

Synthesis and Electrochemical Studies of Hexamethyldibenzotetraaza N_4 -Macrocyclic Complexes of Ni(II) and Cu(II) Metal ions

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Hexamethyldibenzotetraaza[14]annulene type macrocyclic complexes of Ni(II) and Cu(II) have been synthesized by template method. These macrocyclic complexes were characterized by molar conductance, elemental analysis, IR, UV-visible, mass spectra and cyclic voltammetry. On the basis of electronic studies saddle shape distorted octahedral structure have been assigned to these macrocyclic complexes. The redox behaviour of Ni(II) and Cu(II) macrocyclic complexes showed reversible and quasi-irreversible redox process that supported by the i_p/i_{pa} ratio which is in good agreement with Randles-Sevcik equation. These macrocyclic complexes were also studied for the antimicrobial activity against *E. coli*, *P. aeruginosa*, *B. subtilis*, *S. aureus* and *C. albicans* compared with gentamycin as standard drug.

Keywords: Hexamethyldibenzotetraaza[14]annulene, Macrocyclic complexes, Cyclic voltammetry, Antimicrobial activity.

INTRODUCTION

Macrocyclic complexes have received much attention due to their peculiar behaviour. The potential application of macrocyclic complexes have led to a wide spread interest for their studies. Aggregation of tetrapyrrole pigments, in particular, is one of the properties of significance in biological systems [1-6]. These complexes are considered well suited models for naturally occurring macrocyclic systems due to a stable N_4 environment whose coordination chemistry closely resembles to that of porphyrin and corrin ring and structure function relationship [7-9]. Many successful efforts have also been made to achieve peripheral substitution on its framework. The appended substituents are providing the points of attachments for further structural modification. Consequently, the substituent might create the possibility for synthesis of even more complex compounds serving as synthetic models for naturally occurring systems.

A large number of macrocyclic complexes are highly conjugated and exhibit extensive electron delocalization [10]. Macrocycles with conjugation have more interaction with metal orbital and affect the cavity size. Such effects are more influenced in 14-membered macrocycles that encapsulate metal ion and

stabilize unusual oxidation state [11]. In this communication, synthesis and characterization of hexamethyldibenzo-1,4,8, 11-tetraazacyclotetradecatetraene- N_4 macrocyclic complexes of Ni(II) and Cu(II) have been carried out. Electrochemical studies have been carried out by cyclic voltammetry. The formation of reversible and quasi-irreversible redox couple is responsible for kinetic stability of redox couple [12,13].

EXPERIMENTAL

All the chemicals and solvents used were of AR grade. The FT-IR spectral studies were carried out on Shimadzu 8400S spectrophotometer ($4000-400\text{ cm}^{-1}$) by using KBr/DRS system. The electronic spectra were recorded on a Shimadzu 2550 spectrophotometer (200-800 nm) using methanol as a solvent. The molar conductance of these macrocyclic complexes were measured on autoranging Conductivity/TDS Meter TCM 15+ instrument using conc. (10^{-3} M) in acetonitrile. Cyclic voltammetric studies were performed on PGSTAT 101 Autolab Metrohm model 663 VA stand using three electrode system consisting of Pt disc as a working electrode, Ag/AgCl(KCl) as reference electrode, Pt wire as a counter electrode. Tetraethylammonium perchlorate

TABLE-1
ANALYSIS AND PHYSICAL PROPERTIES OF COMPLEXES

Macrocyclic complexes	Colour	m.p. (°C)	Elemental analysis (%): Calcd. (Obsd.)			Molar conductance (ohm ⁻¹ cm ² mol ⁻¹)	m.w.
			C	H	N		
[C ₂₄ H ₂₈ Cl ₂ Ni]	Dark violet	125	57.34 (56.67)	5.57 (6.43)	11.15 (12.94)	25	502.2
[C ₂₄ H ₂₈ Cl ₂ Cu]	Brown	238	56.84 (56.77)	5.52 (5.48)	11.05 (11.02)	15	506.6

was used as supporting electrolytes in the experiment. Elemental analysis and mass studies (LC-MS) was performed at CIL SAIF, Punjab University, Chandigarh, India.

Synthesis of 2,4,9,13,15,20-hexamethyldibenzo-1,4,8,11-tetraazacyclotetradeca-tetraeneN₄ metal(II) macrocyclic complexes [MLCl₂], M= Ni(II),Cu(II): These complexes [MLCl₂] were synthesized according to the literature method [14] by taking 3,4-diaminotoluene (0.224 g, 0.002 mol), acetyl acetone (2 mL, 0.002 mol) and metal salt NiCl₂·6H₂O (0.238 g, 0.001 mol), CuCl₂·2H₂O (0.178 g, 0.001 mol) in methanol as solvent (Scheme-I).

RESULTS AND DISCUSSION

The elemental (C, H, N) analysis and analytical data are given in Table-1. The macrocyclic complexes are soluble in common organic solvents like DMSO, DMF and methanol. Complexes are found to be monomeric by the molecular weight determination. At room temperature the molar conductance of these complexes in acetonitrile were in the range of 15-40 Ω⁻¹ cm² mol⁻¹. Hence, from the conductance data, it is extracted that two chloride ions are covalently bonded to metal ions and showed the non-electrolytic in nature.

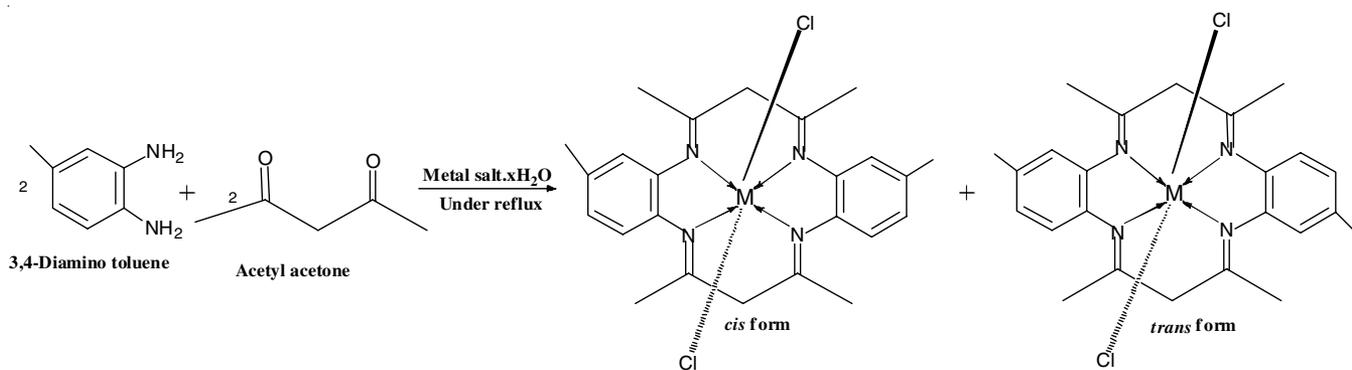
Infrared studies: The IR spectra of macrocyclic complexes showed no characteristic band of >C=O of acetyl acetone and -NH₂ band for primary amine suggesting the complete condensation. A weak absorption band in the region of 2900 cm⁻¹ resulted by C-H(-CH₃) stretching vibration [15] and medium

intensity band at 1580, 1500, 1450 cm⁻¹ for the C-H(-CH₃) bending vibration. The absorption band in the region of 1632-1675 cm⁻¹ resulted from aromatic C=C stretching vibration. The weak absorption band in the region 3099-3030 cm⁻¹ assigned to Ar-H stretching vibration. The C=N stretching frequency occurs at 1625-1580 cm⁻¹ [16] (Table-2).

TABLE-2
VIBRATIONAL FREQUENCIES (cm⁻¹)
OF MACROCYCLIC COMPLEXES

Complex	C=C	-C-H(CH ₃)	C=N	M-N
[C ₂₄ H ₂₈ Cl ₂ Ni]	1632	2830, 1450, 1500	1615	435
[C ₂₄ H ₂₈ Cl ₂ Cu]	1665	2940, 1445, 1550	1594	530

UV-visible spectral studies: The absorption characteristic of macrocyclic complexes were observed at room temperature in the range 200-800 nm on Shimadzu 2550 spectrophotometer of 10⁻³ M solution in methanol and the data is given in Table-3. The band around 253 and 290 nm is due to π → π* and n → π* transition, respectively [17,18]. The spectra of Ni(II) complex observed in the range (422 nm) 23696 cm⁻¹, (402 nm) 24875 cm⁻¹, (392 nm) 25512 cm⁻¹ that indicate transitions ³A_{2g} (F) → ³T_{2g} (F), ³A_{2g} (F) → ³T_{1g} (F), ³A_{2g} (F) → ³T_{1g} (P) [19], whereas the electronic spectra of Cu(II) macrocyclic complex (Fig. 1) show three bands in the region of (539 nm) 18552 cm⁻¹, (568 nm) 17605 cm⁻¹ and (643 nm) 15552 cm⁻¹ that assigned to ²B_{1g} → ²B_{2g}, ²B_{1g} → ²E_g, ²B_{1g} → ²A_{1g}. The observed data for Ni(II) complex, correspond was found octahedral geo-



Scheme-I: Synthesis of macrocyclic complexes, [MLCl₂]; M = Ni(II), Cu(II)

TABLE-3
ELECTRONIC SPECTRAL DATA OF THE MACROCYCLIC COMPLEXES

Complexes	Absorption (cm ⁻¹)	Band assignment	Geometry	ε (dm ³ mol ⁻¹ cm ⁻¹)
[C ₂₄ H ₂₈ Cl ₂ Ni]	23696	³ A _{2g} (F) → ³ T _{2g} (F)	Octahedral	85
	24875	³ A _{2g} (F) → ³ T _{1g} (F)		132
	25512	³ A _{2g} (F) → ³ T _{1g} (P)		45
[C ₂₄ H ₂₈ Cl ₂ Cu]	18552	² B _{1g} → ² B _{2g}	Distorted octahedral	706
	17605	² B _{1g} → ² E _g		39
	15552	² B _{1g} → ² A _{1g}		63

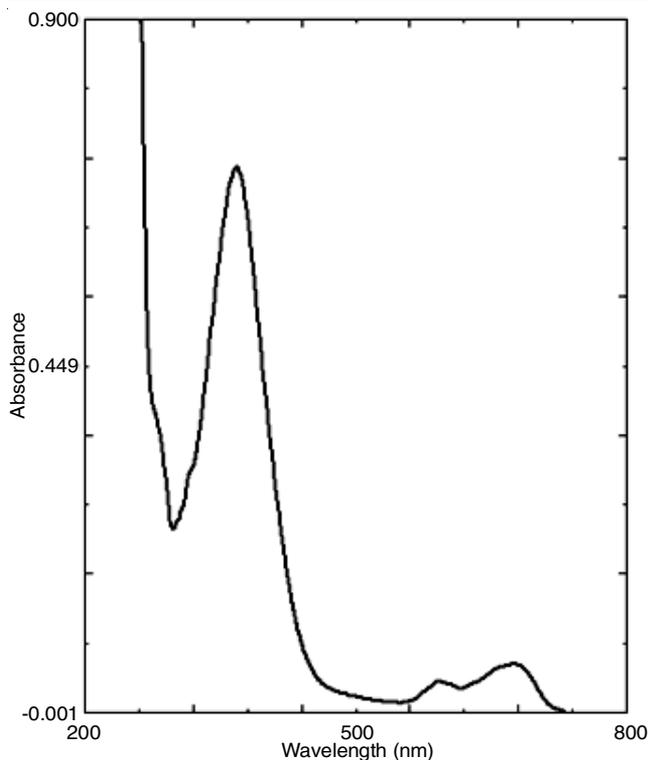


Fig. 1. Electronic spectra of Cu(II) complex (10^{-2} M) in acetonitrile

metry while Cu(II) macrocyclic complex show distorted octahedral geometry [20].

Mass analysis: LC-MS was recorded in positive ion mode and indicates the evidence of the formation of the coordination complex. Many fragments were observed in the spectrum which characterizes the composition of macrocyclic complexes. The mass spectrum of Ni(II) macrocyclic complex showed a more intense base peak at m/z 431 (Fig. 2) and the molecular ion peak at m/z 502.2 which is in good agreement with respect to its molecular formula. Other peaks are observable at m/z 318, 238, 134, 71.

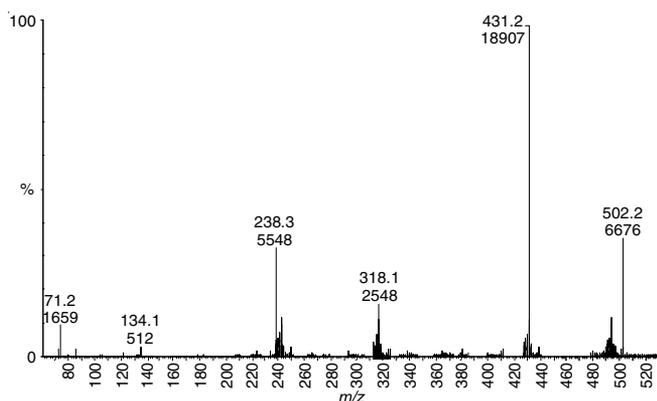


Fig. 2. Mass spectrum of Ni(II) macrocyclic complex

Redox studies: Electrochemical studies of these tetraaza [14] annulene type macrocyclic complexes have been carried out in different solvents. Cyclic voltammetric studies of Ni(II) and Cu(II) macrocyclic complexes were carried out in the range from +2 V to -2 V. Cyclic voltammograms of these macrocyclic complexes observed in DMF (10^{-3} M) solution along with 0.1 M TEAP (tetraethylammonium perchlorate) as sup-

porting electrolyte under nitrogen atmosphere are shown in Figs. 3 and 4. The cyclic voltammetric data of these macrocyclic complexes are given in Table-4. The cyclic voltammogram of Ni(II) macrocyclic complex shows two redox couples corresponding to cathodic and anodic peak. First redox couple Ni(II)/Ni(III) is observed at $E_{1/2} = 0.09$ V, while second redox couple Ni(0)/Ni(II) shows two electron reversible process at $E_{1/2} = 0.05$ V. These redox processes are reversible with corresponding peak separation ΔE (0.14 V) and also supported by the value of peak current ratio. The cyclic voltammogram of complex also shows two separate cathodic peaks at $E_{pc} = +0.62$ V and $E_{pc} = -1.10$ V which are assigned to reduction peak, Ni(II)/Ni(I) and reduction of ligand L/L^{-1} respectively [21]. The cyclic voltammetric data for Cu(II) complex were observed at 100 V/s in the range -1.5 V to +1.5 V. The cyclic voltammogram (Fig. 4) shows a redox couple at $E_{pa} = +0.52$ V and $E_{pc} = +0.25$ V assignable to Cu(II)/Cu(III) which is a quasi-irreversible redox couple with the peak separation 0.27 V and $E_{1/2} = +0.39$ V. Cathodic peaks at $E_{pc} = -0.44$ V and +0.25 V show Cu(II)/Cu(I) and Cu(I)/Cu(0) reduction processes [22].

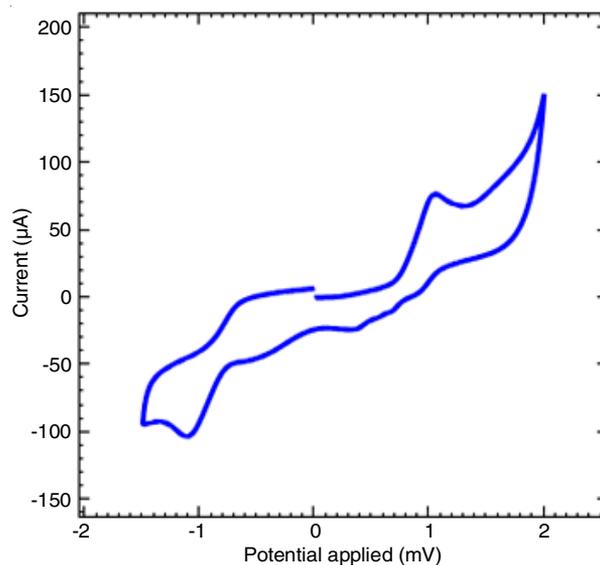


Fig. 3. Cyclic voltammogram of Ni(II) complex

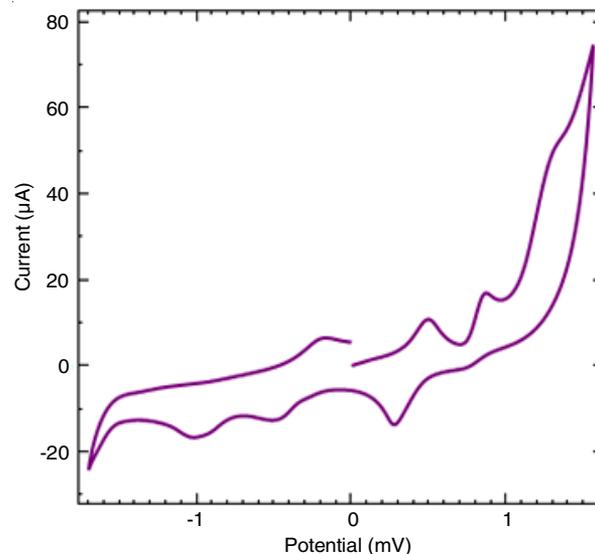


Fig. 4. Cyclic voltammogram of Cu(II) complex

TABLE-4
 ELECTROCHEMICAL DATA FOR Ni(II) AND Cu(II) MACROCYCLIC COMPLEXES

Complexes	E_{pa}^1	E_{pa}^2	E_{pc}^1	E_{pc}^2	ΔE_p	$E_{1/2}$	i_{pa}/i_{pc}
[C ₂₄ H ₂₈ Cl ₂ Ni]	+1.01 V	-0.56 V	+0.87 V	-0.54 V	0.14 V	+0.94 V	1.07
[C ₂₄ H ₂₈ Cl ₂ Cu]	+0.52 V	+0.85 V	+0.25 V	-0.44 V	0.27 V	+0.39 V	0.86

$E_{1/2} = E_{pa} + E_{pc}/2$, $I = i_{pa}/i_{pc}$

The cyclic voltammograms of Cu(II) complex were also recorded in DMF at different scan rate in the range of 50-300 mV s⁻¹. It was found that E_{pa} and E_{pc} increase linearly with increasing scan rate. The cathodic peak potential shifted towards negative potential and the anodic peak shifted towards positive potential. Thus peak separation (ΔE) values increase from 0.20 V to 0.28 V showing deviation of redox process from reversibility whereas peak current increase linearly that showed diffusion controlled process (Fig. 5) hence, follows Randles-Sevick equation [23,24].

$$i = 2.69 \times 10^5 n^{3/2} A D^{1/2} c v^{1/2}$$

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.

Antibacterial activity: Antimicrobial activities of these tetraazamacrocyclic complexes against *E. coli*, *P. aeruginosa*, *B. subtilis*, *S. aureus* and *C. albicans* have been carried out [25] and the observed antibacterial data for these complexes given in Table-5. The antimicrobial activities of these synthetic macrocyclic complexes were evaluated by agar well diffusion method for solvent extract [26]. All the microbial cultures were adjusted to 0.5 McFarland standards, which is visually comparable to a microbial suspension of approximately 1.5×10^8 CFU/mL [27,28]. 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, 6 mm well was cut at the centre of the all agar plates and the wells was filled with test complexes. The medium with only solvent was used as a negative control where as media with gentamycin were used as positive control. The experiments were performed in triplicates. The diameter of the inhibition

 TABLE-5
 ANTIBACTERIAL ACTIVITY (ZONE OF INHIBITION) OF Ni(II) AND Cu(II) MACROCYCLIC COMPLEX

Complexes	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>B. cereus</i>	<i>S. aureus</i>	<i>C. albicans</i>
[Ni LCl ₂]	19	16	17	16	10
[CuLCl ₂]	20	18	19	19	16
Gentamycin	24	24	24	24	20

zone observed around the wells was measured for each pathogen after 24 h of incubation at 37 °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). These complexes were found to be inhibitory against both Gram +ve and Gram -ve bacteria [29,30] and results shows Cu(II) macrocyclic complex was most effective as compared to Ni(II) macrocyclic complex for *P. aeruginosa* and *S. aureus*. 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.

Conclusion

Hexamethyldibenzotetraaza[14]annulene metal (II) (M = Ni(II) and Cu(II) complexes have been synthesized and characterized by various techniques. The macrocyclic complexes were obtained in good yields. The Ni(II) macrocyclic complex attributed to octahedral geometry, whereas Cu(II) macrocyclic complex is assigned to the distorted octahedral geometry. The structures of these complexes were proposed mainly on the basis of spectroscopic and molar conductance data. The cyclic

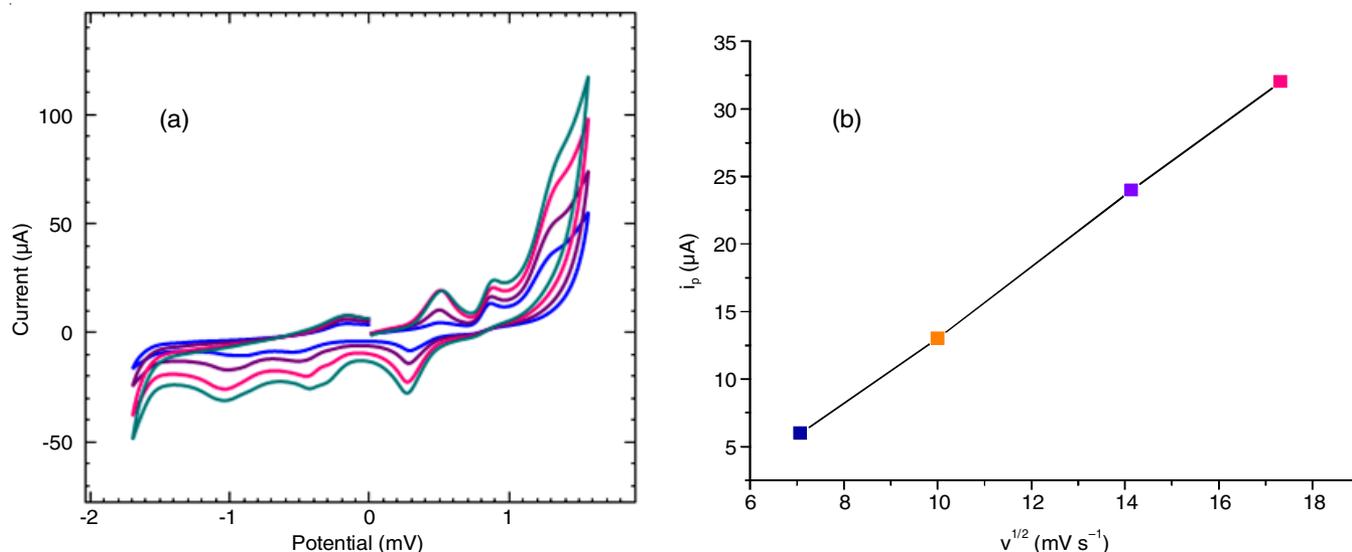


Fig. 5. (a) Cyclic voltammogram at different scan rates (50-300 mV s⁻¹) and (b) Plot of i_p vs. $v^{1/2}$ of Cu (II) macrocyclic complex

voltammetric data showed that the unusual oxidation state of these metal ions stabilized by the macrocyclic frame work and Ni(II) macrocyclic complex having reversible redox process while Cu(II) showed quasi-irreversible redox behaviour.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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