ABSTRACT

The continued interest and quest in designing new macrocyclic ligands and their complexes stem mainly in view of their variety of applications. This interest was stimulated by the possibilities macrocycles offered to the creative chemist to investigate molecular recognition in new ways and therefore suggest ideas for the design and synthesis of novel complexes capable of performing useful functions. Among the macrocycles the synthesis of aza-macrocyclic compounds received considerable attention during the last few decades because of their relationship to biomimetic and catalytic systems and the applications of this type of chelating agents to biology and medicine. They have applications in modern clinical techniques such as magnetic resonance imaging, imaging with radioisotopes and radiotherapy, i.e., techniques where metal complexes with extreme kinetic and thermodynamic stability toward metal release are required. The whole thesis is divided in five different chapters.

First chapter gives a general introduction to macrocyclic complexes and the pioneering work done by eminent scientists. A systematic description of conventional methods of synthesis, the physical and chemical properties, reactivities, functionalities and
applications has been accounted on various types of macrocyclic compounds involving N, P, O, and S donor atoms. The effect of ring sizes, nature of the ligand donors, donor set, donor array, ligand conjugation, ligand substitution, number and sizes of the chelate rings, ligand flexibility and the ligand backbone to tailor specific metal ion or recognition of molecular species has been discussed. The applications of macrocyclic complexes in development of bioinorganic chemistry, therapeutic agents, medically important chemicals, synthetic ionophores etc. have also been highlighted.

Second chapter deals with the basic principles and theories of various techniques used in the characterization of the newly synthesized macrocyclic complexes viz., infrared spectroscopy, nuclear magnetic resonance spectroscopy, electron paramagnetic resonance spectroscopy, ultraviolet and visible spectroscopy, magnetic susceptibility and molar conductance measurements, elemental analyses, thermogravimetric analysis, job's method and antimicrobial activity.

Third chapter describes the synthesis and characterization of 14- and 16-membered octaazamacrocyclic complexes, Dichloro/nitrato [1,2,4,5,8,9,11,12-octaazacyclotetradecane] metal(II), [ML\textsuperscript{3}X\textsubscript{2}], (M =
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Co(II), Ni(II), Cu(II) and Zn(II); X = NO₃ or Cl) and Dichloro/nitrato [1,2,4,5,8,9,10,12,13-octaazacyclohexadecane] metal(II), [ML₂X₂], (M = Co(II), Ni(II), Cu(II) and Zn(II); X = NO₃ or Cl). These macrocyclic complexes were synthesized by reacting hydrazine, formaldehyde and 1,2-dibromoethane or 1,3-dibromopropane with metal ion in a 4:2:2:1 molar ratio. The low molar conductance values measured in DMSO suggest their non-electrolytic nature. The confirmation regarding the formation of macrocyclic framework in the complexes has been achieved by loss of absorption bands characteristics of NH₂ groups of the hydrazine moiety and the presence of ν(N-H) in the region 3210-3260 cm⁻¹ and appearance of proton resonance peaks in the regions, 6.86-6.94, 3.08-3.19, 2.90-2.95 and 1.80-1.90 ppm assigned to (C-NH-N), (N-CH₂-C), (N-CH₂-N) and (C-CH₂-C) protons, respectively in the IR spectra of the complexes and ¹H NMR spectra of Zn(II) complexes, respectively. The magnetic susceptibility data and the band positions in the electronic spectra of Co(II), Ni(II) and Cu(II) complexes ascertained the octahedral geometry of the macrocyclic complexes. However, the EPR spectra of the Cu(II) complexes show g∥ < 2.3 which indicate that they exhibit appreciable covalent character.

The fourth chapter discusses the synthesis and characterization of hexaazamacro cyclic complexes, Dichloro/nitrato [3,5:12,14-dipyridyl
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8,9:17,18-dibenzo-2,4,6,11,13,14-hexacyclooctadecane-1,6,10,15-tetraene] metal(II), [MLX2], (M = Co(II), Ni(II), Cu(II) and Zn(II); X = Cl or NO3), resulted from the template condensation reaction of o-phthalaldehyde and 2,6-diaminopyridine with metal ion in a 2:2:1 molar ratio. The elemental analyses obtained compliment the proposed stoichiometry of the complexes. The IR spectra of all the complexes do not show bands corresponding to amino or carbonyl groups, instead a strong intensity band appeared around 1610 cm⁻¹ assigned to the coordinated v(C=N). The characteristic ring vibrations of the pyridine moiety and the phenyl ring vibrations appeared at their estimated positions. The bands around ~1410, 1230 and 1015 cm⁻¹ indicate the presence of coordinated nitrate group in the complexes derived from metal nitrates. The ¹H NMR spectrum of [ZnL(NO₃)₂] shows a singlet at 8.08 ppm corresponding to the four equivalent imine protons, CH=N (4H). The spectrum shows a triplet (δH 8.05 ppm) and a doublet (δH 7.73 ppm) assigned to the para Ha and meta pyridyl Hb protons, respectively. A doublet and a triplet observed at δ 6.89 ppm and δ 7.26 ppm corresponds to H1 and H2 protons of phenyl moiety, respectively. However, the ¹H NMR spectrum of [ZnL(NO₃)₂] does not show any bands assignable to the uncondensed NH₂ and CO moieties of 2,6- diaminopyridine and o-phthalaldehyde supporting the formation of macrocyclic framework.
The EPR spectra of the Cu(II) macrocyclic complexes show a broad signal in which $g_{||} > g_z$ suggesting that $d_{z^2}$ is the ground state and the $G$ values of 2.00 and 1.91 for $[\text{CuL(NO}_3\text{)}_2]$ and $[\text{CuLCl}_2]$ complexes suggest the exchange interaction between copper centers. The electronic spectral and magnetic moment data of Co(II) and Ni(II) complexes indicate a perfect octahedral geometry around the metal ion while Cu(II) complexes show a distortion in the octahedral geometry.

The fifth chapter describes the synthesis of 16-membered tetraazamacroyclic complexes of the type, $[\text{MLX}_2]$, $[\text{M = Co(II), Ni(II), Cu(II) and Zn(II); L = 3,4;7,8;11,12;15,16-tetrazeno-2,5,10,13-tetraazacyclohexadecane-1,5,9,13-tetraene and X = Cl or NO}_3\text{]}$. The complexes were synthesized from Dichloro/nitrato bis(o-phenylenediamine) metal(II) (A) obtained from o-phenylenediamine and MX$_2$·nH$_2$O by reacting with o-phthalaldehyde (1:2 molar ratio) in MeOH solution. However, the ligand $[\text{L}]$ has been synthesized by demetallation procedure. The preliminary information regarding the formation of ligand and their complexes has been obtained by the absence of bands around ~3400 cm$^{-1}$ and 1650 cm$^{-1}$ corresponding to $\nu$NH$_2$ and $\delta$NH$_2$ for free primary diamine and the absence of band ca ~1700 cm$^{-1}$ characteristic of $\nu$(C=O) of aldehydic moiety and appearance of a strong intensity band at 1620 cm$^{-1}$ attributable to $\nu$(C=N) in their IR
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spectra suggesting the condensation of amino group by aldehydic group. A negative shift of about 20-30 cm\(^{-1}\) indicates the involvement of imine nitrogen in coordination to metal ions. The thermogravimetric analysis results account for the relative stabilities of Ni(II) and Cu(II) complexes and the presence of coordinated chloride and nitrate ions. Analytical data correspond to stoichiometry as \([M(C_{28}H_{20}N_{4})X_{2}]\) for the complexes. The electrical conductance of soluble complexes measured in DMSO show their non-electrolytic nature. The Job's method of continuous variation has been used to determine metal to ligand ratio for copper and cobalt complexes which appear at \(\lambda= 600\) and 500 nm respectively. The same profile was observed when the diagram was constructed at different wavelengths. The bands observed in the electronic spectra of Co(II), Ni(II) and Cu(II) complexes indicate the octahedral geometry around the metal ions. The observed magnetic moments for Co(II), Ni(II) and Cu(II) complexes fall in agreement with their electronic spectral data. A singlet at 88.05 ppm in the \(^1\)H NMR spectrum of \([ZnLCl_2]\) complex further corroborates the IR spectral findings conforming that the condensation between primary amine and a carbonyl group has occurred leading to the formation of a macrocyclic framework. The spectrum further shows four multiplets at 86.89, 87.20, 87.31 and 87.50 ppm assignable to the protons of the benzenoid rings.
However, a slight upfield shift has been noticed in free macrocyclic ligand in $^1$H resonances. The antibacterial activity performed on complexes of Co(II), Ni(II), Cu(II) and Zn(II) against *Escherchia coli*, *Staphylococcus aureus* and *Corynebacterium diphtheriae* was studied. DMSO was used as a negative control and Streptomycin as a standard drug. The results of this study reveal that all the complexes are active against these microorganisms.