CHAPTER-I

REVIEW
1.1 Introduction

Macrocyclic complexes have undergone a phenomenological growth during the past three decades. The impetus for research has been accentuated by the recognition of the fact that the basic structural units of several naturally occurring systems such as: haemoglobin, chlorophyll, vitamin B$_{12}$ and many others contain macrocyclic corrin, porphin or chlorin rings [1]-[3], which have assumed a key role in the biological evolution on our planet. These splendid ligands are commonly bound to metal ions like iron(II), magnesium(II) or cobalt(II). Studies encompassing syntheses, structures and reactivities on man-made and natural macrocycles have been fruitful for a profound understanding of the role of metal ions in biological systems. Metal phthalocyanines$^1$, discovered in 1934 and the related macrocyclic compounds have attracted attention for their industrial applications, catalytic activity for syntheses of unusual organic compounds and for their semiconductor behavior.

It is no surprise that the progress in synthesis of macrocycles suffered a hindrance for a long period due to want of standard procedures required for the high degree of molecular reorganization. Besides, these endeavors were, for the most part, unsuccessful due to associated problems such as: low yields, polymerization during the reaction process, generation of side products and the requirement of large volume of solvents to minimize polymerization and encourage cyclization.
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Von Bayer\(^2,^3\) reported the first synthetic macrocycle \([4]\) by the violent reaction of pyrrole with acetone in presence of a drop of hydrochloric acid with 80% yield. The oxygen analogue macrocycle \([5]\) was isolated by Ackman and coworkers\(^4\) by the condensation of furan with acetone, catalyzed by protons, but the yield was surprisingly low, only 18-20%.

![Diagram 4](image4.png)

![Diagram 5](image5.png)

General methods of approach to macrocycle synthesis began to unveil in 1960 with the momentous work of Curtis\(^5,^6\) when he reported the synthetic macrocycle, \(\text{Me}_6[14]-4,11\text{-dienen}-\text{Ni}^2\), \([6]\), by the action of dry acetone on tris-ethylenediaminenickel(II) perchlorate. In parallel, a novel class molecules know as crown ethers, cryptates and cyclic polypeptides developed by Pederson\(^7\) has grown into an area of major research.

We are inclined to highlight some of the important aspects of macrocyclic complexes in the following sections that would serve as a background to the present investigations which deals with syntheses, elucidation of structures and bonding and electrochemical properties of some macrocyclic complexes of nickel(II), and copper(II).

1.2 Historical Developments

In 1950, Linstead and coworkers\(^8-11\) reported a few synthetic macrocyclic compounds, some of which are potential tri- and tetradentate ligands and are related to porphyrins and phthalocyanines. A decade later Curtis\(^5,^6\) reported the isomeric forms of the synthetic macrocyclic complexes \([6a,6b]\) which not only triggered the research on synthesis of macrocyclic complexes, but also encouraged their multifaceted growth.
Within a couple of years, Schrauzer and coworkers reported the fluoroboro-bridged macrocycle [7] formed by the action of boron trifluoride on dimethylglyoximato nickel(II). However, a spectacular rise was observed in macrocyclic complexes and further enriched by a new class of cyclic polyether compounds familiarly known as ‘Crown Ethers’, discovered by Pederson in 1967. The crown ethers have the ability to strongly hold alkali and alkaline earth metal ions. Immediately after the report on crown ethers, another class of compounds, cryptands, possessing the ability to accommodate a metal ion of suitable size forming an inclusion complex, were synthesized by Lehn and coworkers. Since then, there has been a worldwide conscious effort by a large number of celebrated workers towards the growth of the macrocyclic chemistry.

1.3 Classification

The synthetic macrocyclic ligands can be classified broadly into two categories. In first category, a group of complexes comprising macrocyclic ligands that incorporate nitrogen donor atoms or contain nitrogen in combination with oxygen, sulphur or phosphorus atoms as donors. These ligands generally possess a strong affinity to accommodate 3d-transition
metal ions forming a unique family of complexes; exemplary structures are [8]-[11]. The structure [8] and [9] coordinate about the metal ion in a planar array. The structure [10] is an example of a bicyclomacrocyclic complex where the ligand-cage fully surrounds the metal ion coordinating through six nitrogen atoms. Finally [11] represents a super macrocycle, where five nitrogen atoms coordinate about the uranyl ion in a plane orthogonal to the O=U=O axis. The second category of metal complexes are the cyclic polyethers of “Crown type”; the dibenzo-18-crown-6 [12] illustrates an unique example.

In contrast to the first category of azamacrocycles, the crown ether ligands have a strong tendency to coordinate and exhibit potentially unusual behavior towards non-transitional metal ions\textsuperscript{18} and only a few of their transition metal complexes are known\textsuperscript{19,20}.

\[\begin{align*}
[8] & \quad [9] \\
[12] & \quad \bullet = \text{UO}_2
\end{align*}\]
Macrocyclic ligands having compartments to accommodate more than one metal ion constitute relatively a new area in coordination chemistry. Binuclear complexes can be structurally classified into two categories. In the first category of complexes, the metal ions are embedded within a large macrocycle ring\textsuperscript{21-23} whereas in the second type, two mononuclear macrocyclic units are joined by common groups or bonds\textsuperscript{24,25}. Complexes [13] to [18] represent examples of some of these binuclear macrocyclic complexes and structure [19] is a typical heterobinuclear complex. A unique tetranuclear super macrocycle [20] which accommodates four metal atoms within the cavity of the macrocyclic ring, has been reported\textsuperscript{26}.

\[ R_1 = -(CH_2)_2/-(CH_2)_3-R_2 = \text{Im} = \text{Imidazole} \]

\[ \begin{align*}
R_1 &= \cdot -(CH_2)_2 - \cdot -(CH_2)_3- \\
R_2 &= H/CH_3, \ R_3 = H 
\end{align*} \]
1.4 Synthesis Of Macrocyclic Complexes

The synthetic routes for the preparation of macrocycles require a high degree of molecular reorganization. These are usually prepared either directly by conventional organic syntheses or by in situ procedures, the latter requires the presence of a metal ion that plays a pivotal role in bringing the reacting groups to closer proximity for cyclization.
1.4.1 **Direct Synthesis**

Novel direct synthetic methods for preparing azamacrocycles in reasonable yields are known. Condensation of tosylated reactants, [21] and [22] by heating in dimethylformamide at elevated temperature are examples of such exciting reactions and the tetratosyl derivative, [23] is obtained in good yield (80%). The tosyl groups are easily eliminated by heating the product. [24] is synthesized in concentrated sulfuric acid medium. Synthetic reactions of this type have become general as well as considerably simpler to prepare even macrocycles [25] with increased ring sizes (Scheme 1).
Besides, macrocyclic ligands containing nitrogen, oxygen as donors \[26\] can also be synthesized directly\(^{29}\) and Scheme-2 depicts a representative example.

\[\text{Scheme-2}\]

1.4.2 Template Synthesis

Apart from direct procedures, a galaxy of macrocyclic complexes with various molecular architectures have been synthesized via metal ion template methods. In these processes the cyclization reactions occur either by metal ion induced reactivity of one of the condensing functional groups or by steric factors that govern the appropriate positioning of the reacting moieties in the ring closure step. The function of the metal ion in the template process has been the subject of much discussion and the consensus opinion is that it directs the steric course of reaction and the effect is known as coordination template effect. The template effects have been recognized to be of two types: a kinetic template effect, if the directive influence of the metal ion controls the steric course of a sequence of step-wise reactions and the thermodynamic (or equilibrium) template effect, if the metal ion perturbs an existing equilibrium in the organic moiety by preferential coordination with one of the components.

Majority of the macrocyclic complexes have been synthesized by template methods involving condensation of metal amine precursor complexes with carbonyl compounds. 2,3-pentanedione-bis-(mercaptoethylimino) nickel(II) reacts with the diketone in a basic medium giving rise to the intermediate imine complex which in turn reacts with a dibromo compound to yield the macrocycle\(^{30-32}\) (Scheme-3).
The macrocycle[28] has been recently reported by Suh and coworkers[33] and represents an interesting template condensation of bis-(ethylenediamine) nickel(II) with formaldehyde and a primary amine, (Scheme-4).

These examples of macrocyclic syntheses involve the isolation of intermediate precursor complexes followed by ring closure reactions. But in majority of cases, in situ procedures have been applied to synthesize the macrocyclic ligands involving condensation reactions between the reactants in presence of a metal ion without the isolation of the intermediate.
The isolation of tetraazamacrocycle Me₄[14]tetraene-N₄, [29] by the reaction of 1,3-propanediamine and 2,3-butanedione in presence of iron(II), nickel(II) or cobalt(II) has been achieved this way³⁴,³⁵.

The *in situ* condensation of di or polyamines with a carbonyl moiety in presence of a metal ion is quite facile provided the di-carbonyl moiety incorporates one or more donor atoms between the two carbonyl groups. It is realized that nucleophilic reactions at carbonyl carbon atoms are invariably catalyzed by Lewis acids³⁶ and therefore, the presence of additional and appropriately positioned donor atoms between the carbonyl groups enhances the bonding potentialities with the metal atom³⁷, the additional bonding facilitates the dicarbonyl moiety to form a number of stable chelate rings with the metal atoms. The carbonyl groups thus linked to the metal ion experience enhanced polarization so that nucleophilic attacks by the amines on them become favourable. However the situation is more complex than what has been suggested with regard to simple polarization and the observed enhanced rate is a combination of several factors including polarization³⁸. It is observed that in several reactions where nucleophilic attack occurs at coordinated carbonyl centres, the reaction rate is enhanced and is attributed to favorable entropies of activation than the enthalpic factors³⁹,⁴⁰. The following reaction of the complex [30] with ethylenediamine represent a typical example of the reaction of a coordinated dicarbonyl forming the macrocycle [31].
In situ cyclizations of a series of complexes involving terminal aldehyde functions with suitably placed donor atoms in the backbone are known. In the presence of nickel(II) acetate, the dialdehyde [32] can react with a number of diamines\textsuperscript{42-44} to form macrocycles [33]. The dialdehyde [32] can be used as a suitable precursor to synthesize macrocyclic ligands directly by non-template methods\textsuperscript{45}. But, some quadridentate macrocycles like [34] have not been isolated without metal ions\textsuperscript{46-50}. Similarly, a related type\textsuperscript{51} of macrocyclic ligand [35] with nickel(II), cobalt(II) or zinc(II) metal ions has been synthesized. Reduction of the pyridine ring in the nickel(II) perchlorate complex affords the new piperidine ligand [36] in a square planar geometry. The dialdehyde [37] with various substituents yields nickel(II) macrocycles [38] by metal ion template methods\textsuperscript{52}.

\[ R = -(\text{CH}_2)_2-, -(\text{CH}_2)_3- \]
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Complexes of larger macrocyclic rings are of great interest as they dissociate readily in acidic and basic solutions. Martell, and coworkers\textsuperscript{53} synthesized the ligand [39] as the dihydroperchlorate salt by the reaction of 1,4-diaminobutanemonohydroperchlorate with acetone. The macrocycles of [39] can be reduced\textsuperscript{54} with NaBH\textsubscript{4} under basic conditions in methanol-water solvent to give a mixture of meso [40] and racemic [41] compounds which can be separated by fractional crystallization from xylene.

![Chemical structures: [39], [40], [41]]

Macrocyclic complexes with mixed donor atoms of the type [42] containing two sulphur\textsuperscript{55} or two oxygen atoms\textsuperscript{56} along with two nitrogen donor atoms as well as of the type [43] have been prepared conveniently by in situ synthesis. However, a number of nitrogen and oxygen donor macrocyclic ligands of the types [44] and [45] have been synthesized by non template methods\textsuperscript{57,58} and characterized.

![Chemical structures: [42], [43]]

\[
R_1 = -(CH_2)\text{--}, -(CH_2)_3\text{--}, -CH_2-CH(CH_3)-, \\
R_2 = -(CH_2)\text{--}, -(CH_2)_3\text{--}, \\
X = S \text{ or } O
\]
The macrocycles comprise an interesting class of ligands which are intermediate between the crown polyethers as well as azamacrocycles and are of considerable interest for showing enhanced specificity towards a number of metal ions, increased stability, greater kinetic inertness and more ligand field strength compared to related ligands with only oxygen or nitrogen donor atoms.

Novel macrocycles have been synthesized from dihydrazones or hydrazone metal complex precursors. The hydrazine or hydrazone complexes which contain free terminal -NH$_2$ groups undergo nucleophilic condensation with different ketonic functions. The dihydrazine precursor complex [46] gives the diamagnetic macrocyclic nickel(II) complex [47] by the action of formaldehyde in tetrahydrofuran (THF). The macrocycle [48] is obtained by a similar reaction of formaldehyde on 2,3-butanedionedihydrazone metal complexes or glyoxaldihydrazone complexes. Nickel(II) and cobalt(II) complexes of 6,6'-dihydrazino-2,2'-bipyridyl [49] react with aqueous acetone, to give a 13-membered macrocycle [50]. On complexation, the dihydrazino ligand [49] strongly chelates through the
α-diimine nitrogen atoms of the dipyridyl-moiety and the terminal -NH₂ groups. The coordinated amines of the hydrazine groups are now in a state of high stability and nucleophilicity to react with ketonic functions to yield the macrocycle [50].

The quinquedentate heptaaza macrocyclic ligand [51] has been synthesized from 2,9-di-(N,2'-methylhydrazino)1,10-phenanthroline and 2,6-diacetylpyridine and a range of bivalent metal complexes and their properties have been studied by a variety of techniques, including X-ray diffraction. Derivatives of benzilmonohydrazone [52] react with 1,2-diaminobenzene derivatives in presence of nickel(II) ion to give highly unsaturated hexaaza tetra-coordinated [N₄(N₂)] planar complexes [53].
Another novel series of complexes of the type, \([ M(DAPCH)X_2]\) where \(M=Zn(II), \text{Cd}(II)\) or \(Hg(II)\), \(DAPCH=\text{planar pentadentate ligand derived from 2,6-diacetylpyridine and carbohydrazide, } X=\text{Cl}^-, \text{Br}^-, \text{I}^-, \text{NO}_3^-\) and \(\text{CH}_3\text{COO}^-\) have been synthesized [54]. The complexes contain terminal hydrazine groups to participate in nucleophilic condition and react with 2,6-diacetylpyridine leading to the formation of macrocyclic complexes [55].

Reactivity of the coordinated amines was considered to be severely inhibited for nucleophilic condensation. But Curtis and Sargeson [69] have used the tris-(ethylenediamine) nickel(II) and cobalt(II) complexes as precursors to prepare macrocycles [6] and a series of interesting clathrochelates respectively. A saturated quadricoordinated hexaaza 16-membered macrocyclic nickel(II) complex [56] has been synthesized by the action of formaldehyde on bis-(diethylenetriamine) nickel(II) complex [70]. This is a rare macrocycle that encloses two unusual 7-membered chelate rings.

The well known tetrabenzo macrocyclic complexes [57] are obtained by metal ion assisted self condensation of orthoaminobenzaldehyde [71-75]. The classical chelating ligands like 1,10-phenanthroline can serve as starting materials for the synthesis of quadridentate macrocycles. It has been shown
that 2,9-dichloro-1,10-phenanthroline reacts with 2,9-diamino-1,10-phenanthroline in nitrobenzene in presence of potassium carbonate to form the macrocycle \([58]\) in high yield\(^7\). This reaction provides an example of direct synthesis of another category of macrocycles where the cyclization involves sites that are remote from donor atoms. Copper(II) chloride reacts with the ligand \([58]\) in nitrobenzene to give the neutral copper(II) complex with loss of two protons.

![Diagram 1](image1.png)

A family of charged macrocycles have been synthesized by the reaction of \(\beta\)-diketones such as 2,4-pentanedione with a variety of diamines. Inner macrocyclic complexes of copper(II)\(^7\) and nickel(II) are obtained by condensation of 2,4-pentanedione with triethylenetetraamine \([59]\) or with 1,2-diaminobenzene\(^78,79\) \([60]\) in mild acidic medium. Metal ions in unusual oxidation states, such as gold(II), have been used to isolate macrocycles of this type of ligands. The reaction of gold(III) ethylenediamine complex with 2,4-pentanedione in presence of an aqueous base\(^81,82\) gives the macrocycle \([61]\). But metal ion assisted synthesis of m-phenylenediamine and 1,3-diphenyl-1,3-propanedione gives unchanged\(^83\) macrocycles \([62]\).

![Diagram 2](image2.png)
The β-polyketones, like 2,4,6-heptanetrione and related ligands react with anhydrous ethylenediamine in ethanol medium yielding large ring macrocycles of the type [63]. Although these ligands appear to be binucleating, only mononuclear complexes have been isolated94. A large macrocycle containing eight nitrogen atoms [64] has been synthesized by the reaction of o-phthalonitrile(1,2-benzenedicarbonitrile) on 2,6-diaminopyridine in chloronaphthalene using a non-template procedure95.

A series of 14-membered tetraazatetranato macrocyclic complexes containing easily replaceable acetyl (CH₃CO ) group in the ring have been synthesized by multistep template reaction96.
The macrocyclic complex [65] is obtained from the reaction of 3-(ethoxymethylene)-2,4-pentanedione and ethylenediamine in presence of nickel(II) ions. These ligands are versatile in the sense that the terminal groups could be easily manoeuvred to undergo either condensation or replacement and there is a growing interest to synthesize new macrocycles by this method.

A series of macrocyclic lacunar complexes of the type [66] containing a permanent void have emerged from the quadridentate macrocycle [67] by the reaction of alkylated amines in methyl cyanide medium; the process involves template reactions in which nickel(II) maintains the favourable stereochemistry. The metal ion is stripped of the ligand by dry HCl in methyl cyanide medium and the protonated ligand in isolated as the ZnCl$_4^{2-}$ or PF$_6^-$ salt. Other metal ions like cobalt(II), copper(II) or iron(II) can be introduced into the ligand by suitable reactions. These ligands are unique because of their permanent void and can enclose small molecules like O$_2$, CO, NCS$^-$ and indeed the remarkable ability of cobalt(II), copper(II) and iron(II) complexes of [66] to bind molecular oxygen has been observed. The bridging groups can be made flexible and the cavity size can be altered by synthetic manipulations.
Hexaaza macrocyclic ligands acting as quadridentate donors have been reported. Divalent nickel, cobalt and copper salts react with 2,6-diaminopyridine and 2,4-pentanedione to form complexes of the type \([68]\) with 16-membered \(N_6\) rings; but coordination occurs only through four nitrogen atoms. A similar macrocycle \([69]\) having \(N_4O_4\) donor set but behaving as a quadridentate ligand has been reported.

A galaxy of fluoro-boro bridged macrocycles has been synthesized with considerable ease. Complexes of vicinal dioximes like bis-(dimethylglyoximato)nickel(II), react with strong electrophiles like BF\(_3\), BCl\(_3\) to form macrocycles \([70]\) in which BF\(_2\) units bridge the adjacent oxime groups. Fluoro-boro bridged 14- and 16- membered macrocyclic complexes of cobalt(II), nickel(II) and copper(II) derived from the reaction of 2,4,-pentanedionedioxime \([71]\), 1,2-diphenylethene-1,2-dionedioxime \([70,R=\text{Ph}]\) and 1,2-difurylethene-1,2-dionedioxime \([70,R=C_6H_5O]\) with boron trifluoride etherate have been synthesized and characterized. In the similar way triphenyl aluminium, AlPh\(_3\) is used in place of BF\(_3\) to react with bis-(dimethylglyoximato) complexes, M(Hdmg)\(_2\), \([M=\text{Ni(II)}, \text{Pd(II)} \text{and Cu(II)}]\) to isolate an analogous series of macrocycles. Lewis acids such as SnCl\(_4\), SiCl\(_4\) and H\(_3\)BO\(_3\) also give structurally similar complexes.
1.4.3 Synthesis by Other Methods

Apart from template and non-template methods, a number of macrocyclic complexes have been chemically modified to produce new cyclic ligand complexes. Oxidative dehydrogenation and electrochemical reduction techniques are usually employed for the modification of known macrocyclic complexes to form a series of new macrocycles. The ligand yields the benzo analogue [73]. The saturated precursor Ru(III) macrocycle [74] gives an unsaturated complex [75] by aerial oxidation. However, syntheses of macrocycles by this procedure have not progressed as expected because of their intrinsic instability.

\[ \text{M} = \text{Co(II), Ni(II), Fe(II), Zn(II)} \]
The clathrochelate [76] was synthesized by the action of boron trifluoride with tris-(dimethylglyoximato)cobalt(II) ion96. Besides the aforesaid capping reagent, lewis acids like SnCl₄, SiCl₄ and H₂BO₃ have been used97,98. A series of clathrochelates of iron(II) [76b, 76c] have been synthesized by in situ methods by the reaction of FeCl₂.4H₂O, boric acid, borax and oximes such as dimethylglyoxime99,100, 2,4-pentane-dionedioxime [77] and 1,2-diphenyleneethane-1,2-dionedioxime101 in appropriate alcohols. The mononuclear tris-(2,3-butanedione-dihydrazone) complexes of cobalt(II), iron(II) and nickel(II) having free terminal -NH₂ groups are suitably disposed to form clathrochelates and as a matter of fact, with formaldehyde60,102 give the ring closure product [78].

(a) M = Co(III), X = F, n = 1, R = CH₃
(b) M = Fe(II), X = F, OMe, OEt, OBu, n = 0, R = CH₃
(c) M = Fe(II), X = OH, OMe, OEt, OBu, n = 0, R = C₆H₅

The condensation product of 2-furaldehyde with oxalyldihydrazone is reacted with M(OAc)₂ where M = Co, Ni, Cu, Zn and Cd giving the polymeric coordination complexes of 2-furaldehyde-oxalyldihydrazone103. IR study confirmed the formation of hydrazones with coordination in enolic form
through the azomethine nitrogen, and the absence of coordination between metals and oxygen in the furan ring.

The synthesis of a 18-membered cyclic ligand from the reaction of 2,4,4,11,13,13-hexamethyl-1,5,10,14-tetraazacyclodecane-N,N'-diacetic acid (H₂L) with lanthanides is reported. They have been prepared in aqueous solution by the interaction of H₂L with the nitrates of rare earth and have been characterized by thermal and spectral measurement.

Template condensation reaction of H₂CO with appropriate tetramines and diamines in the presence of nickel(II) or copper(II) produce square planar complexes. These complexes contain 21,3-diazacyclopentane or 1,3-diazaalkylcyclohexane rings in the 6-membered ring that lie in the 5-membered chelate ring. Synthesis and characteristics of [ML]²⁺ are presented. The effects of the ligand structure or the equilibrium, [NiL]²⁺ + 2H₂O = (NiL(H₂O)₂)²⁺, in aqueous solution are described.

A series of ligands of structural importance that prevents the decomposition routes of high-valent middle and latter transition metal centres has been reported. The macrocyclic tetraamide H₄L [79] is derived from the parent acid of the macrocyclic tetraamido N-ligand \([n^4-L]^4\) which stabilized high-valent middle and latter transition metal complexes. The features presented provide insight useful to the development of new compound for high-valent reactive intermediate in catalytic oxidation in chemistry and biology.

The preparation and thermal decomposition of copper(II) complexes of acetone-1-naphthoylhydrazone are studied. From spectral and magnetic measurements copper(II) coordination in all complexes is square planar except for Cu(HL)₂(NO₃)₂, which is octahedrally coordinated. A detail analysis of the thermal decomposition of the complexes showed that they
undergo endothermic decomposition followed by oxidation of the resulting fragments by atmospheric oxygen. The decomposition of the complexes is completed at 760°C and CuO is formed as the final product.

The cobalt(II) and nickel(II) complexes with 2,4-dichloro and 2-methyl-4-chlorophenoxyaceticacidhydrazide and 2,4-dichlorophenoxybutyricacid are prepared\textsuperscript{108} and characterized by TGA electronic and IR spectra. Complexes of cobalt(II), nickel(II), copper(II) and zinc(II) with aryloxyacetic acid hydrazides are synthesized\textsuperscript{109} and characterized by elemental analyses, molecular weight, conductivity measurement, magnetic moment and spectroscopic techniques. The ligands and their metal complexes are tested for \textit{in vitro} growth inhibitory activity against some phytopathogenic fungi and bacteria and it is observed that the coordination of metal ions has pronounced effect on the microbiocidal activity of the ligands.

The complexes of the malonyldihydrazide of salicylaldelyde with lanthanides are prepared by the reaction of H\textsubscript{2}L and Lanthanide(III) chloride in anhydrous ethanol in the presence of NaOH\textsuperscript{110}. They are characterized by elemental analysis, IR and UV spectra and conductivity measurements.

Some macrocyclic condensation products of diphenylglyoxal-bis(S-alkylisothiocarbohydrazonato) nickel(II) with diethyl oxalate [80] and with diphenylglyoxal [81] are synthesized\textsuperscript{111}. These complexes are characterized by X-ray diffraction studies.
Template condensation of \( ML_2H_2O \) (\( M = \text{Cu, Ni; } H_2L = \text{CH}_2[\text{C}(O)\text{NHCH}_2\text{CH}_2\text{NH}_2) \_2 \) with nitroethane and \( H_2CO \) produce the complexes\(^{112} \) of the type \([82]\) and \([83]\). The structures are established from IR, \(^1H \) and \(^{13}C \) NMR and ESR data. The electrochemical oxidation of these complexes and their precursor complexes is studied. The effect of the structural parameters of the macrocyclic ligands is discussed in terms of the spectral and electrochemical properties of their complexes.

Some 14- and 20-membered tetraamide macrocyclic complexes with divalent metal ions are reported\(^ {113} \). They have been prepared via the template condensation of dicarboxylic acid (malonic, succinic, glutaric and phthalic acid) with primary diamines. All the complexes are soluble in most polar solvents. The complexes are characterized by IR, \(^1H \) NMR, mass, ESR electronic spectral studies and magnetic measurements. A square planar geometry for the complexes, \([ML]^2+\), where \( M = \text{Ni(II) and Cu(II)} \) or a tetrahedral geometry for \( M = \text{Co(II) and Zn(II)} \) are assigned.

Iron(II), cobalt(II) copper(II) and zinc(II) complexes of tetraza macrocyclic ligands \([84]\) are prepared by the condensation of 1,2-diaminoethane; 1,3-diaminopropane and o-phenylenediamine with methylacetoacetate or ethylacetoacetate in presence of metal salts at room temperature\(^ {114,115} \). The structure and bonding of macrocyclic complexes are studied from magnetic susceptibility measurements, IR, \(^1H \) NMR, mass, EPR and electronic spectra.
The stereochemistry around the metal ions is octahedral in which four of the coordination sites are occupied by nitrogen atoms of the macrocyclic ligand and the remaining positions are occupied by two chlorides.

Direct reaction of triethylenetetraamine and diethyloxalate in DMF in a 1:1 ratio yielded a 12-membered tetraaza macrocycle i.e. triethylenetetraamineoxamide. Condensation reaction of triethylenetetraamine and diethyloxalate in the presence of divalent hydrated transition metal chlorides \([M = \text{Mn(II), Co(II), Ni(II) and Cu(II)}]\) formed neutral complexes in methanol of similar ratio (1:1:1), the reaction yields ionic 12-membered macrocyclic complexes. Two molecules of water bound to the central metal ion in an octahedral environment while zinc maintains a tetrahedral geometry for being free from \(\text{H}_2\text{O}\). The IR spectral bands show that the two \(\text{C}=\text{O}\) groups of the oxalato species do not participate in coordination. The slight decrease in \(\nu(\text{C}=\text{O})\) suggests bonding of the nitrogen of the amide group to the metal ion. The complexes decompose on dissociation in DMSO.

Three Schiff base macrocycles such as 1,4,7,10-tetraazacyclododeca-5,6,11,12-tetraamineaceticacid-4,6,10,12-tetraene; 1,4,7,10-tetraazacyclododeca-5,6,11,12-tetraaminophenyl-4,6,10,12-tetraene, and 1,4,7,10-tetraazacyclododeca-5,6,11,12-tetraaminopyridyl-4,6,10,12-tetraene are prepared by the reaction of ethylenediamine with oxaamidediaceticacid, oxaamidediphenyl and oxaamide-dipyridyl respectively. Their complexes with 1st row transition metal ions, in different oxidation states (i.e. +2 and +3) are prepared and characterized by physicochemical and spectroscopic methods. The complexes of divalent metal ions are non ionic while those of trivalent metal ions appear to be 1:1 electrolytes. An octahedral geometry is proposed for all the complexes.

A novel, simple approach to the synthesis of macrocyclic dioxotetraamine ligands bearing pendant coordinating groups is described. Reduction of ethyl-benzopyran-3-carboxylate or its derivatives with sodium borohydride and then aminolyzing the products with triethylenetetraamine, without isolation of intermediates, leads to [85]. The ligands are
characterized by elemental analyses, IR, \(^1\)H NMR and mass spectra. These copper (II) complexes have axial symmetry according to their EPR spectra. Two redox processes appeared in the cyclic voltamogram at -0.1 to -0.8 V (vs. SCE); one is the oxidation of phenol and the other is the oxidation of a copper (II) complex to a copper (III) complex.

\[ \text{(4) R=R'=Br} \]

The synthesis of two coordination compounds \([86]\) of cobalt(II) and nickel(II) with a ligand resulting from template condensation reaction of 2,6-pyridinedicarboxylic acid with ethylenediamine is presented\(^{119}\). The formula of the complex is established from elemental analysis, electronic and IR spectra, as well as thermal analysis.

The syntheses of 3,4,10,22-tetraphenyl-1,2,5,6,8,9,12,13-octaazacyclotetradeca-7,14-dione-2,4,9,11-tetraene (DBDCH) \([87 \text{ and } 88]\) and their complexes with divalent metal ions are reported\(^{120}\) \([M = \text{Cu(II), Ni(II), Co(II), Zn(II), Cd(II) and Hg(II)}]\). All compounds are characterized by UV-visible, IR, \(^1\)H NMR and FAB MS spectroscopy.
The macrocycles 2,10-dimethyl-3,4,8,9,15-pentaazabicyclo-[9.3.1]-pentadeca-1(15),2,4,11,13-pentaene-5,7-dione [89] and 2,11-dimethyl-3,4,9,10,16-pentaazabicyclo [10.3.1] hexadeca-1(16),2,10,12,14-pentaene-5,8-dione [90] are prepared\textsuperscript{121} and characterized by elemental, IR and mass spectral data.

New macrocyclic compounds of copper with the ligand DPIH, DPDH, DCIH and DCPDH are synthesized\textsuperscript{122}, where DPIH = 2,6-diacetylpyridine-N-iminodiacetoylhydrazone\textsuperscript{[91]}; DPDH = 2,6-diacetylpyridine-N-pyridine-2,6-dicarboxyloylhydrazone, DCIH = 2,6-pyridinedicarboxyldichloride-N-iminodiacetoylhydrazone and DCPDH = 2,6-pyridinedicarboxyldichloride-N-pyridine-2,6-dicarboxyloylhydrazone. The \textit{in vitro} antimicrobial studies revealed that the macrocyclic complexes are potentially active against a few
bacteria and fungi and exhibit greater biocidal effect as compared to the ligand fragments.

Some tetraaza macrocyclic complexes involving the reaction of oxalic acid dihydrazide\textsuperscript{123,124} complexes have been reported. These complexes have been prepared by the reaction of dihydrazide complexes with diethyl carbonate and carbon disulphide yielding 5:6:5:6 annulated [92] macrocyclic complexes.

![Chemical structure 1](image1)

![Chemical structure 2](image2)

[91]

[92]

There are few complexes in which the monohydrazone complexes of benzil, diacetyl and glyoxal (all α,β-dicarbonyls) and their Schiff base metal complexes have been reported. K. Hussain Reddy et al\textsuperscript{125} have used the bis(benzil)ethylenediamine as precursor for the synthesis of a series of macrocyclic cobalt(II) complexes [93] with varying ring sizes (12-, 14-membered) by using template method. These complexes have been characterized by elemental analyses, conductance, IR and electronic spectra. The spectral data suggest octahedral geometry for all complexes. The cyclovoltametry results suggest that the cobalt complexes derived from aromatic diamines are reduced to more negative potentials.

R\textsubscript{1} = C\textsubscript{2}H\textsubscript{4}; 1,3-C\textsubscript{3}H\textsubscript{6}; 1,2-C\textsubscript{3}H\textsubscript{6}
R\textsubscript{2} = C\textsubscript{2}H\textsubscript{4}; 1,3-C\textsubscript{3}H\textsubscript{6}; 1,2-C\textsubscript{3}H\textsubscript{6}
1,4-C\textsubscript{4}H\textsubscript{6}; 1,2-C\textsubscript{6}H\textsubscript{6}; 3,4-CH\textsubscript{3}C\textsubscript{6}H\textsubscript{3}

[93]
1.5 Synthesis of Polynuclear Macrocycles:

Many studies have been published in the recent literature on binuclear compounds containing similar or dissimilar metal ions, owing to the role played by these metal centres in a variety of fields. The simultaneous presence of two metal ions with a suitable geometry give these complexes particular physicochemical properties which make them very interesting materials for theoretical studies and practical applications. Fleischer et al. reported the binucleating macrocyclic ligand [94] which was synthesized by the reaction of [32] with 1,2,4,5-tetraaminobenzene in methanol. The ligand on treatment with copper(II) or nickel(II) acetate in pyridine incorporates two metal ions with identical \( \text{N}_4^2^- \) donor sets.

\[
\text{M = Ni}^{2+}, \text{Cu}^{2+}
\]

[94]

A series of homobinuclear or heterobinuclear complexes [95 and 96] of copper(II), nickel (II) with acyclic and symmetric or asymmetric cyclic ligands derived from 2,6-diformyl-4- chlorophenol and the polyamines \( \text{NH}_2-(\text{CH})_2-X-(\text{CH})_2\text{NH}_2(X = \text{NH}, \text{S}) \) and/or \( \text{NH}_2-(\text{CH})_2\text{NH}_2 \) are reported together with their physicochemical properties and catalytic activity. Similarly, a family of binuclear macrocyclic complexes [13] and [19] has been conveniently obtained by the metal ion directed syntheses of (2,6-diformyl-4-methyl-phenol) with diamines.
Some 20- and 22-membered binuclear macrocyclic complexes\textsuperscript{130,131} of cobalt(II) and nickel(II) with the ligand [97] have been synthesized by the reaction of 3,6-dimethyl-4,5-diazaocta-3,5-diene-2,7-dione with 1,2-diaminoethane and 1,3-diaminopropane respectively. Polarographic studies of these macrocycles reveal two well-defined reversible reduction waves involving transfer of one electron in each step. In the first step of reduction, the complex is stabilized with metal ions in an ambivalent oxidation state and in the final step both the metal ions are reduced to +1 state. The IR, \textsuperscript{1}H NMR, EPR and electronic spectral studies, magnetic susceptibility and conductance values elucidate the overall geometry and stereochemistry of these complexes. An octahedral geometry around the metal ion is suggested for nickel, cobalt and zinc complexes, while a square planar geometry is proposed for copper complexes.

Rosen\textsuperscript{132} reported the binuclear macrocyclic complexes of [98] which were synthesized by the reaction of 1,4-dihydrazinophthalazine with

\[ M = M' = \text{Cu}^{2+}, \text{Ni}^{2+}, \]
\[ R = -(\text{CH}_2)_2^-, -(\text{CH}_2)_2-\text{NH}(\text{CH}_2)_2^-, -(\text{CH}_2)_2^-\text{S}(\text{CH}_2)_2^- \]
\[ X = \text{NH or S} \]
2,2-dimethoxypropane in presence of nickel(II) salts refluxing over a period of half an hour in dry methanol.

Two macrocyclic nickel complexes joined by common groups are of recent origin. A system comprising two units of macrocyclic ligand with S₂NO donor groups joined by a benzyl group has been effectively isolated by using a non-template synthesis. It forms binuclear complexes with copper(I) and copper(II) [99]. A hydroxo-bridged binuclear copper(II) complex of this ligand has been structurally confirmed from X-ray crystallography. A novel family of dimeric nickel(II) macrocyclic complexes separated by a persistent void, comprising pairs of 16-membered macrocycles held in an approximate face to face orientation by various bridging moieties including -(CH₂)ₙ- (n = 2-8), p-xylyl or duryl groups have been prepared by condensation reactions from monomeric macrocyclic precursor complexes containing suitable terminal substituents.
Another series of double ring octaaza macrocycle i.e. (bis-diazocyclam) [101] has been synthesized by the single step aminolytic condensation of the appropriate tetraester and a linear tetraamine in 1:2 molar ratio.

A binuclear macrocyclic complexes [102] is synthesized by the interaction of formaldehyde with tris-(3,6-dimethyl-4,5-diazaocta-3,5-diene-2,7-dihydrazone) dimetal (II) ions.
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The nickel(II) and iron(II) tetracyclathrochelates have spin triplet and spin quintet ground terms respectively, whereas the cobalt(II) complex has a spin doublet ground terms. Their spectra show some departure form the usual pattern observed for the respective metal ions in octahedral complexes and were interpreted in terms of trigonal prismatic or pseudo-trigonal prismatic approximation. Electrochemical studies of the binuclear clathrochelates reveal that they undergo two-step one-electron redox processes and their electrochemical behaviour is consistent with the proposed structure.

Some binuclear copper(II) complexes of some hexadentate phthalazinehydrazone ligands with strong antiferromagnetic exchange are synthesized. The OH-bridged copper(II) complexes exhibit strong antiferromagnetic exchange which is propagated via a superexchange mechanism through a bridging diazine (N-N) and OH-groups. When the OH-bridge is replaced by a pyrazolato bridge, a dramatic decrease in exchange is observed indicating the importance of hydroxide as a dominant super exchange bridge.

A new bimacrocyclic ligand, 6-(1,4,7,10-tetraaza-12-cyclotridecyl)-1,4,8,11-tetracyclotetradecane is reported in which 13- and 14-membered rings are linked together by a C-C bond. The absorption spectra and cyclic voltamograms showed that it has properties of both the 13-and 14-membered rings. Cyclic voltametry and controlled potential electrolysis showed that the complex can serve as an electrocatalyst for H₂O reduction to produce H₂.

A series of binuclear macrocyclic fluoroboro-bridged complexes of cobalt(II) and nickel(II) are synthesized by reacting BF₃ with M₂(DAADH)₂X₄ where, DAADH represent diacetylazinedihydrazone. The complexes are ionic in nature and the spectral data show the existence of fluoroboro groups as BF₂⁺ and BF₄⁻ species. Polarographic redox studies show three single-electron redox steps and the parameters, viz. $E_{1/2}^{1,2}$ values point to the macrocyclic structure of the complexes.
A new series of binuclear macrocyclic metal complexes were synthesized containing aza, amido and phenol moieties. The ligand 2-hydroxy-5-methyl-N,N-bis(aminotrimethylene)-1,3-benzenedicarboxamide reacted with Cu(ClO₄)₂ and NaOH yielding a binuclear copper complex which further reacted with 4-methyl-2,6-dibenzoylphenol and then demethylated by passing H₂S resulting the complex [104]. This ligand is reduced with NaBH₄ to give [105]. Upon recrystallization from methanol [105].H₂O is isolated. [104] and [105].H₂O are characterized by elemental analysis, mass, IR, and ¹³C NMR spectra. [105].H₂O crystallized as orthorhombic space group.
Capped trigonal prism coordination geometry in a cobalt(II) chelate with a 24-membered macrocyclic ligand in which two ethylenediamine-tetraacetate and two ethylenediamine groups are linked by amide bonds are studied\textsuperscript{141}.

Some 20-, 24-membered macrocyclic binuclear transition metal complexes are synthesized\textsuperscript{142} by template condensation of diethylenetriamine with dicarboxylic acids. The bonding and stereochemistry of the complexes \textsuperscript{[106]} are characterized by IR, \textsuperscript{1}H NMR, EPR and electronic spectral studies, magnetic susceptibility and conductance measurements. Each metal ion is coordinated by two amide nitrogens and two secondary nitrogen of the diethylenetriamine moiety, the fifth and sixth coordination sites are occupied by the anions.

\begin{align*}
Z &= \text{-CH}_2-, \text{-} \text{(CH}_2\text{)}_2- \text{ etc.} \\
M &= \text{Ni(II), Cu(II), Zn(II)} \\
X &= \text{Cl, NO}_3
\end{align*}

[106]

A series of binuclear macrocyclic complexes \textsuperscript{[107]} formed by the action of formaldehyde on (i) tetrathiocyanato-bis-(3,6-dimethyl-2,7-dioxo-4,5-diazaocta-3,5-diene-2,7-dihydrazone) dinickel(II), dicobalt(II) and diiron(II), (ii) perchlorate complexes of copper(II) and (III) corresponding tetrabromo and tetraiodo complexes of cobalt(II) have been reported\textsuperscript{143}. The structure of these complexes have been elucidated on the basis of IR and electronic spectra. These complexes exhibit two well defined diffusion controlled reversible or quasireversible polarographic reduction waves involving transfer of one electron at each step. The intermediate complexes contain the pair of metal ions in mixed oxidation state (M\textsuperscript{+1}, M\textsuperscript{+2}) and in the second step both the metal ions are reduced to +1 oxidation state. In the case
of iron(II), copper(II) complexes, a third wave is observed where one of the metal ions is stabilized in zero valent state indicating the macrocycle to be a strong H-acceptor ligand.

Cobalt(II) complexes\textsuperscript{144} of the type Co\textsubscript{2}L\textsubscript{2}X\textsubscript{4}, (where L represent 3,6-dimethyl-2,7-dioxo-4,5-diazaocta-3,5-diene-2,7-dihydrazine (BAADH) and X = Br\textsuperscript{-}, I\textsuperscript{-}, NO\textsubscript{3}\textsuperscript{-} and SCN\textsuperscript{-}) react with 2,3-butanedione to give 24-membered binuclear macrocyclic complexes [108]. The IR spectra of macrocyclic complexes show two sharp and strong bands near 1600 and 1680 cm\textsuperscript{-1} due to stretching vibrations of coordinated and uncoordinated C=\textsuperscript{N} groups respectively. Their magnetic and electronic spectral data indicate octahedral ligand field around the metal ions. The macrocyclic complexes are reduced in two steps; each step involves transfer of one electron. The -E\textsubscript{1/2} values are partially influenced by the axial ligands and are more pronounced for the second redox step.

Recently a series of homo and bimetallic trinuclear complexes derived from the reaction of benzildihydrazone and different carbonyl compounds [109] has been reported\textsuperscript{145-149}. The metal complexes of bis-benzildihydrazone has been used as metallo-ligands (precursor) and they are reacted with carbonyl compounds like salicylaldehyde and acetyl acetone in the presence of homo-, and hetero- metal salts. These have been characterized on the basis of different spectral studies and other physicochemical methods.
In the above complex the precursor metal occupies the inner N₄-chromophore core while the incoming homo- or hetero- metal ions occupies the outer core with "N₂O₂ chromophore." These complexes constitute an interesting class of compounds because of presence of two different or same metal ions in different crystal field generated by the coordinating atoms.

In the schiff bases derived from benzilmonohydrazine and different amines such as ethylenediamine, propylenediamine, o-phenylendiamine, the metal centre fixes up the free-NH₂ groups of the hydrazine constituent in such a position /orientation that they undergo cyclization reaction with ketones, diketones, aldehydes etc.yielding macrocyclic complexes [109].

However no work involving the exploitation of the -NH₂ groups to introduce another metal centre into the ligand frame work is reported so far. Attempts to synthesize homo-/hetero- bimetallic binuclear complexes by reacting the precursor complex bis-(benzilmonohydrazone) ethylenediamine nickel(II) complexes with different metal salts have been made. The results of such investigations leading to the establishment of structure of the resulted complexes are discussed. The condensation of aliphatic diamine such as H₂N(CH₂)ₙNH₂ (where n = 2, 3) with dicarboxylic acids in the presence of dicyclohexylcarbodiimide and 4-(dimethylamino)-pyridine results in new types of 14-,18- membered tetraamide macrocyclic ligand [110]. These compounds on undergoing reduction with LAH yields series of tetraazamacrocycles [111] which on reaction with transition metals yields corresponding metallo complexes. The ligands and their complexes have been characterized by elemental analyses, mass, IR, ¹H NMR, UV-Visible, EPR spectroscopic, molar conductance and magnetic moment data.
1.6 Reactions of Macrocyclic Complexes

Coordinated macrocyclic ligands are relatively kinetically inert even when they contain the most labile metal ions. Therefore, such systems are regarded ideal for the study of metal ion influenced ligand reactions since ligand dissociation during the course of the reaction is dramatically reduced.

1.6.1 Redox Reaction

Redox reactions employing catalytic and electrochemical methods as well as oxidative dehydrogenation are together the most widely studied group of cyclic ligand reactions. Oxidative dehydrogenation of a number of cyclic ligand complexes has been scanned using a variety of oxidizing substances, mostly the reactions involve the transformation of coordinated secondary amines to imine functions. The reverse process, i.e., hydrogenation of an imine to an amine is also facile in many macrocyclic complexes. Hydrogenation reactions have been usually achieved either catalytically or chemically. In the former case, hydrogenation is performed in presence of Raney nickel or metal catalysts and in the latter, reagents, such as, sodium borohydride are used. Electrochemical methods have been successfully employed for both hydrogenation and dehydrogenation reactions\textsuperscript{94}.

A number of cyclic products containing zero to three imine linkages have been obtained from the nickel(II) complex [34] by a combination of selective hydrogenation and chemical oxidation\textsuperscript{93,151}. Adopting similar redox
reactions a series of nickel(II) complexes with Curtis macrocyclic ligands having zero to four imine groups have been isolated\(^5\).

Available evidences show that redox reactions of these complexes are metal ion dependent with regard to the ease of the reactions as well as the nature of the products formed. These consideration are amply borne by the fact that the oxidation of the Curtis iron(II) complex [73] in acetonitrile by molecular oxygen stepwise yields [74] as the final product\(^{152,153}\). On the other hand, the analogous nickel(II) complex on oxidation\(^5,154\) leads to the tetraimine species [112]. It is generally observed that iron(II) complexes undergo more facile oxidative dehydrogenation than the corresponding nickel(II) analogues\(^{152,153}\). This is illustrated by the behaviour of the diene iron(II) complex [113], that reacts with oxygen in acetonitrile to give an intermediate tetraimine [114] which spontaneously tautomerizes to give [115]. The reactions are reminiscent of the well-known preference of iron(II) for ligands containing \(\alpha\)-diimine linkages\(^{155}\) compared to the characteristics of the analogous nickel(II) macrocycles\(^5\).

\[\text{N} \quad \text{V} \quad \text{V} \quad \text{M} \quad / \quad \text{N} \quad \text{N} \quad " \quad \text{rH} \quad -v / \quad \text{S} \quad \text{Fe} \quad \text{HN} \quad n \quad \text{N} \quad \text{N} \quad 2\text{Fe} \quad [112] \quad [113] \quad [114] \quad [115] \]

Oxidative dehydrogenation discussed above represent examples of introduction of unsaturation adjacent to nitrogen donor atoms. However, incorporation of unsaturation between adjacent carbon atoms in the backbone of a chelate ring are not unknown, though such reactions have been less frequently encountered. Besides imino linkages in the 5-membered and 6-membered chelate rings on the 2,4-pentanedione part of the macrocycle, [59], on reaction with bromine in acetonitrile yields [116], which contains an
additional C=C linkage localized in the 6-membered chelate ring$^{156}$. The copper(II) and nickel(II) complexes of the type $[117]$ undergo oxidative dehydrogenation to $[118]$ with $15\pi$ electrons on treatment with triethyltetrafluoroborate in acetonitrile with introduction of unsaturation between carbon atoms in 5-membered chelate ring$^{157}$. Subsequent reduction of $[116]$ with Sodium borohydride in ethanol gives the macrocycle $[117]$ with $16\pi$ electrons. Cyclic voltametric studies show that $[118]$, $[119]$ and $[120]$ are inter-convertible through a series of one electron reversible redox process. The complex $[120]$ possesses aromatic properties because of the presence of a stable $(4n+2)\pi$ electron ring system.

Several illuminating studies reveal that the mechanism of the ligand oxidative dehydrogenation processes involved a high oxidation state of the central metal atom$^{156-159}$. Oxidation of nickel(II)$^{159,160}$ and iron(II)$^{152,153}$ complexes proceed through the generation of the respective trivalent metal ion followed by intramolecular redox reaction in which the ligand is oxidized. There are instances of iron(III) macrocyclic complexes spontaneously
generating new imine linkages via oxidative dehydrogenation under appropriate conditions.

1.6.2 Thermodynamic Consideration

Macrocyclic complexes are thermodynamically and kinetically more stable than their open chain counterparts. These properties are inherent in the cyclic ligand systems and arise through a concerted action of such factors like chelate effect, enthalpy and entropy changes and are collectively regarded as macrocyclic effect. Thermodynamic studies demonstrate some of the important attributes of this effect.

The term 'macrocyclic effect' was first introduced in 1969 by Cobbiness and Margerum to highlight the large increase in stability constants for the macrocyclic complex $[\text{Cu}([14\text{ane-N}_4])^{2+}$ when compared to that of the equivalent complex ion with a noncyclic ligand $[\text{Cu}(2,3,2\text{-tet})]^{2+}$ [121]. In general terms, the macrocyclic effect refers to the decrease in Gibbs energy, $\Delta G^\circ$ for the metathetic reaction

$$[\text{ML}^{n+} \text{noncyclic} + \text{L cyclic} \rightarrow \text{ML}^{n+} \text{cyclic} + \text{L noncyclic}]$$

Considerable attention has been directed towards separating $\Delta G^\circ$ into its component enthalpic and entropic parts in order to understand the origin of the enhanced stability of macrocyclic complexes. However, the separation is difficult because the macrocyclic complexes display an enhanced kinetic inertness with respect to either their formation in aqueous solution or their degradation.

Earlier attempts are made to separate $\Delta G^\circ$ in order to evaluate $\Delta H^\circ$ involved indirect methods. Recently it has been possible to determine $\Delta H^\circ$ directly by calorimetry\textsuperscript{162,163}. 
The ΔH° for [Cu([14]aneN₄)]²⁺ was obtained from spectroscopic correlation and the enhanced stability of the macrocyclic complex was attributed to both enthalpy and entropy terms arising from a strong Cu-N interaction and a marginal loss in configurational entropy respectively. Hinz and Margerum have reported the ΔH° values for [Ni([14]ane-N₄)]²⁺ and their corresponding open chain precursors from spectrophotometric measurements in a series of papers. It was concluded that the macrocyclic effect was due to a dominant enthalpy contribution (12-14 Kcal/mol⁻¹) and an unfavourable entropy effect. The results were interpreted in terms of different degrees of solvation of the cyclic and noncyclic ligands and a favourable macrocyclic entropy arises due to the difference in the degree of hydration of macrocyclic and noncyclic ligand in aqueous solutions. This interpretation has been proved to be untenable by subsequent calorimetric studies by Paoletti et al. who have found that ΔH° for the same [Ni[14]ane-N₄]²⁺ is -20.3 Kcal mol⁻¹, i.e., 11 Kcal mol⁻¹ less than the previously reported value. The calorimetric data clearly shows a more favourable but small enthalpy effect.

Thermodynamic parameters for the reaction between Cu²⁺ and various macrocycles and their respective open chain counterparts have been obtained polarographically by Kodama et al. The stability constants for the 1:1 macrocyclic N₄ complexes are 10⁴ to 10⁷ folds greater than their respective open chain tetraamines. For the triamine complexes the stability constants do not show appreciable changes. The data show that, the enhanced stability with 12-, 13- and 14-membered cyclic ligands arises due to a more favourable entropy change. However, there are significant, though in some cases minor, contributions from the enthalpy changes. Ligand cyclization has major effects on the enthalpy change but minor effects on complex formation in triamines, [122], [123] and [124] as well as tetraamines.
Thermodynamic parameters for a number of macrocycles determined from direct calorimetric measurements\textsuperscript{173-176} show some differences for the same set of compounds whose thermodynamic data were determined by other methods such as polarography or potentiometry\textsuperscript{168-172}. However, the differences are not appreciable to alter the earlier conclusion\textsuperscript{164-170}.

1.6.3 Effect of Ring Size and Sequence

Thermodynamic consideration have been made with respect to the specificity of ring size and the metal ions radii. For a series of copper(II) and nickel(II) complexes with saturated macrocyclic ligands of different ring sizes it has been observed that of the $\Delta H^\circ$ value reaches a maximum at [14]ane-N$_4$ and falls off sharply on either side. In order to maximize the $\Delta H^\circ$ value, while maintaining the planar arrangement of the metal atom and the four donor atoms in the macrocyclic complex, the size of the metal ion must match closely the size of the aperture in the macrocyclic ligand in its minimum strain conformation. The normal Cu-N distance observed in tetraamine complexes (2.03-2.1 Å) gives the best matching of sizes in the above series with [14]ane-N$_4$ as the ligand. Since in high field octahedral coordination the Ni$^{2+}$ ion has almost the same size as Cu$^{2+}$ [2.07 Å for Ni[14]ane-N$_4$], the maximum $\Delta H^\circ$ is predictably observed for [Ni[14]ane-N$_4$]$^{2+}$. Therefore, it appears that the relative magnitude of the enthalpy of complex formation reflects the strength of metal nitrogen in-plane interactions and is related to electronic (d-d) transitions. The extremely low enthalpy of formation of [Ni[16]ane-N$_4$]$^{2+}$ is due to unfavourable conformation of free ligand and ring strain and a mismatch of ring size for [Cu[16]ane-N$_4$]$^{2+}$.

It is pertinent to rationalize the observed favourable enthalpy terms for macrocyclic complexes over the non-cyclic ligands. The non-cyclic ligand expands energy in arranging their donor atoms around the metal ion and hence experiences steric resistance during the process. On the other hand, the synthetically preoriented macrocyclic ligands have their donor atoms in appropriate positions for coordination and are able to exert the most effective metal donor interactions, particularly if the size of the metal ion is matched.
to that of the aperture in the macrocyclic ligand and have been demonstrated from spectrochemical as well as thermodynamic data.

The zinc(II) macrocyclic complexes show different result than copper(II) and nickel(II) complexes. For zinc(II) complex, the maximum $\Delta H^0$ with 14-membered macrocycle is no longer observed; instead the stabilities fall very slightly, more negative so that there is a marked increase in entropy resistance to complex formation as the size of the macrocyclic ring increases.

Thermodynamic parameters for some saturated pentaaza macrocycles [125], [126], [127] and [128] of various ring sizes with copper(II) and nickel(II) have been reported. The complexes appear to form distorted octahedra in solution with the macrocycles folded. In complexes of [127] and [128], one 6-membered chelate ring apparently lies in the equatorial plane. The thermodynamic data differ from the quadridentate macrocycles. Unlike the tetradentate $N_4$ macrocycles, in which $\Delta H^0$ values reach a maximum for 14-members, the enthalpy terms for nickel(II) pentaaza complexes, lie in the sequence, i.e., 15-member < 17-member < 16-member. The highest enthalpy value for 16-membered ring may be attributed to the presence of 6-membered chelate ring in the equatorial plane and for the 17-membered ring the macrocycle folds up to attain an intermediate conformation. In comparison to
their open chain counterparts [126], the nickel(II) pentaaza macrocycles are not distinctly enthalpy favoured. A gradual decrease of enthalpy value is observed for copper(II) complexes as ring size increases. From the available data, the quadridentate Cu(II)N₄ macrocyclic complexes are entropy governed, whereas pentaamine copper(II) macrocycles are governed by favourable enthalpy terms.

Values of logKₘₙ, ΔH and ΔS have been found potentiometrically or polarographically for the 1:1 reaction between zinc(II), cadmium(II), mercury(II) and lead(II) and macrocyclic polyamine ligands including 9-10 membered triamines, 12-16 membered tetraamines and 15-17 membered pentaamines [169]. The resulting data are compared with those for the relevant linear polyamines and consistently show larger stability constants and more favourable entropy terms with less favourable enthalpy terms as in copper(II) complexes. A survey of the tri-, tetra- and pentaamine systems indicates some correlations between macrocyclic effects and the ratio of the size of the metal ion to the size of the macrocyclic cavity.

1.6.4 Ring Sequence

Marked thermodynamic changes occur by the variation of chelate ring sequence around the metal ion in a macrocycle [179]. The enthalpy changes for the formation of some [Cu(macro)]²⁺ and [Ni(macro)]²⁺ complexes show that alternating sequence of 5- or 6-membered chelate rings is enthalpically preferred and the formation of (5,5,6,6) [129] systems in which both the 5- and 6-membered rings are adjacent is less exothermic by 19.2 KJ mol⁻¹. However, the (5,5,5,7) arrangement [130], causes a dramatic decrease in the enthalpy of formation. Furthermore, the formation of copper complexes [130] is less exothermic than that with the 12-, 13- and 15-membered tetraaza macrocycles indicating that the enthalpic advantage of the 14-membered cavity disappears with the introduction of a 7-membered chelate ring. The enthalpy term for the formation of a metal complex in solution depends on the relative contribution of several factors including gas phase bond enthalpy, solvation and bonding situation. The most symmetrical ligand cyclam [8] (5,6,5,6) exhibits the strongest coordination bonds since it is able to dispose
its donor atoms closer to the sites preferred by metal ions and hence the preferred $\Delta H^0$ value. On the other hand, the location of the nitrogen atom in much less symmetrical for the macrocyclic complexes [130] and formation of Cu-N bonds in much less favoured resulting in unfavourable enthalpy.

![Diagram of macrocyclic complexes]

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1.7 Electrochemical Studies of Macrocyclic Complexes

Electrochemical studies in the realm of coordination compounds\textsuperscript{180,181} and macrocyclic complexes have become a dominating aspect in recent years. Investigations are growing steadily on structurally different complexes to unveil the fundamental relations that govern chemical reactions accompanied by charge transfer. It can be emphasized that these works have explicitly established the ability of certain macrocyclic ligands to stabilize a wide range of oxidation states of the coordinated metal ions\textsuperscript{182-184}. Some of the important and prospective results relating to cobalt, nickel and copper macrocyclic complexes are discussed here.

(i) Nickel(II) complexes

The influence of structural and electronic parameters on the electrochemical redox behaviour of a range of quadridentate N\textsubscript{4} macrocyclic complexes of nickel(II) have been studied\textsuperscript{94,151}. Electrochemical studies\textsuperscript{94} on a range of neutral, [8] and [34], monoanionic [59] and dianionic nickel(II) macrocyclic complexes in acetonitrile demonstrate the facile one-electron oxidation to produce stable nickel(II) species. The neutral complexes form six coordinate nickel(III) complexes, whereas charged complexes invariably produce square planar nickel(III) species. The authenticity of nickel(III) states in these complexes has been established from ESR studies which show...
the unpaired electron to be localized on the nickel ion and not on the ligand skeleton. The electrochemical data further establishes that the relative stabilities of the Ni(macrocycle)$^{3+}$ species expressed by $E_{1/2}$ of the Ni$^{2+}$/Ni$^{3+}$ couple in acetonitrile are sensitive to the ring size, unsaturation and substitution and the $E_{1/2}$ values for 13- to 15-membered rings vary over a substantial range $\sim 0.4$V. The one electron reduction products of these macrocycles exist as either d$^8$ nickel(II) complexes or as metal stabilized anion-radicals, depending upon the nature of ligand unsaturation. The reduction products have been characterized from ESR spectra. In the case of neutral complexes, the ESR spectra fall into two categories. For the complexes of saturated ligands or for those containing isolated imine groups axial symmetric spectra are observed with $g_\perp < g_{||}$. Such spectra unambiguously suggest the presence of nickel(I) d$^9$ species. For complexes containing $\alpha$-diimine groups an isotropic ESR spectrum is observed without any hyperfine splitting and the 'g' value corresponds to that of free electron and the implications are that the unpaired electron in each of these systems is delocalized on the ligand. The one-electron reduction product of such a complex is best explained as nickel(II) coordinated to a stabilized anion-radical ligand. Several electrochemical studies on mononuclear nickel(II) complexes of tetraaza macrocyclic ligand reveal that the intermediate reduced species like nickel(I) or nickel(II) complexed to the ligand radical, react with carbonmonoxide to give paramagnetic penta-coordinated nickel(II) carbonyl adducts$^{185}$.

Polarographic behaviour of the nickel cyclic amines is of considerable interest since it is rather unusual for nickel compounds. With regard to the overall electrochemical reaction, two types of behaviour may be found. The first type is exhibited by compounds, which undergo a two-electron reduction yielding the metal as a product. Most nickel compounds fall into this class. The second type is characteristic of a class of compounds having a delocalized ground state, such as those formed by dithiolene and 1,2-diaminobenzene ligands. These compounds may be considered complexes of nickel(II) with radical anion ligands. Two or more reversible one-electron polarographic waves are obtained. The electronic change is localized mainly
on the ligand so that the valence state of the nickel remains essentially unchanged i.e., it is primarily the ligand that is reduced or oxidized rather than the metal.

(ii) Cobalt(II) Complexes

Some quadridentate macrocyclic complexes of cobalt(III) like [CoL(NO$_2$)$_2$]$^+$, where, L = cyclam, DIM (2,3-dimethyl-1,4,8,11-tetraazacyclo tetradeca-1,3-diene) and TIM containing saturated and unsaturated 14-membered rings have been subjected to polarographic studies in methanol$^{186}$. They show two one-electron reduction waves corresponding to Co$^{3+}$/Co$^{2+}$ and Co$^{2+}$/Co$^{+}$ couples. The results show that an increase in ligand unsaturation leads to an anodic shift of $E_{1/2}$ and has been attributed to greater nephelauxetic effect of the unsaturated ligand.

A series of unsaturated cobalt(II) complexes of the type, [Co(MAC)(CH$_2$CN)$_2$], where MAC represents a series of 14-membered macrocycles varying in their degree and position of ligand unsaturation and substitution have been investigated electrochemically$^{187}$. The $E_{1/2}$ values of the Co$^{2+}$/Co$^{+}$ couple vary in a predictable manner related to ligand unsaturation, the Co$^{3+}$/Co$^{2+}$ couple is, however, insensitive to these structural variations.

A series of fluoroboro-bridged cobalt(III) macrocycles have been subjected to polarographic studies$^{188,189}$. Both Co$^{3+}$/Co$^{2+}$ and Co$^{2+}$/Co$^{+}$ reduction couples in these macrocycles experience anodic shifts in comparison with the parent non-macroyclic complexes. The decrease of the electron density on the metal atoms by the >BF$_2$ bridge and greater nephelauxetic effect have been attributed as the major causes for the observed anodic shifts$^{188,189}$.

(iii) Copper(II) Complexes

The electrochemical behaviour of copper(II) complexes with 14-membered saturated tetraaza macrocycles is reported$^{190}$. Both anodic and cathodic electrode processes involve complicated mechanisms. However, a
cyclic voltammetry at high potential scan rates has allowed evaluation of the $E^{1/2}$ values for Cu$^{3+}$/Cu$^{2+}$ and Cu$^{2+}$/Cu$^+$ couples.

Change of the ligating atoms greatly influences the potentials of metallo complexes. Anodic shift greater than one volt in the half-wave potential of the Cu$^{2+}$/Cu$^+$ couple is observed from the tetraaza Cu(ms-(5,12)-Me$_6$[14]ane-N$_4$)$^{2+}$ complex to the tetrathioether complex$^{191}$ (Cu[14]ane-S$_4$)$^{2+}$. The presence of sulphur as donor atom in the coordinating sphere and coordination stereochemistry$^{192}$ constitute dominant factors in determining the Cu$^{2+}$/Cu$^+$ redox potentials.

Electrochemical investigations of copper(II) complexes$^{193}$ with 4-membered tetraaza macrocycles $^{[34]}$, $^{[131]}$, $^{[132]}$ and $^{[29]}$ which contain different structural features as well as varying degrees of unsaturation have been performed. The $E^{1/2}$ value for the Cu[6]$^{2+/1+}$ redox couple is appreciably less negative than for the Cu[31]$^{2+/1+}$ redox couple, suggesting that the reduction to give copper(I) cation is easier when copper(II) macrocyclic interactions ($\sigma$, in nature) are weaker. Moreover, the rearrangement of 5,5,6,6, chelate ring system of $^{[34]}$ to 5,5,5,7 of $^{[131]}$ makes the reduction to copper(I) easier. Comparison of the behaviour of the complexes with $^{[132]}$ and $^{[29]}$ emphasizes a second effect on the stabilization of copper(II) in tetraaza macrocyclic systems. The Cu(II)/Cu(I) redox change in the tetraene macrocycle $^{[29]}$ occurs at less negative potential than the diene system $^{[132]}$.

\[
\begin{align*}
\text{[131]} & \quad \text{[132]}
\end{align*}
\]

This difference has been explained on the basis of the argument that the copper(I), d$^{10}$ ion transfers electronic charge through a back-donation mechanism into the donor atom system provided it possesses orbitals of
appropriate type and energy. The situation is satisfied with the nitrogen atoms of the imine bonds. Therefore, the easier reduction of the copper(II) complex having four C=N groups speaks of more stabilization of the copper(I) complex, due to establishment of a more extended system of copper(I) -N, π-interaction.  

1.8 Biological Applications of Macrocycles

Macrocyclic complexes have become of monumental importance for their potential applications in diverse fields, the most important being their relation with naturally occurring systems. Though, macrocyclic complexes, identical to naturally occurring ones have not been achieved synthetically, however, our knowledge has widened and a better understanding on the role of metal ions in natural systems is emerging. Heme, chlorophyll and vitamin B_{12} are the three outstanding examples of natural macrocyclic complexes that are vitally important for creative evolution and continuation of life process.

The co-enzyme vitamin B_{12} is a cobalt(III) cyclic complex containing a bonded alkyl ligand in an axial position. Since its discovery a number of compounds containing cobalt(III)-alkyl moieties have been prepared and interest has centered on the factors influencing stabilization of the cobalt-carbon bond. Most of the model compounds capable of stimulation properties of vitamin B_{12} contain unsaturated nitrogen donors such as bis-(dimethylglyoximato)cobalt derivatives in the equatorial plane. It was believed that unsaturation in the equatorial ligand was essential for the formation of stable Co(III)-alkyl bonds. However, stable cobalt(III)-alkyl complexes of saturated macrocycles as cyclam have been isolated from photochemical reaction, which make it clear that neither unsaturation nor a macrocyclic ligand is a pre-requisite for the stabilization of cobalt(III)-alkyl bonds. Nevertheless, unusual redox properties arising from the incorporation of an unsaturated corrin ring in vitamin B_{12} and related co-enzymes are of considerable importance with regard to the biological functions of this important group of compounds.
The iron in cytochrome c, haemoglobin and myoglobin and cobalt in vitamin B₁₂ contain, besides the equatorial macrocyclic environments, an axial coordination position occupied by a heterocyclic base (viz. an imidazole derivative). Planar quadridentate macrocycles containing flexible side chains with appropriately positioned heterocyclic nitrogen donor groups have been synthesized. The side chains are sufficiently long to allow the attached nitrogen donors to coordinate axially with the metal ions. The iron(II) complex [133] provides an example of such a complex which has been synthesized and used as a model for the myoglobin and haemoglobin. Like the natural molecules, it reversibly binds molecular oxygen in solution and in solid state and combines with carbon monoxide more strongly than oxygen.

Porphyrrins and other macrocyclic complexes of cobalt(II) in the presence of slight excess of a coordinating base form low-spin 5-coordinate base adducts of the type, Co(por)B or Co(macro)B, (por = porphyrin, B = base, macro = macrocycle) which reversibly bind oxygen to form high-spin Co(macro)B(O₂) type of complexes. The binding of an axial fifth ligand leads to a square pyramidal arrangement, raising the dₓ² orbital above the dₓᵧ, thus resulting in the configuration (dₓ²)(dᵧ²)(dₓᵧ²)(dₓᵧ)¹. This latter configuration appears to be a necessary precondition for oxygenation. The scheme of oxygenation is considered as follows:

\[
\text{Co(macro)(B) + O}_2 \xrightarrow{\text{KO}_2} \text{Co(macro)(B)(O}_2\text{).}
\]

The nature of dioxygen coordinated complexes has been confirmed from ESR spectra.
Low temperature studies\textsuperscript{219-222} have shown that covalent attachment of an imidazole derivative to the heme group, as occurs in \textsuperscript{133} is not essential for reversible oxygenation. The iron(II) ions in the heme complexes undergo auto-oxidation to iron(III) after binding oxygen and the following mechanism is suggested\textsuperscript{223}. The reversibility is attained when there is a cavity to entrap the \( \text{O}_2 \) molecule and at the same time \( \text{Fe}^{II}\text{O} \)-\( \text{OFe}^{II} \) prevents the formation of oxygen bridged species\textsuperscript{223}.

\[
\text{Fe}^{II} + \text{O}_2 \leftrightarrow \text{Fe}^{II}\text{O} + \text{Fe}^{II} \rightarrow \text{Fe}^{II}\text{O} \rightarrow \text{OFe}^{II} \rightarrow \text{Fe}^{III} \]

Hæmoglobin is an ideal example of a reversible oxygen carrier system in which the heme groups occupy molecular cavities in the globin portion of the molecule\textsuperscript{225}.

Iron complexes with ligands, capable to enclose a bound \( \text{O}_2 \) molecule in a cavity of the organic ligand frame-work have been prepared\textsuperscript{223,225-227}. The synthetic porphyrin derivative iron(II) complex\textsuperscript{225,226} of the ‘picket fence’ ligand \textsuperscript{134} undergoes reversible oxygenation at room temperature in presence of various bases and is diamagnetic like oxyhaemoglobin. Structure of this complex with \( \text{N}\)-methylimidazole as the axial ligand shows the iron(II) ion to be in the plane of the porphyrin ring and the iron-oxygen bond has substantial double bond character\textsuperscript{228,229} and is bent in a manner predicted previously for oxyhaemoglobin\textsuperscript{230}.

![Diagram of complex structure](image-url)
A novel synthetic capped porphyrin complex of iron(II) [135] having an organic cavity above the porphyrin plane is reported\textsuperscript{227}. It forms a dioxygen adduct in the presence of heterocyclic base but the cavity size is unsuitable for entry of small solvent molecules.
REFERENCES


Chapter-I


Chapter-I


Chapter-I


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Chapter-I


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