

## Studies on the Complexes of Transition Metal Ions with Macrocyclic Ligands Containing Nitrogen, Oxygen and Sulphur

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The synthesis of macrocyclic ligands and their metal complexes is a growing area of research in inorganic and bioinorganic chemistry in view of their presence in many biologically significant systems. The synthesis and study of macrocycles have undergone tremendous growth in recent years and their complexation chemistry with a wide variety of metal ions have been extensively studied. Macrocyclic metal complexes are considered to be the model of metalloporphyrins and metalocorrins due to their intrinsic structural properties.

Macrocycles find wide applications in medicine, cancer diagnosis and in treatment of tumors, in metal ion techniques and treatment of kidney stone. Macrocyclic ligands have been used successfully for diverse processes such as separation of ions by transport through artificial and natural membrane, liquid-liquid or solid-solid phase transfer reaction, preparation of ion-selective electrodes, isotope separation and in the understanding of some natural processes through mimicry of metalloenzymes.

The reaction of thiobarbituric acid with diethylenetriamine and diethyl oxalate in a 2:1:1 molar ratio afforded the formation of [exo O<sub>2</sub>] cyclam, ligands 1,4,7,9,12-pentaaza-10,11-dioxo-8,9,12,13-bis-(1'-oxo-3'-thio-2'-hydroypyrimidine)-trideca-7,13-diene (L<sup>1</sup>), similarly the formation of the ligand, 1,4,7,9,12-pentaaza-10,11-dioxo-8,9,12,13-bis-(1',3'-dioxo-6,6-diethyl-2'-hydroypyrimidine)-trideca-7,13-diene (L<sup>2</sup>), was accomplished when 5,5-diethylbarbituric acid was reacted with diethylenetriamine and diethyl oxalate in a 2:1:1 molar ratio. The ligand 1,4,7,9,12-pentaaza-10,12-dioxo-8,9,13,14-bis-(1'-oxo-3'-thio-2'-hydroypyrimidine)-tetradeca-7,14-diene, (L<sup>3</sup>) was synthesized by the reaction of thiobarbituric acid with diethylenetriamine and diethyl malonate, while the ligand 1,4,7,9,13-pentaaza-10,12-dioxo-8,9,13,14-bis-(1',3'-dioxo-6,6-diethyl-2'-hydroypyrimidine)-tetradeca-7,14-diene (L<sup>4</sup>) was formed by the reaction of 5,5-diethylbarbituric acid with diethylenetriamine and diethyl malonate in the 2:1:1 ratios. These macrocyclic ligands have been characterized by elemental analysis, IR

and  $^1\text{H}$  NMR spectroscopic data. The complexes of these ligands with Cr(III), Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) ions have been synthesized. They are characterized by elemental analysis, IR,  $^1\text{H}$  NMR, EPR, UV-visible spectral data, magnetic susceptibility and conductance measurements.

The conductivity values ( $52\text{--}71\text{ ohm}^{-1}\text{ cm}^2\text{ mol}^{-1}$ ) suggest that the complexes of divalent metal ions are 1:1 electrolytes while those of trivalent metal ions ( $11\text{--}27\text{ ohm}^{-1}\text{ cm}^2\text{ mol}^{-1}$ ) are non-electrolytes. On the basis of electronic spectra and magnetic moments the chromium(III) and iron(III) complexes have been assigned octahedral geometry, while the divalent metal complexes are proposed to be tetrahedral, excepting the nickel(II) and copper(II) complexes which are proposed to have a square planar geometry. All these ligands and their complexes have been screened against Gram-positive bacteria, *Staphylococcus aureus* and *Escherichia coli* and they have been found to inhibit the growth of bacteria.

The new ligands, 1,5,8,12-tetraaza-4-(1',1'-dimethylethyl)-2-(1'',1'',2'',2'',3'',3'',3'' heptafluoropropyl)-9,11-(dimethyl)-cyclotetradeca-1,4,8,11-tetraene ( $\text{L}^5$ ), and 1,5,9,13-tetraaza-4-(1',1'-dimethylethyl)-2-(1'',1'',2'',2'',3'',3'',3''-heptafluoropropyl)-10,12-(dimethyl)-cyclohexadeca-1,4,9,12-tetraene ( $\text{L}^6$ ), have been prepared by the reaction of 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione with ethylenediamine and acetyl acetone and 1,1,2,2,3,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione with 1,3-diaminopropane and acetylacetone, respectively. Their complexes with Cr(III) Mn(II), Fe(III), Co(II), Ni(II), Cu(II) and Zn(II) ions have also been synthesized and characterized by elemental analyses, magnetic susceptibility measurements, molar conductances, IR, EPR,  $^1\text{H}$  NMR and UV-Visible spectra. The molar conductance values show that the complexes of Fe(III) and Cr(III) are 1:1 electrolytes, while the Ni(II) and Cu(II) complexes are 1:2 electrolytes and those of Mn(II), Co(II) and Zn(II) appear to be non-ionic. An octahedral structure has been proposed for all these complexes except the of Cu(II) and Ni(II) complexes, which appear to be square planar.

In order to investigate the coordination behavior of these ligands to the metal ion, spectroscopic studies suggested that an octahedral geometry for the trivalent and bivalent metal complexes. The b values indicate a considerable orbital overlap in the metal-ligand bond. All of the compounds inhibit the growth of gram positive, *Staphylococcus aureus* and gram-negative *Escherichia coli* bacteria.

The ligands, disodium salts of thiobarbituric acid ( $\text{Na}_2\text{L}^7$ ) and 5,5-diethylbarbituric acid ( $\text{Na}_2\text{L}^8$ ) and their transition metal complexes of the type  $[\text{M}_2(\text{L}^7)_2]$  and  $[\text{M}_2(\text{L}^8)_2]$ , where  $\text{M} = \text{Mn(II)}, \text{Co(II)}, \text{Ni(II)}, \text{Cu(II)}, \text{Zn(II)}$  have been synthesized. In the present work displacement method is employed for the synthesis of dithiocarbamates. The ligands have been characterized by elemental analysis and IR spectra while their transition metal complexes have been characterized by IR, UV-visible spectroscopic studies, magnetic moments, elemental analysis and molar conductance measurements.

The spectroscopic studies indicate that the ligands ( $\text{L}^7$ ) and ( $\text{L}^8$ ) form binuclear dithiocarbamate macrocyclic complexes with the divalent metal ions. The molar conductivity data suggest that all the complexes are non-electrolytes. The magnetic moment values and electronic spectra reveal that the Ni(II) and Cu(II) complexes are square planar, while Mn(II), Co(II) and Zn(II) complexes are tetrahedral. The C-N stretching frequency is also diagnostic of the chelation of dithiocarbamate groups. The thioureide band appears at  $1440\text{--}1482\text{ cm}^{-1}$ , which is intermediate between  $\nu(\text{C}=\text{N})$  band ( $1640\text{--}1690\text{ cm}^{-1}$ ) and  $\nu(\text{C}-\text{N})$  band ( $1250\text{--}1360\text{ cm}^{-1}$ ) indicating the partial double bond character of carbon-nitrogen bond. The different bands observed between  $1130\text{--}1290\text{ cm}^{-1}$  region are due to coupled vibration of the  $\text{NCS}_2$  group.

All the complexes have been found to exhibit antimicrobial activity against *Staphylococcus aureus* (gram-positive bacteria) and *Escherichia coli* (gram-negative bacteria). The complexes showed better antimicrobial activities as compared to the corresponding ligands.

Two new macrocyclic ligands, 1,4,10,13-tetraazacyclooctadeca-4,9,13,18-tetraene, ( $\text{L}^9$ ) and 1,4,10,13-tetraza-2,3,11,12-bis-(phenyl)-cyclooctadeca-4,9,13,18-tetraene, ( $\text{L}^{10}$ ) have been synthesized by the reaction of glutaraldehyde with ethylenediamine, and glutaraldehyde with *o*-phenylenediamine in a 2:2 molar ratio, respectively. Their transition metal complexes of the type,  $[\text{ML}]\text{Cl}_2$ , where  $\text{L} = \text{L}^9$  and  $\text{L}^{10}$ ,  $\text{M} = \text{Mn(II)}, \text{Co(II)}, \text{Ni(II)}, \text{Cu(II)}, \text{Zn(II)}$  and  $[\text{M}'\text{LCl}_2]\text{Cl}$ , where  $\text{M}' = \text{Cr(III)}$  and  $\text{Fe(III)}$  have also been prepared. In the absence of metal ions the yield of macrocyclic ligands are very low. The complexes were synthesized by the template reaction. In template synthesis the metal ion facilitates the formation of macrocyclic ligands by arranging the ligand precursor fragments in the coordination sphere.

The complexes were characterized by elemental analyses, molar conductance measurements, IR,  $^1\text{H}$  NMR and UV-visible spectra. The observed molar conductance values show that the chromium(III) and iron(III) complexes are 1:1 electrolytes, whereas the divalent metal complexes are 1:2 electrolytes. On the basis of electronic spectral studies and conductance measurements an octahedral structure has been proposed for Cr(III) and Fe(III) complexes. The Mn(II) and Co(II) complexes possess a tetrahedral

geometry, while Ni(II) and Cu(II) complexes are square planar.

The formation of the ligands is supported by the disappearance of  $\nu(\text{C}=\text{O})$  in the 1630–1670  $\text{cm}^{-1}$  region and the appearance of  $\nu(\text{C}=\text{N})$  absorption bands in the 1590–1610  $\text{cm}^{-1}$  region. The appearance of an absorption band in the 310–420  $\text{cm}^{-1}$  region in far IR spectra of the complexes suggests the formation of metal–nitrogen bond. In the case of trivalent metal complexes the two chlorine atoms appear to be covalently bonded while the third one is present outside the coordination sphere. Bands observed at 265–320  $\text{cm}^{-1}$  region in the complexes are assigned to  $\nu(\text{M}-\text{Cl})$  mode.

The results of antibacterial screening of the ligands and their complexes against gram (+) *Staphylococcus aureus* and gram (–) bacteria *Escherichia coli* indicate that compare to the ligands the metal complexes inhibit the growth of bacteria.