CHAPTER I

INTRODUCTION
Although the coordination chemistry of metal complexes with small donor groups is a fascinating area of research the chemistry of large donor groups with complicated structures has also attracted attention. Synthesis of metal complexes with small donor groups containing N, O and S are of particular interest because of their ability to possess extra stability, structural lability, unusual configuration and their sensitivity to molecular environment [1]. The interest in designing metal complexes with small donor molecules stem mainly from their use as antibacterial, antifungal agent [2], models to study magnetic exchange phenomenon [3] therapeutic reagents, in the treatment of metal intoxication and catalysis [4-7]. Recognition of these complexes with such donor groups has led to the development of inexpensive synthetic routes for these compounds [8]. Several classes of ligands and their metal complexes have been synthesized which contain varying combinations of aza, oxa and sulpho ligating atoms which can be tailored to accommodate specific metal ions by fine tuning of the ligand design such as the cavity size, nature of the ligand, ligand substitution, number and sizes of the chelate rings. Multidentate ligands are cyclic molecules consisting of an organic framework interspersed with heteroatom which are capable of interacting with a variety of metal ions.

Acyclic molecules containing the grouping N(CH₂)nN in their structures are among the best characterized chelating agents for transition metal ions. In comparison to acyclic diamines, cyclic diamines are relatively less studied. Piperazine, for instance, does not form bicyclic metal chelates with the smaller transition metal ions such as copper(II) and nickel(II) although its complexes with palladium (II) and iridium(II) have been reported [9]. Assuming that the strain induced in the chelated structure would be reduced if additional methylene groups are introduced between the amine functions, the eight-membered-ring diamine 1,5-diazacyclooctane (daco) [10]
and the seven-membered-ring diamine 1,4-diazacycloheptane (dach) were examined as chelating agents for nickel(II) and copper(II). When nickel(II) and copper(II) salts were treated with daco, planar complexes were obtained regardless of the anion or solvent present [10]. Nickel(II) complexes of dach were also planar (Fig.1). However, the geometry of the dach copper(II) complex is dependent on the solvent and the anions present because both tetra and pentacoordinated complexes could be prepared [11]. Thus a comparison of daco and dach complexes is advantageous since the local environment of the metal ions in the planar, four-coordinated bis complexes is similar and variations in the physical and chemical properties of the two complexes can be attributed to changes in coordination number. In addition, the spectral data may be particularly informative in that the ligand does not contain a π-electron system and all of the absorption maxima can be assigned to either d-d or ligand-to-metal transitions.

Fig.1 Cyclic diamines

Homo and heterobimetallic complexes containing two or more metal centers in close proximity are involved in a variety of important biochemical processes.
[12,13] and are important in materials of technological and industrial significance [14,15]. Heterobimetallic complexes offer an opportunity to study cooperative interaction between metal ions depending on the preferred stereochemical disposition of metal and the bonds formed in coordination. The efficacy of heterobimetallic complexes in asymmetric activation of carbon dioxide and related molecules has been demonstrated [16]. Further, heterobimetallic complexes have potential to mediate chemical reactions of industrial relevance either more efficiently than or, in a different manner, isolated metal centres [17]. Various diamines have been employed for synthesis of chelating agents in the present work. It has been shown that diamines can take part in the activation of the metal surface and also in electron transfer in the reacting system [18]. Moreover, it is a strong coordinating agent that is efficiently applied in supramolecular design.

Desired architectures of heterobimetallic complexes might be achieved by the application of building blocks possessing bridging possibilities due to the presence of sterically accessible donor atoms, H-bonding centres and/or fragments capable of $\pi-\pi$ stacking. These building blocks can be formed by self-assembly of components in one-pot reaction. In this approach, a metal complex as ligand is subsequently self assembled with a second metal centre in the same reaction vessel eliminating several separate steps of building blocks. This approach has been applied to synthesize Cu/Zn and Cu/Cd heterobimetallic complexes [19,20].

The mutual influence between the metal ions leads to polymetallic systems with new physicochemical activities which are being used in the design of molecular magnet or optical devices, molecular probes for selective recognition of charged or neutral molecules and polynuclear catalytic systems [21,22]. The ability to form heterodinuclear complexes is related to the possibility to synthesize stable
mononuclear complexes which can act as “ligand” for further complexation or go through a transmetallation process [23]. Organoheterbimetallics has aroused interest due to applications in catalysis, material synthesis and bioorganometallics [24]. Organo-mercury compounds are important in organic synthesis on account of generation of radical precursors [25]. Monometallic and mixed metallic complexes with bifunctional unsaturated sulphur containing ligands are of great interest in inorganic and metalloorganic chemistry, especially due to their potential with novel electrical and magnetic properties.

Coordination chemistry of Cu(II) continues to be of interest in developing models for copper proteins and in understanding the factors which give rise to infinite variety of distortion for regular stereochemistry. Five coordinate copper complexes are quite common, however, stereochemistry adopted by them ranges between square pyramidal (SP) to trigonal bipyramidal (TBP). Very few complexes with regular SP or TBP geometries are known. They are mostly intermediate between these two extremes [26].

Considerable research effort is currently directed toward polymeric copper complexes with symmetric multidentate corboxylates as bridging ligand [27]. The chemistry of Cu(II) corboxylates with N/S donor ligands are studied widely as they find application in pharmaceuticals, fungicides, catalyst, gas occlusion compounds and solvent extraction process. Moreover, Cu(II) corboxylates with different ligands are potential wood preservatives. Cu(II) corboxylates of different chain length (hexanoates/heptanoates/octanoates/nonanoates) with 2-aminopyridine have been generally reported to be dimeric (green) with paddle-wheel type structure which becomes monomeric (blue) as the concentration of 2-aminopyridine increases [28].
Dithiocarbamate (dtc) is one of the most studied sulphur donor ligands because of its convenient synthesis, exquisite nature of bonding, exceptional stability and biochemical relevance [29]. They form complexes with almost all metals present in periodic table. The dithiocarbamate core M-S₂CNR₂ \((M=\text{metal, } R=\text{alkyl})\) could prove to be of great utility since a wide variety of substituents can be incorporated. The strong chelating ability of dithiocarbamate moiety may be attributed to the small interatomic distance between two sulphur atoms conferring stronger ability between the ligand and the metal ion [30,31]. The special feature of dithiocarbamate ligand is an additional \(\pi\)-electron flow from the nitrogen to sulphur atoms via a planar delocalized \(\pi\)-orbital system. The net effect is the development of strong electron donating ability resulting in a high electron density towards the metal ion. Their dual nature of binding both as symmetrical bidentate and asymmetrical monodentate ligand makes them more specific as a metal chelator. They can bind a metal ion in different modes (Fig.2). By far, the most common of these is the symmetrical chelating mode [30,32].

They can stabilize unusual oxidation states of transition metal ions, a property which has been attributed to the ability of ligands to delocalize positive charge from the metal towards the periphery of the complex [33]. Their strong affinity for the metal ions accounts for enzyme inhibition and thus, makes them biologically significant entities. Metal dithiocarbamates are used as pesticides (propineb, zineb, mane, mancozeb, ziram, thiram etc.) [34], antiviral agents [35], antidote for phytotoxic agents [36], bactericides, prophylactic, and therapeutic agents for metal toxicity [37].
Fig. 2  Coordination mode of dithiocarbamate moiety
Although, they are suitable for the removal of metal ions from organisms, they are also able to alter redistribution, resulting in increased toxicity [38]. They have also been investigated for possible application in chronic alcoholic therapy for instance; tetraethyl thiuram disulfide (disulfiram, teruram) induces alcohol tolerance by inhibition of the acetaldehyde dehydrogenase enzyme [39]. The dithiocarbamate motif is also susceptible to decomposition in aqueous solution, releasing the highly toxic carbon disulfide and amines in the process. They can be useful tectons for the generation of assemblies capable of encapsulating small guest molecules in a selective manner [40].

Self-assembly has been recognized as a powerful methodology for the formation of supramolecular systems. Metal directed self-assembly has numerous advantages over conventional synthesis [41]. The predictable nature of coordination chemistry has been used successfully to generate the metallatopomers (coronands, cryptates, cryptands). The dithiocarbamate is useful in generating macrocyclic complexes because of its self-assembling nature. The coordination of transition metal ions together with an appropriate bis-dithiocarbamate salt results in the formation of dinuclear/ polynuclear complexes. In these dtc derivatives “CuS₄” unit is ubiquitously square-planar which attains an overall distorted octahedral coordination environment via long range intermolecular interactions. Copper centers in these complexes form an infinite chain held together by weak Cu-S interactions with a second Cu dithiocarbamate unit. Based on Cu-S and cationic-anionic interactions these polynuclear complexes exhibit three structural types (Fig.3) leading to the formation of ladder/chains [42].
Fig. 3 Pictorial representation of polynuclear dithiocarbamate complexes
The importance of Schiff base ligands is due to ease and flexibility of their synthetic procedures and their sensitivity towards central metal atom. They may coordinate as a neutral or (after deprotonation) anionic ligand. Sallomi et al. [43-45] have reported the synthesis of tri- and tetradentate Schiff base ligands derived from the condensation of benzoin with acid hydrazide, amino phenols, p-phenylenediamine and their mononuclear and oxygen bridged binuclear complexes with Co(II), Ni(II) and Cu(II).

A number of tridentate dibasic Schiff bases [46] have been shown to force the metal ions to polymerize which results in the formation of complexes with unusual /subnormal magnetic moment value. The magnetic moment of Cu(II) complexes have been observed to decrease with decreasing temperature exhibiting antiferromagnetic spin-spin exchange phenomenon.

Transition metal complexes with quadridentate Schiff bases (Fig.4) of the type I and II have been studied [47]. As the number of carbon atoms in the methyl bridge increases from n=2 to n=3/4, the stereochemistry of the metal(II) complexes [where M=Co(II) and Cu(II)] changes from square-planar to pseudo tetrahedral [48]. Also, more planar nature of naphthalene ring has been observed as compared to benzene ring.

Cukurovali et al. [49] have explored the synthetic possibility of heterocycle of cyclobutane with thiazole due to presence of several reaction sites. It holds promise for the preparation of new thiazole derivatives because 1,1,3-trisubstituted cyclobutane, substituted thiazole and its Schiff base containing mesityl group have not been reported so far. These compounds exhibit anti-inflammatory, antiparasitic, antidepressant activity and liquid crystal property [50].
Fig. 4 Tetradentate Schiff bases

Chatterjee and Mitra [51] have reported a series of Schiff base ligands ($L_1$-$L_5$) of 1,2-phenylenediamine with salicylaldehyde, 2-pyridinecarboxaldehyde and 2-aminophenol, 2-aminomethylpyridine with acetylacetone (Fig.5). Their complexes with ruthenium(III) have been found to catalyze olefin epoxidation and, oxidation of other organic compounds in presence of $O_2$, $H_2O_2$, $ClO_4^-$, pyridine-N-oxide, iodosyl benzene, oxone or $t$-BuOOH.
Fig. 5 Different types of tetradentate Schiff bases
Gupta et al. [52] have synthesized asymmetric compartmental ligand bis(acetylacetone)ethylenediamine which has an enaminoketone structure with intramolecular hydrogen bonding (Fig.6) which is quite obvious.

Structure of complexes with pentadentate N$_3$O$_2$ ligand is unique [53]. Cobalt complexes with pentadentate Schiff base derived from substituted ortho hydroxybenzophenones with amines containing central “NH” or “thioether” functionality have greater solubility than their salicylaldehyde analogues. Because of their greater solubility they are also more suitable for crystal growth [54]. Methyl substituted o-hydroxybenzophenone derivatives (mbpN) are more soluble than the chloride substituted (cbpN) derivatives. On the basis of spectral and magnetic data it has been concluded that Co(II) complexes with salX ligands, (where X=NH, NCH$_3$, NC$_6$H$_5$, PCH$_3$) are five-coordinate but when, X=S or O; it is strange that they are four coordinate. (Fig.7).

The synthesis and X-ray crystal structure of Co(III) complexes with pentadentate ligands have also been reported [55]. Their electrochemical behaviour, effect of axial and equatorial ligation and the effect of mutual steric hindrance between the pentadentate Schiff base ligand [bis-(2-hydroxy-o-naphthaldimine)-N -diethylenetriamine] dianion and ancillary ligands [pyridine/piperidine/pyrrolidine] on their spectral and redox properties have also been discussed. The mutual steric hindrance between pentadentate Schiff base ligand and bulky ancillary ligand affects the Co(III)/Co(II) reduction potential. It shows a relatively good correlation with sigma donor ability of the axial ligands (Fig.8).
Fig. 6 Enaminoketone structure of Schiff base with intramolecular H-bonding

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\text{Fig. 7 Pentadentate Schiff bases}
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Recent interest has been shifted towards the binuclear transition metal complexes in order to study their preparative accessibility, structural variability and magnetic exchange interactions. Since bimetallic complexes may also mimic various biosites in protein and enzymes they can be used in model studies [56]. A Schiff base afforded by the condensation of glycyl-glycine and o-pthalaldehyde, with a phenyl spacer acts as octadentate N4O4 ligand. Multidentate binucleating Schiff base with inbuilt spacer can take up two similar or different metals [57-62, ]. These complexes have shown moderate to good antibacterial activity against Gram-positive and Gram negative bacteria.
A large number of oxo-bridged dinuclear and tetranuclear copper complexes have been shown to exhibit some degree of spin pairing between copper atoms [63] via bridging oxygen atoms (Fig.9). Studies of such compounds have revealed the effect of chelate ring size on their magnetic properties. For instance, when n=2, compounds obey the Curie-Weiss law, and when n=3,4 they are essentially diamagnetic through antiferromagnetic coupling [64]. By molecular weight measurement in solution, it is established that for n=2, the complex is dinuclear and for n=3,4 it is tetranuclear.

Structural studies have demonstrated the existence of a Cu₄O₄ “cubane” core in tetranuclear complexes and different geometrical models have been used to account for the observed magnetic interaction [65]. In view of the known sensitivity of these magnetic interactions to small changes in ring geometry, Willis et al. [66] have prepared a series of substituted tetranuclear complexes to observe the effect of magnetic interaction on ring geometry and effect of chirality with variable R group on degree of super exchange between Cu²⁺ ions.

Metal compounds with stable d¹⁰ electronic configuration are of interest in the field of coordination chemistry. To the best of our knowledge, over thirty zinc metalloenzymes are known in which zinc is tetrahedrally bonded to hard donor atoms [67]. Schiff base complexes of Zn and Cd are reported [68] to exhibit photo physical properties and they can, therefore, be used as effective emitting layer. Moreover, Zn(II) complexes have been shown to act as antitumor, anti-HIV and antimicrobial agents [69]. In this context a variety of Schiff base metal complexes having d¹⁰ configuration, eg. Zn(II), Cd(II), Sn(II) and Pb(II) have been synthesized [70].
Fig. 9  Dinuclear complexes bridged *via* oxygen atom
The effect of steric interaction on coordination geometry has been analyzed [71,72]. The coordination chemistry of mercury is of substantial interest because of its toxic effects [73-76]. The ligand N’N-bis(2,3-dimethoxybezylidene)-1,2-diaminomethane coordinated to the Hg(II) centre via two nitrogen atoms adopts an E,E-configuration. It is important to note that intermolecular non-classical H-bonding of the type C–H…O occurs and, no H-bonding has been observed through iodide ion of HgI₂ which is quite unusual. This has also been supported by the crystal structure of the compound, although no valid reason has been given for such H-bonding [77,78]. On the contrary, the corresponding HgBr₂ and HgCl₂ complexes exhibit both inter and intra molecular non-classical H-bonds of the type C–H…X (where X=O, Br, Cl). This is also unique in itself and has rarely been observed (Fig.10a,b).

Binuclear complexes of compartmental ligand containing unsaturated tetraaza diphenol and its derivatives have received more attention than the mononuclear complexes. Gupta et al. have also synthesized [79,80] mononuclear complexes of oxovanadium (IV), Fe(III), Cu(II), Ni(II) from the [2+2] template condensation of 4-methyl-2,6-di(formyl/benzoyl) phenol with various diamines in the presence of metal ions and studied their electrochemical properties [Fig.11].
Fig. 10a Intramolecular Non-classical C–H---O hydrogen bond

Fig. 10b Inter- and intra-molecular non-classical C–H---X (X=O,Br) hydrogen bond
Fig. 11  Tetraazamacrocyclic complex

R = H(1), Ph(2)
X = C₂H₄, 1,3-C₃H₆, C₆H₄
Macrocycles with a wide spectrum of electronic and structural features are designed and synthesized to explore their application as bioinorganic model, spacer for crystal engineering [81,82]. The macrocyclic ligand systems having both “hard” and “soft” donor atoms are of greater importance because they can easily stabilize metal ions in their high and low oxidation states respectively [83-88]. In this context Tripathi et al. [89] have demonstrated template free synthesis of the first 24- and 28-membered N₄O₂E₂ (H₂L) macrocycles and open ended N₂O₄Se (H₂Lₓ) Schiff base (Fig.12).

![Diagram of macrocycles incorporating “Hard and Soft” donors](image)

E=Se, Te

Fig.12 Macrocycles incorporating “Hard and Soft” donors
Bis-NNO-chelate complexes of tridentate Schiff bases with Co(II) were first prepared by Sacconi et al. [90]. Cationic complexes of Co(III), derived from ortho hydroxyarylketone and diamine, were synthesized by template assistance. It was shown that the ease with which Co(II) compounds are oxidized to Co(III) derivatives depends on the nature of compartmental ligands. In some cases simple air oxidation is sufficient to convert Co(II) halides into Co(III) complexes [91]. The kinetically inert Co(III) compounds can be converted into the kinetically labile Co(II) derivatives in reducing biological environment and provide means for the delivery of NNO-donor ligands, e.g. some cytotoxins, to specific locations. The binding of these complexes with DNA suggests potential applications in antitumour therapy [92]. Many of cobalt complexes contain two metal centers and interactions between them gives interesting magnetic properties.

In some cases the multidentate ligands can be pre-formed before reaction with solutions containing Co(II) or Co(III) halides. However, in other cases ligands are apparently assembled in the coordination sphere of the metal [93]. The crystallographic studies of their complexes with first row transition metals have also been done to see the effect of length of diamine on cavity size (Fig.13).

![Fig.13 Effect of diamines chain lengthening on cavity size](image-url)
Complexes of Schiff base containing amino acids are useful in understanding many biochemical reactions in vivo. The metal poisoning in living organisms is ascertained using these complexes by determining the action of drugs [94]. Amino acids are indispensable building blocks of proteins and perform a huge number of biological functions, as exemplified by the role of enzymes [95].

Schiff bases formed with salicylaldehyde and amino acids (glycine, alanine and leucine) in presence of VOSO$_4$ in alcoholic-aqueous solution yields a mononuclear water bound vanadyl(IV) complex [96] which could not be dehydrated by heating even up to 160 °C [97,98]. Neelkantan and co-workers [99] have described a successful synthesis of eighteen mononuclear Cu(II), Ni(II), Zn(II), Co(II), Mn(II) and VO(II) species chelated by aldimines of o-phthalaldehyde and $\alpha$-amino acids (glycine, l-alanine, l-phenylalanine). Their spectral, redox behavior, biological activities and DNA cleaving nature has been discussed Arun et al. [100] have reported Schiff bases (L$^1$-L$^6$) of 1′-hydroxy-2′-acetonaphthone (HAN) containing chalcogen functionalities (Fig.14). Their complexation with Pd(II), Pt(II), Hg(II) and (p-cymene)Ru(II) has been explored. The crystal structures of ligands L$^1$, L$^3$ and L$^6$ and complexes of Pd(II) with L$^1$, L$^2$, L$^3$ and L$^5$ have been determined. The geometry of Pd is close to square planar in all the cases and the ligands coordinate in a uni-negative tridentate mode. 1′-Hydroxy-2′-acetonaphthone (HAN) has been studied as a proton transfer prototype molecule in gas, solution and nanocavities. The internal hydrogen bonding photoreaction in this molecule leads to keto type structure, and following its formation, an internal twisting motion gives rise to keto rotamers [101]. The presence of chalcogen may tune the catalytic activity of its complex in a new direction. The Pd(II) complexes of L$^1$–L$^6$ show promise as homogeneous catalyst for Heck and Suzuki reactions (Fig.15).
The complexes used as catalyst are based on phosphorus ligands and phosphorus-free ligands. The improved catalytic activity of transition metal complexes with hemilabile ligands has been reported [102]. But many phosphine based catalysts are quite often water and air sensitive. Therefore, catalysis under phosphine-free conditions is a challenge of high importance. A number of phosphine free Pd complexes [103] have been reported to exhibit promising catalytic activity for Heck reaction.

Since complexes of tridentate chalcogenated Schiff bases of [(N, O, E) type ligands, where E = S, Se or Te)] are air and moisture stable they have been used for Heck reaction. A good selectivity for trans-products has been observed. The catalytic activity depends on the halide, while electron-withdrawing groups on the aryl ring increase the reaction rate. The reactivity decreases drastically in the order ArI > ArBr > ArCl.

Suzuki-Miyaura reaction is also among the most important palladium catalyzed cross-coupling reactions of both academic and industrial interest [104,105]. Since phosphorus ligands are air sensitive effort is made to prepare phosphine-free ligands for the Suzuki-Miyaura reaction. Pd(II) complexes offer the advantage of stability under ambient conditions for Suzuki-Miyaura reactions of aryl bromides with phenylboronic acid. Thus chalcogenated Schiff bases of 1'-hydroxy-2'-acetonaphthone (HAN) may yield efficient catalysts for Suzuki-Miyaura cross coupling and Heck reactions.
Fig. 14 Schiff bases involving chalcogen functionality

L¹ = S;   L³ = Se

L² = S;   L⁴ = Se

Fig. 15 Heck and Suzuki reactions
The ligational behaviour of 2-hydroxybenzophenone and 2-hydroxy-4-methoxybenzophenone N-substituted thiosemicarbazones towards Ni(II) and Cu(II) ions has been investigated [106]. The ligands containing methoxy group facilitate the deprotonation of –OH by resonance, more than the –SH. Most of the Ni(II) complexes were found to have subnormal magnetic moments due to square-planar + tetrahedral configuration. The percentage of square-planar to tetrahedral was calculated and found in agreement with the ligand splitting energy (10Dq). Also, Cu(II) complexes show subnormal values due to the interaction between copper centers; the lower the value the higher the interaction. It was found that the substituent has a noticeable effect on the distortion of the complex.

Superoxide anions are reactive oxygen species that can attack biomolecules such as DNA, lipids and proteins to cause many serious diseases. Prachayasittikul and co-workers [107] have reported the synthesis of copper complexes of nicotinic acid with related pyridine derivatives. They were shown to possess superoxide dismutase (SOD) and antimicrobial activities. Particularly, copper complex of nicotinic acid with 2-hydroxypyridine was the most potent SOD mimic. Interestingly, the SOD activity of the copper complexes was demonstrated to be inversely correlated with the electron affinity, but was well correlated with both HOMO and LUMO energies.
References


