SYNTHESIS AND REACTIVITY OF METAL CHELATES WITH BIOLOGICALLY ACTIVE DONOR MOLECULES

ABSTRACT

Thesis Submitted for the Degree of

Doctor of Philosophy

In

Chemistry

By

Afshan Jabeen

Department of Chemistry
Aligarh Muslim University
Aligarh-202002 (India)

1993
The importance and significance of the metal ion chemistry of macrocyclic ligands cannot be overemphasized. The macrocyclic ligands incorporating nitrogen or sulphur or both nitrogen and sulphur donor atoms are of interest because of their potential for providing molecules capable of mimicking various aspects of macromolecular biological system. The design and synthesis of multidentate macrocyclic ligands containing coordination sites for binding several guest species such as hard and soft metal cations is of considerable interest.

Dicopper complexes of a series of binucleating macrocycles such as haemocyanine and cytochrome C oxidase have been used as model of the active centre of some biological metalloenzymes. The chemistry of macrocyclic ligands and its exciting applications has prompted the study undertaken in the present work. An introduction to the same has been described in the first chapter of the thesis.

In the present work several new macrocyclic ligands have been synthesized with a view to prepare complexes which would be helpful in elucidating several aspects of the macromolecular biological systems.
In the second chapter of this project three new types of macrocyclic ligands, 7,12-diamino-1,4,8,11-tetraazacyclotetradeca 8,11-diene ($L_1$), 9,11-dimethyl-1,4,8,12-tetraazacycloptadeca-8,12-diene-7,13-dione ($L_2$), 14-Amino-3-pyridyl-1,4,8,11-tetraazacyclotetradeca-1,3-diene-5-one ($L_3$) and a simple Schiff base ligand N,N'-di-2-(3-pyridyl-1,2,4-triazol-5-yl)ethyl ethylene diamine ($L_4$) derived (a) by the condensation reaction of 4,7-diazadecanediamide with acetylacetone and ethylenediamine (b) by the condensation reaction of 4,7-diazadecanediamide with isoniazid in 1:1 and 1:2 molar ratios have been prepared.

Some first row transition metal ions form the complexes in a 1:1 (Metal : Ligand) ratio with the ligand $L_1$. Molar conductance values of the complexes reveal that the bivalent metal ions are 1:2 electrolytes while complexes of the trivalent metal ions are 1:1 electrolytes in nature. An octahedral geometry has been suggested for Cr(III) and Fe(III) complexes whereas the bivalent metal ions have a tetrahedral geometry. The lanthanide (III) complexes of the above ligands have also been synthesized and characterized by elemental analysis, IR, $^1$H NMR spectra and magnetic moment measurements. The complexes are 1:1 electrolyte in DMSO and are hexacoordinated with an octahedral geometry.
Another series of the complexes of first row transition metal chlorides with the ligands $L_3$ and $L_4$ have also been synthesized. Bivalent metal complexes are 1:2 electrolytes while the trivalent metal complexes are 1:1 electrolytes in DMSO. $^1$H NMR spectra of the ligands and their complexes show a downfield shift after coordination suggesting coordination through the nitrogen atoms of macrocyclic ligands. An octahedral structure has been suggested for Cr(III) and Fe(III) complexes whereas the Cu(II) complexes are square planar. A tetrahedral geometry has been proposed for Mn(II), Co(II), Ni(II) and Zn(II) complexes with the above ligands.

In the third chapter the preparation of three new Schiff base ligands 1,3-(5-chloro-2-hydroxyphenyl)phenyl methylene amino)propane ($L_5$),1,2-(5-chloro-2-hydroxyphenyl) phenyl methylene amino) ethane ($L_6$) and 2-(5-chloro-2-hydroxy -phenyl)phenyl methylene amino)pyridine ($L_7$) derived from the condensation reaction of 5-chloro-2-hydroxybenzophenone with propanediamine, ethylenediamine and 2-aminopyridine has been described. The complexes of these ligands with Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) have been characterized by elemental analysis, magnetic susceptibility measurements and electronic and infrared studies.
Fe(III) and Cr(III) complexes of $L_5$ are soluble in DMSO. The molar conductance values of the complexes suggest a 1:1 electrolytic nature. On the basis of electronic spectra and magnetic moment measurements an octahedral geometry has been proposed for all the complexes with the above ligands. The magnitude of the nephelauxetic parameter $B$ indicates a low degree of covalency in these complexes.

In the case of ligand $L_6$ also only complexes of trivalent metal ion are soluble in DMSO and are 1:1 electrolyte in nature. All the complexes have an octahedral geometry except Co(II) and Ni(II) complexes which presumably have a tetrahedral geometry.

In the case of ligand $L_7$, all the trivalent and bivalent metal ions form the complexes in 1:2 (Metal : Ligand) ratios. The complexes are soluble in DMSO and are ionic in nature. An octahedral geometry has been proposed for all the complexes on the basis of their magnetic moments and characteristic electronic assignments.

The synthesis of two series of first row transition metal chloride complexes with the ligands, 5-Acetoxy-4-(2-hydroxyphenyl)6-methyl-1,4-dihydropyrimidine ($L_8$) and sulphoxide derivative of 5-Acetoxy-4-(2-hydroxyphenyl)6-methyl-1,
4-dihydropyrimidine \((L_9)\) have been carried out and is described in the fourth chapter of this project.

The divalent and the trivalent metal ions form the complexes in 1:2 and 1:1 \((\text{Metal} : \text{Ligand})\) ratios with the ligand \(L_9\). An octahedral geometry has been proposed for Fe(III) and Cr(III) complexes, while the Cu(II), complex has square planar geometry around the metal ion. A tetrahedral geometry has been proposed for Mn(II), Co(II), Ni(II) and Zn(II) complexes with the above ligand. The ligand field parameters \(\Delta Q, B\) and \(p\) have also been calculated for these complexes. The magnitude of nephelauxetic ratio \(p\) indicates a low degree of covalency for the complexes.

In the same chapter the synthesis and characterization of another series of transition metal chloride complexes of ligand \(L_9\) have also been described. The bivalent metal ions form the complexes in 1:2 \((\text{Metal} : \text{Ligand})\) ratio while those of trivalent metal ions form the complexes in 1:1 \((\text{Metal} : \text{Ligand})\) molar ratio respectively. The magnetic moment values and electronic assignments are indicative of an octahedral geometry for all the complexes. The ligand field parameters \(\Delta Q, B\) and \(p\) have also been calculated for the complexes. The value of \(p\) indicates that the covalent character of metal ligand bond is low.
In the fifth chapter of this project, the synthesis and characterization of the complexes of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) with tetradeptate, 2,4,8,10,11-hexaaaza-3,9-bis-4-pyridotetradeca-3,9,12,14-tetraene \( \text{L}_{10} \) derived from isonicotinic acid hydrazide, acetylacetone and propanediamine has been described. Molar conductance values of these complexes measured in DMSO indicate their non ionic nature. On the basis of magnetic moment values and electronic spectral assignments an octahedral geometry has been proposed for all the complexes.

In the same chapter the synthesis and characterization of another series of 1:1 complexes of above ligand with lanthanide (III) chlorides have also been described. These complexes have been characterized by elemental analysis, I.R., u.v-visible spectral studies and magnetic moment measurements. The magnetic moment and electronic spectra suggest that the lanthanide ions are 7-coordinated with an octahedral geometry. The positive values of bonding parameter \( b^k \) and covalency parameter \( \% \) indicate a moderate covalent character of metal ligand bond. The molar conductance values of all the complexes in DMSO reveal that all the complexes are non ionic in nature.
In the last chapter the synthesis of a new macrocyclic ligand 1,4,8,11-tetraazacyclotetradeca-5,7,12,14-tetramethyl- 2,3,9,10-tetrathione ($L_{11}$) has been described. This ligand $L_{11}$ has been prepared by the reaction of dithiooxamide with acetylacetone in 1:1 molar ratio. New transition metal complexes of type ($M L_{11} Cl_2$) where $M$=Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) and ($M L_{11} Cl_2) Cl$ where $M$=Fe(III) and Cr(III), have been synthesized. The molar conductance value of the complexes reveal that the complexes of bivalent metal ions are non ionic while those of trivalent metal ions are 1:1 electrolyte in DMSO, the electronic spectra and magnetic moment are suggestive of an octahedral geometry. On the basis of 10 $Dq$, values it is concluded that the complexes of trivalent metal ions are more stable than that of divalent metal ions.

The macrocyclic Schiff base on reaction with lanthanide (III) chlorides yielded the complexes of general formula ($M L_{11} Cl_3$). The covalent nature of metal ligand bond is indicated by their molar conductance values measured in DMSO. The magnetic moment and electronic spectra also suggest heptacoordinated lanthanide (III) ions.