Chapter-1

INTRODUCTION AND LITERATURE BACKGROUND
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GENERAL INTRODUCTION AND LITERATURE BACKGROUND

1. INTRODUCTION

Our present understanding of coordination compounds is due to ingenious pioneer work of Alfred Werner. Now the chemistry of coordination compounds has become one of the most active branches of inorganic chemistry, which plays a vital role in the chemical industry and as a whole in life itself. The importance of coordination compounds becomes clear when one realises the fact that chlorophyll, which is vital to photosynthesis in plants is a magnesium complex and the prosthetic group of haemoglobin (hemin), which carries oxygen in animal cells is an iron complex.

Since the formulation of Werner's theory of coordination compounds, much advances has been made in the direction of realizing the structure of the coordination compounds and their applications to the various branches of science.

The coordination compounds are characterized depending on the nature of metal ion, the donor atom, the structure of the ligand and the metal-ligand interaction. One of the most important problems of the coordination chemistry has been nature and the metal-ligand bond strength. Considerable work has been done from this point of view to focus various aspects affecting the metal-ligand bond. Usually a metal ion does not form bonds of same strength with two different donor atoms. Similarly particular donor atom cannot form bonds of same strength with different metal ions. Goddard et al have measured the
stability constants of urea, semicarbazide and sulphur and selenium analogues with Zn(II), Cd(II) and Hg(II) metal ions and have compared the relative donor properties of O, S and Se towards a particular metal ion. This affinity order being O << S < Se for Hg and Cd metal ions, while for Zn(II) it is O > S > Se. Likewise Savant et al. have reported the metal-oxygen bond order as Cr(III) > Ni(II) > Zn(II), from the position of M-O stretching mode in far IR region. The study of coordination compounds is therefore, quite interesting. In recent years, much attention has been concentrated on the structural study and reactivity of the complexes.

During the recent past, tremendous upsurge in the study of coordination compounds has been evidenced with ligands having diverse donor atoms in the literature. Many investigators have studied the pharmacological, biological and analytical applications of furan, benzofuran, naphthofuran, derivatives of naphthalene and the compounds containing acyl, oxime, hydrazone, semicarbazone and ester as functional groups. The complexes of the above mentioned compounds have received considerable attention of scientists, except those of naphthofuran derivatives. The brief description of utility of these compounds and their derivatives is described in the section – 2.

2. LITERATURE BACKGROUND

2.1. Furan and its complexes

The chemistry of this heterocycle has developed in spectacular fashion, especially during the last century. It is particularly due to the occurrence of furan nucleus in natural substance and its importance in these compounds.
The opium alkaloids contain furan nucleus in their structure. The efficiency of opium as an analgesic is known from ancient time. Small and coworkers\textsuperscript{12} have extensively investigated the alkaloid morphine present in opium and revealed some interesting correlations between structure and physiological properties of morphine. It was observed that the opening of ether bridge of furan nucleus diminished its analgesic activity considerably. The compounds containing furan moiety fused with benzene nucleus from either sides are found to be present in strepsilin, porphyrilic acid and didymic acid, which are isolated from lichens, have some activity against Avian tubercle and Staphylococcus aureus\textsuperscript{13}.

Furocoumarins is the class of furan derivatives, which exhibit photosensitizing properties. These are important for plant biosynthesis, as they take part in the elaboration of chlorophyll\textsuperscript{14}.

Limaye\textsuperscript{15} has isolated number of furoflavones. Karanjin isolated from seeds of Pongamia glabra is found to be active against leucoderma. Similarly furoisoflavones e.g., coumestrol\textsuperscript{16,17}, are non-steroid phytoestrogenic substances which stimulate animal growth. Furan ring in these substances is known to contribute substantially to this activity.

In addition to these, there are numerous reports\textsuperscript{18-28} regarding synthesis, isolation from natural products, medicinal use and other properties of compounds containing furan nucleus. The detailed description is not relevant to the scope of this thesis.
Huggi et al\textsuperscript{29} have synthesized metal complexes of some furan derivatives like ethyl furan -2- carboxylate (1) and its thiosemicarbazide (2) and evaluated their antibacterial and antifungal activities.

Sharma et al\textsuperscript{30} have reported synthesis of metal complexes involving furoic acid hydrozone as ligand.

2.2. Benzofuran and its complexes

The compounds with benzofuran nucleus are well known as biodynamic agents, possessing various physiological and pharmacological properties. To name a few pharmacodynamic studies\textsuperscript{31-32}, benzofuran compounds have revealed spasmolytic activity and showed some dilatory effects on the heart of rabbits, cause apnea and bradycardia in dogs. The benzofuran compounds possess potential antimicrobial\textsuperscript{33}, analgesic\textsuperscript{34-36}, analeptic\textsuperscript{35}, antiviral\textsuperscript{37} and antiinflammatory\textsuperscript{38} activities. The mycological investigations\textsuperscript{39} on benzofuran compounds have revealed lethal effects on several common dermatofitic fungi. Some of the natural compounds with benzofuran moiety are used as effective medicines\textsuperscript{40} in the treatment of heart diseases and whooping cough and as pesticides\textsuperscript{41}. Few of the compounds can stimulate the rate of germination of seeds\textsuperscript{42}. 
Only a few reports\textsuperscript{43-45} are available about the metal complexes of benzofuran derivatives, which have been characterized on the basis of magnetic and dipole moment measurements, thermogravimetric and spectral studies. Various complexes of \(N\)-(p – toluenesulphonyl)-2-benzofurylcarboxamide (3) were characterized with the help of above mentioned parameters.

\[ \text{3} \]

Raina and Dhar\textsuperscript{46} have reported the interesting colour reactions of benzofuran derivative, 4,6-dihydroxy-coumarane-3-one, with transition metal ions on paper chromatograms. Many complexes of \(\beta\)-hydroxy coumaranones have been reported by other investigators\textsuperscript{47-51}.

Benzofuro[3,2-d]pyrimidines are associated with biological activity\textsuperscript{52}. 2-Acetylbenzofurans are being used as diuretic choleretic agents\textsuperscript{53}.

2.3. Naphthofuran and its complexes

Naphthofuran is a tricyclic heterocycle in which five membered heterocycle containing oxygen atom is condensed with the polynuclear aromatic system naphthalene. Eventhough, there can be several isomers for naphthofurans, the structures of only the four important isomers are given below,
Derivatives of these compounds are reported to exhibit wide spectrum of pharmacological and biological activities.

Weill thevenet et al\textsuperscript{54} have synthesised 7-methoxy-2-nitronaphtho[2,1-b]furan which exhibited considerable mutagenic activity. Veluchamy et al\textsuperscript{55} reported the synthesis of 3,6,9-trimethylnaphtho[1,2-b]furan related to Emmotin-G. The relationship between the structure and the carcinogenic and mutagenic activity of different naphthofurans have been described by Venegas et al\textsuperscript{56-58}.

Some naphthofurans have been reported to induce chromosomal aberrations detected in metaphase, anaphase and telophase - V79 Chinese Hamster cells\textsuperscript{59}. Salmon et al\textsuperscript{60} reported carcinogenic effects of 2-nitronaphthofuran injected subcutaneously in rats.

Mukhanova et al\textsuperscript{61} have synthesized aminomethyl derivatives of naphtho[2,1-b]furan and evaluated them for possible biological activity. These derivatives have been found to exhibit a weak antimicrobial activity.
Mutagenicity of naphthofurans annelated with 1,2-dioxetanes has been reported in the literature\textsuperscript{62}.

Strapelias et al\textsuperscript{63} have studied the influence of methoxy and nitro groups in the oxidative metabolism of naphtho[2,1-b]furans.

Touati et al\textsuperscript{64} investigated target nucleotides involved in binding of DNA of 7-methoxy-2-nitronaphtho[2,1-b]furan [R-7000] (4).

\[
\begin{align*}
\text{NO}_2 \\
\text{OCH}_3
\end{align*}
\]

4

This compound has been proved to be a very potent mutagen that causes sarcomas at the subcutaneous injection site and carcinomas in the forestomach after p.o. administration\textsuperscript{65}.

Gilotdelhalle et al\textsuperscript{66} have investigated clastogenic effects of a nitronaphthofuran after the treatment of seeds or root tip cells. Photooxygenation of 2-methylnaphtho[2,1-b]furan and 2-methyl naphtho[1,2-b]furan was carried out by Hashemi et al\textsuperscript{67}. Carlini et al\textsuperscript{68} have reported three step synthesis of naphthofurans related to (-)-morphine from ortho-benzoquinone monoketals by Diels-Alder and Cope reactions. A series of substituted racemic naphthofurans were synthesized as "hybrid" molecules of the two major prototypical hallucinogenic drug classes and found to possess unexpectedly, affinity for muscarinic receptors\textsuperscript{69}. Recently Al-Hazimi et al\textsuperscript{70} have published a review
article on naturally occurring naphthofuroquinones, in which they have described various naphthofuroquinones isolated from various parts of plants species belonging to nineteen plant families.

However, survey of literature reveals that there are no reports regarding synthesis and characterization of complexes of naphthofuran derivatives, inspite of their pharmacological and medicinal importance, except a report by Arancibia and co-workers\(^7\) on the synthesis of Zn(II) complexes with the reduction product of 2,3-dimethoxy-1-4-naphthoquinone in dimethyl sulfoxide.

2. 4. Complexes of derivatives of 2-hydroxy-1-naphthaldehyde

There are several reports regarding synthesis, characterization, biological and pharmacological activities of complexes derived from 2-hydroxy-1-naphthaldehyde.

Chaurasia and Srivatsava\(^8\) have reported the synthesis and biological evaluation of some novel naphthoxy derivatives and observed that some of these compounds possess promising anthelmintic activity.

Some bivalent metal complexes of 2-hydroxy-1-naphthaldehyde mono semicarbozone have been synthesized by Sahadev et al\(^9\) and their stability constants have been studied. Sharma et al\(^10\) reported potentiometric studies on the complexation equilibrium between some complexes of trivalent lanthanides with biologically active 2-hydroxy-1-naphthaldehyde thiosemicarbazones (5).
Thermal studies on chelation behavior of bivalent metal complexes of biologically active 2-hydroxy-1-naphthaldehyde mono semicarbozones have appeared in literature\textsuperscript{75}.

Nath et al\textsuperscript{76} synthesised organo Sn(IV) complexes of the ligand obtained by condensation of 2-hydroxy-1-naphthaldehyde with glycine and characterised them on the basis of spectral studies. The complexes, thus prepared have been tested \textit{invitro} against bacteria like \textit{Streptococcus faecalis} and fungi like \textit{Candida albicans}, they observed that all the complexes have remarkable antimicrobial activity. The biocidal studies of Cu(II), Ni(II), Zn(II) and Mn(II) complexes of schiff bases derived from 2-hydroxy-1-naphthaldehyde have been carried out by Misra et al\textsuperscript{77}.

2.5. Complexes of ligands containing different functional groups

2.5.1. Complexes of ligands containing acyl group

Hiremath et al\textsuperscript{78} synthesized complexes using 3-amino-2-acetyl benzofuran (6) and characterized them on the basis of magnetic and spectral studies. They observed that carbonyl oxygen of acetyl group and oxygen of the benzofuran nucleus act as donor atoms in the formation of complexes.
Similarly they have also prepared complexes of 3-acetylamino-2-benzofurancarboxamide and 3-acetylamino-2-benzoylbenzofuran. On the basis of IR spectral data they concluded that oxygen atom of $-\text{NHCOCH}_3$ group is not involved in complexation\textsuperscript{79-80}.

Huggi et al\textsuperscript{81} investigated transition and non-transition metal complexes of 3-amino-2-benzoylbenzofuran and showed that oxygen atom of benzoyl group is involved in coordination with metal ions, by studying IR spectral data.

2.5.2. Complexes of ligands containing oxime group

Infrared spectral studies on the complexes of salicylaldoxime indicated that nitrogen atom of azomethine group takes part in forming dative bond with metal ions in complexes\textsuperscript{82}. Oxime of ketones are also known to act as excellent ligands in the formation of complexes. Investigation of IR spectra of such complexes revealed the involvement of azomethine group in complex formation\textsuperscript{83}.

Talati et al\textsuperscript{84} synthesised Ni(II) complexes of vic-oxime-imines and came to the conclusion that both the nitrogen atoms of oxime and imine are involved in complex formation. Potentiometric and infrared studies on oxime of 2-hydroxy benzophenone and their metal chelates have been carried out by Unny et al\textsuperscript{85}, in this case also it has been shown that nitrogen atom of oxime group acts as donor atom.
Outer sphere electron transfer in Fe(III) complex of naphthoquinone oxime has been investigated by AL-Qurashi. Sinha et al. have carried out synthesis, characterisation and reactivity studies of some electrophilic mono and binuclear nitrosyls of Ruthenium(II) containing ketoximates, they assigned square planar geometry to the complexes and suggested the participation of nitrogen atom in complex formation. There are reports in literature regarding synthesis and characterisation of mono and homo binuclear Co(II), Ni(II) and Cu(II) complexes derived from oxime of 3-formylsalicylic acid (7). These complexes have been shown to be associated with remarkable fungicidal activity.

Pokhariyal et al. have characterized the complexes of some divalent metal ions with 8-acetyl-7-hydroxy-4-methylcoumarin oxime on the basis of spectral and thermal studies. Recently, Zekri et al. reported the reactivity of α-benzoin oxime with Mo(VI).

2.5.3. Complexes of ligands containing hydrazone group

The ligand containing hydrazone, which are obtained by the reaction between aldehydes or ketones with hydrazine or substituted hydrazines, act as very good chelating agents. It is because of the presence of two nitrogen atoms in the ligands. Aggarwal et al. investigated the reactions of Titanium(IV) halide
with hydrazine. Similarly chloro titanium(IV) of salicylaldehyde hydrazone and orthohydroxy acetophenone hydrazone have been studied extensively.\textsuperscript{92-93} Complexes of Mn(II), Cu(II), Ni(II) etc., using benzil phenyl hydrazone have been isolated and characterised by Misra et al.\textsuperscript{94} Nawar et al.\textsuperscript{95} carried out research work involving synthesis and spectral studies of bivalent metal complexes of 4-oxo-4H-1-benzopyran-3-carboxaldehyde hydrazone derivatives. Dey et al.\textsuperscript{96} reported the synthesis and characterization of iron(III) complexes of salicylaldehyde-4-methoxybenzoyl hydrazone.

Gouder et al.\textsuperscript{97} have reported synthesis and structural studies on Nb(V) complexes of furoic acid hydrazones (8)

\begin{equation}
\begin{array}{c}
\text{\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \\end{array}
\end{equation}

8

Singh et al.\textsuperscript{98} have carried out very interesting study on complexes of various lanthanides with 2-aminoacetophenone and 2-acetylaminocetophenone-2-thionyl hydrazones and arrived at the conclusion that the increase in chelate ring size is connected with lowering in coordination number. They have also studied inductive effect of methyl group in these complexes. Singh et al.\textsuperscript{99} have reported the synthesis of Zn(II) complexes with some hydrazones.
2.5.4. Complexes of ligands containing semicarbazones group

Survey of literature has revealed that there are only a few reports of using the ligand containing semicarbazone group in the complex formation with various transitional and non-transitional metal ions.

Misra et al\(^\text{94}\) have described the synthesis of complexes of the metal ions with benzil phenyl semicarbazone. Synthesis of some lanthanide complexes of semicarbazones derived from fluorenone have appeared in literature\(^\text{100}\).

\[
R-C=N-N-C-NH_2
\]

Semicarbazone

Recently Pandey and Singh\(^\text{101}\) have reported spectral and biocidal study on some unsymmetrical boron complexes of semicarbazones. The semicarbazones and respective boron complexes have been screened for antifungal activity against, *Macrophomina phaseolina* and *Fusarium oxysporum* and antibacterial activity against *Pseudomonas cepaccola*, *Escherichia coli* and *Staphylococcus aureus*. The results revealed the considerable increase in the toxicity of the complexes as compared to the organic ligand. This observation was in accordance with Tweedy's theory\(^\text{102}\).

2.5.5. Complexes of ligands containing ester group

In this case also, survey of literature revealed that there are only few reports regarding synthesis of complexes with the ligands having ester group.
There are some reports in connection with synthesis, characterization and biological screening of complexes derived from β-ketoester derivatives with various metal ions\textsuperscript{103-110}.

Kumar et al\textsuperscript{111} have investigated the Sb(III) complexes using methyl acetoacetate, ethyl acetoacetate and ethyl benzoyleacetate as ligands (10).

\[
\begin{align*}
R &= C - CH_2 - C - OR' \\
O & \quad \quad O
\end{align*}
\]

Recently synthesis, characterization and electrochemical properties of interesting complexes of Co(II) have been investigated. These complexes have been assigned half-sandwich structure. The preparation of such complexes involved the ligands containing different ester groups\textsuperscript{112}.

The above discussions reveal the importance of furan, benzofuran, naphthofuran and naphthalene derivatives as biologically, pharmacologically and industrially important molecules. Similarly functional groups like acetyl, benzoyl, oxime, hydrazone, semicarbazone and ester play significant role in the formation of complexes with different metal ions. As there are no reports available in literature regarding synthesis of complexes using various naphthofuran derivatives as ligands, it is contemplated to synthesise various naphtho[2,1-b]furan derivatives and to use them as ligands in the formation of complexes with metal ions like Cu(II), Co(II), Ni(II), Cd(II), Hg(II) and Zn(II).

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