Chapter I

GENERAL INTRODUCTION

Coordination chemistry is one of the most active research fields in inorganic chemistry, encompassing a great variety of subjects and phenomena. The spasmodic development that happened in the field of theoretical chemistry has led to the formulation of new theories that suffice to explain almost all the properties of coordination compounds. In addition to that, sophisticated and powerful instrumental facilities to solve many of the puzzling structural problems and study unusual phenomena shown by coordination compounds are available. Consequently coordination chemistry has grown from a readily defined and limited area to the most promising research area in inorganic chemistry. Recently, many properties of coordination compounds have evoked the interest of researchers in other fields of science and now it has become an area of interdisciplinary research. Metal chemotherapy and chelation therapy have now drawn attention as additional outlets for coordination chemistry. Realisation of the involvement of metal ions and the role of metal complexes in biological systems also helped immensely to sustain a live interest in this
field. The end of the last century has witnessed a tremendous upsurge of interest in the study of lanthanide complexes with a variety of multidentate ligands. Schiff bases figured conspicuously among the ligands used in these investigations.

The condensation product of primary amine with carbonyl compounds was first reported by Schiff and the products are often referred to as Schiff bases,\(^1\) which are characterized by the presence of azomethine group, \(>\text{C}=\text{N}−\). Various studies have shown that the presence of a lone pair of electrons on trigonally hybridized nitrogen atom of \(>\text{C}=\text{N}−\) group is of fundamental chemical and biological importance.\(^2\) For the relative ease in the synthesis and also for the synthetic flexibility, Schiff base with widely varying substituents can be obtained by proper choice of reactants. By changing the nature and position of the donor atoms and groups, it is possible to control the size of chelate ring formed and to exploit the effect of substitution. Due to all these factors Schiff bases find applications in many fields of fundamental and applied research. Aromatic Schiff bases or their corresponding metal complexes exert profound catalytic influence on several reactions, \(\text{viz.}\) polymerization, oxidation and decomposition. Several examples which illustrate the usefulness of azomethines in preventing deterioration induced by heat, light, air and oxygen have
been well documented in literature. Antimicrobial activity has been reported for several aromatic azomethine compounds and several aromatic Schiff bases have been shown to possess antifungal activity. Schiff bases are also reported to exhibit antitumour3,4 and cytotoxic5 activities. Thus Schiff base complexes, with a variety of bonding interactions, high degree of catalytic influence and significant biological applications occupied an outstanding role in the development of coordination chemistry. The exponential growth of this rewarding field of research resulted in enormous volumes of publications,6-9 describing various aspects of this important class of metal complexes. However, a potential group of Schiff base complexes which has received comparatively less attention is those derived from heterocyclic systems, particularly those containing thiophene ring system. In spite of their biological significance and potential applications, coordination chemistry of these heterocyclic Schiff bases containing thiophene ring system has not received the special attention it rightly deserves.10,11 Hence it is quite worthwhile to carry out a detailed investigation on metal chelates, especially those of lanthanides, of some polydentate Schiff bases derived from compounds containing thiophene ring system.
Choice of ligand

Azomethine group alone is not sufficient to form metal complexes with substantial stability. If the carbonyl compound and/or the amine containing coordinating functional group is present near the site of condensation, such ligands can sufficiently enhance the stability of the resulting metal complexes. This may lead to chelate effect which enhances the stability of a metal complex. This can be largely attributed to favourable entropy changes that accompany the chelate formation. When donor functions of the polydentate Schiff bases are so situated as to form five and six-membered or two six-membered metal chelate rings, the resulting complex is stable. Stability is further enhanced by chelate ring resonance when the ring structure permits it. It has been observed that of two related multidentate chelating agents, the one forming the greater number of annulated chelate rings with a given metal ion yields the more stable complex. Polyydentate ligands can also confer increased kinetic stability to their metal chelates, since in the bonded state, the ligand virtually envelopes the metal ion and hence blocks access to the attacking species.
The aim of the present investigation has been to work on some heterocyclic Schiff bases derived from thiophene ring system. Thiophene stands as uniquely aromatic among the five membered heterocyclics. The structure of thiophene has been determined by microwave spectroscopy and electron diffraction, but the microwave results are more precise (Fig 1.1). The C(2)-C(3) and C(4)-C(5) distances 1.370 Å are clearly shorter than C(3)-C(4) bond (1.424 Å); however, all three C-C bond lengths differ from normal C(sp²)-C(sp²) double (1.340 Å) and C(sp²)-C(sp²) single (1.480 Å) bond distances. The C-S bonds 1.714 Å are somewhat shorter than normal C(sp²)-S single bond lengths (1.760 Å) but are not nearly as short as C(sp²)-S double bonds (1.610 Å). Thus, the thiophene structure indicates some delocalization of the π-electrons to indicate that the aromatic character of thiophene is not much less than that of benzene. Aromaticity indisputably influences the reactions undergone by thiophene and its spectroscopic properties. Among the five membered ring aromatics, the relative trend in resonance is in the order furan < pyrrole < thiophene and the sulphur atom, the unique component of thiophene, has much to do with this behaviour. Thiophene ring is electron rich and enhancement of the electron enrichment consequently causes an increase in reactivity towards any sort of
electrophile or reagent capable of removing an electron. A survey of literature reveals that thiophene coordination in transition metal complex is an area of recent origin.\textsuperscript{12}

Since our attention has been on Schiff bases containing thiophene nucleus, the search for ligand has been focussed in that direction. A perusal of literature reveals that metal chelates of polydentate Schiff bases containing heterocyclic system have been receiving increased interest.\textsuperscript{10,11} Only limited advance in this field has been made by using Schiff bases derived from thiophene-2-aldehyde and related ligands.\textsuperscript{16-19} It was observed that metal chelates of Schiff bases derived from 2- or 3-aminothiophene are scanty. The poor stability of these aminothiophenes could have frustrated the earnest efforts of ardent researchers to prepare such Schiff bases and their metal complexes. In this investigation the instability of 2-aminothiophene\textsuperscript{20} has been solved by introducing a carboxyethyl group at position-3 and by fusion of thiophene ring system with a cyclohexane ring by Gewald synthesis.\textsuperscript{21} In addition to providing sufficient stability for the amine, the carboxyethyl group (\(-\text{COOC}_2\text{H}_5\)) has provided further scope for reactivity and new coordination site. In this investigation the ligational behaviour of the condensation products of 2-amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[\(\text{b}\)] thiophene and carbonyl
compounds such as isatin, o-hydroxyacetophenone and benzoin has been examined. The ligands investigated are:

a) 2-(N-indole-2-one)amino-3-carboxyethyl-4, 5, 6, 7-tetrahydrobenzo[b]thiophene (ISAT).

b) 2-(N-o-hydroxyacetophenone)amino-3-carboxyethyl-4, 5, 6, 7-tetrahydrobenzo[b]thiophene (HAAT).

c) 2-(N-benzoin)amino-3-carboxyethyl-4, 5, 6, 7-tetrahydrobenzo[b]thiophene (HBAT).

Choice of metal ions

The rapidly developing field of bioinorganic chemistry is the centre of attraction of coordination chemists. One of the rapidly growing areas in this field is the coordination chemistry of lanthanides and actinides. Recent interesting applications of lanthanide(III) complexes as contrast agents for MRI, luminescent strains for fluoro immuno assays and as catalyst for selective cleavage of DNA and RNA are receiving attention. The europium(III) complexes possess a set of properties such as water solubility, inertness to metal release, ligand-sensitized luminescence and reactive peripheral functionalities that make them suitable for luminescent markers for bio-substrates. Site-selective hydrolysis of DNA has been
one of the most attractive and challenging themes for chemists and biochemists. Site-selective DNA hydrolysis was achieved by conjugating cerium(IV) ion with oligonucleotides. The earliest use of lanthanide ions in imaging arose from the need to provide high sensitivity probes for use in bioassay. As lanthanide ions have much longer luminescence lifetimes than conventional fluorescent probes, signals arising from them can be separated from background biological fluorescence using time-gating techniques. The need to image such systems, rather than simply obtain their spectra, became more pronounced with the development of high throughput screening techniques and the use of multi-well plates. Lanthanide based assays have become increasingly commonplace and their use as probes for biochemical systems is gathering more interest especially the application of more than one lanthanide in the assay to provide more detailed information on the analytes present in solution.

Among the prodigious number and variety of transition, innertransition and main group metal complexes of Schiff bases, those formed from trivalent lanthanides are of particular interest because of their structural diversities, biological significance and other multiple applications. A deep survey of literature reveals that transition metal
complexes of polydentate Schiff bases derived from thiophene-2-aldehyde and its derivatives with primary amines have been reported, but those derived from lanthanides are comparatively few. In view of the pronounced applications of lanthanide complexes and the relatively undeveloped coordination chemistry of lanthanides, lanthanum(III), cerium(III), praseodymium(III), neodymium(III), samarium(III), europium(III), gadolinium(III), dysprosium(III), ytterbium(III), and lutetium(III) are selected as metal ions for complexing with polydentate 2-aminothiophene Schiff base in this investigation.

**Coordination chemistry of lanthanides**

The lanthanides are given a unique position in the periodic table due to their various chemical and physical characteristics. The most important of these characteristics are summarized below:

1. In lanthanides the 4f electrons are expected to control their properties. Since these electrons are 'innerseated' and are effectively shielded from the influence of external field by the $5s^25p^6$ octet, the 4f electrons do not have much effect on the properties of lanthanides. This feature distinguishes the lanthanides from the transition metals, in which the 'd' electrons play a vital role in
determining their properties. As a matter of fact, the 4f electrons play only a secondary role in the properties of lanthanides, except their spectral and magnetic properties.

2. The sum of the first three ionization potentials of the lanthanides is comparatively low so that these elements are highly electropositive. They readily form +3 ions in solids, like their oxides, in aqueous ions $[\text{Ln(H}_2\text{O)}_n]^3^+$ and in complexes. These trivalent ions in solution are protected by water molecules, which make the properties of these ions more alike. In addition to the +3 oxidation state, certain lanthanides show +2 oxidation state ($\text{Sm}^{2+}$, $\text{Eu}^{2+}$ and $\text{Yb}^{2+}$) and certain others show +4 oxidation state ($\text{Ce}^{4+}$, $\text{Pr}^{4+}$, $\text{Nd}^{4+}$ and $\text{Tb}^{4+}$) also. However, these oxidation states are always less stable than +3 state. The prime +3 oxidation state, which is common to all the lanthanides, makes the chemistry of lanthanides essentially similar.

3 The steady and significant decrease in sizes of atoms and ions from lanthanum to lutetium — the lanthanide contraction — is a special feature of the lanthanides. As we proceed from lanthanum to lutetium, the nuclear charge and the number of 4f electrons increase by one at each step. Due to the blurred shape of 4f orbital, the shielding of a 4f electron by another is very imperfect, and the
effective nuclear charge experienced by each 4f electron increases, thus causing a reduction in size of the entire 4f shell. The close similarity among the lanthanides, the similarity of chemical properties and the steady decrease in basicity of the lanthanide ions from La$^{3+}$ to Lu$^{3+}$ are some of the direct consequences of lanthanide contraction.

4. The 4f electrons are responsible for the magnetic and spectral properties of the lanthanide ions, but they are shielded from the influence of external fields by the overlying 5s$^2$5p$^6$ octet. This makes a difference in the magnetic and spectral properties of lanthanides from those of transition metals. In the case of lanthanides, the states arising from the various 4f$^n$ configurations are only slightly affected by the surroundings of the ions and hence, these states tend to remain nearly invariant for a given ion in all of its compounds. In addition, the spin orbit coupling constants are quite large (in the order of 1000 cm$^{-1}$). The net result of these properties is that with only a few exceptions (Sm$^{3+}$ and Eu$^{3+}$) the lanthanide ions have ground states with a single well defined value of the total angular momentum $J$, with the next lowest $J$ states at energies many times greater than $kT$ and hence, these higher states are virtually
unpopulated. Therefore, sharp lines are observed in their spectra, and the theoretical magnetic moments are in agreement with the experimental values with the exceptions of Sm$^{3+}$ and Eu$^{3+}$, where the first excited J state is sufficiently close to the ground state and hence, the excited state is populated at ordinary temperatures.

Lanthanides do not form complexes so easily, unlike the transition metals. The important factors that limit the number of lanthanide complexes and mitigate against their formation are the following:

1. The transition metal ions can form stable complexes because of the participation of the outer d orbitals in bonding with the ligands. In the case of lanthanide(III) ions the 4f orbitals are buried deep with a small spatial extension and so they are not easily available for bond formation. Therefore, the approaching ligands encounter only with the completely filled 5s$^2$5p$^6$ octet, and have to look for high energy vacant orbitals for bonding. This results the possibility of complex formation with the lanthanides, and the bonds formed will be usually weak.

2. The lanthanide ions in any oxidation state are large compared to transition metal ions. This minimizes the electrostatic attraction
between the metal ion and the ligand causing reduction in metal-ligand interaction. Hence, again weak bonds are formed between the lanthanide ions and the ligands.

3. During complex formation in aqueous solution, the ligands encounter with stiff competition from water molecules for coordination with the lanthanide ions. Therefore, if the complex formation has to occur, the ligands must be capable of overweighing the competition from water molecules. Hence, only very strong ligands will give stable insoluble complexes in aqueous solution. In alkaline solution, there is additional competition from hydroxide ions which have even better coordinating ability than water molecules. Therefore, even highly basic ligands form sufficient concentration of OH ion by interaction with water to precipitate the lanthanide ions as their hydroxide rather than their complexes. In view of these restrictions the lanthanide complexes are generally isolated from neutral non-aqueous media.

4. In solution, ligand exchange reactions involving the lanthanide species are extremely rapid. This again limits the number of insoluble complexes, and also the possibilities of isomerism. Moreover, a composition found for a solid complex may not often
persist in solutions, and a given complex may not be recovered once it has been dissolved.

5. The lanthanides are classified as 'class a' according to Ahrland et al.\textsuperscript{55}, and as 'hard acids' according to Pearson.\textsuperscript{56} On the basis of both these concepts, the interaction of lanthanide(III) ions with different donor atoms may be in the following order $O > N > S$. A majority of the lanthanide complexes isolated so far are those with oxygen donor ligands. These ligands may be either pure oxygen donors or mixed 'O–N' donors. Complexes with pure nitrogen donors are limited and those with sulphur donor ligands are rare.

6. Complex formation is generally indicated by a distinct colour change for most of the transition metal ions. But in the case of lanthanide(III) ions, complex formation is not always accompanied by a colour change. So in many cases, whether complex formation has occurred or not is not immediately known.

In view of these difficulties, coordination chemistry of lanthanides is rather complicated, particularly in aqueous solution. The important factors that govern the complex formation are:

a) the mol ratio of the ligand to metal ion

b) nature and concentration of the starting materials
c) nature of the solvent used
d) decomposition or hydrolysis of ligands or of the products formed
e) pH of the medium
f) temperature at which the reaction is performed
g) presence of more than one competitive reaction and the resulting equilibria.

Structure and bonding

In contrast to transition metal complexes, where the coordination number for a particular combination of metal ion and oxidation state is often constrained to a particular value, the coordination number in lanthanide complexes appears to be substantially determined by crowding in the coordination sphere, the strength of the positively charged metal ion and the electron-rich ligand. At all events, high coordination numbers are predicted for the lanthanides simply upon the basis of the large size of the lanthanide ion. The coordination numbers exhibited by the lanthanide ions in complexes usually vary from 6 - 12, the most common being 7, 8 and 9. Recently coordination number less than 6 is also reported for lanthanides. Polydentate ligands with short bites often yield complexes
with higher coordination numbers. A large number of molecular geometries are exhibited by the lanthanide complexes because of the variations of coordination numbers.\textsuperscript{188}

The three coordinate complex \([\text{Fe}(\text{N(SiMe}_3\text{)}_2)_3]\) was obtained in 1969 through the use of a bulky silylamide ligand. Extension of this work led to the synthesis of \([\text{Lu}(\text{N(SiMe}_3\text{)}_2)_3]\) (\(\text{Ln} = \text{La} - \text{Lu}\) except \(\text{Pm}\)),\textsuperscript{57-58} shown by diffraction methods to be the first three coordinate lanthanide compounds.\textsuperscript{59-61} Unlike transition metal analogues that have strictly planar \(\text{MN}_3\) cores, the \(\text{MN}_3\) moiety is pyramidal in the lanthanide compound. These compounds were subsequently shown to form four-coordinate\textsuperscript{62} \(\text{Ph}_3\text{PO}\) adducts such as \([\text{La}(\text{N(SiMe}_3\text{)}_2)_3(\text{Ph}_3\text{PO})]\) and indeed five coordinate\textsuperscript{63} bis(nitrile) adducts. More recently four-coordinate and three-coordinate alkyls have been synthesized.\textsuperscript{64-65}

For a six coordinate with six unidentate ligands, octahedral geometry is the ideal polyhedron and distorted octahedral geometries are obtained when the six ligands are not identical. For seven coordination, three geometries are possible - pentagonal bipyramid, monocapped octahedron and monocapped trigonal prism. The relative repulsivities increase in the above order, although the energy differences between them are very small, and the preference for a particular geometry may be decided by packing
forces. The preferred polyhedra for eight coordination expected from the relative repulsivities are square antiprism, triangular dodecahedron, 4,4-bicapped trigonal prism, distorted cube and cube. However, the most commonly observed polyhedra for eight coordination are square antiprism and triangular dodecahedron. The ideal polyhedra for nine coordination are symmetrical tricapped prism and monocapped square antiprism, the former being more common. For ten coordination, the possible polyhedra are bicapped dodecahedron and bicapped square antiprism, the latter being more stable on the basis of interligand repulsivities. The idealized polyhedron for 12 coordination is icosahedron.

However, it is noted that these assignments of ideal polyhedra are only approximations, since the deviations compromise to obtain maximum shielding for the metal ions and minimum interligand repulsion, and hence, do not always lead to ideal geometry.

Bonding in lanthanide complexes is predominantly electrostatic due to the large size of the lanthanide ions and their electronic configuration. However, some evidence for, at least minor, covalent interaction between the lanthanide ions and the ligand, does exist. A naphelauxetic series of ligands has been derived for praseodymium(III) and neodymium(III), which is comparable with that for the transition metal ions. Further
evidence for covalent interaction is provided by the study of NMR spectra of the lanthanide complexes. In the case of diamagnetic lanthanide complexes, the NMR spectra show low field shifts of protons indicating deshielding of the protons due to draining of electron density from the ligand to the metal ion. The shifts of IR spectral bands of donor groups such as C=O, S=O, C=N and the like to lower frequencies in the complexes also suggest definite, but small, covalent interaction between the lanthanide ions and the ligands.

Colours of most of the lanthanide complexes resemble those of the free metal ions. Since the 4f electrons are responsible for the colours, it is evident that these electrons are not disturbed much during the complex formation, and hence, possibility of the participation of 4f orbital in bonding is limited. Perturbation in electronic spectra upon complexation is accounted for in terms of alteration in crystal field symmetry and it does not imply any covalent interaction. Therefore any covalent contribution to bonding must be due to the involvement of 5d or higher orbitals that are normally unoccupied in the lanthanide ions. Magnetic data of the complexes which are also dependent upon the 4f electrons, give no definite indication that these orbitals are involved in bonding. From the above observation it can be argued that the 4f orbitals are spatially less
favourable, and hence, their involvement in bonding, if any, must be weak. Therefore any covalent contribution to bonding must be due to the involvement of 5d or higher orbitals that are normally unoccupied in the lanthanide ions. Although these higher orbitals are energetically less favourable, they are spatially more favourable for bonding than the 4f orbitals.

Present investigation and its significance

The present investigation is concerned with the synthesis, characterization, thermal decomposition kinetics and antimicrobial studies of some lanthanide complexes with three different types of Schiff bases. The Schiff bases prepared in this investigation served effectively under selected conditions as tridentate neutral ligands. Different series of metal complexes could be obtained in the pure state. The ligands and the metal chelates were characterized through microanalytical, conductance, UV-Visible, IR and NMR spectral data wherever possible or applicable, also by magnetic moment measurements, thermogravimetric, X-ray diffraction and cyclic voltammetric studies. The ester function present in the ligands provided new possibilities for coordination and reactivity. Thus transesterification has been carried out successfully with a selected
complex under specified conditions. Thermal decomposition studies have not kept pace with synthetic progress made in this field. Hence thermal decomposition of some complexes has also been studied and the kinetic parameters have been evaluated using Coats - Redfern equation.

The main purpose of this investigation has been to study the ligands and their metal complexes from a structural point of view. The simplicity arising from the formation of only mononuclear complexes has been a definite advantage.

Apart from the structural diversity and versatile reactivity, in view of the biological activities of the parent compounds, it was hoped that these azomethine derivatives and their metal complexes could have pronounced biological activities. The ligands and their complexes have been screened for antibacterial and antifungal activities.

Schiff bases derived from 2-amino-3-carboxyethyl-4,5,6,7-tetrahydrobenzo[b]thiophene and their metal complexes hold exciting possibilities for the future. There is a recent report on the relationship of electrical conductivity as a function of temperature and molecular structure, in Schiff bases derived from 2-amino-3-cyano-4,5,6,7-tetrahydrobenzo[b]thiophene. Various physico chemical investigations such as electrical conductance, thermal activation energy obtained from
electrical conductivity measurements as well as the energy gap calculated from solid state UV spectral studies are consistent with those of semiconductor materials. Similar studies can be extended to the Schiff bases and their metal complexes used in this investigation.

A major stimulus to the study of thiophene and benzothiophene chemistry was the discovery of their importance in the dye industry. It is hoped that metallised thiophene and benzothiophene Schiff base derivatives will be an excellent topic for researchers of this area.

The bioisosteric relationship of thiophene to benzene is an area of immense significance. Several studies of drug analogues in which benzene rings were replaced by thiophene rings have been reported. On the basis of this work, it is quite usual to prepare thiophene derivatives when investigating new series of potential drugs today. Hence a study of bioisosteric relationship among metal chelates of polydentate Schiff bases containing thiophene ring system is quite relevant and fascinating. Hopefully, the above studies will stimulate a broad enquiry of scientific knowledge and technical innovation.