

# Synthesis, Electrochemical and Antimicrobial Studies of Tetraaza Macrocylic Complexes of Cobalt (II)

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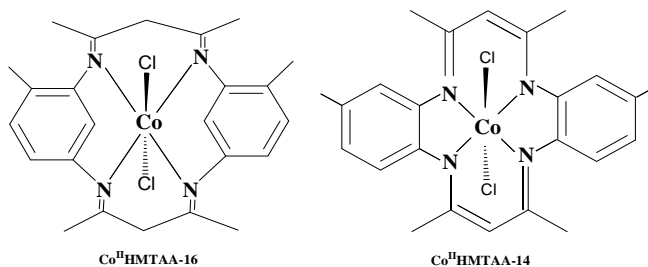
**Abstract**—6,13-Dihydro-Me<sub>6</sub>-dibenzo[b,i][1,4,8,11]-tetraazacyclotetradec-4,7,11,14-tetraene Co(II) and 7,15-Dihydro-Me<sub>6</sub>-dibenzo[b,j][1,5,9,13]-tetraazacyclohexadec-5,8,13,16-tetraene Co(II) macrocyclic complexes have been synthesized by the template method. These synthetic macrocycles analysed by various techniques like Molar conductance, IR, UV-Vis. and Mass spectra etc. Cyclic voltammetric studies were carried out on Pt disc (tip-06.1204.120.) electrode (2mm diameter). The octahedral geometry has been assigned to these macrocycles and attributed to the unusual oxidation state of metal ion which is stabilized by macrocyclic cavity. These synthetic macrocycles were also tested for their biological activities against *E. coli*, *P. aeruginosa*, *B. cereus*, *S. aureus* and *C. albicans* to assess their inhibition potential and were compared with standard drugs like Gentamycin.

## 1. INTRODUCTION

The importance of azamacrocycles is well recognized now-a-days. The design and synthesis of macrocyclic complexes is an interesting area of research. It has been observed that macrocycles exhibit peculiar characteristic features with respect to the size and degree of unsaturation of the macrocyclic cavity and axial ligation. Coordination geometry of tetraazamacrocyclic complexes is known to be octahedral or distorted octahedral saddle shape. Dibenzo[14]annulenes and Dibenzo[16]annulenes macrocyclic ligands have been used as mimicking agent for naturally occurring systems such as porphyrins and corrin rings. Metalloporphyrins exhibit a good redox chemistry and the studies have revealed their general tendency to undergo multiple one electron oxidation processes. The great interest for these type of studies implies that the ligand in various metalloporphyrins undergo a total of two one electron oxidation processes. Many such ligands and complexes have been prepared containing transition metals in the quest of finding their biological functions. Cobalt tetraazaannulene macrocyclic complexes have been found acting as catalyst for the reduction of dioxygen in fuel cells and for the oxidation of hydroquinones. The dibenzo[14]annulene and porphyrin ligands both have four coplanar N-donor atoms and

can easily be deprotonated to form a dianion. The dibenzotetraaza[14]annulenes are anti-aromatic ( $4n \pi$  electrons) and thus, their dianions do not have complete resonance through entire annulene framework but the delocalization remain confined to the 1,3-diiminato linkages. The porphyrins, on the other hand, have delocalization spread over the entire ligand. [1-11]

Keeping all these points in view, the preparation of both, dibenzotetraaza[14]annulenes and dibenzotetraaza[16]annulene macrocyclic complexes of cobalt(II) has been carried out. The dibenzotetraaza[16]annulene macrocyclic complexes possess  $4n+2 \pi$  electrons and having delocalization spread over the entire annulene framework.



Macrocycles are also being studied for their antimicrobial activity. It is necessary to find newer macrocycles for better therapeutic use due to emergence of multidrug resistant bacteria. There are so many transition metal macrocyclic complexes which have shown promise regarding antimicrobial activities. In the present communication, all these studies have been carried out with respect to Co<sup>II</sup>HMTAA-14 and Co<sup>II</sup>HMTAA-16.

## 2. EXPERIMENTAL

FT-IR spectra were recorded on Shimadzu-8400S double beam spectrophotometer by KBr DRS method. Methyl substituted Me<sub>6</sub> dibenzo [1,4,8,11] tetraazacyclotetradecaene-N<sub>4</sub> complexes of Co(II) were prepared by template method.

All the reactants were of AR grade purchased from TCI, India. The microanalysis (C, H, N) and mass spectral studies of these compounds were carried out at Central Instrumental Laboratory (CIL) Panjab University Chandigarh (Eager Xperience and TOF MS ES+6018e3). The electronic spectra were recorded on Double Beam Spectrophotometer (Shimadzu 2450 spectrophotometer) in methanol. The molar conductance of these complexes was recorded on Auto ranging Conductivity/TDS Meter (TCM 15+). The electrochemical studies were carried by using Auto Lab instrument (Metrohm 663 VA Stand) in methanol (MeOH) and dimethylformamide (DMF) containing TEAP as supporting electrolyte by employing cyclic voltammetric techniques. This system contain three electrode system consists of Pt disc electrode (3mm diameter) as a working electrode, Ag/AgCl (3M KCl) reference electrode and Pt wire electrode as auxiliary electrode. Pre-treatment of electrodes was done before every cyclic voltammetric experiments.

### 2.1. Preparation of macrocylic complexes

6,13-Dihydro Me<sub>6</sub> dibenzo [b,i] [1,4,8,11]-tetraazacyclotetradecene cobalt(II) chloride [Co<sup>II</sup>HMTAA-14] and 7,15-Dihydro Me<sub>6</sub> dibenzo [b,j] [1,5,9,13]-tetraazacyclohexadecene cobalt(II) chloride [Co<sup>II</sup>HMTAA-16] were prepared by the template method by the reaction between acetyl acetone (2 moles, 0.400 g), cobalt(II) chloride hexahydrate (1 mole, 0.476 g) with 3,4-diamino toluene (2 moles, 0.488 g) and 2,4-diamino toluene (2 moles, 0.488 g) respectively. The reactants were dissolved in 50-60 ml methanol and the reaction mixture was refluxed for about 6-8 hours. A change in color appeared; the solution was concentrated in rotary evaporator and dried in vacuum. Violet and brown colored crystals of macrocylic complexes Co<sup>II</sup>HMTAA-14 and Co<sup>II</sup>HMTAA-16 respectively were obtained and characterized by various techniques like elemental analysis, UV-VIS, IR and mass spectrometry etc. [11]

## 3. RESULT AND DISCUSSION

**Table 1: Microanalytical data for Co<sup>II</sup>HMTAA-14 and Co<sup>II</sup>HMTAA-16 macrocylic complexes**

Complex	Molar conductance (ohm-1 cm <sup>2</sup> mol <sup>-1</sup> )	M.P (°C)	Mol Wt.	C* (%)	H* (%)	N* (%)
Co <sup>II</sup> HMTAA-14	42	238	502	55.7 (57.4)	5.5 (5.6)	10.1 (11.2)
Co <sup>II</sup> HMTAA-16	36	225	502	55.2 (57.4)	5.4 (5.6)	10.5 (11.2)

\* Theoretical values of microanalysis are given in parenthesis.

### 3.1. Electronic spectral studies

The absorption characteristic of macrocylic complexes were observed in methanol at room temperature in the range 200-800 nm on Shimadzu 2450 spectrophotometer of 10<sup>-3</sup> M solution. The band around 253 and 290 nm are due to  $\pi \rightarrow \pi^*$

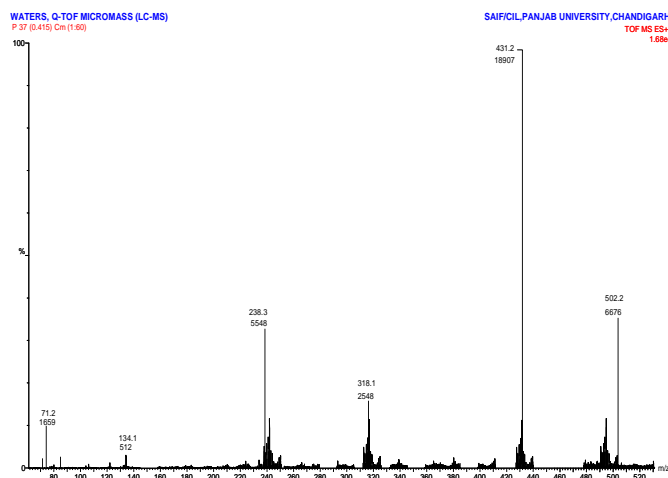
and  $n \rightarrow \pi^*$  transitions respectively. The electronic spectrum of Co<sup>II</sup>HMTAA-14 macrocylic complex shows three bands in the region of (315 nm) 26315 cm<sup>-1</sup>, (352 nm) 28000 cm<sup>-1</sup> and (412 nm) 24271 cm<sup>-1</sup> while for Co<sup>II</sup>HMTAA-16, three bands are in region (325 nm) 30769 cm<sup>-1</sup>, (347 nm) 28818 cm<sup>-1</sup> and (460 nm) 21739 cm<sup>-1</sup>. These bands can be assigned to <sup>4</sup>T<sub>1g</sub>(F) → <sup>4</sup>A<sub>2g</sub>(F), <sup>4</sup>T<sub>1g</sub>(F) → <sup>4</sup>T<sub>2g</sub>(F) and <sup>4</sup>T<sub>1g</sub>(F) → <sup>4</sup>T<sub>1g</sub>(P) transitions. The electronic spectral data in conjugation with molar conductance data suggest the octahedral geometry for both the macrocylic complexes, the chloride ions being at the axial positions.

### 3.2. Mass spectra

The mass spectra of both the macrocylic complexes showed a more intense molecular ion peak (M)<sup>+</sup> at m/z 502 which are in good agreement with respect to their molecular formulae. The mass spectrum of Co<sup>II</sup>HMTAA-16 complex (Fig. 1.) shows a molecular ion peak (M)<sup>+</sup> at m/z 502 and other at m/z 431, 318, 238, 134, 71.

### 3.3. IR Spectra

The two important observations in the spectra of both the complexes are the absence of bands due to free >C=O group (near 1700 cm<sup>-1</sup>) and due to free -NH<sub>2</sub> group (near 3300 cm<sup>-1</sup>) and the presence of strong band near 1500 cm<sup>-1</sup> due to C=N group. The



**Fig. 1: Mass spectrum of Co<sup>II</sup>HMTAA-16 macrocylic complex**

disappearance of these bands and the appearance of a new strong absorption band near 1500 cm<sup>-1</sup> confirms the condensation of the carbonyl group of acetyl acetone and the amino group of diaminotoluenes and the formation of a macrocylic Schiff's base, as these bands may be assigned to  $\nu(\text{C}=\text{N})$  stretching vibrations. The lower value of the frequency of  $\nu(\text{C}=\text{N})$  vibrations may be explained by a drift of the lone pair electron density of the azomethine nitrogen towards the metal atom, indicating that coordination occurs through the nitrogen of the C=N groups. The absorption bands in the region 1400–1450 cm<sup>-1</sup> may be assigned to  $\nu(\text{C}=\text{C})$  aromatic stretching vibrations of the benzene rings. The

medium intensity bands present in the region  $2770\text{--}2950\text{ cm}^{-1}$  may be assigned to the  $\nu(\text{C-H})$  stretching vibrations of the methyl groups. The bands in the region  $700\text{--}831\text{ cm}^{-1}$  may be assigned to the  $\nu(\text{C-H})$  out of plane bending of the aromatic ring. [12-20]

The far infrared spectra show bands in the region  $400\text{--}450\text{ cm}^{-1}$  corresponding to  $\nu(\text{M-N})$  vibrations. The bands in the spectra of all the complexes in the region  $400\text{--}450\text{ cm}^{-1}$  originate from (M-N) azomethine vibrational modes and identify coordination of the azomethine nitrogen.

### 3.4. Cyclic Voltammetry

The cyclic voltammograms of all the complexes, recorded at a scan rate of  $50\text{ mV/s}$  are shown in Fig. 2 and various parameters have been collected in table 2. The CVs of  $\text{Co}^{\text{II}}\text{HMTAA-14}$  and  $\text{Co}^{\text{II}}\text{HMTAA-16}$  are very much similar to each other with slight difference in the values for  $E_{\text{pa}}$  and  $E_{\text{pc}}$ . The CV of  $\text{Co}^{\text{II}}\text{HMTAA-14}$  shows two distinct redox couples at  $+0.76\text{ V}$  and  $+1.09\text{ V}$  whereas  $\text{Co}^{\text{II}}\text{HMTAA-16}$  shows the corresponding redox couples at  $+0.81\text{ V}$  and  $+1.13\text{ V}$  respectively.

Peak currents are found stable over repeated scans. The CVs of all complexes were also recorded varying scan rates from  $25\text{ mV/s}$  to  $500\text{ mV/s}$ . the anodic and cathodic peak potentials were found independent of scan rate for each complex. (Table 2.)

Further, the plots of peak currents against the square root of scan rates were found to be linear, following the Randles-Sevcik equation for reversible electrochemical reactions.

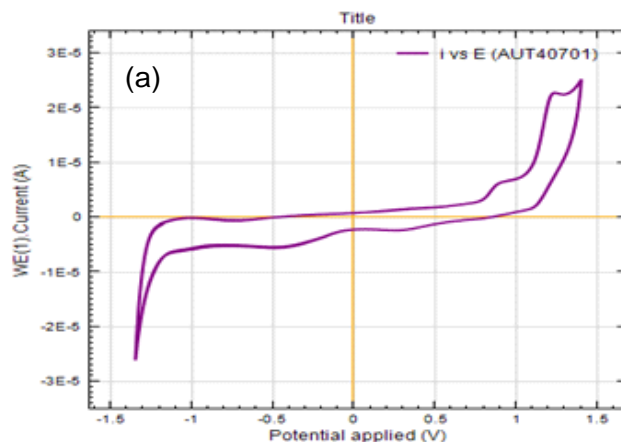
$$i = -2.69 \times 10^5 n^{3/2} AD^{1/2} cv^{1/2}$$

Where  $n$  is the number of electrons transferred,  $A$  is the area of electrode,  $D$  is the diffusion coefficient,  $c$  is the analyte concentration and  $v$  is the scan rate.

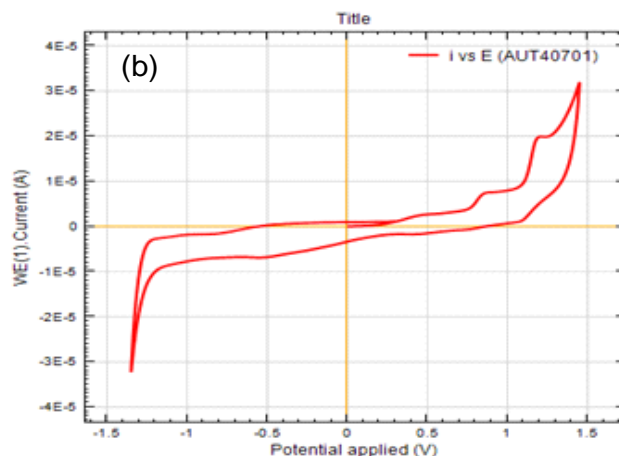
Axial ligation of a base like pyridine is also useful for further proving the nature of electrochemistry of planer  $\text{N}_4$  chelates such as porphyrins and tetraaza annulenes. [21-25] (Fig. 2.) shows the effect of addition of small amount of pyridine on the voltammetry of  $\text{Co}^{\text{II}}\text{HMTAA-14}$ .

**Table 2: Redox potential data for  $\text{Co}^{\text{II}}\text{HMTAA-14}$  and  $\text{Co}^{\text{II}}\text{HMTAA-16}$  complexes in DMF**

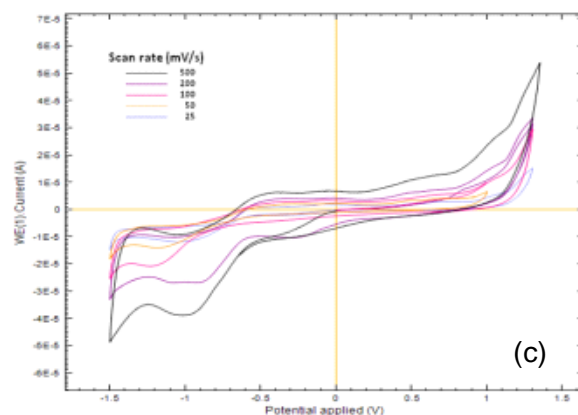
Complex	M <sup>2+/3+</sup>	L <sup>+/0</sup>
$\text{Co}^{\text{II}}\text{HMTAA-14}$	$+0.76\text{ V}$ (88 mV)	$+1.09\text{ V}$ (92 mV)
$\text{Co}^{\text{II}}\text{HMTAA-16}$	$+0.81\text{ V}$ (81 mV)	$+1.13\text{ V}$ (83 mV)
$\text{Co}^{\text{II}}\text{DPTAA}$ [25]	$+0.24\text{ V}$	$+0.56\text{ V}$
$\text{Co}^{\text{II}}\text{HMTAA-14}$ + excess pyridine	$+0.60\text{ V}$	$+0.86\text{ V}$
$\text{Co}^{\text{II}}\text{DPTAA-14}$ + excess pyridine[25]	$+0.02\text{ V}$	$+0.64\text{ V}$



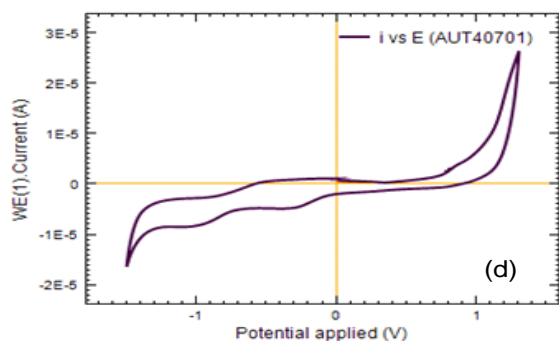
(a) Cyclic voltammogram of  $\text{Co}^{\text{II}}\text{HMTAA-16}$



(b) Cyclic voltammogram of  $\text{Co}^{\text{II}}\text{HMTAA-14}$



(c) Cyclic voltammetry of  $\text{Co}^{\text{II}}\text{HMTAA-14}$  at different scan rates



(d) Cyclic voltammogram of Co<sup>II</sup>HMTAA-14 in presence of pyridine

Fig. 2: Cyclic voltammograms of macrocylic complexes in DMF

### 3.5. Biological activity

Published literature revealed very few antibacterial and antifungal activities of tetraaza macrocylic complexes.[26] In the present study, we have investigated the antibacterial activities of the complexes against *Escherichia coli*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Staphylococcus aureus* and antifungal activity of the complexes against the pathogenic fungus *Candida albicans*. [27]

The antimicrobial activities (against bacteria and yeasts) of the newly synthesized compounds were evaluated by agar well diffusion method [28]. All the microbial cultures were adjusted to 0.5 McFarland standards, which is visually comparable to a microbial suspension of approximately  $1.5 \times 10^8$  cfu/ml [29]. 20 ml of agar media was poured into each Petri plates and each plate were swabbed with 100 ml bacterial inoculums of the test microorganisms and kept for 15 min for adsorption. A 6 mm well was cut at the centre of the all agar plates and the wells was filled with test complexes (1–2 separately). The medium with only solvent was used as a negative control where as media with Gentamycin (standard antibiotic and antifungal drug) were used as positive control. The experiments were performed in triplicates. The diameter of the inhibition zone observed around the wells was measured for each bacterium after 24 h of incubation at 37°C and in case for fungus inhibition zone was measured after 48 h of incubation at 28°C. Antimicrobial activity of all the synthesized compounds was evaluated by measuring the zone of growth inhibition against the test organisms with zone reader (Hi Antibiotic Zone Scale). Results showed Co<sup>II</sup>HMTAA-14 was most effective for *Pseudomonas* and *Staphylococcus*. [30]

However Co<sup>II</sup>HMTAA-16 was more effective than Co<sup>II</sup>HMTAA-14 in case of *E. coli* followed by *Bacillus*. Such alteration in activity may be influenced by the complexity of the cell wall or resistance properties of the bacteria. However, possibilities of subsequent injury to the cell membrane which led to leakage of electrolytes from the cells cannot be ruled out. (Fig. 3.)

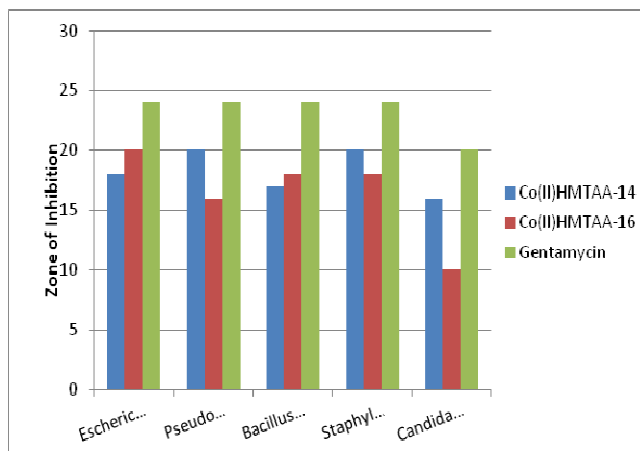


Fig. 3: Comparative study of biological activities of macrocylic complexes with standard drug

## 4. CONCLUSION

Electronic and IR spectral analysis have confirmed octahedral geometry for both the complexes. Voltammetric studies show the reversible one electron redox processes for these complexes and their ligand part. Both the complexes have shown good promise for antibacterial activity against both Gram +ve and Gram –ve bacteria.

## 5. ACKNOWLEDGEMENT

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