CD/133/29/2000
15/06/2000

TO: Dr. Yesehak Worku
Dean, SGS

FROM: Negussie Retta
Head,Chemistry Department

SUBJECT: MSc theses

The MSc students of the Department listed below have incorporated all comments made by the examining panel in their final versions of their theses. This is testified by their respective advisors.

ANALYTICAL STREAM

Ato Kidane Fanta G/Mariam

Advisor: Dr. B.S. Chandravanshi
Title of thesis: Studies on Voltammetric Behavior of Cadmium(II) at N-P-Chlorophenylcinnamohydroxamic Acid Modified Carbon Paste Electrode.
Thesis Grade: Very good

Ato Abraha G/Kidan Asgedom

Advisor: Dr. B. Hundhammer
Title of thesis: Investigation of the ionic composition of Addis Ababa drinking and surface water.
Thesis Grade: Very good

Ato Sisay Tadesse Anshebo

Advisor: Dr. B. Hundhammer
Title of thesis: Ion Transfer Across Membrane Stabilized Liquid Liquid Interface Application to Enzymatic Determination of Urea
Thesis Grade: Good

INORGANIC STREAM

Kebede Keterew Kefene

Title of thesis: Simultaneous Chemical Transport Reaction of Zinc and Cadmium Chalcogenides

Advisor: Dr. V Marx

Thesis Grade: Very good

Sisay Chanyalew Abegaz

Title of Thesis: Calculation of Schottky Defect Formation Energies in Alkali Halides by Numerical Summation of Coloumb, Repulsive, and Van der Waals Interactions.

Advisor: Dr. V Marx

Thesis Grade: Very good

Mulu Gebre Gebremedhin

Title of Thesis: Synthesis and Characterization of Metal Complexes of New Nitrogen Hetrocyclic Chelating System and Study on their Possible Applications.

Advisors: Drs. Negussie Retta and V.J.T. Raju

Thesis Grade: Very good

Mulugeta Ghiday Ma-Asho

Title of Thesis: Synthesis and Structural Studies on Polymeric Metal Complexes Derived from New Multidentate Ligands.

Advisors: Drs. Negussie Retta and V.J.T. Raju

Thesis Grade: Good

PHYSICAL STREAM

Abebaw Adgo Tsegaye

Title of thesis: Electrochemical Behaviours of Substituted Thiophenes

Advisors: Dr. B. Hundhammer/ Dr Wendmagegn Mammo and Prof. Theodros Solomon

Thesis Grade: Good

Terefe Getaneh Habteyes

Title of thesis: Mean Field Theory of Ferroelectricity in Liquid Crystals.
Advisor: Dr. Habtamu Zewdie

Thesis Grade: Very good

SYNTHESIS AND CHARACTERIZATION OF METAL COMPLEXES OF A NEW NITROGEN HETEROCYCLIC CHELATING SYSTEM AND STUDY ON THEIR POSSIBLE APPLICATIONS

A Thesis Submitted to the
School of Graduate Studies
Addis Ababa University

In Partial Fulfillment of the Requirements
for the Degree of Master of Science
in Chemistry

by

Mulu Gebre

June 2000

ADDIS ABABA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

SYNTHESIS AND CHARACTERIZATION OF METAL COMPLEXES OF A NEW NITROGEN HETEROCYCLIC CHELATING SYSTEM AND STUDY ON THEIR POSSIBLE APPLICATIONS

by

MULU GEBRE

DEPARTMENT OF CHEMISTRY
FACULTY OF SCIENCE

Approved by the Examining Board:

Dr. Yonas Chebude, Examiner and Coordinator _____

Dr. Negussie Retta, Advisor _____

Dr. V. J. T. Raju, Advisor _____

Dr. V. Marx, Examiner _____

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TO MY PARENTS

ACKNOWLEDGEMENTS

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Finally, The German Academic Exchange Service (DEUTSCHER AKADEMISCHER AUSTAUSCHDIENST /DAAD) is gratefully acknowledged for financial support during the period of my study.

LIST OF TABLES

SYMBOLS AND ABBREVIATIONS USED

cm = centimeter, nm = nanometer, IR = infrared

UV-VIS = ultraviolet-visible, XRD = x- ray diffraction

^{1}H-nmr = proton nuclear magnetic resonance , WL= wave length

N = normality, S = Siemens

ν = Streching , δ = bending

m.p. = melting point

MeOH = methanol, EtOH = ethanol, NaOH = sodium hydroxide

HCl = hydrochloric acid, DMSO = dimethyl sulphoxide

DMF = dimethylformamide

KBr = potassium bromide

NaCl = sodium chloride

DMG = dimethylglyoxime

EDTA = ethylenediaminetetra-acetic acid

PPh_3 = triphenylphosphine

BU_3N = tributhylamine

LIST OF FIGURES

ABSTRACT

Synthesis and Characterization of Metal Complexes of a New Nitrogen Heterocyclic Chelating system and Study on their Possible Applications.

The condensation of o-phenylene diamines with α- carbonyl compounds results in the formation of a variety of quinoxalines. By suitable choice of α- carbonyl component (oxalic acid), quinoxaline-2, 3- dione has been prepared. The result obtained has been characterized and it is in well agreement with the results reported in literature.

So far there are no reports on the condensation of quinoxaline-2, 3- dione with amines or polyamines. In this study a suitable amine group, 1, 3-diaminopropane, has been selected.

A new oxygen nitrogen chelating system, which is a condensed product of quinoxaline-2, 3-dione with 1, 3-diaminopropane has been isolated and characterized by elemental analysis, electronic and IR spectral data.

New N, N'- bis (3- quinoxaline- 2- one) diaminopropane (BQxDP) complexes of cobalt (II), nickel (II), copper (II), zinc (II), cadmium (II) and mercury (II) have been prepared and characterized by elemental analysis, conductance, IR and electronic spectral data.

The ligand acts as neutral ONN donor system in cobalt (II), nickel (II) and copper (II) complexes. In case of zinc (II), cadmium (II) and mercury (II) complexes it acts as ONNO

donor system.

From the analytical and electronic spectral data all the complexes except copper (II) have been found to be octahedral in geometry. Electronic spectral data supports the formation of a distorted octahedral geometry for copper (II) complex.

The ligand, metal complexes and related compounds have subjected to preliminary studies for antibacterial activity against Bacillus T.I. and E. Coli. In general the ligand and most of the metal complexes are inactive. Only Cd (II) complex shows inhibitory activity against gram +ve Bacillus T.I. at 100 μg/mL concentration. Further studies are necessary to draw worthwhile conclusions.

Chapter 1

INTRODUCTION

A large number of heterocyclic compounds have been investigated for their metal binding properties, which have significantly contributed towards the development of modern coordination chemistry. Substantial contributions in the fields of analytical chemistry, biochemistry, industrial chemistry, catalysis, dyes, and drugs have been documented in the literature [1-3]. Nitrogen heterocyclics have been employed in metal complex formation to a greater extent than the other heterocyclics containing heteroatoms like O, S,----, etc. This is probably due to the availability of a potential lone pair on the nitrogen, which is not totally drawn into the π-cloud of the ring, besides the lone pair: lone pair repulsions and steric restrictions are relatively higher in oxygen and related heterocyclics. Probably, the absence of these is a favorable factor in the greater stabilization of metal complexes through the nitrogen heterocyclics.

Voluminous work on the synthesis, characterization, solution studies and applications of metal complexes of pyridine and various suitably substituted pyridines with functional groups like-CHO, $-COCH_3$, $-NH_2$, $-NHNH_2$, $-(CH_2)_n NH_2$, NO_2, etc., is a classic example to show the potentiality of the heterocyclic nitrogen in metal binding [4, 5-8]. Amongst the diazines, the most extensively studied one is undoubtedly pyrazine, present in the so-called Creutz- Taube complex. The interest in metal complexes of pyrazine and related ligands is due to electron-transfer reactions via ligand aromatic systems [9]. Fused heterocyclics like quinolines, isoquinolines, phenazines, indoles, and pteridines have also contributed towards the development of coordination chemistry.

Quinoxalines (Figure 1), a class of nitrogen heterocyclics with two nitrogen atoms in mutually para disposition has attracted recent attention in the formation of metal complexes [10-12].

Quinoxalines, also known as 1,4-diazanaphthalenes have wide applications in pharmacology , bacteriology and mycology. These compounds have been reported for insecticidal, antibiotic, cytostatic, cytopathogenic, pesticidal, herbicidal, antileukemia, antiamoebic, antidiabetic, antituberculous and receptor antagonistic properties [13 –20].

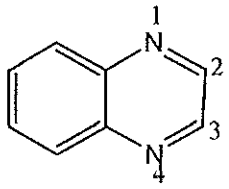


Fig. 1 Quinoxaline

The majority of quinoxalines are of synthetic origin. Quinoxaline is made by condensation of ortho disubstituted benzene with a carbon synthon. The condensation of ortho-phenylenediamines with α-carbonyl compounds results in the formation of a variety of quinoxalines. By suitable choice of α-carbonyl component quinxaline-2, 3-dione (Figure 2) have been prepared.

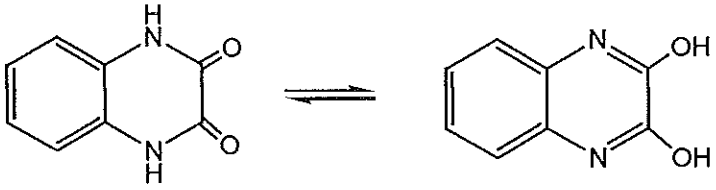


Fig 2 Tautomeric Forms of QxD

The derivatives of quinoxalines have received attention in complex formation in view of two potentially metal binding nitrogen centers present in 1,4-positions of a six membered fused heterocyclic system. Significant chelating abilities could be developed in these through the introduction of suitable substitutions on heterocyclic ring or on benzene ring.

Notable features of complex formation have been documented with quinoxalines having metal binding substituents at positions-2 and –3 and on heteroatoms (N-atoms) at positions-1 and-4. Various disubstituted quinoxalines have been developed as potential chelating ligands wherein other nitrogen heterocyclics like pyridine have been grafted as substituens at positions-2 and-3 resulting in an interesting class of biheteroaromatic compounds [21, 22].

Due to the potential complexing abilities of quinoxalines and their wide applications, it has been aimed to synthesize a new multidentate ligand with quinoxaline function. Literature survey reveals, that quinoxaline-2, 3-dione (QxD) can form condensed products with primary amines. So far there are no reports on metal complexes of QxD with diamines or polyamines.

In general ligands with highly electronegative donor atoms are hard bases while polarizable ligands are soft. A general rule is that stable complexes are those formed between hard acids and hard bases, and soft acids and soft bases (HSAB). The selection of metal ions is based on the HSAB principle and for comparison purposes metal complexes of some heavy metal ions mercury (II) and cadmium (II) were included for study.

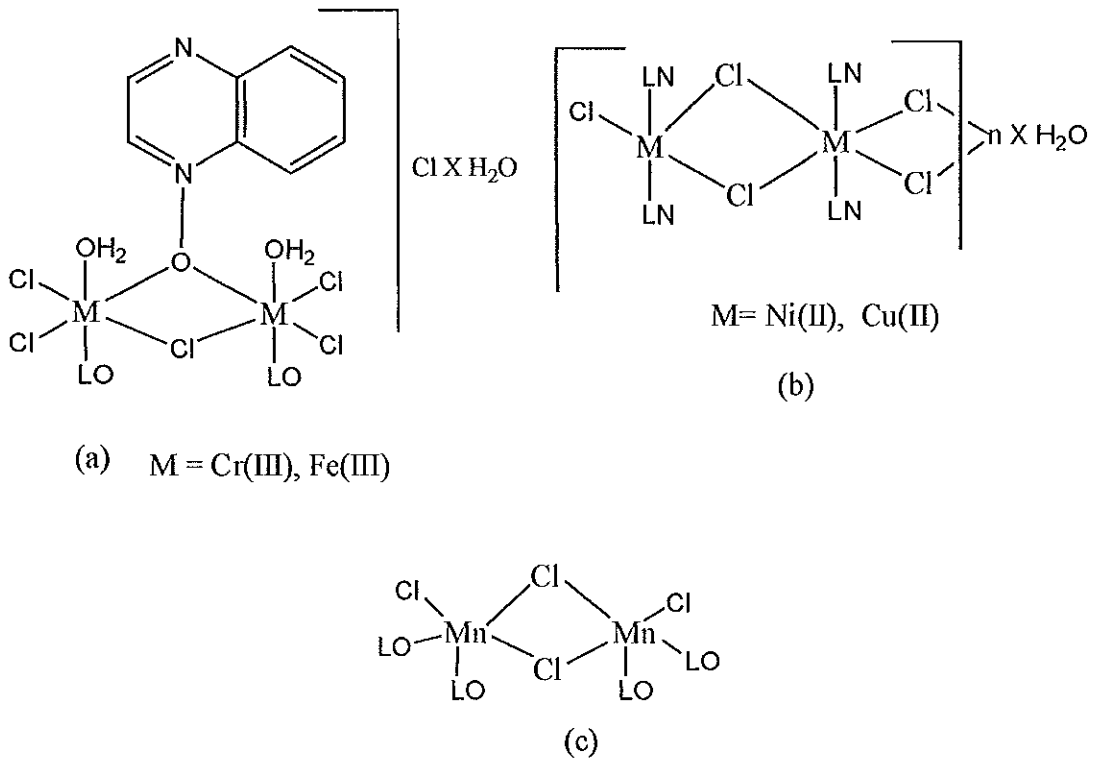
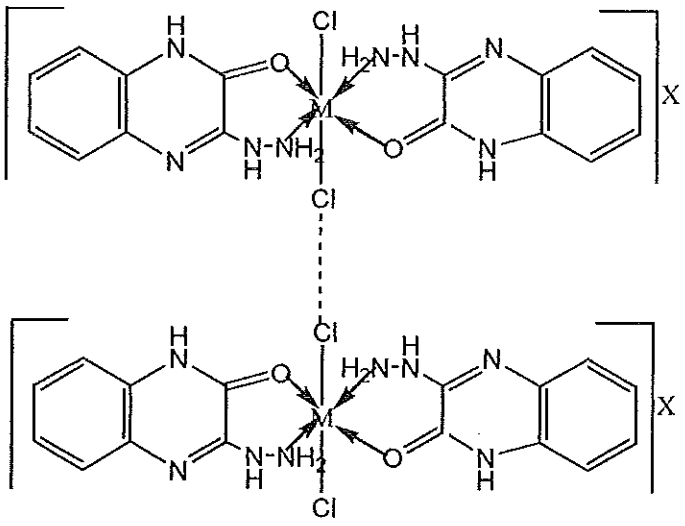


Fig. 3 Metal Complexes Of Quinoxaline -1- Oxide

First row transition (3d) metal complexes with quinoxaline 1,4-dioxide were prepared and characterized by means of spectral and magnetic studies by Chasan et al. [38]. The temperature dependent magnetic susceptibilities of 3d (transition) metal chloride and perchlorate complexes with quinoxaline 1,4- dioxide (L) were measured [40]. Reports on 3d metal perchlorate (ClO_4) complexes indicate bi- or poly-nuclear structures with the exception of penta coordinated monomeric Cu (II) complex of the type [CuL4 ($OClO_3$)] (ClO_4). The spectral and magnetic evidence is reported to be in favour of bi-or poly-nuclear structures, involving terminal (L_1) and bridging quinoxaline-1, 4-dioxide (Figure 4).

Co (II), Ni (II) and Cu (II) complexes with 2-quinoxaline carboxamide were prepared and characterized on the basis of analytical, spectral and magnetic data. It has been found that



M = Fe(III), X= Cl M = Cu(II), X = -

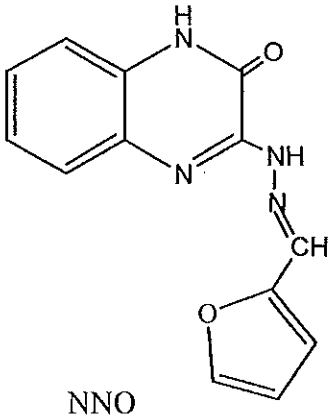
Fig. 6 Metal Complexes of 3- hydrazinoquinoxaline- 2- One

Recently, several biheteroaromatic ligands were synthesized starting with substituted 1,4-quinoxaline like-3 hydrazino-1, 4-quinoxaline-2-one and investigated for complex formation. Many oxygen, nitrogen, sulphur and mixed heterocyclics with suitable carbonyl substituents on condensation with hydrazine-substituted quinoxalines were reported [12].

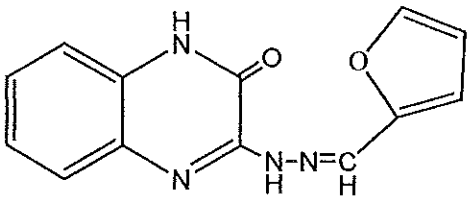
Metal Complexes of N- (2-Furylidene)-N'- (3-Quinxaline-2-One) Hydrazine (FQH).

FQH (Figure 7) was found to be a neutral tridentate ONO / NNO donor through the lactam carbonyl oxygen / azomethine (ring) nitrogen, azomethine nitrogen (hydrazone) and furan oxygen. Based on analytical, conductance, thermal, spectral and magnetic data, octahedral geometry for oxovanadium (IV), chromium (III), manganese (II), iron (III) and zinc (II) complexes, tetrahedral geometry for cobalt (II) complex and trigonal bipyramidal geometry

for nickel complex have been reported. Copper (II) complex has been assigned square planar geometry [12].



NNO



ONO

Fig. 7

Metal Complexes of N- (2-Pyridinilidene)-N'- (3-Quinoxaline-2-One) Hydrazine (PQH).

PQH (Figure 8) has been reported to be a neutral tridentate NNN donor through the azomethine nitrogens (ring and hydrazone) and the nitrogen of pyridine moiety in oxovanadium (IV), chromium (III), manganese (II), iron (III), cobalt (II) and zinc (II) complexes. It acts as ONN donor in nickel (II) and copper (II) complexes. On the basis of analytical, conductance, thermal, spectral and magnetic data, octahedral geometries have been reported for oxovanadium (IV), chromium (III), iron (III), nickel (II) and zinc (II) complexes and square planar geometry for copper (II) complex [12].

Section-C

OBJECTIVIES AND THE SCOPE OF THE PRESENT INVESTIGATION.

Literature survey reveals that the metal complexes of N-heterocyclics like quinoxaline containing one or more amine (polyamine); substituted amine side chains and their derivatives have received limited attention by researchers.

In view of the wide range of applications and the potential metal binding abilities of N-heterocyclics, it has been aimed to synthesize N, N'-bis (3-quinoxaline-2-one) diaminopropane (BQxDP) and study its reactivity towards metal ions.

After preliminary studies, the product (BQxDP) from the condensation of QxD and 1,3-diaminpropane was selected for the investigation. The ligand (BQxDP) is expected to exist as tautomers due to the mobility of the hydrogen between the ring and exocyclic azomethine nitrogens and also the mobility of hydrogen between the ring azomethine nitrogen and hydroxy and can behave as bis-ON donor or ONN donor system and lead to stable metal complexes. These complexes are thought to have interesting structural and application characteristics. BQxDP is expected to be neutral tri / tetra dentate ONN / ONNO donor.

In view of the importance and recent interest on quinoxaline-2, 3- dione derivative ligands, as understood from literature [10-12, 15-20], it is proposed to undertake investigation on **"synthesis and characterization of metal complexes of a new nitrogen heterocyclic chelating system and study on their possible applications."**

Chapter 2

EXPERIMENTAL PART

2.1 Chemicals

Metal salts $NiCl_2$ and $CoCl_2.6H_2O$ (all from BDH) ,$CuCl_2.2H_2O$ (GRAVE), $ZnCl_2$, $HgCl_2$, $CdCl_2.H_2O$ and orthophenylene diamine and oxalic acid dihydrate (all from Riedel-deHaen), 1,3-diaminopropane (Fluka) were used with out purification. Solvents like MeOH, DMSO, EtOH, DMF, 4N HCl, and 1%NaOH, 4% methanolic ammonia solution (in some cases for pH adjustment) were also used as obtained.

2.2 Instruments and Experimental Conditions

Melting points of the products were determined using Bock- Monoscop instrument.

Carbon, hydrogen and nitrogen analysis was carried out using Elementar Vario EL instrument at the laboratory of Geological Survey of Ethiopia.

The metal complexes have been analyzed for metal and chlorine contents using known methods [36, 37]. Cobalt, zinc and cadmium were determined complexometrically with standard EDTA solution [36, 37] while nickel and copper were estimated as Ni $(DMG)_2$ and Cu (α-benzoinoxime). Mercury was determined as mercuric para periodate $Hg_5(IO_6)_2$. The percentages of chlorine in the complexes were determined as silver chloride precipitate.

The electrical conductivities of 10^{-3} M solutions of the complexes in DMSO were obtained using a Philip Harris conductometer at room temperature.

Infrared spectra were recorded using a Pye-Unicam SP 2000 Infrared Spectrophotometer with a range of 4000 – 200 cm^{-1} as KBr disks.

UV–Visible Spectrophotomeric studies of 10^{-3} -10^{-4} M solution of the compounds in the range 200–900 nm were conducted using SPECTRONIC GENESYS 2PC at room temperature.

2.3 Synthesis

2.3.1 Synthesis of quinoxaline-2, 3-dione (QxD)

Orthophenylene diamine (0.05 mole), oxalic acid dihydrate (0.05 mole) and 4 N HCl (30 mL) were heated to boiling for 15 min. A crystalline solid was formed which was then cooled, collected, washed with water and dried. The compound was dissolved in alkali and then acidified with HCl, so that pure product may be obtained. Yield: 3.2 g, m.p. >330 ^{0}C.

2.3.2 Synthesis of N, N'-bis (3-quinoxaline-2-one) diaminopropane (BQxDP)

To a mixture of quinoxaline-2, 3- dione (0.02 mole) and 1,3- diaminopropane (0.12 mole), ethanol (10-20 mL) was added and heated under reflux for 1-2 h and cooled. The precipitate was filtered out, washed with ethanol. DMF was used as a solvent to purify the product. Yield: 3.06 g, m.p. >330 ^{0}C **(found (calculated)**: C, 56.78 (57.28); H, 5.48 (5.56); N, 20.57 (21.09) %, $C_{19}H_{18}N_6O_2.2H_2O$.

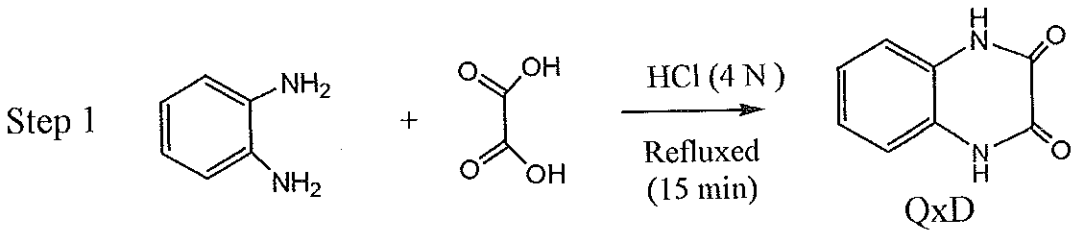
2.3.3 Synthesis of Metal (Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Hg^{2+}) complexes

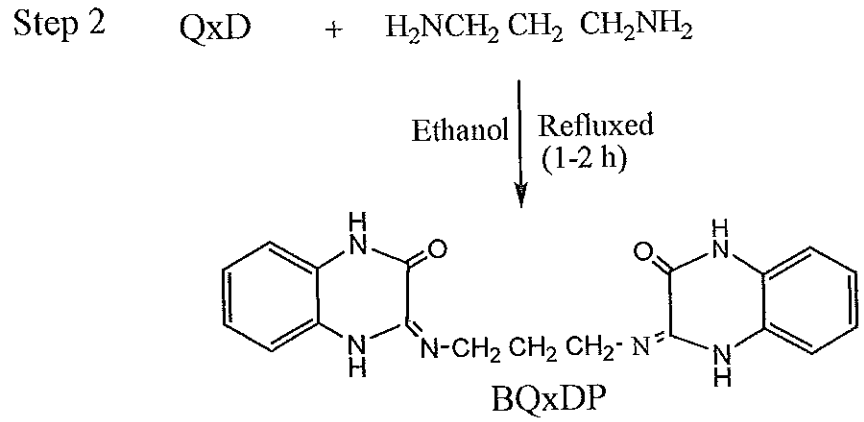
Metal complexes were synthesized following a general procedure as described below.

The ligand (1mmole) was dissolved in hot methanol and to this solution; methanolic solution of divalent metal chloride (1 mmole) was added. The pH of the mixture (in a cobalt and nickel case only) was adjusted to 6.5-7 with methanolic ammonia (4%). The reaction mixture was refluxed for 3-12 h. The colored product, thus, obtained was filtered in hot condition, washed with methanol and dried. The product was then collected and stored in desiccators. Yield: 35-50%.

SCHEME 1

Summary of the synthesis of QxD, BQxDP and metal complexes of BQxDP





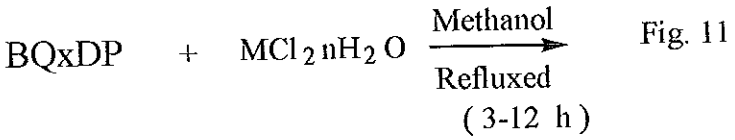


Fig. 11

Chapter 3

RESULTS AND DISCUSSION

The compounds are stable to air and moisture. All the compounds except copper complex don't melt or decompose below 330 ^{0}C. The physical properties of the ligand (BQxDP) and the complexes are summarized on Table-I.

TABLE-I: PHYSICAL PROPERTIES OF BQxDP AND THE METAL COMPLEXES

Compound	Color	Yield (%)	Decomp.Temp. /m.p. (^{0}C)
Ligand (BQxPD)	Colorless	38	>330
Cobalt (II) complex	Rose	45	>330
Nickel (II) complex	Green	40	>330
Copper (II) complex	Blue	45	218-220
Zinc (II) complex	Colorless	50	>330
Cadmium (II) complex	Colorless	35	>330
Mercury (II) complex	Colorless	40	>330

3.1 Analytical Studies

3.1.1 Elemental Analysis

The analytical data of the compounds are given in Table II. Elemental analysis shows metal to ligand ratio as 1:1 in cobalt (II), nickel (II) and copper (II) complexes and 2:1 in zinc (II), cadmium (II) and mercury (II) complexes and are consistent with the proposed compositions. The data also provides evidence for the presence of ammonia in cobalt (II) complex and water molecules and chloride in all the complexes. These observations are in support of the neutral character of the ligand in all the complexes.

3.1.2 Conductivity Data of Metal Complexes

The conductivity measurements were carried out in $1x10^{-3}$ M DMSO solutions. The molar conductance values are given in Table II. The molar conductance values of cobalt (II), nickel (II) and copper (II) complexes are 65.33, 72.42 and 82.57 S cm^2 $mole^{-1}$,respectively. The data shows that these three complexes are 1:1 electrolytes and zinc (II) cadmium (II) and mercury (II) complexes are non-electrolytes [38].

From the elemental analysis and conductivities of cobalt (II), nickel (II) and copper (II) complexes, it can be concluded that out of two chlorides, one is in the ionization sphere while the other is in the coordination sphere. In case of zinc (II), cadmium (II) and mercury (II) complexes all the chlorides are in the coordination sphere.

there is a strong band with three structures which is assignable to ν C=O (exocyclic) likely to be involved in tautomeric and hydrogen bonding interactions (Fig.10). The corresponding ν C=O band in QxD (Fig. 2) appears at a higher frequency due to relatively less number of tautomers and hydrogen bonding interactions. A free ν C=O (exocyclic) in similar compound is generally observed around 1720 cm^{-1} [22] Another sharp characteristic multiple band at 1610 cm^{-1}-1590 cm^{-1} is due to ν C=N (of the exocyclic azomethine functions). Other bands observed at 1550, 1540, 1520-1500 cm^{-1} may be attributed to the ring ν C=N, ν C=C, δ NH and δ OH etc.

The characteristic infrared spectral frequencies of the ligand and metal complexes are presented in Table-III. The comparison of the free ligand infrared spectrum with the spectra of complexes has revealed specific changes in the important regions. These regions are between 3600-2400 cm^{-1}, 1730-1400 cm^{-1} and 1000-200cm^{-1}.

Corresponding to the ligand region of 3680-2700 cm^{-1}, the spectra of metal complexes show more resolved band structures in the range of 3600-3000 cm^{-1}. The better resolution observed in the spectra of the metal complexes can be attributed to disruption in hydrogen bonding interactions during the process of complexation [12].

All the metal complexes show changes in ν C=O and ν C=N (exocyclic) frequencies. IR spectra of the metal complexes show down ward shift in ν C=N (exocyclic) frequencies (Table III) which clearly indicate that the exocyclic azomethine nitrogen is involved in bonding with the metal.

In all the complexes a positive shift in ν C=O frequency has been observed (Table III). This is noted as an indication of metal ligand interaction through particular tautomers, which can stabilize metal complexes preferentially. The positive shift is an indication of a higher carbonyl bond order corresponding to I or IV in Fig.10, of these two, structure I can be considered to be a better chelating system in view of the potential azomethine centers. This, in free state is likely to have ν C=O around 1720 cm^{-1}.

The metal complexes show broad, strong, multistructured bands in the regions 1720-1650 cm^{-1} (Co^{2+}, Ni^{2+} & Cu^{2+}) and 1700- 1665 cm-1 (Zn^{2+}, Cd^{2+} & Hg^{2+}), attributed to ν C=O of the metal complexes which can be classified into two categories: (i) complexes of the transition metal ions Co^{2+}, Ni^{2+} and Cu^{2+} in which the band maxima is at 1720-1725 cm^{-1}, (ii) complexes of non- transition metals in which the band maxima is at 1700 cm^{-1}. Based on this information, it is concluded that both carbonyls in Zn^{2+}, Cd^{2+} and Hg^{2+} complexes are binding centers but one of the carbonyl functions participates in bonding in Co^{2+}, Ni^{2+} and Cu^{2+} complexes (Figure 11).

The non-ligand bands in the region 960-845 cm^{-1}in all the complexes are attributed to the rocking mode of coordinating water (except cobalt (II)) [39]. The non-ligand band at 930 cm^{-1} in cobalt (II) complex is assigned to rocking mode of ammonia molecule [40]. In all the complexes the new bands observed in the region 640-400 cm^{-1} have been assigned to ν M-O and ν M-N frequencies [39], some of the bands in this region can also be assigned to wagging mode of coordinating water [39]. Further, the spectra of the complexes show new bands identified in the region 400-200 cm^{-1} which are assigned to coordinated chloride [39, 41], of these the low energy bands in Zn^{2+}, Cd^{2+}, and Hg^{2+}spectra are assigned to

bridging chloride.

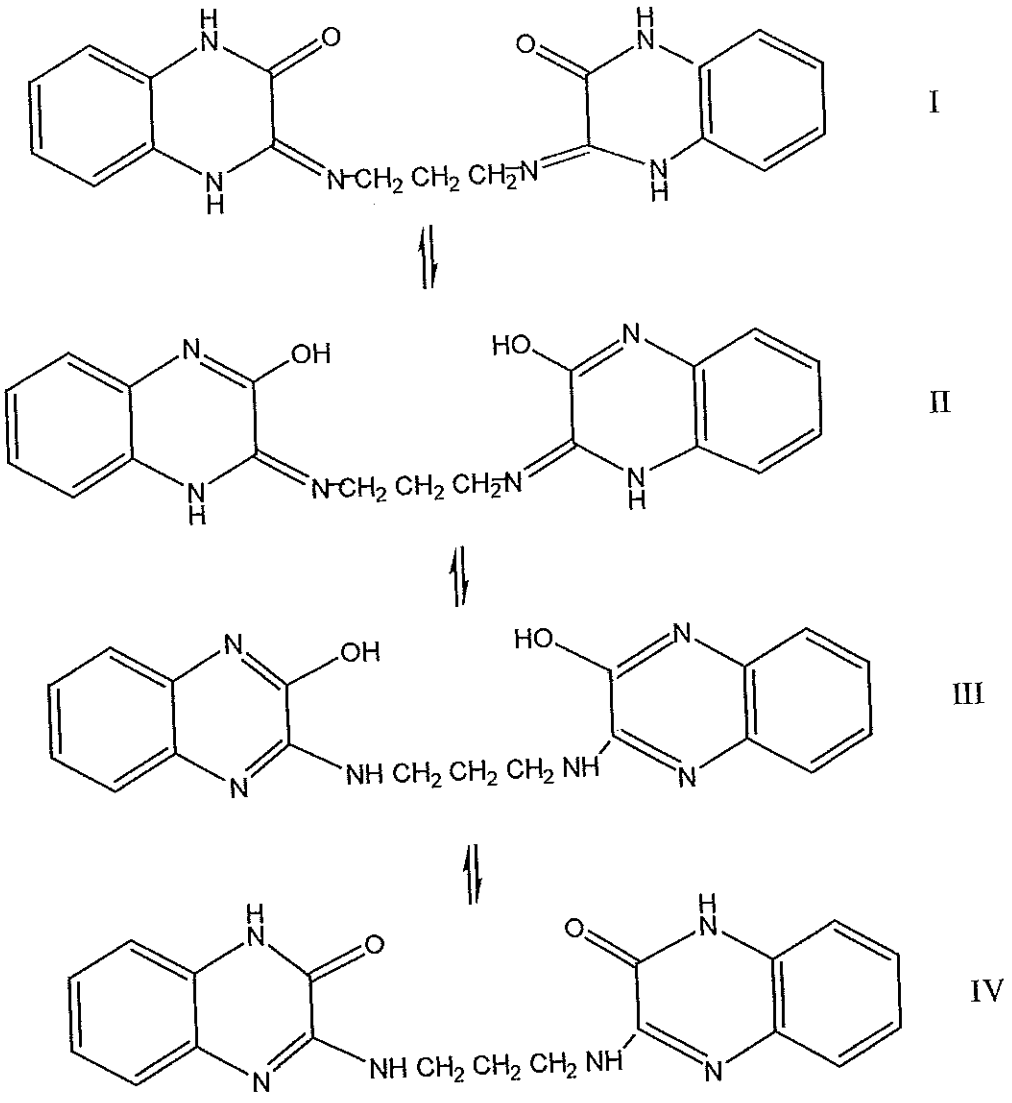
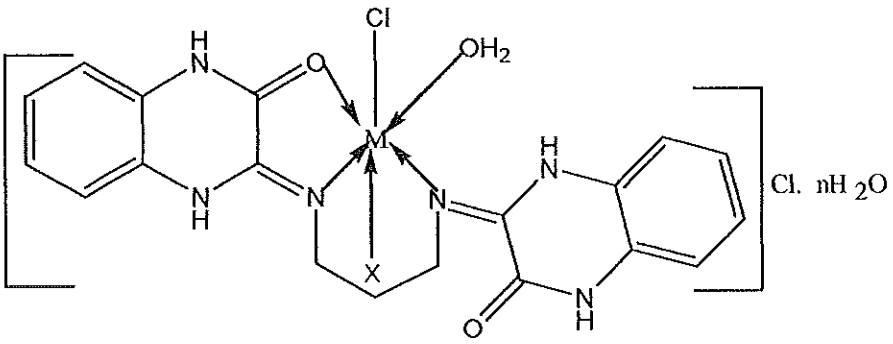
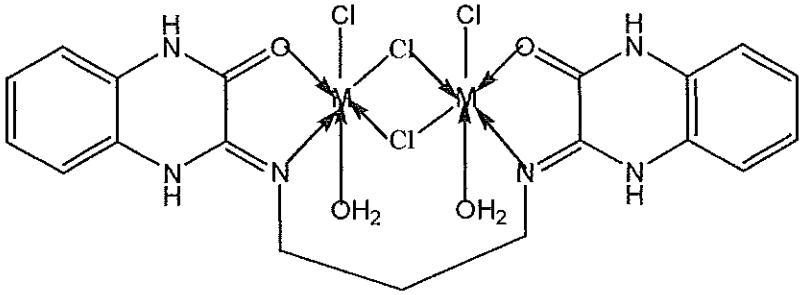


Fig. 10 Tautomeric forms of BQxDP



M = Ni (II), Cu (II) X= OH_2, n =2

M= Co (II) X=NH_3, n =3



M = Zn (II), Cd (II), Hg (II)

Fig.11 Structure of Complexes of BQxDP

3.3 **Electronic Spectral Studies**

The electronic spectrum of ligand (BQxDP) shows number of bands in the range of 47619-28571 cm^{-1}. The band positions are observed at 47619, 43290, 38314, 32680, 31746 and 30864 cm^{-1}. Out of these, the bands observed at 47619, 38314, 31746 and 30864 cm^{-1} may be assigned for the C=N (ring) and C=N (exo) functions [42]. The band at 32680 cm^{-1} is assigned for n $\rightarrow$ π^* transition of carbonyl (C=O) [21]. Band at 43290 cm^{-1} may be attributed to $\pi \rightarrow \pi^*$ transition of benzene ring (C=C). The positions of most of these bands are at relatively higher wavelength region, which could be attributed to the extended conjugation.

TABLE-IV: ELECTRONIC SPECTRAL DATA OF BQxDP COMPLEXES

Complex	Electronic spectral bands, (cm^{-1})	Assignment
$CoLCl_2\ NH_3.4H_2O$	18939	$^4T_1\ (F) \rightarrow {}^4T_1\ (P)$
	16129	$^4T_1\ (F) \rightarrow {}^4A_2$
$NiLCl_2.4H_2O$	22727	$^3A_2 \rightarrow {}^3T_1(P)$
	17544	$^3A_2 \rightarrow {}^3T_1(F)$
	12392	$^3A_2 \rightarrow {}^3T_2$
$CuLCl_2.4H_2.O$	16667 – 12500	$^2B_1 \rightarrow {}^2A_1$
		$^2B_1 \rightarrow {}^2B_2,\ ^2B_1 \rightarrow {}^2E$
$M_2LCl_4.\ 2H_2O$ (M = Zn, Cd and Hg)	-	-

The results discussed above can further be appreciated on the basis of Pearson's HSAB theory. The principle "hard acids prefer to bind to hard bases and soft acids prefer to bind to soft bases" will help in classifying the ligand BQxDP as a borderline case, in spite of the fact that the donor atoms, nitrogen and oxygen, belong to (class a) hard bases.

The lighter transition metal ions Co (II), Ni (II) and Cu (II) belong to (class a) hard acids. while Zn (II) is a borderline acid and Cd (II) and Hg (II) are soft acids (class b) with pseudo

inert gas configuration.

If the ligand BQxDP were a hard base, it would have exhibited better affinity towards hard acids. The present studies show that the ligand prefers the metal ions Zn^{2+}, Cd^{2+} and Hg^{2+} and stabilizes dinuclear complexes through an efficient ONNO donor sequence. With Co^{2+}, Ni^{2+} and Cu^{2+}, the interaction is relatively less intimate resulting in mononuclear complexes through ONO chelation.

Thus it is worthwhile to conclude that, the N, O centers of the ligand don't exhibit hard base characteristics. This may be attributed to the symbiotic effect caused by π-electron system associated with the ligand which imparts polarizability to the donor centers; thus reducing their hardness and transforming the ligand into a borderline $\rightarrow$ soft system.

Chapter 4

PRELIMINARY ANTIBACTERIAL STUDIES

In this chapter results pertaining to preliminary screening of BQxDP and its metal complexes are presented.

Physiological activity may be defined as the final result of a series of interlinked chemical reactions or the observed manifestations of an interference with a delicately balanced system of interdependent, chemical and physical processes. This interference should be effected with out damaging the tissues of the host. Some substances capable of causing such interference are useful as drugs.

Coordinated metal ions have been understood to be essential in the discharge of several vital functions in living organisms. The important aspect of ligand metal interaction in a biological environment is that the bound metal may cause considerable change in the reacting of the organic ligand by (1) changing the electron distribution in the ligand (2) by making a chemically active center of the ligand (3) by structuring the ligand molecules into a particular stereochemical form (4) by providing the conducive pathway for electron addition or removal (5) by increasing the lipo-solubility of the ligand and hence helping to penetrate into a living cell.

Natural products containing the quinoxaline ring are rare. However, the 1, 4-dioxides of quinoxaline-2-carboxylic acid has been isolated from cultures of streptomycin ambrafacieus. This compound and its ester derivatives have been shown to have antibiotic properties. It is

interesting to note that a large number of quinoxaline 1, 4-dioxides have antibacterial activity and this activity is higher in vivo than in vitro and is increased by two orders of magnitude under anaerobic conditions. It has been suggested that the high activity in vivo is possibly due to the quinoxaline acting as a prodrug with the metabolic products acting as effective antibiotic substances [44].

Echinomycin has been shown to be antitumor agent and to have antiviral and antibacterial properties. It has been demonstrated that echinomycin functions by inhibiting RNA synthesis in organism such as staphylococcus aureus. Echinonmycin, levomycin and actinoleutin are members of the quinxaline peptide antibiotic family and all contain one or more quinxaline rings [12, 22].

Amongst synthetic quinoxalines, numerous types of biological activity have been reported. 5,6,7,8-tetra chloroquinxaline and related derivatives have found use in fungicidal formulations. Phosphoric esters of 6-hydroxy quinoxalines have found use insecticidal preparations and phosphoric ester derivatives of 2-hydroxyquinoxalines functions as anthelmintics. Numerous other biological activities have been claimed for many synthetic quinoxalines and these are well documented in the review by Cheeseman and Cookson [45].

Number of quinoxaline dione derivatives like 6,7- dinitro quinoxaline-2, 3-dione and 6-nitro-7- cyano quinoxaine-2, 3- dione were prepared and tested for their antagonized responses mediated by N-methyl-D- aspartate and NMDA associated glycine recognition sites in mouse [22].

There are numerous patents dealing with the biological activity of 2,3- dichloroquinoxalines. Derivatives with 6-sulfonamido function have been patented as microbiocidal agents and 2, 3, 7-trichloro-6-methylaminosulfonyl quinoxaline is patented as anti-cancer drug.

Various 2,3- dichloroquinoxaline-6-sulfonates have antibacterial activity and there are patent claims for the fungicidal and bactericidal antibacterial activity and there are patent claims for the fungicidal and bacterial activity of 6-nitro-2, 3-dichloroquinoxaline [46].

In view of the reported antibacterial activities of substituted quinoxaline and related compounds, it has been aimed to carry out investigations on quinoxaline-2, 3- dione derivative and the corresponding metal complexes, synthesized and characterized in course of this investigation. These studies may throw light on the relation between the activity and the structure. The effect of metallation may bring about appreciable changes in the activities.

The ligand BQxDP and its metal complexes were tested for antibacterial activity on the gram-positive Bacillus thryngiensic isolate. and gram negative Escherichia Coli. The antibacterial activity is assessed by the disc diffusion method.

METHODS AND MATERIALS

Method: Disc diffusion method

Medium: Nutrient Agar

Bacteria: Gram +ve: Bacillus thryngiensic isolate

Gram-ve: Escherichia Coli

Media Composition

Peptone, meat extract, NaCl and distilled water

Methodology

Exponentially growing cultures (24 hrs culture) were taken and seeded on the nutrient agar plates by spreading plate technique. 2 mL of the culture was placed onto the nutrient agar plate and was spreaded all over the plate using a sterile spreader and was allowed to dry.

DMSO solutions (50 μg/mL and 100 μg/mL) containing ligand and metal complexes were prepared and each solution including DMSO and metal salts were absorbed on to each disc (S and S Antibiotic-Assay Disc diam. 0.25 inch). Each disc was placed in the agar plates. Finally the plates were kept in the incubator. They were incubated at 28^0C for 24 hrs.

RESULTS AND DISCUSSION

Results of preliminary studies on antibacterial activities of the ligand BQxDP, metal complexes and related compounds against gram +ve Bacillus thryngiensic isolate and gram –ve Escherichia Coli are presented in Table-V.

The compounds, Hg (II) and Cd (II) exhibit growth inhibitory activity against gram +ve Bacillus thryngiensic isolate species at 100 μg/mL concentrations. Hg (II) salt and its complex are active against both the bacteria at 50 and 100 μg/mL concentrations.

Earlier studies [12] show that quinoxaline dione (QxD) exhibits antimicrobial activity against E.coli and S.aureus. The present ligand that is a condensation product of QxD and 1,3-diamino propane is inactive against E.coli. This indicates that condensation of QxD with the diamine results in deactivation of QxD. This probably shows that both the exocyclic carbonyls are necessary in antimicrobial effects as exhibited by QxD. Such reactions may have application in detoxification of substances like QxD and may form models in the study of structure to activity relations.

The activity of Cd (II) complex, in comparison with the inactive free ligand and free Cd (II) metal ion in comparable concentrations needs consideration. This may be an example of synergistic or combination effect, which is probably due to changes, associated with electronic distribution and stereochemistry of the ligand due to complexation. However, detailed studies are necessary to draw worthwhile conclusions.

TABLE-V: RESULTS OF PRELIMINARY STUDIES ON ANTIBACTERIAL ACTIVITIES OF BQxDP, METAL COMPLEXES AND RELATED COMPOUNDS

Compound	Bacillus Thryngiensic Isolate		Escherichia Coli	
	50 µg/mL	100 µg/mL	50 µg/mL	100 µg/mL
Co (II) salt and complex	-	-	-	-
Ni (II) salt and complex	-	-	-	-
Cu (II) salt and complex	-	-	-	-
Zn (II) salt and complex	-	-	-	-
Cd (II) salt	-	-	-	-
Cd (II) complex	-	+	-	-
Hg (II) salt and complex	+	+	+	+
DMSO	-	-	-	-
BQxDP	-	-	-	-

Where - = inactive, + = active

CONCLUSION

Based on the elemental analysis, conductance measurement, IR and electronic spectral studies, the ligand BQxDP, binds the metal ions through ONN donor set in Co^{2+}, Ni^{2+} and Cu^{2+} complexes, where as in Zn^{2+}, Cd^{2+} and Hg^{2+} complexes it behave as bis-ON (ONNO) donor set. The studies show that the ligand is forming mononuclear Co^{2+}, Ni^{2+} and Cu^{2+} complexes and binuclear Zn^{2+}, Cd^{2+} and Hg^{2+} complexes.

In view of its greater affinity towards Zn^{2+}, Cd^{2+}, Hg^{2+} ions, the ligand may be classified as a borderline case of HSAB system. While BQxDP is inactive against Bacillus T.I. and E. Coli, its Cd (II) complex shows growth inhibition at 100 μg/mL concentration.

REFERENCES

1. Bedell, S.A; Martell, A.E, *Inorg. Chem.*, **1983**, 22, 364.
2. Dutta, R. L.; Hussan, K M., *Indian J. Chem.*, **1984,** 23A, 30.
3. Chohan, Z.; Hussan; Pervez; Humayun, Synth. React. *Inorg.Met.Org.Chem.*, **1993**,23, 1061.
4. Crawford, V. H.; Hatfield, W.E., *Inorg. Chem.*, **1977**, 16, 1336.
5. Kolks, G.; Lippard, S.J., *J. Am. Chem. Soc.*, **1977**, 99, 5804.
6. Livinstone, M., *Transition. Met. Chem.*, **1986**, 5, 77
7. Zuber, M., *Transition. Met. Chem.*, **1986**, 11, 5.
8. Mann, L.V.K.; Jeffers, C.J.; McCleverty, A.J; Ward, D.M., *J. Chem. Soc. Dalton Trans.*, **1998,** 3029.
9. Citrin, P.H.; Ginsberg, A.P., *J. Am. Chem. Soc.*, **1981**, 103, 3673.
10. Dikonda, S. R.; Parupalli, V. A. L.; Raju,V. J. T., *Trans. Met.Chem.*, **1994,** 19, 75.
11. Dikonda, S. R.; Raju, V. J. T.; Parupalli, V. A. L., *Indian J. Chem.*, **1999**, 38A, 385.
12. Goverdhan, K., Ph.D. thesis: " Synthesis and Structural studies on first row transition metal complexes of new biheteroaromatic ligands derived from 3-hydrazinoquinoxaline-2-one", submitted to Osmania University, **1997**.
13. Iland, C.N., *Nature*, **1948**, 161, 1010.
14. Junja, O.; Sasamat, S., *J. Med. Chem.*, **1996**, 39,3971.
15. Fabbiopaul, F.; Lang, S. A.; Lin, Y.; Cufcik, T.; Andrew, S., *J. Med. Chem.*, **1980**, 23, 201.
16. Carinna, T.; Citterio, A.; Crolla, T.; Minisci, F., J. Chem. Soc. Perkin I, **1977**, 865.
17. Mason, S. F., *Chem. Soc.* (London), **1955**, 3, 139.
18. Brigneil, P. J.; Katritzky, A. R.; Reavill, R.E.; Cheeseman, G. W. H., *J. Chem. Soc.*B, **1967**, 1241.
19. Sarsfield, A.A.; Blears, D. J.; Danyluck, S. S., *Tetrahedron*, **1967**,23,2927.
20. Cheeseman, G. W. H.; Katrizky, A. R.; Ridgeuell, B. J., *J. Chem. Soc.*, **1963**, 3764.
21. Schmidt, K. J.; Hamman, I.; Brit.Pat, *Chem. Abstr.*, **1969**, 72,973.
22. Sandhya Rani, D., Ph. D. thesis: "Synthesis and Structural elucidation of transition metal complexes derived from multidentate 2,3-disubstituted quinoxalines", submitted to Osmania University, **1995**.
23. Dhumwad, S.D.; Guadasi, K.B.; Goudar, T.R., *Indian J. Chem.*, **1994**, 34A, 320.

24. Syamal, A.; Kale, K.S., *Indian J. Chem.*, **1977**, 15A, 431.

25. Chasan, D.E.; Pytlewski, L.L; Owens, C.; Karayannis, N.M., *J. Inorg. Nucl. Chem.*, 1976, 38, 799.

26. Chasan, D.E.; Pytlewski, L.L; Owens, C.; Karayannis, N.M., *J. Inorg. Nucl. Chem.*, **1977**, 39, 585.

27. Chasan, D.E.; Pytlewski, L.L; Owens, C.; Karayannis, N.M., *Inorg. Chem. Acta*, **1977**, 24, 219.

28. Chasan, D.E.; Pytlewski, L.L; Owens, C.; Karayannis, N.M., *J. Inorg. Nucl. Chem.*, **1978**, 40, 1019.

9. Sanyal, G.S; Modak, A.B.; Mudi, A.K., *Indian J. Chem.*, **1981**, 20A, 510.

30. Corbin, R.D., *Inorg. Chem.*, **1981**, 20, 2084.

31. Boyde, S.; Garner, C.D.; Clegg, W., *J. Chem. Soc. Dalton Trans.*, **1987**, 1083.

32. Boyde, S.; Garner, C.D.; Enemark, J.H.; Ortega, R.B., *Polyhedron*, **1986**, 5, 177.

33. Boyde, S.; Garner, C.D.; Enemark, J.H.; Bruck, M.A.; Kristofoski, J.G., *J. Chem. Soc. Dalton Trans.*, **1987**, 2267.

34. Boyde, S.; Garner, C.D.; Enemark, J.H.; Bruck, MA.; Kristofoski, J.G., *J. Chem. Soc. Dalton Trans.*, **1987**, 1083.

35. Lakshmi, P.V.A, Ph.D. thesis: "Synthesis structural elucidation of transition metal complexes derived from some biologically active quinoxaline derivatives", submitted to Osmania University, **1993**.

36. Vogel, I. Textbook of Quantitative Inorganic Analysis, 3rd ed., Longman, London, **1961**.

37. Lever, A.B.P. Inorganic electronic spectroscopy, 2nd Edit., Elsevier, Amsterdam, **1984**.S

38.Costes, J.P; Gareia, M.I.F, *Transition Met. Chem.*, **1988**, 13, 132.

39. Nakamoto, K. Infrared and Raman Spectra of Coordination Compounds, 4th ed., Intersience, New York, **1986**.

40. Manapatra, B.B.; Patel, B.K., *Transition Met. Chem.*, **1987**,12, 49.

41. Tarafdar, M.T.H.; Ali, M.A., *Canadian J. Chem.*, **1978**,56,2000.

42. Kuge, Y.; Yamada, S., *Bull. Chem. Soc.*, **1972**, 45, 799.

43. Jolly, W.L. Modern Inorganic Chemistry, 2nd ed., McGraw-Hill, Singapore, **1991**.

44. Edwards, M.L., *J. Med. Chem.*, **1975**, 18, 637.

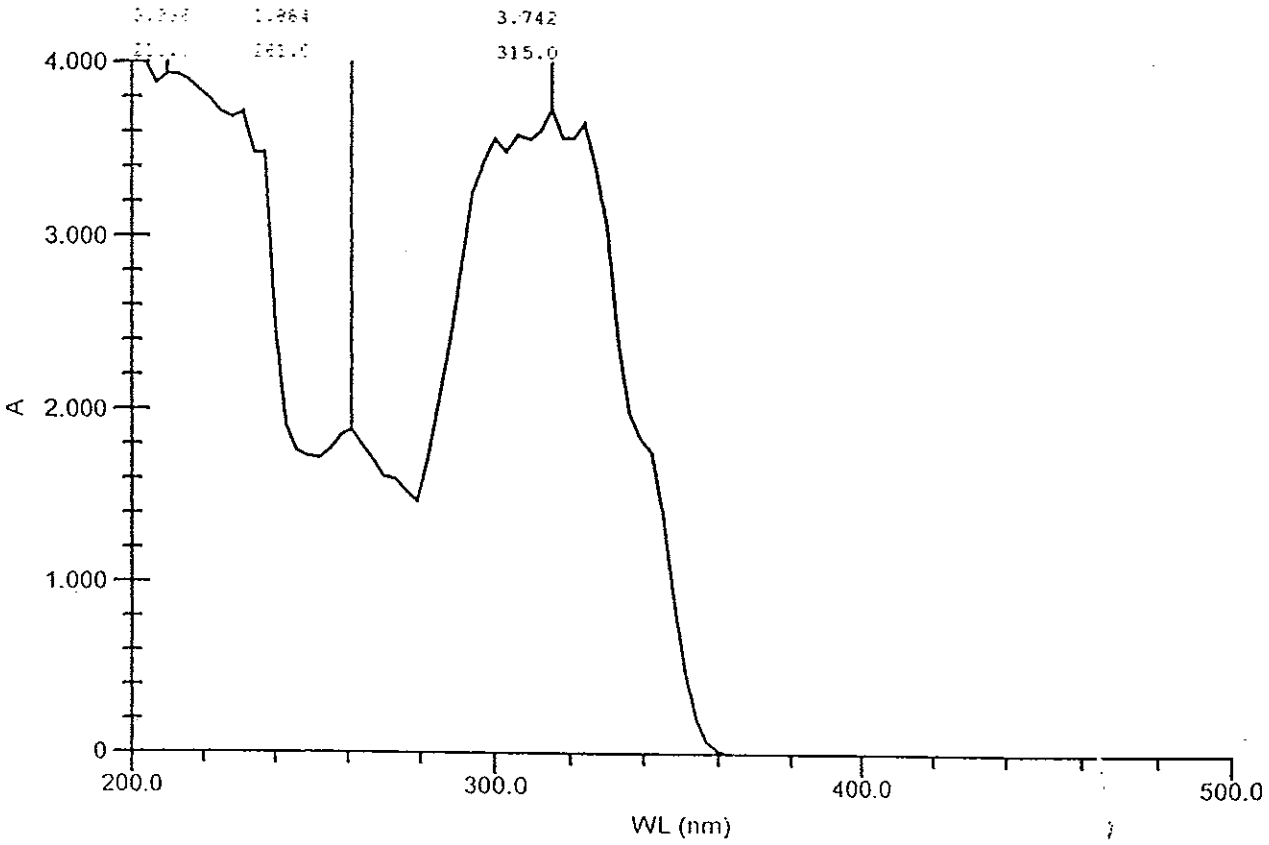
45. Cheeseman, G.W.; Cookson, R.F., Chemistry of Heterocyclic Compounds, Weissbergen, Taylor series, **1979**, 35.

46. Freedlander, B.C.; Frust, A., *Chem. Abstr.*, **1953**, 47, 2877.

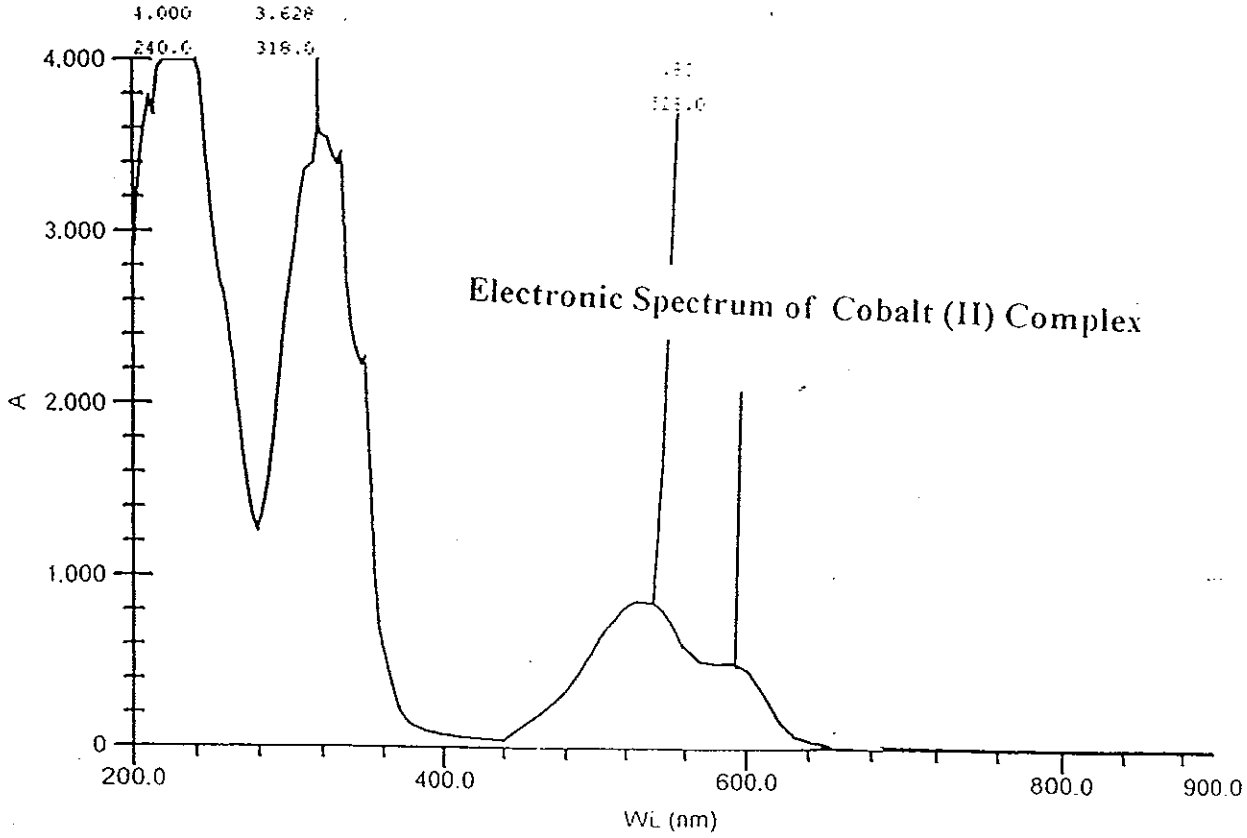
APPENDIX

22 May 2000 4:42

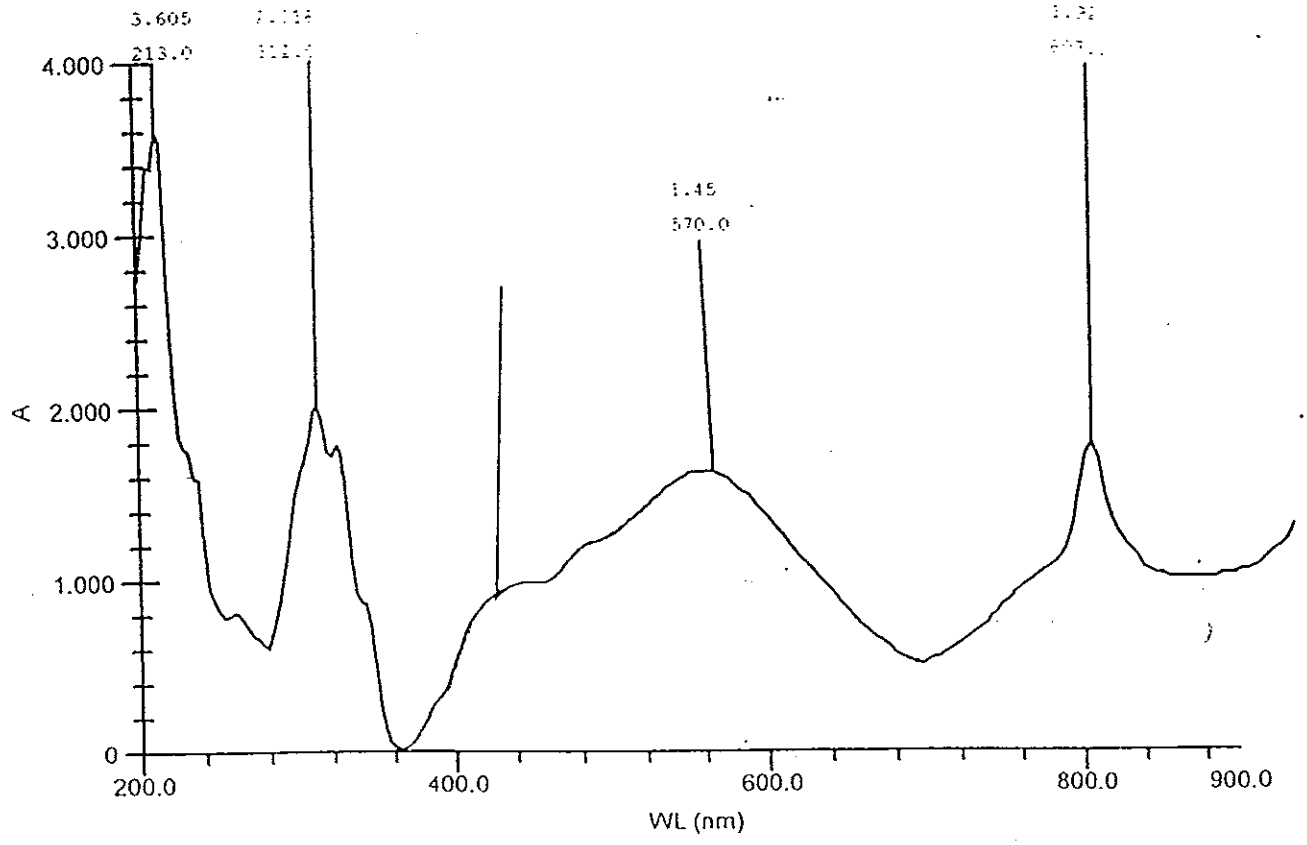
Application:	SCANNING
Data Name:	BQxDP
Start Wavelength:	201.0
Stop Wavelength:	399.0



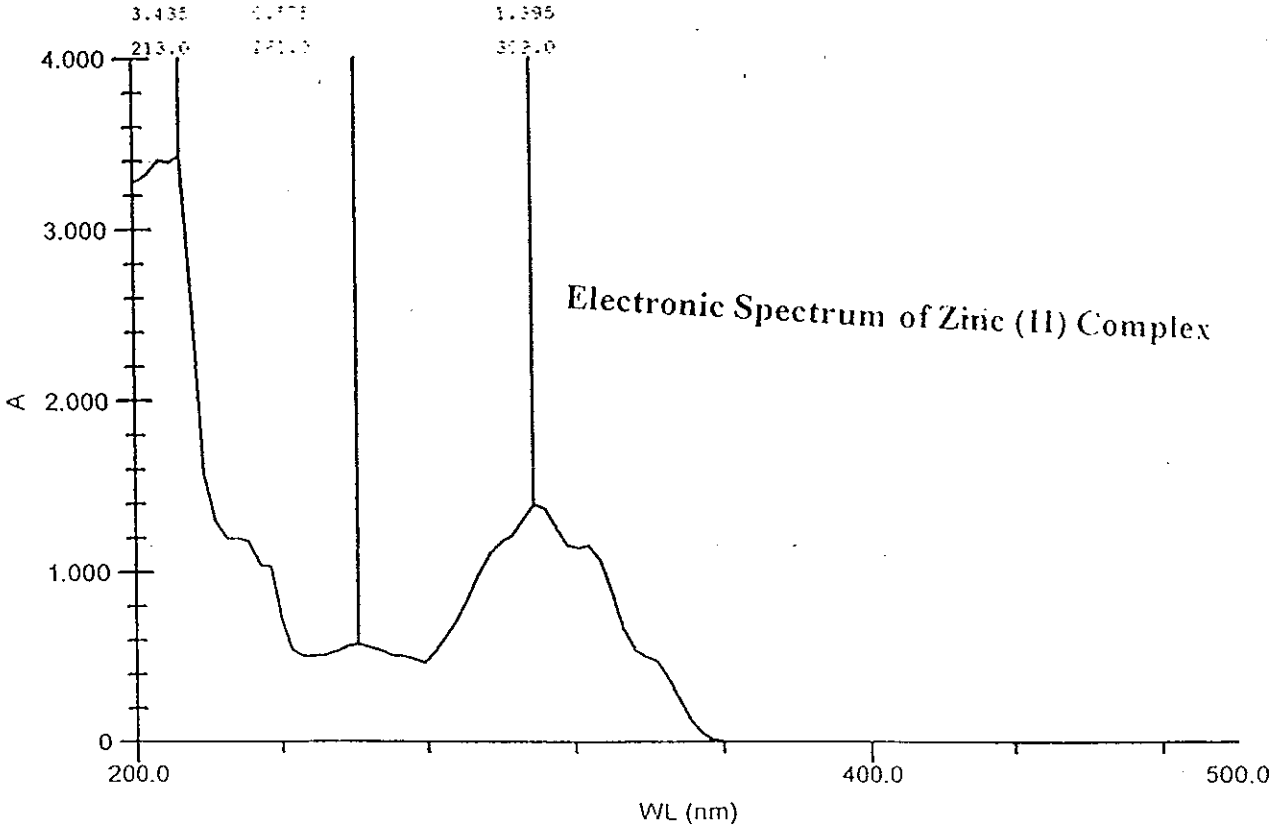
Electronic Spectrum of the Ligand (BQxDP)



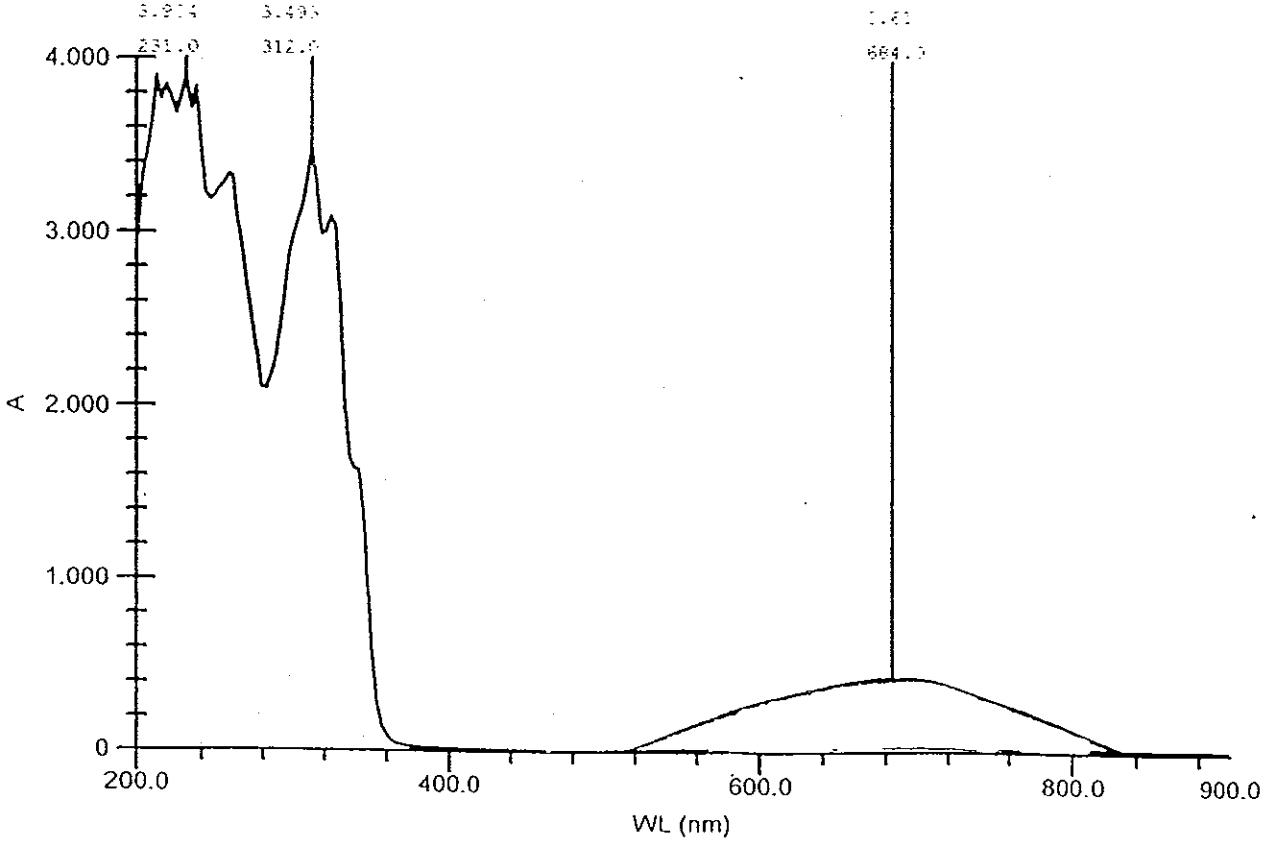
Electronic Spectrum of Cobalt (II) Complex



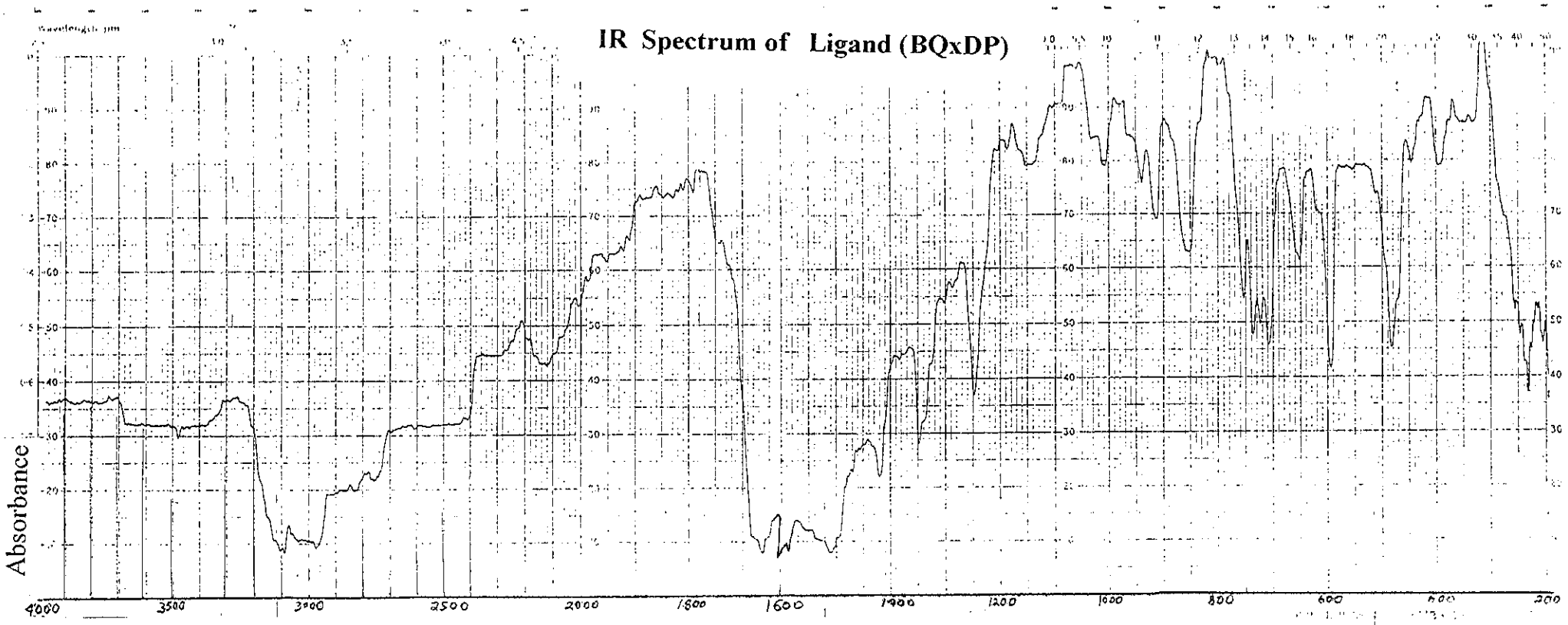
Electronic Spectrum of Nickel (II) Complex

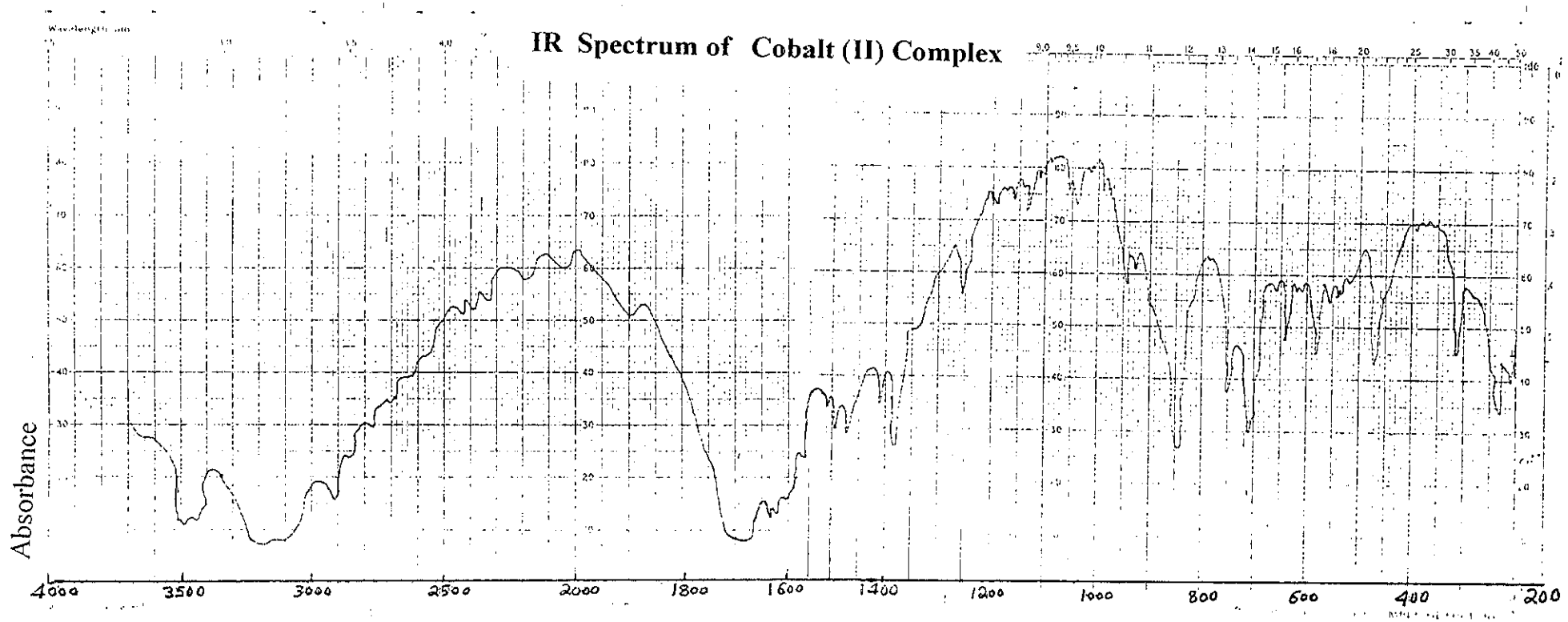


Electronic Spectrum of Zinc (II) Complex



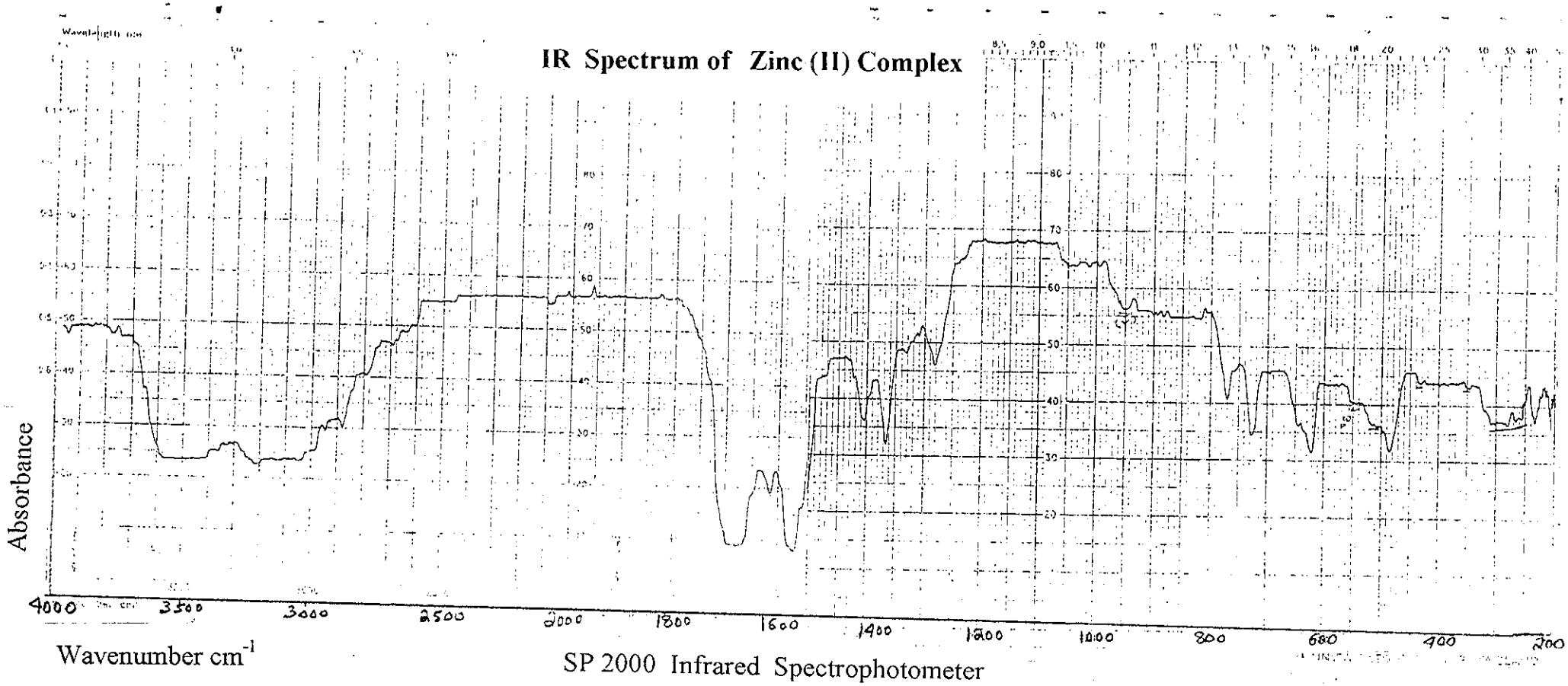
Electronic Spectrum of Copper (II) Complex


IR Spectrum of Ligand (BQxDP)
Absorbance
4000
3500
3000
2500
2000
1800
1600
1400
1200
1000
800
600
400
200
Wavenumber cm-1
SP 2000 Infrared Spectrophotometer



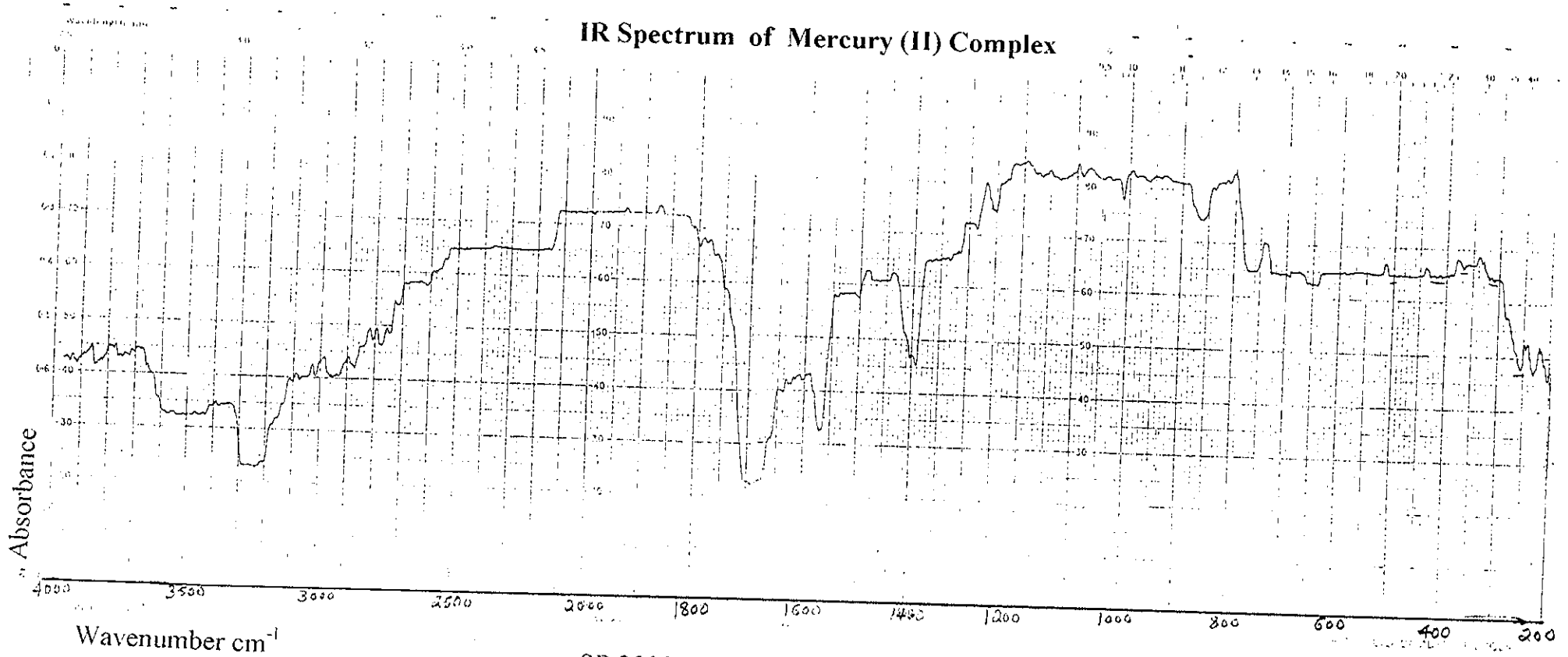
SP 2000 Infrared Spectrophotometer

IR Spectrum of Zinc (II) Complex



SP 2000 Infrared Spectrophotometer

IR Spectrum of Mercury (II) Complex



SP 2000 Infrared Spectrophotometer