SYNTHESIS AND CHARACTERISATION OF BIOLOGICALLY IMPORTANT METAL COMPLEXES

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SUNITHA. S

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALICUT
KERALA, PIN – 673 635.

JULY 2008

Dr. K.K.ARAVINDAKSHAN
Professor of Chemistry
University of Calicut.

Calicut University P.O.
Kerala, PIN 673635.
28th July, 2008.

CERTIFICATE

This is to certify that the thesis bound herewith is an authentic record of the research work carried out by **Ms. SUNITHA.S** under my supervision in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry of the University of Calicut and further that no part thereof has been presented before for any other degree.

Dr. K.K. Aravindakshan
(Research Guide)

DECLARATION

I, Sunitha. S, here by declare that the thesis entitled **Synthesis and characterisation of biologically important metal complexes** submitted to the University of Calicut in partial fulfilment of the requirements of the Doctoral degree in Chemistry, is a bonafide research work done by me under the supervision and guidance of Dr. K.K.Aravindakshan.

I further declare that the thesis has not previously formed the basis for the award of any other degree, diploma or similar title.

Calicut University Campus, **SUNITHA. S**
28th July, 2008.

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PREFACE

Schiff bases have proved to be of utmost importance to mankind ever since its synthesis. They are important in the field of biology and medicine and they help immensely in inorganic drug research. They find use in dye industry and in other chemical industries because they can be used as catalysts. Recently they are being used in the field of genetic engineering as they are used in the photocleavage of deoxyribonucleic acid (DNA). A lot of research work have been carried out on Schiff bases. They have also been complexed with transition metal ions and with lanthanide metal ions. A perusal of the literature has shown that no work has been done on the Schiff bases formed by the condensation of 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone with primary amines like aniline, phenylhydrazine and benzoylhydrazine. Schiff bases obtained by condensing the above heterocyclic ketone with isoniazid, an antitubercular drug had been synthesized, characterised and complexed with lanthanide ions but not with transition metal ions.

In the present work, four Schiff bases have been synthesized by condensing 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone with aniline, isoniazid, phenylhydrazine and benzoylhydrazine. They have been complexed with transition metal ions.

The thesis has been divided into two parts, Parts I and II.

Part I deals with the syntheses and characterisation of the four Schiff bases and their transition metal complexes. It consists of six chapters.

Chapter I gives an introduction of the earlier work done on Schiff bases, their complexes and their applications.

Chapter II gives the details of the materials used, the methods adopted and the details of the instrumentation used.

Chapter III describes the synthesis and characterisation of the Schiff base, BMPPA and its complexes with the salts of cobalt(II), nickel(II) and copper(II).

Chapters IV, V and VI describe the syntheses and characterisation of the Schiff bases, BMPPI, BMPPPH and BMPPBH, respectively and their complexes with the salts of cobalt(II), nickel(II) and copper(II).

Part II deals with the biological applications of the Schiff bases and their transition metal complexes. It consists of two chapters. Chapter I makes an introduction to the earlier work done on the antibacterial and the antifungal activity of the Schiff bases and their metal complexes.

Chapter II describes the materials used and the methods adopted to study the antibacterial and the antifungal activity of some of the Schiff bases and their metal complexes.

The references cited in the text have been arranged in serial order at the end of each chapter.

CHAPTER I

INTRODUCTION

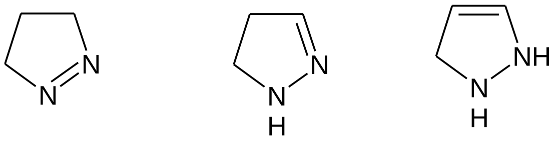
Heterocyclic compounds are widely distributed in nature which are essential to life.[1] Genetic material DNA is also composed of heterocyclic bases-pyrimidines and purines. A large number of heterocyclic compounds, both synthetic and natural, are pharmacologically active and are in clinical use. Several heterocyclic compounds have applications in agriculture as insecticides, fungicides, herbicides, pesticides, etc. They also find applications as sensitizers, developers, antioxidants, copolymers etc. They are used as vehicles in the synthesis of other organic compounds. Chlorophyll -photosynthesizing and haemoglobin -oxygen transporting pigments are also heterocyclic compounds. Huge amount of research work is generated on various phases of heterocyclic chemistry.

Pyrazole is a pi-excessive heterocyclic[2] and contains two nitrogen atoms, pyrazole type and pyridine type at the positions 1 and 2. Benzo-fused pyrazole (II) is known as benzopyrazole or more commonly indazole with the numbering as shown in the structures I and II (Fig.1). Pyrazole exists in three partially reduced forms III, IV and V with the different positions of double bond (Fig.2).

I

II

Fig.1 Structures of pyrrole (I) and indazole (II)



III

IV

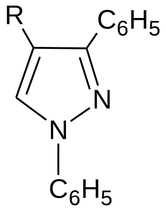
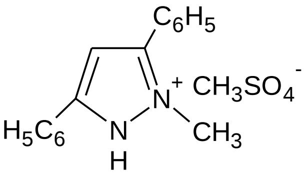
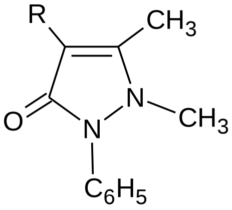
V

Fig.2 The partially reduced forms of pyrazole

Pyrazole ring is incorporated into many of the commercially available pharmaceuticals, agrochemicals and dyesuffs. Some important pyrazole derivatives with their activity are listed in Table 1.

TABLE 1

PYRAZOLE DERIVATIVES AND THEIR ACTIVITIES

STRUCTURE	NAME	ACTIVITY
	Difenamizole	Analgesic, anti-inflammatory and antipyretic
	Difenzoquat	Herbicide
	3-pyrazolin-5-one	Analgesic, anti-inflammatory and antipyretic

Pyrazole exists in two identical tautomeric forms with the movement of proton between two annular nitrogen atoms.[4] Thus two nitrogen atoms are indistinguishable (Fig.3a). But asymmetrically substituted pyrazole exists in two non-separable tautomers due to the rapid interconversion of tautomers, although one tautomeric form predominates over the other (Fig.3b). Therefore, 3-substituted pyrazole is identical with 5-substituted pyrazole. The numbering of such compounds is complicated and the atoms are identified by two numbers. If $R=CH_3$, the compound is named as 3(5)methylpyrazole.

Fig.3a Tautomerism in pyrazole

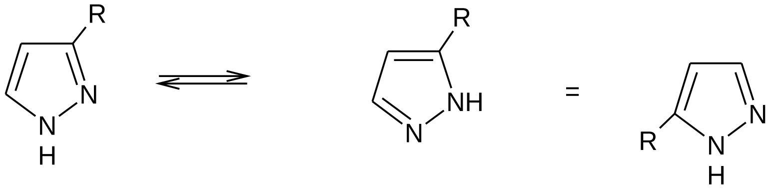


Fig.3b Tautomerism in substituted pyrazole

Pyrazole is a colourless solid,[5] m.p.70ºC and it is a weak monoacidic base with pK_a 2.53. Other pyrazoles are similarly weak bases and although they form salts, these dissociate very readily. They are aromatic compounds. The ring system is more stable than pyrrole and less reactive. Nevertheless, electrophilic substituion reactions occur readily enough, the attack being at the 4- position. Bromination can be effected in organic solvents, and hypobromite also gives the

4-bromo derivative. Direct iodination occurs, using iodine and sodium acetate. Nitration and sulphonation reactions are less facile, but in these cases, the reagent presumably has to attack the pyrazole salt, which is clearly deactivated towards electrophilic substitution. In this respect, it is note- worthy that the nitration of N-phenylpyrazoles occurs so that the first nitro group enters the benzene ring. Pyrazoles are relatively stable to oxidation, and methylpyrazoles are oxidised to pyrazolecarboxylic acids by treatment with alkaline $KMnO_4$ or chromic acid.

A. Pyrazolones and their applications

Theoretically, there are three types of pyrazolones, but only derivatives of 3-pyrazolones (Fig.4) and 5-pyrazolones (Fig.5) are known. They are, of course tautomeric substances.

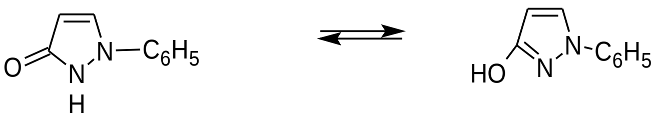


Fig.4 Tautomers of 1-phenyl-3-pyrazolone

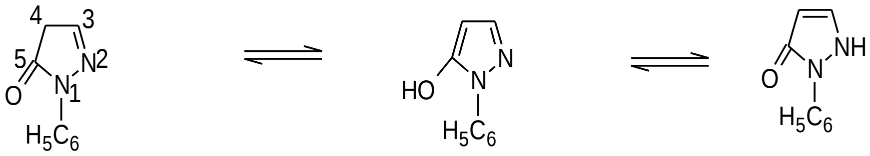


Fig.5 Tautomers of 1-phenyl-5-pyrazolone

The 5-pyrazolones have been very extensively studied. Several useful drugs and dyestuffs contain this system. The most common method of synthesis involves reaction of a hydrazine with a β-keto ester and this method is capable of very wide variation. The first pyrazole derivative to be described was made by this method. Knorr, a pupil of Emil Fischer, had been impressed by the versatility of phenylhydrazine. He accordingly treated it with ethyl acetoacetate, apparently expecting to obtain an aminoquinoline. However, the product was later shown to be 3-methyl-1-phenyl-5-pyrazolone and on methylation, it gave 2,3-dimethyl-1-phenyl-5-pyrazolone. Knorr's interest in quinine led to the testing of this compound as a febrifuge and it was patented even before the correct structure had been established. It is commonly known as antipyrine.[6] It has been very widely used as an antipyretic and analgesic drug, but has been somewhat displaced recently by better and safer drugs. Early attempts to improve antipyrine led to the introduction of aminopyrine or pyramidone (Fig.6), which have been extensively used in medicine.

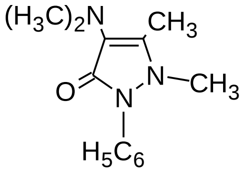


Fig.6 Aminopyrine (Pyramidone)

The pyrazolone dyes are derivatives of 5-pyrazolone. The azo dyes are generally made by diazo coupling with a pyrazolone which is unsubstituted in the 4-position, and many of these derivatives have achieved very considerable commercial importance. Tartrazine, for eg., is a yellow dye prepared from phenylhydrazine-p-sulphonic acid and oxaloacetic ester, followed by coupling with diazotised sulphanilic acid (Fig.7) . It is extremely fast to light; it is used as a wool dye and also for the artificial colouring of processed foods. Many related dyes are known, and many have found applications in colour photography.

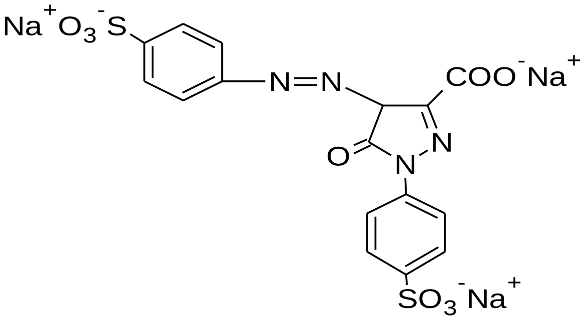


Fig. 7. Structure of tartrazine

B. Complexes containing multifunctional 1,2,4-triazole as co-ligand:

Substituted 1,2,4-triazoles have attracted attention owing to their bactericidal,[7] fungicidal[8] and pharmacological activities[9,10] in addition to their uses as antiulcer-[11] and blood pressure-lowering agents.[12] Triazoles are also the subject of extensive studies in view of their synthetic uses and other theoretical aspects.[13] Hence the commercially available 4-amino-3-hydrazino-5-mercapto-1,2,4-triazole was selected as co-ligand since it possesses properties that can be exploited for use as complexing agent with ruthenium(II) polypyridyls (Figs.8 & 9). Ruthenium(II) polypyridyls have opened a new door for enthusiastic researchers since they act as probes for DNA and hence are potential therapeutic agents.[14]

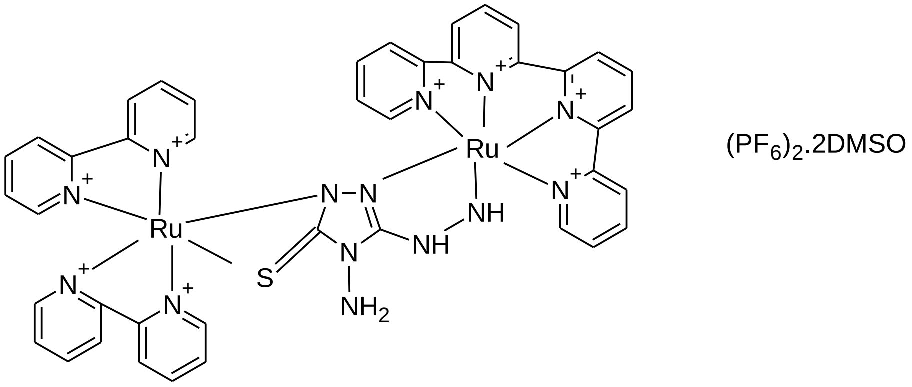


Fig. 8 Proposed structure for $Ru_2L(bpy)_4(PF6)_2$.2DMSO

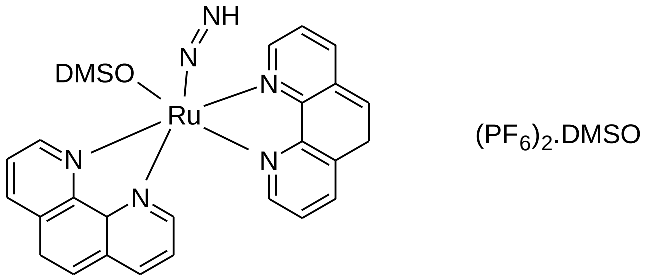


Fig.9 Proposed structure for $[Ru(N_2)(phen)_2DMSO](PF_6)_2$.DMSO

C. Schiff bases as complexing agents

1. Schiff bases derived from o-phenylenediamine

Schiff bases of o-phenylenediamine and its complexes have a variety of applications including biological,[15] clinical[16] and analytical.[17] Earlier work have shown that some drugs showed increased activity when administered as metal chelates rather than as organic compounds[15,16] and that the coordinating possibility of o-phenylenediamine has been improved by condensing with a variety of carbonyl compounds. The synthesis of a tetradentate ligand formed by the condensation of o-phenylenediamine and acetoacetanilide was reported.[18] This ligand system has both nitrogen and oxygen donor sites. It coordinates with the metal ion in a tetradentate manner through the enolisable carbonyl group of the acetoacetanilide moiety and the azomethine nitrogen atoms of the Schiff base. The structure of the ligand is shown in Fig.10.

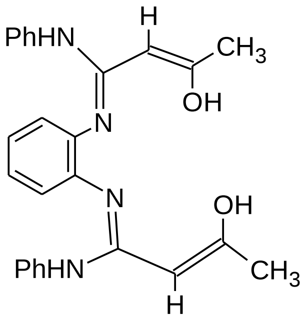
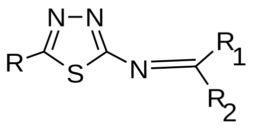


Fig.10 Structure of the ligand

The analytical data of the complexes corresponded to the general formula ML while that of the manganese complex was MnL.H_2O. Magnetic moment values of the complexes at room temperature were consistent with square planar geometry around the central metal ion except for the Mn(II) and VO(II) complexes which showed octahedral and square pyramidal geometries respectively. The chelates showed no appreciable conductance and this supported their neutral nature. Thermal analysis showed that the manganese complex lost two water molecules at about 170ºC , which suggested the presence of two molecules of water coordinated to the central metal ion. This was further confirmed by its characteristic IR spectrum.

2. Schiff bases derived from 2-amino-5-aryl-1,3,4-thiadiazole

The synthesis and structural features of Co(II), Ni(II), Cu(II) and Zn(II) complexes of Schiff bases derived from the condensation of 2-amino-5-phenyl-1,3,4-thiadiazole with 2-hydroxy1-1-naphthaldehyde (HL^1) or 2-hydroxyacetophenone (HL^2) and derived from 2-amino-5-(2-methoxyphenyl)-1,3,4-thiadiazole and 2-hydroxybenzaldehyde (HL^3) or 2-hydroxyacetophenone(HL^4) were synthesized and characterised by elemental analyses, molar conductance, magnetic measurements, infrared and electronic spectral studies. The analytical data show 1:2 metal to ligand stoichiometry of the complexes. Magnetic moments, along with electronic spectral data, suggest a distorted octahedral geometry for the Co, Ni and Cu complexes, whereas, a tetrahedral structure was proposed for the Zn complexes. The presence of water molecules in the Co(II), Ni(II) and Cu(II) complexes was also indicated by the thermal studies. Thiadiazoles (Fig.11) have been reported to display fungicidal properties by virtue of the –N=C-S- linkage, which is a possible toxophore in many pesticides.[19] 2,5-Disubstituted-1,3,4-thiadiazoles have been found to possess bacteriostatic, herbicidal, radio protective and diuretic properties.[19-21]



R=C_6H_5	R_1=H	R=2 $HOC_{10}H_5$
R=C_6H_5	R=CH_3	R=2 OHC_6H_4
R =2 $OCH_3C_6H_4$	R=H	R=2 HOC_6H_4
R =2 $OCH_3C_6H_4$	R=CH_3	R=2 HOC_6H_4

Fig.11 Structure of the Schiff bases

The thermograms of the complexes showed no mass-loss upto ~ 100°C indicating the absence of lattice water. Sharp endothermic peaks observed in the range 162-240°C for the complexes of Co(II), 108-170°C for Ni(II) and 115-150°C for Cu(II) in the DTA curves , in conjunction with the mass-loss in the TG curves corresponding to two water molecules, confirmed the stoichiometry $ML_2.H_2O$ for the Co(II), Ni(II) and Cu(II) complexes. Thereafter, the decomposition of the ligands took place continuously upto ~700°C giving metal(II) oxide as residue. However, the mass-loss started at 238°C in the case of Zn(II) complexes and continued slowly and linearly. Finally a stable plateau was obtained in the TG curve, corresponding to the zinc oxide. The general order of the stabilities on the basis of the DTG peak temperatures and partial decomposition temperatures was:Zn>Co>Cu>Ni.

The magnetic moments of the Cu(II) complexes were in the range 1.93-1.82 B.M., indicating the presence of one unpaired electron per copper ion. Their electronic spectra showed a broad envelope around 700-689 nm due to the $^{2}E_{g} \rightarrow {}^{2}T_{2g}$ transition in an octahedral field. The broadening of the band may be due to Jahn-Teller effect. The observed magnetic moments [(-93.0 to 6.0) x 10^{-4} cgs units] of the Zn(II) complexes indicated their diamagnetic behaviour. All the electronic spectra showed a broad band in the region 230-260 nm and a weaker band in the range 275-325 nm which are characteristic of heterocyclic systems with extended conjugation associates with π-π* transitions.[22] A band in the region

335-380 nm may be due to the secondary band of benzene ring /intramolecular charge transfer band within the ligand moiety.

The position of υ_1 and the values of the electronic parameters such as 10 Dq and β calculated from the υ_2 and υ_3 transitions indicated the presence of an octahedral environment around the Co(II) ion and Ni(II) ions, in conformity with the conclusions drawn from the magnetic moment values.[23] The β values for the Co(II) and Ni(II) complexes were found to be less than unity, indicating partial covalency in the metal-ligand due to the presence of appreciable orbital overlap.[23]

Based on the analytical results, spectral data, magnetic moments and thermal behaviour, they suggested a distorted octahedral stereochemistry for the Co(II), Ni(II) and Cu(II) complexes and tetrahedral coordination for the Zn(II) complexes (Fig.12).

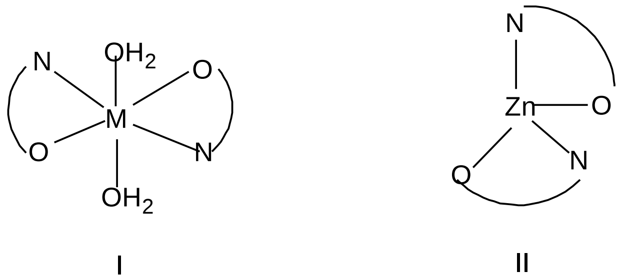


Fig. 12 Proposed structures for the (I) $ML_2.H_2O$ and II ZnL_2 (where M=Co,Ni and Cu; NO=coordinating sites for L).

D. Applications of Schiff Bases

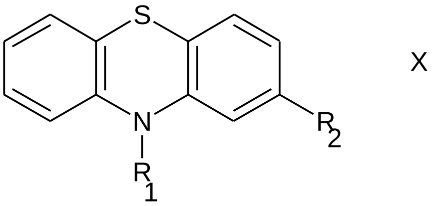
1. As catalysts

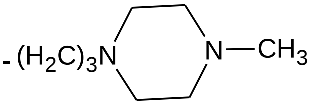
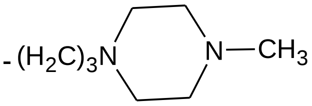
The isolation and structural investigation of dioxobridgedmolybdenum(IV) and tungsten(IV) complexes with methoxypromazine(MP), prochlorperazine(PCP) and trifluoperazine(TFP) and their interactions with biologically important compounds such as L-cysteine and L-histidine were reported. Molybenum as a trace element plays an important role in metabolic processes.[24] Complexes of molybdenum(V) and molybdenum(VI) with cysteine,[25]histidine[26] and organic sulphur compounds[27] are of interest as models for molybdenum-containing enzymes. These enzymes are known to catalyse a number of important biological oxotransfer reactions where the valence of molybdenum alternates between +6 and +4 in reactions with substrates and subsequent reactivation.[28] N-alkylphenothiazines(NAP) (Table 2) are versatile anticholinergic, antihistamine and antiemetic compounds.[29] The study of metal-phenothiazine complexes has gained much importance in recent years due to their potential pharmacological activities. The possible use of metal-phenothiazine complexes as fungicides and increase in their fungicidal activity by complexation of phenothiazines with copper(II),[30] dioxouranium(VI),[31] yttrium(III)[32] and lanthanides(III)[33] have been reported.

The interaction of ammonium molybdate tetrahydrate or sodium tungstate dihydrate with N-alkylphenothiazines resulted in the formation of M(IV)-NAP complexes (Table 2). The reduction of M(VI) to M(IV) may be attributed to the behaviour of N-alkylphenothiazines which are excellent electron donors.

TABLE 2

STRUCTURES, TRIVIAL AND SYSTEMATIC NAMES OF N-ALKYLPHENOTHIAZINES

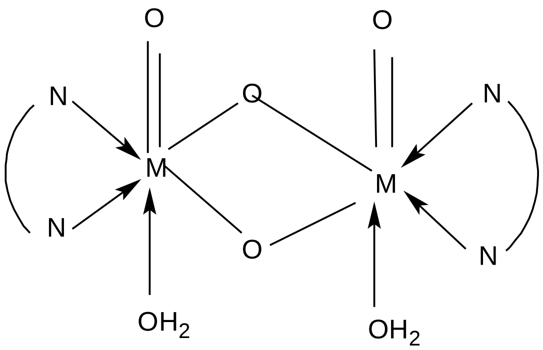


TRIVIAL(SYSTEMATIC) NAME OF THE LIGAND	R_1	R_2	X
Methoxypromazine maleate (MPM) 10-[3-(Dimethylamino)propyl] 2-methoxy phenothiazine meleate)	$-CH_2)_3N(CH_3)_2$	$-OCH_3$	$C_4H_4O_4$
Prochlorperazine dimaleate (PCPD) 10-[3-(4-Methyl-1-piperazinyl)propyl]2-chloro phenothiazine dimaleate)		-Cl	2 $C_4H_4O_4$
Trifluoperazine hydrochloride (TFPH) 10-[3-(4-Methyl-1-piperazinyl)propyl]2-trifluoromethyl phenothiazine hydrochloride)		$-CF_3$	HCl

The maleate or chloride ions of the ligand go into solution during the reaction and do not participate in the coordination with metal ions. The analytical data corresponded with the formula $[M_2O_4(L)_2(H_2O)_2]$, where M=molybdenum or tungsten and L=methoxypromaxine, prochlorperazine or trifluoperazine.

The complexes were coloured, non-hygroscopic, and stable at room temperature for long periods. They did not possess sharp melting points. The complexes were insoluble in water and common organic solvents but soluble in DMF and DMSO. The molar conductance values measured in DMF indicated the non-electrolytic nature of the complexes. Ion-exchange studies showed that the complexes were neutral. These results were consistent with the stoichiometry assumed for the complexes on the basis of analytical data.

The interactions of M(IV)-NAP complexes with biologically important compounds such as L-cysteine and L-histidine were carried out to determine the ease of substitution of the coordinated ligands. These interactions resulted in the immediate formation of solid complexes by the displacement of the NAP ligands. The complexes thus obtained were quite stable for long periods. They exhibited low magnetic moments in accordance with dimeric M(IV)-NAP complexes due either to spin-spin interaction or to direct metal-metal bond. The analytical- and magnetic data of the complexes showed that there is no significant change in the composition or structure of the substituted products. Based on the above discussions, the following structure was proposed for the M(IV)-NAP complexes (Fig.13).

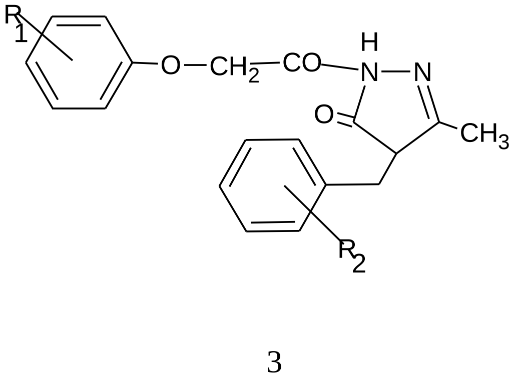


M=Mo(IV) or W(IV) and L=N-alkylphenothiazine

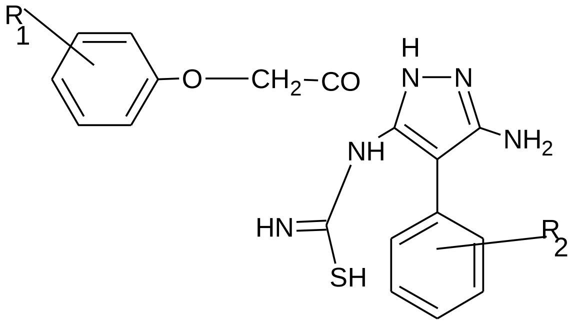
Fig.13 Structure of M(IV)-NAP complexes

2. <u>As histaminic agents</u>

5-pyrazolones are known to possess antiinflammatory,[34,35] antipyretic,[36] antifungal,[37] antidiabetic,[38] analgesic,[39] vasodilating, respiration stimulating[40] and hypotensive[41] properties. Several reports have appeared in literature which highlight their chemistry and uses.[42] Some bis-heterocyclic compounds like 4-substituted aroyloxy-methyl-carbonyl-3-methyl-4-substitutedphenyl-6-imino-4,7-dihydro-1,3-thiazino-(5,4-d) pyrazolones(Fig.14) have been reported and these compounds have been tested for antihistaminic activity. These compounds have shown histamine-like activity instead of antihistaminic activity.



3



4

	R_1	R_2
a	H	H
b	4-Cl	4-Cl
c	4-CH_3	4-Cl
d	H	4-CH_3
e	4-Cl	H
f	4-CH_3	4-Cl
g	H	2-OCH_3
h	4-Cl	4-CH_3
I	4-CH_3	H
j	H	4-Cl
k	4-Cl	2-OCH_3
l	4-CH_3	4-CH_3

Fig.14 Structures of the *bis*-heterocyclic compounds

The overnight tested guinea pig weighing 400-600g was selected. The drugs used were histamine and selected samples of 3a, 3f, 3h, 3k, 4b, 4f, 4h and 4k. The stock solution of histamine at a concentration of 1 mg/ml was prepared and selected compounds were made into suspension using 1 % Tween-80 at a concentration of 40 mg/mL. The tyrode physiological solution was also prepared for guinea pig ileum preparation.

One piece of the ileum(2-3 cm long) was selected and the top and bottom ends with lumen openings were tied by a thread. It was mounted in organ bath containing tyrode solution at 32-35ºC with oxygen supply. After 30 minutes, the responses due to histamine and due to histamine samples at various concentrations were recorded on the smoked drum. The results indicated that the samples of compounds 3b, 3f, 3h, 4b, 4f, 4h and 4k have shown histaminic-like activity instead of antihistaminic activity.

The chemistry[43] and wide range of pharmaceutical properties of 2-pyrazoline-5-one derivatives, like germicides,[44] antimicrobial agents,[45] antiactinics,[46] antidiuretics,[47] analgesics and antipyretics,[48] antifungals,[49] antihistaminics,[50] anti-M.tuberculosis,[51] antirheumatics,[52] antibacterial[53] and similar such diseases have been cited. Sulpha drugs are well known chemotherapeutic agents. 2-pyridine carboxylic acid hydrazide [54,55] and their derivatives are generally used as antibacterial agent.

3. For potentiometric and polarographic study

Phenylazo-5-pyrazolones are of great importance in technical dye chemistry.[56] They are also used as indicators in complexometric titrations.[57] Snavely *et al* [58] prepared metal complexes of some of these dyes and determined their stabilities. The study of Eu(III) complexes with 1-phenyl-3-methyl-4-

benzoyl-5-pyrazolone dyes by potentiometric and polarographic methods has been presented.

The potentiometric titration indicated that the free ligand is diprotic(H_2L). The first step corresponds to the phenolic group and the second step to deprotonation of hydrazo moiety. The titration curves were greatly altered in presence of Eu(III) and corresponded to complex formation according to

$$2H_2L + Eu^{3+} \rightarrow EuL_2^- + 4H^+$$

The stability constants were calculated using Irving-Rossotti expression[59] and were found to depend on the structure of the ligand.

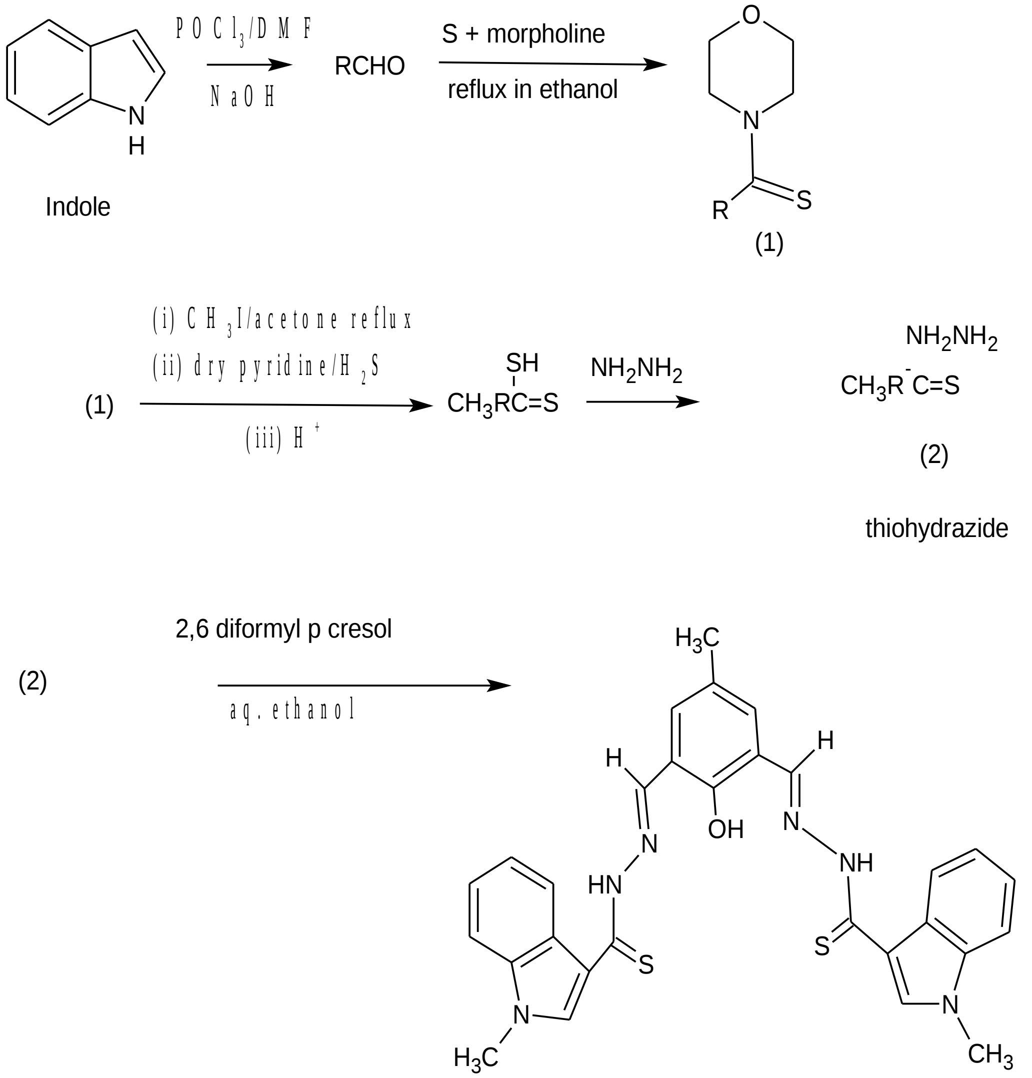
Polarographic studies were carried out in solutions containing $1.5x10^{-3}$ M ligand in universal buffer of pH=10, in dioxane-water mixture (40%,v/v). This amperometric titration could thus be applied successfully for the determination of trace quantities of Eu(III) by azopyrazolone ligands and *vice versa*. The above amperometric titration could be used to determine precisely the composition of the Eu(III) azopyrazolone complex by means of reverse molar ratio.[60]

4. Design of synthetic models

A novel dinucleating pentadentate Schiff base, resulting from the condensation of 2,6-diformyl-p-cresol and N-methyl-indoyl-3-thiohydrazide and its Zn complex have been prepared and characterised on the basis of elemental analysis, IR, UV-Visible ,^{1}H NMR and C^{13} NMR studies. The ligand was acyclic and consisted of a phenolate head unit with two inbuilt azomethine shoulders and two indole thiohydrazide arms forming SNONS coordinating sites. NMR and IR spectral studies showed that the ligand existed in thioketo form. Each Zn ion in the dinuclear core was in tetrahedral environment with endogenous phenolate bridging and exogenous acetate bridging. The zinc complex in DMF exhibited fluorescence. Zinc-containing, carboxylate-bridged bimetallic centres were widespread structural motifs in hydrolytic metalloenzymes such as phosphatase and amino peptidases and some synthetic dinuclear Zn(II) complexes were found to have functions in RNA hydrolyse and dephosphorylation.[61-66]

A thiohydrazide moiety was built on N-methyl indole and its framework was extended to construct a compartmental ligand by condensing it with dicarbonyl compound and to synthesize zinc complex to study its coordinating behaviour. By synthesising these compounds, Revankar *et al*[67] were heading towards the design of synthetic models of sulphur-rich zinc enzymes.

Scheme 1 outlines the synthesis of 2,6-Diformyl-p-cresol-bis[N-methylindoyl-3-thiohydrazone].



2,6-diformyl-p-cresol-bis(N-methylindolyl)-3-hiohydrazome

Scheme 1

The moderately intense broad band for the zinc complex in the region 350-425nm in the electronic spectra was assigned to S → Zn(II) ligand to metal charge-transfer transition (LMCT). The LMCT maxima for the phenolate complex showed line broadening, with a tail running into the visible part of the spectrum. This may result from a phenolate to Zn(II) LMCT band being superimposed on the low energy side of S → Zn(II) LMCT. Except this, the complex showed no appreciable absorptions in the region above 450 nm in DMF solution, in accord with the d^{10} electronic condiguration of the Zn(II) ion.

Fluorescence spectra of the complex showed a strong emission band at 486 nm when excited with 350 nm radiation, at room temperature with a sample concentration of 0.1mmol in DMF. Generally, fused-ring systems like indole and its derivatives show fluorescence. The free ligand showed an enhanced fluorescent intensity on complexation with diamagnetic zinc ion. The emission was neither MLCT (metal-to-ligand charge transfer) nor LMCT in nature. It was tentatively assigned to intraligand (π-π) fluorescence , since a similar emission was also observed for the free ligand, but with reduced intensity. It was known that lone pairs of electron on nitrogen and on thioamide chromophore could quench the fluorescence of indole moiety through photo-induced electron transfer. Draining out of these pairs of electrons on to the metal orbital via complex formation caused a suppression of this fluorescence quenching and, therefore, resulted in fluorescence intensity. The formation of metal chelates with metal ions, in general, also promoted fluorescence by promoting rigidity and minimizing internal vibrations. At higher concentration (1 mmol), the fluorescence intensity decreased considerably due to self-quenching. The proposed structure of the complex is given in Fig. 15.

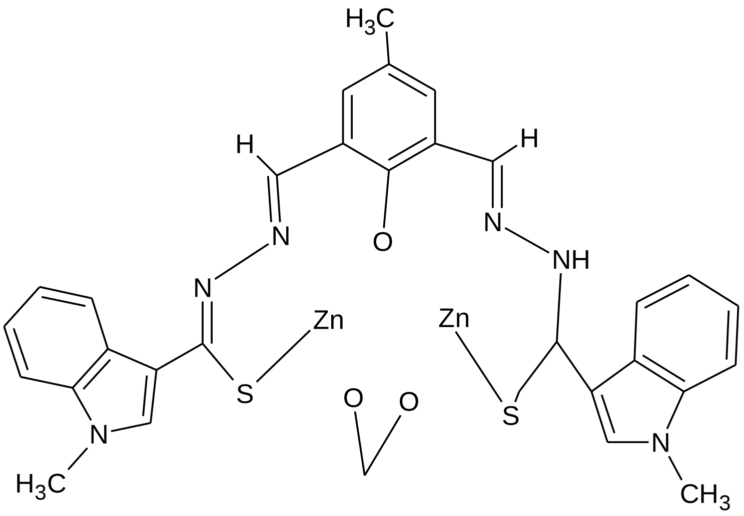
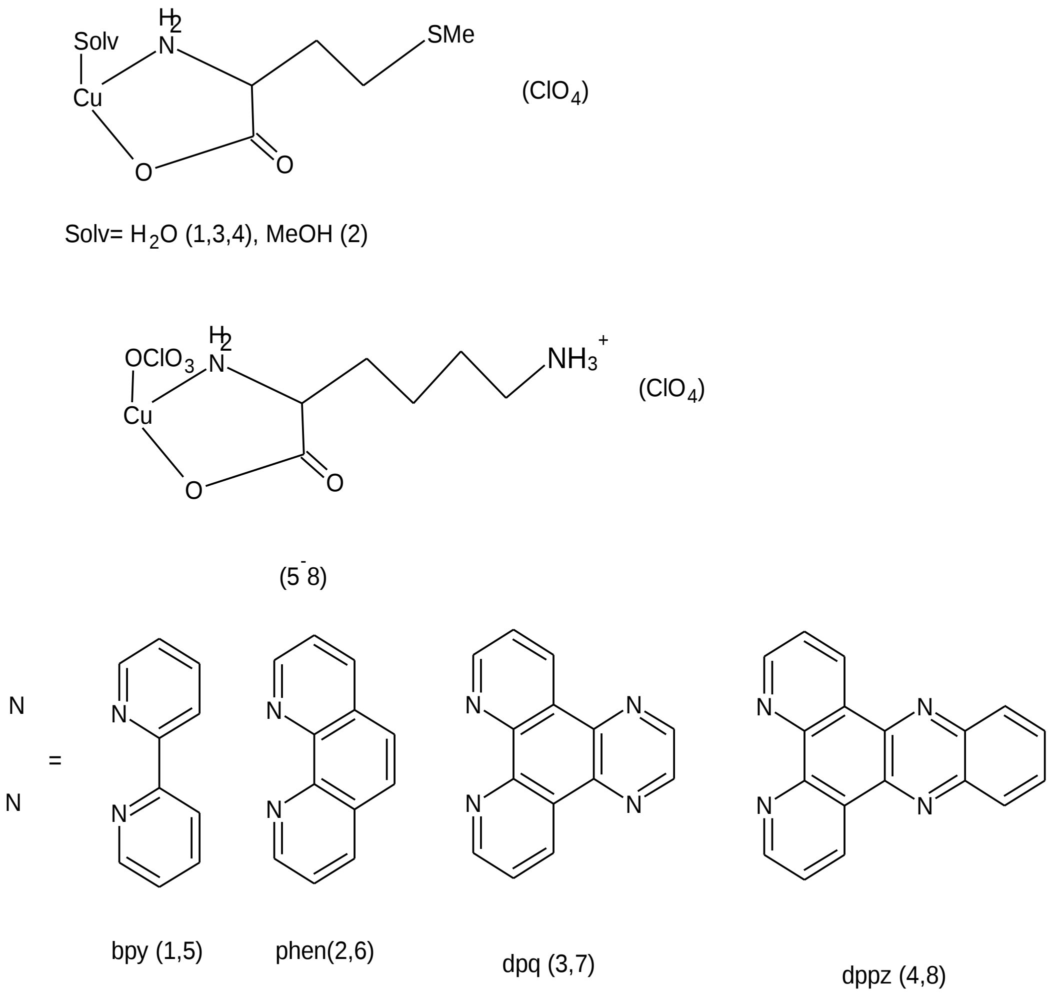


Fig. 15 Proposed structure of the complex

5. Photocleavage of DNA

Transition metal complexes that are suitable for binding and cleaving double-stranded DNA are of considerable interest due to their various applications in nucleic acid chemistry like foot-printing and sequence– specific binding agents, for modeling the restriction enzymes in genomic research and as structural probes for therapeutic applications in cancer treatment.[67-77] Cleavage can be achieved by targeting its basic constituents like base and/or sugar by an oxidative pathway or by hydrolysis of phosphoester linkages. Iron and copper complexes are known to be useful for oxidative cleavage of DNA involving nucleobase oxidation and/or degradation of sugar by abstraction of deoxyribose hydrogen atom(s),while complexes containing Lewis acids like copper(II) and zinc(II) are suitable for hydrolytic cleavage of DNA. Oxidative cleavage of DNA could take place by chemical or photochemical means. Sigman and coworkers have reported *bis*(phen)copper(I) complex as the first copper-based “ chemical nuclease” that cleaves DNA in the presence of H_2O_2 and a thiol.[68,78] Similarly, the anticancer antibiotic bleomycins containing iron cleave DNA in an oxidative manner.[79,80]

New ternary copper(II) complexes of the type “A-Cu(II) B” where the aminoacid (A) , like L-methionine(L-met) or L-lysine(L-lys) and the DNA binder (B) such as phenanthroline bases are covalently linked to the metal ion to explore the effect of the metal ion on the photo-induced DNA cleavage activity of the complexes were reported. (Scheme 2). The complexes of formulation [Cu(L-met)B(Solv)](ClO_4) (1-4)[81,82] and [Cu(L-lys)B(ClO_4)]ClO_4) (5-8)[83] where B is a heterocyclic base like 2,2′bipyridine(bpy,1,5), 1,10-phenanthroline(phen,2,6), dipyrido[3,2-d:2′,3′-f]quinoxaline(dpq,3,7) and dipyrido[3,2-a:2′,3′-c]phenazine(dppz,4,8), show efficient photo induced DNA cleavage activity on irradiation with red light at 632.8 nm which is close to the photoactivation wavelength used for PDT drug Photofrin. Organometallic amino acid complexes were also known to photochemically cleave DNA on exposure to UV radiation.[84] The photo-induced DNA cleavage activity of the L-met complexes was studied at 365 nm UV and 632.8 nm CW He-Ne laser(3 mW). The bpy complex was cleavage inactive as this complex did not bind to DNA. The cleavage activity of the dpq and dppz complexes was significantly better than the phen complexes. The cleavage activity of the L-lysine complexes has been studied at 365 nm and 694 nm (pulsed ruby laser, 1/6 Hz,20ns). The complexes showed efficient red light induced DNA cleavage activity with the L-lysine species being more active than the L-methionine analogues.



Scheme 2

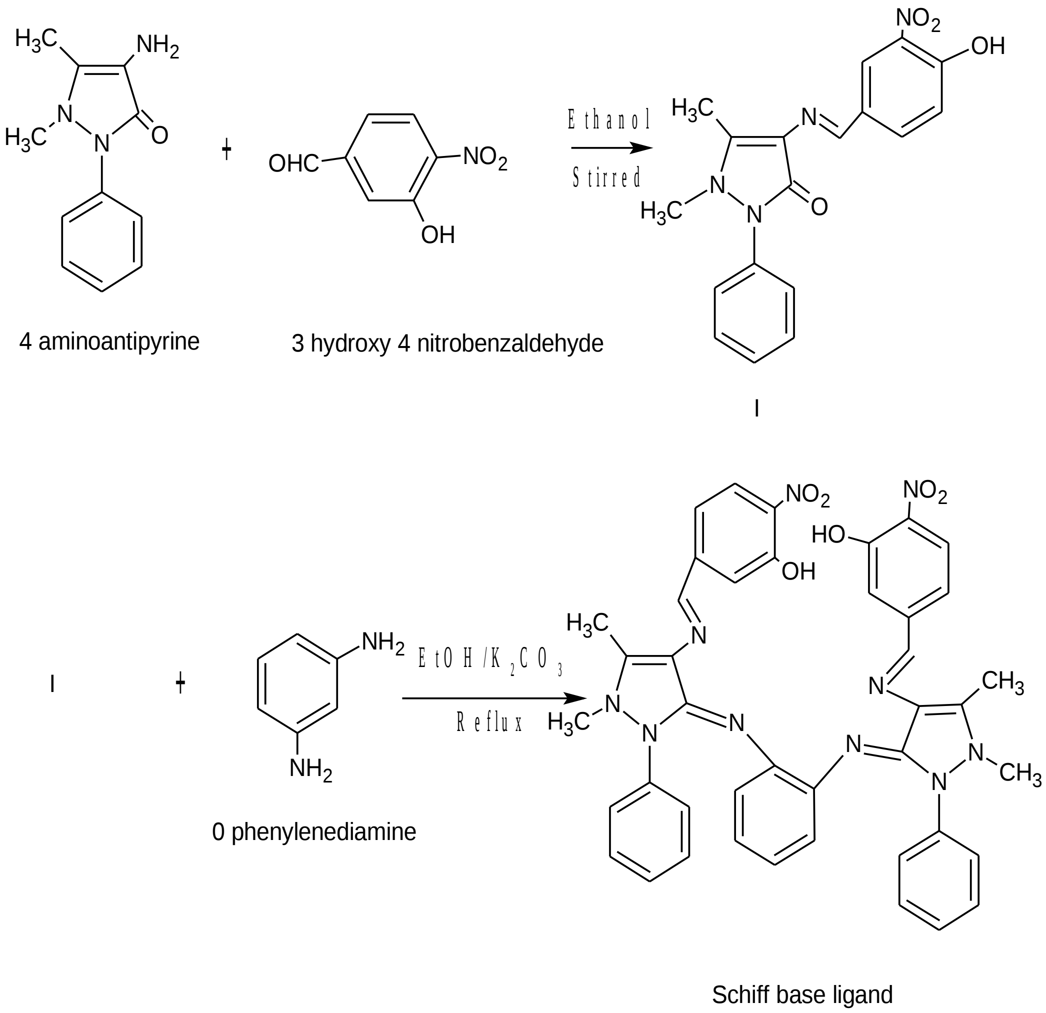
The photosensitizing effect of L-met and L-lys on copper–bound form was evidenced from the cleavage activity of their phen complexes as phen ligand itself was not a photosensitizer.

Photo-induced DNA cleavage activity of the binary and ternary copper(II) complexes revealed the important roles of the paramagnetic transition metal, DNA binder phenanthroline bases and the photosensitizers. Red-light induced DNA cleavage activity of the present complexes was of significance as binding of transition metal like copper(II) to porphyrin bases leads to reduction in cleavage activity. Long wavelength DNA cleavage activity made these copper(II) complexes potential candidates for further design of molecules suitable for photodynamic therapy (PDT) applications and as alternatives to the PDT anticancer drug, Photofrin.

The red light-induced DNA cleavage activity of the *bis*-dpq copper(II) complex was of importance for designing analogous complexes while hybrid quinoxalines for cellular applications and towards understanding the function of quinoxaline-based antitumour antibiotics in the presence of bio-essential copper ions. The ternary aminoacid copper(II) complexes were also useful for designing peptide-based conjugates containing metal ion for cellular application. Suphur containing ligands with their longer triplet state lifetimes were suitable for activation of molecular oxygen. DNA cleavage under anaerobic conditions has potential advantages in therapeutic applications.

DNA cleavage activity of the copper(II) complexes on red light exposure presented the first direct evidence for the dual involvement of the copper (II) d-d band and the ligand-to-metal charge transfer band in the photosensitization process leading to the an efficient DNA cleavage activity at wavelengths within the PDT window. This work has opened up a new area of research involving 3d-metal complexes for photocleavage of DNA with an objective for future PDT applications.

The synthesis, characterisation, redox, antimicrobial and DNA cleavage studies of transition metal complexes containing Schiff base derived from 4-aminoantipyrine, 3-hydroxy-4-nitrobenzaldehyde and o-phenylenediamine have been reported(Scheme 3). The Schiff base of 4-aminoantipyrine and its complexes have a variety of applications in biological, clinical, analytical and pharmacological areas.[85-87] It had been reported earlier that some drugs showed increased activity when administered as metal complexes rather than as organic compounds.[88,89] Deoxyribonucleic acid (DNA) is the primary target molecule for most anticancer and antiviral therapies according to cell biologists. Investigations on the interaction of DNA with small molecules are important in the design of new types of pharmaceutical molecules. Since the chemical nuclease activity of transition metal complexes was discovered in the 1980s,[90,91] studying the interaction model and the mechanism of transition metal complexes with DNA and exploring the application of metal complexes in antineoplastic medication, molecular biology and bioengineering has become hotspots in recent years. Some kind of metal complexes interacted with DNA could induce the breakage of DNA strands by appropriate methods. In the case of cancer genes, after DNA strands are cleaved, the double DNA strands break The replication ability of cancer gene is destroyed. Copper complex could cleave DNA in the presence of ascorbate or hydroquinone.[92]



Scheme 3. Formation of Schiff base ligand

The cleavage efficiency of the Cu, Ni and Co complexes compared to that of the control is due to their efficient DNA binding ability. The metal complexes were able to convert supercoiled DNA into open circular DNA . The proposed general oxidative mechanisms and account of DNA cleavage by hydroxyl radicals via abstraction of a hydrogen atom from sugar units that predict the release of specific residues arising from transformed sugars, depending on the position from which the hydrogen atom is removed. The cleavage is inhibited by free radical scavengers implying that hydroxyl radical or peroxy derivatives mediate the cleavage reaction. The reaction is modulated by a metallocomplex bound hydroxyl radical or a peroxo species generated from the co-reactant H_2O_2.

The CT DNA gel electrophoresis experiment was conducted at 35ºC using our synthesized complexes in the presence of H_2O_2 as an oxidant. The results indicated that at very low concentration, few complexes exhibit nuclease activity in the presence of H_2O_2. Control experiment using DNA alone does not show any significant cleavage of CT-DNA even on longer exposure time. It had been concluded that the copper, nickel and cobalt complexes cleaved DNA as compared to control DNA while other complexes did not cleave DNA in the presence of H_2O_2. Probably this may be due to the formation of redox couple of the metal ions and its behaviour.

6. Analytical applications

a) Separation of Cu(II) and Zn(II)

Amberlite IRC-50 was functionalized by 8-aminoquinoline group and the resulting resin was characterised by elemental analyses, infrared spectra and metal ion capacities. The resin was very useful for preconcentration, separation and sequential determination of trace amounts of copper and zinc by atomic absorption spectrometry.

Separation of Cu(II) and Zn(II) has been achieved by many workers using the chelating groups like imidazole,[93] 4-(2-thiazolylazo)resorcinol,[94] pyragallol,[95] pyrocatechol,[96] 6-mercaptopurine[97], etc. Solid surfaces having heterocyclic donor sites have specific activity towards transition metal ion.[98] 8-aminoquinoline

(AQ) contains heterocyclic nitrogen donors and incorporation of this ligand into polymeric matrix may lead to a solid surface which may be effective for the separation of copper and zinc from each other.

Separation of Cu(II) and Zn(II) were mixed in 100 ml of double distilled water and passed through the column loaded with 1 g of AQ resin after maintaining the pH at desired level. Sorbed Cu(II) was eluted completely with about 10 bed volume 1 M neutral SSA and sorbed Zn(II) was eluted completely with 25 ml of 1M HCl. The result showed that 98.9% Cu(II) and 99.0% Zn(II) could be recovered from the binary mixtures of these two ions.

The results showed that resin containing 8-aminoquinoline group was very selective for Cu(II) and Zn(II) due to the presence of heterocyclic nitrogen of the pyridine moiety and may be followed by chelation via N atom of amide residue. The resin thus had an immense potentiality for the effective preconcentration of trace copper and zinc from biological matrices. Microwave-assisted digestion followed by atomic absorption spectroscopy(AAS) allowed reliable determination of these two metals in biological samples in which copper and zinc may be present at low levels. Thus this method for the determination of copper and zinc in biological samples was an attractive one.

b) Spectrophotometric determination of nickel(II)

Aqueous solution of salicylaldehyde guanylhydrazone (SAG) gave an yellow coloured complex with Ni(II) in alkaline medium, which led to the development of simple and rapid spectrophotometric method for the determination of nickel.

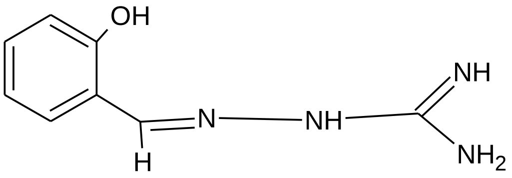


Fig. 16 Structure of SAG

A stock solution of SAG (0.01 mol) was prepared in distilled water. A stock solution containing 1mg/ml nickel was prepared by dissolving nickel chloride hexahydrate(A.R) in distilled water containing a little concentrated HCl and was standardised using dimethylglyoxime.[99] The working solution was prepared by appropriate dilution. The buffer solution was prepared by mixing appropriate amount of borax and NaOH.

To an aliquot of the solution containing about 10 µg of Ni(II) was added 0.6 ml of the reagent (SAG) solution (1.0 x 10^{-3}M), pH of the solution was adjusted to 9.52 by adding borax buffer solution (1.0 ml) and made upto 10 ml with distilled water. The absorbance of the complex was measured at 370 nm against the reagent blank. The concentration of nickel was determined from a calibration curve.

7. Industrial applications

2-Thiorotic acid (6-hydroxy-2-mercaptopyrimidine-2-carboxylic acid) was used a new spectrophotometric reagent for the determination of copper(II) ion in the pickle liquor discharged from a copper wire treatment plant at Bhilai Wires Limited, Bihar. 2-Thiorotic acid ($C_5H_4O_3N_2S$) was synthesised according to a reported method[100] by subjecting 2-thiouracyl-4-aldehyde to Cannizaro reaction. A 0.02 M solution of the reagent (98.9%) was prepared in 100 ml of a solvent mixture of pyridine-ethanol-water(75:20:5, v/v). Aqueous solution of cupric sulphate 0.5 mg Cu/ml was used.

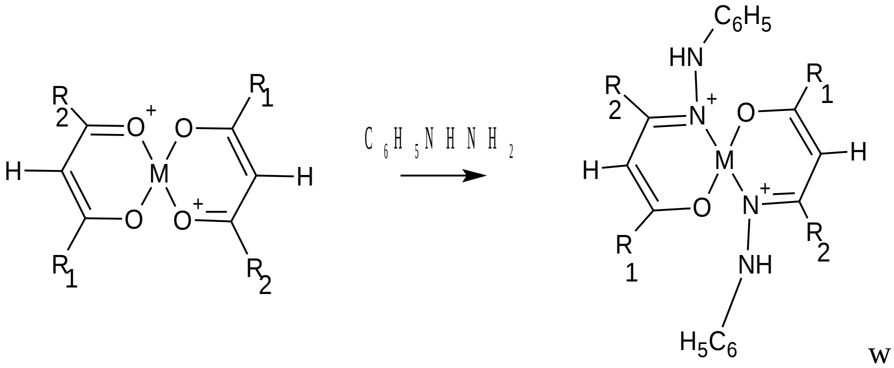
Aliquots of Cu(II) solution containing 1.5-3.0 mg of Cu(II) were treated with equal volume of the reagent solution, and the mixture was diluted to 100 ml using the same solvent mixture and allowed to stand for 10 min. The absorbances were measured at 660 nm using a Systronics 103 spectrophotometer. A calibration graph was also constructed.

In three different experiments, each with a set of five, containing 1.5, 2.4 and 3.0 mg (100 ml) of Cu(II) , the standard deviation values were, respectively, 0.0022, 0.0013 and 0.0045. The molar absorptivity and the Sandell's sensitivity were found to be $1.04 \times 10^2\ dm^3mol^{-1}cm^{-1}$ and $0.6240\ \mu gcm^{-2}$ respectively.

For estimation of copper (II) in the waste liquor , iron in aliquots (5 ml) was removed as hydrated oxide (1:10 ammonia). The filtrate after removal of excess ammonia was adjusted to pH~ 7 (dilute H_2SO_4), treated with 2-thioorotic acid (0.02M; 5 ml) and adjusted to a definite volume by the diluent solutions. After 10 minutes, the absorbance was measured at 660 nm and the Cu(II) content was determined from the calibration curve. A mean value of 985 mg dm^{-3} was obtained from three experiments.

8. As antimicrobial agents

The formation of phenylhydrazones is a characteristic reaction of carbonyl group with phenylhydrazine. Phenylhydrazones were synthesized by the condensation of phenylhydrazine with β-diketones/β-keto esters of Co(II), Co(III), Ni(II) and Cu(II) complexes and their antimicrobial activities were studied.[101] It is well known that pyrazole derivatives are formed when β-diketone/β-ketoester reacts with phenylhydrazine.[102] But in this case, metal phenylhydrazone derivatives were formed which was due to central metal atom of the metal β-diketone/β-ketoester. The presence of metal prohibits the possibility of the formation of pyrazole ring derivatives. This fact was supported by IR, UV and magnetic susceptibility data. In several similar systems, the formation of metal phenylhydrazone derivatives have been established.[103-105] Therefore the probable reaction could be written as given in Fig. 17.



where M=Cu(II), Co(II), Ni(II)

R_1=R_2=CH_3 in β-diketone

R_1=OC_2H_5; R_2=CH_3 in β-ketoester

Fig. 17 Formation of phenylhydrazones

All the product complexes were screened *in vitro* for their antibacterial activity against the gram-positive bacteria, Escherichia coli by well-diffusion technique. All the product complexes showed better inhibitory zone at a concentration of 1000µg/10µL. Decreasing the concentration by about ten times, the inhibitions of the complexes was also decreased about half the value. All the product complexes were screened *in vitro* for their antifungal activity against Candida albicans. In all the complexes the MIC(minimum inhibitory concentration) values were found to be less than 10µg/10µL which showed the better inhibitory effect.

9. As antitumour agents

1,4-Dibenzoyl-3-thiosemicarbazide(DBtsc) contains oxygen, sulphur and nitrogen as potential donor atoms and is liable to form deprotonated complexes by the loss of hydrazinic proton(s) *via* enolisation/thioenolisation. The complexes of this ligand with 3d-metal ions were synthesized and their antifungal, antibacterial and *in vitro* antitumour activity were studied.[106]

Antibacterial activities of the ligand and the soluble complexes were evaluated by the disc diffusion technique. All the thiocyanato and chloro complexes inhibited the growth of Pseudomonas flauracences, whereas the ligand and the other complexes were inactive against other seven tested bacteria.

The antifungal activities of the ligand and the soluble complexes were studied by the spore germination technique. The ligand [M(DBtsc-HCl], where [M=Co(II) or Ni(II) and Zn(DBtsc-H)(SCN)] showed moderate activity against Aspergillus flavus, while [M(DBtsc-H)(SCN)], where M=mangansese(II) or cobalt(II)], [Ni(DBtsc-H)(SCN) (H_2O], [Mn(DBtsc)Cl_2] and [Zn(DBtsc-H)Cl] showed good antifungal activity against A. flavus. The ligand showed poor activity, while [M(DBtsc-H)(SCN)], where [M=cobalt(II) or zinc(II) and [Zn(DBtsc-H)Cl] showed moderate activity against Aspergillus niger. [Mn(DBtsc-H)(SCN), [Ni(DBtsc-H)(SCN)(H_2O)], [M(DBtsc-H)Cl], where [M=cobalt (II) or nickel(II)] and [Mn(DBtsc)Cl_2] showed good antifungal activity against A. niger. [Cu(DBtsc-H)(SCN)H_2O] and [Cu(DBtsc-H)Cl] exhibited excellent antifungal activity against both the fungi.

In vitro DNA synthesis inhibition assay was performed. The percentage inhibition of incorporation was calculated as follows

% inhibition=1-(CPM in treated tumour cells /CPM in untreated tumour cells) x100

where CPM=counts per minute.

An MTT assay was used to measure the cytotoxic effect of the ligand and its complexes.

It has been found that the percentage of cell growth in the presence of DBtsc was less than its Cu(II) thiocyanato/chloro complexes. Percentage inhibition of thymidine incorporation data showed that the ligand has a pronounced inhibitory effect on DNA synthesis, whereas its metal complexes have less inhibitory effect. The ligand showed higher inhibition of thymidine incorporation in Jurket and Daltons lymphoma tumour cells than

[Cu(DBtsc-H)(SCN)(H2O)] and [Cu(DBtsc-H)Cl]. Further, the MTT assay performed at 10μg cm^{-3} corroborated the same finding as was evident from the low LD_{50} values for the ligand than those of [Cu(DBtsc-H)(SCN)(H_2O)] and [Cu(DBtsc-H)Cl]. It has been found that the growth inhibition of tumour cells was due to apoptosis in the case of the ligand, whereas the antitumour activity of the copper(II) complexes was not due to apoptosis. It appeared that the metal complexes inhibit cellular growth by binding with DNA.

E. Scope of the present investigation

Pyrazole (1,2-diazole) is isomeric with imidazole (1,3-diazole), an integral part of the well-known histidine molecule, which provides an important binding site in biological systems, playing a vital role in metal-protein interactions.[107,,108] During recent years, a substantial amount of research has been generated around the studies involving the coordination characteristics of both imidazole and pyrazole–derived (model) ligands from various aspects in order to have meaningful information regarding the binding sites of the *in vivo* metal ions.

A perusal of the literature revealed that 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone is an excellent chelating agent[109] and their complexes are becoming increasingly important as biochemical, analytical and antimicrobial reagents.

However, Schiff bases of 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone and their metal complexes are not studied widely, especially those of first row transition metal ions. As the ligands contain several potential coordinating sites, the syntheses and characterisation and the study of biological activity is attempted here. It is expected to form metal complexes in 1:2 (metal:ligand) molar ratio.

Four Schiff base ligands obtained by condensing amines like aniline, isoniazid, phenylhydrazine and benzoylhydrazine with 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone were synthesized. They were complexed with first row transition metal ions viz., Co(II), Ni(II) and Cu(II) which are bioactive. Co(II) was chosen because it is very challenging to study the interaction between Co(II) ions and heterocyclic nitrogen compounds, that occur in biological systems. It is also well-known that heterocyclic compounds play a significant role in many biological systems, especially 6-membered ring system being a component of several vitamins and drugs.[110] The *bis*(dimethylglyoximato)Co(III) system is generally known as cobaloximes and are ideal systems for structural comparisons.[111,112] Biggotto *et al*[113]prepared cobalt complexes in an attempt to derive extended model systems for Vitamin B_{12}. Some tetradentate Schiff base cobalt complexes were characterized as oxygen carriers. [114,115]

Ni(II) forms a large number of square planar complexes stabilised by strong nickel-ligand covalent bonding.[116,117] Moreover, many Ni(II) complexes have a wide range of biological activity.[118]

The Cu(II) complexes of Schiff bases are biologically active and they exhibit enhanced activities as compared to their parent ligands. Copper is a micronutrient as well as a trace element for living beings, depending upon the concentration level.[119] Moreover, Cu(II) forms many stable complexes with many Schiff bases which are biologically active and can be used as models.

The chlorides, nitrates and acetates of these metal ions were used for complexation. These metal ions were chosen as they are capable of forming complexes with a wide range of biological activity. Different anions were chosen with a view to obtain structural variety, varied physical and chemical properties and much more diverse biological applications. In order to establish the structures of the ligands and the complexes, elemental analyses, conductance, magnetic susceptibility measurements, ^1H NMR, IR and electronic spectral analyses were used.

Antibacterial and antifungal activities of the ligands and a number of selected complexes were investigated.

CHAPTER II

MATERIALS AND METHODS

A brief account of the reagents and apparatus used and the methods adopted for the synthesis, characterisation of the ligands and complexes are presented here. Detailed descriptions are provided in appropriate contexts.

A. Materials

Analar grade chemicals (BDH, Sarabhai, Qualigens, E.Merck, Loba-Chemie or Glaxo) were used for the synthesis. For the preparation of the ligands, ethylacetoacetate, phenlhydrazine, aniline, isoniacid, benzoylchloride and hydrochloric acid were used.

The metal salts used for the synthesis of the complexes were the acetates, chlorides and nitrates of Co(II), Ni(II) and Cu(II).

The solvents made use of for the synthesis, purification and analyses of the ligands and the complexes were diethylether, ethanol, methanol, petroleum ether, dimethylformamide and dimethylsulphoxide. Ethanol and methanol were distilled before use.

B. Synthesis of ligands and complexes.

Four Schiff base ligands, namely, BMPPA, BMPPI, BMPPPH and BMPPBH were synthesized. First of all, 1-phenyl-3-methyl-5-pyrazolone was synthesized. This was converted to 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone. This was condensed with various amines, namely, aniline, isoniazid, phenylhydrazine and benzoylhydrazine. The pyrazolone and the amines were refluxed in ethanol for 2-3 hours. On cooling, solid separated. This was filtered, washed with ethanol and dried under vacuum.

The complexes were prepared by refluxing a mixture of the solutions of the metal salt and the ligand in 1:2 molar ratio. The solvents used were methanol, ethanol, DMF, etc. In some case, the complexes were precipitated on mixing the ligand solution and metal salt solution in hot condition. In some cases, the complex was precipitated during refluxing itself, which was separated, washed with suitable solvent and dried. In some other cases, after refluxing for 2-3 hours, the solid which separated was washed repeatedly with ethanol, filtered and dried. In some other cases, after refluxing for 2-3 hours, the solution was concentrated over a water bath and the viscous mass obtained was shaken with petroleum ether(60-80 range) and left as such for a few days. The solid complex separated was filtered and dried in vacuum.

C. Instruments and methods of analysis.

The purity of the compounds was checked by standard methods of semimicroanalyses. Known methods were adopted for the estimation of metal contents of the complex. A definite quantity of the complex was digested three to four times with a mixture of concentrated nitric acid and concentrated hydrochloric acid and the residue was extracted with distilled water and the solution was used for the estimation. Cobalt and copper were estimated complexometrically using EDTA. Nickel was estimated colorimetrically using a Systronics photoelectric colorimeter, by coverting it to dimethylglyoximato complex in alkaline medium. The anions present in the complexes were estimated by standard methods. The chlorides were estimated by Volhard's method. Carbon, hydrogen and nitrogen were estimated by making use of VarioEL III CHNS analyzer at SAIF, Cochin University of Science and Technology, Kochi. The melting points of the ligands and that of the complexes were determined using sulphuric acid bath method and standard melting point apparatus. Conductance measurements were carried out at room temperature using Equiptronics conductivity bridge and dip-type conductivity cell using 10^{-3}M solution of the complex in DMF/DMSO. The magnetic susceptibilities of the complexes at room temperature were measured using a Evans Magnetic susceptibility balance. The Sherwood Scientific Magnetic Susceptibility Balance (M.S.B) was used to determine the magnetic susceptibility values for the complexes at room temperature. The balance is a result of collaboration with Prof. D.F. Evans of Imperial College, London and is designed as a replacement for a traditional Guoy balance system. The Evans method uses the same configuration as the Guoy method, but, instead of measuring the force which a magnet exerts on the sample, the equal and opposite force which the sample exerts on a suspended permanent magnet is observed. $Hg[Co(NCS)_4]$ was used as a calibrant. Diamagnetic corrections were applied using Pascal's constants for various atoms and structural units.

The infrared spectra of the ligands and the complexes were recorded in the range 4000-400 cm^{-1} on a spectrophotometer as their KBr pellets at Calicut

University, and at SAIF, IIT, Madras and on a Perkin-Elmer spectrophotometer at Madurai Kamaraj University, Madurai. The diffuse reflectance spectra of the complexes were recorded using a JASCO UV-Visible spectrophotometer in the University of Calicut.

The ^{1}H NMR spectra of the complexes were recorded in DMSO-d_6 on a Advance III 500 MHz Bruker spectrometer, at SAIF, IIT, Madras, Chennai.

The antibacterial studies were performed at National Centre for Marine Cyanobacteria. The antifungal studies were performed at EUMIC Analytical Lab and Research Institute, Woriyur, Tiruchirappalli. The reference work was carried out at Calicut University, IISc. Bangalore, National College, Tiruchirappalli, at Bharathidasan University and at Annamalai University . Online reference was also done.

CHAPTER III

Co(II), Ni(II) AND Cu(II) COMPLEXES OF N-[PHENYL(METHYLPHENYL-5-PYRAZOLYL)METHYLIDENE]ANILINE (BMPPA)

The chemistry of pyrazole-5-ones and its derivatives has attracted considerable attention of coordination chemists by virtue of their applicability as potential ligands for a large number of metal ions. It is also found that the 4-position of pyrazole-5-one system is reactive as it undergoes coupling reactions with aryl diazonium salts to furnish 4-arylazo derivatives and complexes of such azo dyes having an azole nucleus are well known.[1-4] Some planar and octahedral complexes of the sulphates of Cu(II) and Ni(II) with different 3-methyl-4-arylazo-pyrazole-5-ones were synthesized.[5] Pyrazole-5-one and its derivatives are not only biologically active but also find applications in photography and dye industry.[6] 4-acyl-3-methyl-1-phenyl-5-pyrazolone has been used to extract Mn(II).[7]

5-pyrazolones possess various biological activities.[8,9] The substituted pyrazolones act as monodentate, bidentate and sometimes tridentate ligands towards transition- and inner transition metals.[10-14] They have been gaining increasing importance as chelating agents for the extraction of metals.[15-17] In view of the ligational behaviour and biological importance[8,9] of 5-pyrazolones and its derivatives,[18,19] the syntheses of pyrazolone derivatives of sulphonamides have been attempted by the reaction of aminoguanidine nitrate with products obtained from the reaction between diazonium salts and active methylene compounds.[20] The syntheses of neutral mixed-ligand cyanonitrosyl $\{CrNO\}^5$ complexes of chromium(I) with some N-alkylanilines, viz., N-methylaniline, N-ethyl-o-toluidine, N-ethyl-p-toluidine and 2-pyrazolin-5-one derivatives *viz.,* 4-benzoyl-1-(4′tolyl)-5-one and 4-phenacyl-1-(4′-tolyl)-3-methyl-2-pyrazolin-5-one were performed and characterised.[21]

Schiff bases derived from 4-acetyl-2,3-dimethyl-1-(4′methylphenyl)-3-pyrazoline-5-one and aromatic amines were synthesized and spectral studies on the octacoordinated dioxouranium(VI) complexes were carried out.[22] Lanthanide nitrate and perchlorate complexes with the Schiff base 4-(pyridine-2′carboxalidene)aminoantipyrine derived from pyridine-2-carboxaldehyde and 4-aminoantipyrine were reported.[23] Spectral and thermal studies of dioxouranium(VI) sulphate complexes of some Schiff bases of 4-aminoantipyrine were carried out.[24]

A perusal of the literature revealed that no work has been done on the transition metal complexes of the Schiff base derived from aniline and 1-phenyl-3-methyl-4-benzoyl-5-pyrazolone. The present work involves the synthesis of a new type of bidentate/tetradentate ligand formed by the condensation of aniline with 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone. This ligand system (Fig.3.1) has three sites which may offer coordination, *i.e.,* azomethine nitrogen, the pyrazolone ring oxygen and the pyridine ring nitrogen atoms. Hence it is worth while to synthesize and characterize the complexes of N-[phenyl(methylphenyl-5-pyrazolyl)methylidene]aniline (BMPPA)*(L) and to conduct detailed investigations on the structure and the biological activities of these compounds.

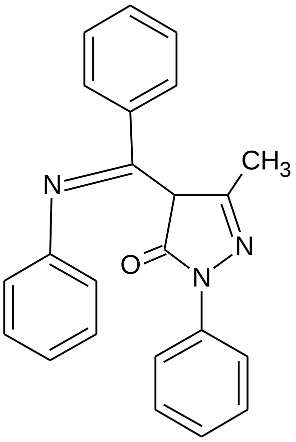


Fig.3.1

Suggested structure for

N-[phenyl(methylphenyl-5-pyrazolyl)methylidene]aniline, (BMPPA) (L)

A. Experimental

1. Materials and methods

Specifications regarding the reagents used, the procedural details adopted for the syntheses and the characterisation of the ligand and the complexes are given in Chapter II.

1. Synthesis of the ligand, N-[phenyl(methylphenyl-5-pyrazolyl)methylidene]aniline (BMPPA)

The synthesis of the ligand consists of the following three stages.

---

*The systematic name of the compound is 5-methyl-2-phenyl-4-phenyl(phenylimino)methyl]-2,4-dihydro-3H-pyrazol-3-one. But for the sake of convenience, the name N-[phenyl(methylphenyl-5-pyrazolyl)methylidene]aniline and the short form ‘BMPPA’ are adopted in this thesis.

a) Preparation of 3-methyl-1-phenyl-5-pyrazolone

Mixed together (49ml, 0.384 mol) of ethylacetoacetate and phenylhydrazine (36.5 ml, 0.37 mol) in a large china dish. Heated the mixture on a boiling water bath in a fume cupboard for about two hours and stirred from time to time with a glass rod. Allowed the heavy reddish syrup to cool, added about 100 ml of ether and stirred the mixture vigorously. The syrup, which was insoluble in ether, solidified within 15 minutes. Filtered the solid at the pump and washed it thoroughly with ether to remove the coloured impurities. Recrystallised from hot water to obtain colourless crystals of the pyrazolone. Yield: 52 g (80 %)

b) Preparation of 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone(BMPP)

3-Methyl-1-phenyl-5-pyrazolone(15 g, 0.082 mol) was placed in a flask equipped with a reflux condenser and a magnetic stirrer and dissolved in 60-80 ml of freshly distilled ethanol by heating. Calcium hydroxide(12 g) were added followed by the addition of benzoyl chloride (9.9 ml) dropwise within one minute. The reaction mixture became a thick paste and the temperature increased during the first few minutes. The mixture was heated to reflux for 30 minutes. The calcium complex in the flask was decomposed by pouring the mixture into 2N hydrochloric acid (200 ml) which caused cream coloured crystals to separate. The crystals were collected on a Buchner funnel. They were recrystallized from ethanol-water mixture which was slightly acidified to destroy any undecomposed calcium complex. Yield**:** 15.6 g (65 %).

c) Preparation of BMPPA

Dissolved (2.7840 g, 0.01 mol) BMPP in minimum quantity of ethanol and refluxed. Added an ethanolic solution of aniline (1 ml, 0.0109 mol) to the hot refluxing solution. Refluxed for 3 hours. On cooling, the lemon yellow coloured crystals obtained were filtered at the pump, washed with ethanol and dried. Yield:2.3250 g (65.8 %) m.p. = 162ºC.

3. Synthesis of the complexes of BMPPA

Complexes of the ligand with the iodide and nitrate of Co(II), the acetate of Ni(II) and the acetate, chloride, nitrate and sulphate of Cu(II) were synthesized.

a) Complexes of iodide and nitrate of Co(II)

Added a methanolic solution of the metal salt to a methanolic solution of the ligand in 1:2 molar ratio and stirred for 20 minutes. While being stirred itself, the colour changed to brown. Refluxed for 0.5 hour and left overnight. Filtered off the dark brown solid which separated, washed with methanol and dried in vacuum.

b) Complexes of $Ni(CH_3COO)_2$, $CuSO_4$ *and* $Cu(NO_3)_2$

Dissolved the ligand in methanol by heating. Added an aqueous solution of the metal salt to the refluxing ligand solution, in 1:2 metal: ligand ratio. An aqueous solution was chosen as the solubility of the metal salt in methanol was very low, and refluxed for 2 hours. A green solid was formed. This was filtered at the pump, washed with methanol and dried under vacuum.

c) Complex of $Cu(CH_3COO)_2$

Dissolved the ligand in methanol by the application of heat. Added an ethanolic solution of the metal salt to the refluxing ligand solution in 1:2 metal: ligand ratio. Within 15 minutes, a red brown solid was formed. Filtered the solid at the pump and dried under vacuum.

d) Complex of $CuCl_2$

Dissolved the ligand (0.3510 g) in minimum of methanol by the application of heat. Added a methanolic solution of $CuCl_2.2H_2O$ (0.08474 g) to the refluxing solution of the ligand and refluxed for 7.5 hours. Reduced the volume to half by evaporating off the solvent. A green solid separated which was washed with methanol and dried in vacuum.

B. Results and discussion

The data obtained from analytical and physico-chemical studies have been correlated in a logical way to explain the properties, bonding and structures of the compounds.

1. Characterisation of the ligand, BMPPA.

The ligand, BMPPA was lemon yellow in colour with a melting point of 162ºC. The analytical data showed closed agreement with the suggested formula of $C_{23}H_{19}N_3O$. It was further characterised by ^1H NMR and IR spectral data.

a) ^{1}H NMR spectrum

The ^{1}H NMR spectrum of the ligand, BMPPA are recorded in (Table 3.1) and the spectrum is shown in Fig. 3.2. The spectrum exhibited a number of signals which were characteristic of the compound. The assignments were made by reference to generalised charts of chemical shits of protons attached to carbin atims and on the basis of analogous structures, known earlier.[25,26] The singlet at 1.4 δ was due to the methyl group at 3 position of the pyrazolone ring. The multiplet observed in the range 7.0-7.5 δ was assigned to the aromatic protons. The singlet at 8.0 δ was assigned to the proton at 4 position of the pyrazolone ring. Singlets at 2.3 and 3.4 δ are due to DMSO–d_6 and H_2O. The singlet at 12.8 δ may be due an impurity.

b) IR spectrum

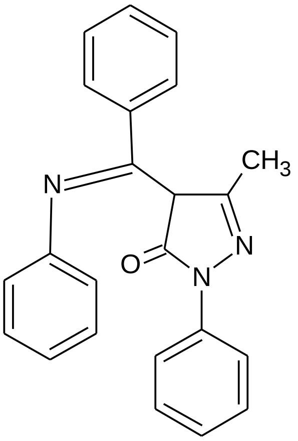
The infrared spectrum of the ligand BMPPA showed a number of absorption bands which were characteristic of different groups present in it (Table 3.2). Assignments were made by simple inspection and by reference to generalized charts of characteristic group frequencies and on the basis of analogous structures, known earlier.[25,26] The bands present at 1628 cm^{-1} and at 1226 cm^{-1} have been assigned to >C=N and C-N stretching vibrations, respectively. The characteristic frequency due to the stretching of the aromatic keto group, at 1650 cm^{-1} [26,27] was not present in the spectrum, which indicated that condensation between BMPP and aniline was complete. The band at 1500 cm^{-1} has been assigned to >C=O group of the pyrazolone ring. The bands due to the in plane bending of the aromatic C-H stretching are usually found in the range 1250-950 cm$^{-1.}$ The bands at 1138 cm^{-1},

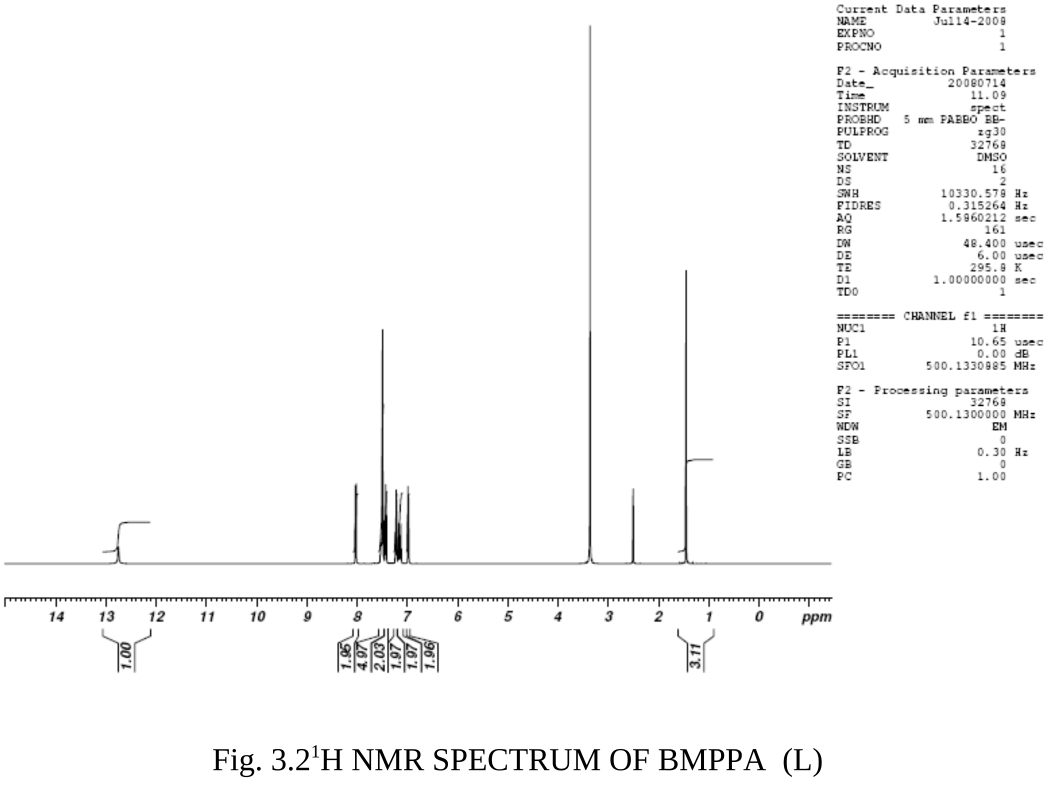
TABLE 3.1

SIGNIFICANT ^{1}H NMR PEAKS OF BMPPA AND THEIR ASSIGNMENTS

CHEMICAL SHIFT * (δ ppm)	PROTON ASSIGNMENT
8.0 s	H at C-4
7.5-7.4 m 7.2-7.1 m 7.0 m	Aromatic protons
1.4 s	CH_3- protons at C-3
2.4 s	DMSO
3.4 s	H_2O

* s = singlet; m = multiplet





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Current Data Parameters
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PROCNO                    1

F2 - Acquisition Parameters
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Time                  11.09
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PULPROG                zg30
TD                    32768
SOLVENT                DMSO
NS                       16
DS                        2
SWH               10330.578 Hz
FIDRES             0.315264 Hz
AQ                1.5860212 sec
RG                      161
DW                   48.400 usec
DE                     6.00 usec
TE                    295.8 K
D1               1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
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P1                    10.65 usec
PL1                    0.00 dB
SFO1            500.1330885 MHz

F2 - Processing parameters
SI                    32768
SF              500.1300000 MHz
WDW                      EM
SSB                       0
LB                     0.30 Hz
GB                        0
PC                     1.00
```

Fig. 3.2 ^{1}H NMR SPECTRUM OF BMPPA (L)

TABLE 3.2

SIGNIFICANT IR BANDS OF BMPPA AND THEIR ASSIGNMENTS

BAND FREQUENCY * cm-1	ASSIGNMENT
1628 (s), (sh)	>C=N- stretch
1598 (s), (sh)	>C=C< stretch
1535 (s), (sh)	Aromatic C-C stretch
1500 (s), (sh)	>C=O stretch
1385 (s), (sh)	CH_3- symmetric deformation
1226 (m),(sh)	C-N stretch
1138 (m),(sh)	Aromatic C-H stretch
1007 (m),(sh)	-do-
906 (w),(sh)	-do-
770 (s), (sh)	Out-of-plane bending vibration of aromatic C-H
760 (s), (sh)	-do-
698 (s), (sh)	-do-
655 (m),(sh)	C-H deformation

* s= strong; sh= sharp; m= medium; w= weak

1007 cm^{-1} and 906 cm^{-1} have been assigned to these modes of vibrations. The most characteristic frequencies of aromatic groups were found below 900 cm^{-1}, usually in the range 600-900cm^{-1}, due to the out-of-plane bending vibration of the aromatic C-H. The bands at 770cm^{-1}, 760 cm^{-1} and 698 cm^{-1} have been assigned to these modes of vibrations.

2 Formulae and general properties of the complexes

All the complexes were found to be coloured, stable to light, heat and moisture and non-hygroscopic solids. Some of them looked crystalline in nature. The solubility of these complexes in common organic solvents was very low, but they were soluble in DMF/DMSO. The analytical data (Table 3.3) and the molar conductance values in DMF(Table 3.4) showed that the complexes had the formula [ML_2X_2] except the sulphato complex which had the general formula [ML_2X]. The spectral and magnetic data also confirmed these suggested formulae.

3. Molar conductance

The molar conductance of 10^{-3} M solutions in DMF/DMSO of the BMPPA complexes were determined a room temperature and the values are given in Table 3.4). The range of molar conductance in DMF[28] for 1:1, 1:2 and 1:3 electrolytes are 65-90,130-170 and 200-240 $ohm^{-1}cm\ mol^{-1}$, respectively, and for the 1:4 electrolytes it is above 450 $ohm^{-1}\ cm\ mol^{-1}$. An approximate value for Ω_m at 10^{-3} M for the solutes in DMSO given by Sears *et al*[29] is 35 $ohm^{-1}\ cm^2\ mol^{-1}$. Greenwood *et al* [30] have suggested 50-70 $ohm^{-1}\ cm^2\ mol^{-1}$ as the range for 1:1 electrolytes in

TABLE 3.3

ANALYTICAL DATA OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPA

COMPOUND	EMPIRICAL FORMULA	F.WT. *	COLOUR	YIELD %	FOUND (CALCULATED) %				
					METAL	C	H	N	ANION
BMPPA (L)	$C_{23}H_{19}N_3O$	353	Lemon yellow	66	-	77.01 (78.19)	5.25 (5.38)	11.80 (11.89)	-
$[Co(L)_2I_2]$	$CoC_{46}H_{38}N_6O_2I_2$	1018.93	Brown	42	5.65 (5.78)	55.26 (54.17)	3.70 (3.73)	8.21 (8.24)	-
$[Co(L)_2(NO_3)_2]$	$CoC_{46}H_{38}N_8O_8$	888.93	Brown	42	6.60 (6.63)	64.09 (62.10)	4.25 (4.27)	14.38 (14.40)	-
$[Ni(L)_2(CH_3COO)_2]$	$NiC_{50}H_{44}N_6O_6$	882.71	Pale green	40	6.60 (6.65)	66.74 (67.97)	4.30 (4.98)	9.95 (9.52)	-
$[Cu(L)_2(CH_3COO)_2]$	$CuC_{50}H_{44}N_6O_6$	887.54	Black	53	7.10 (7.16)	68.14 (67.60)	4.98 (4.96)	9.48 (9.46)	-
$[Cu(L)_2Cl_2]$	$CuC_{46}H_{38}N_6O_2Cl_2$	840.54	Green	52	7.49 (7.56)	66.74 (65.67)	4.99 (4.52)	10.25 (9.99)	8.50 (8.45)
$[Cu(L)_2(NO_3)_2]$	$CuC_{46}H_{38}N_8O_8$	893.54	Green	51	7.05 (7.11)	62.12 (61.78)	4.20 (4.25)	12.57 (12.53)	-
$[Cu(L)_2SO_4]$	$CuC_{46}H_{38}N_6O_6S$	865.54	Green	50	7.29 (7.34)	65.16 (63.77)	5.11 (4.39)	10.07 (9.70)	-

* F. Wt. = FORMULA WEIGHT

TABLE 3.4

MOLAR CONDUCTANCES OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPA

COMPLEXES	Ω_m ohm^{-1} cm^2 mol^{-1}	SOLVENT
$[Co(L)_2I_2]$	10.75	DMF
$[Co(L)_2(NO_3)_2]$	0.0	DMF
$[Ni(L)_2(CH_3COO)_2]$	10.75	DMF
$[Cu(L)_2(CH_3COO)_2]$	0	DMSO
$[Cu(L)_2Cl_2]$	30.23	DMF
$[Cu(L)_2(NO_3)_2]$	0.0	DMSO
$[Cu(L)_2SO_4]$	10.75	DMF

DMSO. All the complexes showed values lower than those expected for 1:1 electrolytes, indicating their non-electrolytic nature. The analytical data and spectral studies also supported the suggested formulae.

4. Magnetic behaviour

Magnetic measurements can provide information on the electronic structure, oxidation state and in some cases on the symmetry of the central transition metal ion. Magnetic measurements indicate the electronic configuration of the d shell of the transition metal, particularly if the transition metal occupies position isolated from one another.[31] The magnetic susceptibilites, diamagnetic corrections and the effective magnetic moments from the observed magnetic susceptibilities are given in the Table 3.5.

In complexes, the metal ions are generally separated from one another by magnetically inactive ligands, preventing the interaction between the metal atom which would otherwise give rise to ferromagnetism or antiferromagnetism. These types of magnetism are, therefore, of subordinate importance from the view-point of coordination chemistry. The paramagnetic properties of the complexes, as a result of the isolating effect of the ligands, yield direct information on the electronic configuration of the central atom. For complexes containing large organic ligands, measurement of diamagnetic susceptibility may also be of importance, if exact knowledge of the paramagnetic susceptibility is required.

TABLE 3.5

MAGNETIC SUSCEPTIBILITY AND MAGNETIC MOMENTS OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPA

COMPOUND	χ_g x 10^{-6}	χ_m x 10^{-6}	$\chi_{m\,corr}$	μ_{eff}	T (K)
$[Co(L)_2I_2]$	9.34	9511.78	9925.16	4.84	294.7
$[Co(L)_2(NO_3)_2]$	5.64	3658.27	4071.65	3.10	294.7
$[Ni(L)_2(CH_3COO)_2]$	4.25	3751.60	4164.96	3.14	294.7
$[Cu(L)_2(CH_3COO)_2]$	1.37	1218.32	1631.70	1.96	294.7
$[Cu(L)_2Cl_2]$	1.56	1307.68	1721.07	2.02	295.0
$[Cu(L)_2(NO_3)_2]$	2.13	1768.17	2181.55	2.27	294.7
$[Cu(L)_2SO_4]$	0.6385	552.65	966.03	1.51	295.0

χ_g = mass susceptibility
χ_m = molar susceptibility
$\chi_{m\ corr}$ = corrected molar susceptibility
μ_{eff} = effective magnetic moment
T=Temperature in Kelvin

The d^7 (high-spin) configuration contributes an orbital moment to the magnetic moment, both in ions and in complexes. Hence, the μ_{eff} values measured experimentally differ from the spin-only moment. The d^8 and the d^9 configurations do not contribute an orbital moment to the magnetic moment, either in ions or in complexes. But in Ni(II) and Cu(II) complexes, discrepancies are observed. This is due to the fact that spin-orbital coupling in the ion can mix the ground state representing no orbital momentum with higher levels of identical multiplicity. The participation of these higher levels result in a small orbital contribution in these cases where it is not to be expected. In these cases, the magnetic moment can be calculated from the following formula

$$\mu_{eff}=\mu_0(1-\alpha\ \lambda/\Delta),$$

where μ_0 is the spin-only moment, λ the spin-only coupling constant, Δ is the difference in the energy between the ground state and the higher state and α a constant. The values of λ are positive for d^1 to d^5, and negative for d^6 to d^{10}. This explains why the values of the magnetic moment measured are smaller in, chromium(III) complexes and greater in copper(II) complexes than the spin-only values.[32]

The magnetic moment of Co(II)–methylpyrazine(mp) and Co(II)2,5-dimethylpyrazine(dmp) mixed complexes of octahedral symmetry are in the range 4.37 to 5.40 B.M.[32] The magnetic data of the Co(II) complexes reveal that they are high-spin. These are much higher than the spin-only value for 3 unpaired electrons. The ground state electron population $t_{2g}^5e_g^2$ permits orbital contribution to the magnetic moment. In addition to this unquenched orbital moment, spin-orbit coupling occurs by mixing of the first excited state ($t_{2g}^4e_g^3$) with the ground state.[33] The slightly lower magnetic moment values, as compared to those assigned for high-spin octahedral cobalt(II)[34] complexes imply, that the complexes probably belong to an orbital singlet ground state with distorted octahedral environment.[35] This also suggests that the complexes belong to a group of lower symmetry(C_2).[36]

The low-spin octahedral Co(II) complexes has ground state ^2E_g and hence no orbital contribution is expected. Therefore, the observed values are very close to the spin-only value for one unpaired electron, i.e., 1.73 B.M. In the tetrahedral high-spin complexes of Co(II), the ground term is $^4A_2$ and there is no orbital contribution. The expected magnetic moment is close to the spin-only value for the three unpaired electrons, i.e., 3.87 B.M. However, the observed values are usually in the range 4.40-4.80 B.M. The high values are due to spin-orbit coupling perturbation. In the case of four coordinate low-spin complexes, which are square-planar in geometry, it is difficult to predict accurately the magnetic properties. A magnetic moment above 1.73 B.M. ,the spin-only value for one unpaired electron, is expected and values in the range 2.20-2.70 B.M. are observed.[33] In the present work, the iodo and the nitrato complexes showed a magnetic moment of 4.84 and 3.10 B.M.. which corresponded to high spin octahedral geometry (Table 3.5).

Octahedral nickel(II) ($3d^8$) has the ground state $t_{2g}^6e_g^2$ so that the orbital multiplicity of the electronic state must be one. This electronic state is symbolised as $^3A_{2g}$. The next excited configuration is $t_{2g}^5e_g^3$. The excited state is $^3T_{2g}$ which has an orbital moment. When the energy difference between the $^3A_{2g}$ state and the $^3T_{2g}$ excited state is small, as in the case with nickel(II) octahedral complexes, there is a scope of being mixed up which means that the ground state loses its pure A character and gains T character. Since both the ground state and the excited state possess the same spin multiplicity but different orbital multiplicities, the former cannot make a perfect distinction between the two orbital multiplicities. We thus observe that nickel(II) octahedral complexes register magnetic moment values above spin-only values although the ground state is devoid of any orbital moment.[34]

For tetrahedral geometries, there is an appreciable orbital contribution of the $^3T_1$ ground state and the magnetic moment values are in the range 3.60-4.00 B.M. Large distortions and inequalities in the field of coordinated ligands may result in magnetic moments with small orbital contributions and the observed values can be as low as 3.20 B.M. Ni(II) square-planar complexes have a spin-singlet ground state and hence are diamagnetic.[35] In the present work, the acetato complex showed a magnetic moment of 3.14 B.M. suggesting an octahedral geometry (Table 3.5).

The magnetic moment values for the present copper complexes are comparable to the μ_{eff} values observed for many of the reported mononuclear copper(II) complexes.[36] The complex of Cu(II) with morpoline-N-thiohydrazone of benzaldehyde, cinnamaldehyde and cyclohexanone displayed magnetic moment values in the range 1.84-1.91 B.M., suggesting that they are magnetically dilute and probably possess tetragonal structure. In the present work, the acetato, chloro, nitrato and sulphato complexes showed magnetic moments of 1.96, 2.02, 2.27 and 1.51 B.M., respectively indicating that they have distorted octahedral geometries(Table 3.5).

5. Electronic spectra

Electronic absorption spectroscopy is one of the principal physical techniques currently used for studying transition metal complexes. The electronic absorption spectrum often provides quick and reliable information about the arrangement of ligands around the metal ion. For example, in some cases, octahedral complexes are readily distinguished from the tetrahedral ones on the basis of the position and intensity of their absorption bands. The number of bands, their frequencies and molar absorptivities should be considered for the assignments.[37]

The electronic absorption bands of metal complexes resulting from the d-d transitions are often referred to as ligand field or crystal field bands because their energies shift with the positions of the ligands in the spectrochemical series. Further, splitting of the bands may occur due to Jahn-Teller distortion, spin-orbit coupling and inequivalencies of the ligands. Transition metal complexes often show strong bands arising from charge-transfer transitions from the ligand to the metal or vice versa. Very little is known about the effect of the charge transfer transitions localised on the ligands.

The Orgel- and Tanabe-Sugano diagrams are now universally used for the interpretation of the spectra of transition metal complexes. For high -spin d^7 systems, the ground term is ^4F with a low lying ^4P excited term. As a consequence, the spectra are reminiscent of analogous d^2 and d^3 complexes. The most important d^7 species is undeniably cobalt(II) known in all coordination numbers from 8 to 2, however, coordination numbers 6 and 4 dominate.[38]

Six coordinate octahedral or pseudooctahedral species will exhibit three transitions, none of which correspond in energy with 10 Dq. However,

$$\upsilon_1 \quad {}^4T_{2g} \rightarrow {}^4T_{1g}$$

$$\upsilon_2 \quad {}^4A_{1g} \rightarrow {}^4T_{1g}$$

$$\upsilon_3 \quad {}^4T_{1g}(P) \rightarrow {}^4T_{1g}$$

the energy difference υ_2-υ_1 is exactly equal to 10 Dq. Unfortunately the υ_2 transition is usually very weak (formally two electron) and rarely unequivocally observed.

Tetrahedral species also exhibit three transitions:

$$\upsilon_1 \quad {}^4T_2 \rightarrow {}^4A_2$$

$$\upsilon_2 \quad {}^4T_1 \rightarrow {}^4A_2$$

$$\upsilon_3 \quad {}^4T_1(P) \rightarrow {}^4A_2$$

All the three can be observed, though υ_1 lies at low energy in the near infrared region. Both octahedral and tetrahedral species display rich spin forbidden transitions, whose intensity is often enhanced by intensity stealing. As a consequence, the identification of the spin-allowed bands can be equivocal.

In the present work, the spectra of the brown iodo complex of Co(II) showed transitions at 694, 593 and 525 nm and were assigned to the ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ transitions,[39-41] respectively (Table 3.6). The broad band in the region 525 -694 nm has been assigned to the transition ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$ in an approximately octahedral field.

The bands at 820, 690 and 530 nm in the spectrum of the nitrato complex of Co(II) have been assigned to the transitions ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ and ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$, respectively. This indicates octahedral geometry around Co(II).

The nickel(II) species are of special interest existing in all coordination numbers from 7 to 2. There probably exists more electronic spectroscopic data for nickel(II) ions than for any other metal ion.[42]

The three spin-allowed transitions from ${}^3A_{2g}$ to ${}^3T_{2g}$, ${}^3T_{1g}$ and ${}^3T_{1g}(P)$ generally fall within the range 1428-769, 909-500 and 526-370 nm, respectively, with intensities less than 30 l mol^{-1} cm^{-1} in regular octahedral systems. In addition, two spin-forbidden bands are usually quite prominent. One is the transition to ${}^1E_g$ near the second spin-allowed transition and the second is primarily to ${}^1T_{2g}$ between the second and third spin-allowed band.[42]

In the present work, three bands at 770, 740 and 440 nm have been observed for the acetato complex of nickel(II) (Table3.6). These have been assigned to the transitions, ${}^3A_{2g} \rightarrow {}^3T_{2g}$, ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ and ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$, respectively, in an octahedral symmetry. The maxima of the absorption bands for these complexes are within the region usually found for paramagnetic pseudo-octahedral nickel(II) complexes.[43]

TABLE 3.6

ELECTRONIC SPECTRAL BANDS OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPA AND THEIR ASSIGNMENTS

COMPLEX	BANDS(nm)	ASSIGNMENT	GEOMETRY
$[Co(L)_2I_2]$	694 593 525	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}$ ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	Distorted octahedral
$[Co(L)_2(NO_3)_2]$	820 690 530	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$ ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$	Octahedral
$[Ni(L)_2(CH_3COO)_2]$	770 740 440	${}^3A_{2g} \rightarrow {}^3T_{2g}$ ${}^3A_{2g} \rightarrow {}^3T_{1g}(F)$ ${}^3A_{2g} \rightarrow {}^3T_{1g}(P)$	Octahedral
$[Cu(L)_2(CH_3COO)_2]$	680 398	${}^2E_g \rightarrow {}^2E_g$	Distorted octahedral
$[Cu(L)_2Cl_2]$	548 493	${}^2E_g \rightarrow {}^2T_{2g}$ Charge transfer	Distorted octahedral
$[Cu(L)_2(NO_3)_2]$	686 306	${}^2E_g \rightarrow {}^2E_g$ Charge transfer	Distorted octahedral
$[Cu(L)_2SO_4]$	650 525	${}^2E_g \rightarrow {}^2E_g$ Charge transfer	Distorted octahedral

A survey of the electronic spectroscopy of copper(II) complexes presents difficulty because of the lack of definitive statements which can be made to relate spectra with structure. Moreover, because of the general ease with which copper(II) complexes can be made, there is an extraordinary amount of spectroscopic information available in the literature. The electronic spectra of copper(II) complexes show a single broad poorly resolved absorption band in the visible region. Copper(II) complexes frequently exist in highly distorted stereochemistries.[44,45] However, in parallel with nickel(II), copper(II) systems with square-planar or close to square-planar stereochemistry, will have no electronic absorption below 1000 nm. Similarly, tetrahedral or close to tetrahedral copper(II) will absorb primarily in the red- and near infrared.

Since the ground state in an octahedral field is the Jahn-Teller unstable ^2E_g, very few regular octahedral copper(II) complexes exist.[45,47-50]

In the present work, the acetato, chloro and nitrato complexes of copper(II) display two broad bands in the regions 686-548 nm and 525-306 nm (Table 3.6). They have been assigned to the $^2E_g \rightarrow {}^2T_{2g}$ and charge-transfer transitions, respectively, in an approximately octahedral ligand field. The nature of the spectral bands and the paramagnetic behaviour of the copper(II) complexes indicate a distorted octahedral configuration around copper(II) ion.[51]

6. Infrared spectra

a) Complex

During complex formation, when ligands coordinate to the central metal atom, the newly established metal-ligand coordinate bonds change the electronic structure, the state of energy and the symmetry of the ligands. These changes affect the vibration of the ligand, and consequently its vibrational spectrum. The new molecule (the complex) comprising the ligands will perform new vibrations, which are not exhibited by the free ligands. The structure and symmetry of the complex molecule, the strength of the coordinate bonds, as well as its interaction with the environment (solvent, ions bound in the outer sphere and other molecules) all affect the vibrational spectrum of the complex. This is the reason why experimental procedures involving the recording and analysis of vibrational spectra *i.e.,* infrared and Raman spectroscopy, have become important tools in coordination chemistry.[52]

One of the important advantages of infrared spectroscopy, compared with other methods of structural analysis (X-ray diffraction, electron spin resonance, etc), is that it affords information on the structure of the molecules quickly, without requiring tiresome evaluation methods.[52] The significant vibrational bands of the complexes, investigated here, and the assignments are given in the Table 3.7.

Assignments are made on the basis of comparison with similar known systems and by reference to tables of spectral data.[27] All the complexes of BMPPA showed downshift in the characteristic absorption frequency of the azomethine group. This indicates that the nitrogen atom of the azomethine group is coordinated to the metal.

The band at 1628 cm^{-1} observed in the spectrum of the ligand was absent in all the complexes. Instead, bands appeared in the ranges of 1560-1531 cm^{-1} and were assigned to the coordinated azomethine groups present in them.

In addition to these, new bands were present in the lower frequency region of the spectra of all these complexes. These bands appeared in the range 665-650 and at 585 cm^{-1} in the spectra of the Co(II) complex, at 685 and 585 cm^{-1} in the spectrum of the Ni(II) complex and in the ranges 685-679 and 607-580 cm^{-1} in the Cu(II) complexes. The first one was assigned to the stretching vibrations of the M-N bonds and the second one to that of the M-O bonds formed during complexation. The M-O bond is due to coordinated nitrate or acetate anion or due to coordinated oxygen atom of the 5-pyrazolone ring of the ligand.

The absence of sharp bands in the region 3441-3060 cm^{-1} in the spectra of all the complexes and the ligand indicates that N-H group is not present in the ligand and in the complexes. The absence of a broad band in this region is an indication of the absence of coordinated water as well. Elemental analyses also corresponded to the absence of coordinated water in the complexes.

b) IR features of coordinated anions in the complexes

IR spectroscopy has been used to determine the status of the anions in the complexes.

TABLE 3.7

SIGNIFICANT BANDS IN THE IR SPECTRA OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPA AND THEIR ASSIGNMENTS

COMPOUNDS	ASSIGNMENTS AND BAND FREQUENCIES * (cm^{-1})								
	υ C=N	υ C =O	υ COO^- asy	υ COO- sym	υ SO_4^{2-} coordinated	υ M-N	υ M-O	υ M-X	υ NO_3^{--} coordinated
BMPPA (L)				-	-				-
$[Co(L)_2I_2]$	1570 m,sh	1460 s	-	-	-	650 m,sh	585 w,sh	330 m,sh	-
$[Co(L)_2(NO_3)_2]$	1570 m,sh	1460 s,sh	-	-	-	665 m,sh	585 w,sh	-	1460 s,sh 1360 s,sh 1010 w,sh
$[Ni(L)_2(CH_3COO)_2]$	1531 s,sh	1460 s,sh	1632 sh	1376 m,sh	-	685 m,sh	585 w,sh	-	-
$[Cu(L)_2(CH_3COO)_2]$	1550 s,sh	1460 s,sh	1640 s	1360 m,sh	-	680 m,sh	590 w	-	-
$[Cu(L)_2Cl_2]$	1580 s,sh	1460 s,sh	-	-	-	680 m,sh	580 m	366 m,sh	-
$[Cu(L)_2(NO_3)_2]$	1550 s,sh	1460 s,sh	-	-	-	685 m,sh	580 w	-	1450 s,sh 1360 s,sh 1010 w,sh
$[Cu(L)_2SO_4]$	1610 s,sh	1432 s,sh	-	-	1210s,sh 1142 s,sh 1008 s,sh	679 s,sh	607 m,sh	-	

s = strong; m = medium; w = weak; sh = sharp *i) Acetato complexes*

Extensive infrared studies have been made on metal complexes of carboxylic acids.[53] The carboxylate ion may coordinate to a metal in one of the following modes

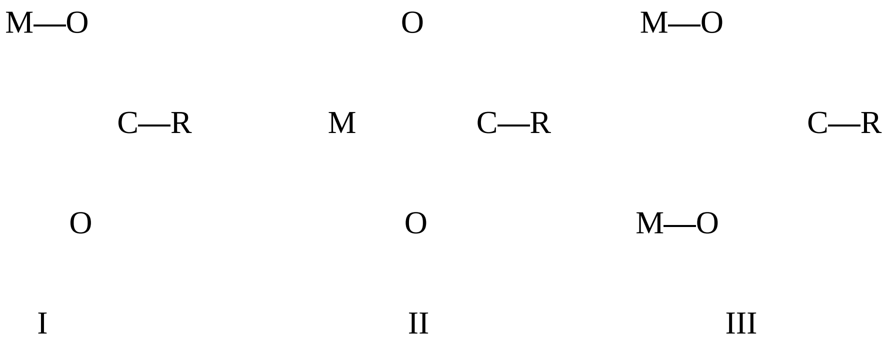

Fig. 3.2. Modes of coordination of carboxylate ion to a metal

The $\upsilon_a(CO_2^-)$ and $\upsilon_s(CO_2^-)$ of free acetate ion are at about 1560 and 1416 cm^1, respectively. In the unidentate complex (structure I), $\upsilon(C{=}O)$ is higher than $\upsilon_a(CO_2)$ and $\upsilon(C—O)$ is lower than $\upsilon_s(CO_2)$. As a result, the separation between the two $\upsilon(CO)$ is much larger in unidentate complexes than in the free ion. The opposite trend is observed in the bidentate (chelate) complex (structure II); the separation between the $\upsilon(CO)$ is smaller than that of the free ion in this case. In the bridging complex (structure III), however, two $\upsilon(CO)$ are close to the free ion values.

In the present work, two strong bands at 1632 and 1376 cm^{-1} observed in the spectra of the complex of Ni(II) and two strong bands at 1640 and 1360 cm^{-1} in the spectra of the Cu(II) complex (Table 3.7) are assigned to $\upsilon(C{=}O)$ and $\upsilon(C—O)$, respectively. Since the separation between the two υ(CO) is much larger than that in the free ion, we conclude that the acetate ion coordinates to the nickel(II) ion and copper(II) in an unidentate fashion.

Linkage isomerism involving the acetate group has been reported by Baba and Kawaguchi.[54]

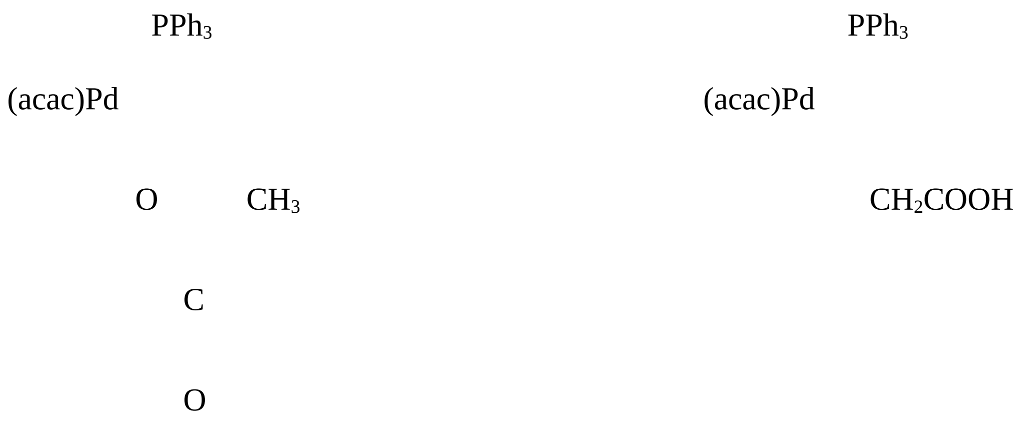

Fig. 3.3. Linkage isomerism in acetate group

The O- isomer exhibits υ(C=O) at 1640 cm^{-1}, whereas the C-isomer shows υ(C=O) at 1670 and 1650 and υ(OH) at 2700-2500 cm^{-1}. The absence of bands at 2700-2500 cm^{-1} indicates that the complex is an O- isomer. This is also confirmed by the presence of M-O bond.

ii) Halo complexes

Halogens (X) are the most common ligands in coordination chemistry. Several review articles[55-57] summarize the results of extensive infrared studies on halogeno complexes. In most cases, υ(M-X) can readily be assigned by halogen or metal (isotope) substitution.

The bands due to M-halogen vibrations are usually observed below 400 cm^{-1}. A band of medium intensity was observed at 330 cm^{-1} in the spectra of the iodo complex of cobalt(II) indicating the presence of M-I bond (Table 3.7). The non-conducting nature of the complexes showed that the iodide ions were coordinated to the Co(II) ion.

Terminal M-X stretching bands appear in the regions of 750-500 cm^{-1} for M-F, 400-200 cm^{-1} for M-Cl, 300-200 cm^{-1} for M-Br and 200-100 cm^{-1} for M-I. Several factors govern υ(M-X).[58] If other conditions are equal, υ(M-X) is higher as the oxidation state of the metal is higher.

In the present work, the band at 366 cm^{-1} is assigned to Cu-Cl bond (Table 3.7).

ii) Nitrato complexes

The structures and vibrational spectra of a large number of nitrato complexes have been reviewed by Addison *et al*[59] and Rosenthal.[60] X-ray analyses showed that the NO_3^- ion coordinates to a metal as a unidentate, symmetric- and asymmetric chelating bidentate, and bridging bidentate ligand of various structures. It is rather difficult to differentiate these structures by vibrational spectroscopy since the symmetry of the nitrate ion differs very little among them (C_{2v} or C_s). Even so, vibrational spectroscopy is still useful in distinguishing unidentate and bidentate NO_3^- ions.

Originally, Gatehouse *et al*[61] noted that the unidentate NO_3^- ion exhibits three NO stretching bands, as expected for its C_{2v} symmetry. For example, $[Ni(en)_2(NO_3)_2]$ (unidentate) exhibits three bands as follows

υ_5 (B_2)	1420 cm^{-1}	υ_a(NO_2)
υ_1 (A_1)	1305 cm^{-1}	υ_s(NO_2)
υ_2 (A_1)	(1008) cm^{-1}	υ(NO)

whereas $[Ni(en)_2NO_3]ClO_4$ (chelating bidentate) exhibits three bands as follows

υ_1(A_1)	1476 cm^{-1}	υ(N=O)
υ_5(B_2)	1290 cm^{-1}	υ_a(NO2)
υ_2(A_1)	(1025) cm^{-1}	$\upsilon_{s(}$NO2)

The separation between the two highest frequency bands is 115 cm^{-1} for the unidentate complex, whereas it is 186 cm^{-1} for the bidentate complex.

Thus Curtis and Curtis[62] concluded that $[Ni(dien)(NO_3)_2]$ contains both types, since it exhibits bands due to unidentate (1440 and 1315 cm^{-1}) and bidentate (1480 and 1300 cm^{-1}) NO_3^- ions. In general, the separation of the two highest frequency bands is larger for bidentate than for unidentate coordination if the complexes are similar. However, this rule does not hold good if the complexes are markedly similar.

In the present work, three strong bands at 1460, 1360 and 1010 cm^{-1} were observed in the spectra of Co(II) complex and at 1450, 1360 and 1010cm^{-1} in the spectra of Cu(II) complex (Table 3.7). These were assigned to υ_a(NO_2), υ_s (NO_2) and υ(NO) vibrations, respectively indicating that unidentate coordination of the nitrate ion to the Co(II) ion has taken place. The separation of the two highest frequency bands were 100 and 90 cm^{-1} in the Co(II) and Cu(II) complexes, respectively. Moreover, the absence of any band at 1290 cm^{-1} due to $\upsilon_a(NO_2)$ indicated that bidentate coordination has not taken place.

iv) *Sulphato complex*

When a ligand of relatively high symmetry coordinates to a metal, its symmetry is lowered and marked changes in the spectrum are expected because of the changes in the selection rules. This principle has been used extensively to determine whether acido anions such as SO_4^{2-} and CO_3^{2-} coordinate to metals as unidentate, chelating bientate or bridging bidentate ligands. Although symmetry lowering is also caused by the crystalline environment, this effect is generally much smaller than the effect of coordination.[63]

The free sulphato ion belongs to the high symmetry point group, T_d. Of the four fundamentals, only υ_3 and υ_4 are infrared active. If the symmetry of the ion is lowered by complex formation, the degenerate vibrations split and Raman active modes appear in the infrared spectrum.[64] The lowering of the symmetry caused by the coordination is different for the unidentate and bidentate complexes, as shown below.

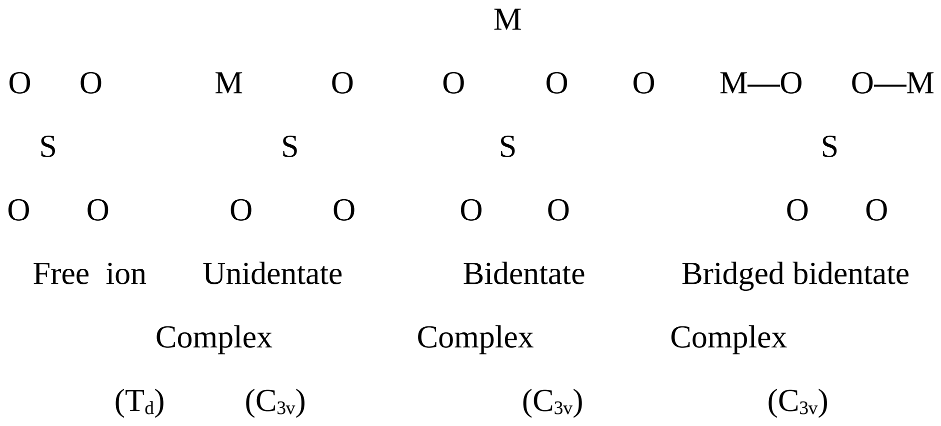

Fig. 3.4 Modes of coordination of sulphate group to a metal

In an approximately tetrahedral geometry, υ_3 and υ_4 do not split and υ_2 does not appear; although υ_1 is observed, it is very weak. When the symmetry is lowered from T_d to C_{3v}, as in unidentate coordination, υ_1 and υ_2 appear with medium intensity; moreover, υ_3 and υ_4 each splits into two bands. In bridged bidentate complexes, both υ_1 and υ_2 appear with medium intensity and υ_3 and υ_4 each splits into three bands. These results suggest that the symmetry is further lowered and probably reduced to C_{2v}.

The chelating bidentate SO_4^{2-} group was discovered by Barraclough and Tobe,[65] who observed three bands (1211,1176 and 1075 cm^{-1}) in the υ_3 region of $[Co(en)_2SO_4]Br$. These frequencies are higher than those of the bridging bidentate complex. Eskenazi et al[66] also found the same trend in Pd(II) sulphato complexs. Thus the distinction between briding and chelating sulphato complexes can be made on this basis.

In the present work, two medium intensity bands at 906 and 547 cm^{-1} have been observed. These have been assigned as υ_1 and υ_2 bands, respectively. Three bands in the region 1210, 1142 and 1008 cm^{-1} have also been observed and have been assigned as υ_3 bands. Thus the sulphato group in this complex is concluded to be a chelating bidentate ligand. This is also confirmed by analytical data(Table 3.3).

C. Conclusions

The iodo and nitrato complexes of Co(II), acetate complex of Ni(II) and Cu(II) and the chloro, nitrato and sulphato complexes of Cu(II) of BMPPA have been synthesized and characterised. The physico-chemical properties of all the complexes were studied and they were found to have the general formulae $[ML_2X_2]$. The structures suggested for these compounds are given in Figs. 3.3 and 3.4.

In these complexes, BMPPA acted as a neutral bidentate ligand. It provided two coordination sites, viz., the nitrogen atom of the azomethine group and the oxygen atom of the 5-pyrazolone ring system. The microanalytical, electrical conductance, magnetic and spectral data were logically correlated and the formulae and structures of the complexes were established.

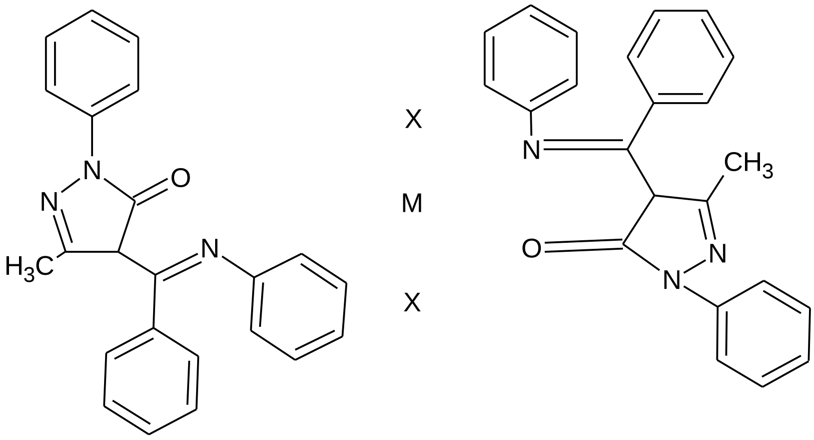

Fig.3.3 Suggested structure for $[ML_2X_2]$where M=Co(II), Ni(II) or Cu(II) and X=CH_3COO^-, I^- or NO_3^-

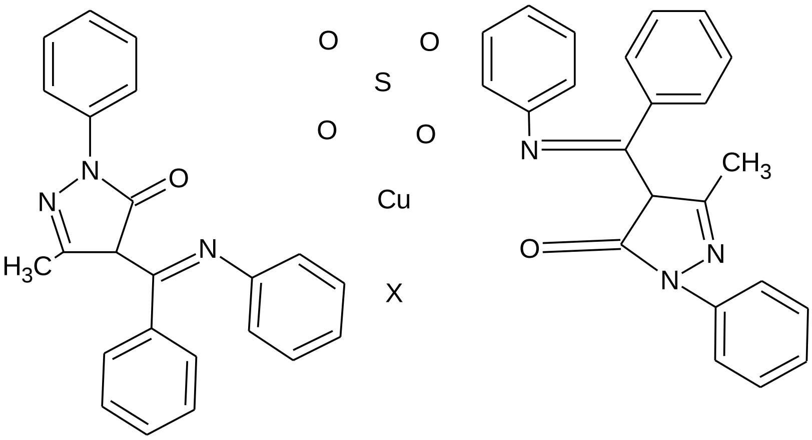

Fig. 3.4 Suggested structure for $[Cu(L)_2SO_4]$

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CHAPTER IV

Co(II), Ni(II) AND Cu(II) COMPLEXES OF N′-[PHENYL(METHYLPHENYL-5-PYRAZOLYL)METHYLIDENE]PYRIDINE-4-CARBOHYDRAZIDE
(BMPPI)

Schiff's bases or anils are the compounds having >C=N-N< linkages, which have immense applications as catalysts, stabilizers, pigments, dyes and drugs. They have good ability to form chelates with many metal ions.

A search through the literature has revealed that 2-hydroxy-1-naphthaldehyde isonicotinoyl hydrazone (NIH) and several other aroylhydrazone chelators possess anti-neoplastic activity due to their ability to bind intracellular ion. Richarson *et al*[1] have examined the structure and properties of NIH and its Fe(III) complex inorder to obtain further insight into its anti-tumour activity. Two tridentate NIH ligands deprotonate upon coordination to Fe(III) in a meridional fashion to form a distorted octahedral, high-spin complex.

Isonicotinic acid hydrazide or isoconitinylhydrazide, commonly known as isoniazid, is an antibacterial agent which has been used to treat tuberculosis. It interacts with microbial cell walls. Isoniazid can form Schiff's bases with diketones such as acetoacetanilide. Acetoacetanilide isonicotinylhydrazone and its metal chelates exhibit anticancer activity. The studies on N-methyl-acetoacetanilide isonicotinylhydrazone and its metal chelates revealed that they were active against pathogenic fungal strains. Five new metal chelates of ω-bromoacetoacetanilide isonicotinylhydrazone have been synthesized by Aravindakshan *et al.*[2] The ligand behaved as a tridentate monoanion or as a tridentate dianion in the complexes. These compounds were characterised mainly by elemental analyses, conductivity measurements and electronic, infrared and nuclear magnetic resonance spectral studies. Antifungal studies of these compounds against four selected pathogenic fungal strains using a cup-plate technique were carried out. The ligand and its metal chelates were active against all the fungal strains investigated. However, the chelates were found to be more active than the ligand.

The three isonicotinoyl hydrazones *viz.*, anisaldehyde isonicotinoyl hydrazone(AINH), 2-furaldehyde isonicotinoyl hydrazone (FINH), 2-thiophenealdehyde isonicotinoyl hydrazone (TINH) have been synthesized and characterised on the bases of their elemental analysis, magnetic susceptibility, IR, electronic and NMR spectral studies.[3] The ternary complexes of Ni(II) and Cu(II) with these hydrazones and neutral bidentate bases phen and bipy are octahedral and the presence of acetate and /or water molecule was revealed by the study of their IR spectra, force constants and thermal degradation pattern. Suitable structures have been assigned to these ternary complexes.

A new series of transition metal complexes of Schiff bases isonicotinic acid (2-hydroxybenzylidene)hydrazide, HL, have been synthesized. The Schiff base reacted with dipositive metal ions as monobasic tridentate ligand to yield mononuclear complexes of 1:2 (metal:ligand) except with copper(II) which formed complexes of 1:1 (metal:ligand). The ligand and its metal complexes were characterised by elemental analyses, IR, UV-vis, mass and ^{1}H NMR spectra, as well as magnetic moment, conductance measurements and thermal analyses. All complexes have octahedral configurations except copper(II) complex which has a square planar geometry distorted towards tetrahedral, while the uranium(II) complex favours hepta- coordination. The ligand and its metal complexes were tested against one strain gram positive bacteria (Staphylococcus aureus), gram negative bacteria (Escherichia coli) and Fungi (Candida albicans). The tested compounds exhibited high antibacterial activities.[4]

When isoniazid and pyridoxal were mixed in equimolar quantities a hydrazone was formed which was able to complex with iron. The oral administration of this compound to rats in single doses of 25-100 mg/kg led to an increase in faecal iron excretion up to 8 times the normal level. In tissue culture the compound was able to remove iron from Chang cells. The results suggested that the compound might be of potential value for the oral therapy of iron overload.[5]

2-Acetylpyridineisonicotinoyl hydrazone (Hapinh) complexes of VO(II), manganese(II), cobalt(II), nickel(II), copper(II) and zinc(II) having 1:1 metal-ligand stoichiometry have been prepared and characterised by elemental analyses, molar conductance, magnetic susceptibility, electronic, infrared, ESR and NMR (^{1}H and ^{13}C) studies. Octahedral/distorted octahedral geometry has been assigned for the VO(II), manganese(II), nickel(II), copper(II) and zinc(II) complexes while tetrahedral and trigonal bipyramidal configurations have been suggested for the cobalt(II) adduct and deprotonated complexes, respectively. IR and NMR spectral studies suggested a tridentate behaviour of Hapinh and apinh$^-$ species in the adducts and deprotonated complexes, respectively.[6]

A new series of 12 complexes of cobalt(II) and nickel(II) with N-isonicotinamide-2,4-dichlorobenzaldimine(INH-DCB) with the general composition MX_2.n(INH-DCB) [M=Co(II) or Ni(II), X= Cl^-, Br^-, $NO3^-$, NCS^- or CH_3COO^-, n=2; x=ClO_4^-, n=3] have been synthesized by Agarwal *et al*[4]. The nature of bonding and the stereochemistry of the complexes have been deduced from elemental analyses, infrared, electronic spectra, magnetic susceptibility and conductivity measurements. An octahedral geometry has been suggested for all the complexes. The metal complexes were screened for their antifungal and antibacterial activities on different species of pathogenic fungi and bacteria and their bipotency has been discussed.[7]

A perusal of the literature revealed that no work has been done on the transition metal complexes of the Schiff base derived from isoniazid and 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone. The present work involves the synthesis of a new type of bidentate/tetradentate ligand formed by the condensation of isoniazid with 4-benzoyl-3-methyl-1- phenyl-5-pyrazolone.

The ligand system (Fig. 4.1) has five sites which may offer coordination, i.e., azomethine nitrogen, the pyrazolone ring oxygen atom, nitrogen atom of –N-H group, oxygen atom of carbonyl group and nitrogen atom of the pyridine moiety. Hence it was considered worth while to synthezise this ligand and to complex it with first row transition metal ions with a view to characterise them and also to study their biological activity.

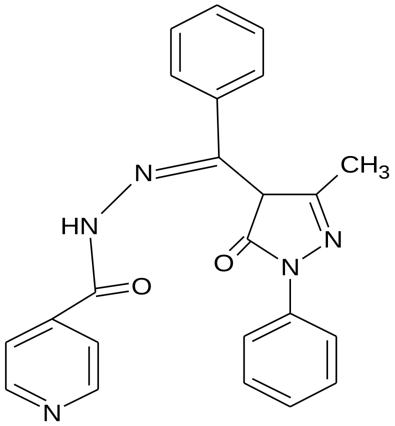

Fig.4.1

Suggested structure for N′-[phenyl(methylphenyl-5-pyrazolyl)methylidene]pyridine-4-carbohydrazide,* (BMPPI) (L)

A. Experimental

1. Materials and methods

Specifications regarding the reagents used, the procedural details adopted for the synthesis and the characterisation of the ligand and the complexes are given in Chapter II.

2. Synthesis of the ligand, N′[phenyl(methylphenyl-5-pyrazolyl)methylidene]pyridine-4-carbohydrazide (BMPPI)

The synthesis of the ligand consists of the following three stages**.**

---

*The systematic name of the compound is N′-[(1E-(3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)(phenyl)methylidene]pyridine-4-carbohydrazide. But for the sake of convenience the name N′[phenyl(mehylphenyl-5-pyrazolyl)methylidene]pyridine-4-carbohydrazide and the short form ‘BMPPI’ are adopted in this thesis.

a) Preparation of 3-methyl-1-phenyl-5-pyrazolone

Mixed together (49ml, 0.384 mol) of ethylacetoacetate and phenylhydrazine (36.5 ml, 0.37 mol) n a large china dish. Heated the mixture on a boiling water bath in a fume cupboard for about two hours and stirred from time to time with a glass rod. Allowed the heavy reddish syrup to cool, added about 100 ml of ether and stirred the mixture vigorously. The syrup, which was insoluble in ether, solidified within 15 minutes. Filtered the solid at the pump and washed it thoroughly with ether to remove the coloured impurities. Recrystallised from hot water to obtain colourless crystals of the pyrazolone. Yield: 52 g (80 %)

b) Preparation of 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone (BMPP)

3-methyl-1-phenyl-5-pyrazolone (15 g, 0.0862 mol) was placed in a flask equipped with a reflux condenser and a magnetic stirrer and dissolved in 60-80 ml of freshly distilled ethanol by heating. Calcium hydroxide (12 g) were added followed by the addition of benzoyl chloride (9.9 ml) dropwise within one minute. The reaction mixture became a thick paste and the temperature increased during the first few minutes. The mixture was heated to reflux for 30 minutes. The calcium complex in the flask was decomposed by pouring the mixture into 2N hydrochloric acid (200 ml) which caused cream coloured crystals to separate. The crystals were collected on a Buchner funnel. They were recrystallized from ethanol-water mixture which was slightly acidified to destroy any undecomposed calcium complex. Yield: 15.6 g (65 %).

c) *Preparation of BMPPI*

Dissolved BMPP (14.161 g, 0.05 mol) in ethanol by heating and kept under reflux. Added an ethanolic solution of isonicotinic acid hydrazide (6.862 g, 0.05 mol) to the refluxing solution and refluxed for 3 hours and left overnight. The red coloured crystals formed were filtered at the pump and washed with ethanol and dried. Yield: 12.7690 g, 62.98%.

3. Syntheses of the complexes of BMPPI

Complexes of the ligand with the acetate, chloride and nitrate of cobalt(II), acetate and chloride of nickel(II) and acetate, chloride and nitrate of copper(II) were synthesized.

a) *Complex of $Co(CH_3COO)_2$ and $CoCl_2$*

Dissolved the ligand in methanol by heating and refluxed. Added a hot methanolic solution of cobalt(II) acetate tetrahydrate to it in drops. The colour changed immediately from yellow to brown. Refluxed for 2 hours. A dark red solid was formed. Cooled and filtered at the pump and washed thoroughly with methanol and dried.

b) *Complex of $Co(NO_3)_2$*

Dissolved the ligand in methanol by heating and refluxed. Added a methanolic salt solution to the refluxing solution of the ligand. Refluxed for 3.5 hours. Reduced the volume to half and cooled in a refrigerator. A dark brown solid was formed. Filtered the solid at the pump, washed with methanol and dried.

c) *Complex of Ni(CH_3COO)$_2$*

Dissolved the ligand in methanol-ethanol mixture by heating and refluxed. Added a methanolic solution of the metal salt to the refluxing solution of the ligand, in drops. The colour of the solution changed and solid started forming even before the metal salt solution was completely added. Stopped heating and added the rest of the metal salt solution to the mixture in the flask. A brown solid was formed. Cooled and filtered at the pump, washed thoroughly with methanol and dried in vacuum.

d) *Complexes of $NiCl_2$*

Dissolved the ligand in methanol by heating and refluxed. Added a methanolic solution of the metal salt to the refluxing solution of the ligand and refluxed for hours. Reduced the volume to half by evaporation and allowed to cool. Filtered the solid at the pump, washed thoroughly with methanol and dried in vacuum.

e) *Complexes of $Cu(CH_3COO)_2$, $CuCl_2$ and $Cu(NO_3)_2$*

Dissolved the ligand in methanol by heating. Added a methanolic solution of the metal salt to the refluxing solution of the ligand. As soon as the solutions were mixed, the colour changed to green-brown. Stopped heating and added the rest of the metal salt solution. Cooled and filtered at the pump, washed thoroughly with methanol and dried in vacuum.

B. **Results and discussion**

The data obtained from analytical and physico-chemical studies have been correlated in a logical way to explain the properties, bonding and structure of the compounds.

1. Characterisation of the ligand, BMPPI

The ligand BMPPI is red in colour with a melting point of 212ºC. The analytical data showed close agreement with the suggested formula of $C_{23}H_{19}N_5O_2$. It was further characterised by IR spectral- and elemental analysis data.

a) IR spectrum

The infrared spectrum of the ligand BMPPI showed a number of absorption bands which were characteristic of different groups present in it (Table 4.1). A sharp band at 3020 cm^{-1} has been assigned to N-H stretching vibration. This suggested that the –NH group of the hydrazine moiety was not involved in coordination to the metal ions. A sharp band at 1610 cm^{-1} was due to υC=O vibration. A broad band between 720-740 cm^{-1} was assigned to N-H δ. A sharp band at 1000 cm^{-1} is due to N-N stretching vibration. A sharp band at 1550 cm^{-1} is assigned to >NHC=O stretching vibration. The bands due to the in plane bending of aromatic C-H stretching were found in the 1300-1000 cm^{-1} region. . Strong bands in the region 1400-1600 cm^{-1} were due to skeletal vibrations involving carbon-carbon stretching within the ring. The skeletal vibrational bands have overlapped with the C-N and the -NH-C=O stretching vibrational bands. Two distinct bands occurring at 2920 and 2880 cm^{-1} were due to asymmetrical and symmetrical

TABLE 4.1

SIGNIFICANT IR BANDS OF BMPPI AND THEIR ASSIGNMENTS

BAND FREQUENCY * (cm-1)	ASSIGNMENT
3020 sh	N-H stretch
2920 sh	Asymmetric C-H stretch
2880 sh	Symmetric C-H stretch
1610 s	>C=O stretch
1600-1400 s	Skeletal vibrations of the aromatic ring
1550 s	>NHCO stretch & N-H bend
1470	Asymmetric bending vibration of CH_3-
1370	Symmetric bending vibration of CH_3 -
1300-1000	In-plane bending of the aromatic C-H
1000 sh	N-N stretch
810-600 s	Out-of-plane bending of ring C-H
810 s	Out-of-plane ring bending of 4-substituted pyridine
740-720 br	N-H bend
730 s	Out-of-plane ring bending of a4-sunstituted pyridine

* s = strong; sh = sharp; br = broad

stretching C-H (of methyl group) modes of vibration, respectively.[8] The symmetrical bending vibration (δs CH_3) occurred at 1370 cm^{-1} and the asymmetrical bending vibration (δ_{as} CH_3) at 1470 cm^{-1}. The absorption band near 1375 cm^{-1}, arising from the symmetrical bending of the methyl C-H bonds, is very stable in position when the methyl group is attached to another carbon atom.[8] Strong bands in the range 810-600 cm^{-1} observed in the spectrum were due to the out-of-plane bending of the ring C-H bonds bending (β ring) modes of the 4-substituted pyridine ring.[8]

2. Formulae and general properties of the complexes

All the complexes were found to be coloured solids, stable to light, heat and moisture. Some of them had crystalline nature. The solubilities of these complexes in common organic solvents were very low but they were soluble in DMF or DMSO. The analytical data (Table 4.2) and the molar conductance values in DMF or DMSO (Table 4.3) showed that the complexes had the formula $[ML_2X_2]$ except the chloro complex of Cu(II) which had the formula $[CuL_2Cl_2]H_2O$. The spectral and magnetic data also confirmed the suggested formulae.

3. Molar conductance

The molar conductance of 10^{-3} M solutions in DMF/DMSO of the BMPPI complexes were determined at room temperature and the values are given in Table 4.3. All the complexes showed values which were lower than that expected for 1:1 electrolytes indicating their non-electrolytic in nature.[9] The analytical data and spectral studies also supported the suggested formula.

TABLE 4.2

ANALYTICAL DATA OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPI

COMPOUND	EMPIRICAL FORMULA	F.WT. *	COLOUR	YIELD %	FOUND (CALCULATED) %				
					METAL	C	H	N	ANION
BMPPI (L)	$C_{23}H_{19}N_5O_2$	397	Red	63	-	69.50 (69.52)	4.72 (4.78)	17.61 (17.63)	-
$[Co(L)_2(CH_3COO)_2]$	$CoC_{50}H_{44}N_{10}O_8$	970.93	Dark brown	45	6.00 (6.06)	56.17 (56.85)	4.07 (3.91)	14.58 (14.42)	-
$[Co(L)_2Cl_2]$	$CoC_{46}H_{38}N_{10}O_4Cl_2$	923.93	Dark brown	42	6.29 (6.38)	59.59 (59.74)	4.86 (4.11)	14.97 (15.15)	7.50 (7.68)
$[Co(L)_2(NO_3)_2]$	$CoC_{46}H_{38}N_{12}O_{10}$	976.93	Dark red brown	40	5.89 (6.03)	57.85 (56.50)	4.08 (3.89)	16.20 (17.20)h	-
$[NI(L)_2(CH_3COO)_2]$	$NiC_{50}H_{44}N_{10}O_8$	970.71	Light brown	53	5.98 (6.04)	60.85 (61.81)	4.50 (4.53)	14.95 (14.42)	-
$[Ni(L)_2Cl_2]$	$NiC_{46}H_{38}N_{10}O_4Cl_2$	923.71	Light green	52	6.30 (6.36)	59.60 (59.75)	4.95 (4.11)	15.12 (15.16)	7.50 (7.68)
$[Cu(L)_2(CH_3COO)_2]$	$CuC_{50}H_{44}N_{10}O_8$	975.54	Red orange	51	6.45 (6.51)	57.73 (56.58)	3.94 (3.90)	14.55 (14.35)	-
$[Cu(L)_2Cl_2]\ H_2O$	$CuC_{46}H_{40}N_{10}O_5Cl_2$	946.54	Pale green	50	6.05 (6.71)	57.78 (58.32)	3.94 (4.01)	14.62 (14.79)	7.45 (7.50)
$[Cu(L)_2(NO_3)_2]$	$CuC_{46}H_{38}N_{12}O_{10}$	981.54	Yellow brown	52	6.31 (6.47	57.04 (56.23)	4.00 (3.87)	17.87 (17.12)	-

* F. Wt. = FORMULA WEIGHT

TABLE 4.3

MOLAR CONDUCTANCES OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPI

COMPLEXES	Ω_m ohm^{-1} cm^2 mol^{-1}	SOLVENT
$[Co(L)_2(CH_3COO)_2]$	20.15	DMSO
$[Co(L)_2Cl_2]$	40.3	DMF
$[Co(L)_2(NO_3)_2]$	10.08	DMF
$[Ni(L)_2(CH_3COO)_2]$	20.15	ETHANOL
$[Ni(L)_2Cl_2]$	30.23	DMF
$[Cu(L)_2(CH_3COO)_2]$	20.15	DMF
$[Cu(L)_2Cl_2]H_2O$	10.08	DMF
$[Cu(L)_2(NO_3)_2]$	0.0	DMSO

4. Magnetic behaviour

The mass susceptibility, molar susceptibility, corrected molar susceptibility and the effective magnetic moment values for the cobalt(II), nickel(II) and copper(II) complexes are tabulated in Table 4.4. The values 1.18, 1.03 and 2.86 B.M. for the acetato. chloro and nitrato complexes of cobalt(II) indicated that they deviate significantly from the calculated spin-only moments. Smaller but significant discrepancies between experimental moments and calculated spin-only moments are found for complexes with A_2, A_{2g}, E and E_g ground states. These discrepancies are caused by angular momentum introduced to the ground state by a mixing in of higher T states. Theory shows that the magnetic moment of such a complex can be calculated from the relation[10]

$\mu = (1-\lambda'/\Delta)]n(n+2)]^{½}$ where λ' is the spin-orbit coupling parameter and Δ is the ligand field splitting.

Octahedral weak-field cobalt(II) complexes such as $(NH_4)_2[Co(H_2O)_6](SO_4)_2$ have room temperature moments of 5.00 to 5.10, in remarkably close agreement with the value of 5.10 obtained from the above relation. Octahedral strong-field cobalt(II) complexes appear to be very rare. However, $K_2Pb[Co(NO_3)_6]$ has been reported to have $\mu = 1.80$, in fair agreement with the value estimated by using the above relation. The effective magnetic moments reported in the present work for the cobalt(II) complexes indicated that they were octahedral strong-field complexes.

TABLE 4.4

MAGNETIC SUSCEPTIBILITY DATA OF COBALT(II), NICKEL(II) AND COPPER(II) COMPLEXES OF BMPPI

COMPLEX	χ_g x 10^{-6}	χ_m x10^{-6}	$\chi_{m(corr)}$ x 10^{-6}	μ_{eff}	T (K)
$[Co(L)_2(CH_3COO)_2]$	0.0882	86.68	587.81	1.18	295.7
$[Co(L)_2Cl_2]$	0.8613	795.94	1225.26	1.03	296.3
$[Co(L)_2(NO_3)_2]$	3.0574	2986.44	3469.56	2.86	295
$[Ni(L)_2(CH_3COO)_2]I$	1.441	1399.50	1399.50	2.12	296.3
$[Ni(L)_2Cl_2]$	2.929	2705.74	3199.86	2.75	295.7
$[Cu(L)_2(CH_3COO)_2]$	1.938`	1890.6	2319.32	1.18	296.3
$[Cu(L)_2Cl_2]H_2O$	2.673	2482.41	2976.53	2.66	296.1
$[Cu(L)_2(NO_3)_2]$	2.229	2188.26	2670.38	2.51	296.1

χ_g = mass susceptibility
χ_m = molar susceptibility
$\chi_{m\ corr}$ = corrected molar susceptibility
μ_{eff} = effective magnetic moment
T=Temperature in Kelvin

The effective magnetic moments for the acetato and chloro complexes of nickel(II) tabulated in Table 4.4 are 2.12 and 2.75 B.M., respectively. These values are commensurate with six-coordinate spin-free nickel(II) complexes.[11]

The effective magnetic moment for the acetato, chloro and nitrato complexes of copper(II), tabulated in Table 4.4 are 1.18, 2.66 and 2.51 B.M., respectively. These values are in accord with their distorted octahedral configurations[12] as expected. The lower value for μ_{eff} exhibited by the acetato complex than the spin-only value expected for octahedral complexes may be due to metal-metal interaction.[13]

5. Electronic spectra

In general, in high-spin six coordinate complexes, two principal regions of absorption are observed.[13-19] The important electronic spectral bands of the complexes and their probable assignments are given in Table 4.5.

In the acetato complex of cobalt(II), a broad band at 650 nm is observed which has been assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$ transition. This suggests an octahedral environment with tetragonal distortion[20] around cobalt(II) ion.

In the chloro complex of cobalt(II), a broad band at 851 nm is observed, which has been assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, (υ_1) transition. This suggests an octahedral environment around cobalt(II) ion.

In the nitrato complex of cobalt(II), a broad and intense band has been observed at 520 nm which has been assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)(\upsilon_3)$ transition. This suggests an octahedral environment around cobalt(II) ion.[20]

TABLE 4.5

ELECTRONIC SPECTRAL BANDS OF COBALT(II),NICKEL (II) AND COPPER(II) COMPLEXES OF BMPPI

COMPLEX	BANDS(nm)	ASSIGNMENT	GEOMETRY
$[Co(L)_2(CH_3COO)_2]$	650	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$	Octahedral
$[Co(L)_2Cl_2]$	851	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$	Octahedral
$[Co(L)_2(NO_3)_2]$	520	$^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$	Octahedral
$[Ni(L)_2(CH_3COO)_2]$	529 600	$^3A_{2g} \rightarrow {}^3T_{2g}$ $^3A_{2g} \rightarrow {}^3T_{2g}(P^4)$	Octahedral
$[Ni(L)_2Cl_2]$	806 610	$^3A_{2g} \rightarrow {}^3T_{2g}$ $^3A_{2g} \rightarrow {}^3T_{2g}(P)$	Octahedral
$[Cu(L)_2(CH_3COO)_2]$	~550 ~650	$^2E_g \rightarrow {}^2T_{2g}$	Distorted octahedral
$[Cu(L)_2Cl_2]H_2O$	~525 ~600	$^2E_g \rightarrow {}^2T_{2g}$	Distorted Octahedral
$[Cu(L)_2(NO_3)_2]$	~525 ~600	$^2E_g \rightarrow {}^2T_{2g}$	Distorted octahedral

The configuration d^8 is essentially prone to form four coordinate diamagnetic planar derivatives, especially with stronger field ligands, where steric hindrance impedes high coordination numbers.[21-43] Such complexes typically have a single band at 556-400 nm of intensity generally near 50-500 l mol-1 cm^{-1} and are often orange, yellow or red. A second, more intense band may be seen near 435-333 nm which is often charge transfer in origin. Square-planar complexes differ from tetrahedral and pseudo-tetrahedral complexes in that absorption below 1000 nm is not seen (except perhaps for some vibrational structure), the crystal field strength in a square-planar complex being very high.

Diamagnetism is a consequence of eight electrons being paired in the four lower lying d orbitals. The upper orbital is x^2-y^2 (b_{1g}) in monodentate NiL_4 D_{4h} systems, where the x,y Cartesian coordinates pass through the Ni-L bonds. However, it is to be noted that if bidentate ligands are used, the x,y coordinates are usually written to bisect these bidentate ligands. Under such circumstances, the upper orbital is xy (b_{2g}). The four lower orbitals are often so close together in energy, that individual transitions therefrom to the upper d level, cannot be distinguished –hence the single absorption band.[44]

In the electronic spectra of the acetato complex of nickel(II), two bands at 529 and 600 nm were observed which are assignable to $^3A_{2g} \rightarrow {}^3T_{2g}$ and $^3A_{2g} \rightarrow {}^3T_{2g}(P)$ transitions, respectively, assuming octahedral geometry. The effective magnetic moment value of this complex also supports this geometry.[45]

In the chloro complex of nickel(II), two broad bands at 806 and 610 nm have been observed. They have been assigned as $^3A_{2g} \rightarrow {}^3T_{2g}$ and $^3A_{2g} \rightarrow {}^3T_{1g}(P)$

transitions, respectively.[46] Hence it was concluded that this complex has octahedral geometry.

The electronic spectrum of the acetato complex of copper(II) exhibited one broad band at ~ 550 and ~ 650 nm with λ_{max} at 598 nm, assignable to $^2E_g \rightarrow {}^2T_{2g}$ transition has been observed in support of a distorted octahedral configuration.[47] The effective magnetic moment of the complex was 1.18 B.M. The electronic spectral data[48] coupled with magnetic moment values[49] suggested a distorted octahedral geometry for the complex.

The electronic spectrum of the chloro complex of copper(II) exhibited one broad band at ~ 525 and ~ 600 nm with maximum at 550 nm, assignable to $^2E_g \rightarrow {}^2T_{2g}$ transition has been observed in support of a distorted octahedral configuration.[50] The electronic spectral data[47] coupled with magnetic moment values[46] suggested a distorted octahedral geometry for the complex.

The electronic spectrum of the nitrato complex of copper(II) exhibited one broad band at ~525 nm and at 600 with a maximum at 558 nm, assignable to $^2E_g \rightarrow {}^2T_{2g}$ transition has been observed in support of a distorted octahedral configuration.[49] The electronic spectral data[50] coupled with magnetic moment values[51] suggested a distorted octahedral geometry for the complex.

4. Infrared spectra

a) Complexes

The IR spectra of the complexes in the solid state contain characteristic bands due to vibrations of M-N, M-O, >C=N-, C-N, N-H, etc bands and are assigned accordingly. Assignments have been made on the basis of comparison with similar known systems and by reference to tables of spectral data.[51] The structurally important bands are tabulated in Tables 4.6 & 4.7. The ligand displayed a band at 3020 cm^{-1} which was almost undisplaced in all the complexes indicating that the N-H group of the hydrazine moiety were not involved in coordination to the metal. The absence of broadening of the band due to υ N-H indicated the absence of intramolecular hydrogen bonding between the carbonyl oxygen and the –NH of the hydrazine group.[51] The band due to υC=N which appeared at 1585 cm^{-1} in the ligand was shifted to lower frequencies in the complexes (1570-1540 cm^{-1}) (Tables 4.6 & 4.7) indicating that the azomethine nitrogen atom was coordinated to the metal atom. The band at 1610 cm^{-1} due to υC=O of the pyrazolone ring in the ligand was also shifted to lower frequencies in the complexes (1595-1550 cm^{-1}) suggesting that the oxygen atom of the pyrazolone ring was also involved in coordination to the metal atoms. The bands in the region 480-420 and 400-360 cm^{-1} have been assigned to υM-O and υM-N bonds.

b))IR features of coordinated anions in the complexes

IR spectroscopy has been used to determine the status of the anions in the complexes.

i) *Acetato complexes*

The acetato complexes showed bands at ~ 1600 and 1320 cm^{-1} due to asymmetric and symmetric υCOO^- stretching bands, respectively, which were consistent with the monodentate[52] acetate group. The band at ~ 350 cm^{-1} was assigned to (υ Co-OAc).[52]

TABLE 4.6

SIGNIFICANT BANDS IN THE IR SPECTRA OF THE CHLORO AND NITRATO COMPLEXES OF Co(II), Ni(II) AND Cu(II) OF BMPPI AND THEIR ASSIGNMENTS

COMPOUNDS	ASSIGNMENTS AND BAND FREQUENCIES * (cm^{-1})									
	υ N-H	υ C =N	υ C= O (cm^{-1})	δ N-N-H	υ CO ring	υ M-N	υ M-O	υ M-Cl	υ H_2O	υ NO_3^- coordinated
BMPPI (L)	3020 m,sh	1585 s,sh	1610 s	1538 s,sh	1470 s, sh	-	-	-	-	-
$[Co(L)_2Cl_2]$	3010 m	1570 s,sh	1595 s,sh	1530 m,sh	1445 s,sh	360 w	480 w	335 w		
$[Ni(L)_2Cl_2]$	3020 m	1550 s,sh	1575 s,sh	1520 m,sh	1450 s,sh	380 w,sh	460 w	280 w	-	-
$[Cu(L)_2Cl_2]H_2O$	3020 m	1550 s,sh	1580 s,sh	1530 m,sh	1450 s,sh	380 w,sh	480 w	420 w	3400-3300 br	-
$[Co(L)_2(NO_3)_2]$	3030 m	1540 s,sh	1570 s,sh	1500 m,sh	1410 s,sh	380 w	480 w	-		1450 sh 1280 sh 1020 sh
$[Ni(L)_2(NO_3)_2]$	3020 m	1550 s,sh	1575 s,sh	1530 m,sh	1410 s,sh	400 w	460 w	-		1465 s 1280 m 1020 m
$[Cu(L)_2(NO_3)_2]$	3020 m	1550 s,sh	1550 sh	1530 m,sh	1450 s,sh	380 w, sh	420 w	-		1450 s 1260 m 1020 s

* s = strong; m = medium; w = weak; sh = sharp

TABLE 4.7

SIGNIFICANT BANDS IN THE IR SPECTRA OF THE ACETATO COMPLEXES OFCo(II), Ni(II) AND Cu(II) OF BMPPI AND THEIR ASSIGNMENTS

COMPOUND	υ N-H	υ C =N	υ C= O (cm^{-1})	δ N-N-H	υ CO ring	υ M-N	υ M-O	υ COO$^-$ asym	υ COO$^-$ sym
BMPPI (L)	3020 m	1585 s,sh	1610 s	1538 s,sh	1470 s, sh	-	-	-	
$[Co(L)_2(CH_3COO)_2]$	3010 m	1550 s,sh	1570 s,sh	1530 s,sh	1450 s,sh	470 m	380 w	1600 sh	1320 sh
$[Ni(L)_2(CH_3COO)_2]$	3020 m	1540 s,sh	1570 s,sh	1500 m,sh	1455 s,sh	490 w,sh	380 w	1600 sh	1320 sh
[Cu(L)(CH3COO)2]	3020 m	1540 s,sh	1550 s,sh	1530 m,sh	1450 s,sh	490 w,sh	380 w	1600 sh	1320 sh

* s = strong; m = medium; w = weak; sh = sharp

ii) Chloro complexes

The band at ~ 335 cm^{-1} in the chloro complex of cobalt(II) has been assigned to Co-Cl bond, i.e., the chlorine atom present was terminal and not bridging.[53] The presence of a broad band in the region 3400-3300 cm^{-1} in the copper complex indicated the presence of water molecule. This was confirmed by elemental analyses (Table 4.2). A medium band at 420 cm^{-1} in the spectrum was assigned to Cu-Cl bond. This suggested that the chloride ion was present inside the coordination sphere, which has been confirmed by molar conductance value. A medium band at 280 cm^{-1} in the spectrum of the chloro complex of nickel(II) indicated the presence of Ni-Cl bond suggesting that the chloride anion was present inside the coordination sphere.

iii) Nitrato complexes

Two weak bands were observed at ~1720 and ~ 1700 cm^{-1} in the spectrum of the nitrato complexes which suggested that the nitrato group was monodentate in these complexes[54] and the band in the range 330-350 cm^{-1} was assigned to $\upsilon(Co\text{-}NO_3)$. Moreover, three additional bands at ~1450, ~1280 and ~1020 cm^{-1} were observed in the spectra of the complexes, which were assigned to υ_4, υ_1 and υ_2 modes of coordinated nitrate ion. Since the magnitude of separation of υ_4 and υ_1 modes is ~170 cm^{-1}, it is ascertained that the nitrate ions are coordinated unidentatively.[55]

C. Conclusions

The acetato, chloro and the nitrato complexes of cobalt(II), nickel(II) an copper(II) have been synthesised and characterised. The physico-chemical properties of all the complexes have been studied and they were found to have the general formula $[ML_2X_2]$ except the chloro complex of copper(II), which showed the formula $[CuL_2Cl_2](H_2O)$. The structures suggested for these compounds are given in Fig. 4.2

In these complexes, BMPPI acted as a neutral bidentate ligand. It provided only two coordination sites, viz., the nitrogen atom of the azomethine group and the oxygen atom of the pyrazolone ring system, though five potential ligating sites were available in the ligand. The microanalytical, electrical conductance, magnetic and spectral data were logically correlated and the formulae and the structures of the complexes were established.

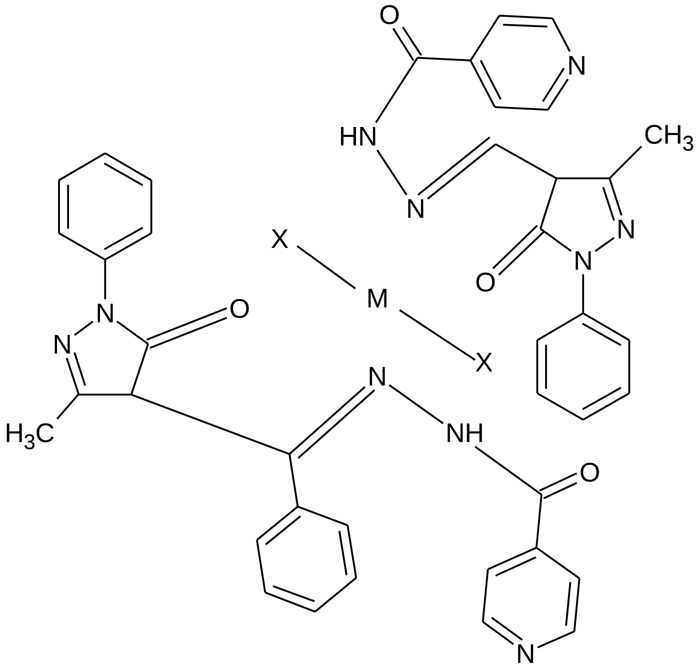

Fig.4.2 Suggested structure for $[ML_2X_2]$ where M=Co(II), Ni(II) or Cu(II) and X= CH_3COO^-, Cl^- or NO_3^-

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CHAPTER V

Co(II), Ni(II) AND Co(II) COMPLEXES OF METHYLPHENYL-4-[PHENYL(PHENYLHYDRAZONO)METHYL]-3-PYRAZOLONE

(BMPPPH)

A search through the literature proves that a lot of work has been carried out to understand the complexing behaviour of various ligands. One of the important ligands used for the study is hydrazone. Choudhary et al[1] have studied the complexing behaviour of thiohydrazide and thiohydrazone [2,3] by synthesizing the complexes of bivalent cobalt, nickel, copper, zinc, cadmium and palladium with morpholine-N-thiohydrazone of benzaldehyde (benzmthH), cinnamaldehyde (cinmthH) and cyclohexanone (cyclmthH). These thiohydrazones (LH) have donor sites similar to the corresponding thiosemicarbazones but alkyl substitutions for NH_2 hydrogens on ($-CS-NH_2$) contributed a large electon density on sulphur atom of ligand and made them better donor molecules tpwards metal ions.

Anhydrous cupric chloride in dry methanol reacted with cyclmthH forming [Cu(cyclmthH)Cl_2], but other thiohydrazones formed inner *bis*-chelate [CuL_2]. (LH = benzmthH or cinmthH). Cadmium chloride formed [CdLHCl_2] with benzmthH, cinmthH and cyclmthH as well. With metal acetate and chloride in case of palladium(II) in neutral aqueous ethanol, these ligands formed neutral inner complexes ML_2 (M = cobalt(II), copper(II), nickel(II), zinc(II) and cadmium(II)). The colour, magnetic moment values and reflectance spectra of [Co(cyclmth)$_2$] differed appreciably from other *bis*-chelates [CoL_2], L = benzmth or cinmthH). The marked change in donor behaviour of cyclmthH can be attributed to pronounced electron pushing character, absence of delocalised π-electron in metal chelate ring and large steric volume of cyclohexanone altered the geometric disposition of ligand molecule. In general, the complexes were insoluble in water but dissolved slightly in ethanol and methanol. The solubility of cyclmthH complexes was greater in organic solvents than in others. In DMF, the electrical conductance values of the complexes were negligible indicating their non-ionic character. The complexes zinc(II), cadmium(II) and palladium(II) were diamagnetic, whereas the copper(II), cobalt(II) and nickel(II) complexes were paramagnetic. The diamagnetism of the palladium(II) complexes indicated their square-planar structure.[4] The room temperature magnetic moment values of the cobalt(II) complexes (3.98-4.52 B.M.) and that of the nickel(II) complexes (3.20-3.32 B.M.) occured in the range of tetrahedral complexes.[5] The copper(II) complexes displayed magnetic moment values in the range 1-84-1.91 B.M., suggesting that they were magnetically dilute and probably possess tetragonal structure.[6] The values for $[Co(cyclmthH)_2]$ (4.52 B.M.) were typical of tetrahedral molecule.[6] A slight lowering of the values of $[Co(benzmthH)_2]$ (3.98) and $[Co(cinmthH)_2]$ (4.12 B.M.) could be attributed to spin-state equilibrium.

In view of the biological importance of molybdenum,[7] several new oxomolybdenum(V) and dioxomolybdenum(VI) complexes of Schiff bases derived from isonicotinic acid hydrazide (INH) and salicylaldehyde (INHSAL), furan-2-aldehyde(INFAL), 2-hydroxy-1-naphthaldehyde (INHNAL), 4-dimethylamino-benzaldehyde (INHDAB), 2-hydroxyacetphenone(INHHAP) or p-chlorobenzaldehyde (INHPCB) have been prepared[8] having formulae MoOLClX, MoO_2LY

(L=INHSAL, X= H_2O, Y=CH_3OH), $MoOLCl_2$, MoOLClZ, MoO_2L (L=INHSAL, Z= NCS), $MoOLCl_2X$, MoOLClZX, $MoO_2L(OH)Y$ (L=INHFAL), $MoOLCl_2X$, $MoO_2L(OH)X$ (L=INHDAB)), $MoOLCL_2$, MoO_2LY (L=INHHAP), $MoO_2L(OH)_2$ (L=INHPCB). The complexes have been characterised by elemental analyses, molar conductance, magnetic moment values, infrared, electronic, ^1H NMR and ESR spectral data.

The synthesis and evaluation of sulphonylhydrazones of phthalimido acetaldehyde as anticancer agents have been carried out by Utpal Sandyal *et al*[9]. Marginal to moderate *in vivo* activity of some arylsulphonylhydrazones of substituted benzaldehydes and nitrosalicylaldehydes in murine Ehrlich Ascites Carcinoma (EAC) have been reported.[10] They have also described the highly significant anticancer activity of phthalmustine which contain the basic nitrogen mustard antitumour functionality embedded in the phthalimido moiety.[11] As part of their ongoing anticancer drug development programme,[12] they have prepared phthalimido derivatives containing arylsulpholylhydrazones of 2-pyridinecarboxaldehyde-1-oxide functionality.

The behaviour of 4-arylhydrazono-3-methyl-2-pyrazolin-5-ones towards acetylation, hydroxymethylation, Mannich reaction and chlorosulphonation have been carried out by Metwally *et al*[13] in view of the fact that pyrazoles[14] represent one of the most active classes of heterocyclic compounds possessing a wide spectrum of biological activities. A new series of 1-substituted-4-arylhydrazono-3-methyl(or phenyl)-2-pyrazolin-5-ones and 4-arylhydrazono-3-methyl (or phenyl)-5-phenylsulphonylpyrazoles, using the corresponding 4-arylhydrazono-3-methyl-2-

pyrazolin-5-ones have been synthesised by them. The presence of the cyclic –CONH- linkage in the aryl hydrazonopyrazolones prompted them to investigate their behaviour towards acetylation, hydroxymethylation, aminomethylation and chloromethylation.

Jolly *et al*[15] have synthesized a number of aryl thiosemicarbazones and 2-oxo-Δ^2-thiazolin-2-ylhydrazones and have tested for *in vitro* activity against M. tuberculosis($H_{37}R_v$ strain) and antiviral activity for AIDS.

The syntheses and spectral features of 2-acetylpyridine (N-benzoyl)glycylhydrazone (2-ApBzGH) with manganese(II), cobalt(II), nickel(II), copper(II), zinc(II), cadmium(II) and mercury(II) have been reported by Lonibala [16] and co workers. The analytical data of the complexes suggested that 2-ApBzGH could form complexes in both 1:1 and 1:2 ratios. The electrical conductance showed 1:1 electrolytic nature of the adducts. IR, ^1H and ^{13}C NMR spectra suggested tridentate behaviour of 2-ApBzGH coordinating through hydrazide >C=O, azomethine nitrogen and ring nitrogen as a neutral ligand in the adducts and uninegative ligand in the deprotonated complexes though keto-enol tautomertism. The highly shielded ^{113}Cd chemical shift value suggested more ionic bonding in the complexes.

The synthesis, crystal structure and catalytic reactivity of hydrazone Schiff base-manganese(II) complexes were reported by Hassan Hosseini-Monfared and co workers.[17] Five dissymmetric tridentate Schiff base ligands, containing a mixed donor set of ONN and ONO were prepared in the reaction of benzhydrazide with the appropriate salicylaldehyde and pyridine-2-carbaldehyde and characterised by

FT-IR, ^1H and ^{13}C NMR. The results suggested that the Schiff bases HL^1(benzoic acid(2-hydroxy3-methoxy-benzylidene)-hydrazide), HL^2(benzoic acid(2,3-dihydroxy-benzylidene)-hydrazide), HL^3(benzoic acid(2-hydroxy-benzylidene)-hydrazide) and HL^4(benzoic acid(5-bromo-2-hydroxy-benzylidene)-hydrazide) coordinated as univalent anions with their tridentate O,N,O donors derived from the carbonyl- and phenolic oxygen and azomethine nitrogen. L^5(benzoic acid pyridine-2-yl methylene-hydrazide) was a neutral tridentate Schiff base with N,N,O donors. ESI-MS for the complexes Mn-$L^{2,3,5}$ provided evidence for the presence of multinuclear complexes in solution. The catalytic ability of Mn-L^{1-5} complexes were examined and found that highly selective epoxidation (>95%) of cyclohexene was performed by iodosylbenzene in the presence of these complexes and imidazole in acetonirile.

Literature survey indicated that the complexes of the ligand derived from 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone and phenylhydrazone have not been reported so far. So it was thought worthwhile to synthesise the hydrazone, (BMPPPH)* (L) by condensing 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone and phenylhydrazine, to synthesize their transition metal complexes, to characterise them and to study their biological activity..

The ligand, BMPPPH (Fig.5.1) has three sites which may offer coordination, i.e., azomethine nitrogen, the pyrazolone ring oxygen atom and the nitrogen atom of the –NH group of the hydrazine moiety.

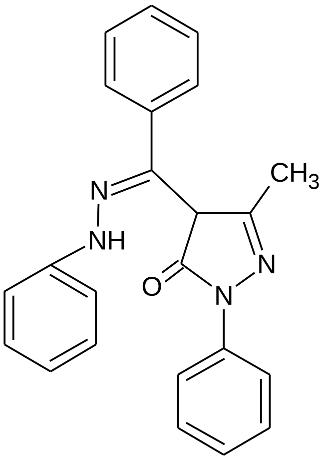

Fig.5.1

Suggested structure for methylphenyl-4-[phenyl(phenylhydrazono)methyl]-3-pyrazolone, (BMPPPH) (L)

A. Experimental

1. Materials and methods

Specifications regarding the reagents used, the procedural details adopted for the syntheses and the **c**haracterisation of the ligand and the complexes are given in Chapter II.

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*The systematic name of the compound is 5-methyl-2-phenyl-4-[(1E)-phenyl(phenylhydrazono)methyl]-2,4-dihydro-3H-pyrazol-3-one. But for the sake of convenience, the name methyl-phenyl-4-[phenyl(phenylhydrazono)methyl]-3-pyrazolone and the short form ‘BMPPPH’ are adopted in the thesis.

2. Synthesis of the ligand, BMPPPH

The synthesis of the ligand consisted of three stages. First, 3-methyl-1-phenyl-5-pyrazolone was prepared and benzoylated to give 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone the preparations of which are given in Chapter III. The synthesis of the ligand, BMPPPH is given below.

Dissolved BMPP(14.0950 g, 0.0507 mol) in minimum quantity of ethanol by heating. Added an ethanolic solution of phenylhydrazine (5.0 mL 0.0507 mol) to the hot solution. Cooled and added 1 ml of concentrated sulphuric acid. A yellow-green solid was formed. Cooled and added some more of ethanol and refluxed for 0.5 h. On cooling, bright yellow coloured crystals were obtained. Filtered at the pump, washed with ethanol and dried. Yield: 12.3570 g, 66.2 %

3. Syntheses of the complexes of BMPPPH

Complexes of the ligand with the acetates of nickel(II) and copper(II), chlorides of nickel(II) and copper(II), nitrates of cobalt(II) and copper(II) were synthesized.

a) Complex of $Co(NO_3)_2$

Dissolved BMPPPH in ethanol by heating. Added an ethanolic solution of cobalt(II) nitrate hexahydrate to it in 1:2 metal:ligand molar ratio, followed by the addition of 80 mL of sodium acetate-acetic acid buffer solution of pH=4 and heated for twenty minutes. Added water whence some solid started to form. Continued heating for 1.5 hours and cooled. Filtered the solid at the pump, washed with ethanol and dried.

b) Complex of Ni($CH_3COO)_2$

Dissolved BMPPPH in ethanol by heating. Added an ethanolic solution of nickel(II) acetate tetrahydrate to the solution in drops in 1:2 metal:ligand molar ratio and heated on a water bath for 45 minutes. A green solid was formed at the bottom of the beaker. Cooled, filtered the solid at the pump, washed with ethanol and dried.

c) Complex of $NiCl_2$

Dissolved BMPPPH in ethanol by heating. Added an aqueous solution of nickel(II) chloride hexahydrate to the solution in drops, in 1:2 metal:ligand molar ratio. Added 70 ml of sodium acetate-acetic acid buffer solution of pH=4.7 and heated on a water bath for one hour and left overnight. A brown solid that formed was filtered at the pump, washed with ethanol and dried.

d) Complex of Cu($CH_3COO)_2$

Dissolved BMPPPH in ethanol by heating. Added an aqueous solution of copper(II) acetate monohydrate to it in drops, in 1:2 metal:ligand molar ratio, whence the colour changed to pale green. Heated on a waterbath for an hour, and stirred occasionally. Filtered the solid at the pump, washed with ethanol and dried.

e) Complex of $CuCl_2$

Dissolved BMPPH in minimum quantity of ethanol by heating. Added an aqueous solution of copper(II) chloride dihydrate to the above solution, in drops in 1:2 metal: ligand molar ratio. Added 10 ml of sodium acetate-acetic acid buffer solution of pH=4.7 stirred and heated on a waterbath for one hour. Filtered the green-yellow precipitate at the pump, washed with ethanol and dried.

f) Complex of $Cu(NO_3)_2$

Dissolved BMPPPH in minimum quantity of ethanol by heating. Added an aqueous solution of copper(II) nitrate trihydrate to the above solution in drops in 1:2 metal: ligand molar ratio. The colour changed to black. Added 20 ml of sodium acetate-acetic acid buffer solution of pH=4.7 and heated for a few minutes. A green precipitate was formed. Filtered the solid at the pump, washed with ethanol and dried.

B. Results and discussion

The data obtained from analytical and physico-chemical studies have been correlated in a logical way to explain the properties, bonding and structures of the compounds.

1. Characterisation of the ligand, BMPPPH

The ligand BMPPH was bright yellow in colour with a melting point of C. The analytical data showed close agreement with the suggested formula of $C_{23}H_{20}N_4O$. It was further characterised by IR spectral and elemental analysis data.

a) IR spectrum

The infrared spectrum of the ligand BMPPPH showed a number of absorption bands which were characteristic of different groups present in the molecule (Table 5.1). Assignments have been made by reference to generalised charts of characteristic group frequencies and on the basis of analogous structures, known earlier.[18] The sharp band at 3325 cm^{-1} has been assigned to –NH group. A sharp band of medium intensity at 1632 cm^{-1} has been assigned to >C=O group. The sharp band at 1250 cm^{-1} has been assigned to C-N stretching vibration. The sharp band of medium intensity at 953 cm^{-1} has been assigned to υ(N-N)vibration of the hydrazono moiety. The appearance of the azomethine υ(C=N) vibration in the Schiff base, BMPPPH at lower frequency 1578 cm^{-1}, in comparison with the normal value (1675 cm^{-1}), indicated the involvement of the azomethine nitrogen atoms in hydrogen bonding. The sharp band at 3198 cm^{-1} was attributed to aromatic C-H stretching band. Strong and medium intense bands between 690 and 837 cm^{-1} resulted from the out-of-plane bending of the ring C-H bonds. In-plane bending bands appeared in the 1300-1000 cm^{-1} region. Skeletal vibrations, involving carbon-carbon stretching within the ring, were found in the 1600-1585 and 1500-1400 cm^{-1} regions.

2. Formulae and general properties of the complexes

All the complexes were found to be coloured, stable to light, heat and moisture and non-hygroscopic solids. Some of them looked crystalline in nature. The solubility of these complexes in common organic solvents was very low, but they were soluble in DMF/DMSO. The analytical data (Table 5.2) and the molar conductance values (Table 5.3) showed that the complexes had the formula $[ML_2X_2]$. The spectral and magnetic data also confirmed the suggested formulae.

TABLE 5.1

SIGNIFICANT IR BANDS OF BMPPPH AND THEIR ASSIGNMENTS

BAND FREQUENCY * (cm-1)	ASSIGNMENT
3325 (s)	-NH stretch
3198 (s)	Aromatic C-H stretch
1632 (s) (m)	>C=O stretch
1578 (s)	>C=N stretch
1300-1000 (s)	In-plane bending of aromatic ring protons
1250 (s)	C-N stretch
953 (s) (m)	N-N stretch
837 (s) (m)	Out-of-plane bending of the ring C-H
690 (s) (m)	-do-

* s = strong; m= medium

TABLE 5.2

ANALYTICAL DATA OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPPH

COMPOUND	EMPIRICAL FORMULA	F.WT. *	YIELD %	FOUND (CALCULATED) %				
				METAL	C	H	N	ANION
BMPPPH (L)	$C_{23}H_{20}N_4O$	368	66	-	75.12 (75.00)	5.40 (5.44)	15.20 (15.22)	-
$[Co(L)_2(NO_3)_2]$	$CoC_{46}H_{40}N_{10}O_8$	918.93	42	6.40 (6.41)	61.01 (60.07)	4.70 (4.35)	15.60 (15.24)	-
$[Ni(L)_2(CH_3COO)_2]$	$NiC_{50}H_{46}N_8O_6$	912.71	44	6.39 (.6.43)	65.90 (65.74)	5.07 (5.04)	12.32 (12.27)	-
$[Ni(L)_2Cl_2]$	$NiC_{46}H_{40}N_8O_2Cl_2$	865.71	45	6.70 (6.78)	64.00 (63.76)	4.62 (4.62)	13.00 (12.94)	8.14 (8.20)
$[Cu(L)_2(CH_3COO)_2]$	$CuC_{50}H_{46}N_8O_6$	917.54	43	6.89 (6.93)	65.94 (65.39)	4.97 (5.01)	12.32 (12.21)	-
$[Cu(L)_2Cl_2]$	$CuC_{46}H_{40}N_8O_2Cl_2$	870.54	43	7.25 (7.30)	63.56 (63.41)	4.64 (4.59)	12.80 (12.87)	8.09 (8.16)

$[Cu(L)_2(NO_3)_2]$	$CuC_{46}H_{40}N_{10}O_8$	923.54	43	6.79 (6.88)	59.68 (59.77)	4.30 (4.33)	15.12 (15.16)	-

* F.WT. = FORMULA WEIGHT

TABLE 5.3

MOLAR CONDUCTANCES OF Co(II) , Ni(II) AND Cu(II)COMPLEXES OF BMPPBH

COMPLEX	Ω_m ohm^{-1} cm^2 mol^{-1}	SOLVENT
$[Co(L)_2(NO_3)_2]$	10.75	DMF
$[Ni(L)_2(CH_3COO)_2]$	0.0	DMSO
$[Ni(L)_2Cl_2]$	0.0	DMSO
$[Cu(L)_2(CH_3COO)_2]$	10.75	DMSO
$[Cu(L)_2Cl_2]$	20.15	DMSO
$[Cu(L)_2(NO_3)_2]$	0.0	DMSO

3. Molar conductance

The molar conductance of 10^{-3} M solutions in DMF/DMSO of the BMPPH complexes were determined at room temperature and the values are given in Table 5.3. All the complexes showed values which were lower than that expected for 1:1 electrolytes indicating their non-electrolytic nature.[19] The analytical data and spectral studies also supported the suggested formula.

4. Magnetic behaviour

The mass susceptibility, molar susceptibility, corrected molar susceptibility and the effective magnetic moment values for the cobalt(II), nickel(II) and copper(II) complexes are tabulated in Table 5.4. The value of 5.68 B.M. calculated for the nitrato complex suggested high-spin octahedral geometry with very high contributions attributable to the three-fold degeneracy of $^4T_{1g}$(F) ground term.[20,21] The observed high value of μ_{eff} may be due to the mixing of the ground state with the excited state. The electronic spectra also supported octahedral geometry.

The magnetic moment values of 1.93 and 2.40 B.M. for the acetato and chloro complexes of nickel(II) also deviated significantly from the value expected for metal ion in the d^8 configuration. In a large number of tridentate ONO donor metal complexes, lower magnetic moment have been reported[22] which had been attributed to antiferromagnetic interactions as a consequence of dimeric or polymeric structural arrangements. Bur in the present work, the lower value than the one expected is due to metal-metal interaction.[20]

TABLE 5.4

MAGNETIC SUSCEPTIBILITY DATA OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPPH

COMPLEX	χ_g x10^{-6}	χ_m x 10^{-6}	$\chi_{m\,corr}$ x 10^{-6}	μ_{eff}	T(K)
$[Co(L)_2(NO_3)_2]$	14.62	13436.62	13651.79	5.68	296.1
$[Ni(L)_2(CH_3COO)_2]$	1.49	1359.83	1575.02	1.93	295.7
$[Ni(L)_2Cl_2]$	2.54	2201.60	2416.79	2.40	296.1
$[Cu(L)_2(CH_3COO)_2]$	1.88	1722.04	1937.22	2.14	295.9
$[Cu(L)_2Cl_2]$	1.70	1476.11	1691.30	2.00	295.7
$[Cu(L)_2(NO_3)_2]$	2.00	1845.37	2060.56	2.21	295.7

χ_g = mass susceptibility
χ_m = molar susceptibility
$\chi_{m\,corr}$ = corrected molar susceptibility
μ_{eff} = effective magnetic moment
T=Temperature in Kelvin

The magnetic moment values 2.14, 2.00 and 2.21 B.M. calculated for the acetato, chloro and nitrato complexes of copper(II) indicated that they were in the required range for complexes with D_{4h} symmetry.[23]

5. Electronic spectra

The important electronic spectral bands of the complexes and their probable assignments are given in Table 5.5 and the solid reflectance spectra are shown in Figs.5.2-5.5. In the nitrato complex of cobalt(II), a broad band between 525 and 650 nm, centered at 565 nm was observed which has been assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(P)$ transition(Fig.5.2). This suggested an octahedral environment around cobalt(II) ion. The shoulder at 448 nm may be assigned to $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$ transition. The position, intensity considerations, the magnetic moment values and analytical data favoured octahedral geometry.[24-26]

The solid reflectance spectrum of the acetato complex of nickel(II) showed a broad band between 700 and 800 nm centered at 742 nm and a shoulder at 440 nm(Fig.5.3). The former has been assigned to $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)(\upsilon_2)$ transition and the latter to $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)(\upsilon_3)$ transition. A broad band between 750 and 850 m centered at ~800 nm has been observed in the spectra of the chloro complex of nickel(II) and has been assigned to $^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)(\upsilon_2)$ transition. The positions and assignments of these bands suggested octahedral environment around nickel(II) ion in the complexes.[27]

TABLE 5.5

ELECTRONIC SPECTRAL BANDS OF Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPPH AND THEIR ASSIGNMENTS

COMPLEX	BANDS(nm)	ASSIGNMENT	GEOMETRY
$[Co(L)_2(NO_3)_2]$	~ 565 448	$^4T_{1g} \rightarrow {}^4T_{2g}(P)$ $^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$	Octahedral
$[Ni(L)_2(CH_3COO)_2]$	~742 440	$^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ $^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$	Octahedral
$[Ni(L)_2Cl_2]$	~800	$^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$	Octahedral
$[Cu(L)_2(CH_3COO)_2]$	~ 602	$^2E_g \rightarrow {}^2T_{2g}$	Distorted octahedral
$[Cu(L)_2Cl_2]$	~526	$^2E_g \rightarrow {}^2T_{2g}$	Distorted octahedral
$[Cu(L)_2(NO_3)_2]$	~547	$^2E_g \rightarrow {}^2T_{2g}$	Distorted octahedral

Fig. 5.2. ELECTRONIC SPECTRUM OF $[Co(L)_2(NO_3)_2]$

Fig. 5.3. ELECTRONIC SPECTRUM OF $Ni(L)_2(CH_3COO)_2]$

The solid reflectance spectra of the acetato and chloro complexes of copper(II) are shown in Figs.5.4 & 5.5.. Broad bands around 602, 526 and 547 nm in the acetato, chloro and nitrato complexes, respectively were observed.. They have been assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition in an octahedral field. The broadening of the band may be due to Jahn-Teller effect[28] and suggested a distorted octahedral geometry around copper(II) ion.

6. Infrared spectra

a) Complexes

The significant vibrational bands observed in the infrared spectra of the complexes investigated here and their assignments are given in the Table 5.6. The infrared spectrum of the Schiff base, BMPPPH exhibited a strong sharp band at 3325 cm^{-1}, characteristic of –NH stretching vibration. It was present in the spectra of the complexes, suggesting the non-involvement of the –NH group of the hydrazono moiety in coordination to the metal ions. The absence of strong and broad bands in the range 3260-3285 cm^{-1} indicated the absence of coordinated water molecules. This was also supported by the absence of bands around 890 cm^{-1} in the spectra of the complexes which wre due to the wagging and rocking modes of coordinated water molecules.[29,30] The azomethine υ(C=N) vibration underwent a shift to lower frequency ~ 1567 cm^{-1}) on complex formation, suggesting coordination of the azomethine nitrogen to the metal ion. This observation agreed with those of previous studies.[31,32] The υ(N-N) vibration observed at 953 cm^{-1} in the ligand was unchanged in the complexes , indicating thereby that the nitrogen of the hydrazono moiety was not involved in coordination.[33] The band at 1632 cm^{-1}

Fig. 5.4. ELECTRONIC SPECTRUM OF $Cu(L)_2(CH_3COO)_2]$

Fig. 5.5. ELECTRONIC SPECTRUM OF $[Cu(L)_2Cl_2]$

TABLE 5.6

SIGNIFICANT BANDS IN THE IR SPECTRA OF THE Co(II), Ni(II) AND Cu(II) COMPLEXES OF BMPPPH AND THEIR ASSIGNMENTS

COMPOUNDS	ASSIGNMENTS AND BAND FREQUENCIES * (cm^{-1})									
	υ N-H	υ C =N	υ C= O (cm^{-1})	δ N-N-H	υ M-N	υ M-O	υ M-X	υ COO- asym	υ COO- sym	υ NO_3^- coordinated
BMPPPH (l)	3325 m,sh	1578 s,sh	1632 s	1539s,sh	-			-		-
$[Co(L)_2(NO_3)_2]$	3269 m,sh	1554 s,sh	1612 s,sh	1533s,sh	470 w,sh	619 m,sh	-	-	-	1437 s,sh 1157 m,sh 1020 m,sh
$[Ni(L)_2(CH_3COO)_2]$	3292 m,sh	1554s,sh	1612 s,sh	1533 s,sh	360 w,sh	619 m,sh	-	1500 sh	1369 sh	-
$[Ni(L)_2Cl_2]$	3323 m	1562 s,sh	1612 s,sh	1529 m,sh	439 m,sh	603 w,sh	~400 w	-	-	-
$[Cu(L)_2(CH_3COO)_2]$	33210 m	1568 s,sh	1620 s,sh	1529 m,sh	470 w	619 w,sh	-	1599 s,sh	1381 s,sh	
$[Cu(L)_2Cl_2]$	3020 m	1550 s,sh	1575 s,sh	1530 m,sh	490 w	611 w	~455`	-	-	
$[Cu(L)_2(NO_3)_2]$	3338 m,sh	1560 s,sh	1599 s,sh	1535 s,sh	462 w,sh	615 s,sh	-	-	-	1440 m,sh 1280 w,sh 1020 w,sh

* s = sharp; m = medium; w = weak; sh = sharp

assigned to the υ(C=O) frequency of the pyrazolone ring of the Schiff base was observed in the region 1620-1575 cm^{-1} in the spectra of the complexes. This shift towards lower frequencies suggested that the carbonyl oxygen of the pyrazolone ring was involved in coordination.[34] The coordination through the oxygen and nitrogen atoms was further supported by the occurrence of new bands in the regions 619-603 cm^{-1} and 490-360 cm^{-1} , which may be assigned[29,35] to the υ(M-O) and the υ(M-N) vibrations, respectively, in the spectra of all the complexes.

b) IR features of coordinated anions in the complexes

IR spectroscopy has been used to determine the status of the anions in the complexes.

i) Acetato complexes.

The infrared spectrum of the acetato complex of copper(II) showed two sharp bands at 1599 and 1381 cm^{-1} assigned to $\upsilon_a(COO^-)$ and $\upsilon_s(COO^-)$ vibrations respectively(Table 5.7). The former was greater and the latter was at a lower frequency than that of the free acetate ion i.e., 1560 and 1416 cm^{-1}.[36] Hence, the separation between the two υ(CO) was very large, suggesting unidentate coordination of the acetate ion to the copper(II) ion.

ii) *Chloro complexes*

The band at ~ 400 cm^{-1} in the infrared spectrum of the chloro complex of nickel(II) has been assigned to Ni-Cl bond, i.e., the chlorine atom present was terminal and not bridging.

iii) *Nitrato complexes*

The infrared spectrum of the nitrato complex of copper(II) complex showed bands at 1440, 1280 and 1020 cm^{-1} which were assigned, respectively, to υ_4, υ_1 and υ_2 modes of coordinated nitrate ion. Since the magnitude of separation of υ_4 and υ_1 modes was 160 cm^{-1}, it was ascertained that the nitrate ions are coordinated unidentatively.[37]

C. Conclusions

The acetato complexes of nickel(II) and copper(II), nitrato complexes of cobalt(II) and copper(II) and chloro complexes of nickel(II) and copper(II) have been synthesized and characterised. The physico-chemical properties of all the complexes were studied and they were found to have the general formula $[ML_2X_2]$. The structures suggested for these compounds are given in Fig.5.7.

In these complexes, BMPPPH acts as a neutral bidentate ligand. It provided two coordination sites, viz., the nitrogen atom of the azomethine group and the oxygen atom of the 5-pyrazolone ring system. The microanalytical, electrical conductance, magnetic and spectral data have been logically correlated and the formulae and the structures have been established.

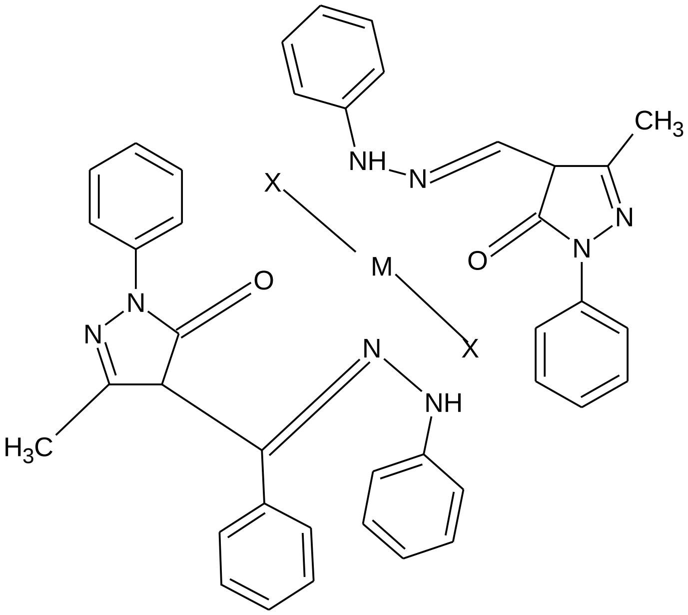

Fig. 5.7 Suggested structure for [ML_2X_2] where M=Co(II), Ni(II) or Cu(II) and X= CH_3COO^-, Cl^- or NO_3^-

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CHAPTER VI

Cu(II) COMPLEXES OF METHYLPHENYL-4-[PHENYL(BENZOYLHYDRAZONO)METHYL]-3-PYRAZOLONE

The synthesis, spectral and electrochemical studies of mixed-ligand oxovanadium(IV) and oxovanadium(V) complexes incorporating the tridentate ONO donor Schiff base derived from acetylacetone and benzoylhydrazine have been carried out by Tapas Ghosh and coworkers.[1] The complexes have been characterised by elemental analyses and by IR, EPR, NMR and UV-VIS spectroscopic studies. The complexes with N,N donor ligands are one electron paramagnetic displaying axial EPR spectra and exhibiting two ligand –field transitions in the visible region, whereas the complexes with OC donor ligands are diamagnetic and display only LMCT bands.

Complexes of *bis*acetylmonoxime phenylacetylhydrazine(H_2BMPH) with cobalt(II), cobalt(III), nickel(II), copper(II), palladium(II) and uranyl(VI) have been prepared and characterised by chemical- and thermal(TG,DTG,DTA) analyses, molar conductivity, spectral (IR, NMR, visible, UV) and magnetic moment measurements.[2] Changes in selected vibrational absorptions of the ligand upon coordination were discussed. The molar conductivities for the complexes lie in the non-electrolytic range. Based on magnetic- and spectroscopic data, the structures for the complexes were proposed as follows. Ocahedral for $[Co(H_2BMPH)_2(OAc)]$ and $[Ni(HBMPH)Cl(H_2O)]$, tetrahedral for $[Co(H_2BMPH)Cl_2]$, square-planar for $[Cu(HBMPH)Cl(H_2O)]$, $[Cu(BMPH)]_2$, $[Ni(BMPH)]_2$ and Pd(II) complexes. TG, DTG and DTA data suggested a mechanism for degradation of the complexes which was a function of temperature. The solid [Co(HBMPH)$_2$(OAc)] complex had a unique decomposition exotherm profile which can be used as a rapid and sensitive tool for the detection of an acetate containing complex.

The preparation and characterisation of the complexes of 4-benzoylsemicarbazone-1-phenyl-3-methyl-2-pyrazolin-5-one with vanadyl(IV), chromium(III), manganese(II), iron(II), cobalt(II), nickel(II), copper(II), zinc(II) and uranyl(VI) ions have been carried out by Shah etal.[3] Elemental analyses indicated a metal-ligand ratio of 1:3 for iron(III) and chromium(III) complexes and 1:2 for all the other complexes. The conductivity measurements suggested non-ionic behaviour of the complexes in ethanol. Elemental analyses, magnetic and electronic spectral studies of the iron(II) complexes suggested that it has been oxidised to iron(III) during its preparation. The magnetic moment (6.40 B.M.) of the complex was greater than a spin-only value, indicating the presence of ferromagnetic impurity in it.

With an effort to study extensively the transition metal complexes of sulphur donor ligands , a few complexes of cobalt(II), nickel(II) and copper(II) of N-benzoyl-N′-(pyrid-2-yl)thiocarbamide have been synthesised and characterised by Patel *et al*.[4] The analytical data showed the metal-ligand ratio of 1:2 for all the complexes. Low molar conductance values (60-100 Ω^{-1} cm^2 mol^{-1}) indicated non-electrolytic nature of the complexes. Most of the complexes melted above 200ºC. The molecular weight measurement (Rast’s camphor method) indicated that all the complexes were monomeric in nature. The magnetic moment- and the electronic spectral data proved that the complexes have octahedral geometry.

There has not been any report on the Schiff base obtained by condensing 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone with benzoylhydrazine. The ligand, (BMPPBH) (L) (Fig.6.1) has four potential ligating sites, viz., the nitrogen atom of the azomethine group, oxygen atom of the 5-pyrazolone group, the oxygen atom of the amide group and nitrogen atom of the hydrazono moiety. Hence it was considered worthwhile to synthesise the above Schiff base and to complex it with copper(II) metal salts, to characterise them and to study their biological activity.

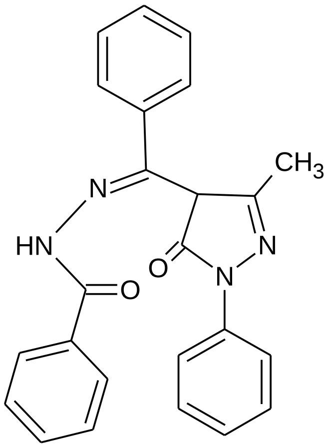

Fig. 6.1

Suggested structure for methylphenyl-4-[phenyl(benzoylhydrazono)methyl]-3-pyrazolone, (BMPPBH) (L)

A. Experimental

1. Materials and methods

Specifications regarding the reagents used, the procedural details adopted for the syntheses and the characterisation of the ligand and the complexes are given in Chapter II.

2. Synthesis of the ligand, BMPPBH

The synthesis of the ligand consists of three stages. First, 3-methyl-1-phenyl-5-pyrazolone was prepared. This was benzoylated to give 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone the preparation of which are given in Chapter III. The synthesis of the ligand, BMPPBH is given below.

a) Preparation of the ligand, BMPPBH

The preparation of the ligand consists of two stages. First, benzoylhydrazine was prepared. Second, it was converted to the ligand by refluxing it with 4-benzoyl-3-methyl-1-phenyl-5-pyrazolone.

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*The systematic name of the compound is N-[(1E)-(3-methyl-5-oxo-1-phenyl-4,5-dihydro-1H-pyrazol-4-yl)(phenyl)methylidene)benzoylhydrazide. Bur for the sake of convenience, the name methylphenyl-4-[phenyl(benzoylhydrazono)methyl]-3-pyrazolone and the abbreviation BMPPBH has been adopted in the thesis.

i) Preparation of benzoylhydrazine

Mixed together ethylbenzoate (30 mL, 0.2 mol) and hydrazinehydrate (10mL, 0.2 mol) in a round bottom flask and refluxed for 2.5 hours and cooled. Filtered the cream coloured crystals at the pump, washed with ethanol and dried.

ii) Preparation of BMPPBH

Dissolved benzoylhydrazine (7.0 g, 0.0515 mol) in minimum quantity of ethanol by heating. Added an ethanolic solution of BMPP (14.268 g, 0.0513 mol) to it and refluxed for four hours and cooled. Filtered the bright yellow crystals at the pump, washed with ethanol and dried. Yield: 8.4g, 42%

m.p. = 192ºC.

3. Syntheses of the complexes of BMPPBH.

Complexes of the ligand with the acetate, chloride and nitrate of copper(II) were synthesized.

a) Complexes of $Cu(CH_3COO)_2$, $CuCl_2$ and $Cu(NO_3)_2$

Dissolved BMPPBH in mimimum quantity of ethanol by heating. Added an ethanolic solution of the appropriate metal salt in 1:2 metal : ligand molar ratio to the hot solution of the ligand. Added 20 mL of sodium acetate-acetic acid buffer solution of pH=4.7 to it and refluxed for 1.15 hours. A green solid was formed. Cooled, filtered the solid at the pump, washed

A. Results and discussion

The data obtained from analytical and physico-chemical studies have been correlated in a logical way to explain the properties, bonding and structures of the compounds.

1. Characterisation of the ligand, BMPPBH.

The ligand is bright yellow in colour with a melting point of 192ºC. The analytical data showed close agreement with the suggested formula of $C_{24}H_{20}N_4O_2$. It was further characterised by IR- and elemental analyses data.

a) IR spectrum

The infrared spectrum of the ligand BMPPBH showed a number of absorption bands which were characteristic of different goups present in the molecule(Table 6.1). Assignments have been made by reference to generalised charts of characteristic group frequencies and on the basis of analogous structures, known earlier.[5] The sharp band at 3348 cm^{-1} has been assigned to –NH group. A sharp and medium intense band at 1712 cm^{-1} has been assigned to >C=O group. The sharp band at 1161 cm^{-1} has been assigned to C-N stretching vibration. The medium intense sharp band at 1022 cm^{-1} has been assigned to υ(N-N)vibration of the hydrazono moiety. The appearance of the azomethine υ(C=N) vibration in the Schiff base, BMPPPH at lower frequency 1643 cm^{-1}, in comparison with the normal value (1675 cm^{-1}), indicated the involvement of the azomethine nitrogen atoms in hydrogen bonding.. The sharp band at 2974 cm^{-1} is attributed to aromatic C-H stretching band. Strong and medium intense bands between 702 and 856 cm^{-1} result

TABLE 6.1

SIGNIFICANT IR BANDS OF BMPPBH AND THEIR ASSIGNMENTS

BAND FREQUENCY * (cm-1)	ASSIGNMENT
3348 sh	N-H stretch
2974 sh	Aromatic C-H stretch
1712 m,sh	>C=O stretch
1643	>C=N stretch
1600-1585	Skeletal vibrations
1500-1400	-do-
1300-1000	In-plane C-H bending vibrations
1161 sh	C-N stretch
1022 m,sh	N-N stretch
856 s,	Out-of-plane bending of aromatic ring C-H
702 s	-do-

* s = strong; m = medium; sh = sharp

from the out-of-plane bending of the ring C-H bonds. In-plane bending bands appear in the 1300-1000 cm^{-1} region. Skeletal vibrations, involving carbon-carbon stretching within the ring, are found in the 1600-1585 and 1500-1400 cm^{-1} regions.

2. Formulae and general properties of the complexes

All the complexes were found to be coloured, stable to light, heat and moisture and non-hygroscopic solids. Some of them looked crystalline in nature. The solubility of these complexes in common organic solvents was very low, but they were soluble in DMF/DMSO. The analytical data (Table 6.2) and the molar conductance values (Table 6.3) showed that the complexes had the formula $[ML_2X_2]$ except the nitrato complex of copper(II), which had the formula $[ML_2X]X$ The spectral and magnetic data also confirmed the suggested formulae.

3. Molar conductance

The molar conductance of 10^{-3} M solutions in DMF/DMSO of the BMPPBH complexes were determined at room temperature and the values are given in Table 6.3. The acetato and chloro complexes showed values which were lower than that expected for 1:1 electrolytes indicating their non-electrolytic in nature. The nitrato complex showed a value which is expected for 1:1 electrolyte.[6] The analytical data and spectral studies also supported the suggested formula

TABLE 6.2

ANALYTICAL DATA OF Cu(II) COMPLEXES OF BMPPBH

COMPOUND	EMPIRICAL FORMULA	F.WT. *	COLOUR	YIELD %	FOUND (CALCULATED) %				
					METAL	C	H	N	ANION
$[Cu(L)_2(CH_3COO)_2]$	$CuC_{52}H_{46}N_8O_8$	973.54	Pale green	42	6.50 (6.53)	64. 02 (64.10)	4.70 (4.73)	11.42 (11.50)	-
$[Cu(L)_2Cl_2]$	$CuC_{48}H_{40}N_8O_4Cl_2$	926.54	Green	43	6.79 (6.86)	62.77 (62.17)	4.22 (4.32)	11.98 (12.09)	7.61 (7.67)
$[Cu(L)_2(NO_3)]NO_3$	$CuC_{48}H_{40}N_{10}O_{10}$	979.54	Green	43	6.42 (6.49)	59.02 (58.50)	4.74 (4.08)	13.99 (14.29)	-

* F. Wt. = FORMULA WEIGHT

TABLE 6.3

MOLAR CONDUCTANCES OF Cu(II) COMPLEXES OF BMPPBH

COMPLEX	Ω_m ohm^{-1} cm^2 mol^{-1}	SOLVENT
$[Cu(L)_2(CH_3COO)_2]$	10.75	DMF
$[Cu(L)_2Cl_2]$	10.75	DMF
$[Cu(L)_2(NO_3)]NO_3$	100.75	DMF

4. Magnetic behaviour

The magnetic moment values were determined and the values are tabulated in Table 6.4. The magnetic moment values of 2.13, 2.32 and 2.29 B.M. calculated for the acetato, chloro and nitrato complexes of copper(II) indicated that they are in the required range for complexes with D_{4h} symmetry.[23]

5. Electronic spectra

The important electronic spectral bands of the complexes and their probable assignments are given in Table 6.5 and the solid reflectance spectra are shown in Figs.6.2- 6.4 In the acetate complex of copper(II), two broad bands centered around 572 and 271 nm and a shoulder around 225 nm have been observed. The band centered at 572 nm has been assigned to $^2E_g \rightarrow {}^2T_{2g}$ and the other two to charge transfer transitions. In the chloro complex of copper(II), a broad band between 550 and 500 nm, centered at 544 nm has been observed, which has been assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition in an octahedral field. The broadening of the band may be due to Jahn-Teller effect.[7]

In the nitrato complex of copper(II), a highly intense band at 567 nm has been observed. This has been assigned to $^2E_g \rightarrow {}^2T_{2g}$ transition. Two shoulders at ~200 nm and 271 nm have also been observed. They have been assigned to charge transfer transitions. It is to be noted that among all the complexes investigated, the above nitrato complex of copper(II) alone is electrolytic in nature and it alone shows an intense band at 567 nm in the solid reflectance spectrum. The other

TABLE 6.4

MAGNETIC SUSCEPTIBILTY AND MAGNETIC MOMENT DATA OF Cu(II) COMPLEXES OF BMPPBH

COMPLEX	χ_g x10^{-6}	χ_m x 10^{-6}	$\chi_{m\ corr}$ x 10^{-6}	μ_{eff}	T(K)
$[Cu(L)_2(CH_3COO)_2]$	1.821	1721.60	1926.61	2.14	295.6
$[Cu(L)_2Cl_2]$	2.080	1869.20	2284.40	2.32	294.7
$[Cu(L)_2(NO_3)]NO_3$	2.121	2018.63	2226.26	2.29	295.0

χ_g = mass susceptibility
χ_m = molar susceptibility
$\chi_{m\ corr}$ = corrected molar susceptibility
μ_{eff} = effective magnetic moment
T=Temperature in Kelvin

TABLE 6.5

ELECTRONIC SPECTRAL BANDS OF Cu(II) COMPLEXES OF BMPPBH AND THEIR ASSIGNMENTS

COMPLEX	BANDS(nm)	ASSIGNMENT	GEOMETRY
$[Cu(L)_2(CH_3COO)_2]$	~ 572 ~271 ~225	$^2E_g \rightarrow {}^2T_{2g}$ Charge transition	Distorted octahedral
$[Cu(L)_2Cl_2]$	~544	$^2E_g \rightarrow {}^2T_{2g}$	Distorted octahedral
$[Cu(L)_2(NO_3)]NO_3$	567 ~200 271	$^2E_g \rightarrow {}^2T_{2g}$ Charge transition	Distorted octahedral

Fig. 6.2. ELECTRONIC SPECTRUM OF [Cu(L)$_2$(CH$_3$COO)$_2$]

Fig. 6.3. ELECTRONIC SPECTRUM OF $[Cu(L)_2(Cl_2]$

Fig. 6.4. ELECTRONIC SPECTRUM OF $[Cu(L)_2(NO_3)_2]$

complexes are non-electrolytic in nature and the bands in the solid reflectance spectra do not show intense bands.

6. Infrared spectra

a) Complexes

The significant vibrational bands of the complexes investigated here and the assignments made are given in the Table 6.6.

The ligand spectra and the spectra of the complexes differ from each other. The band at 3348 cm^{-1} assigned to –NH group is almost unchanged in the complex when compared to that in the spectrum of the ligand (Table 6.1), suggesting the non-involvement of –N-H group in complex formation. A sharp and intense band at 1600 cm^{-1} has been assigned to the free >C=O group indicating that it is not involved in complex formation. The sharp band at 1712 cm^{-1} has been assigned to >C=O group of the pyrazolone group. This lowering of the frequency is indicative of involvement of oxygen atom of the 5-pyrazolone ring in complex formation to the metal ion. The band at 1643 cm^{-1} due to the >C=N stretching vibration is lowered to 1629-1589 cm^{-1} indicating that the azomethine nitrogen atom is coordinated to the metal ion. Moreover, the presence of bands in the far infrared region support the presence of M-N and M-O bonds in complexes.

b) IR features of coordinated anions in the complexes

IR spectroscopy has been used to determine the status of the anions in the complexes.

TABLE 6.6

SIGNIFICANT BANDS IN THE IR SPECTRA OF THE Cu(II) COMPLEXES OF BMPPBH AND THEIR ASSIGNMENTS

COMPOUND	ASSIGNMENTS AND BAND FREQUENCIES * (cm^{-1})								
	υ N-H	υ C =N	υ C= O (cm^{-1})	δ N-N-H	υ M-N	υ M-O	υ M-X	υ COO- asym	υ COO- sym	υ NO_3^- coordinated
BMPPBH (L)	3348 m, sh	1643 s,sh	1712m,sh	1575 s,sh	-	-	-	-		-
$[Cu(L)_2(CH_3COO)_2]$	3348 s,sh	1629 s,sh	1699 s,sh	1531 s,sh	401 w,sh	611 w,sh	-	1531 s,sh	1377 s,sh	
$[Cu(L)_2Cl_2]$	3333 m,br	1589 s,sh	1699 s,sh	1521 s,sh	459 w,sh	655 m,sh	366 m,sh	-	-	-
$[Cu(L)_2(NO_3)]NO_3$	3377 s,br	1599 s,sh	1670 s,sh	1535 s,sh	453 m,sh	623 w,sh	-	-	-	1437 s,sh 1178 w,sh 1026 m,sh

br = broad; s = strong; sh = sharp; m = medium; w= weak *i) Acetato complex*

Two intense bands at 1531 and 1377 cm^{-1} (Table 6.6) have been observed in the acetato complex of copper(II) and have been assigned to υ(C=O) and υ(C-O), respectively. Since the separation between the two υ(CO) was much larger than that in the free ion, we concluded that the acetate ion has coordinated to the copper(II) ion in an unidentate fashion.

ii) Chloro complex

The sharp band at 366 cm^{-1} in the infrared spectrum of the chloro complex of copper(II) has been assigned to Cu-Cl bond, i.e., the chlorine atom present is inside the coordination sphere .

iii) Nitrato complex

The infrared spectrum of the nitrato complex of copper(II) complex exhibited three bands at 1477, 1178 and 1026 cm^{-1} which are assigned respectively to υ_1, υ_5 and υ_2 modes of coordinated nitrate ion. Since the magnitude of separation between the tho highest frequency bands was larger (299 cm^{-1}) than that in the free ion, it is ascertained that the nitrate ions are coordinated bidentatively.[8]

The elemental analyses data indicate that both the nitrate ions are present in the complex but the molar conductance values indicate that out of the two nitrate ions present one of them is present outside the coordination sphere.

C. Conclusions

The acetato, chloro and the nitrato complexes of copper(II) have been synthesised and characterised. The physico-chemical properties of all the complexes have been studied and they were found to have he general formula $[ML_2X_2]$ except the nitrato complex $[ML_2X]X$. The structures suggested for these compounds are given in Figs.6.5 & 6.6.

In these complexes, BMPPBH acts as a neutral bidentate ligand. It provided only two coordination sites, viz., the nitrogen atom of the azomethine group and the oxygen atom of the pyrazolone ring system, though five potential ligating sites are available in the ligand. The microanalytical, electrical conductance, magnetic and spectral data were logically correlated and the formulae and the structures of the complexes were established.

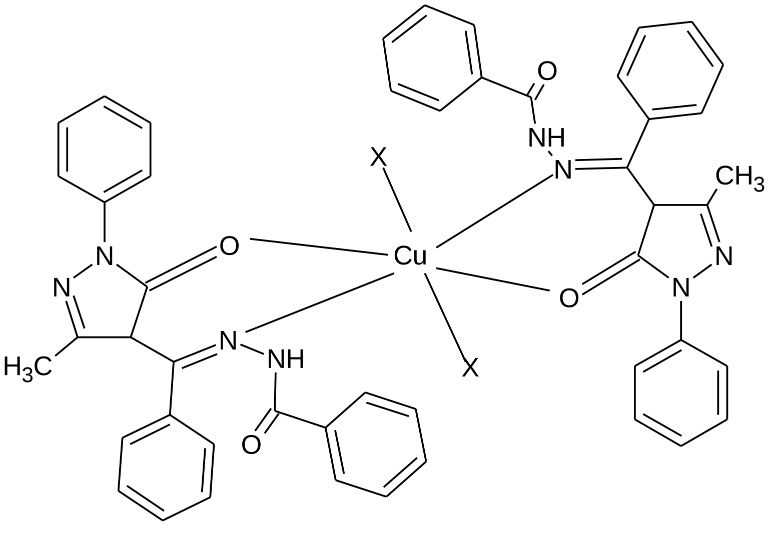

Fig. 6.5

Suggested structure for $[CuL_2X_2]$ where X= $CH_3COO^{- r}$ or NO_3^-

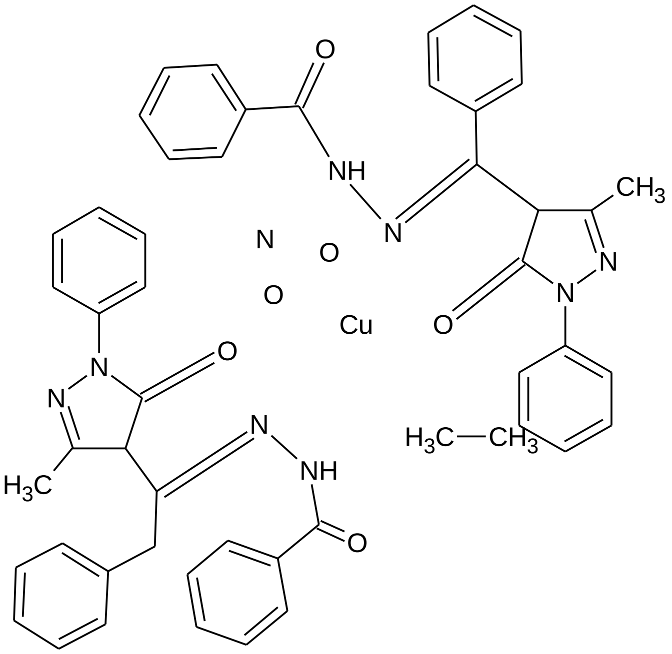

Fig. 6.6.

Suggested structure for $[Cu(L)_2X]X$Where X= NO_3^-

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CHAPTER I

INTRODUCTION

A. Antibacterial studies

The earth came into being an almost incomprehensibly distant 4.5 billion years ago.[1] For the first several millions of years of its existence the earth was a ball of molten rock. Then, as millennia passed, a thin crust formed over the hot core, and violent volvanic activity filled the days and nights. Now the earth was awash with energy. There was radiation from the sun, lightning from intense electrical storms and heat form radioactive decay and the ever present volcanic eruptions. In the incessant rains and the tropically warm oceans, organic molecules were forming – amino acids, proteins, nucleotides and carbohydrates- the stuff that one day would compose living things.

For the first billion years, the earth was as barren as life as the surface of moon is today. Then about 3.5 billion years ago, microscopic cells, the first living things, came into being. Although scientists are uncertain how these cells arose, they are reasonably sure that these first life forms were bactaeria. The ancient bacteria (like the modern forms) were tiny, single-celled creatures, with little evidence of internal structure. Organisms like those are called prokaryotes, a name that reflects the absence of a nucleus.

Bacteria (or prokaryotes) were the only inhabitants of the earth for over 2 billion years, nearly half of the planet’s existencxe. Then about 1.3 billion years ago, the eukaryotes evolved. The organisms, typified by protozoa, fungi, plants and animals, have larger cells with nuclei and complex internal srtructure. Although the eukaryotes were larger organisms, the bacteria were not threatened because by that time bacteria had the advantage- they were well-established and in ful swing.

And what a group they were!. Growing wildly in the oxygen-free atmosphere of earth, the ancient bacteria chemically combined carbon of carbon dioxide to form methane (not unlike we find in a swamp today). Then the photosynthetic bacteria evolved. These forms are called cyanobacteria.(or blue-green algae). Cyanobacteria used their chlorophyll pigments in the process of photosynthesis to capture light energy and produce carbohydrates or energy-storage compounds. In so doing, they played a decisive role in earth's development because photosynthesis dramatically increased the atmospheric concentration of oxygen form 1% to the current 21%. More than any other organism on earth, cyanobacteria were catalytsts foe the oxygen-based chemistry that now pervades earthly life.

All the contemporary bacteria developed from the evolutionary experiments that Mother Nature performed on these ancient forms, and the results have been spectacular, for modern bacteria have come to cccupy every conceivable niche on earth. Every crack, every crevice, every cranny-whether at the bottom of a 6 mile deep Pacific Trench, at the pinnacle of Mount Everst, or in the blazing desert of the Sahara – contains some sort of bacterial life. A single pinch of rich soil contains over a billion bacteria. Indees, a handful of that same soil combines more bacteria than all the people who have ever lived on planet earth.

It should not be surprising that bacteria occupy a critical place in the web of life. Many bacterial species make major contributions to the mineral balance of the world by metabolising the nutrients in fresh water, marine and terrestrial environments. The bacteria residing in the soil influence the earth's ecology by breaking down the remains of all that die and recycling the elements. And certain bacterial species do what few other species of organisms on earth can do. They trap nitrogen form the air and convert to substances used by plants to make proteins, protein that ultimately winds up on our plates as grains, meat and dairy products.

In industries and biochemical laboratories, bacteria are both work horses and lab rats. Growing in enormous numbers in mammoth fermentation tanks, bacteria carry on their day-to-day chemical routines and yield products as substantial value. For example, they manufacture organic compounds, they produce fermented foods; they synthesize antibiotics and vitamins; and they serve as biological factories for genetic engineering.

Despite all the good they do, bacteria also pose a threat to human beings because a small percentage of species cause infectious diseases. Indeed, human history is replete with accounts of ravaging epidemics of cholera, plague, typhoid fever and syphilis. But even as the great 'slate-wipers' of history, bacteria may have served a useful purpose in giving the human population an opportunity to renew and improve itself. Some revolutionary biologists argue that bacteria are the key agents of natural selection for the human species, i.e., in a sense. they help improve our species by selecting the fitter individuals through the distasteful task of infectious disease. As our constant companion, bacteria have impacted our lives in some ways, that are clear and in some ways that have not yet been discovered.

1. A short account of Pseudomonas

Pseudomonas aeruginosa and other members of this group of gram-negative bacilli are opportunistic pathogens[2] that frequently cause hospital-acquired infections, particularly in ventilator patients, burn patients, and those with chronic debility. Many sites can be infected, and infection is usually severe. Diagnosis is by culture. Antibiotic choice varies with the pathogen and must be guided by sensitivity studies because resistance is common.

a) Epidemiology

Pseudomonas is ubiquitous and favors moist environments. In humans, P. aeruginosa is the most common pathogen, but infection may result from P. paucimobilis , P. putida , P. fluorescens, and P. acidovorans. Other important hospital-acquired pathogens formerly classified as Pseudomonas include Burkholderia cepacia and Stenotrophomonas maltophilia. Burkholderia pseudomallei causes a distinct disease known as melioidosis that is mostly limited to the Asian tropics. P. aeruginosa can be found occasionally in the axilla and anogenital areas of normal skin but rarely in stool unless antibiotics are being given. In hospitals, the organism is frequently found in sinks, antiseptic solutions, and urine receptacles. Transmission to patients by health care practitioners may occur, especially in burn and neonatal ICUs.

b) Diseases Caused by Pseudomonas

Most P. aeruginosa infections occur in hospitalized patients, particularly those who are debilitated or immunocompromised. P. aeruginosa is the 2nd most common cause of infections in ICUs. HIV-infected patients, particularly those in advanced stages, are at risk for community-acquired P. aeruginosa infections. Pseudomonas infections can develop in many anatomic sites, including skin, subcutaneous tissue, bone, ears, eyes, urinary tract, and heart valves. The site varies with the portal of entry and the patient's vulnerability. In hospitalized patients, the 1st sign may be overwhelming gram-negative sepsis.

c) Skin and soft-tissue infections

In burns, the region below the eschar can become heavily infiltrated with organisms, serving as a focus for subsequent bacteremia—an often lethal complication. Deep puncture wounds of the foot are often infected by P. aeruginosa. Draining sinuses, cellulitis, and osteomyelitis may result. Drainage from puncture wounds often has a sweet, fruity smell. External otitis with purulent drainage, common in tropical climates, is the most common form of Pseudomonas infection involving the ear. A more severe form, referred to as malignant external otitis, can develop in diabetic patients. It is manifested by severe ear pain, often with unilateral cranial nerve palsies, and requires parenteral therapy. Ecthyma gangrenosum in neutropenic patients is a skin lesion pathognomonic for P. aeruginosa. It is characterized by erythematous, centrally ulcerated, purple-black areas about 1 cm in diameter found most often in other infections the axillary or anogenital areas.

d) Respiratory tract infections

P. aeruginosa is a frequent cause of ventilator-associated pneumonia. In HIV-infected patients, Pseudomonas most commonly causes pneumonia or sinusitis. Pseudomonas bronchitis is common late in the course of cystic fibrosis. These isolates have a characteristic mucoid colonial morphology.

2. Bacteria affecting wheat

The most common bacterial pathogens that attack wheat are grouped under the names *Xanthomonas translucens* and *Pseudomonas syringae.*[3] Pathovars (bacterial strains pathogenic to a specific host or hosts) included in *X. translucens* can cause significant crop losses, while the ones grouped under *P. syringae* may severely affect the grain quality of wheat and are widely distributed in many temperate and subtropical wheat-growing regions. There is also a range of other bacterial diseases that have a more limited distribution or may cause crop losses just in certain localities.

3. Escherichia coli (E. coli)

E. coli (Escherichia coli) is one of several types of bacteria[4] that normally inhabit the intestine of humans and animals (commensal organism). Some strains of *E. coli* are capable of causing disease under certain conditions when the immune system is compromised or disease may result from an environmental exposure.

E. coli bacteria may give rise to infections in wounds, the urinary tract, biliary tract, and abdominal cavity (peritonitis). This organism may cause septicemia, neonatal meningitis, infantile gastroenteritis, tourist diarrhea, and hemorrhagic diarrhea. An *E. coli* infection may also arise due to environmental exposure. Infections with this type of bacteria pose a serious threat to public health with outbreaks arising from food and water that has been contaminated with human or animal feces or sewage. This type of bacteria has been used as a biological indicator for safety of drinking water since the 1890s. Exposure may also occur during hospitalization, resulting in pneumonia in immunocompromised patients or those on a ventilator.[2]

Escherichia coli (*E. coli*), is one of the most common coliform bacteria types. Detection of *E. coli* is definite evidence of fecal pollution. *E. coli* are facultatively anaerobic gram-negative rods that live in the intestinal tracts of animals. They can grow in the presence or the absence of oxygen. Under anaerobic conditions, *E. coli* grow by fermentation, producing mixed acids and gases as end products. They can also grow by anaerobic respiration, utilizing NO_3, NO_2, or fumarate. This versatility is what gives *E. coli* its ability to adapt to its intestinal (anaerobic) and its extraintestinal (aerobic or anaerobic) habitats.

As a pathogen, *E. coli* is best known for its ability to cause intestinal diseases. Five classes of *E. coli* can result in diarrheal diseases, but three specific pathogenic strains—enterotoxigenic, enteropathogenic, and enteroinvasive—cause problems when present in the water supply. All three of these types can cause acute diarrhea. An outbreak of *E. coli*-induced diarrhea can have a fatality rate as high as 40 percent in newborn children.

Since 1885, when it was first isolated from childrens's faeces and described by the German dermatologist Theodor Escherish,[5] scientific attention has been lavished on the E. coli to such an extent that it is today probably the best understood free-living organism.

E. coli is an almost universal inhabitant of the gut of humans and other warm-blooded animals where it is the predominant facultative anaerobe though only a minor component of the total microflora. Generally,a harmless commensal, it can be an opportunistic pathogen causing a number of infections such as gram-negative sepsis, urinary tract infections, pneumonia in immunosupressed patients and meningitis in neonates. Its common occurrence in faeces, ready culturability, generally non-pathogenic character and survival characteristics in water led to the adoption of E. coli as an indicator of faecal contamination and the possible presence of enteric pathogens such as S. typhi in water. This usage has been transferred to foods where greater circumspection is required in interpreting the significance of positive results.

4. Antibacterial drugs

Drugs that kill or inhibit microbes[6] have dominated strategies aimed at combating bacterial diseases. This approach has several shortcomings. For instance, drugs may be toxic, useful antibiotics can have adverse side reactions. Microbes can become resistant to the action of certain drugs. Therefore, an alternative, more subtle strategy is to interfere with the ability of pathogens to gain a hold on the body in the first place.

Trypanosoma cruzi, a vector-borne protozoan is the etiologic agent of Chagas' disease, which manifests as potentially fatal cardiomyopathy or dilations in the digestive tract.[7] Azole antimicrobial agents have been discovered to have antitrypanosomal activity by inhibition of synthesis of ergosterol, which is integral to the parasite cell membrane.[8,9] Azoles, which were developed as antifungal drugs, are widely used clinically to treat mycotic infections. In fungi, azoles inhibit the cytochrome P-450 enzyme lanosterol 14α-demethylase, causing the accumulation of 14α-methylsterols and the decreased production of ergosterol.[10,11] Miconazole and econazole were the first of these inhibitors tested in *T. cruzi* and showed potent growth inhibition.[12] Ketoconazole was shown to inhibit ergosterol synthesis in *T. cruzi* epimastigotes. Other studies showed that ketoconazole, itraconazole, and fluconazole were active in inhibiting intracellular multiplication of parasites and in protecting against lethal infection in mice.[8]

5. Drug resistance

Microbial drug resistance is a tremendous clinical problem that affects all classes of microorganisms. Resistance to azole antimicrobial agents, specifically, has become an impediment to the effective treatment of infections due to *Candida* and *Torulopsis* species.[10] This problem is particularly serious in the population with AIDS, in whom it is estimated that >33% of candida isolates are resistant to fluconazole.[13] Poor clinical outcome and in vitro resistance have been correlated.[14] In yeast several different mechanisms of azole resistance have been discovered,[10] the most common being efflux pumps which extrude the drug from the intracellular space.

Malaria caused by drug-resistant *Plasmodium falciparum* has become the leading health threat to populations in tropical and subtropical regions.[15] Resistance to antifolate drugs is principally due to structural changes in the target enzymes.[16]

The findings suggest that *T. cruzi* resistance to azoles may occur clinically in humans, particularly because therapies involve long courses to effect a cure. Resistance to azole drugs has the potential to be an impediment to the progress being made in the treatment of *T. cruzi* infections.

B. Antifungal studies

The agents (pathogens) that cause soilborne diseases of peanut are various fungi and nematodes that survive in the soil[17] and infect one or more parts of the plant at or below the soil surface. Soilborne diseases can severely limit peanut yields, particularly in fields where long rotations with non-host crops are not practised. Southern blight and Sclerotinia blight are probably the most widespread and destructive of the soilborne diseases. There are several other soilborne diseases that are less common, but still important where they occur.

1. Aspergillus Crown Rot

Aspergillus crown rot commonly results in seedling blight, but also may affect older plants from mid- to late-season. The fungus that causes crown rot, *Aspergillus niger(A. niger)*, is different from the species that causes aflatoxin contamination of harvested kernels. A. niger is present in most peanut soils and is a common contaminant of peanut seed. However, outbreaks of the disease are sporadic and appear to be related to the prior occurrence of one or more stresses.

Extreme heat or fluctuations in soil moisture during the seedling stage, poor seed quality, seedling damage from pesticides or cultivation, and feeding by root and stem boring insects are stresses thought to aggravate the disease. The economic importance of Aspergillus crown rot is difficult to assess. Generally scattered plants are affected, although standing losses of 50% have been reported in isolated fields.

Lucia Pitzurra *et al* have reported a new azole derivative of 1,4-benzothiazine[18] which increases the antifungal mechanisms of natural effector cells. The synthesis and antifungal activities of 1,4-benzothiazine derivatives for evaluation of the effect of substitution of the aromatic ring with the 1,4-benzothiazine nucleus, which shows some antifungal activity when it is part of fluconazole – and miconazole – like analogues, have been reported. Of these derivatives, 7-[1-[4-chlorobenzyl}oxy]-2-(1H-1-imidazolyl)ethyl]-4-methyl-3,4-dihydro-2H-1,4-benzothiazin-3-one(FS5) shows good efficacy against systemic candidiasis in a murine experimental model. Their results showed that the FS5 azole derivative of 1,4-benzothiazine significantly prolongs the survival and decreases the kidney fungal byrden of mice systematically infected with C albicans. This new antifungal agent appears to work *in vivo* as a toxic agent against C. albicans and as a promoter of antifungal mechanisms in natural immune cells.

2. Diseases caused by Aspergillus[19]

Allergic bronchopulmonary aspergillosis (ABPA) is a condition which produces an allergy to the spores of the *aspergillus* moulds. It is quite common in asthmatics; up to 20% of asthmatics might get this at some time during their lives. ABPA is also common in cystic fibrosis patients, as they reach adolescence and adulthood. The symptoms are similar to those of asthma: intermittent episodes of feeling unwell, coughing and wheezing. Some patients cough up brown-coloured plugs of mucus. The diagnosis can be made by X-ray or by sputum, skin and blood tests. In the long term ABPA can lead to permanent lung damage (fibrosis) if untreated.

The treatment is with steroids by aerosol or mouth (prednisolone), especially during attacks. Itraconazole (an oral antifungal drug) is useful in reducing the amount of steroids required in those needing medium or high doses. This is beneficial as steroids have side-effects like thinning of the bones (osteoporosis) and skin and weight gain, especially when used for a long time.

3. How do people contract *Aspergillus* diseases?

Aspergillus spores are found everywhere in the environment including the air we breathe. The spores can therefore enter everyone's lungs and can also enter wounds. This is how all *Aspergillus* diseases are contracted, although the underlying reasons for the different types of *Aspergillus* diseases differ. Invasive aspergillosis occurs almost exclusively in people with a damaged immune system. Most people's natural immunity to *Aspergillus* means that they easily kill *Aspergillus* spores that enter their body. However, if someone has a damaged immune system, (for example due to leukaemia) they lose their natural protection and may develop invasive aspergillosis. Aspergilloma, sinus disease and ABPA often occur in people with an apparently healthy immune system. Individuals with ABPA are allergic to the *Aspergillus* spores that enter their lungs and they "overreact" to small numbers of

Aspergillus spores that most people happily tolerate. This may happen with sinus disease as well. Normally, in sinus disease and Aspergilloma, *Aspergillus* becomes lodged in the lung or sinus often due to a cavity in these organs. Occasionally individuals with a healthy immune system are infected with *Aspergillus*. This is rare, however exposure to very large numbers of spores can lead to severe allergic lung disease called extrinsic allergic alveolitis. The most famous example of this is Farmers Lung, where farmers are exposed to massive numbers of *Aspergillus* spores in silage.

4. Metal complexes as antifungal agents

A series of antibacterial and antifungal amino acid-derived compounds and their cobalt(II), copper(II), nickel(II), and zinc(II) metal complexes have been synthesized and characterized by their elemental analyses, molar conductances, magnetic moments, and IR, and electronic spectral measurements.[20] The ligands were derived by condensation of *β*-diketones with glycine, phenylalanine, valine, and histidine and act as bidentate towards metal ions (cobalt, copper, nickel, and zinc) via the azomethine-N and deprotonated-O of the respective amino acid. The complexes were screened for *in vitro* antifungal activity against *Trichophyton longifusus, Candida albicans, Aspergillus flavus, Microsporum canis, Fusarium solani, and Candida glaberata*. The results of these studies show the metal(II) complexes to be more antifungal against one or more species as compared to the uncomplexed ligands.

The case is reported of a 73-year-old diabetic man with malignant otitis externa due to Aspergillus niger. Cure was achieved with a 3 week course of intravenous of amphotericin B, followed by oral itraconazole for 3 months.[21] It has been reported by Boni E. Elewski[22] that antimycotic agents like fluconafluconazole and itraconazole offer high cure rates and good safety profiles for onycho onuchomycosis, a fungal nail infection.

5. Limitations of traditional antifungal agents

The kingdom of fungi comprises more than 100,100 species of yeasts and moulds. They are eukaryotic organisms with a true nucleus and nuclear membrane and with a cell wall that contains chitin. It is the ergosterol in the cell wall of yeasts and moulds, however, that constitutes the fungal cell's Achilles heel. All currently prescribed antifungal agents act in one way or the other to inhibit ergosterol synthesis. The azole drugs include the older imidazole, ketoxonazole and the new triazoles, itraconazole and fluconazole. Griseofulvin, the mainstay of treatment for decades of onychomycosis is active against growing hyphae and may also affect nucleic and synthesis and arrest fungal cell mitosis in metaphase.[23]

Developed in the 1980s ketonazole was the first orally active imidazole with a relatively broad specrum of activity against dermatophytes, some yeasts and moulds. However, the long-term use of oral ketoconazole in onychomycosis which is necessary to effect improvement or cure, is limited by the occurrence of side effects and significant drug interactions. Patients who take ketoconazole on a long-term basis are obliged to undergo regular liver function tests. Other adverse effects of ketoconazole therapy include hypersensitivity reactions, nausea, vomiting, headache, pain, pruritus and fever.[24]

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CHAPTER II

ANTIMICROBIAL STUDIES

This chapter describes the antibacterial activities of the ligands BMPPA(L_1), BMPPI(L_2), BMPPPH(L_3), BMPPBH(L_4) and that of the complexes, $[Ni(BMPPA)_2(CH_3COO)_2]$, $[Cu(BMPPA)_2Cl_2]$, $[Cu(BMPPA)_2SO_4]$, $[Co(BMPPI)_2(CH_3COO)_2]$, $[Co(BMPPI)_2Cl_2]$, $[Co(BMPPI)_2(NO_3)_2]$, $[Cu(BMPPI)_2(CH_3COO)_2]$, $[Cu(BMPPI)_2Cl_2]$ and $[Cu(BMPPBH)_2Cl_2]$. It also describes the antifungal studies of the ligands BMPPA, BMPPI, BMPPPH, BMPPBH and that of the complexes $[Co(BMPPA)_2I_2]$, $[Ni(BMPPA)_2(CH_3COO)_2]$, $[Cu(BMPPA)_2(CH_3COO)_2]$, $[Cu(BMPPA)_2Cl_2]$, $[Cu(BMPPA)_2(NO_3)_2]$, $[Co(BMPPI)_2(CH_3COO)_2]$, $[Co(BMPPI)_2I_2]$, $[Co(BMPPI)_2Cl_2]$, $[Co(BMPPI)_2(NO_3)_2]$, $[Ni(BMPPI)_2(CH_3COO)_2]$, $[Ni(BMPPI)_2Cl_2]$, $[Ni(BMPPI)_2(NO_3)_2]$. $[Cu(BMPPI)_2(CH_3COO)_2]$, $[Cu(BMPPI)_2Cl_2]$, $[Cu(BMPPI)_2SO_4]$, $[Cu(BMPPPH)_2(CH_3COO)_2]$, $[Cu(BMPPI)_2(NO_3)_2]$, $[Ni(BMPPPH)_2(NO_3)_2]$,$[Ni(BMPPPH)_2Cl_2]$, $[Cu(BMPPPH)_2Cl_2]$, $[Cu(BMPPPH)_2(NO_3)_2]$, $[Co(BMPPBH)_2(CH_3COO)_2]$ $[Cu(BMPPBH)_2Cl_2]$ and $[Cu(BMPPBH)_2(NO_3)_2]$. The details of the synthesis and characterisation of these complexes are presented in Part I.

A. Materials and methods

1. Antibacterial studies

a) Intended Use of nutrient agar[1]

Nutrient Agar 1.5% is used for cultivating a variety of microorganisms and with the addition of blood or other enrichment can be used for cultivating fastidious microoganisms.

b) Explanation

This medium is a slightly alkaline general-purpose medium. Since the medium contains 0.8% sodium chloride, it can be used as a base for enrichment with blood, ascitic fluid or other supplements for cultivating fastidious microorganisms. Beef extract is the commercially prepared dehydrated form of autolysed beef and is supplied in the form of a paste. Peptone is casein (milk protein) that has been digested with the enzyme pepsin. Peptone is dehydrated and supplied as a powder. Peptone and Beef extract contain a mixture of amino acids and peptides. Beef extract also contains water soluble digest products of all other macromolecules (nucleic acids, fats, polysaccharides) as well as vitamins and trace minerals. Although we know and can define beef extract in these terms, each bach can not be chemically defined. There are many media ingredients which are complex: yeast extract, tryptone, and others. The advantage of complex media is that they support the growth of a wide range of microbes.

Agar is purified from red algae in which it is an accessory polysaccharide (polygalacturonic acid) of their cell walls. Agar is added to microbiological media only as a solidification agent. Agar for most purposes has no nutrient value. Agar is an excellent solidification agent because it dissolves at near boiling but solidifies at 45°C. Thus, one can prepare molten (liquid) agar at 45°C, mix cells with it, then allow it to solidify thereby trapping living cells. Below 45°C agar is a solid and remains so as the temperature is raised melting only when >95°C is obtained.

c) Principles of the Procedure

Beef extract and peptone provide the nitrogen, vitamins, amino acids and carbon sources in Nutrient Agar 1.5%. Sodium chloride maintains the osmotic balance so that red blood cells will not rupture when blood is added as supplement. Agar is the solidifying agent.

d) Formula

Nutrient Agar 1.5%

Approximate Formula Per Liter

Beef Extract	3.0 g
Peptone	5.0 g
Sodium Chloride	8.0 g
Agar	15.0 g

2. Antifungal studies

a) Intended use of potato agar medium[2]

Potato dextrose agar is used for the cultivation, isolation and enumeration of yeasts and moulds from foodstuffs and other materials.

Potato dextrose agar (abbreviated "PDA") and potato dextrose broth (abbreviated "PDB") are common microbiological media made from potato infusion, and dextrose (corn sugar). Potato dextrose agar is the most widely used medium for growing fungi and bacteria which attack living plants or decay dead plant matter. Common organisms that can be cultured on PDA are yeasts such as *Candida albicans* and *Saccharomyces cerevisiae* and molds such as *Aspergillus niger*.

b) Mode of Action

Carbohydrate and potato infusion promote the growth of yeasts and moulds while the low pH value partially inhibits the growth of the accompanying bacterial flora. If the medium is to be used for fungal counts, the pH should be adjusted to approximately 3.5. Fungi grow on this medium to develop typical morphology.

B. Experimental

a) Preparation of nutrient agar medium

Weighed out accurately 0.3 g of beef extract and placed it in a flask. Weighed accurately 5.0 g of peptone and added to the same flask. Added 200 ml of distilled water and swirled to dissolve the peptone and beef extract. Checked the pH. It was found to be 7.0. Weighed out 15.0 g of agar and added to the flask. Heated the medium to boiling to dissolve the agar. Stopped heating as soon as it began to boil . Allowed it to cool a few minutes and poured the melted agar onto petridishes and closed them with lids and allowed to solidify.

Inoculated the culture (E. coli) evenly onto the agar using a L glass rod. Rotated the plate 90 degrees and continued spreading the sample. The discs containing varying concentrations of the complexes in DMSO were placed over the agar surface. Closed the lid and incubated the plates at 37C for 24 h. After 24 h, the plates were examined. The zones of inhibition were measured using a measuring scale.

Potato infusion is made by boiling 200g of sliced (washed but unpeeled) potatoes in water for 30 minutes and then decanting or straining off the broth. Dextrose (corn sugar) is then added (20 g/L) and the medium is sterilized by autoclaving.[4] at 121 C, at 15 lbs pressure for 15 minutes. They were then aseptically poured on to sterile petriplate and allowed to solidify.

The fungi Aspergillus niger culture was swabbed on each petriplate containing the dextrose agar medium. Wells were made on the agar plate and then aseptically transferred 100 µl concentration of chemical solution to the wells aseptically.

The agar plates were incubated at 37C for 24 to 72 h. After incubation, the plates were observed for zone formation. The zone of inhibition were measured in mm using a measuring scale.

C. Results and discussion

1. <u>Antibacterial studies</u>

The results of the antibacterial activity against E. coli are tabulated in Table 2.1. The minimum inhibitory concentration was found to be different in different complexes. The results showed that the ligand, BMPPA was inactive against

TABLE 2.1

ANTIMICROBIAL ACTIVITY STUDY ON E. COLI

COMPLEX	ZONE OF INHIBITION(MM) AT DIFFERENT CONCENTRATIONS CONCENTRATION(µg/L)				MINIMUM INHIBITION CONCENTRATION (µg/L)
	0.5	1.0	1.5	2.0	
BMPPA (L_1)	NI*	NI	NI	NI	NI
$[Ni(L_1)_2(CH_3COO)_2]$	NI	0.7	0.7	0.8	1.0
$[Cu(L_1)_2Cl_2]$	1.7	1.9	2.3	2.4	0.5
$[Cu(L_1)_2SO_4]$	1.2	1.7	1.9	2.0	0.5
BMPPI (L_2)	1.0	1.2	1.2	1.0	0.5
$[Co(L_2)_2(CH_3COO)_2]$	0.5	0.6	NI	0.7	1.0
$[Co(L_2)_2Cl_2]$	NI	NI	NI	NI	NI
$[Co(L_2)_2(NO_3)_2]$	0.7	0.8	0.9	1.0	0.5
$[Cu(L_2)_2(CH_3COO)_2]$	1.2	1.4	1.5	1.7	0.5
$[Cu(L_2)_2Cl_2]$	0.7	0.7	0.8	1.5	0.5
BMPPBH (L_4)	0.7	0.9	1.0	1.2	2.0
$[Cu(L_4)_2Cl_2]$	NI	NI	NI	0.8	NI

* NI = NO INHIBITION

E. coli but its complexes [Cu(BMPPA)$_2$Cl$_2$] and [Cu(BMPPA)$_2$SO$_4$] were found to be active against the bacteria. The ligand, BMPPI exhibited antibacterial activity but the zones of inhibition were less than that in the complex [Cu(BMPPI)$_2$(CH$_3$COO)$_2$]. The ligand , BMPPBH and its complex [Cu(BMPPBH)$_2$Cl$_2$] were found to exhibit antibacterial activity (Figs.2.1 - 2.7).

2. Antifungal studies

The results are tabulated in Table 2.2 and the figures are shown in Figs 2.8 -.2.10. The results indicate that the ligands and the complexes were found to exhibit antifungal activity. The results indicate that the complexes [Co(BMPPA)$_2$I$_2$], [Cu(BMPPA)$_2$(CH$_3$COO)$_2$], [Cu(BMPPA)$_2$(NO$_3$)$_2$] and [Cu(BMPPA)$_2$Cl$_2$] exhibit greater antifungal activity against A. niger than the ligand, BMPPA. Similarly, [Ni(BMPPI)$_2$(CH$_3$COO)$_2$] exhibits greater antifungal activity than the ligand, BMPPI and the other complexes have almost the same activity as that of the ligand. The complexes [Ni(BMPPPH)$_2$(NO$_3$)$_2$], and [Cu(BMPPPH)$_2$(NO$_3$)$_2$] exhibit greater antifungal activity than the ligand, BMPPPH. The complexes [Co(BMPPBH)$_2$(CH$_3$COO)$_2$] and [Cu(BMPPBH)$_2$(NO$_3$)$_2$] exhibit greater antifungal activity than the ligand, BMPPBH.

The results prove that the transition metal complexes can be preferred to organic compounds by the drug manufacturers.

TABLE 2.2

ANTIFUNGAL ACTIVITY STUDY ON ASPERGILLUS NIGER

COMPLEX	ZONE OF INHIBITION (mm)
BMPPA (L_1)	11
$[Co(L_1)_2I_2]$	14
$[Ni(L_1)_2(CH_3COO)_2]$	10
$[Cu(L_1)_2CH_3COO)_2]$	15
$[Cu(L_1)_2Cl_2]$	13
$[Cu(L_1)_2(NO_3)_2$	13
BMPPI (L_2)	15
$[Co(L_2)_2CH_3COO)_2]$	14
$[Co(L_2)_2I_2]$	13
$[Co(L_2)_2(Cl_2)]$	15
$[Co(L_2)_2(NO_3)_2]$	13
$[Ni(L_2)_2(CH_3COO)_2]$	20
$[Ni(L_2)_2Cl_2]$	17
$[Ni(L_2)_2(NO_3)_2]$	13
$[Cu(L_2)_2(CH_3COO)_2]$	14
$[Cu(L_2)_2Cl_2]$	13
$[Cu(L_2)_2(NO_3)_2]$	16
$[Cu(L_2)_2SO_4)]$	16
BMPPPH (L_3)	13
$[Ni(L_3)_2Cl_2]$	10
$[Ni(L_3)_2(NO_3)_2]$	17
$[Cu(L_3)_2(CH_3COO)_2]$	8
$[Cu(L_3)_2Cl_2]$	8
$[Cu(L_3)_2(NO_3)_2]$	19
BMPPBH (L_4)	9
$[Co(L_4)_2(CH_3COO)_2]$	14
$[Cu(L_4)_2Cl_2]$	10
$[Cu(L_4)_2(NO_3)_2]$	13

D. Conclusion and scope

Man cannot live without air. The air we breathe is full of microbes which cause innumerable diseases, most of which prove to be fatal if immediate attention is not given. The earlier antibacterial and antifungal drugs like fluconazole and itraconazole which contain azole nucleus in them pose a threat to humans due to the adverse side effects which they create. A perusal of the literature proves that many of the bacteria are resistant to drugs. Hence it was thought worthwhile to try to find out better drugs which have greater antibacterial and antifungal activities than the earlier drugs and also which do not pose any threat to humans or animals. The antibacterial and the antifungal activity results discussed above prove that the effort to synthesize transition metal complexes with a view to make a rapid stride in drug industry, has been a success.

The results indicate that the effort to synthesise biologically active metal complexes was very successful, and that more research work could be done in the field of coordination chemistry which would be very useful in drug research. A perusal of the literature proves that many of the bacteria are resistant to drugs. So work in this area has to be extended inorder to synthesize new and newer drugs.

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