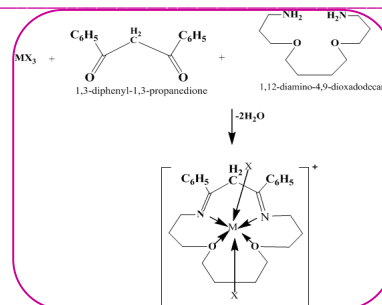




## SYNTHESIS AND CHARACTERIZATION STUDIES OF MACROCYCLIC COMPLEXES OF CHROMIUM (III)

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### ABSTRACT

A new mixed aza-oxo macrocycle complexes viz., 3,16-diaza-7,12-dioxo-cycloheptadecane with a transition metals Cr(III) in butanol, has been synthesised by the [1+1] cyclocondensation of  $\beta$ -diketones such as 2,4-pentanedione, 1-phenyl-1,3-butanedione and 1,3-diphenyl-1,3-propanedione with dioxadamines such as 1,12-diamino-4,9-dioxadodecane. Different techniques like elemental analysis, FT-IR, FAB mass spectroscopy, magnetic properties, and their biological activities were characterized to complexes.

**KEYWORDS:** Synthesis; Cr (III) complexes;  $N_2O_2$  macrocyclic complexes; biological activities.

### INTRODUCTION

Synthetic Macrocyclic complexes have received wide attention during the recent years [1]. Due to various molecular topologies and sets of donor atoms [2], attractive physical and chemical properties and their applications have been found in various scientific areas [3, 4, 5, 6]. They exhibit various biological properties, such as antitumor, antibacterial, antiviral, antifungal, anti-carcinogenic etc., due to their ability to form tetradentate chelate with essential heavy metal ions, bonding through nitrogen, sulphur, and oxygen [7, 8, 9, 10]. Metal ion complexes with macrocyclic ligands have importance due to their resemblance with organic compounds such as cobalamine and porphyrin [12, 11]. I have developed aza-oxo macrocyclic metal complexes, containing ( $N_2O_2$ -donor) of 3d transition metal series.

### EXPERIMENTAL

#### Materials

$Cr(NO_3)_3 \cdot 9H_2O$  (CDH), 1,12-diamino-4,9-dioxadodecane (Aldrich) 2,4-pentanedione(Aldrich), 1-phenyl-1,3-butanedione (Aldrich) and 1,3-diphenyl-1,3-propanedione (Aldrich) and 1-butanol (Merck) were distilled before use.

#### Analytical methods and measurements

Chromium was determined volumetrically by EDTA using Eriochrome Black T as indicator<sup>13</sup>. The FTIR spectra were recorded as KBr pellets in the region  $4000-200\text{ cm}^{-1}$  on a SHIMADZU-JAPAN8400S Spectrophotometer. FAB-mass spectra were recorded on Jeol SX102/DA-600 mass spectrometer/Data System using Argon/Xenon (6kV, 10mA) as the FAB gas. Electronic spectra were recorded in DMSO in the range of 200nm-800nm on a SYSTRONICS UV-VIS Spectrophotometer.

### ANTIBACTERIAL SCREENING

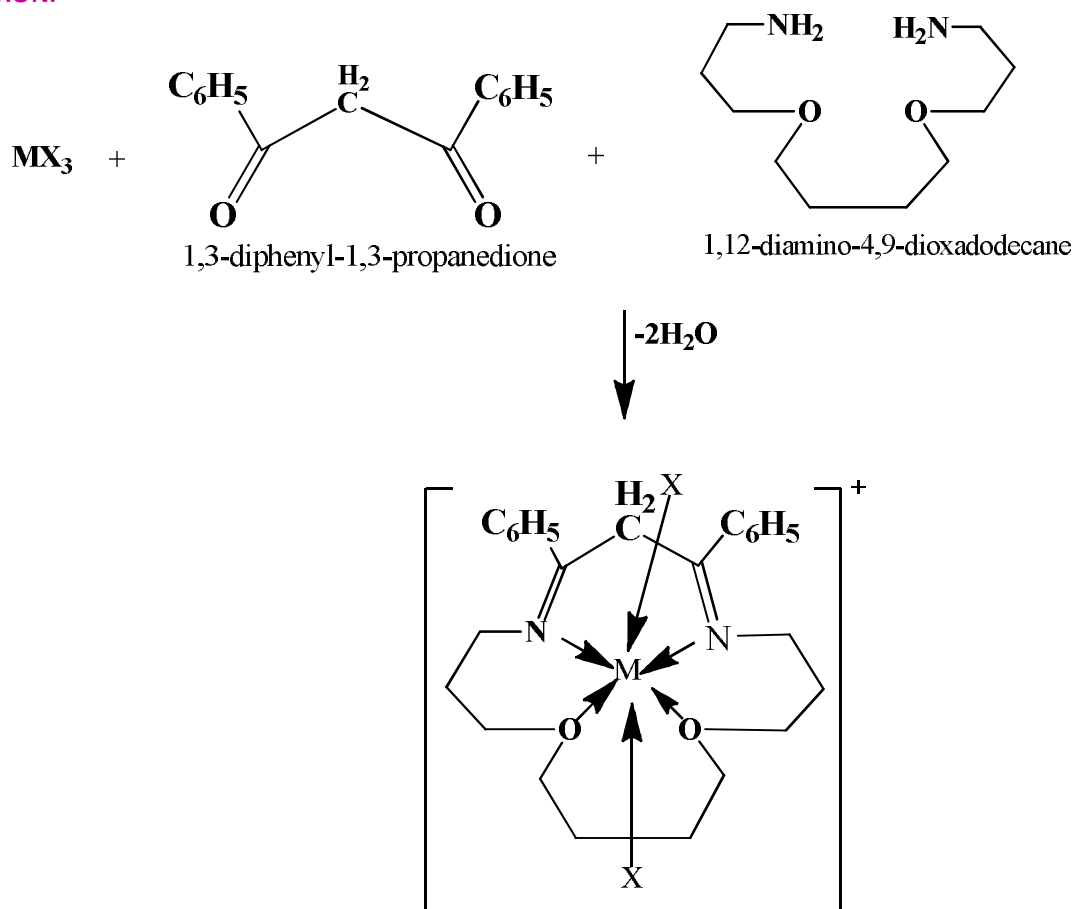
The in vitro antibacterial activities of the ligands and metal complexes were tested by using Muller Hinton agar by well diffusion method against a gram negative bacterial strain *Pseudomonas aeruginosa*

(ATCC 27853), and a gram positive bacterial strain *Bacillus subtilis*. The bacterial strains grown on nutrient agar at 35°C for overnight were suspended in a saline solution and adjusted to a turbidity of 0.5 McFarland standards. The suspension was used to inoculate. Wells were punched in the agar with the help of a sterile metallic borer and filled with (50µl) of the test extract (10mg/mL). Plates were incubated in air at 37°C (approx) for 16-18 hours (approx). Antibacterial activities were evaluated by measuring diameters of the inhibition zone in millimeters carefully. DMSO and amoxicillin (5mg (w/v)) was used as a reference standard antibiotic drug.

### Synthesis of Cr (III) complexes of oxa-azamacrocycles derived from β-diketones

To Cr(NO<sub>3</sub>)<sub>3</sub>.9H<sub>2</sub>O (.81gm) dissolved in 10 ml of n-butanol was added dropwise a butanolic solution of 1,3-diphenyl-1,3-propanedione (0.453gm in 10 ml of n-butanol) under continuous stirring. Then a butanolic solution of 0.413gm of 1,12-diamino-4,9-dioxadodecane was added and the contents were stirred for approximately 5-6 hours. The solid product was filtered, washed with n-butanol and dried under reduced pressure. A similar procedure was adopted for the synthesis of Cr (III) complexes of macrocycles derived from 2,4-pentanedione, and 1-phenyl-1,3-butanedione with 1,12-diamino-4,9-dioxadodecane.

### REACTION:

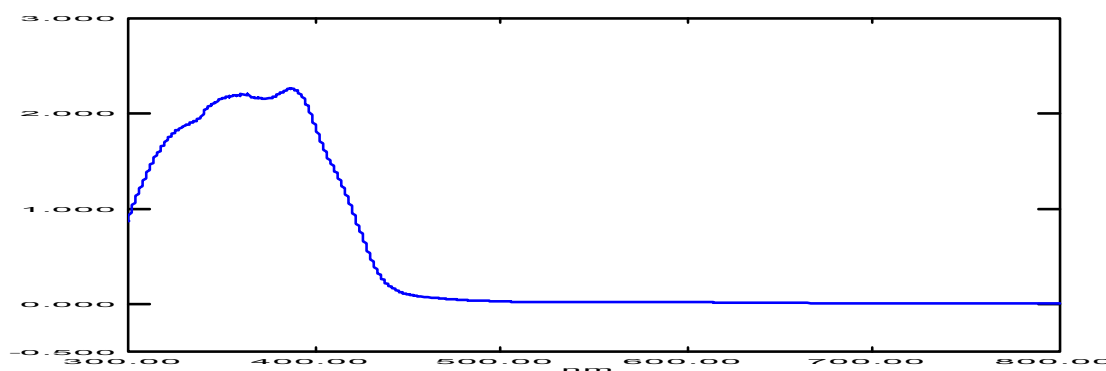


M (III) Complexes of 17-membered N, O-donor macrocycles, whereas M = Cr

## RESULT AND DISCUSSION

### Magnetic moments

Chromium (III) complex shows magnetic moments corresponding to three unpaired electrons, i.e. 3.83 B.M., expected for octahedral chromium(III) complexes<sup>14,15-17</sup>. Six coordinated Cr(III) complexes with octahedral symmetry show three spin allowed bands in the range of 18000-30000cm<sup>-1</sup>



### IR Spectra

It was noted that two bands present in the spectrum of 1,12-diamino-4,9-dioxadodecane at 3340 and 3380 cm<sup>-1</sup>, corresponding to the  $\nu(\text{NH}_2)$  group, were absent from the infrared spectra of all the complexes. Furthermore, no strong absorption band was observed near 1720 cm<sup>-1</sup> indicating the absence of the  $>\text{C}=\text{O}$  group of the 1,3-diphenyl-1,3-propanedione. The disappearance of these bands and the appearance of a new strong absorption band in the range 1590–1629 cm<sup>-1</sup> confirms the condensation of the carbonyl group of 1,3-diphenyl-1,3-propanedione and the amino group of 1,12-diamino-4,9-dioxadodecane and the formation of and the formation of a macrocyclic Schiff's base,<sup>18</sup> as these bands may be assigned to  $\nu(\text{C}=\text{N})$  stretching vibrations<sup>19</sup>. The lower value of the  $\nu(\text{C}=\text{N})$  vibrations may be explained by a drift of the lone pair electron density of the azomethine nitrogen towards the metal atom<sup>20</sup>, indicating that coordination occurs through the nitrogen of the C=N groups. A medium intensity absorption band in the region 1400–1500 cm<sup>-1</sup> may be assigned for phenyl ring absorption<sup>21</sup>. The presence of the absorption bands at 1408–1440, 1290–1320 and 1010–1030 cm<sup>-1</sup> in the IR spectra of all the nitrate complexes suggest that the nitrate groups are coordinated to the central metal ion in a unidentate fashion<sup>22</sup>.

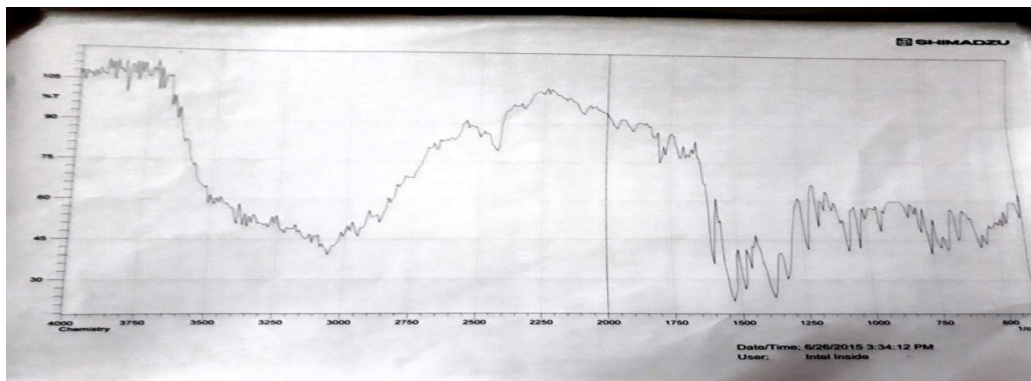


Fig-1: IR spectra of  $[\text{Cr}(\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$

### APPLICATION

All synthesized macrocyclic complexes were tested for in vitro antibacterial activity against some bacterial strains using spot-on-lawn on Muller Hinton Agar. Two test pathogenic bacterial strains viz *Bacillus subtilis* and *Pseudomonas aeruginosa* were considered for determination of MIC (Minimum Inhibitory Concentration) of selected complexes.

**Table 1: Antimicrobial sensitivity of Chromium metal complexes**

S.NO	Concentration (10mg/ml)		<i>Bacillus subtilis</i> Test zone of inhibition(mm)	<i>Pseudomonas aeruginosa</i> Test zone of inhibition (mm)
1	[Cr(C <sub>25</sub> H <sub>32</sub> N <sub>2</sub> O <sub>2</sub> )(NO <sub>3</sub> ) <sub>2</sub> ] <sub>2</sub> NO <sub>3</sub> (10mg/ml DMSO)	20 $\mu$ l	No zone of inhibition	No zone of inhibition
		40 $\mu$ l	No zone of inhibition	No zone of inhibition
		60 $\mu$ l	No zone of inhibition	No zone of inhibition
		80 $\mu$ l	No zone of inhibition	No zone of inhibition
2	Amoxicillin(5mg (w/v))		29	32

**Table 2: Since no Zone of inhibition was obtained for the given concentrations, an antimicrobial assay so further conducted at higher concentrations of the test samples against *Bacillus subtilis* and *Pseudomonas aeruginosa*.**

S.NO	Sample concentration (50ul loaded/well)		<i>Bacillus subtilis</i> Test zone of inhibition (mm)	<i>Pseudomonas aeruginosa</i> Test zone of inhibition (mm)
1	[Cr(C <sub>25</sub> H <sub>32</sub> N <sub>2</sub> O <sub>2</sub> )(NO <sub>3</sub> ) <sub>2</sub> ] <sub>2</sub> NO <sub>3</sub> (10mg/ml DMSO)	1 $\mu$ l	No zone of inhibition	No zone of inhibition
		2 $\mu$ l	No zone of inhibition	No zone of inhibition
		3 $\mu$ l	No zone of inhibition	No zone of inhibition
		4 $\mu$ l	No zone of inhibition	No zone of inhibition
		5 $\mu$ l	No zone of inhibition	No zone of inhibition
		6 $\mu$ l	No zone of inhibition	No zone of inhibition
		7 $\mu$ l	No zone of inhibition	No zone of inhibition
		8 $\mu$ l	No zone of inhibition	No zone of inhibition
		9 $\mu$ l	No zone of inhibition	No zone of inhibition
		10 $\mu$ l	No zone of inhibition	No zone of inhibition
2	Amoxicillin(5mg (w/v))		25	32

**FAB mass spectra:**

The mass spectra of trivalent chromium (III) macrocyclic complexes derived from cyclocondensation of azaoxo macrocyclic ligand and  $\beta$ -diketone have been recorded. All the spectra exhibit parent peaks due to molecular ions  $[M]^+$ . The proposed molecular formula of these complexes was confirmed by comparing their

molecular formula weights with m/z values. The molecular ion peaks and other fragments arising from the thermal cleavage of the complexes have been given in Table 3

S.NO	COMPLEXES	MOLECULAR ION PEAK [M+]	IMPORTANT PEAK DUE TO COMPLEXES FRAGMENTATION
1	$[\text{Cr}(\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$	$[\text{Cr}(\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$ [M+] = 506	$[\text{Cr}(\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_2)(\text{NO}_3)_2]^+ = 444$ $[\text{Cr}(\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_2)(\text{NO}_3)]^+ = 382$ $[\text{Cr}(\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_2)]^+ = 320$ $[\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_2]^+ = 268$
2	$[\text{Cr}(\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$	$[\text{Cr}(\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$ [M+] = 568	$[\text{Cr}(\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_2)(\text{NO}_3)_2]^+ = 506$ $[\text{Cr}(\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_2)(\text{NO}_3)]^+ = 444$ $[\text{Cr}(\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_2)]^+ = 382$ $[\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_2]^+ = 330$
3	$[\text{Cr}(\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$	$[\text{Cr}(\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$ [M+] = 630	$[\text{Cr}(\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2)(\text{NO}_3)_2]^+ = 568$ $[\text{Cr}(\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2)(\text{NO}_3)]^+ = 506$ $[\text{Cr}(\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2)]^+ = 444$ $[\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2]^+ = 392$

Table 3: Fragmentation pattern of Chromium complexes

#### ANALYSES AND CHARACTERIZATION OF MACROCYCLIC COMPLEXES: CONCLUSIONS

S.No	Complexes Molecular wt(gm)	Colour and Yield	Analysis % Found (calculated)					Decom Temp. (C <sup>o</sup> )
			M	C	H	O	N	
1	$[\text{Cr}(\text{C}_{15}\text{H}_{28}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$ 506.437	Blackish (42%)	10.28 (10.26)	35.58 (35.57)	5.59 (5.57)	34.75 (34.73)	13.84 (13.82)	180
2	$[\text{Cr}(\text{C}_{20}\text{H}_{30}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$ 568.51	Greenish yellow (13%)	10.00 (9.14)	41.91 (42.25)	5.85 (5.32)	45.83 (45.02)	24.44 (24.68)	192
3	$[\text{Cr}(\text{C}_{25}\text{H}_{32}\text{N}_2\text{O}_2)(\text{NO}_3)_2]\text{NO}_3$ 630.583	Light Green (41%)	9.39 (8.24)	47.17 (47.61)	5.10 (5.12)	40.75 (40.59)	22.68 (22.21)	210

Based on elemental analyses, magnetic moments, electronic, IR and mass spectral and structural studies, a octahedral structure may be proposed for these complexes.

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