



# Studies of Trivalent Transition Metal Macrocyclic Complexes and Its Antimicrobial Activities

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## Abstract

The new series of two new Macrocyclic complexes have been synthesized bearing the formula  $M(III)[DPDTPH](BF_4)_2$  and  $M [DCDTPH](BF_4)_2$ , where  $M= Cr(III)$ ,  $DPDTPH = 2,6$ -diacetyl pyridine- $N-N'$ -dithiodipropionyl dihydrazone and  $DCDTPH = 2,6$ - pyridine dicarbonyl di chloride-  $N-N'$ -dithiodipropionyl dihydrazone and  $(BF_4)=$  Tetrafluoroborate. The ligand and complexes have been analyzed for elemental analysis, spectral studies, and conductivity measurements. Different techniques like FT-IR, electronic spectra were used to investigate the structural features of the synthesized compounds. Electronic absorption and IR spectra indicate octahedral geometry. The biological screening of ligand and complexes against bacteria and fungi shows the complexes have been found to be manifold active biologically than the ligand.

**Keywords:** Macrocyclic complexes, FT-IR, spectral and biological studies.

## Introduction

Synthesis and characterization of macrocyclic ligand has been very important area of current research in coordination chemistry at all over the world due to its wider application in all the field, particularly antibiotic, transport of ion and unusual binding properties<sup>1</sup>. Macrocyclic complexes are thermodynamically more stable and more selective metal ion chelates than open chain analogue so the study of macrocyclic complexes is a growing class of research<sup>2-4</sup>. In living systems, metal ions play an important role as catalyst for many biological reactions. The activity of such metal ions depends on their confinement within approximately planar, tetra dentate and totally enclosed macrocyclic ligands, which themselves are highly conjugated species<sup>5-7</sup>. Macrocyclic complexes of transition metal ions have received great attention due to their biological activities, including antiviral, anticarcinogenic<sup>8</sup>, antifertile<sup>9</sup>, antibacterial and antifungal<sup>10</sup>. Some Macrocyclic complexes of lanthanides e.g.  $Gd^{3+}$  are used as MRI contrast enhancing agents<sup>11-12</sup>. Macrocyclic Nickel complexes have been reported<sup>13</sup> as DNA recognition and oxidation while macrocyclic copper complexes find use in DNA binding and cleavage<sup>14</sup>. In view of the above discussion, in this paper we report the synthesis, spectral and biological investigation of Cr(III) dithiodipropionic acid and hydrazide hydrate.

## Material and Methods

All the chemicals and solvents used of A.R. grade, purchased from Aldrich, Himedia, Merck and CDH and were used as received.

**Synthesis of Ligand:** The ligand, dithiodipropionic acid dihydrazide was formed by mixing 1:2 stoichiometric quantities

of transparent dithiodipropionic acid ester (2.38 gm, 0.01M) solution and hydrazine hydrate (0.83cm<sup>3</sup>, 0.02M) were mixed in 20ml ethyl alcohol with continuous stirring. The obtained solution was refluxed over a water bath at 40-50°C for around 5-6 hours. The obtained bright-white crystal in bottom round flask was concentrated and cooled overnight and were filtered, washed with alcohol and ether then dried in vacuum over anhydrous  $CaCl_2$  in a desiccator.

**Synthesis of Metal Complex I:** 1:1:1 stoichiometric quantities of ligand (2.38 gm, 0.01M), Chromium Acetate (242 gm, 0.01M) and 2,6-diacetyl pyridine (1.63gm., 0.01M) were mixed in 20 ml. ethanol with continuous stirring. The obtained solution was refluxed over a water-bath for around 6-7 hours and concentrated. Then a little of sodiumtetrafluoroborate was added and the solution was cooled overnight, crystals separated out. These Dark – green crystals were filtered, washed with alcohol and then dried in vacuum over anhydrous  $CaCl_2$  in a desiccator.

**Synthesis of Metal Complex II:** 1:1:1 stoichiometric quantities of ligand (2.38gm, 0.01M), chromium acetate (2.42 gm, 0.01M) and 2, 6-pyridine dicarbonyldichloride (1.90 gm, 0.01M) were mixed in 20 ml. ethanol with continuous stirring. The obtained solution was refluxed over a water-bath for around 6-7 hours and concentrated. Then a little of sodiumtetrafluoroborate was added and the solution was cooled overnight, crystals separated out. These parrot-green crystals were filtered, washed with alcohol and then dried in vacuum over anhydrous  $CaCl_2$  in a desiccator.

**Analytical and physical measurements:** The elemental analysis helps in fixing the stoichiometric composition of the ligand and metal complexes. The carbon, hydrogen, nitrogen, oxygen analyzed by sophisticated analytical instrument facility

such as Elemental Analyzer (*Thermo Scientific 338 35210*) and for weighing by Micro Balance (*Mettler Toledo Model XP<sub>6</sub>*). Melting point determine by (*Make-VEEGO, Model-VMP-PM*). For metal estimation, using gravimetric method of analysis *Vogel's Quantitative Inorganic Analysis (seventh edition) revised by G.SVEHLA*. Infra-red spectra of synthesized compounds were recorded on (*Perkin-Elmer, Model No.-C91158*) in the range 4000-400  $\text{cm}^{-1}$ . The electronic spectra of complexes in DMSO were recorded on a UV-VIS-NIR (Cary5E) spectrophotometer at room temperature.

**Infra-Red Data:** The band due to the  $-\text{NH}_2$  group disappeared completely in the complexes. The band due to the  $-\text{NH}$  group did not show any change in the spectra of complexes, confirming that the Nitrogen of  $-\text{NH}$  group did not take part in reaction whereas a sharp band was seen in the range of  $1310\text{cm}^{-1}$  proving that  $-\text{NH}_2$  group is present in the ligand. Some entirely

new absorption band appeared in the spectra of complexes viz. band around  $580\text{-}570\text{cm}^{-1}$  due to M-N group, a band around  $470\text{-}460\text{cm}^{-1}$  due to M-O group and a band around  $360\text{-}350\text{cm}^{-1}$  due to presence of M-S group. These new band confirmed the coordination of nitrogen and sulphur with the metal atom in the complexes.

**Electronic Data:** The synthesized macrocyclic complexes are stable in air, completely insoluble in water and common organic solvents, but they are soluble in DMSO. The electronic spectra of the complexes recorded in DMSO (HPLC grade). All the absorption bands in electronic spectra were found for complexes in the range of  $12,100\text{-}12,050\text{cm}^{-1}$  attributed to  ${}^2\text{E}_g \rightarrow {}^2\text{T}_{2g}$  transition and in the range of  $24,300\text{-}24,250\text{cm}^{-1}$  attributed to  $\text{L} \rightarrow \text{M}$  charge transfer transition. These transition confirmed the octahedral geometric of the complexes.

**Table-1**  
**Elemental Analysis and Molar Conductivity Data of the Ligand and Newly Synthesized Cr(III) Macrocyclic Complexes**

Compound	M.P. ( $^{\circ}\text{C}$ )	Color	Yield (%)	Elemental Analysis (%) (F/C)				Molar Conductivity ( $\text{Ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ )
				C	H	N	M	
DTDPDH	159	Bright-white	1.96 gm.	30.11 (30.21)	5.71 (5.87)	23.44 (23.49)	-	-
Cr(III)[DPDTPH]( $\text{BF}_4$ ) <sub>2</sub>	260	Dark-green	2.39 gm.	30.01 (30.34)	3.51 (3.54)	11.69 (11.80)	8.46 (8.76)	113.79
Cr(III)[DCDTPH]( $\text{BF}_4$ ) <sub>2</sub>	289	Parrot-green	2.75 gm.	24.46 (24.60)	2.27 (2.36)	11.00 (11.04)	8.19 (8.20)	113.85

**Table-2**  
**Infra-red Spectral Data of Ligand and Newly Synthesized Cr(III) Macrocyclic Complexes**

Functional Groups	DTDPDH	Cr(III)[DPDTPH]( $\text{BF}_4$ ) <sub>2</sub>	Cr(III)[DCDTPH]( $\text{BF}_4$ ) <sub>2</sub>
$-\text{CH}_2$	2970	2940	2930
$-\text{NH}_2$	1310	-	-
$-\text{NH}$	3380	3380	3370
N-N	1020	980	970
C-H	850	810	820
$>\text{C}=\text{N}$	-	1620	1610
$>\text{C}=\text{O}$	1750	1690	1680
M-N	-	580	570
M-O	-	470	460
M-S	-	360	350

**Table-3**  
**Absorption Bands (in  $\text{cm}^{-1}$ ) of Macrocyclic Complexes in Electronic Spectra**

Complexes	Transition ( $\text{cm}^{-1}$ )	
	${}^2E_g \rightarrow {}^2T_{2g}$	L $\rightarrow$ M
Cr(III)[DPDTPH](BF <sub>4</sub> ) <sub>2</sub>	12100	24250
Cr(III)[DCDTPH](BF <sub>4</sub> ) <sub>2</sub>	12050	24300

**Minimum Inhibitory Concentration (MIC):** The MIC values determine by the sets to of “two fold serial dilution method”. In this method 1 ml. of seeded broth (obtained by 1:100 dilution of the indicated micro-organism in broth) was taken in ten well sterilized tubes (3x100mm. size) keeping the first test tube empty 2ml. of each of the seeded broth was prepared having 100 $\mu\text{g/ml}$ . and test compound in two tubes. A and B respectively (prepared by dissolving 0.2 ml. and 0.3 ml. of the stock solutions (1  $\mu\text{g/ml}$ .) in 1.8 ml. and 1.7 ml of broth respectively). Contents of the tube A were placed in the first empty tube using a fresh sterilized pipette. 1 ml. contents from the B tube were withdrawn and added to second tube and mixed well. Similarly, 1 ml. contents from the first tube were withdrawn and added into the third tube and mixed well. 1ml. contents from the third tube were pipette out with other fresh sterilized pipette and added into fourth tube and shaken well. This gradient dilution process was continued for all the ten test tubes using a fresh pipette each time. 1ml. contents were taken out from the tenth tube and rejected. All the test tubes were labeled with 100  $\mu\text{g/ml}$ ., 75  $\mu\text{g/ml}$ ., 50  $\mu\text{g/ml}$ ., 25  $\mu\text{g/ml}$ ., 12.5  $\mu\text{g/ml}$ ., 6.25  $\mu\text{g/ml}$ ., 3.125  $\mu\text{g/ml}$ ., 1.562  $\mu\text{g/ml}$ ., 0.78  $\mu\text{g/ml}$ . and 0.39  $\mu\text{g/ml}$ . respectively. 1ml. of each of the seeded broth and broth was placed in two separate tubes for the control of culture and control of broth media respectively in each set of above experiments simultaneously. All the above sets of tubes were incubated in BOD incubator for the respective indicated micro-organisms. The tube having the highest dilution showing no visible turbidity was chosen. The amount of the test compound in this tube was the minimum inhibitory concentration.

## Results and Discussion

In the present paper we have synthesized and characterized Cr(III)Macrocyclic complexes, formulated as

Cr(III)[DPDTPH](BF<sub>4</sub>)<sub>2</sub> and Cr(III)[DCDTPH](BF<sub>4</sub>)<sub>2</sub>. Both the complexes are solid and colored. Complexes are stable at room temperature. The ligand and macrocyclic complexes are bright-white, dark-green and parrot- green colored and are soluble in DMSO and DMF. All compounds give satisfactory elemental analyses results as shown in the table-1. In infra-red spectral data table-2 Nitrogen, Oxygen and Sulphur are suitably placed for coordination towards the metal ion, has been proposed for both complexes, absence in ligand confirm a octahedral geometry of complex I and complex II. On the basis of analytical and spectral data octahedral structures have been tentatively proposed for both complexes. Electronic spectral data of ligand and Cr(III) Macrocyclic complexes shown in table-3. The Minimum inhibitory concentration (MIC) value in molar concentration shown in table-4 of ligand and complexes compared. The antimicrobial screening data confirms that the metal complexes exhibit a higher inhibitory effect than the free ligand. Present observations may serve as a guide for studying the control release of these complexes that could be a promising future in the field of infectious diseases.

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**Table-4**  
**Minimum Inhibitory Concentration (MIC) value in Molar Concentration [ $\times 10^{-4}$ ] of Ligand and Newly Synthesized Cr(III) Macrocyclic Complexes**

Compounds	Activity against bacterial strain			Activity against fungal strain	
	E. coli (Gram Negative)	Salmonella (Gram Negative)	S. aureus (Gram Positive)	A. brasiliensis	C. albicans
DTDPDH	0.605	0.622	0.619	0.585	0.590
Cr(III) [DPDTPH] (BF <sub>4</sub> ) <sub>2</sub>	0.210	0.208	0.210	0.210	0.211
Cr(III) [DCDTPH] (BF <sub>4</sub> ) <sub>2</sub>	0.195	0.190	0.191	0.185	0.192

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