

# Preparation and Properties of Macrocyclic Ligand and Its Complexes Derived From Trimethoprim and L-Tyrosine

Ms B.Mary Juliet<sup>1</sup> Dr M.Amaladasan<sup>2</sup>

<sup>1</sup>Research Scholar Department of Chemistry,

St.Joseph's college (Autonomous), Tiruchirappalli-620002(T.N), India

mjuliet1830@gmail.com

**Abstract:** Macrocyclic complexes of Mn<sup>II</sup>,Co<sup>II</sup>,and Cu<sup>II</sup> using a macrocyclic ligand derived by the condensation of Trimethoprim and L-Tyrosine by elemental analysis, molecular mass determination ,conductance and the spectral studies like IR, Electronic spectra.The spectral data suggest that the complexes of metal chlorides have octahedral geometry and that of metal sulphates have tetrahedral geometry.

**Key words:** Trimethoprim, macrocyclic Schiff-base complexes,L-Tyrosine, Mn<sup>II</sup>, Co<sup>II</sup> and Cu<sup>II</sup>.

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## 1. INTRODUCTION

Coordination Chemistry of macrocyclic ligand has been a fascinating area of current research in inorganic chemistry all over the world due to its wider applications and the unusual binding abilities<sup>1-4</sup>.From the literature survey,it is found that a great deal of interest has been shown in pyrimidine and its derivatives due to their biological importance as constituents of nucleic acids<sup>5</sup>. In this work,incorporation of pyrimidine moiety into the macrocyclic frame work is found to enhance the rigidity and binding ability of the ligands towards the transition metal ions<sup>6</sup>.A Novel synthesis of N<sub>8</sub>- macrocyclic ligand of pyrimidine based trimethoprim has been reported.The present work also deals with the interaction of Mn<sup>II</sup>,Co<sup>II</sup> and Cu<sup>II</sup> metal ions with the ligand.

The study of stereochemistry and chemical reactivity of the Coordination compounds of the macrocycles will help us to understand the relationship between chemical structure and biological activity of macrocycle<sup>7</sup>.

## 2. MATERIALS AND METHODS

### 2.1 Macrocyclic ligands

All the reagents used in the preparation of macrocyclic Ligands and their metal complexes were of reagent grade(Merck).The solvents used for the synthesis of macrocyclic ligands and metal complexes were distilled before use.

All other chemicals were of AR grade and used without further purification.The microelemental analysis was carried

out using Heraeus CHN-Rapid analyser.

IR spectra (KBr) on a bruker IFs-60-VFT-IR Spectrometer. The electronic spectra (methanol) were on the Beckman model 25 spectrometer. The conductivity was measured on a conductivity bridge at 25<sup>o</sup>C using dip type platinised platinum electrode.

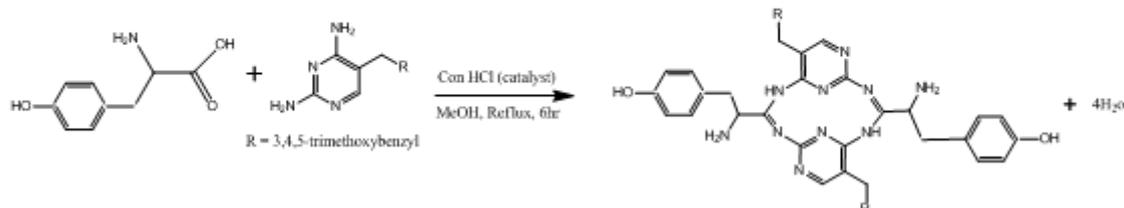
### 2.2 Synthesis of Macrocyclic Ligand

Trimethoprim and L-Alanine were condensed to give macrocyclic ligand by the reported method<sup>8</sup>. Trimethoprim (0.01m) was dissolved in methanol(50 ml) solvent.L-Tyrosine(0.01 m) was dissolved in methanol (50 ml) solvent. Both the solutions taken into round bottom flask. Then add two drops of Con.Hcl. The reaction mixture was allowed to reflux up to six hours at 60<sup>o</sup>C.It was then concentrated to half of the volume and set aside for two days. The resulting white crystals were washed with methanol and ether then dried. The crude recrystallised from methanol.

### 2.3 Synthesis of Macrocyclic complexes

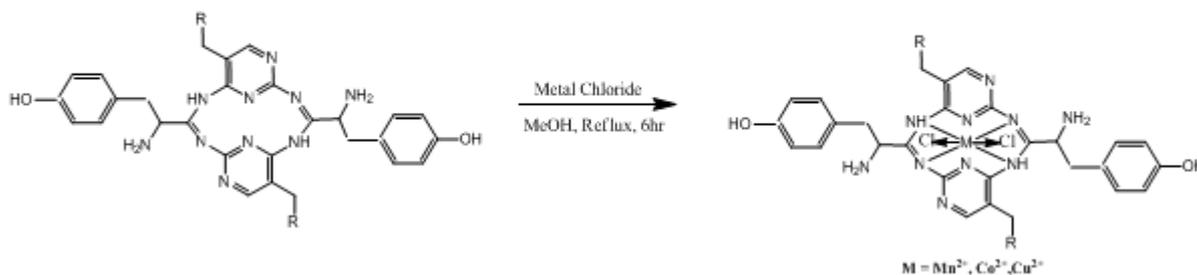
A solution of the hydrated metal chloride and metal sulphate (0.01m) in methanol (50 ml) was added to a round bottom flask containing (0.01) solution of the macrocyclic ligand in methanol (50 ml) the mixture was reflux up to six hours. It was then concentrated to half of the volume and set aside for two days. The microcrystalline compound which separated out was filtered washed with methanol-ether mixture (1:1) and dried in vacuum over anhydrous calcium chloride<sup>9-10</sup>.

Scheme:1



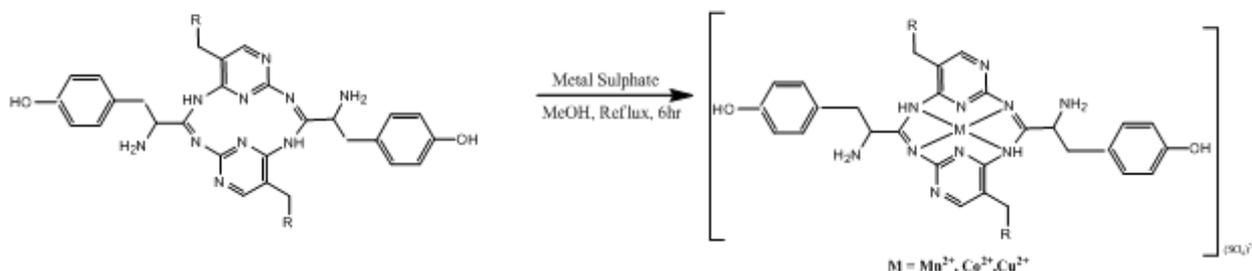
Scheme:1. Synthesis of ligand

Scheme:2



Scheme:2. Synthesis of Metal complex with Chloride

Scheme:3



Scheme:3. Synthesis of Metal complex with Sulphate

### 3. RESULTS AND DISCUSSION

All the complexes were soluble in water, acetonitrile, ethanol, methanol and DMSO. They were thermodynamically stable up to 290°C. From the analytical data (Table 1) the complexes can be represented  $[M(C_{46}H_{50}N_{10}O_8)Cl_2]$  and  $[M(C_{46}H_{50}N_{10}O_8)SO_4]$  Where  $M = Mn^{II}, Co^{II}, Cu^{II}$ .

The molecular mass and the analytical results were in good agreement with the proposed compositions of the complexes.

#### 3.1 Molar conductivities

The molar conductance of these macrocyclic complexes in acetonitrile were measured and then calculated molar conductance value are reported in

Table-1. The conductivities of the complexes were in the range of 10–16  $\Omega^{-1} cm^2 mol^{-1}$  and 80–120  $\Omega^{-1} cm^2 mol^{-1}$ . Which is characteristics of 1:0 electrolytes, suggest that all of them are non-electrolytes. The presence of chloride ions & sulphate ions is evident only after decomposition of the complexes, probably due to their presence in the coordination sphere. Based on the conductance, metal chloride complexes are assigned the structure  $[M(ML)Cl_2]$ ,  $[M(ML)SO_4]$ , ML-Macrocyclic ligand. M-Metal.

#### 3.2 Magnetic moments

The magnetic moments of the complexes showed that they

are all high spin type. The magnetic moment of the complexes are given in Table-1. The metal chloride & sulphate complexes have magnetic moments, which suggest octahedral and tetrahedral configuration around metal ions. Manganese(II) chloride complex has magnetic moment 5.99 B.M.  $Mn^{II}$  high spin complexes show in general magnetic moment very close to the spin only value of 5.92 B.M. suggest octahedral geometry. manganese(II) sulphate are 5.73 B.M. respectively suggesting tetrahedral coordination for the metal ion.

The prepared cobalt(II) chloride complex has magnetic moment of 4.8 B.M. this value is very close to the spin only value of 3.25 B.M. for octahedral complexes. Cobalt(II) sulphate it is higher than the spin only value of 3.98 B.M. which indicates the tetrahedral geometry.

The magnetic moment of Cu(II) chloride complex was lower than the spin only value of 1.46 B.M. which may be due to distortion. The macrocyclic complex of Cu(II) chloride exhibit magnetic moment 1.40 B.M. supported that the distorted octahedral geometry<sup>12</sup>.

The Cu(II) sulphate complex with the magnetic moment 1.76 B.M. indicated the presence one paramagnetic electron and tetrahedral geometry.

#### 3.3 Electronic spectra

The electronic spectra of the  $Mn^{II}$  complex exhibits two

bands at 40,816  $\text{cm}^{-1}$ , 37,171  $\text{cm}^{-1}$  and which are assigned to  ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{1g}(\text{G})$ ,  ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{G})$  transition respectively. These observations reveal that the stereochemistry of this complex is consistent with the six coordinated octahedral geometry. The electronic spectra of  $\text{Co}^{\text{II}}$  complexes consist in general of three spin-allowed transition, although it will not always be possible to observe all the three bands. In the electronic spectra of high spin octahedral complexes of  $\text{Co}^{\text{II}}$  one should expect three bands corresponding to the transitions,  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$ ,  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{1g}(\text{P})$  and  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}(\text{F})$ . Once the  $\text{Co}(\text{II})$  chloride complex displays a very broad band at 19,342  $\text{cm}^{-1}$  which is assigned to  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$  transition of distorted octahedral geometry. The

$\text{Co}(\text{II})$  sulphate complex and gave a bands 40,323  $\text{cm}^{-1}$ , 12,136  $\text{cm}^{-1}$  it was for the  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{A}_{2g}(\text{F})$  transition of tetrahedral geometry.

The electronic spectra of these complexes display bands corresponding to the transitions  ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$ ,  ${}^2\text{B}_{1g} \rightarrow {}^2\text{B}_{2g}$ ,  ${}^2\text{B}_{1g} \rightarrow {}^2\text{E}_g$ . Copper(II) chloride complex displays a band at 11,792  $\text{cm}^{-1}$  due to  ${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$  transition, characteristics of octahedral geometry<sup>13</sup>. The copper(II) sulphate complex displays a band at 18,622  $\text{cm}^{-1}$ , 13,316  $\text{cm}^{-1}$  due to  ${}^2\text{T}_{2g} \rightarrow {}^2\text{E}_g$  transition, characteristics of tetrahedral geometry.

**Table-1. Colour, Conductance, Magnetic moment and analytical data of the complexes of Ligand**

S.N O	Ligand/complex	colour	M.W (Calcd)	Molar Conductance $\text{Ohm}^{-1}$ $\text{cm}^2\text{mol}^{-1}$	Magnetic Moments (B.M)	Analysis % Found (Calculated)				
						C	H	N	M	X
1	$\text{L}(\text{C}_{46}\text{H}_{50}\text{N}_{10}\text{O}_8)$	white	870	--	--	62.44 63.44	5.50 5.79	15.88 16.08	---	---
2	$[\text{Mn}(\text{L})\text{Cl}_2]$	Pale brown	996	11.7	5.99	50.39 55.43	5.9 5.06	15.28 14.05	5.25 5.51	6.98 7.10
3	$[\text{Mn}(\text{L})\text{SO}_4)_2$	shine	1021	87.20	5.73	54.97 54.06	4.96 4.93	13.58 13.71	5.32 5.38	3.25 3.14
4	$[\text{Co}(\text{L})\text{Cl}_2]$	pink	1000	15.9	4.8	53.53 55.21	5.23 5.04	13.45 13.98	5.87 5.89	6.99 7.08
5	$[\text{Co}(\text{L})\text{SO}_4)_2$	Sky blue	1025	99.30	3.98	51.49 53.85	5.08 4.91	12.93 13.09	5.38 5.74	2.69 3.13
6	$[\text{Cu}(\text{L})\text{Cl}_2]$	green	1005	14.6	1.46	49.59 54.96	4.99 5.01	14.98 13.93	5.89 6.32	7.10 7.04
7	$[\text{Cu}(\text{L})\text{SO}_4)_2$	Light green	1027	118.00	1.76	53.09 53.61	5.09 4.89	14.59 13.89	6.01 6.17	3.08 3.11

### 3.4 IR Spectra

The Infra Red spectra of the macrocyclic complexes are very useful in determining the coordination groups of the ligand. The shifts in the peaks indicate the mode of linkage in the complexes. Comparison of the IR spectra of macrocyclic ligand and the complexes confirmed the formation of the complexes. Spectra indicated that trimethoprim and L-Tyrosine moieties are present. The stretching and bending vibrations of the  $-\text{NH}_2$  group of amino acid were observed at 3605 and 835  $\text{cm}^{-1}$  respectively in the IR spectrum of the free macrocyclic ligand as well as in the macrocyclic complexes of  $\text{Mn}^{\text{II}}$ ,  $\text{Co}^{\text{II}}$ ,  $\text{Cu}^{\text{II}}$  chlorides and sulphates. This clearly indicated that the amino group did not take part in coordination.

The band at 3320 and 1667  $\text{cm}^{-1}$  observed for the N-H and C=N vibrations of the free ligand were found to have a negative shift of 40-60  $\text{cm}^{-1}$  and 20-30  $\text{cm}^{-1}$ <sup>14-18</sup> respectively in all the complexes of  $\text{Mn}^{\text{II}}$ ,  $\text{Co}^{\text{II}}$ ,  $\text{Cu}^{\text{II}}$ . The band 519-447  $\text{cm}^{-1}$  was assigned to M-N stretching in the complexes as there was a coordination through nitrogen. The M-Cl vibration were identified through the bands appeared around 380-300  $\text{cm}^{-1}$  for those complexes that were involved in the chloride coordination<sup>19</sup>. In the sulphate complexes a very strong and broad band appeared near 1104  $\text{cm}^{-1}$  which was indicative of the non-coordinating sulphate species<sup>20</sup>.

The bands at 615 and 766  $\text{cm}^{-1}$  were assigned to the in-plane and out-of-plane bending motions of aromatic ring

indicating the non-coordination of the nitrogens in the pyrimidine ring. Thus, it might be quadridentate and macrocyclic compound the macrocyclic ring, not involving the nitrogen atoms of the pyrimidine. It was in accordance with the fact that quadridentate macrocycles could be formed more readily than the hexa- or quinquidentate

ligands<sup>21</sup>. It was very interesting to note that the imine and amine nitrogens were equally active and excluded the weak and less stable coordination by the pyrimidine nitrogen<sup>22</sup>.

### CONCLUSION

Conductivity measurement indicates that the metal complexes are non-electrolytes in nature. The spectral data suggest that the complexes of metal chlorides have octahedral geometry and that of metal sulphate have tetrahedral geometry. No evidence is found for the participation of nitrogen atoms of pyrimidine and amino group of the amino acid in the co-ordination.

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Engineering.

She is doing ph.d part time in inorganic chemistry at Bharathidasan university, Trichy, Tamilnadu India. presently she is working as a Associate Professor in the Department of chemistry, Dhanalaksmi Srinivasan college of Engineering and Technology, Chennai.

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