

Full Paper

Synthesis, Characterization, Electrochemical and Antimicrobial Studies of N₄-Macrocycles of Cobalt(II) and Nickel(II) Metal Ions

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Abstract- The precise analysis of redox chemistry of MN₄-based macrocyclic complexes is of great importance because of stabilization of unusual oxidation states of metal ions by macrocyclic ligand and thus have various applications in biochemistry, electrochemistry, electrocatalysis, pharmaceuticals etc. In this work, MN₄-macrocyclic complexes of Co (II) and Ni(II) transition metal ions have been synthesized by using template condensation method. Further, the MN₄-macrocyclic complexes were characterized by elemental, molar conductance and multiple spectroscopic analysis. The spectral and elemental analysis suggested that both complexes would possess the saddle shape distorted octahedral geometry. Further, the electrochemical investigation of both complexes was carried out by cyclic voltammetry. Both complexes showed quasi-reversible one-electron transfer redox process indicating the stabilization of oxidation state of central metal ions. Moreover, the MN₄-macrocyclic complexes have shown to have good antimicrobial activity against the various pathogens such as *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Bacillus subtilis* (*B. subtilis*) and *Staphylococcus aureus* (*S. aureus*).

Keywords- Synthesis; Co(II); Ni(II); Macrocyclic complex; Cyclic Voltammetry

1. INTRODUCTION

The chemistry of MN_4 -macrocyclic complexes is of paramount importance due to their diverse technological and medicinal applications. In addition, the synthesis of new MN_4 -macrocyclic complexes can be carried out by altering the substituents on ligand framework [1-2]. In particular, the oxide minerals of manganese and iron in aqueous phase on reaction with polyamines macrocyclic ligands can be useful as functional catalysts. Cytochrome P450, catechol dioxygenase, methane monooxygenase, and lipo oxygenase [3-7] are naturally occurring complexes and displayed exceptional efficiency and specificity towards various biological reactions. In recent years, much attention has been paid for design and synthesis of similar macrocyclic complexes that imitate features of the spectral and biochemical properties [8-9]. Particularly, the macrocyclic ligand comprising four nitrogen donor atoms with a greater degree of unsaturation, known as tetraazamacrocyclic ligand and primarily influenced by its structure and the type of the central metal ion. Due to the applications of tetraaza complexes in catalysis and their importance for processing of various systems, the coordination chemistry of square-planar metal complexes involving nitrogen donor ligands has generated considerable interest amongst researchers in recent times [10-14].

A large no of highly conjugated tetrazamacrocyclic ligands with extensive electron delocalization have been synthesized. Highly conjugated ligands provide greater orbital metal interaction and reduced 'center' size during the metal complex formation. These results are much more affected in [14]-membered macrocyclic rings encapsulating metal ion to stabilize the higher and lower oxidation states of central metal ion [15]. Previously, we have designed [14] and [16]-membered tetraaza macrocyclic cyclic complexes of various transition metals exhibiting their catalytical and biological applications [5, 16].

In this work, we have synthesized and characterized [14]-membered macrocyclic complexes of Co(II) and Ni(II) transition metals by template method strategy. Further, the chemical and structural characterization of the macrocyclic complexes were carried out to confirm the proposed structure and other features of [14]-membered macrocyclic rings with different metals. The electrochemical behavior of synthesized macrocyclic complexes was evaluated by employing cyclic voltammetry. In addition, the antimicrobial activity of these complexes has been carried out against several pathogens.

2. EXPERIMENTAL

2.1. Material and methods

All the chemicals and solvents used were of AR grade. FT-IR spectra were recorded on a "Shimadzu 84090S spectrophotometer" by employing the KBr DRS system. The UV-Vis spectral studies were performed in methanol on a "Perkin Elmer 2450 spectrophotometer". The electrochemical investigation of the metal complexes was carried out by cyclic

voltammetric technique on a platinum disc electrode (2 mm diameter) at PGSTAT 101 model metrohm 663 VA stand instrument. The current-voltage curves were obtained in the Nova 19 software. A three-electrode system was used consisted of Pt disc as a “working electrode” and Ag/AgCl as “reference electrode”, Pt as a “counter electrode”. Tetraethylammoniumperchlorate (TEAP) was used as a supporting electrolyte. Melting point recorded on an electrically heated block apparatus (Gallen Kamp). The mass spectral analysis was carried out on waters, Q-TOF Micromass (LCMS).

2.2. Preparation of macrocyclic complexes

For the synthesis of Co(II) complex, 10 mL methanolic solution of 2 mole of 2,3-diamino toluene (2,3-DAT) was gradually added to 10 mL methanolic solution of 2 mole of acetylacetone (AA) with constant stirring. To this mixture, added 10 mL methanolic solution of one mole of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ and refluxed for about 6 h until a dark brown colored mixture was obtained. The resulting mixture was concentrated using rotary evaporator and the concentrate was placed in desiccator overnight and recrystallized in methanol which results in the brown colored compound [16]. In the similar manner, Ni(II) complex was also prepared by taking one mole of $\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$ in place of $\text{CoCl}_2 \cdot 6\text{H}_2\text{O}$ metal salt.

2.3. Preparation of Microbial Culture

The antimicrobial activity of the synthesized macrocycles was assessed by agar well dispersion method [17]. All the bacterial colonies were developed in accordance with 0.5 McFarland guidelines, which is outwardly equivalent to a microbial suspension of around 1.5×10^8 cfu/ml [18]. 20 ml of agar media was filled in each Petri dish and poured with 100 ml bacterial inoculum of the test microorganisms and kept for 15 min for adsorption. After that 6 mm wall was cut at the centre of the all agar plates, and loaded up with 100 μl of synthesized complexes.

The DMSO solvent was utilized as a negative control media where Gentamycin (standard anti-infection and antifungal medication) were utilized as positive control media. The experiments were performed three times. After 24 h of incubation at 37°C for each complexes, antimicrobial activity was performed by measuring zone of inhibition precisely in mm with respect to Gentamycin. However, in case of fungus, the zone of inhibition was estimated after 48 h of incubation at 28°C [19].

3. RESULTS AND DISCUSSION

Both macrocyclic complexes were synthesized following template method. This method is an effective and selective in situ approach and proceeds in the presence of metal ions to promote the cyclization reaction by d-orbital directing effect and thus enhancing the yield of the products

remarkably [20-21]. Thus, 2 mole of acetyl acetone (AA) and 2 mole of 2,3-diamino toluene (2,4-DAT) was condensed in the presence of one mole $MCl_2 \cdot 6H_2O$ metal salt to give the macrocyclic complex $[MLCl_2]$ as showed in Fig. 1. The macrocyclic complexes were characterized by spectral, and molar conductivity measurement.

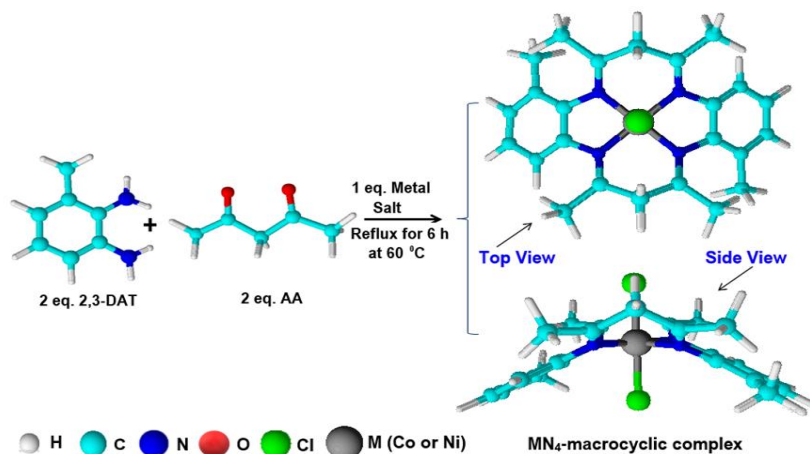


Fig. 1. Proposed synthesis scheme for the preparation of macrocyclic complexes, $[MLCl_2]$ $M=Co(II)$, $Ni(II)$ and the optimized structure of the CoN_4 -macrocyclic complex

The synthesized macrocyclic complexes were soluble in dimethyl sulfoxide (DMSO), dimethylformamide (DMF), and methanol (MeOH) solvents and also found to exist in their monomeric form as supported by their mass spectral studies. The analytical data for both complexes is given in Table 1.

Table 1. The micro-analytical and physical data of the complexes

Macrocyclic complex	Color	M.P(°C)	% Analysis (Calc. & Obsd.)				(% yield)	M.Wt Found (Calc.)
			Metal	C	H	N		
CoN ₄ -Complex	Brown	153	13.67	66.83	12.99	12.99	62	502
			12.67	65.43	12.59	12.59		
NiN ₄ -Complex	Dark Brown	125	13.63	66.86	6.50	13.00	76	502
			12.87	66.67	6.43	12.94		

The FT-IR spectral studies were taken into account to confirm the functional groups of the proposed structure of complexes. The FTIR spectra of both complexes showed the absence of free carbonyl ($>C=O$) and free amine ($-NH_2$) features of used AA and DAT, respectively, while the appearance of a weak absorption band near at 2900 cm^{-1} and 1497 cm^{-1} can be assigned to the CH_3 stretching vibration and aromatic $C=N$ asymmetric stretching vibration, respectively. Additionally, a less intense peak at 3079 cm^{-1} was attributed to the

aromatic C-H stretching. These results confirmed the main characteristics of both N_4 -complexes (Fig. 2 (a-b)) [20].

Next, Ultraviolet-visible (UV-Vis) studies were performed in the 10^{-3} M solution of MeOH at room temperature in the range of 200-800 nm to confirm the electron structure of the macrocyclic complexes. The peak near at 255 and 280 nm is assignable to the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ electronic transition, respectively. The electronic spectra of CoN_4 -complex show three bands at 26315 cm^{-1} (315 nm), $(352\text{ nm})\ 28000\text{ cm}^{-1}$, and $(412\text{ nm})\ 24271\text{ cm}^{-1}$ that can be assigned ${}^4T_{1g}(F) \rightarrow {}^4A_{2g}(F)$, ${}^4T_{1g}(F) \rightarrow {}^4T_{2g}(F)$, ${}^4T_{1g}(F) \rightarrow {}^4T_{1g}(P)$. In similar way, the spectra observed for NiN_4 -complex also indicated three peaks at $(422\text{ nm})\ 23699\text{ cm}^{-1}$, $(402\text{ nm})\ 24875\text{ cm}^{-1}$, $(392\text{ nm})\ 25510\text{ cm}^{-1}$ corresponding to ${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$, ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$, ${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(p)$ electronic transitions (Fig. 2c) [21].

Table 2. The electronic data for both MN_4 -macrocycles

Complexes	Geometry	cm^{-1}	D_q	$B_{\text{complex}}/B_{\text{ion}}$	Covalency (%)
CoN_4 -complex	octahedral	26315,28000,24271	1272	0.718	28%
NiN_4 -complex	octahedral	23,699,24875, 25512	1048	0.698	30%

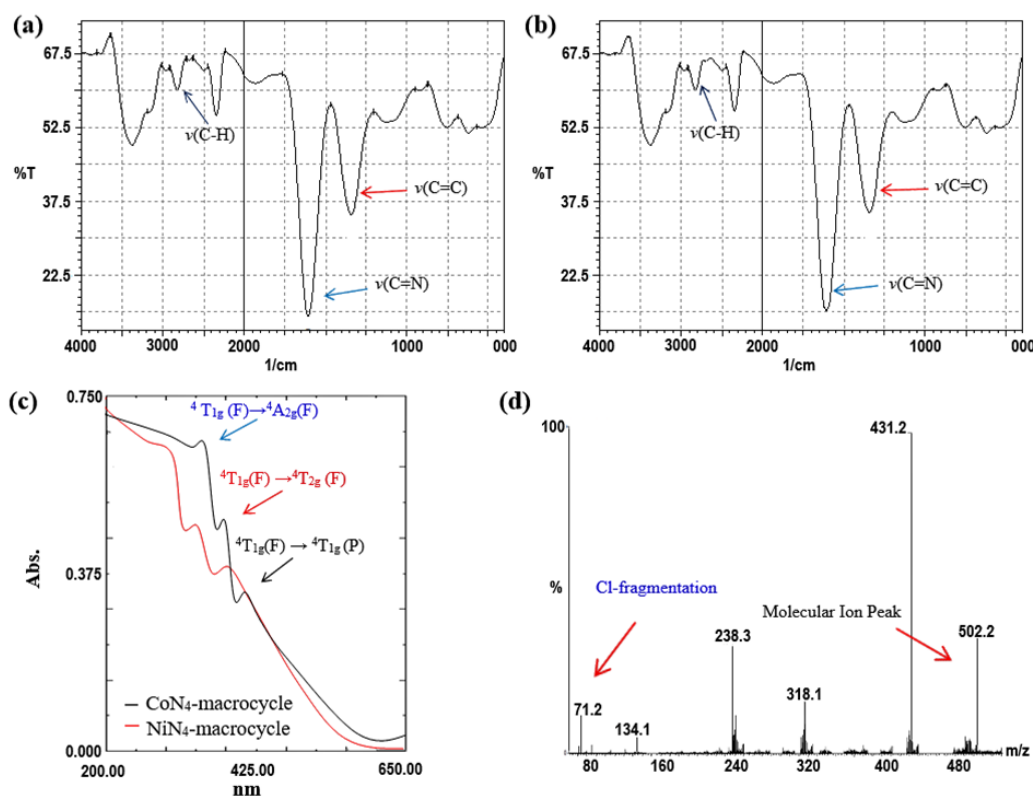


Fig. 2. FT-IR spectra of (a) CoN_4 -complex, and (b) NiN_4 -complex, (c) UV-Vis spectra of both complexes, and (d) Mass spectra of CoN_4 -complex

Further, the ligand field parameters for both complexes were calculated and the nephelauxetic parameter β is used to determine covalent characters of the complexes. The value of Dq parameter could be calculated by using transitions through the Orgel energy level diagram [22]. Various ligands field parameters assigned to appreciate the covalent character of these complexes. The electronic and ligand field parameters data for both complexes is given in Table 2.

The mass spectral investigations showed the molecular ion peak for CoN₄-complex at m/z 502, while other peaks at m/z 431, 316, 238, 134, 71.2 can be attributed to the several fragments corresponding to methyl, benzyl and chloride units as shown in fig. 2d. Similarly, NiN₄-complex exhibited molecular ion peak at m/z 501.71 with other fragments at m/z 466, 334, 465, 431 [23]. These results are fully in agreement with the proposed chemical structure of the complexes.

3.1. Electrochemical studies

The electrochemical investigations of the synthesized complexes were carried out in the +2 V to -2 V potential window to predict their redox behavior. The cyclic voltammogram (CV) of CoN₄-complex (Fig. 3a) and NiN₄-complex (Fig. 3b) were recorded using 10^{-3} mol/dm³ concentration and 0.1 M TEAP as supporting electrolyte in a mixed solvent (dimethyl formamide + Acetonitrile) under the nitrogen atmosphere at 100 mV/s scan rate. The CV of CoN₄-complex complex showed a well-defined cathodic peak at $E^{\circ} = -0.51$ V for $\text{Co}^{2+} \rightarrow \text{Co}^{+}$ conversion while one other reversible redox couple was also appeared at $E^{\circ} = -0.94$ V corresponding to ligand redox process L/L^{-} . Similarly, CV of NiN₄-complex was also recorded in the same experimental conditions and observed almost similar redox processes with CoN₄-complex, indicating the $\text{Ni}^{2+} \rightarrow \text{Ni}^{+}$ conversion at $E^{\circ} = -0.29$ V and a redox couple $E^{\circ} = -0.68$ V corresponding to ligand redox process. These results suggested that both complexes adopted similar electrochemical reaction pathway in the electrolytic media and possess similar electronic as well as chemical structure [24].

The substitution of a hydrogen atom by methyl groups in aromatic rings as well as macrocyclic ring makes these complexes more soluble in organic solvents. The electrochemical behavior of these macrocyclic complexes has been observed having different geometry like saddle shape as proposed from spectroscopic data. Further, the quasi reversibility of the redox process was supported by the peak separation and i_{pa}/i_{pc} ratio that is close to unity. The plots of i_p against the $v^{1/2}$ were found to be linear followed by the Randles-Sevcik equation (eq. 1) as showed in fig. 3 (c-d) [25]:

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

where n ; number of transferred electrons, A ; area of electrode, D ; diffusion coefficient, c ; analyte concentration, and v ; scan rate.

These studies are very necessary to understand the fundamental of H₂, O₂ and CO₂ electrocatalysis with MN₄-macrocyclic complexes because these complexes play pivotal role for the enhancement in sluggish kinetics of H₂, O₂ and CO₂ molecules at electrode surface [26].

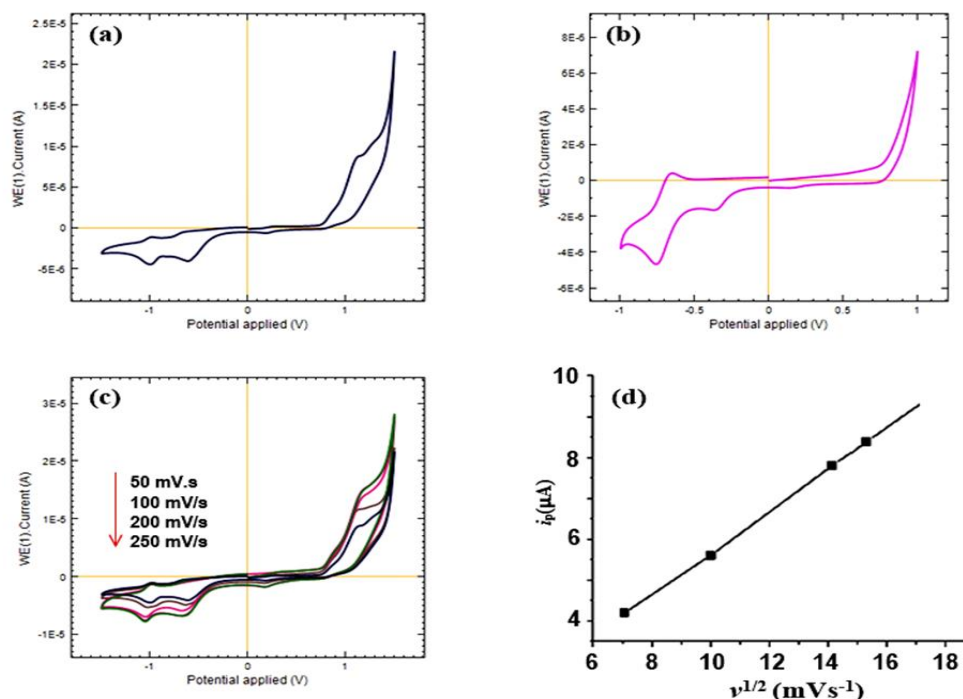


Fig. 3. Cyclic voltammogram of (a) CoN₄-complex, and (b) NiN₄-complex, both CVs were recorded at 100 mV/s scan rate (c) CoN₄-complex recorded at various scan rates, and (d) plots of *i*_p against the *v*^{1/2}. All the CVs were recorded in -2 V to +2 V potential window vs. Ag/AgCl reference electrode.

3.2. Antimicrobial activity

The antibacterial activity for both complexes against the *Escherichia coli* (*E. coli*), *Pseudomonas aeruginosa* (*P. aeruginosa*), *Bacillus subtilis* (*B. subtilis*) and *Staphylococcus aureus* (*S. aureus*) was assessed by estimating the zone of inhibition with zone peruses (Hi Antibiotic Zone Scale).

Both complexes were found to be potent models against both Gram +ve and Gram -ve bacteria and the results demonstrated that CoN₄-complex is more effective as compared to NiN₄-complex for *P. aeruginosa* and *S. aureus* [28-30]. Such adjustment in antimicrobial activity might be affected by the unpredictability of the cell divider or opposition properties of the bacteria. However, the possibilities of subsequent injury to the cell which prompted spillage of electrolytes from the cells can't be precluded. The observed antibacterial data for both complexes is given in Table 3.

Table 3. Antimicrobial activity of the complexes

Complexes	<i>E. coli</i>	<i>P. aeruginosa</i>	<i>B. cereus</i>	<i>S.aureus</i>
CoN ₄ -complex	20	21	18	21
NiN ₄ -complex	21	19	20	20
Gentamycin	24	24	24	24

4. CONCLUSION

In this work, [14]-membered tetraazamacrocyclic complex of Co(II) and Ni(II) transition metal ions have been synthesized by using template method. On the basis of spectral studies, the octahedral geometry has been assigned for both complexes. The electrochemical studies were carried out by using cyclic voltammetry in -2.0 to +2.0 V potential window vs Ag/AgCl at 100 mVs⁻¹ scan rate. The findings showed the interesting results for stabilization of unusual oxidation states of metal ions. Further, both complexes were checked for their antimicrobial activity, the results suggested that the complexes exhibited almost similar antimicrobial activity with the standard drug ‘Gentamycin’ against both Gram +ve and Gram -ve bacteria.

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