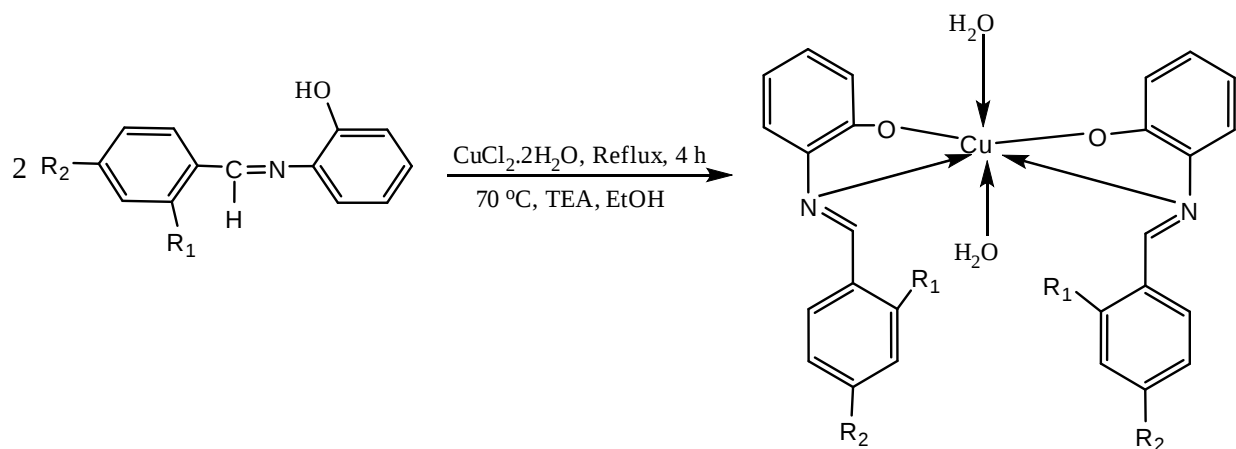
The copper complexes (**CuL1-CuL6**) and cobalt complexes (**CoL1-CoL6**) were obtained by reacting the Schiff bases and metal salts in ratio 2:1 (Scheme 25-30). The reaction afforded stable compounds. The complexes were relatively soluble in common organic solvents and were purified by washing with ethanol to remove traces of unreacted starting materials.

Table 25: Schiff base copper(II) complexes with different substituents at *o*- and *p*-positions

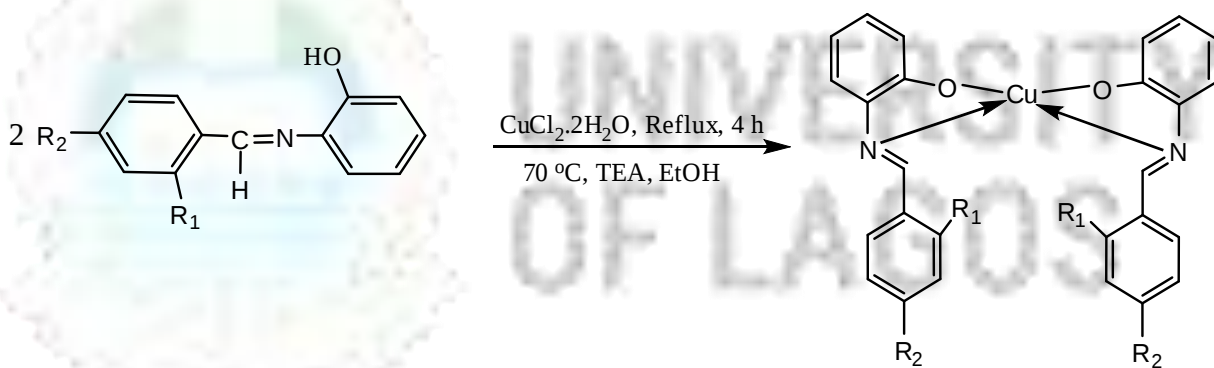
SBMC	R ₁	R ₂
CuL1	OMe	H
CuL2	Cl	H
CuL3	NO ₂	H
CuL4	H	OMe
CuL5	H	Cl
CuL6	H	NO ₂



Scheme 25: Synthesis of 2-aminophenol SB copper complexes (CuL1, CuL2, CuL4, CuL5)



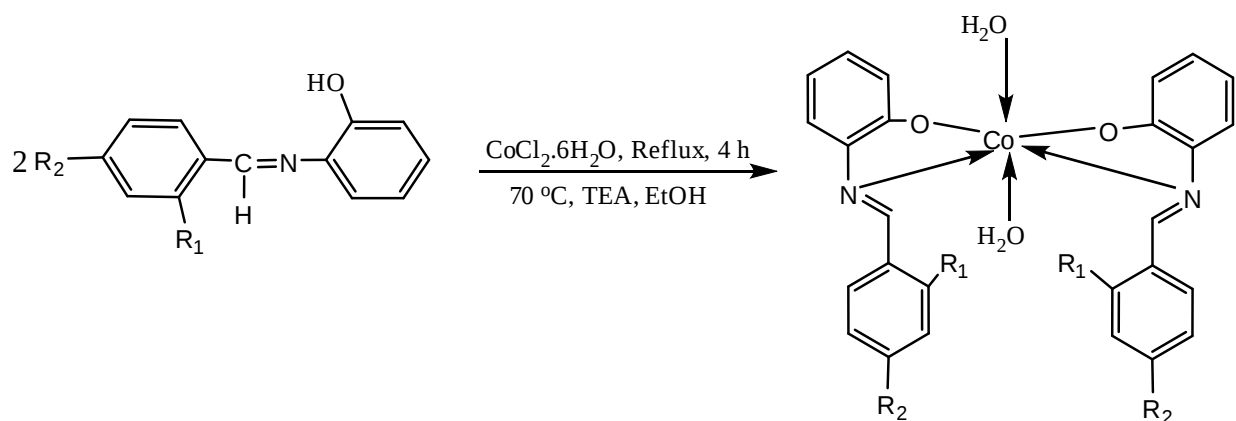
Scheme 26: Synthesis of 2-aminophenol SB copper complex (CuL3)



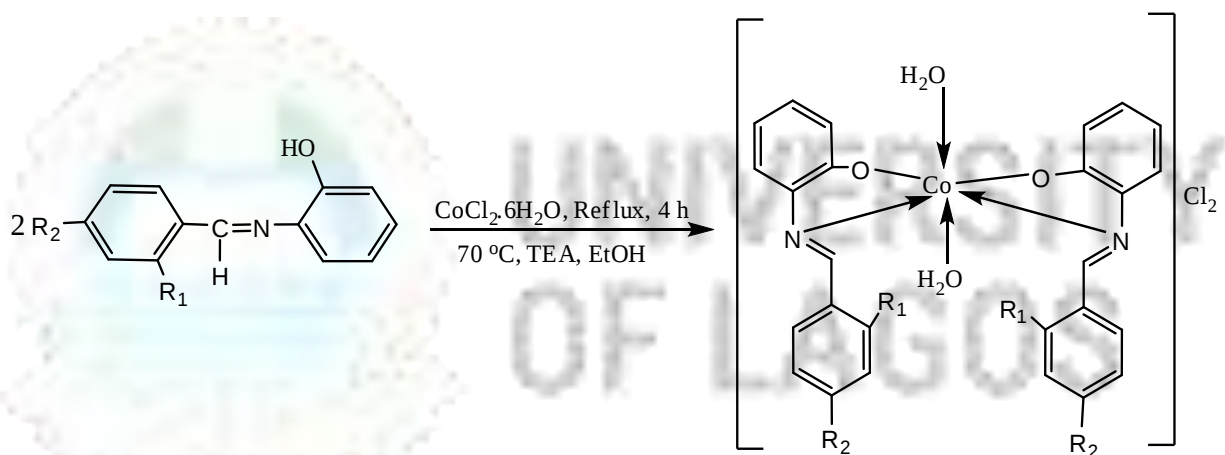
Scheme 27: Synthesis of 2-aminophenol SB copper complex (CuL6)

Table 26: Schiff base cobalt(II) complexes with different substituents at *o*- and *p*-position

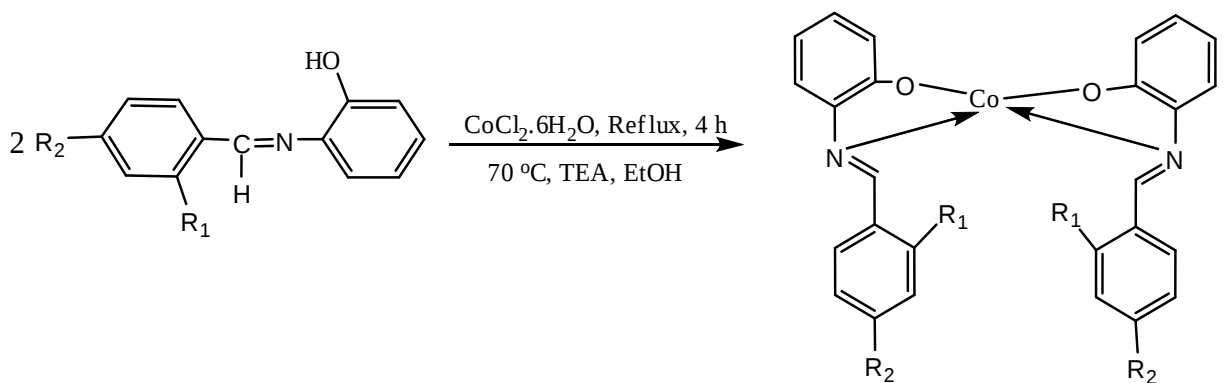
SBMC	R_1	R_2
CoL1	OMe	H
CoL2	Cl	H
CoL3	NO_2	H
CoL4	H	OMe
CoL5	H	Cl
CoL6	H	NO_2



Scheme 28: Synthesis of 2-aminophenol SB cobalt complexes (CoL1, CoL2, CoL3, CoL5)



Scheme 29: Synthesis of 2-aminophenol SB cobalt complex (CoL4)



Scheme 30: Synthesis of 2-aminophenol SB cobalt complex (CoL6)

5.1.1 Physical and Analytical Data of 2-aminophenol Schiff Bases and Metal Complexes

The melting points of *o*-substituted Schiff bases (Table 5a) varied in the order $\text{Cl} < \text{NO}_2 < \text{OMe}$ while the metal complexes decomposed above 250 °C. The yield obtained ranges between 58-72 % for Schiff base ligands L1-L3 and 40-61 % for Schiff base metal complexes CuL1-CuL3, CoL1-CoL3. For the *p*-substituted compounds (Table 5b), the melting points of the Schiff bases follow the order $\text{NO}_2 > \text{Cl} > \text{OMe}$ while the metal complexes decomposed above 250 °C. The yield obtained ranges between 63-77 % for Schiff base ligands L4-L6 and 52-87 % for Schiff base metal complexes CuL4-CuL6 and CoL4-CoL6. The electronic effect and position of substituents groups on aromatic ring influences the reactivity, stability and properties of the compounds (Bu *et al.*, 1997). The yield of 2-aminophenol ligands and its complexes follow the order $\text{NO}_2 > \text{OMe} > \text{Cl}$. These were observed for the *o*- and *p*-substituted compounds in (Tables 5a and 5b). Resonance stability may have led to greater yield of NO_2 and OMe substituted compounds. In considering the position of the substituent groups, the order of $p > o$ was observed. This order can be attributed to absence of steric effects in *p*-substituted compounds.

The Schiff bases and metal complexes were subjected to micro analysis to confirm the purity of synthesized compounds. The results of micro analysis (C, H, N) were in agreement with the molecular formula. The metal content analysis of the complexes reveal the percentage metal ion per mole of complex. Copper(II) complexes of 2-aminophenol Schiff base with OMe and Cl substituents (bis(2-(2-methoxybenzylideneamino)phenol)copper(II), **CuL1**, bis(2-(2-chlorobenzylideneamino)phenol)copper(II), **CuL2**, bis(2-(4-methoxybenzylideneamino)phenol)copper(II) **CuL4**, bis(2-(4-chlorobenzylideneamino)phenol)copper(II), **CuL5**) contained 2 moles of copper per mole of the complex while other complexes had one mole of metal ion per mole of the complex. These complexes with increased metal content can be explained on the basis of its

ligands having the OH (2-aminophenol) close to the imine group, enhancing chelation. Complexes of the form $\text{Cu}_2\text{Cl}_2(\text{L})_2$ containing 2 moles of copper per mole of complex has been reported from 2-acetylpyridine and s-benzylthiocarbamate with polar substituents (s-4-methoxybenzyl and s-4-fluorobenzyl) (Beshir *et al.*, 2008).

5.1.2 Spectroscopic data of 2-aminophenol Schiff bases and metal complexes

The IR spectra of the Schiff bases (Tables 6a and 6b) reveal bands in the region $1625\text{-}1556\text{ cm}^{-1}$ attributed to the C=N bond. In order to determine the bonding mode of Schiff base to the metal ion, the IR spectra of the Schiff bases were compared with those of the corresponding metal complex. Since metal-ligand complexation involves the use of lone pairs of electrons, functional groups of interest are those containing hetero atoms in the ligand. These groups are expected to be involved in complexation and therefore the position of bands for the functional groups will vary in metal and ligand. New peaks are also guided peaks as well as water in chelation.

In the spectra of the SB and SBMC, a shift in IR band ($1625\text{-}1596\text{ cm}^{-1}$) o-methoxy-substituted compounds, ($1616\text{-}1570\text{ cm}^{-1}$) o-chloro-substituted compounds, ($1626\text{-}1556\text{ cm}^{-1}$) o-nitro-substituted compounds indicates coordination of azomethine nitrogen to metal ion (Agarwal *et al.*, 1999, Nishat *et al.*, 2010). This trend was also observed in p-substituted compounds; ($1618\text{-}1593\text{ cm}^{-1}$), ($1601\text{-}1577\text{ cm}^{-1}$), ($1623\text{-}1595\text{ cm}^{-1}$). The presence of OMe and NO_2 groups increased IR stretching frequency for (C=N) while Cl group decreased the IR stretching frequency. These may be attributed to electronic effects (resonance effects in OMe, NO_2 and inductive effects in Cl) (Abd El-Wahab *et al.*, 2004). This effect follows the order $o > p$. A comparison between spectra of SB and SBMC also show a band characteristic of $\nu(\text{C-O})$ 1284 cm^{-1} , 1270 cm^{-1} , 1269 cm^{-1} in o-OMe, Cl, NO_2 substituted Schiff bases and 1271 cm^{-1} ,

1250 cm^{-1} , 1250 cm^{-1} in SBMC respectively due to C-O-M formation (Nishat *et al.*, 2010). A shift to lower wavenumber due to coordination of metal ion to hydroxyl oxygen in *p*-substituted compounds reveal peaks in the spectra at 1245-1178 cm^{-1} , 1238-1212 cm^{-1} and 1299-1274 cm^{-1} for OMe, Cl and NO_2 substituted compounds respectively. The presence of coordinated water is indicated by a broad band in the region 3307-3441 cm^{-1} (Patil *et al.*, 2011). The new bands in the spectra of metal complexes 418-485 cm^{-1} and 529-594 cm^{-1} is assigned to stretching frequencies of $\nu(\text{M-N})$ and $\nu(\text{M-O})$ bond formation (Jouad *et al.*, 2001, Nishat *et al.*, 2010).

5.1.3 ^1H NMR Data of 2-aminophenol Schiff Bases

The formation of Schiff base was confirmed by spectroscopic data. The ^1H NMR of all Schiff bases exhibits a singlet in the region 7.89-8.26 δ . This based on previous reports is attributed to the imine proton (Raman *et al.*, 2010, Mounika *et al.*, 2010). The signal vary with nature and substituent position. Schiff bases with electron donating groups (OMe) appear upfield (lower chemical shift) due to increase in the electron density in the vicinity of the proton which causes shielding from the magnetic field while SBs with electron withdrawing groups (Cl, NO_2) appear at a lower field (higher chemical shift) as a result of low electron density in the vicinity of the proton. These effects were evident in the synthesized Schiff bases. Schiff bases with **OMe, Cl and NO_2** substituted in *o*-position (Table 7a) showed singlet at 8.17, 8.26 and 8.25 δ (s, 1H, CH=N) due to azomethine protons. These trend were also observed for *p*-substituted ligands (Table 7b); 7.89, 7.98, 8.37 δ . These effects and trends were also exhibited in the phenolic -OH, (9.17, 9.21, 9.15 δ) for *o*-substituted SBs, (8.63, 8.65, 8.77 δ) for *p*-substituted SBs. The three protons of OCH_3 groups for *o*- and *p*-substituted SBs resonated in the region 3.93 and 3.91 δ

respectively as expected. The aromatic protons showed signal in the region 6.88-8.07 δ (Nishat *et al.*, 2010). This follows the order $o > p$.

5.1.4 Electronic Absorption Data and Magnetic Moment Measurement of 2-aminophenol Schiff Bases and Metal Complexes

The electronic absorption spectra of Schiff bases and their metal complexes were recorded at room temperature using chloroform and DMF as solvents. The electronic spectra measurements were used in assigning the stereochemistries of the metal ions in the complexes based on the position of $d-d$ transition peaks. The Schiff bases exhibited two absorption bands; a high energy band attributed to $\pi \rightarrow \pi^*$ transitions of the aromatic rings and a lower energy band due to $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the nitrogen of the azomethine group (Issa *et al.*, 2005, Tuna *et al.*, 2006). The absorption spectra of 2-aminophenol SBs features an intense band system with maxima at 35,842-36,630 cm^{-1} and 27,777-28,100 cm^{-1} attributed to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ for o -substituted SBs (Table 8a). In the p -substituted ligands (Table 8b), absorption bands were observed in the region 34,482-36,496 cm^{-1} and 27,567-28,169 cm^{-1} due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$. A shift to longer wavelength (lower energy) is usually observed for imine group with electron withdrawing substituents while electron donating substituents cause shift to shorter wavelength (higher energy) (Bottcher *et al.*, 1997). Substitution of chloro and nitro groups in o - and p -positions in SBs shifts the bands to longer wavelength (28,571, 28,100 cm^{-1} and 28,168, 27,839 cm^{-1}), the opposite is true for methoxy substituted SBs (27,777 cm^{-1} and 27,567 cm^{-1}) for o - and p -substituted positions. The effect on the position of substituent groups follows the order $o > p$. In the metal complexes, imine transitions shifted to longer wavelength due to $d-d$ transitions and charge transfer transitions confirming the coordination of SB to metal ion (Abd El-Wahab, 2007, Lever, 1984). The metal complexes exhibited different absorption bands in

solvents of different polarities. A pronounced change in position of a UV-vis absorption band is associated with increasing solvent polarity, which usually lead to bathochromic (red) shift while the corresponding is called a hypsochromic (blue) shift (Reichardt, 2003, Hemmateenejad *et al.*, 2012). The effect of solvents (chloroform and DMF) on the SBMCs lead to bands of different wavelengths and intensities. Electronic absorption spectra of Schiff base metal complexes in chloroform shows hypsochromic shift, while in DMF bathochromic shift is observed. The spectra of Cu(II) complexes in DMF for methoxy and chloro substituted *o*- and *p*- complexes (**CuL1 Figure 36**, **CuL2 Figure 37**, **CuL4 Figure 39**, **CuL5 Figure 40**) showed broad bands centered at 22,988 cm⁻¹, 22,799 cm⁻¹, 22,988 cm⁻¹, 22,883 cm⁻¹, which could be attributed to the ²A_{1g}(F) → ²B_{1g}(P) transitions characterized Cu(II) ion in a square-planar geometry (Al-Sha'alan, 2007, Nishat *et al.*, 2010). The shift of the absorption band to lower energy than that expected for the square planar complexes may be due to the distortion of the square-planar geometry towards tetrahedral (Gruber *et al.*, 1968, Al-Sha'alan, 2007). The room temperature magnetic moments values of 1.52, 1.60, 1.56, 1.52 BM for the complexes, indicates that, as expected, magnetic exchange occurs between the two copper ions which may have led to lower values than expected (1.7-2.2 BM) (Lever, 1984). On the basis of the magnetic data, the copper(II) complexes probably has a binuclear structure (Sonmez and Sekerci, 2007, Karabocek *et al.*, 2007). The square-planar geometry of these complexes is further confirmed by the measured magnetic moment values (Gruber *et al.*, 1968, Lever, 1984, Al-Sha'alan, 2007). The *o*- and *p*-substituted nitro copper(II) complexes (**CuL3 Figure 38**, **CuL6 Figure 41**) exhibited two absorption bands. The bands around 31,250-22,727 cm⁻¹ and 30,088-22,988 cm⁻¹ is due to charge transfer and ²B_{1g} → ²B_{2g} transitions in a tetrahedral field (Lakshmi *et al.*, 2011). The cobalt(II) complexes with substituents at *o*-position exhibited two distinct bands at 22,471-23,255 cm⁻¹ and 30,030-

31,250 cm⁻¹ due to ${}^4A_{2g}(F) \leftarrow {}^4T_{1g}(F)$ and ${}^4T_{1g}(P) \leftarrow {}^4T_{1g}(F)$ transitions usually observed in octahedral complexes.

Octahedral, tetrahedral and square-planar cobalt(II) complexes show magnetic moments between 4.7-5.2, 4.2-4.8 and 2.2-2.9 BM respectively (Lever, 1984, Al-Sha'alan, 2007). The magnetic moment of Co(II) complexes were seen at 5.46, 5.29 and 5.32 BM within the expected range of 4.7-5.2 BM for high spin octahedral complexes (Fetoh *et al.*, 2000, Mounika *et al.*, 2010). A similar trend (exception CoL6 assigned ${}^4A_2 \rightarrow {}^4T_1(F)$ and ${}^4A_2 \rightarrow {}^4T_1(P)$ transitions in tetrahedral complexes (West, 1962) was observed for the corresponding Co(II) complexes with substituents at *p*-position. The observed magnetic moment value for **CoL6** is 4.28, which is characteristic of mononuclear tetrahedral complexes (Aboaly and Khalil, 2001, Tuna *et al.*, 2006).

5.1.5 Thermal Analysis Study of 2-aminophenol Schiff Base Metal Complexes

Thermal analysis plays an important role in studying the thermal stability and decomposition path way of the compound. The thermal decompositions were studied using TG-technique. During the heating of the SBMCs, the complexes underwent a series of thermal changes associated with a weight loss of the compound. Analysis of the obtained TG-curves is given in (Tables 9a and 9b) and the correlations between the different decomposition steps of the complexes with the corresponding weight losses are discussed in terms of the proposed formulae of the complexes. Figures 45a, 45b-48a, 48b is a representative spectra for thermal analysis of SBMCs under study.

All the complexes lost adsorbed water except **CoL4** and **CoL6** which lost an organic moiety at an equivalent range before the final decomposition for all the complexes. The data from the thermogravimetric analysis indicates that the decomposition of the complexes proceeds in four

steps except **CoL1** which exhibited six decomposition steps. The final decomposition products were metal oxides formed above 700 °C except **CuL6** which decomposed above 500 °C.

The thermogram of **CuL1** representing *o*-substituted complex shows four decomposition steps within the temperature range 71-786 °C. The first step of decomposition within the temperature range 71-227 °C corresponds to the loss of water molecules with a mass loss of 2.83 % (calcd. 3.12 %). The onset of decomposition of the complex occurred at 295-343 °C due to initial loss of an organic moiety (C₁₃H₉NCl) from the aromatic ring with a mass loss 34.68 % (calcd. 34.98 %). Before the process of decomposition is completed, a second moiety C₁₅H₁₃NCl starts to dissociate at 361-504 °C with a mass loss of 25.64 % (calcd. 26.06 %). The complete decomposition of Schiff base metal complex occurred at 504 °C leaving a residue that corresponds to copper oxide. A similar TGA curve was observed for **CuL2** and **CuL3**. The thermogram shows four stages of decomposition within the temperature range 70-220 °C corresponds to the loss of water molecule, while the second and third stages involve the loss of organic moieties and finally the residue as copper oxide.

The cobalt complexes also exhibited mass loss corresponding to the formula suggested from the analytical data. The TGA curve of **CoL1** for *o*-substituted complex gave six decomposition steps as illustrated in **Figure 44**. The first step of decomposition corresponds to the loss of water molecules within the temperature range 85-236 °C (mass loss 2.90 %; calcd. 3.29 %).

The second, third, fourth and fifth steps of decomposition within the temperature range of 270-313 °C, 340-480 °C, 510-560 °C and 590-789 °C correspond to removal of the ligand moieties C₂H₄N (mass loss 8.11 %; calcd. 7.67 %), C₆H₄ (mass loss 13.90 %; calcd. 13.89 %), C₂H₅ (mass loss 5.07 %; calcd. 5.30 %) and C₁₃H₉N (mass loss 49.44 %; calcd. 49.36 %) respectively leaving CoO as a residue. The **CoL2** and **CoL3** complexes were stable up to 76 °C and 70 °C

after which their decomposition started and was completed at 898 °C. The cobalt complexes decomposed and produce CoO as their residue in four steps in the temperature range 76-218, 238-429, 455-631, 680-897 °C and 70-221, 238-356, 385-627, 637-797 °C corresponding to the loss of H₂O, C₁₃H₉NCl, C₆H₇, C₆H₅ and H₂O, C₁₂H₉N, C₆H₅N, C₅H₄ respectively.

The thermoanalytical data of copper and cobalt complexes with substituent at *p*-position shows four steps of mass losses at temperature range from 68-900 °C. The results of thermal decomposition of **CuL4** **Figure 46** shows the first three steps of decomposition within the temperature range 68-481 °C in which loss of water molecule, C₁₅H₁₂N and C₁₃H₁₀N occur with an estimated mass loss of 58.85 % (calcd. 59.25 %). These steps were accompanied by endothermic peak at 324 °C and exothermic peak at 337 °C in the DSC curve **Figure 47**.

The cobalt(II) complex **CoL4** exhibited four decomposition steps within the temperature range 77- 810 °C in which decomposition of the organic ligand occurred, leaving metal oxides as residue with total mass loss of 98.64 % (calcd. 98.74 %). These were confirmed by the presence of endothermic peak at 317 °C and exothermic peak at 330 °C.

The TGA curve of copper(II) (**CuL5**, **CuL6**) and cobalt(II) (**CoL5**, **CoL6**) complexes decomposed within the temperature range of 68-900 °C correspond to loss of water, organic moiety and metal oxides. In all steps, decomposition occurred and residues of metal oxides were left. This is further confirmed from the endothermic and exothermic peaks through all stages of decomposition.

Thermal decomposition of the complexes show good agreement with the formula suggested from the analytical data. The temperature of maximum rate of decomposition of the metal complexes were high, these suggest that the metal complexes have high thermal stability due to chelation

(Nishat *et al.*, 2010). The effect of substituent and its positions were not affected in the decomposition steps.

5.1.6 Antibacterial Activity of 2-aminophenol Schiff Bases and Metal Complexes

The antibacterial activity of 2-aminophenol Schiff bases and their metal complexes are related to the nature and position of substituent groups. Structure activity-relationship of Schiff bases of 2-aminophenol derivatives were studied in relation to nature and position of substituent groups. The Schiff bases **L1-L6** and their metal complexes **CuL1-CuL6**, **CoL1-CoL6** were tested against six human pathogenic bacteria; *Escherichia coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538), *Pseudomonas aeruginosa* (ATCC 19582), *Bacillus cereus* (10702), *Enterococcus faecalis* (ATCC 29212) and *Klebsiella pneumoniae* (ATCC 10031). Ampicillin was used as a reference compound. The paper disc diffusion method was used to evaluate the antibacterial activity of the synthesized SBs and SBMCs while the 96-micro plate dilution technique was used in determining the minimum inhibitory concentration.

The *in-vitro* antibacterial activity of 2-aminophenol Schiff bases recorded in Tables 18a and 18b for *o*- and *p*-substituted compounds show that SB ligands **L1**, **L2**, **L4**, **L5** have moderate activity against the tested organisms in comparism with ligands **L3** and **L6** which revealed no activity except **L6** which showed activity against *B. cereus* and *E. coli*. The activity may have arisen from the substituents (methoxy and chloro) at *o*- and *p*-position which play an important role in antibacterial activity (Benarde *et al.*, 1967, Zhang *et al.*, 2006) in addition to the presence of imine groups which is involved in transamination reactions in biological systems (Shawali *et al.*, 1985, Mohamed, 2006). The high activity of **L1** and **L4** ligands (methoxy substituted at *o*- and *p*-positions) from the MICs may be due to the presence of electron donating group (Jayabalakrishnan and Natarajan, 2002, Sari *et al.*, 2003). A comparative study of the growth

inhibitory zone values of Schiff bases and its metal complexes indicates that metal complexes exhibited higher antibacterial activity than the free ligands and the same were observed from minimum inhibitory concentration results given in Tables 21a and 21b. This is probably due to the greater lipophilic nature of the complexes. Such increased activity of the metal complexes can be explained on the basis of overtone's concept and Tweedy's chelation theory (Tweedy, 1964, Mounika *et al.*, 2010). According to overtone's concept of cell permeability, the lipid membrane that surrounds the cell favors the passage of only lipid soluble materials, hence, liposolubility is considered to be an important factor that controls antibacterial activity. On chelation or complexation, the polarity of the metal ion will be reduced to a greater extent due to the overlap of the ligand orbital and partial sharing of positive charge of metal ion with donor groups (Panchal *et al.*, 2006). Further, it increases the delocalization of π electrons over the whole chelate ring and enhances the lipophilicity of the complexes. This increased lipophilicity enhances the penetration of the complexes into lipid membrane and thus block the metal binding sites on enzymes of microorganisms. This can be attributed to increased activity of 2-aminophenol Schiff base complexes. SBMC from 2-APH containing 2 moles of copper per mole of complex (**CuL1** and **CuL2**) exhibited a higher antibacterial activity. This may be due to increased chelation. Lipophilicity of 2-aminophenol SB complexes may have led to inhibition of metabolic pathway by deactivation of various cellular enzymes (Nora, 2007). This result corroborate Jadhav *et al.*, 2010, Mounika *et al.*, 2010 report that mode of action of SBMC was based on chelation theory. In addition, increased activity of 2-aminophenol SB complexes with methoxy and chloro substituents (**CuL4**, **CuL5**, **CoL4**, **CoL5**) exhibited very low MIC values in the range 0.31-0.62 mg/ml (OMe substituents) and 0.15-0.62 mg/ml (Cl substituents). Minimum inhibitory concentration value of 0.28-1.27 mg/ml has been attributed with extremely strong

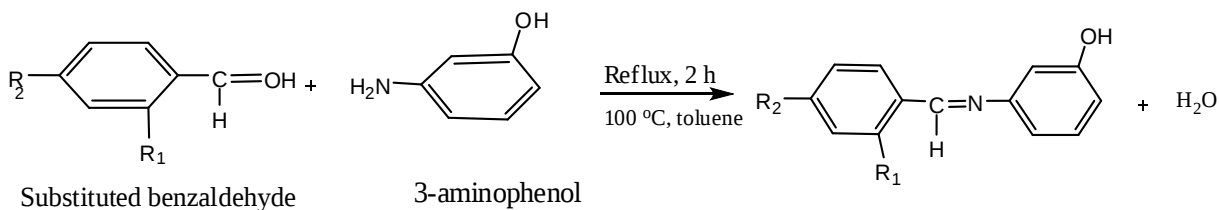
activity while MIC values of 1.81-8.85 mg/ml is attributed with weak activities (Aligiannis *et al.*, 2001). These low MIC values can be attributed to the substituents at *para* position which have the ability to intercalate between bases of DNA. These results are in agreement with Xia *et al.*, 2007 which reports that methoxy and chloro groups at *p*-position significantly increase activity.

5.2 Synthesis of 3-aminophenol Schiff Bases and Metal Complexes

Schiff bases (**L7-L12**) were synthesized by condensation of equimolar quantities of 3-aminophenol with methoxy, chloro and nitro substituted benzaldehydes in toluene (Scheme 31). Three of the compounds (**L7-L9**) had the substituents in *o*-position and the other three in *p*-position (**L10-L12**). The synthesized Schiff bases were recrystallized from toluene. The reaction afforded stable product.

Table 27: Schiff bases (L7-L12) with different substituents at *o*- and *p*-position

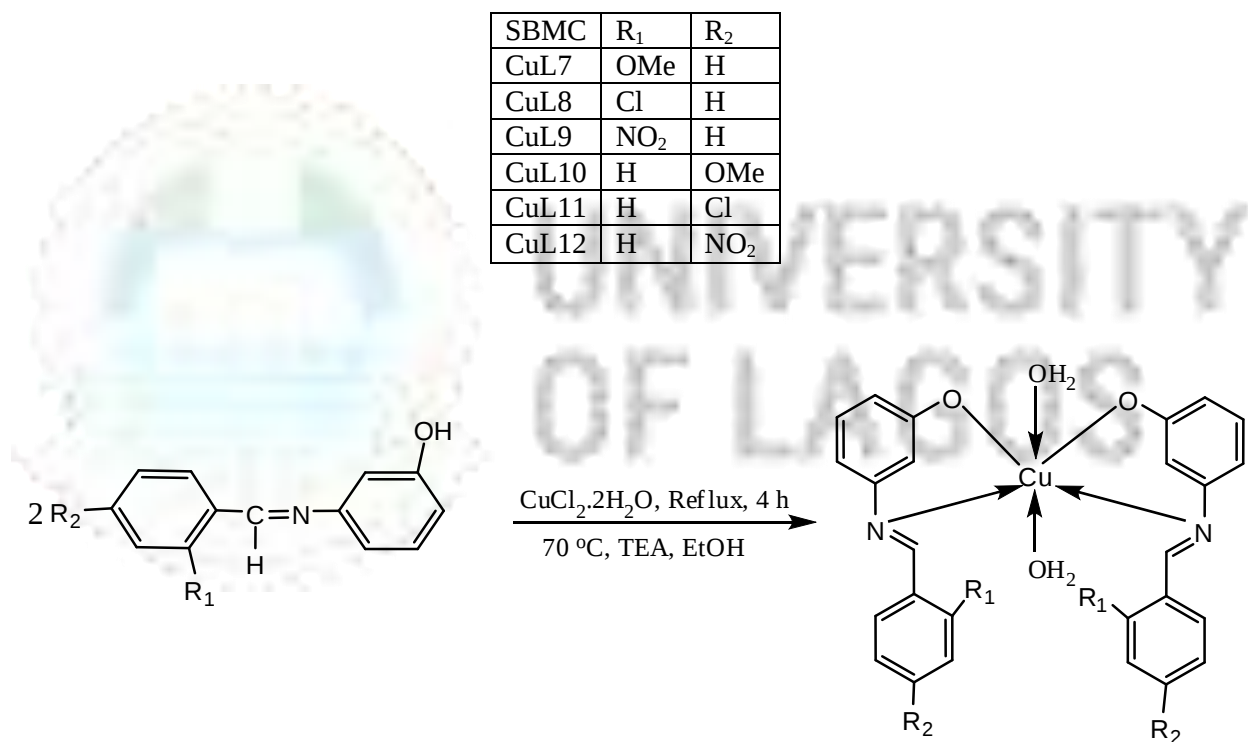
Ligand	R ₁	R ₂
L7	OMe	H
L8	Cl	H
L9	NO ₂	H
L10	H	OMe
L11	H	Cl
L12	H	NO ₂



Scheme 31: Synthesis of 3-aminophenol Schiff bases (L7-L12)

The copper complexes (**CuL7-CuL12**) were obtained by reacting the Schiff bases and metal salts in ratio 2:1 (Scheme 32). The reaction afforded stable compounds. The complexes were relatively soluble in common organic solvents and were purified by washing with ethanol to remove traces of unreacted starting materials.

Table 28: Schiff base copper(II) complexes with different substituents at *o*- and *p*- position



Scheme 32: Synthesis of 3-aminophenol SB copper complexes (CuL7-CuL12)

5.2.1 Physical and Analytical Data of 3-aminophenol Schiff Bases and Metal Complexes

The melting points of *o*-substituted Schiff bases Table 10a varied in the order OMe>NO₂>Cl while the metal complexes decomposed above 250 °C. The yield obtained follows the order

NO₂<Cl<OMe and ranges between 47-58 % for Schiff base ligands L7-L9 and 44-69 % for Schiff base metal complexes CuL7-CuL9.

For the *p*-substituted compounds Table 10b, the Schiff bases and metal complexes decomposed except OMe substituted ligand which melted in the range 148-149 °C. The yield obtained showed that Cl>NO₂=OMe and ranges between 47-52 % for Schiff base ligands L7-L9 and 42-60 % for Schiff base metal complexes CuL7-CuL9. The yield of purified products obtained for 3-aminophenol compounds were rather low which were attributed to challenges in synthesis and purification. The position of substituents reveal that the yield of *o*- and *p*-substituted compounds were not affected as steric effect was reduced.

The Schiff bases and metal complexes were subjected to micro analysis to confirm the purity of synthesized compounds. The results of micro analysis (C, H, N) were in agreement with the molecular formula. The metal content analyses of the complexes reveal the percentage of metal ion per mole of complex. Copper(II) complexes of 3-aminophenol Schiff bases contained 1 mole of copper per mole of the complex.

5.2.2 Spectroscopic data of 3-aminophenol Schiff bases and metal complexes

The IR spectra of the Schiff bases Tables 11a and 11b reveal bands in the region 1617-1586 cm⁻¹ attributed to the C=N bond. In order to determine the bonding mode of Schiff base to the metal ion, the IR spectra of the Schiff bases were compared with those of the corresponding metal complex. In the spectra of the SB and SBMC, a shift in IR band (1586-1581 cm⁻¹) *o*-methoxy-substituted compounds (1617-1586 cm⁻¹) *o*-chloro-substituted compounds, (1606-1593 cm⁻¹) *o*-nitro-substituted compounds indicates coordination of azomethine nitrogen to metal ion (Mohamed *et al.*, 2006, Raman *et al.*, 2010). This trend was also observed in *p*-substituted compounds; (1612-1592 cm⁻¹), (1616-1572 cm⁻¹), (1603-1590 cm⁻¹). The presence of OMe and

NO₂ groups increased IR stretching frequency for (C=N) while Cl group decreased the IR stretching frequency. These may be attributed to electronic effects (resonance effects in OMe, NO₂ and inductive effects in Cl) (Abd El-Wahab *et al.*, 2004). This effect follows the order $p > o$. A comparison between spectra of SB and SBMC also show a band characteristic of $\nu(\text{C-O})$ 1238 cm⁻¹, 1217 cm⁻¹, 1211 cm⁻¹ in *o*- OMe, Cl, NO₂ substituted Schiff bases and 1235 cm⁻¹, 1221 cm⁻¹, 1218 cm⁻¹ in SBMC respectively due to C-O-M formation (Nishat *et al.*, 2010). A shift to lower wavenumber due to coordination of metal ion to hydroxyl oxygen in *p*-substituted compounds reveal peaks in the spectra at 1280-1170 cm⁻¹, 1219-1160 cm⁻¹ and 1214-1195 cm⁻¹ for OMe, Cl and NO₂ substituted compounds respectively. The presence of coordinated water is indicated by a broad band in the region 3327-3368 cm⁻¹, in corroboration with band observed around 800 cm⁻¹ which is due to bending vibration of H₂O indicating that these complexes are hydrated (Al-Shihri and Abdel-Fattah, 2003, Abd El-Wahab, 2007). The new bands in the spectra of metal complexes 437-458 cm⁻¹ and 504-541 cm⁻¹ is assigned to stretching frequencies of $\nu(\text{M-N})$ and $\nu(\text{M-O})$ bond formation (Jouad *et al.*, 2001, Nishat *et al.*, 2010).

5.2.3 ¹H NMR Data of 3-aminophenol Schiff Bases

The ¹H NMR of all Schiff bases exhibits a singlet in the region 7.87-8.39 δ . This based on previous reports is attributed to the imine proton (Raman *et al.*, 2010, Mounika *et al.*, 2010). The signal vary with nature and substituent position. Schiff bases with electron donating groups (OMe) appear upfield (lower chemical shift) due to increase in the electron density in the vicinity of the proton which causes shielding from the magnetic field while SBs with electron withdrawing groups (Cl, NO₂) appear at a lower field (higher chemical shift) as a result of low electron density in the vicinity of the proton. These effects were evident in the synthesized Schiff bases. Schiff bases with **OMe, Cl and NO₂** substituted in *o*-position Table 12a showed singlet at

8.11, 8.23 and 8.17 δ (s, 1H, CH=N) due to azomethine protons. These trend were also observed for *p*-substituted ligands in Table 12b; 7.87, 7.95, 8.39 δ . These effects and trends were also exhibited in the phenolic -OH, (8.89, 9.11, 8.91 δ) for *o*-substituted SBs (8.47, 8.57, 8.71 δ) for *p*-substituted SBs. The three protons of OCH₃ groups for *o*- and *p*-substituted SBs resonated in the region 3.91 and 3.33 δ respectively as expected. The aromatic protons showed signal in the region 6.12-8.11 δ (Nishat *et al.*, 2010). This follows the order *o* > *p*.

5.2.4 Electronic Absorption Data and Magnetic Moment Measurement of 3-aminophenol Schiff Bases and Metal Complexes

The electronic absorption spectra of Schiff bases and their metal complexes were recorded at room temperature using chloroform and DMF as solvents. The electronic spectra measurements were used in assigning the stereochemistries of the metal ions in the complexes based on the position of *d-d* transition peaks. The Schiff bases exhibited two absorption bands; a high energy band attributed to $\pi \rightarrow \pi^*$ transitions of the aromatic rings and a lower energy band due to $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the nitrogen of the azomethine group (Issa *et al.*, 2005, Tuna *et al.*, 2006). The absorption spectra of 3-aminophenol SBs features an intense band system with maxima at 34,843-38,461 cm^{-1} and 28,328-29,498 cm^{-1} attributed to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ for *o*-substituted SBs Table 13a. In the *p*-substituted ligands Table 13b, absorption bands were observed in the region 33,783-34,722 cm^{-1} and 28,248-29,585 cm^{-1} due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$. A shift to longer wavelength (lower energy) is usually observed for imine group with electron withdrawing substituents while electron donating substituents cause shift to shorter wavelength (higher energy) (Bottcher *et al.*, 1997). Substitution of chloro and nitro groups in *o*- and *p*-positions in SBs shifts the bands to higher wavelength (28,328 cm^{-1} , 28,595 cm^{-1} and

28,248 cm^{-1} , 28,932 cm^{-1}), the opposite is true for methoxy substituted SBs (29,498 cm^{-1} and 29,585 cm^{-1}) for *o*- and *p*-substituted positions respectively. In the metal complexes, imine transitions shifted to longer wavelength due to *d-d* transitions and charge transfer transitions confirming the coordination of SB to metal ion (Abd El-Wahab, 2007). Three possible transitions are expected for Cu(II) ion in octahedral geometry, but when they are very close in energy, they often appear in the form of a single broad band (Narang *et al.*, 1994, Raman *et al.*, 2010). The electronic spectra of 3-aminophenol Cu(II) complexes showed one broad absorption band in the region 26,525-27,932 cm^{-1} Tables 13a and 13b attributed to the $\pi \rightarrow$ copper(II), that is ligand-to-metal charge transfer (LMCT) transition (Al-Hazmi *et al.*, 2005, Raman *et al.*, 2010). The broadness of the observed band may be due to Jahn-Teller effect which enhances the distortion of octahedral geometry (El-Asmy *et al.*, 1990). The magnetic moments values of 1.70-1.78 BM which supports an octahedral geometry was observed for the Cu^{2+} complexes. The magnetic moment values of the complexes indicate the presence of one unpaired electron (Serin, 2001, Chandra *et al.*, 2004).

5.2.5 Antibacterial Activity of 3-aminophenol Schiff Bases and Metal Complexes

The antibacterial activity of 3-aminophenol Schiff bases and their metal complexes are related to the nature and position of substituent groups. Structure activity-relationship of Schiff bases of 3-aminophenol derivatives were studied in relation to nature and position of substituent groups. The Schiff bases **L7-L12** and their metal complexes **CuL7-CuL12** were tested against six human pathogenic bacteria; *Escherichia coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538), *Pseudomonas aeruginosa* (ATCC 19582), *Bacillus cereus* (10702), *Enterococcus faecalis* (ATCC 29212) and *Klebsiella pneumoniae* (ATCC 10031). Ampicillin was used as a reference compound. The paper disc diffusion method was used to evaluate the antibacterial activity of the

synthesized SBs and SBMCs while the 96-micro plate dilution technique was used in determining the minimum inhibitory concentration. The *in-vitro* antibacterial activity of 3-aminophenol Schiff bases and metal complexes against the tested bacteria are summarized in Tables 19a and 19b. The antibacterial screening indicate that most of the ligands have higher antibacterial activity than the metal complexes. These were also reflected in the MIC values. The MIC values of the Schiff bases and the Cu(II) complexes against six human pathogenic bacteria are presented in Tables 22a and 22b. Several reports have shown that metal complexes exhibit increased activity than the free ligands due to the presence of metal ion in the complex (Hodnett and Dunn, 1972, Imran *et al.*, 2007, Atmaram and Kiran, 2011), but the results of this research reveal that some Schiff base ligands can exhibit activity more than the metal complexes. This was observed in compounds **L11** (chloro substituent at *p*-position) and **L12** (nitro substituent at *p*-position). Position of substituents has been found to play an important role in modifying DNA adducts. Highest antibacterial activity have been reported in *para*-substituted compounds due to interaction with specific amino acid residue or lie in a hydrophobic pocket in the binding site of the receptor (Trumpp-Kallmeyer *et al.*, 1992). Electron withdrawing effect of chlorine by induction promotes ionization which is one of the important factors governing activity on DNA and RNA (Benarde *et al.*, 1967). Nitro substituted compounds have been reported to stabilize microtubules (globular proteins) and as a result interfere with the normal breakdown of microtubules during cell division by blocking the polymerization of tubulins into microtubules (Baluja *et al.*, 2009, Giannicchi *et al.*, 2013). These can be attributed to the antibacterial activity exhibited by **L11** and **L12** Schiff bases, hence the broad antibacterial activity against the tested organisms except against *E.coli*. It is known that chelation tends to make ligands act as more powerful and potent bactericidal agent and this was confirmed by the fact that the **CuL10**

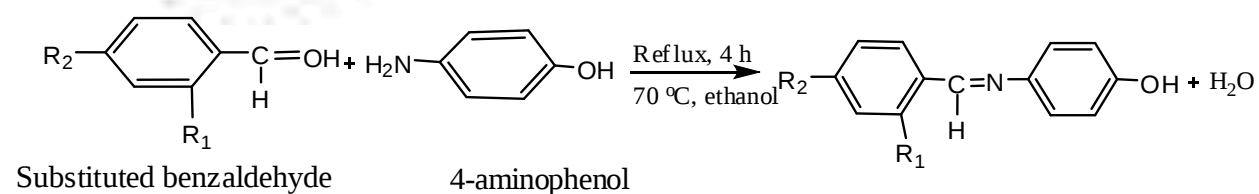
complexes showed antibacterial activity against all bacteria strains than the free ligand. This can be attributed to the chelating theory (Panchal *et al.*, 2006).

5.3 Synthesis of 4-aminophenol Schiff Bases and Metal Complexes

Schiff bases (**L13-L18**) were synthesized by condensation of equimolar quantities of 4-aminophenol with methoxy, chloro and nitro substituted benzaldehydes in ethanol (Scheme 33). Three of the compounds (**L13-L15**) had the substituents in *o*-position and the other three in *p*-position (**L16-L18**). The synthesized Schiff bases were recrystallized from ethanol. The reaction afforded stable products.

Table 29: Schiff bases (L13-L18) with different substituents at *o*- and *p*-position

Ligand	R ₁	R ₂
L13	OMe	H
L14	Cl	H
L15	NO ₂	H
L16	H	OMe
L17	H	Cl
L18	H	NO ₂



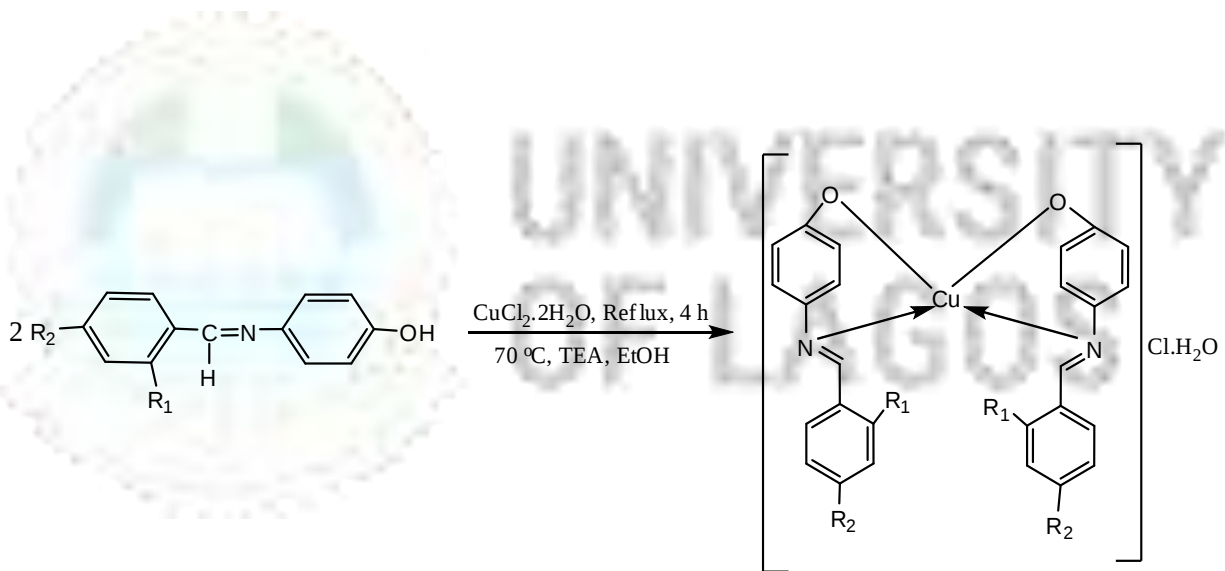
Scheme 33: Synthesis of 4-aminophenol Schiff bases (L13-L18)

The copper complexes (**CuL13-CuL18**) were obtained by reacting the Schiff bases and metal salts in ratio 2:1 (Scheme 34-35). The reaction afforded stable compounds. The complexes were

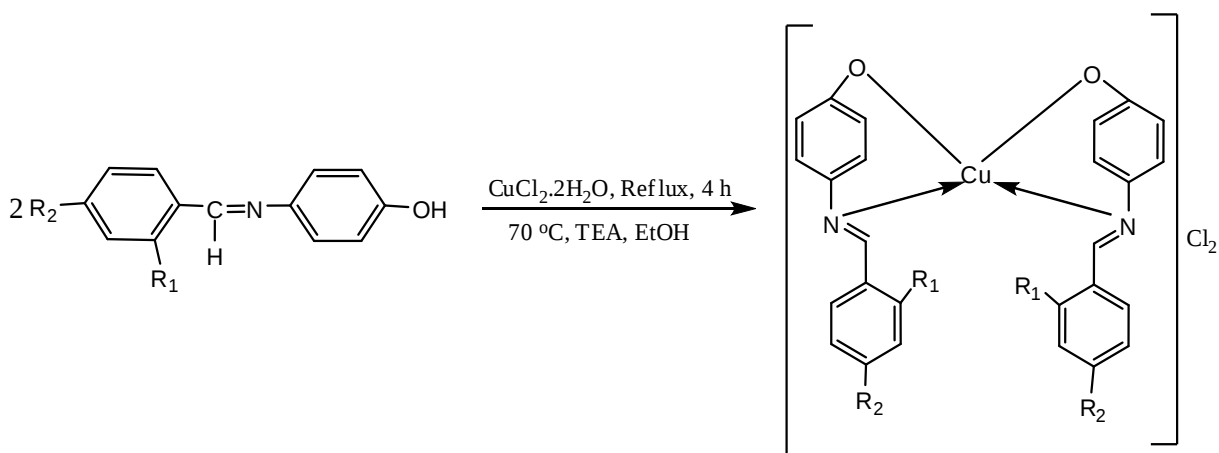
relatively soluble in common organic solvents and were purified by washing with ethanol to remove traces of unreacted starting materials.

Table 30: Schiff base copper(II) complexes with different substituent groups

SBMC	R ₁	R ₂
CuL13	OMe	H
CuL14	Cl	H
CuL15	NO ₂	H
CuL16	H	OMe
CuL17	H	Cl
CuL18	H	NO ₂



Scheme 34: Synthesis of 4-aminophenol SB copper complexes (CuL13-CuL15)



Scheme 35: Synthesis of 4-aminophenol SB copper complexes (CuL16-CuL18)

5.3.1 Physical and Analytical Data of 4-aminophenol Schiff Bases and Metal Complexes

The melting points of *o*-substituted Schiff bases Table 14a varied in the order $\text{OMe} > \text{Cl} > \text{NO}_2$ while the metal complexes decomposed above 250°C . The yield obtained follow the order $\text{OMe} > \text{NO}_2 < \text{Cl}$ and ranges between 54-93 % for Schiff base ligands L13-L15 and 41-47 % for Schiff base metal complexes CuL13-CuL15.

For the *p*-substituted compounds Table 14b, the melting points of the Schiff bases follow the order $\text{OMe} > \text{Cl} > \text{NO}_2$ while the metal complexes decomposed above 250°C . The yield obtained ranges between 49-70 % for Schiff base ligands L16-L18 and 40-47 % for Schiff base metal complexes CuL16-CuL18. The electronic effect and position of substituents groups on aromatic ring influences the reactivity and stability of the compounds. The type of substituent groups in 4-aminophenol compounds played a great role in accounting for the yield of the synthesized compounds. Methoxy substituted compounds gave the highest yield for *o*- and *p*-substituted positions. This resulted in over 70 % yield (*o*- 92 %, *p*- 70 %) Tables 14a and 14b. The nitro and chloro substituted compounds were comparable in their yield. The yield of 4-aminophenol ligands and its complexes follow the order $\text{OMe} > \text{Cl} > \text{NO}_2$. These were observed for the *o*- and *p*-

substituted compounds. Resonance stability may have led to greater yield of OMe substituted compounds. In considering the position of the substituent groups, the order of $o > p$ were observed. The Schiff bases and metal complexes were subjected to micro analysis to confirm the purity of synthesized compounds. The results of micro analysis (C, H, N) were in agreement with the molecular formula. The metal content analysis of the complexes reveal the percentage metal ion per mole of complex. Copper(II) complexes of 4-aminophenol Schiff bases contained 1 mole of copper per mole of the complex.

5.3.2 Spectroscopic Data of 4-aminophenol Schiff Bases and Metal Complexes

The IR spectra of the Schiff bases Tables 15a and 15b reveal bands in the region 1625-1604 cm^{-1} attributed to the C=N bond. In order to determine the bonding mode of Schiff base to the metal ion, the IR spectra of the Schiff bases were compared with those of the corresponding metal complex. In the spectra of the SB and SBMC, a shift in IR band (1614-1593 cm^{-1}) *o*-methoxy-substituted compounds, (1625-1609 cm^{-1}) *o*-chloro-substituted compounds, (1620-1604 cm^{-1}) *o*-nitro-substituted compounds indicates coordination of azomethine nitrogen to metal ion (Mohamed *et al.*, 2006, Raman *et al.*, 2010). This trend was also observed in *p*-substituted compounds; (1618-1584 cm^{-1}), (1604-1589 cm^{-1}), (1623-1591 cm^{-1}).

The presence of OMe and NO₂ groups increased IR stretching frequency for (C=N) while Cl group decreased the IR stretching frequency. These may be attributed to electronic effects (resonance effects in OMe, NO₂ and inductive effects in Cl) (Abd El-Wahab *et al.*, 2004). This effect follows the order $o > p$. A comparison between spectra of SB and SBMC also show a band characteristic of $\nu(\text{C-O})$ 1262 cm^{-1} , 1273 cm^{-1} , 1269 cm^{-1} in *o*- OMe, Cl, NO₂ substituted Schiff bases and 1257 cm^{-1} , 1255 cm^{-1} , 1252 cm^{-1} in SBMC respectively due to C-O-M formation (Nishat *et al.*, 2010). A shift to lower wavenumber due to coordination of metal ion to hydroxyl

oxygen in *p*-substituted compounds reveal peaks in the spectra at 1260-1253 cm⁻¹, 1271-1252 cm⁻¹ and 1247-1256 cm⁻¹ for OMe, Cl and NO₂ substituted compounds respectively. The presence of coordinated water is indicated by a broad band in region 3320-3352 cm⁻¹ (Al-Shihri and Abdel-Fattah, 2003, Abd El-Wahab, 2007). The new bands in the spectra of metal complexes 429-517 cm⁻¹ and 504-565 cm⁻¹ is assigned to stretching frequencies of $\nu(\text{M-N})$ and $\nu(\text{M-O})$ bond formation (Jouad *et al.*, 2001, Nishat *et al.*, 2010).

5.3.3 ¹H NMR Data of 4-aminophenol Schiff Bases

The ¹H NMR of all Schiff bases exhibits a singlet in the region 8.00-8.61 δ . This based on previous reports is attributed to the imine proton (Raman *et al.*, 2010, Mounika *et al.*, 2010). The signal vary with nature and substituent position. Schiff bases with electron donating groups (OMe) appear upfield (lower chemical shift) due to increase in the electron density in the vicinity of the proton which causes shielding from the magnetic field while SBs with electron withdrawing groups (Cl, NO₂) appear at a lower field (higher chemical shift) as a result of low electron density in the vicinity of the proton. These effects were evident in the synthesized Schiff bases. Schiff bases with **OMe, Cl and NO₂** substituted in *o*-position Table 16a showed singlet at 8.00, 8.21 and 8.29 δ (s, 1H, CH=N) due to azomethine protons. These trend were also observed for *p*-substituted ligands Table 16b; 8.35, 8.61, 8.53 δ . These effects and trends were also exhibited in the phenolic -OH, (8.89, 8.93, 8.98 δ) for *o*-substituted SBs, (9.43, 9.57, 8.61 δ) for *p*-substituted SBs. The three protons of OCH₃ groups for *o*- and *p*-substituted SBs resonated in the region 3.96 and 3.83 δ respectively as expected. This follows the order *o* > *p*.

5.3.4 Electronic Absorption Data and Magnetic Moment Measurement of 4-aminophenol Schiff Bases and Metal Complexes

The electronic absorption spectra of 4-aminophenol Schiff bases and their metal complexes were recorded at room temperature using chloroform and DMF as solvents. The electronic spectra measurements were used in assigning the stereochemistries of the metal ions in the complexes based on the position of $d-d$ transition peaks. The Schiff bases exhibited two absorption bands; a high energy band attributed to $\pi \rightarrow \pi^*$ transitions of the aromatic rings and a lower energy band due to $n \rightarrow \pi^*$ transition of the non-bonding electrons present on the nitrogen of the azomethine group (Issa *et al.*, 2005, Tuna *et al.*, 2006). The absorption spectra of 4-aminophenol SBs features an intense band system with maxima at $36,630\text{--}37,313\text{ cm}^{-1}$ and $28,169\text{--}29,761\text{ cm}^{-1}$ attributed to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ for *o*-substituted SBs Table 17a. In the *p*-substituted ligands Table 17b, absorption bands were observed in the region $34,482\text{--}38,759\text{ cm}^{-1}$ and $27,666\text{--}29,395\text{ cm}^{-1}$ due to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$. A shift to longer wavelength (lower wavenumber) is usually observed for imine group with electron withdrawing substituents while electron donating substituents cause shift to shorter wavelength (higher wavenumber) (Bottcher *et al.*, 1997). These were not observed in 4-aminophenol SBs as both substituents exhibited similar shift in wavelength. This can be attributed to *p*-effect in 4-aminophenol SBs due to the position of OH group which is *p*- to the imine group.

The substitution of methoxy, chloro and nitro groups in *o*-positions in SBs shifts the bands to lower wavelength ($29,154\text{ cm}^{-1}$, $29,761\text{ cm}^{-1}$ and $28,168\text{ cm}^{-1}$). These were also observed in *p*-positions in the SBs ($29,030\text{ cm}^{-1}$, $29,395\text{ cm}^{-1}$ and $27,666\text{ cm}^{-1}$) for methoxy, chloro and nitro groups. The effect on the position of substituent groups follows the order $o = p$. In the metal complexes, imine transitions shifted to longer wavelength due to $d-d$ transitions and charge

transfer transitions confirming the coordination of SB to metal ion (Abd El-Wahab, 2007, Lever, 1984). The metal complexes exhibited different absorption bands in solvents of different polarities. A pronounced change in position of a UV-vis absorption band is associated with increasing solvent polarity, which usually lead to bathochromic (red) shift while the corresponding is called a hypsochromic (blue) shift (Reichardt, 2003, Hemmateenejad *et al.*, 2012). The effects of solvents (chloroform and DMF) on the SBMCs lead to bands of different intensities. Electronic absorption spectra of all Schiff base metal complexes in DMF shows *d-d* transitions which were not observed in chloroform for all the SBMCs. This can be attributed to solvent effect. In all the complexes, *d-d* transitions were observed in the range 20,833-23,109 cm^{-1} and 20,080-25,839 cm^{-1} which may be assigned to $^2B_{1g} \rightarrow ^2B_{2g}$ transition in a tetrahedral geometry. The observed magnetic moment value for Cu(II) complexes falls in the range 1.80-1.88 BM suggestive of tetrahedral geometry.

5.3.5 Antibacterial Activity of 4-aminophenol Schiff Bases and Metal Complexes

The antibacterial activity of 4-aminophenol Schiff bases and their metal complexes are related to the nature and position of substituent groups. Structure activity-relationship of Schiff bases of 4-aminophenol derivatives were studied in relation to nature and position of substituent groups. The Schiff bases **L13-L18** and their metal complexes **CuL13-CuL18** were tested against six human pathogenic bacteria; *Escherichia coli* (ATCC 8739), *Staphylococcus aureus* (ATCC 6538), *Pseudomonas aeruginosa* (ATCC 19582), *Bacillus cereus* (10702), *Enterococcus faecalis* (ATCC 29212) and *Klebsiella pneumoniae* (ATCC 10031). Ampicillin was used as a reference compound. The paper disc diffusion method was used to evaluate the antibacterial activity of the synthesized SBs and SBMCs while the 96-micro plate dilution technique was used in determining the minimum inhibitory concentration.

The *in-vitro* antibacterial activity of 4-aminophenol Schiff bases and metal complexes all have the capacity of inhibiting the metabolic growth of the investigated bacteria to different extent. This inhibitory capacity is influenced by the presence and position of substituent groups. The *in-vitro* antibacterial activity and minimum inhibitory concentration is presented in Tables 20a, 20b and 23a, 23b respectively. From the data, Schiff base with nitro substituent at *o*-position (**L15**) exhibited antibacterial activity against all tested bacteria, except against *E. coli* in which the reference compound ampicillin showed antibacterial activity higher than the SB (**L15**). Besides the **L15** SB, complexes were found to be more potent than the free ligands. This can be explained on the basis of chelation theory (Panchal *et al.*, 2006). While chelation is not the only criterion for antibacterial activity, it is intrinsic to know that substituent groups and their positions contribute to antibacterial activity. Copper complexes with chloro and nitro substituents at *p*-position (**CuL17** and **CuL18**) were found to exhibit broad antibacterial activity based on the MIC values. Antibacterial activity is an intricate blend of several contributions such as lipophilicity, steric hindrance, the metal ion and the ligand, the nature and position of substituent groups on the compound.

CHAPTER SIX

6.0 SUMMARY OF FINDINGS AND CONCLUSION

6.1 Summary of Findings

A total of forty-two (**42**) compounds were synthesized and fully characterized using micro analysis, infrared spectroscopy, ^1H NMR spectroscopy, electronic absorption spectroscopy, atomic absorption spectroscopy, magnetic moment measurements, thermal gravimetry analysis and differential scanning calorimetry.

From the total of forty-two (**42**) compounds synthesized, thirty (**30**) are new compounds which consist of the following: Schiff bases of 3-aminophenol (**6**) to the best of my knowledge. These include; 3-(2-methoxybenzylideneamino)phenol (L7), 3-(2-chlorobenzylideneamino)phenol (L8), 3-(2-nitrobenzylideneamino)phenol (L9), 3-(4-methoxybenzylideneamino)phenol (L10), 3-(4-chlorobenzylideneamino)phenol (L11), 3-(4-nitrobenzylideneamino)phenol (L12).

The research reports the synthesis of 2-aminophenol Schiff base metal complexes (**12**) for the first time to the best of my knowledge;

bis(2-(2-methoxybenzylideneamino)phenol)copper(II) CuL1, bis(2-(2-methoxybenzylideneamino)phenol)cobalt(II) CoL1, bis(2-(2-chlorobenzylideneamino)phenol)copper(II) CuL2, bis(2-(2-chlorobenzylideneamino)phenol)cobalt(II) CoL2, bis(2-(2-nitrobenzylideneamino)phenol)copper(II) CuL3, bis(2-(2-nitrobenzylideneamino)phenol)cobalt(II) CoL3, bis(2-(4-methoxybenzylideneamino)phenol)copper(II) CuL4, bis(2-(4-methoxybenzylideneamino)phenol)cobalt(II) CoL4, bis(2-(4-chlorobenzylideneamino)phenol)copper(II) CuL5, bis(2-(4-chlorobenzylideneamino)phenol)cobalt(II) CoL5, bis(2-(4-nitrobenzylideneamino)phenol)copper(II) CuL6, bis(2-(4-nitrobenzylideneamino)phenol)cobalt(II) CoL6.

3-aminophenol Schiff base metal complexes (**6**) were synthesized for the first time to the best of my knowledge;

bis(3-(2-methoxybenzylideneamino)phenol)copper(II) CuL7, bis(3-(2-chlorobenzylideneamino)phenol)copper(II) CuL8, bis(3-(2-nitrobenzylideneamino)phenol)copper(II) CuL9, bis(3-(4-methoxybenzylideneamino)phenol)copper(II) CuL10, bis(3-(4-chlorobenzylideneamino)phenol)copper(II) CuL11, bis(3-(4-nitrobenzylideneamino)phenol)copper(II) CuL12.

Schiff base metal complexes (**6**) from 4-aminophenol were also synthesized for the first time to the best of my knowledge. These are;

bis(4-(2-methoxybenzylideneamino)phenol)copper(II) CuL13, bis(4-(2-chlorobenzylideneamino)phenol)copper(II) CuL14, bis(4-(2-nitrobenzylideneamino)phenol)copper(II) CuL15, bis(4-(4-methoxybenzylideneamino)phenol)copper(II) CuL16, bis(4-(4-chlorobenzylideneamino)phenol)copper(II) CuL17, bis(4-(4-nitrobenzylideneamino)phenol)copper(II) CuL18.

A study of structure-activity relationship of 2-, 3- and 4-aminophenol Schiff bases showed that 2-aminophenol Schiff base with methoxy substituent at *o*-position (bis(2-(2-methoxybenzylideneamino)phenol)) exhibited antibacterial activity against gram –ve bacteria, 3-aminophenol Schiff base with chloro and nitro substituent at *p*-position (3-(4-chlorobenzylideneamino)phenol and 3-(4-nitrobenzylideneamino)phenol) exhibited activity against gram-ve and gram +ve bacteria while 4-aminophenol Schiff base with nitro substituent at *o*-position (bis(4-(2-nitrobenzylideneamino)phenol)) exhibited activity against gram+ve bacteria.

An evaluation of antibacterial activity of Schiff base copper and cobalt complexes of aminophenols show that antibacterial activity of Schiff base metal complexes of 2- and 4-aminophenol were improved upon complexation with metal salts. 2-aminophenol Schiff base

metal complexes exhibited high activity against all tested bacteria. Some 4-aminophenol Schiff base metal complexes (bis(4-(4-chlorobenzylideneamino)phenol)copper(II), bis(4-(4-nitrobenzylideneamino)phenol)copper(II)) exhibited antibacterial activity against all tested bacteria. Antibacterial activity of 2- and 4-aminophenol Schiff base metal complexes were better compared to reference compound, ampicillin

6.2 CONCLUSION

The synthesis and characterization of six (6) new Schiff base ligands and twenty-four (24) new Schiff base metal complexes have been reported with physicochemical and spectroscopic analysis. The ligands are bidentate in their complexation to the metal salt through imine nitrogen and hydroxyl oxygen. The complexes adopt octahedral, tetrahedral and square-planar geometry. The antibacterial study reveals that the complexes have higher activity than the free ligands except with 3-aminophenol ligands. Antibacterial activities were compared with the activity of ampicillin as a reference compound and compounds (**CuL1, CuL2, CuL4, CuL5, CuL17, CuL18, CoL2, CoL3, CoL4, CoL5, and CoL6**) were found to be more active than ampicillin. The effect of Schiff base ligands with metal ions on microorganisms was found to be synergistic. This study sheds further light on the chemical and the biological behavior of the ligands in the presence of metal ions which may help to understand the chelation process of this class of ligands.

The results obtained validate the hypothesis that Schiff bases having substitution with methoxy and chloro groups at the phenyl ring are good candidates for antibacterial activity while nitro group at different positions in the aromatic ring have varying antibacterial activity.

CHAPTER SEVEN

7.0 CONTRIBUTIONS TO KNOWLEDGE

1. This study gives the first report of Schiff base ligands synthesized from 3-aminophenol and Schiff base metal complexes of 2, 3, 4-aminophenol derivatives to the best of my knowledge.
2. This research provides *in-vitro* antibacterial activity of 2-aminophenol metal complexes. The study reported significantly higher activities than the reference compound ampicillin
3. Results of the research have indicated that 2-aminophenol Schiff base metal complexes can be employed as active ingredient in development of broad spectrum antibacterial agent (antiseptic/disinfectant), while 4-aminophenol Schiff base metal complexes can be used in formulation of narrow spectrum antibacterial agent (antiseptics).
4. This study reveals that nature and position of substituent has a great impact on biological activity of 3-aminophenol Schiff base, 2- and 4-aminophenol Schiff base metal complexes.

7.1 FUTURE WORK

Future research in this area to complement the findings reported can include the following:

- Synthesis of cobalt complexes of 3- and 4-aminophenol Schiff bases
- Surface test in the presence and absence of organic matter
- Effect of proteinaceous substances on the antibacterial activities of the compounds
- Determination of contact times for different organism
- X-ray crystallographic studies of Schiff base metal complexes of aminophenols

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