CHAPTER I

INTRODUCTION
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The condensation of primary amines with carbonyl compounds was first reported by Schiff and since then the condensation products are referred to as Schiff bases.

The coordination complexes of a wide variety of Schiff-base ligands have been extensively studied and reviewed. Those with ligands containing sp\(^2\)-hybridized nitrogen atoms, particularly when acting as bi- or poly-dentate ligands, give very stable coordination compounds. Of them, diimine ligands containing the 1,4-diaza-1,3-butadiene skeleton (N=CC=N) with two conjugated C=N iminic bonds, have attracted most interest. Closely related to those are the di-Schiff base ligands containing two N sp\(^2\) donor atoms as part of a non-conjugated (=NCCN=) system. Those derived from salicylaldehyde and diamines (N,N'-bis(salicylidene) ethylenediamine) are recognized chelating agents, giving complexes of almost all metal ions, in which complex formation is determined by metal-nitrogen and metal-oxygen bonds.

Mikuriya and coworkers made a detailed study of crystal structure and magnetic properties of alkoxobridged copper(II) complexes with Schiff base ligand (Fig. 1). Recently, Ceder et al. have synthesized the organometallic complexes containing di-Schiff bases acting as neutral bidentate (NiX(R)NN) ligands.
Haikarainen et al.\textsuperscript{11} have synthesized and characterized new bulky salen type ligands (Fig. 2) and their complexes with first row transition metals, Mn, Fe, Co, Ni and Cu.

The metal derivative of these ligands have drawn substantial attention from the researchers for their biological activities.\textsuperscript{12-15} Many Schiff base ligands have also been derived from sulpha drugs\textsuperscript{16-17} and their coordination chemistry studied.\textsuperscript{18-21} The molecules of life such as amino acids have been exploited for the synthesis of Schiff base ligands and their transition metal complexes.\textsuperscript{22-31} Schiff-base metal complexes are
considered to be a new kind of potential anticancer and antivirus reagent.\(^{32-33}\) However, the antitumor activities of these compounds are difficult to measure because of their low solubility in both aqueous and organic media. Moreover, since they are administered as suspensions, the particle size may affect their activities. Recently, Xiao and Zhang\(^{34}\) have successfully synthesized a novel water soluble polymeric Schiff-base nickel(II) complex and studied its interaction with Calf thymus DNA.

Chemistry of isatin (indole-2,3-dione) dates back well to the 19\(^{th}\) century because of its relationship with the pigment indigo. Isatin and some of its relatively simple derivatives are pharmacologically relevant e.g. isatin "inhibits natriuretic peptide-induced hyperthermia in rats"\(^{35}\) and some of its semicarbazones show anticonvulsive activity.\(^{36}\)

Isatins have a major importance in organic chemistry as they can be used for the synthesis of a variety of heterocyclic compounds, such as indoles and quinolines.\(^{37}\) The synthetic versatility of these compounds has led to their extensive use in the pharmaceutical industry since they can be used as raw materials for drug synthesis.

In nature, isatin and substituted isatins are found in plants,\(^{38}\) for instance the melosatin alkaloids (methoxy phenylpentyl isatins),\(^{39}\) and also in humans as they are metabolic derivatives of adrenalin.\(^{40}\)

Several Schiff bases and hydrazones of substituted isatins were prepared by reacting isatin and aromatic primary amines/hydrazines.\(^{41-42}\)
Recently, a new series of the corresponding Schiff base was synthesized by reacting isatin with formaldehyde and diphenyl amine.\textsuperscript{43}

We also have synthesized Schiff bases from the condensation of isatin with (a) ethylenediamine (L\textsuperscript{5}) and diethylenetriamine (L\textsuperscript{6}). The complexation of divalent and trivalent metal ions have further been investigated.

Macrocyclic chemistry is now a well established interdisciplinary field bridging organic and inorganic coordination chemistry. The multidentate macrocycles give rise to unique, rather cryptic geometries\textsuperscript{44-45} on complexation with metal ion.

The recognition of a metal ion by a macrocyclic ligand and modification of the properties of the resulting complex is controlled to a large extent by a match between the size of the metal ion and the cavity provided by the macrocycle. The chemistry of macrocyclic compounds is, therefore, considered as an important field of research due to the encapsulation capability of a metal ion within a ligating framework.

The macrocyclic ligand (Fig. 3) has been prepared by metal-templated, Schiff-base condensation of 2,6-dicarbonylated pyridine and 1,2-diaminocyclohexane.\textsuperscript{46} Their efficiency as catalysts for double-stranded DNA hydrolysis and NMR imaging have also been reported by Bligh and coworkers.\textsuperscript{47} Recently Tsubomura et al.\textsuperscript{48} have reported the crystal structure of metal complexes of that ligand. The framework of the
The macrocycle is so flexible that the complexes can adopt a variety of conformations. Most complexes of such ligands adopt a folded butterfly conformation. Ayala et al.\textsuperscript{49} and some other workers\textsuperscript{50-52} have pointed out that there is a correlation between the size of the metal ion encapsulated and the cavity formed by the macrocycle. Generally, the complexes containing large metal ions have a tendency to show planar conformation. On the other hand, the ones containing small metal ions show folded conformation.\textsuperscript{48}

![Diagram of macrocyclic ligand]

**Fig. 3**

Macrocyclic ligands can be synthesized either by metathesis or via template synthetic routes. The latter is preferred because of the conformational requirements of the reacting species. Hori et al.\textsuperscript{53} have prepared the macrocyclic ligand by template method in the following way (a) the preparation of an acyclic proligand possessing N(amine)$_2$O$_2$ and O(formyl)$_2$O$_2$ metal-binding sites and (b) the 1:1 condensation of the
proligand with a diamine by a template reaction Fig. 4. Template method
gives high yielding and selective routes to new ligand and their complexes.

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\begin{align*}
&\text{Fig. 4} \\
&\text{The coordination chemistry of transition metals in (+II) oxidation} \\
&\text{state (M = Cu(II), Ni(II) or Pt(II)) with macrocyclic tetraamine N}_4 \text{ has} \\
&\text{extensively been studied.}^{54-56} \text{ Especially, the 14-membered tetraamine} \\
&\text{macrocycles incorporate metal ions into their N}_4 \text{ cavities to form kinetically} \\
&\text{and thermodynamically stable complexes.}^{57} \text{ For example, the 1,4,8,11-} \\
&\text{tetraazacyclotetradecane-5,7-dione ligand (dioxocyclam) possess two} \\
&\text{amide and two secondary amine groups.}^{58} \text{(Fig. 5)} \\
&\text{In the present work, the synthesis and characterization of two} \\
&\text{tetraaza 12 and 13 membered Schiff base macrocycle derived from the} \\
&\text{reaction of triethylenetetraamine with benzil (L}^7 \text{) and acetylacetone (L}^8 \text{)}
\end{align*}
\]
has been described. Their complexes with transition metal have been synthesized and characterized by various physicochemical methods.

![Image of a molecular structure](image)

**Fig. 5**

The coordination properties of macrocycles bearing pendant groups have attracted great deal of attention.\(^59\text{-}62\) The crystal and molecular structure of [3-(4-pyridiniumcarbonyl)1,3,5,8,12-pentaazacyclotetradecane] nickel(II) was described\(^63\) in which pyridine acts as a pendant group. Metallocyclam subunit has been appended to pyridine through metal template procedure which involves the condensation of amides of 3 and 4-pyridine carboxylic acid with formaldehyde and nickel(II) complex with the open chain tetraamine. These metallocyclam units act as building blocks of supramolecular system.

Recently, a new pyridine armed aza crown ether was prepared with the reductive amination of monoaza-15 crown-5 with sodium borohydrideacetate in 1,2-dichloroethane.\(^64\) (Fig. 6)

Indeed macrocyclic systems incorporating appended 2-pyridyl methyl arms have been documented to exhibit a wide variety of interesting
and often novel metal coordination behaviour.\textsuperscript{65}

Recently Gou and coworkers\textsuperscript{66} prepared four novel tetranuclear copper(II) complexes of 2:2 macrocyclic Schiff bases with functional

\begin{align*}
&H_2L^1 : X = CH_3, \text{Ar} = \text{Furanyl}, & H_2L^2 : X = Cl, \text{Ar} = \text{Furanyl} \\
&H_2L^3 : X = Cl, \text{Ar} = \text{Phenyl} & H_2L^4 : X = CH_3, \text{Ar} = \text{Phenyl}
\end{align*}
pendant arms \( (\text{H}_2\text{L}^{1-4}) \), by the condensation of sodium 2,6-diformyl-4-X-phenolate \( (X = \text{Cl, CH}_3) \) with the reduced 1:1 Schiff base of diformyl-4-X-phenolate \( (X = \text{Cl, CH}_3) \) with the reduced 1:1 Schiff base of 2,2',2"-tris(amo-noethyl)amine (tren) and 2-formyl furan (or benzaldehyde) followed by in situ transmetallation with copper(II) perchlorate (Fig. 7).

Lindoy and Dong\(^{57}\) have also synthesized a series of tetraaza \( N \)-benzoylated cyclam derivative by treating benzyl bromide and cesium carbonate to a stirred solution of 1,4,8-tris(tert-butoxy-carbonyl)-1,4,8,11-tetraazacyclotetradecane in dry acetonitrile. Deprotonation by using 3M HCl-MeOH results in the formation of cyclam derivative (Fig. 8).

![Diagram of cyclam derivatives](image_url)  
Fig. 8
In this thesis some new 13, 14 and 17 membered Schiff base macrocycles (L₁, L₂, L₃ and L⁴) containing pendant groups and their transition metal complexes have been synthesized with a view to studying the nature of the complexes. The possibility of the binding of the pendant group has also been explored. For this purpose, the 4-aminoantipyrine was allowed to react with (a) ethylenediamine and (b) propanediamine to form Schiff base which was further allowed to react with benzoylacetic acid resulting in the formation of N₄ macrocycles (L³) and (L⁴) respectively. In the same way, the macrocycles (L¹) and (L²) have been obtained from a Schiff base derived from the condensation of 4-aminoantipyrine with acetylacetone and its subsequent reaction with (a) 1,6-diaminohexane and (b) 1,3-diaminopropane.

Chemistry of heterobimetallic complexes has assumed importance, owing to their diverse application in homogeneous catalytic processes, in enzyme model systems for metalloproteins, viz. superoxide dismutase, oxidases, peptidases and magnetic exchange between the paramagnetic centers. Bioinorganic chemists have made considerable efforts to study the active sites involving more than one metal center due to their diversity in biology e.g. dicopper sites in hemocyanin and tyrosinase, diiron(III) sites in ribonucleotide reductase and heterobimetallic sites of iron(III) and copper(II) in respiratory cytochrome oxidase, which catalyses
the four electron reduction of dioxygen to water in the mitochondria of eukaryotic cells.

Heterobinuclear complexes containing cyclopentadienyl rings have attracted increasing interest in the chemistry of metal complexes.\textsuperscript{74}

![Fig. 9.](image)

In this thesis, the synthesis and characterization of heterotrinuclear complexes of type \([\text{Cu}(\text{ppn})_2\text{Cl}_2\{\text{Ti}(\text{Cp})_2\}_2]\) and \([\text{Cu}(\text{en})_2(\text{NO}_3)_2\{\text{Ti}(\text{Cp})_2\}_2]\) are reported, where ppn-H\textsubscript{2} = 1,3-diaminopropane, en-H\textsubscript{2} = 1,2-diaminoethane and Cp = cyclopentadienyl.

Dithiocarbamate is another class of versatile chelating ligands and forms stable complexes which display interesting and often quite novel properties. Much attention has been devoted to the study of dialkyldithiocarbamates\textsuperscript{75-77} and their respective complexes with a wide variety of cations. They are also used as fungicides, pesticides, vulcanization accelerators, floatation agents and high pressure lubricants.\textsuperscript{78} Dithiocarbamates were chosen for two reasons: first, they provide varying degree of charge to the overall complex. Second, they can
be easily prepared from the readily available secondary amines or amino acid derivatives.

Dithiocarbamate ligands have generally been found to coordinate to a transition metal ion as a bidentate\textsuperscript{79-80} or a monodentate ligand\textsuperscript{80-81} (A and B).

![Diagram](image)

(A) \hspace{1cm} (B)

The dithiocarbamate ions have been used widely in analyses of many elements, because the ions form chelate complexes, which exhibit high extractabilities into organic solvents, with many kinds of metal ions.\textsuperscript{82} Recently, some bioactivities of the dithiocarbamate ions such as inhibition of growth of cancer cells has made dithiocarbamate important in the field of biology and medicine. Since these bioactivities significantly alter with coexistence of heavy metal ion, a relationship between the metal dithiocarbamate and the bioactivities has become significant.

Mixed ligand complexes of the type \([\text{M(dtc)}_2(\text{bpy})]\) and \([\text{M(dtc)}_2(\text{phen})]\) (where \(\text{M} = \text{Mn}(\text{II}), \text{Co}(\text{II}), \text{Ni}(\text{II}), \text{Cu}(\text{II})\) and \(\text{Zn}(\text{II})\), dtc = diethyldithiocarbamate, bpy = 2,2'-bipyridine and phen = 1,10-phenanthroline) were synthesized by the replacement of two Cl\(^-\) ion in \([\text{M(bpy)}\text{Cl}_2]\) and \([\text{M(phen)}\text{Cl}_2]\) by \(\text{N,}\text{N}'\)-diethyldithiocarbamate. Effort has
been made to explore whether diethyldithiocarbamate bonded to a metal ion is in bidentate or monodentate fashion. The complexes are further characterized by elemental analyses, IR, electronic, EPR and $^1$H NMR spectra, magnetic moments and conductivity measurements.
REFERENCES


