



# International Journal of Pharmaceutical Research and Development (IJPRD)

Platform for Pharmaceutical Researches & Ideas

[www.ijprd.com](http://www.ijprd.com)

## SYNTHESIS AND CHARACTERIZATIONS OF MACROCYCLI LIGAND AND ITS COMPLEXES DERIVED FROM TRIMETHOPRIM AND DIETHYLMALONATE.

P.Victor Arockiadoss\*<sup>1</sup>, Dr.M.Amaladasan<sup>1</sup>

<sup>1</sup>Postgraduate and Research Department of Chemistry, St.Joseph's college (Autonomous), Tiruchirappalli-620002(T.N) INDIA

### ABSTRACT

Macrocyclic complexes of  $Mn^{II}$ ,  $Co^{II}$ ,  $Ni^{II}$  and  $Cu^{II}$  using a macrocyclic ligand derived by the condensation of Trimethoprim and Diethylmalonate have been prepared and characterized by electronic, IR and NMR spectral studies as well as magnetic moment and conductivity. On the basis of spectral studies an octahedral geometry has been proposed for all the complexes.

**Key words:** Trimethoprim, Diethylmalonate,  $Mn^{II}$ ,  $Co^{II}$ ,  $Ni^{II}$  and  $Cu^{II}$

### Correspondence to Author



**P.Victor Arockiadoss**

Postgraduate and Research  
Department of Chemistry, St.Joseph's  
college (Autonomous),  
Tiruchirappalli-620002(T.N) INDIA

**Email:** [avemaria.p@gmail.com](mailto:avemaria.p@gmail.com)

### INTRODUCTION

The chemistry of macrocyclic ligands has been known for several decades.<sup>1</sup> Generally, macrocyclic polyamides are prepared by reaction of polyamine with either the diester salt of dicarboxylic acid or the dicarboxylic acid dichloride<sup>2-4</sup>. Three novel complexes of  $Cu(II)$ ,  $Co(II)$  and  $Zn(II)$  using macrocyclic ligand derived by the condensation of diethyl phthalate and benzidine have been designed, synthesized and characterized<sup>5</sup>. The Schiff base condensation of 2,6-diamino pyridine with 1,3-diphenyl 1,3-dipropandione in the presence

$Ni(II)$ ,  $Co(II)$  and  $Cu(II)$  chloride in boiling methanol gives the complexes of the 16-membered macrocycle<sup>6</sup>. New family of 15-membered tetraamide macrocyclic complexes have been synthesized by template condensation reaction of o-aminobenzoic acid with aliphatic or aromatic diamines and diethyl malonate<sup>7</sup>. Macrocyclic ligands are defined as cyclic molecules generally consisting of organic frames, either aliphatic or aromatic units into which the donor atoms are interspersed<sup>8</sup>. The macrocyclic ligands have been synthesized by the condensation reaction of diethyl

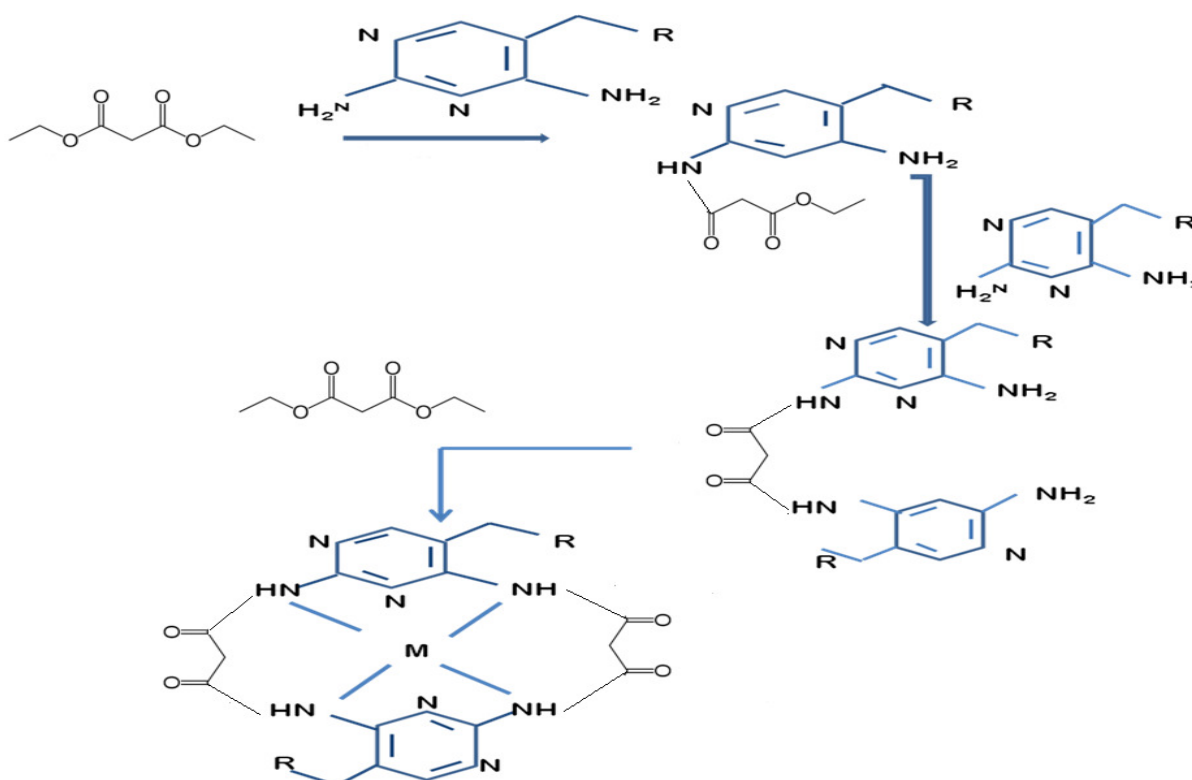
phthalate with *o*-phenylene diamine<sup>9</sup>. The present work deals synthesis and physicochemical studies of a new series of macrocyclic complexes bearing tetra amide groups derived from trimethoprim with Diethylmalonate in the presence of transition metal ions as template.

## EXPERIMENTAL

All the chemical 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. Proton NMR spectra were recorded on a EM 300-30 MHz NMR spectrometer in DMSO. IR spectra of the samples were recorded on a Shimadzu FTIR-8400s spectrophotometer in 4000-400  $\text{cm}^{-1}$  range in a KBr pellet. The electronic

**Fig:1 Macrocylic ligand,**

**R=3,4,5-trimethoxybenzyl.**



## Synthesis of Macrocylic complexes

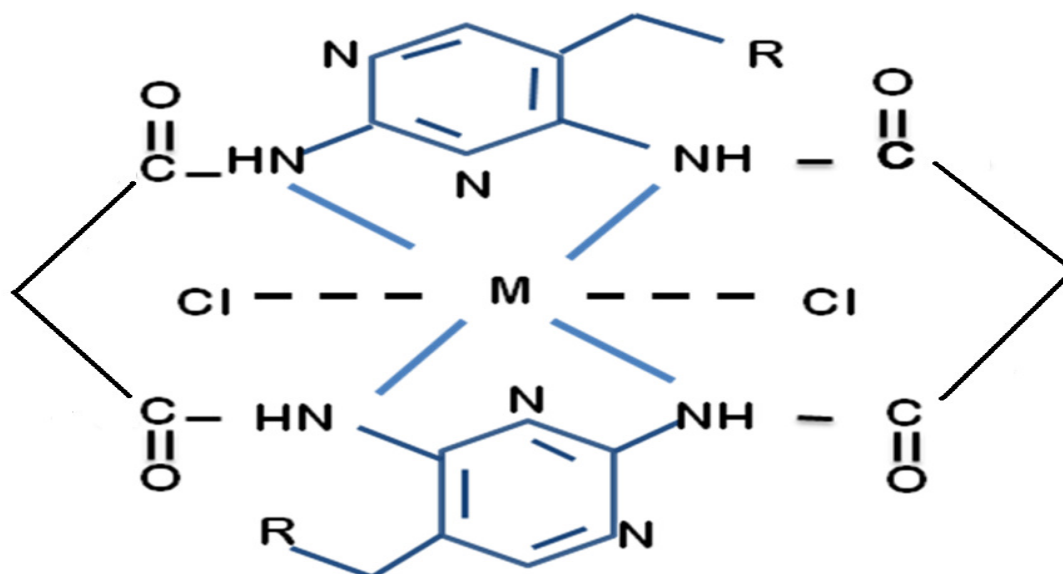
A solution of macrocyclic ligand (5mmol) in ethanol (20ml) was added to a solution of metal chloride (5mmol) in ethanol (10ml) and the mixture was refluxed for three hours and it was then

concentrated to half of the volume and set aside for two days. The microcrystalline compound which separated out was filtered, washed with ethanol-ether mixture (1:1) and dried in vacuum over anhydrous calcium

## Synthesis of Macrocylic Ligand

Trimethoprim and Diethylmalonate were condensed to give macrocyclic ligand by the reported method<sup>5,9-10</sup>. 50 ml ethanolic solution of Trimethoprim (10mmol) was added to the 50 ml of ethanolic solution of Diethylmalonate (10mmol) and refluxed for three hours. Then the solution was reduced to one third on a water bath. The resulting light brown colour crystals were washed with ethanol and ether then dried. The crude product was recrystallised from ethanol, the desired products were obtained.

concentrated to half of the volume and set aside for two days. The microcrystalline compound which separated out was filtered, washed with ethanol-ether mixture (1:1) and dried in vacuum over anhydrous calcium



**Fig:2 Macrocylic complexes**

## RESULTS AND DISCUSSION

All the complexes were found to be colour and soluble in water, acetonitrile, ethanol and DMSO. They were thermodynamically stable up to 350°C.

### Molar conductivities

The molar conductances of these macrocyclic complexes in acetonitrile were measured and then calculated molar conductance value are reported in Table. The conductivities of the complexes were in the range of 10 – 50  $\text{Ohm}^{-1} \text{Cm}^2 \text{mol}^{-1}$ <sup>11</sup>. Which is characteristics of 1:0 electrolytes, suggest that all of them are non –electrolytes. The presence of chloride 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  $[\text{M}(\text{ML})\text{Cl}_2]$ . ML-Macrocyclic ligand. M-Metal.

### Magnetic moments

The magnetic moments of the complexes (Table) reveal that they are all high spin type. The manganese (II) chloride complex with the magnetic moment value 5.65 B.M. supported an octahedral geometry around the  $\text{Mn}^{\text{II}}$  ion. The magnetic moments values of  $\text{Co}^{\text{II}}$  and  $\text{Ni}^{\text{II}}$  were 4.72 and 3.46 B.M, respectively suggesting consistency with their octahedral environment<sup>12</sup>. The  $\text{Cu}^{\text{II}}$  Complex shows magnetic moment value of 1.58 B.M. expected for

one unpaired electron, which offers possibility of a distorted octahedral geometry.<sup>12</sup>

### Electronic spectra

The electronic spectra of the  $\text{Mn}^{\text{II}}$ ,  $\text{Co}^{\text{II}}$ ,  $\text{Ni}^{\text{II}}$  and  $\text{Cu}^{\text{II}}$  complexes were recorded in ethanol solution and spectral data were presented in table.  $\text{Mn}^{\text{II}}$  complex exhibits two very weak bands at 23255  $\text{Cm}^{-1}$  and 26,315  $\text{Cm}^{-1}$  which are assigned to  ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{G})$  and  ${}^6\text{A}_{1g} \rightarrow {}^4\text{T}_{2g}(\text{D})$  transition respectively. These observations reveal that the stereochemistry of this complex is consistent with the six coordinated octahedral geometry. The electronic spectral of  $\text{Co}^{\text{II}}$  complexes show bands at 21276  $\text{Cm}^{-1}$ . this band was assignable to  ${}^4\text{T}_{1g}(\text{F}) \rightarrow {}^4\text{T}_{2g}(\text{F})$  transitions respectively in an octahedral environment. The  $\text{Ni}^{\text{II}}$  complex exhibit two absorption bands at 20833  $\text{Cm}^{-1}$  and 24390  $\text{Cm}^{-1}$  assignable to  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{F})$  and  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$  transitions respectively in an octahedral environment.<sup>13</sup> The  $\text{Cu}^{\text{II}}$  complexes shows a bands in the 25641  $\text{Cm}^{-1}$  and 21276  $\text{Cm}^{-1}$  region assigned to  ${}^2\text{B}_{1g} \rightarrow {}^2\text{F}_g$  and  ${}^2\text{B}_{1g} \rightarrow {}^2\text{B}_{2g}$  transitions respectively corresponding to a distorted octahedral geometry. The high intensity bands observed around 34000  $\text{Cm}^{-1}$  for all the complexes in the U.V region may be assigned as a metal to ligand charge transfer excitation.<sup>7</sup>

**Table-1.** Colour, Conductance, magnetic moments and electronic spectra of the macrocyclic complexes.

Sl. no	Complexes	Colour	Molar conductance $\text{Ohm}^{-1} \text{Cm}^2 \text{mol}^{-1}$	Magnetic moments (B.M)	Electronic spectra		Stereo chemistry
					Energy $\text{Cm}^{-1}$	Assignment	
1	[Mn(ML)cl <sub>2</sub> ]	Light brown	32.14	5.65	26,954	${}^6A_{1g} \rightarrow {}^4T_{2g}(D)$	Octahedral
2	[Co(ML)cl <sub>2</sub> ]	Grey	35.25	4.72	14705	${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$	Octahedral
3	[Ni(ML)cl <sub>2</sub> ]	LightGreen	29.88	3.46	25641	${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$	Octahedral
4	[Cu(ML)cl <sub>2</sub> ]	Green	27.03	1.58	20833	${}^2B_{1g} \rightarrow {}^2B_{2g}$	Distorted Octahedral

**IR Spectra**

The Infra Red spectra gave some important information regarding to the skeleton of the complexes. the IR spectra of the macrocyclic ligands show characteristics bands for  $\nu(\text{N-H})$  at  $3462 \text{ Cm}^{-1}$ ,  $\nu(\text{C=O})$  at  $1660 \text{ Cm}^{-1}$  and  $\nu(\text{C-N})$  at  $1447 \text{ Cm}^{-1}$ . in all the complexes  $\nu(\text{N-H})$  bands were shifted by  $60\text{-}85 \text{ Cm}^{-1}$  to lower frequencies, due to coordination of the NH groups. The  $\nu(\text{C-N})$  bands were also shifted by  $10\text{-}25 \text{ Cm}^{-1}$  due to participation of the azomethine groups in coordination. On the other hand, the stretching vibrations of  $\nu(\text{C=O})$  was not affected in all the complexes, which indicates that the carbonyl groups are not involved in coordination to the metal. The coordination of nitrogen to the metal atom is supported by the appearance of a new band in the region  $510\text{-}504 \text{ Cm}^{-1}$  assignable to  $\nu(\text{M-N})$  vibration.<sup>9</sup>

**<sup>1</sup>H NMR spectra**

The proton magnetic resonance spectrum of the macrocyclic ligand was taken in DMSO solvent. the spectrum shows four different types of protons. Since signals are observed at four different regions from the TMS (Internal standard).the intensities of the peaks are in the ratio 9:2:2:6. <sup>1</sup>H NMR spectrum of the macrocyclic ligand display peaks at  $\delta 3.7(4\text{H}, \text{S}, -\text{CH}_2)$ :  $\delta 5.7(18\text{H}, \text{M}, \text{O}-\text{CH}_3)$ :  $\delta 6.1(4\text{H}, \text{S}, \text{Pyridine-H})$ :  $\delta 6.6(2\text{H}, \text{S}, \text{ring NH})$ :  $\delta 7.5(4\text{H}, \text{S}, \text{Ar-H})$ . Thus the <sup>1</sup>H NMR spectrum confirms the presence of Trimethoprim and Diethyl phthalate moieties in the macrocyclic product. All the above along with the absence of any band

Available online on [www.ijprd.com](http://www.ijprd.com)

characteristics of  $\text{NH}_2$  OR  $\text{OC}_2\text{H}_5$  protons, support the proposed macrocycle<sup>7,14</sup>.

**CONCLUSION**

Conductivity measurement indicates that the metal complexes are non-electrolytes in nature. The magnetic moments of all the complexes reveal that they are all of high spin type with paramagnetic nature. Electronic spectra data support that all the metal complexes have octahedral. The IR spectra data reveal that the macrocyclic ligand coordinated through four amino nitrogen of the macrocyclic ring and there is no indication of pyrimidine nitrogen in coordination. Based on the various physiochemical studies such as conductivity, magnetic susceptibility, electronic and IR spectral studies octahedral geometry may be proposed for all the complexes

**ACKNOWLEDGEMENT**

I have great pleasure in expressing my deep sense of gratitude to **Dr.M.Amaladasan**, Associate Professor, Department of chemistry, St.Joseph's college(Autonomous),Trichy-2 for having motivated and supervised me into this work .I extended my sincere thanks to authorities of St.Joseph's college(Autonomous),Trichy-2 for the facility and support .

**REFERENCES**

1. L.F.Lindoy, the chemistry of macrocyclic ligand complexes, Cambridge university press Cambridge 1989.

2. N.W.Alcock,P.Moorie,H.A.A.Omar and C.J.Reader,j.chem.soc.dalton trans 1987 2643
3. I.Tabushi,H.Okino and Y.Kuroda,Tetrahedron Lett.1976,48,4339
4. P.J.M.Lehn and F.Montavon,Tetrahedron Lett.1972,44,4557.
5. N. Raman\* and S. Parameswari, The Korean Society of Mycology, 35(2): 65-68 (2007)
6. Ashok kumar singh,sudeshna Chandra,Randhir singh,J.Indian Chem.Soc.1997,74,5
7. Omar S.M. Nasman, Journal of Al Azhar University–Gaza (Natural Sciences), (2007), Vol. 9, page: 53-59
8. Karn.J.L.Busch,D.H,Inorg.chem.1969,8,1144
9. N. Raman\*, J. Joseph, A. Senthil Kumara Velan1 and C. Pothiraj1, The Korean Society of Mycology, 34(4): 214-218 (2006)
10. Amaladasan.M “synthesis of N<sub>8</sub>macrocyclic ligands by poly phosphoric acid-catalysed condensation of trimethoprim and amino acids. Indian journal of chemistry section –B 1998
11. \*P.Victor Arockiadoss and Dr.M.Amaladasan “Synthesis and characterization of Tetradentate N<sub>8</sub>-MacrocyclicLigand and its Complexes.” International Journal of ChemTech Research
12. Burger,k.coordination chemistry,experimental methods;Butter worth:London1973
13. Halli.M.B,Vijayalaxmi and patil.B,Res.J.Chem.Environ,Vol15(2) June 2011
14. Amaladasan.M studies on the interaction of Mn (II),Co(II),Ni(II),Cu(II) and Zn with 18 – Membered N<sub>6</sub> macrocycles. (1998)

\*\*\*\*\*